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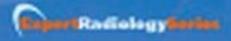
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# ABDOMINAL IMAGING



## SAHANI | SAMIR

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**Abdominal Imaging** 

## **Abdominal Imaging**

## Second Edition

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I dedicate this book to my wife, Susan, whose love and support make everything possible; to my son, Noah, whose curiosity brings me profound happiness; to my daughter, Sophie, whose loving smile makes me deeply grateful for all I have; and to my parents, Charlotte and Moshe, who sacrificed much so that I could achieve something meaningful. ANTHONY E. SAMIR

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### PREFACE

In 2013, when Elsevier approached us to create an updated, revised, and shortened second edition of *Abdominal Imaging*, we had some concerns. Even though the book had been successful and well-received by many colleagues and friends, we both wondered whether there truly is a need for an abbreviated, but comprehensive text? And would we have the time to work on it, adding the myriad updates to do justice to our fast-moving specialty?

Fortunately, we have had the privilege of working with a fine team of outstanding associate editors, section editors, and new chapter authors. Joe Grajo, MD and Nicole Horst, MD, truly outstanding radiologists and clinical fellows in our department, did superb work editing, collating, and organizing the work of our section editors. Together with the initial authors of the many chapters in this book, Melissa Price, MD, Colin McCarthy, MD, Aiofe Kilcoyne, MD, Rani Sewatkar, MD, Koichi Hayano, MD, Surabhi Bajpayi, MD, Naveen Kulkarni, MD, Arash Anvari, Luzeng Chen, Manish Dhyani, and Abe Thomas, MD all did an outstanding job of editing and revising the many chapters that went into this book. New chapters were contributed by Arash Anvari, MD, Manish Dhyani, MD, Luzeng Chen, MD, Koichi Hayano, MD, Naveen Kulkarni, MD, and Surabhi Bajpayi, MD. We are truly proud to have worked with such an outstanding team.

The new edition has been extensively updated and contains new images and the latest information about new technologies in abdominal imaging. This new edition is available both in a print edition and as part of the online *Clinical Key*. This platform comprises an online tool with high yield content and numerous annotated images in an easy-to-use format specifically designed for rapid retrieval of clinically useful information.

Our objective in the Second Edition of *Abdominal Imaging* is the same as in the first: to provide you, the reader, with a reference that is both comprehensive and that incorporates features more typically found in handbooks—short, readable sentences, key fact boxes, summary tables, abbreviated reference lists, listings of important review articles, and, above all, a highly integrated knowledge base that allows readers to rapidly access key content from any Internet-connected computer anywhere in the world.

This text is necessarily the work of many people: The numerous chapter authors of the first edition, Associate Editors, Section Editors, and authors of the new chapters. To all of you—we are profoundly grateful for your work. Our efforts would not have been possible without the understanding and strong support of our families and colleagues. We have also been privileged to work with an outstanding team at Elsevier. Marybeth Thiel demonstrated patience and perseverance dealing with busy editors—with you the project would never have been completed. Robin Carter—thank you for inviting us to complete the second edition.

As with the first edition, editing this book has been a tremendous education. We've learned so many new and interesting information about our own subspecialty that we believe there is something exciting in these pages for everyone from the seasoned subspecialist to the busy generalist.

## Plain Radiography of the Abdomen

ERNESTO TOMEI | VITO CANTISANI | ANDREA MARCANTONIO | UGO D'AMBROSIO | KOICHI HAYANO

#### **Technical Aspects**

A plain abdominal radiograph must be read with a complete knowledge of the clinical situation. The patient's history and results of the physical examination and laboratory studies are always important to evaluate an acute abdomen, which may be caused by various different diseases. Obtaining plain films with the patient supine and erect and that include the diaphragm is the classic approach. Because chest abnormalities may produce an acute abdomen, a chest posteroanterior radiograph is sometimes ordered.

The standard abdominal radiograph is a supine projection: x-rays are passed from front to back (anteroposterior projection) in a patient lying on his or her back (Figure 1-1). In some circumstances, an abdominal radiograph taken with the patient erect is requested; its advantage over a supine film is the visualization of air/fluid levels. A decubitus film (with the patient lying on his or her side) is also of use in certain situations, especially to visualize fluid levels in the large bowel.

It is important, as with any imaging technique, that the technical details of an abdominal radiograph are assessed. The date the film was taken and the name, age, and sex of the patient are all worth noting. This ensures you are reviewing the correct film with the correct clinical information, and it also may aid your interpretation. Unless the order is specifically labeled, the film is taken with the patient supine. The best way to appreciate normality is to look at as many films as possible, with an awareness of anatomy in mind. Although an abdominal radiograph is a plain radiograph, it has a radiation dose equivalent to 50 posteroanterior chest radiographs or 6 months of standard background radiation.<sup>1</sup>

#### **Pros and Cons**

Many techniques may be used to acquire images of the abdomen, including ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI), but the plain abdominal radiograph is the technique that is most readily available in the emergency situation when a patient presents with acute abdominal pain.

Radiographs should never be requested without due consideration. They expend resources and expose the patient to ionizing radiation. They are an adjunct to a careful history and thorough physical examination.

The abdominal radiograph has the advantage of low cost. It is easy to perform and can be done on uncooperative patients, and, if correctly carried out and carefully interpreted,<sup>2</sup> it can still be used with a dual purpose. It can be used to evaluate catheter placement; identify ingested, inhaled, or introduced foreign bodies or free air in patients with a gastrointestinal perforation (conditions for which the examination is often

diagnostic); or assess a condition of intestinal occlusion or an abdomen in the postoperative phase. It also can be of use in documenting the intestinal morphodynamics, the findings of which at the direct examination of the abdomen depend on both the cause of the acute pathologic process and the time when the examination is performed with respect to the onset of the insult.3 In addition, plain abdominal radiographs are an accessible, relatively inexpensive, convenient, and accurate method of detecting retained surgical needles. They can be used effectively to locate needles over 10 mm in length retained in the abdomen, with a sensitivity of 92% in this size range. In this scenario, plain abdominal radiographs should continue to be used after incorrect needle counts. It is also recommended that the requesting physician provide the radiologist the size of the lost needle. However, for missing needles of 10 mm or less in length, the utility of plain abdominal radiographs is more debatable.4

Conversely, criticisms of requests for abdominal films often quote a low number of cases in which the diagnosis or management was changed by the radiographic findings. The diagnostic value is questionable, and very often there is no clear indication. In the majority of cases, the results are negative or nonspecific. In fact, as reported in a recent article by Kellow and colleagues,<sup>5</sup> the results of abdominal radiography are neither sensitive nor specific. Flak and Rowley<sup>6</sup> suggested that there are only two clinical entities in which sensitivity of abdominal radiography approaches 100%: free intraperitoneal air and, to a lesser extent, bowel obstruction. For the latter indication, a prospective trial conducted by Frager and associates<sup>7</sup> determined that clinical and radiographic evaluation was never precise enough to provide the exact location or cause of small bowel obstruction. Furthermore, Taourel and coworkers<sup>8</sup> demonstrated that not only is CT valuable in making a more accurate diagnosis but also that clinical treatment was correctly modified in 21% of patients because of the additional information provided by using CT. Therefore, abdominal radiography appears of limited value in the initial diagnosis of obstruction. For the indication of free air, the diagnosis is better made by evaluation of a chest radiograph obtained with the patient erect.9 In addition, only a few physicians are aware of the relatively high radiation dose of an abdominal film, which is equal to 50 chest radiographs.<sup>10</sup>

#### Controversies

In the 1950s, gastrointestinal radiology consisted of plain abdominal films and single-contrast barium studies to assess gastrointestinal diseases.<sup>11</sup> Today, the plain radiograph still may be the first step to evaluate acute abdominal diseases. However, with the advent of CT and ultrasonography, the importance of the plain abdominal film is decreasing. In past years, plain radiography was also used to help diagnose abdominal pathologic



Figure 1-1 Normal anteroposterior abdominal plain film.

processes such as stones in the kidney, gallbladder, or bladder. Plain radiography is now limited to emergency radiology in the acute abdomen. However, despite the undoubted advantages of the speed of examination, the multiplanar capabilities, and the objectivity of interpretation, CT subjects the patient to a higher dose of ionizing radiation.<sup>12</sup> The role of plain radiography of the abdomen in the diagnosis of acute abdomen needs to be reconsidered.<sup>13</sup> According to some authors, plain radiography should be performed only in patients for whom there are known advantages, such as in the case of suspected gastrointestinal perforation,<sup>14</sup> intestinal occlusion, ingestion of or the search for foreign bodies,<sup>15</sup> and assessment of the postoperative abdomen<sup>16</sup>; in these cases, it is still the examination of choice, and only if it does not prove diagnostic should a CT examination be recommended.<sup>17</sup> In addition to these situations, however, there is another indication: the ability of plain radiography to assess the evolution of intestinal morphodynamism, that is, the variations in the motility, shape, and position of the small bowel in acute pathologic conditions.<sup>18</sup> Even though in the first instance assessing the cause or the precise site of the obstruction is advisable, differentiating at least a mechanical ileus from a paralytic ileus,<sup>1</sup> and above all having an understanding of the seriousness and the extension of the cause and the time elapsed since its onset<sup>20</sup> can prove clinically more useful. Few comparisons of plain abdominal radiographs and CT scans exist in the literature. Siewert and associates<sup>21</sup> reported on 91 admitted patients with acute abdominal pain who eventually received CT because of continuing symptoms or failure to respond to therapy. In this series, treatment was changed after CT in 25 patients (27%), but the authors did not state the relative contribution of the plain abdominal radiographs to the pre-CT diagnosis. In particular, the percentage of patients who had abnormal plain abdominal radiographs was not given. A retrospective review of 23 patients with proved mesenteric infarction compared plain abdominal radiographs with CTs and showed that 6 patients (26%) had abnormal plain abdominal radiographs only, 8

patients (35%) had abnormal CTs only, and in only 1 patient (4%) were both tests abnormal.<sup>22</sup> Both studies were normal or nonspecific in 8 patients (35%). That 26% of patients had signs of an acute abdominal syndrome shown only on plain abdominal radiographs and not on CT is in sharp contradiction to our findings, in which the plain abdominal radiographs provided minimal additional information in 2 of 74 patients (3%) and at the cost of 33 (57%) potentially misleading false-negative results. There are several possible explanations. Mesenteric infarction may represent one of a series of specific syndromes that have either relatively low CT sensitivity, high plain abdominal radiograph sensitivity, or both. In the review just cited, no patients were diagnosed on plain abdominal radiographs, CT, or clinical course with this syndrome. Other possibilities include individual or institutional variations in radiologic interpretations or improvement in the interpretation of CTs for this and other syndromes over the past decade. The increased imaging capabilities of this newer technology would most likely make the test characteristics of the newer CT scanners even more favorable. Despite these limitations, for emergency department patients with acute abdominal, flank, or back pain, in whom a CT is likely to be obtained, a preliminary plain abdominal radiograph adds almost no additional information and is potentially misleading. Given the utilization of resources required for plain abdominal radiographs as well as the time delay to obtain them, some authors believe that patients in whom the clinical suspicion of significant intra-abdominal pathology is high should go directly to CT.23

#### **Normal Anatomy**

As with any plain radiograph, only five main densities may be distinguished, four of which are natural: black for gas, white for calcified structures, gray representing a host of soft tissue, and a slightly darker gray for fat (because it absorbs slightly fewer x-rays). Metallic objects are seen as an intense bright white. The clarity of outlines of structures depends, therefore, on the differences among these densities. On the chest radiograph, this is easily shown by the contrast between lung and ribs as black air against the white calcium-containing bones. These differences are much less apparent on the abdominal radiograph because most structures are of similar density, mainly soft tissue. A systematic approach to plain abdominal radiographs will help avoid errors in interpretation. Interpretation of the abdominal radiograph depends on the assessment of the bowel gas pattern, solid organ outlines, a search for abnormal calcification, and a review of the skeleton. A search should be made for extraluminal gas. A bowel gas pattern distinguishing the colon from the small bowel may be difficult. The presence of solid feces and the distribution, caliber, and mucosal pattern of the bowel help in deciding whether a particular loop of bowel is stomach, small intestine, or colon. The presence of solid feces indicates the large bowel, which also may be recognized by the incomplete haustral band crossing the colonic gas shadow. Haustra are usually present in the ascending and transverse colon but may be absent from the splenic flexure and descending colon. The valvulae conniventes of the small bowel are closer together and cross the width of the bowel. The distal ileum when dilated can appear smooth, which makes differentiation more difficult. The small bowel when obstructed is generally centrally positioned with numerous loops of tighter curvature than the large bowel. Maximal small bowel caliber is 3.5 cm in the jejunum and

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**Figure 1-2** Diverticulitis and peridiverticulitis. There is no evidence of bowel distention at the level of either the colon or the small bowel. It is possible to see a mild air dilation of the small bowel. The cecum seems to be medially moved (*arrow*).

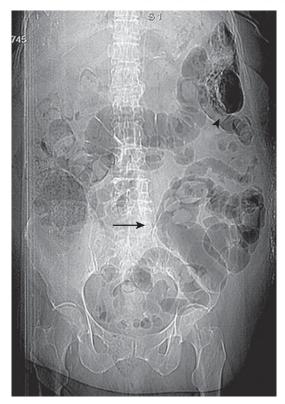
2.5 cm in the ileum. Maximal caliber of the transverse colon on plain films is taken to be 5.5 cm in diameter, and the maximal cecal diameter is 9 cm. Solid organs, the liver edge, renal outlines, and the splenic tip may all be demonstrated.

#### **INTRALUMINAL GAS**

One should begin by looking at the amount and distribution of gas in the bowels (intraluminal gas). There is considerable normal variation in the distribution of bowel gas (Figure 1-2). On the abdominal radiograph taken with the patient erect, the gastric gas bubble in the left upper quadrant of the film is a normal finding. Gas is also normally seen within the large bowel, most notably the transverse colon and rectum. Small and large bowel also can be distinguished, most easily when dilated, by their different mucosal markings. Small bowel has valvulae conniventes that traverse the full width of the bowel; large bowel has haustra that cross only part of the bowel wall. These features are important in the next part of this series, which considers abnormal intraluminal gas. Occasionally, fluid levels in the small bowel are a normal finding. Fecal matter in the bowel gives a "mottled" appearance. This is seen as a mixture of gray densities representing a gas/liquid/solid mixture.

#### **EXTRALUMINAL GAS**

Gas outside the bowel lumen is invariably abnormal (Figure 1-3). The largest volume of gas one might see is likely to be under the right diaphragm; this occurs after a viscus has been perforated. This gas within the peritoneal cavity is termed



**Figure 1-3** Mesenteric ischemia and spleen infarction. Abdominal radiograph shows a colonic dilation (*arrow*) that is especially marked at distal segments. Furthermore, extracolonic air collections are visible at the spleen level (*arrowhead*) in the upper left quadrant. Bowel dilation is evident without the finding of bowel obstruction.

#### BOX 1-1 AREAS TO SEARCH FOR ABNORMAL EXTRALUMINAL GAS

- Under the diaphragm
- In the biliary systemWithin the bowel wall

*pneumoperitoneum.* Gas in the right upper quadrant within the biliary tree is a "normal" finding after sphincterotomy or biliary surgery, but it can indicate the presence of a fistula between the biliary tree and the gut. One must beware of gas in the portal vein, because this can look very similar to biliary air. Gas in the portal vein is always pathologic and frequently fatal. It occurs in ischemic states, such as toxic megacolon, and it may be accompanied by gas within the bowel wall (intramural gas) (Box 1-1).

#### CALCIFICATION

Calcium is visible in a variety of structures, both normal and abnormal, and becomes more common with advancing age. Calcification should be identified and anatomically located. In some locations (e.g., vascular calcification), it is common and benign. Vascular calcification may be seen within the aorta, in the splenic artery in the left upper quadrant, or in the pelvis. Abdominal aortic aneurysms are usually below the second lumbar vertebra. Calcification can make them obvious and can give a rough indication of the internal diameter. Abdominal ultrasonography is required for accurate assessment and to determine the need for surgery or follow-up. Uterine fibroids can become calcified.

Calcified renal tract stones should be looked for around the renal outlines and down the line of the ureters. More rarely, calcified gallstones are seen in the right upper quadrant or a calcified (porcelain) gallbladder is present. The pancreas lies at the level of the T9 to T12 vertebrae. Calcification occurs in chronic pancreatitis and may show the whole outline of the gland.

In the pelvic region, bladder calculi may occasionally be seen. Bladder stones are usually quite large and often multiple. Calcification of a bladder tumor also may occur. Schistosomiasis may produce calcification of the bladder wall.

Other causes of pelvic calcification include phleboliths, calcified fibroids, and, rarely, calcification in ovarian dermoids, which may also contain teeth and hair.

#### SOFT TISSUES AND BONE

A review of the soft tissues entails evaluating the outlines of the major abdominal organs. Observing these structures is made easier by the fatty rim (properitoneal fat lines) surrounding them. In fact, the loss of these fat planes may indicate an ongoing pathologic process, such as peritonitis.

The liver is seen in the right upper quadrant and extends downward a variable distance. The tip of the right lobe may be seen extending below the right kidney; this is a normal variant called Riedel's lobe. The spleen may be visualized (especially in thin individuals) even when of normal size. It enlarges inferiorly and toward the left lower quadrant. It is often possible to identify both kidneys and the psoas shadows within the retroperitoneum. The kidneys are lateral to the midline in the region of the T12 to L2 vertebrae. (*Note:* A useful way to identify vertebrae is that the lowest one to give off a rib is T12 and thus can serve as a reference point.)

Soft tissue masses or abscess can sometimes be identified on plain films. An abscess generally has a rather heterogeneous density because of the presence of gas and necrotic tissue. Mass lesions are of soft tissue density and will displace bowel gas shadows.

The assessment of bones entails evaluating the spine and pelvis for evidence of a bony pathologic process. Osteoarthritis frequently affects the vertebral bodies, as well as the femoral and the acetabular components of the hip joint. Paget's disease may be identified commonly along the iliopectineal lines of the pelvis. The bone survey should also include a check for fractures, especially subtle femoral neck fractures in elderly persons. The spine and pelvis are also common locations for metastatic deposits. In the spine, this is classically seen as "the absent pedicle."

#### ARTIFACTS

"Human-made" structures should be correctly identified. These may be iatrogenic (put there by health care professionals), accidental (put there by the patient or another person), or projectional (lying in front of or behind the abdomen but spuriously projected within it on the abdominal radiograph). Examples of iatrogenic structures would be surgical clips, an intrauterine contraceptive device, a renal or biliary stent, an endoluminal aortic stent, or an inferior vena cava filter. Accidental findings include bullets or an object in the rectum. Projectional findings include pajama buttons, coins in pockets, or body piercings.

#### **Pathologic Findings**

Abdominal radiographs obtained with the patient erect are requested to look for fluid levels in obstruction or ileus. Air under the diaphragm may be seen in an erect film if the bowel has been perforated, although a chest radiograph is more commonly obtained to look for that sign (Figure 1-4). An abdominal radiograph is of no value in hematemesis. Avoiding obtaining erect films when unnecessary and avoiding plain films for hematemesis will reduce the level of radiation exposure.

#### **RENAL COLIC**

If a patient presents with groin pain, the possibility of renal colic is high; therefore, a kidney/ureter/bladder (KUB) view is requested. Approximately 90% of renal stones are radiopaque. Uric acid stones may be missed. False-positive findings may occur from phleboliths, which are most common in the pelvic veins, and false-negative findings occur from small stones. On the right, calcification may represent gallstones but only a minority of gallstones are radiopaque. The presence of gall-stones does not confirm biliary colic as the cause of pain because



**Figure 1-4** Sigmoid carcinoma. Wide sickle-shaped free air is evident under the right hemidiaphragm (*large arrow*). A small, linear, free air collection is also shown along the lower margin of the liver (*small arrows*). Marked air distention of jejunum with a transitional area between dilated jejunum and normal ileum is visible (*arrowheads*).

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gallstones become more frequent with age and are often asymptomatic.

#### INTESTINAL OBSTRUCTION

Erect and supine films are used to confirm the diagnosis. Obstruction of the small bowel shows a ladder-like series of small bowel loops, but this also occurs with an obstruction of the proximal colon. Fluid levels in the bowel can be seen in upright views. Distended loops may be absent if obstruction is at the upper jejunum. Obstruction of the large bowel is more gradual in onset than small bowel obstruction. The colon is in the more peripheral part of the film, and distention may be very marked. Fluid levels also will be seen in paralytic ileus when bowel sounds will be reduced or absent rather than loud and tinkling as in obstruction. In an erect film, a fluid level in the stomach is normal, as may be a level in the cecum. Multiple fluid levels and distention of the bowel are abnormal.

#### PERFORATION OF THE INTESTINE

If the bowel has been perforated and a significant amount of gas has been released, it will show as a translucency under the diaphragm on an erect film. Gas will also be found under the diaphragm for some time after laparotomy or laparoscopy.

#### **APPENDICITIS**

An appendicolith may be apparent in an inflamed appendix in 15% of cases, but as a diagnostic point in the management of appendicitis the plain radiograph is of very limited value, although it may be of value in infants.

#### INTUSSUSCEPTION

Intussusception occurs in adults and children. A plain abdominal radiograph may show some characteristic gas patterns. A sensitivity and specificity of 90% adds to this rather difficult diagnosis, but ultrasonography is vastly superior.

#### **BODY PACKERS**

An increasing problem occurs with people who swallow drugs, usually in condoms, to evade detection. There may be signs that the drugs are leaking, but the carrier is unwilling to disclose the fact for fear of a long prison term, even at risk to life. A plain abdominal radiograph will show 90% of cases, but there will be false-positive findings in 3%. Therefore, a positive result is likely to be true but a negative result does not exclude the clinical suspicion adequately and an ultrasound examination may be considered (Boxes 1-2 and 1-3).

#### BOX 1-2 KEY TO DENSITIES IN ABDOMINAL RADIOGRAPHS

- Black—gas
- White—calcified structuresGray—soft tissues
- Darker gray—fat
- Intense white-metallic objects

#### Pathophysiology

#### SMALL BOWEL

The small bowel contains a small amount to no gas in normal individuals, so it is not visible on a plain film. The presence of more gas than normal should be viewed with suspicion and interpreted in the proper clinical setting. Some clinical situations, such as indigestion or viral enteritis, show an increase of intestinal gas, usually without air/fluid levels; these are selflimiting diseases, and usually they do not need diagnostic efforts.

Intestinal obstruction is a common radiographic finding in an emergency department. Distended intestinal loops with air/ fluid levels with scarcely visible colonic gas are among the most commonly seen features of small bowel obstruction; the clinical history of the patient may be the key to the diagnosis in the case of suspected postoperative adhesions, Crohn's disease, or a known tumor. In some cases, however, depending on the gas and fluid distribution it is not impossible to have a near-normal plain film with a true obstruction. On the other hand, diffuse peritoneal metastasis may produce air/fluid levels without obstruction. The level of the intestinal obstruction may be, in some cases, understood; however, in prestenotic loops the fluid may be abundant and gas not visible so that only proximal loops are distended by gas. Again, fluid-filled intestinal loops showing the cause of obstruction either of the bowel wall or extraintestinal are often easily seen at CT. The diagnosis of strangulation requires expertise because the intramural gas and a rigid loop are well-known features but not so commonly seen. It should be remembered that the shape of valvulae conniventes is also generally preserved in severe distention so that they can be used to differentiate small intestinal disease from colonic disease.

The adhesions are not directly seen, but a transition zone (dilatation of the bowel followed by a collapsed loop) without any other visible cause of obstruction may lead to the diagnosis in a patient with a history of surgery.

CT performed after a plain abdominal film can be obtained without oral contrast administration, but intravenous administration of a contrast agent usually cannot be avoided in these often severely ill patients.

A set of CT criteria that may help surgeons decide if a patient needs surgery for small bowel obstruction has been implemented.<sup>24</sup> Although plain radiography can be used with good results by experienced surgeons, CT has been reported to have 100% sensitivity in complete obstruction.<sup>25</sup> Daneshmand and colleagues compared CT to plain radiography and found a sensitivity and specificity of 75% and 53% for plain film, respectively, and 92% and 71% for CT; they suggest that CT can be used as the primary diagnostic tool for small bowel obstruction.<sup>26</sup> The approach to evaluate patients with small bowel

#### BOX 1-3 RADIOGRAPHIC REVIEW POINTS

- Technical specifics of the radiograph
- Amount and distribution of gas
- Extraluminal gas
- Calcification
- Soft tissue outlines and bony structures
- · latrogenic, accidental, and incidental objects



**Figure 1-5** Volvulus. Visible fecal material (*arrow*) is evident in the right colon, whereas the left and sigmoid colon are not represented. Moderate distention of bowel in the upper abdomen can be seen. In the left lower quadrant, a mass is suspected because of the lack of intestinal air.

obstruction is not generally accepted; however, CT is considered the preeminent imaging modality to evaluate these patients.<sup>27</sup>

#### COLON

Because of the presence of haustra, feces, and gas, understanding diseases of the colon is apparently easier than recognizing diseases of the small bowel on a plain radiograph. An obstruction of the sigmoid colon shows the transition from a dilated to a nondilated colon, and it is not difficult to recognize. On the other hand, an obstruction of the ascending colon may be similar, in some cases, to an obstruction of the last ileal loop. Colonic obstruction producing a severe cecal dilatation greater than 10 to 11 cm is an indication for immediate surgery, to avoid perforation. In elderly constipated patients, a sigmoid volvulus is among the possible causes of obstruction; the dilated sigmoid that is seen as a "kidney bean" also may mimic an abdominal mass. Cecal volvulus, seen in younger patients, produces distention of the cecum (Figure 1-5). In both cases, CT can provide crucial information.

Severe clinical situations such as perirectal or perisigmoidal abscesses or a carcinoma infiltrating bowel wall without obstruction may have a completely normal appearance on a plain film (Figure 1-6); these situations are easily seen on CT.

Distention of the colon, often accompanied with diffuse distention of the small bowel without mechanical obstruction, is the feature of paralytic or adynamic ileus. The intestinal distention may be limited to some part of the intestine so that it may be difficult to distinguish mechanical from paralytic ileus.



**Figure 1-6** Perisigmoid abscess. Note enlargement of the hepatic area (*arrowheads*). Small bowel and colon are within the normal range for size.

The clinical situation of the patient may be enough, in some cases, to make the diagnosis. If the diagnosis is not clear, CT is mandatory.

Ischemic bowel disease produces many different abnormalities on a plain radiograph, ranging from intestinal distention to a gasless abdomen. "Thumbprinting" is a famous, but not so specific, feature of intestinal ischemia. A linear shadow of gas within the bowel wall is difficult to detect on a plain film; when visible, it indicates a poor prognosis.

Toxic megacolon may be a lethal complication of ulcerative colitis. A plain film shows a dilatation of the transverse colon greater than 6 to 8 cm with loss of haustra. The loss of a haustral pattern is important to distinguish a patient with an obstruction of the distal colon from a patient with colitis, in which a haustral pattern is usually lost, even with mild disease. Small bowel distention, often with air/fluid levels, may be seen in a subgroup of patients with severe ulcerative colitis at higher risk for both toxic megacolon and multiple organ dysfunction syndrome. The poor response to therapy and the persistence of gastrointestinal distention are monitored with plain radiography, which is important to evaluate patients who need colectomy.<sup>28</sup>

#### MISCELLANEOUS FINDINGS

Free intraperitoneal or subphrenic air is commonly seen in postoperative patients, and the only thing to do is wait for its resorption. A deep intestinal or colonic biopsy also can produce, as a rare complication, free or subphrenic air collection. Perforation of a duodenal ulcer or perforation of a diverticulum of the colon are not as common causes of extraintestinal air collections.

Cholecystitis, pancreatitis, and other causes of acute abdomen in which a collection of air or fluid may be misleading

#### **Key Points**

- The history, physical examination, and laboratory findings are always important to evaluate an acute abdomen, which may be caused by a number of different diseases.
- Plain radiography should be performed as an initial imaging modality in patients for whom there are known advantages, such as those with suspected gastrointestinal perforation, intestinal occlusion, and ingestion of or in a search for foreign bodies, and in the assessment of the postoperative abdomen to detect retained needles. In

SUGGESTED READINGS

- Anonymous: Best evidence topic reports: role of plain abdominal radiograph in the diagnosis of intussusception. *Emerg Med J* 25:106–107, 2008.
- Brazaitis MP, Dachman AH: The radiologic evaluation of acute abdominal pain of intestinal origin: a clinical approach. *Med Clin North Am* 77:939– 961, 1993.
- Burkill G, Bell J, Healy J: Small bowel obstruction: the role of computed tomography in its diagnosis

and management with reference to other imaging modalities. *Eur Radiol* 11:1405–1422, 2001.

- Gupta H, Dupuy DE: Advances in imaging of the acute abdomen. Surg Clin North Am 77:1245– 1263, 1997.
- Hayes R: Abdominal pain: general imaging strategies. *Eur Radiol* 14(Suppl 4):L123–L137, 2004.
- Kidmas AT, Ekedigwe JE, Sule AZ, et al: A review of the radiological diagnosis of small bowel obstruc-

the rectum is preferred to diagnose this lesion.

should now be assessed by ultrasonography or CT. Fecaloma is

easy to detect on a plain film; however, a digital exploration of

addition, another indication is the ability of plain radiography to assess the evolution of intestinal morphodynamism, which is the variation in the motility, shape, and position of the small bowel in acute pathologic conditions.

- The lack of positive findings on abdominal radiography is falsely reassuring in nontrauma emergency department patients.
- Further imaging is often required to better characterize abnormalities identified at abdominal radiography.

tion using various imaging modalities. *Niger Post-grad Med J* 12:33–36, 2005.

- Reuchlin-Vroklage LM, Bierma-Zeinstra S, Benninga MA, et al: Diagnostic value of abdominal radiography in constipated children: a systematic review. Arch Pediatr Adolesc Med 159:671–678, 2005.
- Roszler MH: Plain film radiologic examination of the abdomen. Crit Care Clin 10:277–296, 1994.

#### REFERENCES

- Levine MS: Plain film diagnosis of the acute abdomen. *Emerg Med North Am* 3:541–562, 1985.
- 2. Baker SR: The abdominal plain film: what will be its role in the future? *Radiol Clin North Am* 31:1335–1344, 1993.
- Grassi R, Di Mizio R, Pinto A, et al: Semeiotica radiografica dell'addome acuto all'esame radiologico diretto: ileo riflesso spastico, ileo riflesso ipotonico, ileo meccanico ed ileo paralitico. *Radiol Med* 108:56–70, 2004.
- 4. Ponrartana S, Coakley FV, Yeh BM: Accuracy of plain abdominal radiographs in the detection of retained surgical needles in the peritoneal cavity. *Ann Surg* 247:8–12, 2008.
- 5. Kellow ZS, MacInnes M, Kurzencwyg D, et al: The role of abdominal radiography in the evaluation of the non-trauma emergency patient. *Radiology* 248:887–893, 2008.
- Flak B, Rowley VA: Acute abdomen: plain film utilisation and analysis. *Can Assoc Radiol J* 44:423–428, 1993.
- Frager DH, Baer JW, Rothpearl A, et al: Distinction between postoperative ileus and mechanical small-bowel obstruction: value of CT compared with clinical and other radiographic findings. *AJR Am J Roentgenol* 164:891–894, 1995.
- Taourel P, Pradel J, Fabre JM, et al: Role of CT in the acute non-traumatic abdomen. *Semin Ultrasound CT MR* 16:151–164, 1995.
- McCook TA, Ravin CE, Rice RP: Abdominal radiography in the emergency department: a prospective analysis. *Ann Emerg Med* 11:7–8, 1982.

- Campbell JP, Gunn AA: Plain abdominal radiographs and acute abdominal pain. Br J Surg 75:554–556, 1988.
- 11. Goldberg HJ, Margulis AR: Gastrointestinal radiology in US: an overview of the past 50 years. *Radiology* 216:1–7, 2000.
- Baker SR: Musings at the beginning of the hyper-CT era. *Abdom Imaging* 28:110–114, 2003.
- Feyler S, Williamson V, King D: Plain abdominal radiographs in acute medical emergencies: an abused investigation? *Postgrad Med J* 78:94–96, 2002.
- Grassi R, Pinto F, Rotondo A, et al: Contributo della radiologia tradizionale alla diagnosi di pneumoperitoneo. In Pinos A, editor: *Pneumoperitoneo*, Napoli, 1996, Guido Gnocchi, pp 7–158.
- Baker SR: Plain films and cross-sectional imaging for acute abdominal pain: unresolved issues. Semin Ultrasound CT MRI 20:142–147, 1999.
- 16. Frassineti A: La Radiologia dell'Addome Acuto Postoperatorio. Padua, Piccin, 1982.
- 17. Wiest P, Roth P: *Fundamentals of emergency radiology*, Philadelphia, 1996, WB Saunders, pp 96–112.
- Taourel P, Kessler N, Lesnik A, et al: Nontraumatic abdominal emergencies: imaging of acute intestinal obstruction. *Eur Radiol* 12: 2151–2160, 2002.
- Krestin GP, Choyke PL: Acute abdomen: diagnostic imaging in the clinical context, Stuttgart, 1996, Georg Thieme, p 139.

- Silen W: Cope's early diagnosis of the acute abdomen, New York, 2005, Oxford University Press, p 159.
- Siewert B, Raptopoulos V, Mueller M, et al: Impact of CT on diagnosis and management of the acute abdomen in patients initially treated without surgery. *AJR Am J Roentgenol* 168:173– 178, 1997.
- Smerud MJ, Johnson CD, Stephens DH: Diagnosis of bowel infarction: a comparison of plain films and CT scans in 23 cases. *AJR Am J Roentgenol* 154:99–103, 1990.
- Nagurney JT, Brown DF, Novelline DA, et al: Plain abdominal radiographs and CT scans. Am J Emerg Med 17:668–671, 1999.
- 24. Jones K, Mangram AJ, Lebron RA, et al: Can a computed tomography scoring system predict the need for surgery in small-bowel obstruction? *Am J Surg* 194:780–784, 2007.
- Frager D, Medwid SW, Baer JW, et al: CT of small bowel obstruction: value in establishing the diagnosis and determining the degree and cause. *AJR Am J Roentgenol* 162:37–41, 1994.
- Daneshmand S, Hedley CG, Stain SC: The utility and reliability of CT in the diagnosis of small bowel obstruction. *Am Surg* 65:922–926, 1999.
- 27. Ros PR, Huprich JE: ACR appropriateness criteria on suspected small bowel obstruction. *J Am Coll Radiol* 3:838–841, 2006.
- Latella G, Vernia P, Viscido A, et al: GI distension in severe ulcerative colitis. Am J Gastroenterol 5:1169–1175, 2002.

2

## Fluoroscopic Study of the Abdomen and Fluoroscopic Contrast Media

NAVEEN M. KULKARNI | PRITISH AHER | KOICHI HAYANO

Fluoroscopy is a type of imaging technique in which real-time movements of body organs and radiopaque contrast material are visualized. During a fluoroscopic examination, the operator or radiologist controls the functions of radiography equipment and x-ray tubes for real-time imaging of the patient. In abdominal imaging, fluoroscopy has a role in the diagnosis of various clinical conditions with gastrointestinal studies, postoperative studies, genitourinary studies, and more.

#### **Technical Aspects**

#### FLUOROSCOPY

#### History

Early fluoroscopes had an x-ray tube and fluorescent screen made of barium platinocyanide. Gradually, the screens were replaced by cadmium tungstate and then zinc-cadmium sulfide, which produced a yellow-green emission.<sup>1</sup>

Fluoroscopy has evolved from the early days of images on a fluoroscopic screen of poor quality, a dark radiography room, and eye adaptation with red goggles to improved images with image intensifiers, video-recorders, and a variety of C-arm machines. Currently, it is available in many different configurations for use in various clinical applications. With technologic advancements in hardware and image processing, fluoroscopy has gained substantially both qualitatively and quantitatively. The introduction of flat-panel detectors, highquality image intensifiers with video-recording capabilities, state-of-the-art C-arm design, and digital units has revolutionized the field of fluoroscopic imaging.<sup>1,2</sup> The superior spatial and contrast resolution combined with faster image reconstruction and reduced radiation along with a variety of safe and effective contrast media has empowered fluoroscopy with advanced capabilities in the diagnostics and interventional realm. A variety of fluoroscopic units are now commercially available, and the components of basic fluoroscopic equipment are shown in Figure 2-1. The main uses of fluoroscopy are listed in Box 2-1.

#### Patient Preparation

It is important to have the patient empty his or her stomach to increase the sensitivity of the fluoroscopy examination, because food and food residue can mimic disease. Informed consent is required, and any medical history such as heart disease, asthma, allergy, thyrotoxicosis, and hypersensitivity to drugs should be elicited. Also important to consider: What medications (e.g., insulin) is the patient using? Is the patient pregnant or breastfeeding? Has there been a recent diagnosis of small bowel obstruction or perforation and, if so, what were the surgical details?

Patients scheduled for a double-contrast barium enema must adhere to a clear liquid diet for 24 hours before the procedure. Laxatives may be prescribed to ensure thorough bowel cleansing, and on the morning of the examination a bisacodyl suppository is given per rectum.

However, in the acute/emergency or postoperative setting, patient preparation is usually optional. Moreover, in this setting, iodinated contrast media are preferred over barium sulfate because the latter might interfere with a surgical procedure and any extraluminal collection of barium may create confusion with a diagnosis on subsequent examinations.<sup>3-5</sup> A medical history of severe hypersensitivity to iodinated contrast media or certain medications should be obtained if the procedure requires its use.

#### FLUOROSCOPIC EXAMINATIONS

Fluoroscopic examinations are of two types: single-contrast studies and double-contrast studies (Box 2-2). Single-contrast studies are performed either with barium or with iodinated contrast media.<sup>67</sup> For double-contrast media, air or carbon dioxide is used (Figure 2-2).<sup>89</sup>

#### Gastrointestinal Fluoroscopic Procedures

- Stomal examinations, enema through ileostomy or colostomy for patency, recurrence of disease, and leak
- Feeding tube studies
- Oral cholecystogram and T-tube cholangiogram
- Hydrostatic reduction of pediatric abdominal emergencies such as intussusceptions and sigmoid volvulus

#### **Genitourinary Fluoroscopic Procedures**

- Cystography for evaluation of urinary bladder and vesicoureteric reflux
- · Voiding cystourethrography for visualization of urethra
- Retrograde urethrography for anterior urethra
- Hysterosalpingogram for uterus and fallopian tubes

#### Interventional Procedures

- Placement of vascular catheter and stents
- Percutaneous biliary drainage procedures
- Urologic procedures: Retrograde pyelography, percutaneous nephrostomies, and suprapubic cystotomies

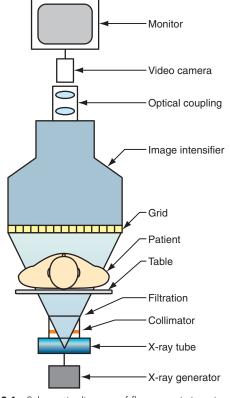
#### Other Examinations

- Sinogram
- Fistulogram

#### **Fluoroscopic Contrast Agents**

Fluoroscopic contrast agents are compounds that enable improved visualization of internal luminal structures, spaces, and tracts and also delineate tubes and catheters on fluoroscopy or radiography (Figure 2-3).

Fluoroscopic contrast agents can be divided into two types: positive contrast and negative contrast. A positive contrast medium absorbs x-rays more strongly than the surrounding tissue or organ being examined and appears radiopaque. A





negative contrast medium absorbs x-rays less strongly and hence appears radiolucent. Positive contrast media are barium and iodine compounds (Figures 2-4 and 2-5). Negative contrast media can be obtained by air or carbon dioxide (Figure 2-6).<sup>10,11</sup>

#### BARIUM

The higher the concentration of the barium sulfate suspension, the thinner are the layers that can be identified in the radiograph. The more viscous is the suspension, the better is the

#### BOX 2-1 MAIN USES OF FLUOROSCOPY

- Gastrointestinal imaging
- Genitourinary imaging
- Angiography
- Other:
- Intraoperative
- Foreign-body removal
- Musculoskeletal

#### BOX 2-2 SINGLE-CONTRAST VERSUS DOUBLE-CONTRAST STUDIES

#### SINGLE-CONTRAST STUDIES

- Precise control of barium column
- Easier identification of filling defects
- In suspected perforation, single contrast with water-soluble medium preferred
- Can be used to evaluate mechanical problems (e.g., obstruction, fistula)
- Optimal for patients unable to swallow gas-forming tablets

#### DOUBLE-CONTRAST STUDIES

- Thick barium coats lumen, and effervescent tablets ingested to distend lumen with air
- Produced see-through effect with better assessment of mucosal details
- Better distention and separation of the bowel loops
- Better detection of small mucosal lesions, polyps, ulcers

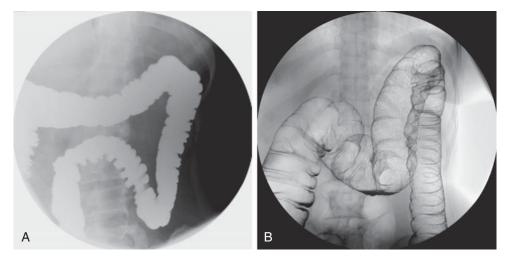


Figure 2-2 Spot radiograph of the mid-transverse colon obtained during single-contrast (A) and double-contrast (B) barium enema. The mucosal details are well seen on the double-contrast study.

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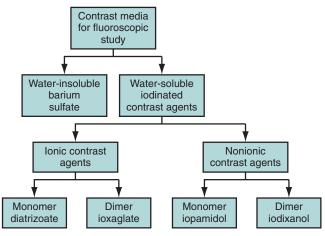


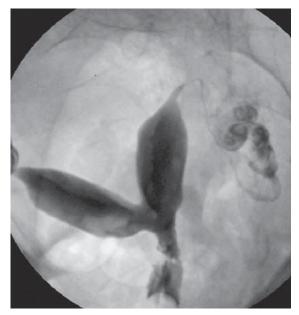
Figure 2-3 Contrast media used in fluoroscopy.



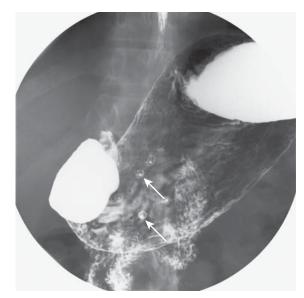
**Figure 2-4** Spot film single-contrast barium sulfate study of esophagus shows a pulsion diverticulum from the lower esophagus.

penetration into the finest folds and the more differentiated are the structures that become visible. Different barium preparations available for use are shown in Figure 2-7. Various barium suspensions used for the evaluation of different parts of gastrointestinal tract are depicted in Table 2-1.

Properties desirable for the conventional upper gastrointestinal and per-oral small bowel examinations include suspension stability, good coating ability for double-contrast views, and resistance to flocculation in the small intestine.<sup>3,4</sup> For dense, uniform coating in the esophagus, stomach, duodenum, and colon, it is also desirable that the barium suspension have the



**Figure 2-5** Spot film from hysterosalpingography using iodinated contrast media shows a bicornuate uterus with free spill.

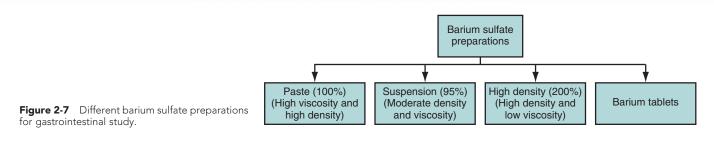


**Figure 2-6** Spot film of double-contrast barium study of stomach showing multiple aphthoid ulcers (*arrows*).

ability to delineate fine mucosal surface details with reasonable flow rate and resistance to flocculation.<sup>3,4,8</sup>

#### WATER-SOLUBLE CONTRAST AGENTS

Water-soluble contrast agents can be divided into ionic or nonionic agents or, depending on the osmolarity, as high- and lowosmolar agents (see Figures 2-3 and 2-8). Ionic contrast media have higher osmolarity and more side effects. Nonionic contrast media have lower osmolarity and tend to have fewer side effects.<sup>10,11</sup> Water-soluble organic iodine compounds are used in certain circumstances in which barium is contraindicated—for instance, in suspected perforation of gut into the free peritoneal



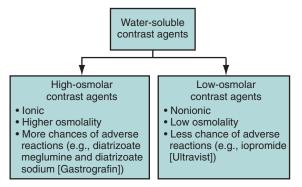


Figure 2-8 Water-soluble contrast agents.

TABLE 2-1	Barium Formulations for Tract Radiography	r Gastrointestinal	
Gastrointestinal Tract Study		Barium Formulations (%)	
Barium swallow		Single contrast: 50-100 w/v Double contrast: 250 w/v	
Upper gastrointestinal tract (stomach and duodenum)		Single contrast: 35-80 w/v Double contrast: 250 w/v	
Small bowel follow-through		40-60 w/v	
Enteroclysis		50-95 w/v	
Retrograde ileography		20-25 w/v	
Barium	n enema	Single contrast: 12-25 w/v Double contrast: 60-120 w/v (80 commonly used)	

w/v, Weight/volume.

cavity, in postoperative cases to look for a leak, or when the risk for aspiration into the lung is high. Barium leakage into the peritoneal cavity can lead to formation of granuloma, and aspiration into the lung can leak to pneumonitis or pulmonary edema.<sup>5,6</sup>

In general, to achieve good radiographic opacification of the gastrointestinal tract it is recommended that 60% or higher solutions of ionic contrast agents be used. Although ionic contrast agents stimulate intestinal peristalsis and result in more rapid visualization of distal small bowel loops as compared with barium preparations, this effect is quickly nullified by the dilution effect in the bowel secondary to hyperosmolarity of these agents.<sup>10-12</sup> Ideally, one of the nonionic contrast agents should be used when indicated for evaluation of gastrointestinal tract. Iodinated contrast agents such as diatrizoate meglumine preparations (Gastrografin and Hypaque) are commercially available for oral use (Figure 2-9). For genitourinary fluoroscopic procedures, ionic contrast agents such as Renografin and Cystografin



**Figure 2-9** Gastrografin enema performed in a neonate with intestinal obstruction shows microcolon.

are preferred over nonionic contrast agents in most institutions owing to the lower cost.

#### GASTROGRAFIN

Gastrografin (diatrizoate meglumine and diatrizoate sodium) is a commercially available oral contrast medium for opacification of gastrointestinal tract. This preparation is particularly indicated when use of a more viscous agent such as barium sulfate, which is not water soluble, is not feasible, or is potentially dangerous.

#### Oral Administration

Adult oral dosage usually ranges from 30 to 90 mL (11 to 33 g iodine), depending on the type of the examination and the size of the patient. For infants and children younger than 5 years of age, 30 mL (11 g iodine) is usually adequate; for children 5 to 10 years of age, the suggested dose is 60 mL (22 g iodine). These pediatric doses may be diluted 1:1, if desired, with water, carbonated beverage, milk, or mineral oil. For very young (<10 kg) and debilitated children, the dose should be diluted as 1 part Gastrografin in 3 parts water.

#### Enemas or Enterostomy Instillations

Gastrografin should be diluted when it is used for enemas and enterostomy instillations. When used as an enema, the suggested dilution for adults is 240 mL (88 g iodine) in 1000 mL

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of tap water. For children younger than 5 years of age, a 1:5 dilution in tap water is suggested; for children older than 5 years of age, 90 mL (33 g iodine) in 500 mL of tap water is a suitable dilution.

#### Oral Gastrografin Indications

Indications for oral use of Gastrografin include the following:

- Cystic fibrosis and subacute intestinal obstruction, because risk for obstruction in the small bowel is greater with barium
- Intestinal perforation
- Suspected tracheoesophageal fistula and pyloric stenosis, to avoid barium aspiration
- Recent rectal biopsy, recent surgery, to visualize postoperative leak, or to visualize ileostomy or colostomy loops
- Infants and neonates with suspected intestinal obstruction, necrotizing enterocolitis, unexplained pneumoperitoneum, gasless abdomen, other bowel perforation, esophageal perforation, or postoperative anastomosis

For genitourinary evaluation, the ionic contrast agents are preferred over the nonionic agents owing to the cost factor. However, in patients with a previous history of allergic reactions, nonionic agents are preferred. The dose and dilution depend on the investigation and body part examined.

#### EQUIPMENT FACTORS

Equipment factors include the following:

- Source-to-image distance
- Fluoroscopic kilovoltage peak
- Fluoroscopic milliampere
- Focal spot
- Field of view
- Grid use
- Fluoroscopic acquisition mode
- Dose rate selection
- Video frame rate

#### PATIENT FACTORS

Patient factors are listed in Box 2-3.

#### SIDE EFFECTS

#### Barium

- The side effects of barium include the following: • Bloating
  - Constipation (severe or continuing)

#### SUGGESTED READINGS

Gelfand DW, Ott DJ, Chen YM: Optimizing singleand double-contrast colon examinations. *Crit Rev Diagn Imaging* 27:167–201, 1987.

Maglinte DD, Romano S, Lappas JC: Air (CO2) double-contrast barium enteroclysis. *Radiology* 252:633–641, 2009. Nolan DJ: Barium examination of the small intestine. *Br J Hosp Med* 6:136–141, 1994.

Op den Orth JO: Use of barium in evaluation of disorders of upper gastrointestinal tract: current status. *Radiology* 173:601–608, 1989.

Rubesin SE, Maglinte DD: Double-contrast barium enema technique. *Radiol Clin North Am* 41:365– 376, 2003.

Schueler BA: The AAPM/RSNA physics tutorial for residents: general overview of fluoroscopic imaging. *Radiographics* 20:1115–1126, 2000.

#### BOX 2-3 PATIENT FACTORS IN GASTROINTESTINAL FLUOROSCOPY

#### ABILITY TO INGEST CONTRAST

 To get high-quality images, a relatively large volume of contrast agent needs to be ingested fairly quickly.

#### MOBILITY

- Multiple positions required for gastrointestinal examinations, particularly double-contrast examinations
- Limited mobility results in fewer diagnostic images.
- Weight
- Tables have weight limits.
- Maximal radiographic technique is required, and exposure is often suboptimal.
- Cramping (severe)
- Nausea or vomiting
- · Stomach or lower abdominal pain
- Tightness in chest or troubled breathing
- Wheezing

Some people have reported sensitivity to the flavoring substance and exposure to latex (in gloves and tubes) used in barium contrast studies. Allergic reactions to barium sulfate suspensions are estimated to occur at a rate of less than 2 per million.

#### Iodinated Oral Contrast Media

The side effects of iodinated oral contrast media may vary from mild reactions such as itching or a rash to rare life-threatening reactions such as shock. These media should be used with caution in patients with known hypersensitivity to iodine, bronchial asthma, eczema, and thyroid disorders such as thyro-toxicosis. Also, patients with inflammatory bowel disease and those with conditions in which there is absorption of contrast media from a mucosal surface may have increased chances of a reaction.<sup>13</sup> With oral administration patients may experience nausea, vomiting, diarrhea, and stomach cramps.

#### **Pros and Cons**

Fluoroscopic examinations may be affordable, but results depend on various factors, including the skill of the radiologist, quality of fluoroscopic equipment, and the patient's weight and compatibility. However, as compared with advanced modalities such as CT or MRI, fluoroscopy has limitations in crosssectional imaging and radiologic tissue diagnosis.

#### REFERENCES

- Cowen AR, Davies AG, Sivananthan MU: The design and imaging characteristics of dynamic, solid-state, flat-panel x-ray image detectors for digital fluoroscopy and fluorography. *Clin Radiol* 63:1073–1085, 2008.
- Schueler BA: The AAPM/RSNA physics tutorial for residents: general overview of fluoroscopic imaging. *Radiographics* 20:1115–1126, 2000.
- 3. Op den Orth JO: Use of barium in evaluation of disorders of upper gastrointestinal tract: current status. *Radiology* 173:601–608, 1989.
- 4. Nolan DJ: Barium examination of the small intestine. Br J Hosp Med 6:136–141, 1994.
- Tanomkiat W, Galassi W: Barium sulfate as contrast medium for evaluation of postoperative anastomotic leaks. *Acta Radiol* 41:482–485, 2000.
- 6. Gottesman L, Zevon SJ, Brabbee GW, et al: The use of water soluble contrast enemas in the diagnosis of acute lower left quadrant peritonitis. *Dis Colon Rectum* 27:84–88, 1984.
- 7. Stollman N, Raskin JB: Diverticular disease of the colon. *Lancet* 363:631–639, 2004.
- Rubesin SE, Maglinte DD: Double-contrast barium enema technique. *Radiol Clin North Am* 41:365–376, 2003.
- Gelfand DW, Ott DJ, Chen YM: Optimizing single- and double- contrast colon examinations. Crit Rev Diagn Imaging 27:167–201, 1987.
- Jobling JC: Air versus carbon dioxide insufflation in double contrast barium enemas: the role of active gaseous drainage. *Br J Radiol* 69:89–90, 1996.
- Ott DJ, Gelfand DW: Gastrointestinal contrast agents: indications, uses, and risks. JAMA 249:2380–2384, 1983.
- Rubin JD, Cohan RH: Iodinated radiographic contrast media: comparison of low-osmolar with conventional ionic agents [corrected]. *Curr Opin Radiol* 3:637–645, 1991.
- Kory LA, Epstein BS: The oral use of iodinated water-soluble contrast agents for visualizing the proximal colon when barium enema examination reveals complete obstruction. *Am J Roentgenol Radium Ther Nucl Med* 115:355–359, 1972.

## Abdominal Ultrasound Imaging: Anatomy, Physics, Instrumentation, and Technique

LUZENG CHEN

Ultrasonography is low in cost, noninvasive, and highly portable, and it allows real-time imaging in multiple operatorcontrolled planes. As a result, it is the most widely used cross-sectional imaging modality worldwide. The principal challenge with ultrasonography is greater user-dependence than computed tomography (CT) or magnetic resonance imaging (MRI).

#### **Basic Physics**

#### DEFINITION

Humans can hear sound that vibrates from 20 Hertz (Hz) to 20,000 Hz. *Ultrasound* is the term given to describe sound at frequencies above 20,000 Hz, beyond the range of human hearing. Frequencies of 3 to 7 megahertz (MHz) are commonly used for abdominal ultrasound.

#### **PROPERTIES OF ULTRASOUND**

Ultrasound waves propagate as longitudinal waves in soft tissues. Acoustic impedance is an intrinsic physical property of a medium defined as the density of the medium multiplied by the velocity of ultrasound wave propagation in the medium. Acoustic interfaces exist between materials that have different acoustic impedances. Reflection, refraction, and scatter occur when ultrasound waves meet an acoustic interface. The greater the acoustic impedance difference between two sides of the interface, the greater is the ultrasound energy that will be reflected.

The relationship among frequency (f), velocity (c), and wavelength ( $\lambda$ ) is  $\lambda = c/f$ . The higher the frequency, the shorter is the wavelength. In theory, the distance that can be measured by ultrasound is  $\frac{1}{2}\lambda$ . The shorter the wavelength, the better the resolution will be. With the wavelength shortened, the attenuation will be greater. So a low-frequency probe should generally be selected to examine the deep organs of the abdomen (e.g., liver, kidney, pancreas), and high-frequency probes should be selected to examine superficial tissues (e.g., abdominal wall, appendix) (Figures 3-1 and 3-2).

The velocity of ultrasound is affected by the density and elasticity of the material it traverses; as a result, ultrasound travels at varying velocities through different tissues. Current commercially available ultrasound machines cannot determine which tissues underlie the transducer and instead assume an average tissue velocity of 1540 m/s in their image reconstruction algorithms. The value is obtained from averaging the velocity in normal soft tissue (Figure 3-3).<sup>1</sup>

#### SAFETY

The American Institute of Ultrasound in Medicine has addressed ultrasound safety and bioeffects, as follows: "No independently confirmed adverse effects caused by exposure from present diagnostic ultrasound instruments have been reported in human patients in the absence of contrast agents." Biological effects (such as localized pulmonary bleeding) have been reported in mammalian systems at diagnostically relevant exposures, but the clinical significance of such effects is not known. Ultrasound should be used by qualified health professionals to provide medical benefit to the patient. Ultrasound exposures during examinations should be as low as reasonably achievable.<sup>2</sup>

#### **INSTRUMENTATION**

A diagnostic ultrasound machine is commonly composed of a transducer (probe) and main body. An electronic transducer is composed of a large number of piezoelectric materials. Ultrasound is produced from piezoelectric material that vibrates in response to the application of electrical energy. Piezoelectric material can be arranged on a plane (linear transducer) or a curved surface (curved transducer). Linear high-frequency transducers are typically used for superficial tissue imaging—for example, appendix, abdominal wall, and scrotum. Low-frequency curved array transducers are typically used for abdominal and obstetric/gynecologic imaging, in which the curvature of the array and penetration depth facilitate large field of view imaging.

When ultrasound travels through tissues, reflection, refraction, and scatter will occur at acoustic interfaces. The reflected and/or scatted ultrasound waves are detected by the transducer and analyzed. Each echo is displayed at a point in the image that corresponds to the relative position of its origin within the body. The brightness of each point in the image is related to the strength of the echo. This form of ultrasound imaging is termed *B-mode* (brightness mode) sonography and is often colloquially termed "gray scale" sonography or "conventional" sonography.

#### General Abdominal Ultrasonography

Ultrasonography can be used to visualize solid structures in the abdomen, the abdominal wall, and some gastrointestinal lesions. The vasculature within these organs can be evaluated by color Doppler, power Doppler, or spectral modes. Body markers or anatomic labels are used to illustrate the position of the patients

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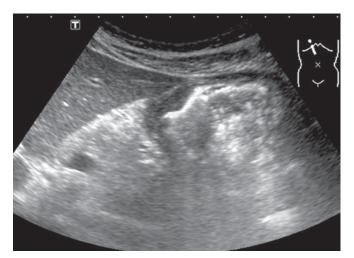
and transducer. A basic glossary of ultrasound terms is listed in Table 3-1.

#### EQUIPMENT

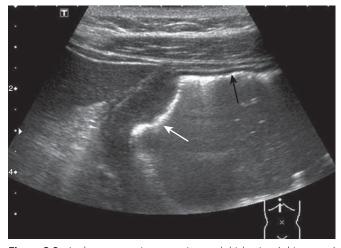
An ultrasound machine capable of real-time imaging should be used to examine the abdominal organs. The equipment should be adjusted to obtain acceptable resolution. For adults, a curved probe with frequencies between 2 and 5 MHz is most commonly used. A linear probe with frequencies between 5 and 7 MHz is most commonly used when the abdominal wall and appendix are examined. Image quality should be optimized while keeping total ultrasound energy exposure as low as reasonably achievable.

#### PREPARATION FOR EXAMINATION

The patient should not eat or drink for 8 hours before the abdominal ultrasound. If fluid is essential to prevent dehydration or take medicine, only water should be given. When the bladder needs to be examined, 400 to 600 mL water should be taken orally 2 hours before examination to ensure there is



**Figure 3-1** Gastric cancer. Gastric mural thickening demonstrated by 3.5-MHz curved probe.



**Figure 3-2** In the same patient, gastric mural thickening (*white arrow*) and normal gastric wall (*black arrow*) were demonstrated with greater spatial resolution using a 7.0-MHz linear probe.

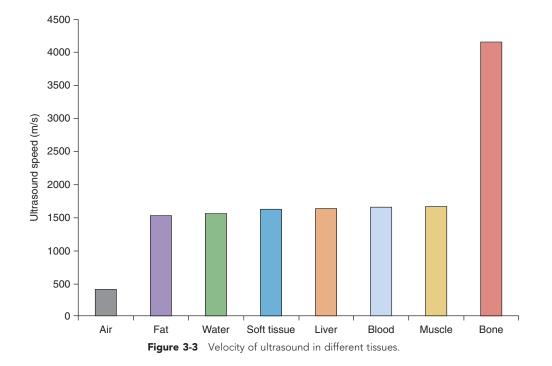


TABLE 3-1	Basic Ultrasound Glossary		
Term		Description	Example
Anech	oic	Without echoes; displayed as black in the image	Normal urine and bile
Нурое	choic	Tissues that create dimmer echoes than adjacent tissues	Cortex of lymph nodes, some tumors
Hypere	echoic	Tissues that create brighter echoes than adjacent tissues	Air, bone, perinephric fat
Acoust	tic shadow	The decreased echogenicity of tissues that lie behind a structure that causes marked attenuation or reflection of the ultrasound waves	Typically deep to solid structures (stones, bone) or air
Acoust	tic window	A tissue or structure that offers little obstruction to the ultrasound waves and can therefore be used as a route to obtain images of a deeper structure	Bladder full of urine, gallbladder full of bile
Cystic		A fluid-filled structure (mass) with thin or thick walls, with or without strong back wall reflections and enhancement of the echoes behind the cyst	Liver, renal cysts common
Solid		Tissue that does not include fluid spaces; will be multiple internal echoes and moderate attenuation of the ultrasound	Solid tumor, liver, muscle

enough urine in the bladder. Emergency ultrasonography can be performed at any time, but the image quality may be affected by air in stomach and bowel.

#### Normal Ultrasound Image

#### LIVER

The normal liver parenchyma appears homogeneous, interrupted by the portal vein, hepatic vein, and their branches. The echogenicity of the liver should be compared with that of the right kidney. The liver can be similar or more echogenic than normal kidney. The hepatic veins, the main portal vein, and the right and left branches of the portal vein should be seen clearly (Figure 3-4).

#### GALLBLADDER AND BILE DUCT

On the longitudinal scan, the gallbladder will appear as an anechoic, pear-shaped structure. It is variable in position, size, and shape, but the normal gallbladder is seldom more than 40 mm wide. The thickness of normal gallbladder wall is no more the 3 mm (Figure 3-5). The intrahepatic bile ducts usually are located above the corresponding portal branches. The common bile duct (CBD) is located anterior the portal vein. The normal diameter of the CBD is less than 6 mm. Ultrasonography has limited capacity to detect small lesions within the distal CBD. Sometimes, tiny stones in the CBD can be detected (Figure 3-6).

#### PANCREAS

The pancreas has approximately the same echogenicity as the adjacent liver and should appear homogeneous. However, pancreatic echogenicity increases with age. The contour of the normal pancreas is smooth. The shape and the size of the pancreas are variable. The diameter of the pancreatic duct should not exceed 2 mm. The tail of pancreas is often difficult to demonstrate, because of gas in the stomach and bowel. If there is no clinical contraindication, it may be helpful to give the patient 300 to 500 mL water to drink when scanning the pancreas (Figure 3-7). The pancreatic tail also occasionally can be demonstrated through the spleen (Figure 3-8).

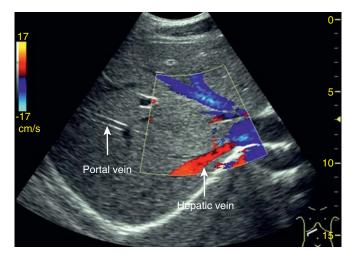


Figure 3-4 Normal liver parenchyma, portal vein, and hepatic vein.

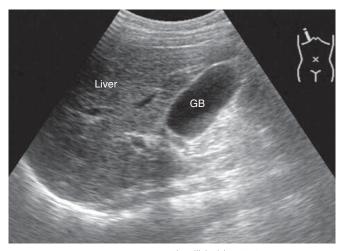
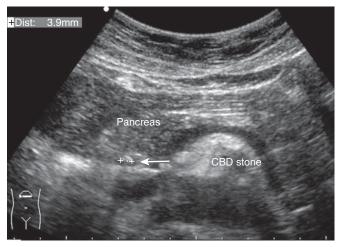


Figure 3-5 Normal gallbladder (GB).



**Figure 3-6** Tiny stone with acoustic shadowing within the intrapancreatic common bile duct (*CBD*).

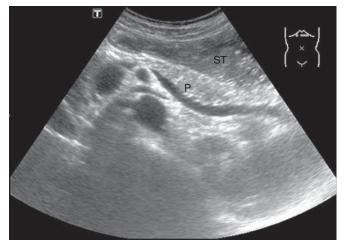
#### SPLEEN

The spleen should show a uniform homogeneous echo pattern. It is slightly less echogenic than the liver. The length of the normal spleen is no more than 12 cm, and the thickness is no more than 4 cm (Figure 3-9).

#### KIDNEY AND ADRENAL GLAND

The renal capsule appears as a bright, smooth, echogenic line around the kidney. The cortex is less echogenic than the liver but more echogenic than the adjacent renal pyramids. The renal pyramids are poorly defined hypoechoic areas in the medulla of the kidney. The central echo complex (the renal sinus) is hyperechoic relative to renal parenchyma. The renal arteries and veins are readily seen at the renal hilus and around the aorta. Like other visceral arteries, the renal artery has high diastolic blood flow (Figures 3-10 and 3-11).

The adrenals are located above and medial to the kidneys. Except in infants, the adrenal glands are not easily visible with ultrasound (Figure 3-12).



**Figure 3-7** Normal body and tail of pancreas were demonstrated after drinking 300 mL water. *P*, Pancreas; *ST*, stomach.

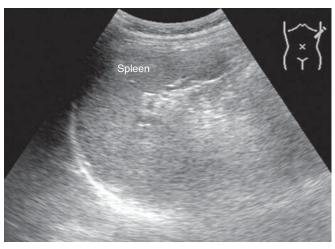
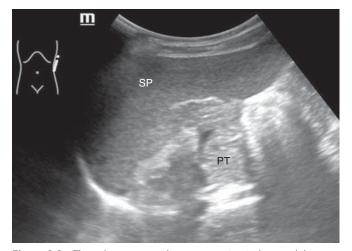


Figure 3-9 Normal spleen.



**Figure 3-8** The spleen was used as an acoustic window, and the pancreatic tail can be demonstrated clearly. *PT*, pancreatic tail; *SP*, spleen.

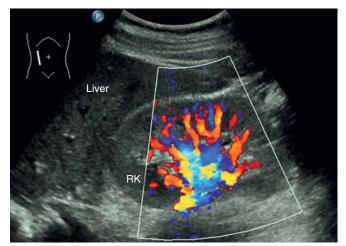


Figure 3-10 Normal right kidney (RK).

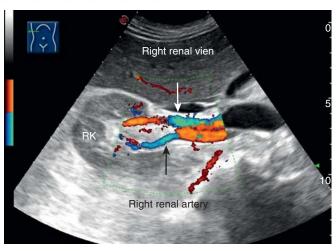
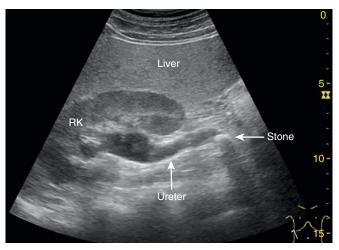
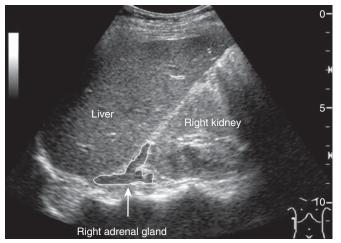


Figure 3-11 Normal right kidney (*RK*), right renal artery and vein.



**Figure 3-13** Right renal pelvis and upper right ureter were distended, a stone with acoustic shadow was demonstrated in the lumen of the right ureter. *RK*, Right kidney.



**Figure 3-12** Enlarged right adrenal gland in a patient with Cushing's syndrome.

#### URETERS, BLADDER AND PROSTATE

The normal ureters are usually not readily visible, but can be demonstrated when distended (Figure 3-13). The bladder should be evaluated while distended with urine, because bladder tumors may not be detected in an empty bladder. The full urinary bladder appears as a large, rounded, anechoic area arising from the pelvis. The thickness of the bladder wall will vary with the degree of distention. When distended, the normal bladder wall is less than 4 mm thick (Figure 3-14).

The prostate can be divided into four glandular zones: the peripheral zone, transitional zone, central zone, and periure-thral glandular area. It is difficult to identify these zones with transabdominal sonography. Transrectal ultrasound can delineate the prostate zonal anatomy and is useful for guiding prostate biopsy (Figure 3-15).

#### SCROTUM

The normal testes are oval, homogeneous, and hyperechoic. Often a small amount of physiologic fluid is present within the scrotum around the testes. The epididymis lies on the inferior

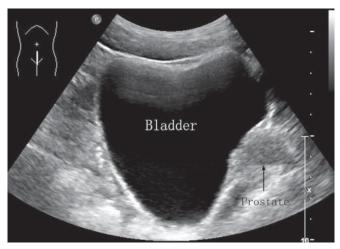
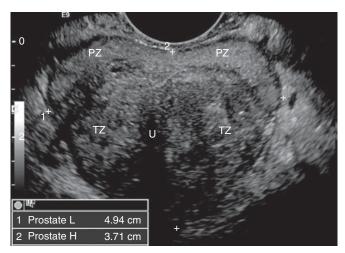


Figure 3-14 Normal full urinary bladder. SAG, Sagittal plane.



**Figure 3-15** Transrectal axial view of benign prostatic hyperplasia. *PZ*, Peripheral zone; *TZ*, transitional zone; *U*, urethra.

aspect of the testis and is more echogenic than the testis. It is subdivided into a head, body, and tail. Doppler ultrasound can demonstrate the blood vessels within the testis, epididymis, and cord (Figure 3-16).

#### DIGESTIVE TRACT

The abdominal part of the esophagus can be detected by ultrasonography, lying inferior to the diaphragm and anterior to the aorta. With transverse scans, the esophagus is seen behind the left lobe of the liver. When empty, the fundus of the stomach will be star-shaped. The gastric body can be demonstrated easily on transverse scanning, just anterior to the pancreas. The layers of gastric wall can be demonstrated by using a 5- to 7-MHz probe with the lumen filled with liquid (Figure 3-17). The ultrasound image of the bowel varies greatly depending on the degree of fullness and content in bowel. If the bowel is full of fluid, the mucosa of the bowel can be demonstrated clearly. Peristalsis can be seen in the small bowel but rarely in the colon. A normal appendix can sometimes be demonstrated by ultrasonography as a tubular structure with a blind end and a diameter less than 8 mm (Figure 3-18).

#### **RETROPERITONEAL GREAT VESSELS**

The aorta may be identified as a pulsating tubular structure. The cross-sectional diameter of the adult aorta varies from approximately 3 cm at the xiphoid to 1 cm at the bifurcation. The celiac trunk and superior mesenteric artery can be demonstrated easily (Figure 3-19). The diameter of the inferior vena cava normally collapses during inspiration and expands during expiration.

#### ABDOMINAL WALL AND PERITONEUM

The normal epidermis is a hyperechoic layer measuring 1 to 4 mm in thickness. The subcutaneous fat layer is relatively hypoechoic and of variable thickness. The muscular layer is

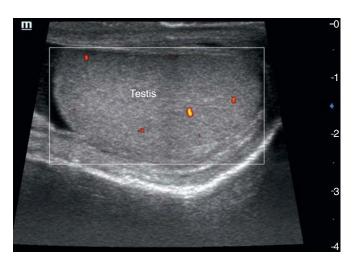
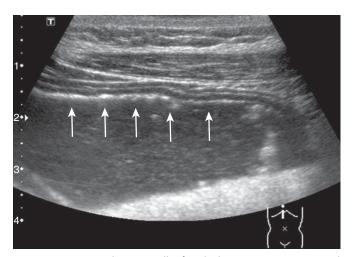


Figure 3-16 Normal testis. An oval, homogeneous, and hyperechoic testis



Figure 3-18 Normal appendix. A diameter 0.36-cm tubular structure with a blind end.



**Figure 3-17** Normal gastric wall. After drinking 300 mL water, normal layers of stomach (*arrows*) were demonstrated with a 7.0-MHz linear probe.

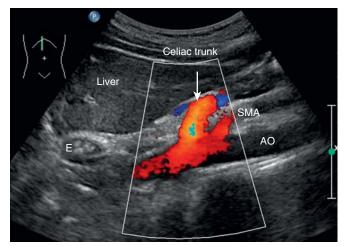


Figure 3-19 Celiac truck, superior mesenteric artery (SMA), and abdominal aorta (AO). *E*, esophagus.

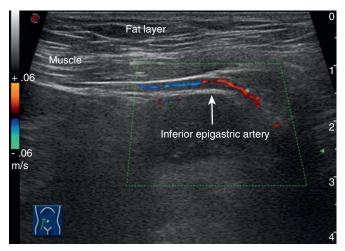


Figure 3-20 Normal abdominal wall. Muscle, fat layer, and inferior epigastric artery.

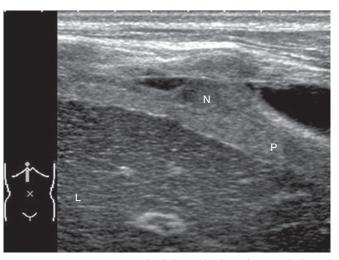


Figure 3-21 In a patient with abdominal tuberculosis, a thickened peritoneum (P) and a small nodule (N) are demonstrated with a linear probe. L, Liver.

usually more echogenic than the subcutaneous fat layer. Individual muscle bundles showing uniform texture and orientation can be demonstrated. Abdominal wall blood vessels and nerves can be demonstrated (Figure 3-20).

The normal peritoneum is very thin and cannot be demonstrated by ultrasonography. The omenta are composed of peritoneal folds and include a double layer of peritoneum, blood vessels, lymphatics, and a variable amount of fat. Normal omentum may be difficult to separate from surrounding fat on sonography. When the peritoneum and the greater omentum become thickened or nodular, they can be evaluated by ultrasonography with high-frequency transducers (Figure 3-21).

## **SUGGEST READINGS**

Rumack CM, Wilson SR, Charboneau JW, et al: Diagnostic ultrasound, ed 3, St. Louis, 2005, Mosby. World Health Organization: *Manual of diagnostic ultrasound*, ed 2, Geneva, 2011, World Health Organization.

#### REFERENCES

- 1. Sahani D, Samir A: *Abdominal imaging*, St. Louis, 2011, Saunders.
- 2. American College of Radiology, Society of Radiologists in Ultrasound: *Prudent Use and Clinical*

*Safety*. <http://www.aium.org/officialstatements/ 34>. 4

# Tissue Harmonic Imaging and Doppler Ultrasound Imaging

ARASH ANVARI | XIAOZHOU MA | SOMESH LALA | BIJAL JANKHARIA | VISHAKHA MAZUMDAR

# **Tissue Harmonic Imaging**

# **TECHNICAL ASPECTS**

*Fundamental frequency* is the original frequency of the acoustic beam emitted from the transducer. *Harmonic* wave generation is an acoustic phenomenon. Harmonic waves are integer multiples of the fundamental frequency.

The second harmonic (twice the fundamental frequency) is currently used for tissue harmonic imaging (THI). With THI, the fundamental frequency is eliminated with image processing techniques. THI advantages include improved signal-to-noise ratio and artifact reduction.<sup>1,2</sup>

# **CLINICAL APPLICATIONS**

THI improves image quality and conspicuity, and has been shown to be useful in multiple clinical scenarios, including (1) obesity, (2) hollow structures (e.g., cysts, gallbladder, urinary bladder) (Figure 4-1), and (3) the deep-seated major vessels (inferior vena cava [IVC] and abdominal aorta) (Figure 4-2).

# **Doppler Ultrasound Imaging**

Doppler ultrasonography is a noninvasive technique that provides information about the condition of blood vessels and blood flow direction. It also measures flow velocity and can be used to evaluate the vascularity of mass lesions. Color and pulsed-wave Doppler imaging provide complementary information, including spatial orientation and a time velocity spectrum, respectively.<sup>3</sup>

#### **TECHNICAL ASPECTS**

Doppler examination requires five technical parameters (5 Ps), as follows:

- *Patient preparation:* Fasting is required for a Doppler examination of the abdomen.
- *Probes:* Commonly used probes are the (1) curvilineararray probes (low frequency, 3 to 5 MHz), (2) phasedarray probes (low frequency, 2 MHz), and (3) linear-array probes (high frequency, 4 to 10 MHz).<sup>4</sup>
- *Person:* The sonographer should have a considerable amount of expertise to perform a Doppler examination such as understanding of the normal anatomy, pathophysiology, and signature patterns of abdominal vessels.
- *Picture quality (machine):* To obtain good picture quality, the radiologist should consider the following operational parameters: (1) an appropriate anatomic window, (2)

depth of field, (3) frame rate, (4) flow sensitivity with adjusted gain settings, (5) image vessel of interest at a Doppler angle of 30 to 60 degrees, and (6) low wall filter settings (if these are high, significant velocity information can be lost). The recorded color flow should occupy the full anteroposterior diameter or cross-sectional area of the vessel without color flow aliasing and noise in the surrounding tissues.

• *Positioning:* The various positions required for imaging every individual vessel.

# PROS AND CONS OF DOPPLER IMAGING

#### Pros

- Noninvasive
- Readily available and cost-effective
- Portability: Can be done by the bedside in sick or debilitated patients
- Differentiating vascular and nonvascular structures (e.g., porta hepatis) (Figure 4-3)
- Provides information about the patency of blood vessels, direction of flow turbulence, phasicity, jet, impedance, and so on
- Quantification of stenosis and direct measurement of flow lumen reduction
- Tissue characterization of tumors

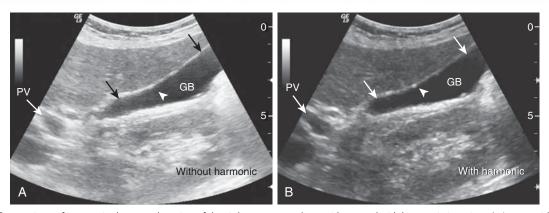
#### Cons

- Operator dependency.
- Doppler imaging is technically difficult to perform in obese patients and in those with overlying bowel gas or a distended abdomen, especially when desiring visualization of the mesenteric vessels, the portosplenic confluence, or renal artery origin; performing portosystemic collateral mapping; evaluating a shunt anastomosis; and so on.
- Good spectral analysis cannot be achieved in patients who cannot hold their breath (e.g., acutely ill patients).
- Graft surveillance at the level of the distal abdominal aorta and iliac arteries is difficult.
- Abdominal aortic calcifications can be an obstacle in visualization of renal artery origin.

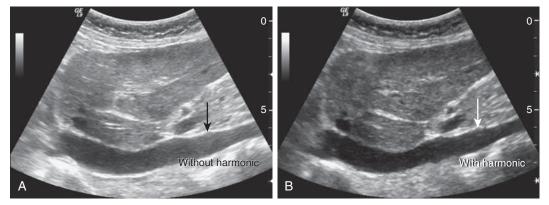
# NORMAL ANATOMY OF ABDOMINAL VESSELS

The normal appearance and signature pattern of abdominal vessels—the portal vein (Figure 4-4), hepatic vessels, mesenteric vessels (Figures 4-5, 4-6, and 4-7), renal vessels (Figure 4-8), abdominal aorta (Figure 4-9), and IVC—are summarized in

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**Figure 4-1** Comparison of images in the same location of the right upper quadrant without and with harmonic imaging. A, Image without harmonic imaging: the fundus and neck areas (*arrows*) of the gallbladder (*GB*) and intraportal venous area (*PV, arrow*) appear echogenic and cloudy. **B**, With harmonic technique, the figure shows a clear GB and portal venous structure. In addition, the tiny calcification on the anterior wall of the GB (*arrow-head*) is well shown on the harmonic image in **B** but invisible in the blurred image in **A**.



**Figure 4-2** Comparison of image conspicuity without/with harmonic imaging in the sagittal plane of the left liver and the long axis of the inferior vena cava (IVC). The *arrows* point to the intra-IVC area, which is obviously cloudy and blurring in the nonharmonic image (A) compared with the harmonic image (B).

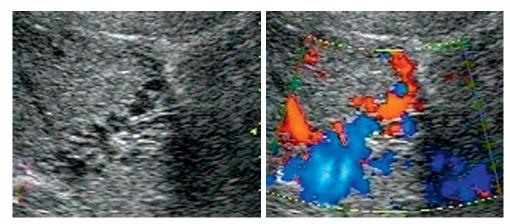
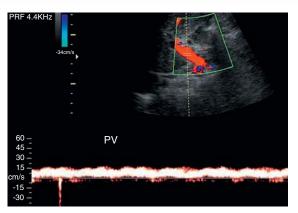
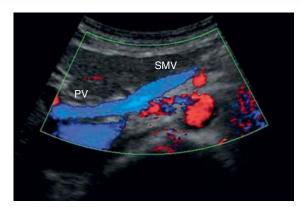


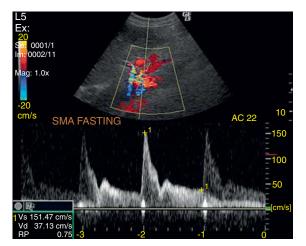
Figure 4-3 Transverse Doppler imaging centered at midclavicular line reveals multiple collateral vessels in the porta hepatis that mimic dilated intrahepatic biliary radicles.



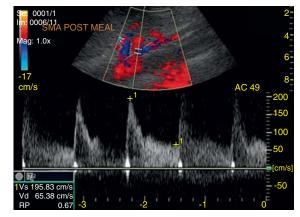
**Figure 4-4** Normal portal vein (*PV*). Pulsed Doppler image of the portal vein shows normal undulating signature pattern with phasic flow. Peak systolic velocity = 15 cm/s.



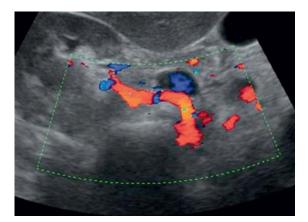
**Figure 4-5** Superior mesenteric vein (*SMV*). Long-axis view shows a normal SMV becoming confluent with the portal vein (*PV*).



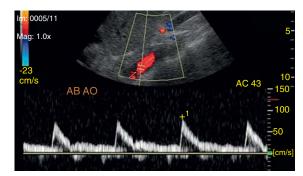
**Figure 4-6** Superior mesenteric artery (*SMA*). Long-axis view shows normal high-resistance waveform patterns of artery in fasting. Peak systolic velocity = 151 cm/s; resistive index = 0.75.



**Figure 4-7** Superior mesenteric artery (*SMA*). Postprandial Doppler image reveals low-resistance waveform pattern with increase in peak systolic velocity. Resistive index = 0.6.



**Figure 4-8** Normal right renal artery. Right coronal oblique view with anterolateral transverse approach shows the course of the renal artery from the hilum to the origin.



**Figure 4-9** Abdominal aorta (*AB AO*). Long-axis view of the proximal abdominal aorta shows high-resistance flow with brief flow reversal. Doppler angle = 43 degrees.

TABLE 4-1         Normal Appearance and	Signature Patterns of Abdominal Vessels	
Vessel	Identification	Normal Signature Pattern
Portal vein: normal caliber = 13 mm (quiet respiration)	Anechoic structure, which runs in transverse plane and converges on the porta hepatis Surrounded by a sheath of echogenic fibrous tissue	Undulating continuous waveform pattern with subtle phasic variation Hepatopetal flow (toward the liver)
Hepatic vein: normal caliber = 3 mm (measured 2 cm from inferior vena cava)	Longitudinally oriented sonolucent structures within liver parenchyma Best visualized with transverse subxiphoid approach to see the three main trunks with the inferior vena cava	Triphasic pulsatile waveform pattern with hepatofugal flow Naked margins
Hepatic artery: normal velocity = 30-60 cm/s	Vascular structure anterior to portal vein	Low-resistance flow with spectral broadening
Inferior vena cava: normal caliber = 2.5 cm	Anechoic structure in the midline to the right of the aorta and anterior to the spine Upper part best visualized using liver as an acoustic window	Pulsatile flow near the heart: "sawtooth pattern" Phasic flow distally
Abdominal aorta: Normal caliber = 2.3 cm (men), 1.9 cm (women)	Hypoechoic tubular pulsatile structure with echogenic walls best seen by longitudinal midline approach	High-resistance waveform pattern with a brief period of reversed flow (see Figure 4-9)
Mesenteric vessels: normal caliber <10 mm	Superior mesenteric artery is surrounded by a triangular mantle of fat. It is to the right of the superior mesenteric vein, which runs parallel to the superior mesenteric artery (see Figures 4-6 and 4-7)	Superior mesenteric artery fasting view: High-resistance waveform pattern with sharp systolic peaks with absent late diastolic flow Postprandial shows low-resistance waveform pattern.
Celiac artery	Best visualized in transverse plane, in which the T-shaped bifurcation of vessel into hepatic and splenic artery is characteristic	Low-resistance type of waveform
Renal artery and vein	Origin of artery is slightly caudad to superior mesenteric artery and best seen by transverse midline approach. Left renal vein is seen between superior mesenteric artery and aorta. Right renal vein can be traced from inferior vena cava	Artery: Low-resistance flow with broad systolic waveform and forward flow during diastole Vein: Phasic with velocity varying with respiration and cardiac activity

(Table 4-1).<sup>5</sup> Portosystemic collateral vessels (Figures 4-10) and splenorenal collateral vessels (Figure 4-11) are explained in detail in Table 4-2.<sup>6,7</sup>

# **Clinical Applications**

### PORTAL HYPERTENSION

#### **Common Causes**

- *Prehepatic:* Portal vein thrombosis (idiopathic, hypercoagulable states, pancreatitis), portal vein compression (tumor, trauma, lymphadenopathy)
- Intrahepatic: Cirrhosis
- *Posthepatic:* Budd-Chiari syndrome (idiopathic, hypercoagulable states, trauma, web, and tumor).

#### **Diagnostic Criteria**

# Gray-Scale Imaging Findings

- Portal vein dilatation is greater than 13 mm.
- Superior mesenteric vein and splenic vein are greater than 10 mm.
- Lack of caliber variation in splanchnic veins is less than 20%.
- In thrombosis, there may be partial visualization or failure to visualize the portal vein (chronic) or echogenic material within distended lumen (acute) (Figures 4-12 and 4-13).
   Doppler Imaging Findings

Portal Vein

- Thrombosis: Absence of flow; malignant thrombus causes pulsatile flow, whereas bland thrombus does not (Figure 4-14).
- Continuous monophasic flow is seen.
- Reduction in velocity is from 7 to 12 cm/s.
- Abnormal hepatofugal flow may be the only sign (Figure 4-15).<sup>7,8</sup>
- Gallbladder varices may be associated with portal vein thrombosis (spontaneous portosystemic shunt) (Figure 4-16).
- Chronic: Echogenic/nonvisualized portal vein occurs with cavernoma formation (Figure 4-17).<sup>7</sup>
- Aneurysmal dilatation of the portal vein occurs (Figure 4-18).

Hepatic Artery

- The hepatic artery is dilated with increased resistance (resistive index > 0.78).
- Hepatic Vein (Budd-Chiari Syndrome)
- Thrombus formation occurs (Figure 4-19).
- The vein cannot be visualized.
- Stenosis and size reduction are noted as less than 3 mm (Figure 4-20).
- Decreased, absent, or reversed flow occurs in hepatic vein.
- Communicating intrahepatic venous collateral vessels can be seen.

Text continued on p. 32

# TABLE Portosystemic Collateral Vessels: Diagnostic Criteria

Site	Portosystemic
Gastroesophageal junction. Normal coronary vein diameter <6 mm	Between coronary/short gastric veins and systemic esophageal veins
Paraumblical vein (falciform ligament) Normal = 2 mm hepatopedal flow	Between left portal vein and systemic epigastric veins near umbilicus
Gastroepiploic (see Figure 4-6)	Between gastroepiploic and esophageal/ paraesophageal veins
Splenorenal and gastrorenal (splenic and renal hilum)	Between splenic, coronary, short gastric, and left adrenal or renal veins
Intestinal	Veins of ascending/descending colon, duodenum, pancreas, liver anastomosis with renal, phrenic and lumbar veins (systemic tributaries)
Hemorrhoidal (perianal region)	Superior rectal vein anastomoses with systemic middle and inferior rectal veins

#### Appearance

- Coronary veins >7 mm are abnormal. Prominent cephalad-directed vessel arising from portal vein opposite superior mesenteric vein
- Solitary vein originating from left portal vein courses inferiorly through falciform ligament and anterior abdominal wall to umbilicus, demonstrating hepatofugal flow
- Cephalad directed vessel along the inferior border of the left lobe
- Splenorenal (see Figure 4-11). Tortuous, inferiorly directed vessels between spleen and upper pole of left kidney

Collateral pathways identification on ultrasonography depends on the amount of air in the bowel at the time of study

Rectal/pararectal varices can be detected with transvaginal or transrectal ultrasonography, cannot be visualized on transabdominal ultrasonography

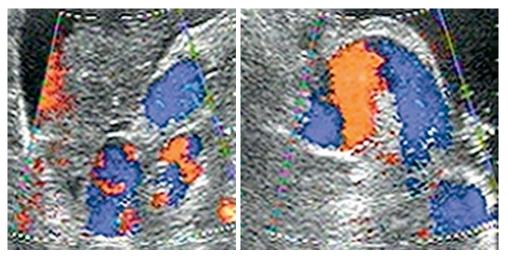


Figure 4-10 Portosystemic collateral vessels. Long-axis view shows large, tortuous, left gastric vein collateral vessels along the inferior border of the left lobe of the liver.

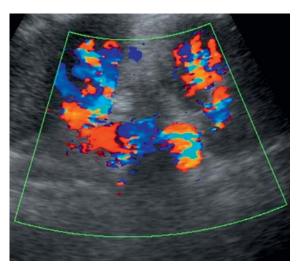


Figure 4-11 Splenorenal collateral vessels. Transverse image of the left kidney shows tortuous collateral vessels between the splenic and renal hila.

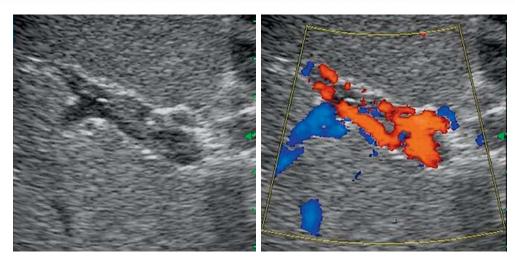


Figure 4-12 Partial portal vein occlusion. Transverse imaging of the portal vein shows echogenic thrombus within the vein with incomplete filling on color flow Doppler imaging.

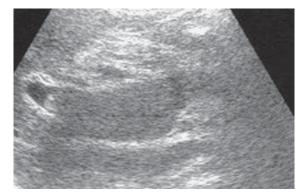


Figure 4-13 Acute portal vein occlusion. Transverse image of the intrahepatic portal vein shows distended portal vein with thrombus within.

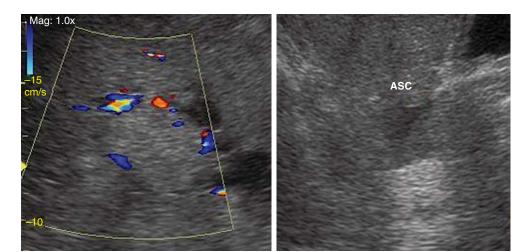


Figure 4-14 Tumor thrombus from renal mass. Transverse image of the liver reveals echogenic material within the portal vein with peripheral flow along its walls. ASC, Ascites.

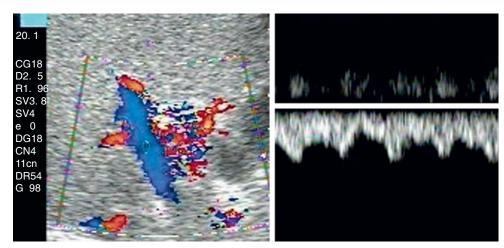


Figure 4-15 Cirrhosis. Long-axis view of the liver shows hepatofugal flow (away from the liver) in the portal vein. Note that the signature pattern is below the baseline.

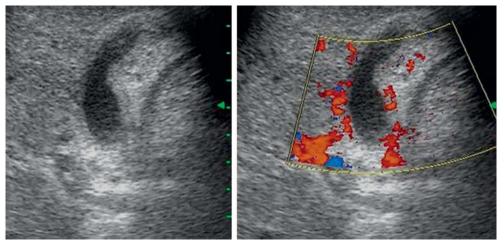


Figure 4-16 Gallbladder varices. Transverse imaging of the liver shows hepatopetal collateral vessels involving the gallbladder wall.

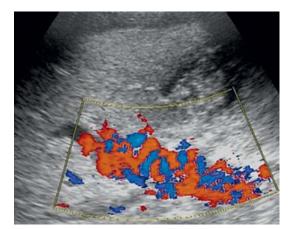


Figure 4-17 Chronic portal vein thrombosis. Serpiginous tortuous collaterals along the portopancreatic axis suggestive of cavernoma formation.

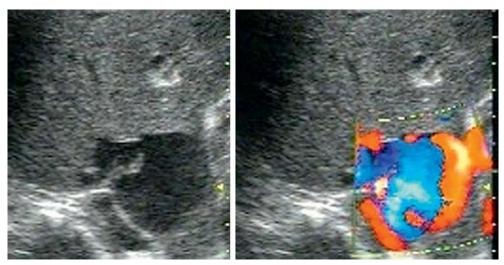


Figure 4-18 Portal vein aneurysm. Long-axis view of the liver shows aneurysmal dilatation of the portal vein with to-and-fro flow within.

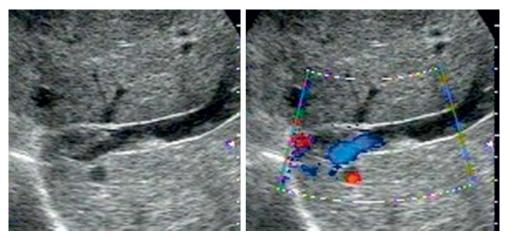


Figure 4-19 Budd-Chiari syndrome. Right coronal oblique view shows echogenic thrombus partially obstructing the right hepatic vein.

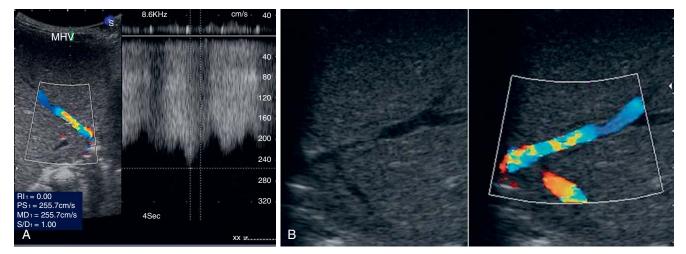


Figure 4-20 Budd-Chiari syndrome. A and B, Gray-scale and color Doppler imaging. Transverse subxiphoid approach shows focal narrowing and significant increase in peak systolic velocity in middle hepatic vein (MHV).

The reader is referred to Table 4-3 for the specifics of diagnostic imaging for portal hypertension.

# Transjugular Intrahepatic Portosystemic Shunt

Transjugular intrahepatic portosystemic shunt (TIPS) refers to portal decompression through a percutaneously established shunt between the hepatic and portal veins with an expandable metallic stent (Figure 4-21).<sup>9</sup> It is done for esophageal and gastric variceal hemorrhage or refractory ascites in advanced liver disease with portal hypertension.

TABLE 4-3	I litracound imaging of Portal Hyportonsion				
		Prehepatic	Hepatic	Posthepatic	
Portal vein flow direction		Hepatopedal	Hepatofugal	Hepatofugal	
Portal vein caliber (>13 mm)		Increased	Increased	Normal or increased	
Liver t	exture/size	Normal	Altered	Altered	
	ite lobe ertrophy	_	+	+	
	ic wedge ssure	Normal	High	High	
Secondary signs of portal hypertension (splenomegaly, ascites, portosystemic collateral vessels)		+	+	+	

**Doppler Imaging Findings.** Post-TIPS spectral analysis should show high-velocity turbulent flow (90 to 110 cm/s) and uniform flow at the portal and IVC ends. Abnormal findings include generalized decrease in shunt velocity to less than 60 cm/s, localized increase in shunt velocity, irregular filling defects, and absence of flow in the shunt.

### Liver Transplantation

Doppler imaging plays an important role in assessing vascular complications of liver transplants, which is the most frequent cause of graft loss. Most of the complications involve the IVC, portal vein, and hepatic artery (Figure 4-22). The complications are commonly seen as a result of discrepancy in vessel caliber between the donor and the recipient, faulty surgical technique, and hypercoagulable states. The diagnostic criteria are listed in Table 4-4.

#### Mesenteric Ischemia

Mesenteric ischemia may be classified as occlusive or nonocclusive. Occlusion accounts for 75% of acute intestinal ischemia (Figure 4-23). Mesenteric artery embolus and plaque secondary to rheumatic heart disease or atherosclerosis and venous occlusion resulting from infection or hypercoagulability states are the common causes (Figure 4-24). The diagnostic criteria are listed in Table 4-5.<sup>10-13</sup>

# **Renal Artery Stenosis**

Atherosclerosis accounts for 75% of the causes of renal artery stenosis, whereas fibromuscular dysplasia accounts for 15%. Renal artery stenosis is hemodynamically significant when the luminal narrowing is 50% to 60% (Figure 4-25). The diagnostic criteria are listed in Box 4-1.<sup>14-19</sup>

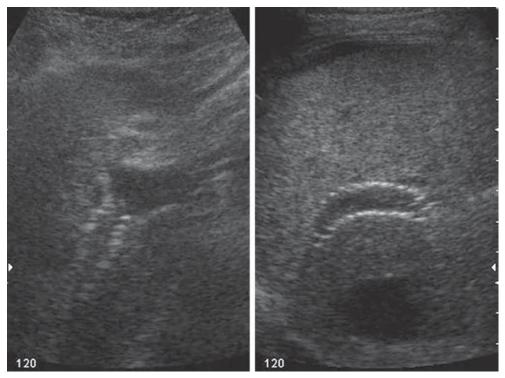
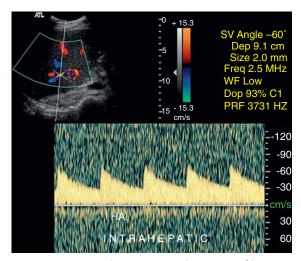
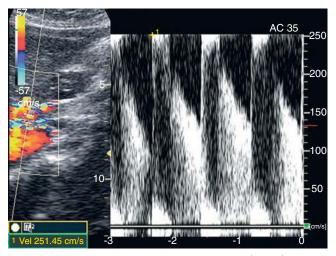


Figure 4-21 Transjugular intrahepatic portosystemic shunt (TIPS). Right coronal view of liver shows a TIPS between the portal and hepatic veins.



**Figure 4-22** Liver transplant. Post-transplant image of hepatic artery (*HA*) shows a normal low-resistance spectral waveform pattern with a renal resistive index of 0.57.



**Figure 4-23** Superior mesenteric artery stenosis. Atherosclerotic narrowing of the artery reveals significant increase in peak systolic velocity (251 cm/s) at its origin suggestive of moderate stenosis.

TABLE	Vascular Complications of Liver Transplant:
4-4	Diagnostic Criteria

Complication	Diagnostic Criteria
Anastomotic narrowing of portal vein/inferior vena cava	Thinned-out portal vein with poststenotic dilatation
Thrombus/stenosis in portal vein	Filling defect in portal vein Focal narrowing at anastomotic site with increase in velocity
Thrombus/stenosis in inferior vena cava	Focal increase in velocity at stenotic/anastomotic site Dilatation of inferior vena cava proximal to stenosis Damped waveform with absent periodicity in subanastomotic inferior vena cava
Hepatic artery stenosis	Increase in peak systolic velocity >200-300 cm/s and poststenotic turbulence Intrahepatic tardus parvus distal to stenosis
Hepatic artery thrombosis	Absence of flow

TABLE	Illuse ound Imparing of Mecontoxic lock onio
4.5	Ultrasound Imaging of Mesenteric Ischemia

Acute Ischemia	Chronic Ischemia
Gray-scale findings: Bowel wall thickening (normal, <2 mm) <sup>11</sup> Doppler findings: Arterial: Mesenteric artery not always well visualized, absence of arterial flow in the wall of the ischemic colon <sup>12</sup> Venous: Dilated vein with echogenic thrombus and no flow within (see Figure 4-24) <sup>13</sup>	Doppler findings: Stenosis (≥70%); superior mesenteric artery shows increase in peak systolic velocity >275 cm/s and end-diastolic velocity >45 cm/s with poststenotic turbulence (see Figure 4-23). <sup>14</sup> Celiac artery shows increase in peak systemic velocity >200 cm/s and end-diastolic velocity >55 cm/s. Low-resistance pattern in fasting is diagnostic of mesenteric ischemia.

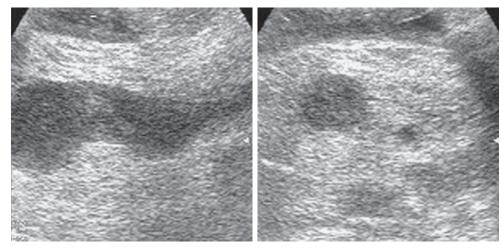
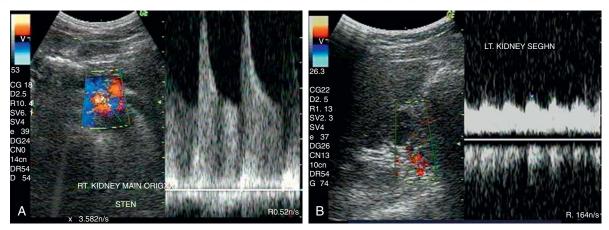


Figure 4-24 Superior mesenteric vein thrombus. Transverse and long-axis epigastric views show distended vein with thrombus within.



**Figure 4-25** Renal artery stenosis. A and B, Color Doppler image and spectral analysis at the level of right renal artery origin show significant increase in peak systolic velocity (251 cm/s) with poststenotic turbulence in the segmental artery.

### BOX 4-1 ULTRASOUND IMAGING OF RENAL ARTERY STENOSIS

#### DIRECT SIGNS

- Peak systolic velocity greater than 180 to 200 cm/s with poststenotic turbulence: Significant stenosis (see Figure 4-25)<sup>16</sup>
- Renal aortic ratio greater than 3.5
- No flow detected: Arterial occlusion

#### **INDIRECT SIGNS**

- Dampened appearance: Tardus parvus pulse
- Loss of early systolic peak
- Acceleration time >80 ms (0.08 s) (see Figure 4-25, B)<sup>17</sup>
- In mild stenosis <50% intrarenal Doppler is normal<sup>18</sup>
- Difference in renal resistive index between normal and abnormal kidney

**Renal Vein Thrombosis.** The common causes of renal vein thrombosis are dehydration (in neonates) and low flow states, trauma, and tumor (in adults). The thrombotic process begins in the small intrarenal veins, reducing venous flow. In the acute stage, hemorrhagic renal infarction occurs from ruptured vessels and capillaries. Formation of collateral vessels begins at 24 hours and peaks 2 weeks after onset of occlusion. The diagnostic criteria are listed in Box 4-2.

#### Renal Parenchymal Disease

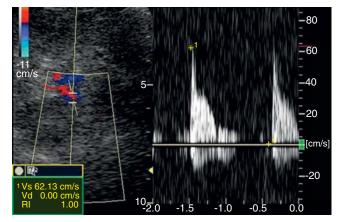
Flow resistance within the renal parenchyma may be increased by a variety of acute and chronic parenchymal disorders (Figure 4-26).<sup>20</sup> The diagnostic criteria are listed in Box 4-3.<sup>21</sup>

### Renal Transplantation

Baseline ultrasound and Doppler imaging are mandatory 2 days after renal transplantation surgery. Doppler imaging plays an important role in assessing transplant-related complications. The normal renal resistive index in the parenchyma should not exceed 0.7 (Figure 4-27).

## **Parenchymal Complications**

• Acute tubular necrosis: On gray-scale imaging, there is increased cortical echogenicity. On Doppler imaging,



**Figure 4-26** Renal parenchymal disease. Spectral analysis of renal artery at the hilum reveals high-resistance waveform pattern with absent end-diastolic flow. Resistive index = 1.00.

#### BOX 4-2 ULTRASOUND IMAGING OF RENAL VEIN THROMBOSIS

#### GRAY SCALE

- Enlarged kidney with focal or generalized areas of increased echogenicity
- Loss of corticomedullary differentiation
- Thrombus within distended renal vein/inferior vena cava

#### DOPPLER

- Main renal vein not traceable into inferior vena cava
- Steady, less-pulsatile venous flow compared with contralateral renal vein
- Renal resistive index greater than 0.7 or reversed end-diastolic arterial flow

there is an increase in the renal resistive index to more than 0.7. Renal biopsy is required to confirm the diagnosis.

• Acute interstitial rejection: This occurs secondary to edema with lymphocytic infiltration. In vascular rejection, proliferative endovasculitis and thrombosis occur.

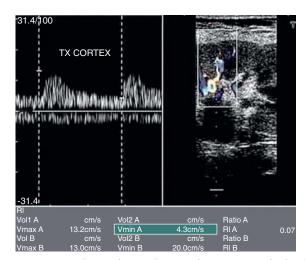
#### BOX 4-3 ULTRASOUND IMAGING OF RENAL PARENCHYMAL DISEASE

#### **GRAY SCALE**

- Hyperechogenicity with or without loss of corticomedullary differentiation
- Acute: Enlarged/normal kidney
- Chronic: Small shrunken kidney

#### DOPPLER

- Acute: Increase in renal resistive index greater than 0.7
- Chronic: Increased renal resistive index with or without absent end-diastolic Doppler (see Figure 4-26)



**Figure 4-27** Renal transplant. Color Doppler imaging at the level of the cortex using a high-frequency probe (7.5 to 10 MHz) shows normal low-resistance waveform pattern. Resistive index = 0.67. *TX*, Transplant kidney cortex.

 Diagnostic criteria: On gray-scale imaging, increased size and echogenicity of the graft with prominent pyramids are seen. On Doppler imaging, a renal resistive index greater than 0.9 is said to have a 100% positive predictive value.<sup>22</sup>

#### **Vascular Complications**

- Allograft renal artery stenosis occurs at the allograft artery origin (short segment), which is almost always the result of a surgical complication. A later complication (long segment stenosis) commonly results from intimal hyperplasia or scarring. The findings are similar to those of renal artery stenosis.<sup>23</sup>
- Vascular occlusion (rare, arterial and venous) occurs as a result of rejection or faulty surgical technique. The findings are similar to those of renal arterial occlusion and renal vein thrombosis, respectively.
- Arteriovenous fistula occurs most commonly as a result of biopsy trauma. There is a high-velocity, low-resistance flow in the feeding artery, a pulsatile "arterialized waveform" in the draining vein, and exaggerated focal color around the lesion, called the *visible bruit*.
- Pseudoaneurysm is commonly seen as a result of biopsy, mycotic infection, or anastomotic leakage. On gray-scale

#### BOX 4-4 ULTRASOUND IMAGING OF THE INFERIOR VENA CAVA

#### **GRAY SCALE**

- Distention of inferior vena cava
- Echogenic material within the lumen

#### DOPPLER

- Absence of flow
- Loss of triphasic waveform pattern
- Flow reversal in distal segment secondary to collateralization



Figure 4-28 Longitudinal midline color flow image shows a large abdominal aortic aneurysm (A) with peripheral thrombus.

imaging, it can resemble a cyst, but on Doppler imaging there is a to-and-fro waveform with a high-velocity jet at the aneurysm neck.

### Abdominal Aorta

**Aneurysm.** The common causes of aortic aneurysm are atherosclerosis, trauma, infection, and hypertension. Aortic aneurysms can be associated with visceral, iliac, and femoral aneurysms and stenosis (Figures 4-28 to 4-29). On ultrasonography, there is focal widening of the aorta more than 3 cm. Analysis of the aneurysm should include its dimension, shape, location, and extent and documentation of thrombus and involvement of any branches.

**Dissection.** The common causes of aortic dissection are hypertension, Marfan's syndrome, and Ehlers-Danlos syndrome. Usually, dissection begins in the thorax; less than 5% occur in the abdomen. An intimal defect results in separation of the intima and adventitia by blood flow having gained access to the media of the aortic wall, splitting it into two.

On gray-scale imaging, there is a thin echogenic membrane (intimal flap) "fluttering" in the lumen. On color Doppler imaging, blood flow is seen in both true and false channels, with higher velocity in the true lumen and retrograde flow being common in the false lumen (Figure 4-30).

# Inferior Vena Cava

The common causes of the IVC obstruction are neoplastic, idiopathic, thrombotic extension from femoroiliac veins and IVC filters, congenital webs, and extrinsic compression. The diagnostic criteria are listed in Box 4-4.<sup>24</sup>

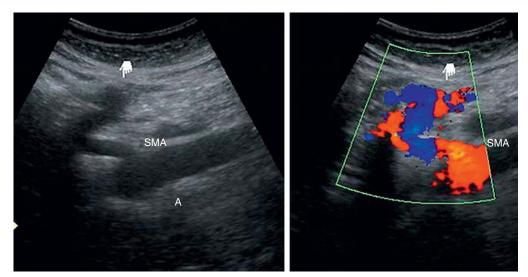


Figure 4-29 Superior mesenteric artery (SMA) aneurysm. Transverse midline imaging shows an aneurysm (A) in the distal artery with turbulent flow within on color Doppler imaging.

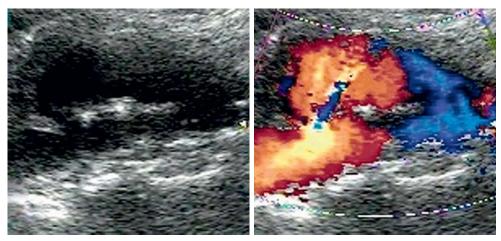


Figure 4-30 Longitudinal midline gray scale and color Doppler imaging show an abdominal dissection with an intimal flap and flow within true and false lumens.

# Summary

Although most abdominal vessels have a common origin, they have different signature patterns on Doppler ultrasound imaging. It is important to understand normal and abnormal flow patterns and know the importance and limitations of Doppler imaging to arrive at a definitive diagnosis.

# **Key Points**

- Harmonic ultrasound imaging reduces image artifacts.
- Doppler imaging is useful in portal hypertension, chronic mesenteric ischemia, and renal transplants.
- There are technical limitations in performance of the examination owing to respiratory variation, obesity, and poor patient preparation.

# **SUGGESTED READINGS**

Foley DW, Erickson SJ: Color Doppler flow imaging. AJR Am J Roentgenol 156:3–13, 1991. Hoskins P, Martin K, Thrush A, editors: *Diagnostic ultrasound: physics and equipment*, ed 2, Cambridge, 2010, Cambridge University Press. Ponziak M, Zagzebski J, Scanlan KA: Spectral and color Doppler artifacts. *Radiographics* 12:35–44, 1992.

## REFERENCES

- Anvari A, Forsberg F, Samir AE: A primer on the physical principles of tissue harmonic imaging. *Radiographics* 35(7):1955–1964, 2015. doi: 10.1148/rg.2015140338.
- Ma Q, Ma Y, Gong X, et al: Improvement of tissue harmonic imaging using the pulseinversion technique. Ultrasound Med Biol 31: 889–894, 2005.
- Scoutt LM, Zawin ML, Taylor KJW, et al: clinical applications. *Radiology* 174:309–319, 1990.
- Taylor KJW, Burns PN, Woodcock JP, et al: Blood flow in deep abdominal and pelvic vessels: ultrasonic pulsed-Doppler analysis. *Radiology* 154:487–493, 1985.
- Kruskal JB, Newman PA, Sammons L: Optimizing Doppler in color flow US: application to hepatic sonography. *Radiographics* 24:657–675, 2004.
- Rumack CM, Wilson SR, Charboneau JW, et al: Diagnostic ultrasound, ed 3, St. Louis, 2004, Mosby.
- 7. Zwiebel WJ: *Introduction to vascular ultrasonography*, ed 4, Philadelphia, 2000, WB Saunders.
- Wachsberg R, Bharamipur P, Sofocleous C: Hepatofugal flow in portal venous system: pathophysiology, imaging findings, and diagnostic pitfalls. *Radiographics* 22:123–140, 2002.
- 9. De Gaetano AM, Lafortune M, Patriquin H, et al: Cavernous transformation of the portal vein: pattern of intrahepatic and splanchnic collateral circulation detected with Doppler sonography. *AJR Am J Roentgenol* 165:1151–1155, 1995.

- Liewer M, Hertzberg B, Heneghon J, et al: Transjugular intrahepatic portosystemic shunts (TIPS): effects of respiratory state and patient position on the measurement of Doppler velocities. *AJR Am J Roentgenol* 175:149–152, 2000.
- Dietrich CF, Jedrzejezyk M, Ignee A: Sonographic assessment of splanchnic arteries and the bowel wall. *Eur J Radiol* 64:202–212, 2007.
- Danse EM, Van Beers BE, Jamart J, et al: Prognosis of ischemic colitis: comparison of color Doppler sonography with early clinical and laboratory findings. *AJR Am J Roentgenol* 175:1151–1154, 2000.
- Amrapurkar DN, Patel ND, Jatania J: Primary mesenteric venous thrombosis: a study from western India. *Indian J Gastroenterol* 26:113– 117, 2007.
- Lim HK, Lee WJ, Kim SH: Splanchnic artery stenosis or occlusion: diagnosis at Doppler US. *Radiology* 211:405–410, 1999.
- Soulez G, Oliva VL, Turpin S, et al: Imaging of renovascular hypertension: respective values of renal scintigraphy, renal Doppler US, and MR angiography. *Radiographics* 20:1355–1368, 2000.
- House MK, Dowling RJ, King P, et al: Using Doppler sonography to reveal renal artery stenosis: an evaluation of optimal imaging parameters. *AJR Am J Roentgenol* 173:761–765, 1999.
- Ripolles T, Aliaga R, Morote V, et al: Utility of intrarenal Doppler ultrasound in the diagnosis of renal artery stenosis. *Eur J Radiol* 40:54–63, 2001.

- de Cobelli F, Venturini M, Vanzulli A, et al: Renal arterial stenosis: prospective comparison of color Doppler US and breath-hold, threedimensional dynamic, gadolinium-enhanced MR angiography. *Radiology* 214:373–380, 2000.
- Leiner T, De Haan MW, Nelemans PJ, et al: Contemporary imaging techniques for the diagnosis of renal artery stenosis. *Eur Radiol* 15:2219– 2229, 2005.
- Dwivedi US, Bishoyi SC, Shukla RC, et al: Renal resistive index: differentiation of obstructive from non-obstructive hydronephrosis. *Indian J Urol* 14:17–21, 1998.
- Buturović-Ponikvar J, Visnar-Perovic A: Ultrasonography in chronic renal failure. *Eur J Radiol* 46:115–122, 2003.
- Grant EG, Tessler FN, Perrella RR: Clinical Doppler imaging. AJR Am J Roentgenol 152:709– 713, 1989.
- 23. Gottlieb RH, Lieberman JL, Pabico RC, et al: Diagnosis of renal artery stenosis in transplanted kidneys: value of Doppler waveform analysis of the intrarenal arteries. *AJR Am J Roentgenol* 165:1441–1446, 1995.
- Rossi AR, Ponziak MA, Zarvan NP: Upper inferior vena caval anastomotic stenosis in liver transplant recipients: Doppler US diagnosis. *Radiology* 187:387–389, 1993.

# Advanced Ultrasound Techniques: Liver Elastography, Contrast-Enhanced Ultrasonography, and Four-Dimensional Ultrasound

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# **Elastography**

# PRINCIPLE

Physicians have long used the technique of palpation in the clinical setting. The underlying principle of palpation lies in the ability to feel stiffer tissue in the background of softer tissue when pressed (palpated). Ultrasound brings this concept to the imaging platform wherein the deformation caused by a force can be imaged, and that deformation can be quantified either visually or quantitatively. Pathologic tissue in any organ is usually stiffer than normal healthy tissue, and thus the technology has a wide range of applications.

# IMAGING BASED ELASTOGRAPHY TECHNIQUES

### Strain Elastography

Strain elastography (also known as real-time elastography) uses B-mode imaging as the only ultrasound technique. In this technique, the force applied over tissue is very similar to that of palpation, wherein the ultrasound operator applies force over the tissue of interest using the ultrasound transducer. This applied force causes deformation of the tissue, which can be visualized with ultrasound. Given the inherent association of operator-dependent applied nonquantifiable force, strain elastography is significantly affected by interobserver and intraobserver variability.

## Shear Wave–Based Elastography

Shear wave elastography (SWE) is a technique that uses acoustic radiation force to induce microscopic tissue movements, producing tissue shear waves. Depending on whether the movement of the tissue itself is measured or whether the speed of the shear waves is measured, the technique is classified either as acoustic radiation force impulse imaging or SWE imaging. Given that the acoustic radiation force is quantifiable and constant (not observer dependent), both deformation force and tissue deformation are known in these techniques. Quantitative estimates of tissue stiffness, expressed as Young's modulus or shear wave velocity, can be obtained.

# Liver Elastography

Elastography of the liver has been predominantly used for estimation of liver fibrosis in the setting of diffuse liver disease and for the noninvasive estimation of portal hypertension.

# DIFFUSE LIVER DISEASE

#### Background and Epidemiology

The prevalence of diffuse liver disease in the United States is estimated to be as high as 14.78%.<sup>1</sup> In 2010, cirrhosis secondary to diffuse liver diseases resulted in an estimated 49,500 U.S. deaths and 1.95% of all global deaths.<sup>2,3</sup> Diffuse liver disease has several causes, including hepatic viral disease, alcoholic liver disease, nonalcoholic fatty liver disease, and autoimmune hepatitis.<sup>4</sup>

#### Pathophysiology

Regardless of cause, chronic diffuse liver disease follows a common pathophysiologic pathway of fibrosis to severe fibrosis and eventually cirrhosis (Figure 5-1). The cost of managing and treating cirrhosis is extremely high and often requires liver transplantation.

## Imaging

The goal of managing diffuse liver disease is to prevent progression to cirrhosis. Therefore, reliable liver fibrosis staging is necessary to meet this goal. Unfortunately, no conventional imaging modality (i.e., ultrasound, computed tomography [CT], or magnetic resonance imaging [MRI]) has shown good sensitivity or specificity for diagnosing early or severe fibrosis. Most current imaging modalities have a high sensitivity for the diagnosis of cirrhosis, but this renders the goal of management ineffective.

## Liver Biopsy

Liver biopsy currently remains the gold standard for estimation of liver fibrosis. However, liver biopsy has a number of limitations: (1) invasiveness with an estimated mortality rate of up to 0.13% and a postprocedure pain rate of up to 63.9%,<sup>5-8</sup> (2) cost, (3) interobserver variability,<sup>9,10</sup> and (4) sampling error (only 1/50,000th of the liver is sampled).<sup>11</sup>

# HEPATITIS C

#### Epidemiology

Hepatitis C (HCV) is the most common hepatic viral disease worldwide, with an estimated prevalence of 5.2 million in the United States<sup>12</sup> and more than 185 million worldwide.<sup>13</sup>

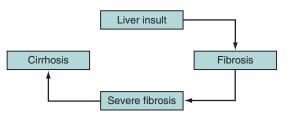
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# Pathophysiology

HCV progresses insidiously and typically remains asymptomatic for decades, represented by the fact that that only 15% to 30% of HCV-infected patients progress to cirrhosis over a 20- to 30-year period.<sup>14-16</sup> It has been shown that liver fibrosis of stage F2 or greater is predictive of subsequent cirrhosis in HCVinfected patients.<sup>17</sup> Recent advances in therapy have been successful in curing HCV. However, these treatments are very expensive, with a per-patient drug expenditure of approximately \$80,000.<sup>18</sup> Treatment is therefore usually allocated to those at risk for developing cirrhosis.

#### ULTRASOUND ELASTOGRAPHY

Shear wave elastographic approaches have good accuracy for the diagnosis of F2 or greater liver fibrosis in patients with HCV.<sup>19-21</sup> This technique can noninvasively distinguish varying degrees of liver fibrosis that appear identical on standard B-mode acquisition (Figures 5-2 and 5-3). SWE has also shown high accuracy for the diagnosis of cirrhosis (F4 disease).<sup>20,21</sup>



**Figure 5-1** Pathophysiology of liver fibrosis. Irrespective of the cause of chronic liver disease, if left undiagnosed and hence untreated, it progresses to cirrhosis.

# HEPATITIS B

### Epidemiology

An estimated 2 billion people worldwide are infected with hepatitis B (HBV).<sup>22</sup> However, the majority of infected people clear the virus and only a small minority remains chronically infected. Those chronically infected can develop cirrhosis secondary to chronic liver inflammation. This at-risk population comprises over 350 million people globally.<sup>22</sup>

#### Pathophysiology

Similar to HCV, the finding of F2 or greater fibrosis on liver biopsy carries an increased risk for subsequent cirrhosis in patients with chronic hepatitis B.<sup>23</sup> Therefore, the imaging diagnosis of early fibrosis is of paramount importance.

## Imaging

Similar to HCV, conventional imaging (ultrasound, CT, MRI) has no role in the diagnosis of early fibrosis in this cohort of patients. Hence, elastography is a great diagnostic imaging tool for this population.<sup>24</sup>

# NONALCOHOLIC FATTY LIVER DISEASE

## Epidemiology

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disorder, with a prevalence of 17% to 46% in the United States<sup>25</sup> and a worldwide prevalence of 6% to 35%.<sup>26</sup>

### Pathophysiology

NAFLD can essentially be categorized in two forms: simple steatosis (~80% of cases), and (2) nonalcoholic steatohepatitis (NASH, 20% of cases), in which excess liver fat is associated with inflammation.<sup>26</sup> From a clinical standpoint, it is essential

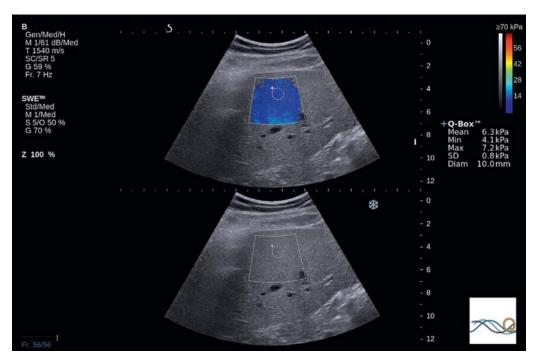
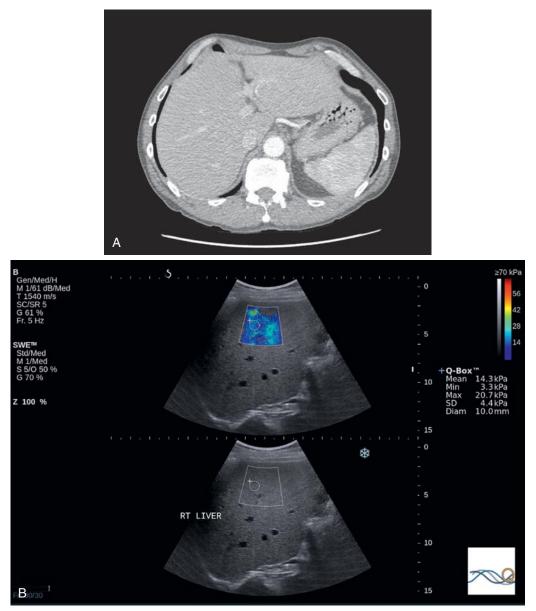


Figure 5-2 Shear wave elastogram of a 67-year-old man with chronic hepatitis C with stage F0 fibrosis on pathologic examination shows an estimated liver Young's modulus of 6.3 kPa.



**Figure 5-3** A, Contrast-enhanced computed tomography of a 55-year-old man with chronic hepatitis C shows no apparent abnormality in the liver. B, Shear wave elastogram shows an estimated liver Young's modulus of 14.3 kPa. The patient had stage F3 fibrosis on pathologic examination from liver biopsy. B-mode appearance is identical to that in the patient with F0 fibrosis, shown in Figure 5-2.

to accurately distinguish the 20% with NASH at risk for cirrhosis from the 80% with simple steatosis who will not progress and require no treatment.<sup>27</sup>

#### Imaging

**Ultrasound.** Ultrasound has a modest sensitivity (67%) and specificity (77%) as a screening tool for steatosis. However, it has no role in distinguishing inflammation and fibrosis.<sup>28</sup>

**Computed Tomography and Magnetic Resonance Imaging.** CT and MRI can quantify liver fat, but conventional CT and MRI cannot distinguish simple steatosis and NASH, which currently requires nontargeted liver core biopsy. **Ultrasound Elastography.** In elastography, early studies have shown promise in making this differentiation. SWE has shown an area under the receiver operating characteristic curve (AUC) of 0.944 in differentiating F2 or greater fibrosis.<sup>29</sup> Similarly, studies have shown AUCs of 0.90 to 0.97 in differentiating F3 or greater fibrosis.<sup>30,31</sup>

# PORTAL HYPERTENSION

#### Cause

The hallmark of cirrhosis is portal hypertension. However, the diagnosis is best made by measuring the hepatic venous pressure gradient (HVPG).<sup>32</sup>

# Pathophysiology

The onset of portal hypertension after the development of cirrhosis is progressive. However, depending on severity, there is significant variation among the four stages with varying degrees of survival. The median 1-year survival in the four stages of cirrhosis has been reported to be 99%, 97%, 80%, and 43%, respectively.<sup>33</sup>

#### Imaging

**Ultrasound, Computed Tomography, and Magnetic Reso-nance Imaging.** Conventional imaging has high sensitivity for the detection of cirrhosis. However, there is a limited role in the diagnosis of HVPG.

**Ultrasound Elastography.** Ultrasound elastography has used both liver and spleen stiffness as a direct assessment of portal hypertension. Spleen stiffness measurements can be independently used as good predictors of clinically significant portal hypertension using elastography. For diagnosing clinically significant portal hypertension, a liver stiffness value of 24.6 kPa with SWE has been reported to have a sensitivity, specificity, and accuracy of 81%, 88%, and 82%, respectively.<sup>34</sup>

# **Contrast-Enhanced Ultrasound**

Investigations of contrast-enhanced ultrasound in the abdomen are predominantly performed on liver, kidney, pancreas, and spleen for screening of anatomic structures, lesion characterization, and blood volume and perfusion evaluation.

The common enhancing patterns of focal liver lesions are well established in contrast-enhanced ultrasound (Figure 5-4). The typical patterns of liver lesions include (1) contrast absence

(e.g., cyst or small hemangioma); (2) diffuse hyperechoic enhancement (e.g., hepatocellular carcinoma [HCC], hypervascular metastasis, and focal nodular hyperplasia [FNH]) (Figure 5-5); (3) heterogeneous enhancement (e.g., large HCC); (4) diffuse heterogeneous enhancement (e.g., HCC, lymphoma, metastasis); (5) rim-like enhancement (e.g., abscess, metastasis, cholangiocarcinoma); (6) peripheral nodular enhancement (e.g., hemangioma) (Figure 5-6); (7) spoke-like enhancement (e.g., FNH); and (8) stippled heterogeneous or "basket sign" (e.g., HCC). Malignant lesions usually manifest a rapid washout, owing to arteriovenous shunts in the portal venous phase, and centripetal filling is not seen.<sup>35</sup> Benign lesions usually manifest in an isoechoic homogeneous enhancing pattern. The residual central hypoechoic area is often a specific pattern for the diagnosis of FNH.<sup>36</sup>

# **Four-Dimesional Ultrasound**

Technical advances in ultrasound have led to earlier diagnoses and improved monitoring of disease progression.<sup>37</sup> One such advancement, three-dimensional (3D) volumetric ultrasound, has been reported to be more efficient than 2D imaging in some applications, such as fetal imaging<sup>38</sup> (with no additional side effects).<sup>39,40</sup> 4D ultrasound allows for dynamic imaging, such as observation of fetal activity.<sup>38,41</sup>

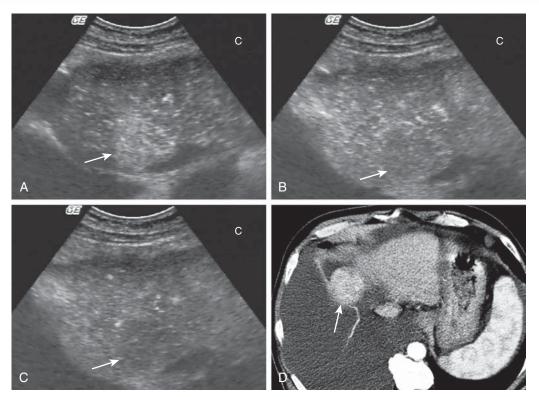
4D ultrasound is the evolution of 3D imaging and is defined as real-time 3D ultrasound imaging. In other words, a "time axis" is added to 3D imaging to make the 3D image animated or updated in real time, providing a "live show" in a 3D view of the target.<sup>39,42</sup> Depending on different settings, 4D ultrasound can be used to show surface anatomy, such as the fetal face and gallbladder polyps (Figures 5-7 and 5-8).

**Figure 5-4** Illustrations of enhancing patterns of focal liver lesions in contrast-enhanced ultrasonography.

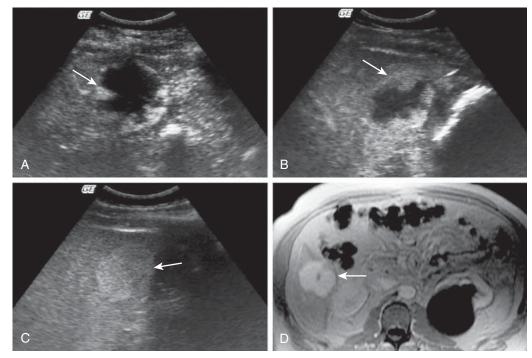
Arterial phase patterns	Illustration	Portal/Late phase patterns	Illustration
Contrast absence (hypoechoic/hypovascular)		Contrast absence (hypoechoic/hypovascular)	
Diffuse homogeneous hyperechoic	$\bigcirc$	Diffuse homogeneous hyperechoic	$\bigcirc$
Heterogeneous		Heterogeneous	
Diffuse dotted	$\bigcirc$	Residual central hypoechoic area	*
Diffuse heterogeneous			
Rim-like	$\bigcirc$		
Peripheral nodular			
Spoke-like			
Stippled heterogeneous (basket sign)			

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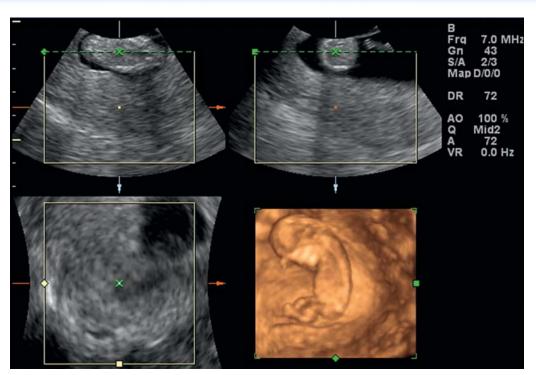
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**Figure 5-5** Images from a 66-year-old man with cirrhosis show a hypoechoic mass (*arrows*) in the transverse plane of ultrasound and computed tomography (CT) images. **A**, Image captured at 14 seconds after the administration of an ultrasound contrast agent represents the diffuse heterogeneous contrast enhancement (*arrow*) in the early arterial phase. **B**, Image captured at 47 seconds represents the microbubble washout (*arrow*) quickly beginning in the portal venous phase. **C**, Image captured at 78 seconds demonstrates the full washout of microbubbles (*arrow*) in the hypoechoic mass. **D**, Corresponding contrast-enhanced CT image demonstrates the early arterial phase contrast enhancement (*arrow*). This lesion was histopathologically proved to be hepatocellular carcinoma.



**Figure 5-6** Images from a 59-year-old man show a large hypoechoic mass (arrows) in the sagittal plane during contrast-enhanced ultrasonography that was incidentally discovered in segment 7 of the liver. **A**, Image captured at 23 seconds after the administration of an ultrasound contrast agent represents a typical peripheral nodular contrast enhancement pattern in the early arterial phase. **B**, Image captured at 47 seconds shows the microbubbles gradually centripetally filling in during the portal venous phase. **C**, Image captured at 161 seconds demonstrates the microbubbles to finally fill out the hypoechoic mass, which appears as homogeneous hyperechoic enhancement. The enhancing patterns demonstrate the lesion was a typical hemangioma. **D**, Corresponding contrast-enhanced magnetic resonance image in the portal venous phase confirmed the lesion was a hemangioma.



**Figure 5-7** Multiplanar four-dimensional image of an early pregnancy. This image illustrates the typical layout in a 3D/4D display. The *upper left*, *upper right*, and *lower left* images are usually the transverse, sagittal, and coronal planes of the region of interest (ROI); the green cross (X) and dashed line (—) represent the central point and line of the ROI of each plane, which can be adjusted by the operator. The lower right image is the reconstructed 3D/4D image corresponding to the ROIs selected in the prior three planes. (*Courtesy LOGIQlibrary, GE Healthcare.*)

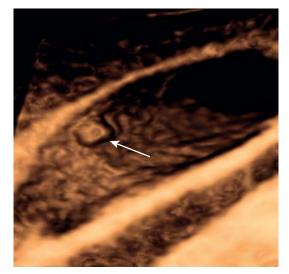


Figure 5-8 Single reconstructed three-dimensional image of the gallbladder. A polyp (arrow) in the anterior wall of the gallbladder neck is well shown using opacity mode. (Courtesy LOGIQlibrary, GE Healthcare.)

#### SUGGESTED READINGS

Dhyani M, Anvari A, Samir AE: Ultrasound elastography: liver. *Abdom Imaging* 19:1–11, 2015. Yoshioka K, Hashimoto S, Kawabe N: Measurement of liver stiffness as a non-invasive method for diagnosis of non-alcoholic fatty liver disease. *Hepatol Res* 45:142–151, 2015.

#### REFERENCES

- 1. Younossi ZM, Stepanova M, Afendy M, et al: Changes in the prevalence of the most common causes of chronic liver diseases in the United States from 1988 to 2008. *Clin Gastroenterol Hepatol* 9:524–530.e1-quiz e60, 2011.
- 2. Murray CJL, Abraham J, Ali MK, et al: The state of US health, 1990–2010: burden of diseases, injuries, and risk factors. *JAMA* 310:591–608, 2013.
- 3. Mokdad AA, Lopez AD, Shahraz S, et al: Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. *BMC Med* 12:145, 2014.
- Schölmerich J, Holstege A: Aetiology and pathophysiology of chronic liver disorders. *Drugs* 40(Suppl 3):3–22, 1990.
- Actis GC, Olivero A, Lagget M, et al: The practice of percutaneous liver biopsy in a gastrohepatology day hospital: a retrospective study on 835 biopsies. *Dig Dis Sci* 52:2576–2579, 2007.
- Cadranel JF, Rufat P, Degos F: Practices of liver biopsy in France: results of a prospective nationwide survey. For the Group of Epidemiology of the French Association for the Study of the Liver (AFEF). *Hepatology* 32:477–481, 2000.
- van der Poorten D, Kwok A, Lam T, et al: Twenty-year audit of percutaneous liver biopsy in a major Australian teaching hospital. *Intern Med J* 36:692–699, 2006.
- Sparchez Z: Complications after percutaneous liver biopsy in diffuse hepatopathies. *Rom J Gastroenterol* 14:379–384, 2005.
- Bravo AA, Sheth SG, Chopra S: Liver biopsy. N Engl J Med 344:495–500, 2001.
- Rousselet M-C, Michalak S, Dupré F, et al: Sources of variability in histological scoring of chronic viral hepatitis. *Hepatology* 41:257–264, 2005.
- Bedossa P, Dargère D, Paradis V: Sampling variability of liver fibrosis in chronic hepatitis C. *Hepatology* 38:1449–1457, 2003.
- Chak E, Talal AH, Sherman KE, et al: Hepatitis C virus infection in USA: an estimate of true prevalence. *Liver Int* 31:1090–1101, 2011.
- Mohd Hanafiah K, Groeger J, Flaxman AD, et al: Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology* 57:1333–1342, 2013.
- 14. Rosen HR: Clinical practice: chronic hepatitis C infection. N Engl J Med 364:2429–2438, 2011.
- Thein H-H, Yi Q, Dore GJ, et al: Estimation of stage-specific fibrosis progression rates in chronic hepatitis C virus infection: a metaanalysis and meta-regression. *Hepatology* 48: 418–431, 2008.
- 16. Poynard T, Bedossa P, Opolon P: Natural history of liver fibrosis progression in patients with

chronic hepatitis C. The OBSVIRC, METAVIR, CLINIVIR, and DOSVIRC groups. *Lancet* 349: 825–832, 1997.

- Wong GL-H: Prediction of fibrosis progression in chronic viral hepatitis. *Clin Mol Hepatol* 20:228–236, 2014.
- Brennan T, Shrank W: New expensive treatments for hepatitis C infection. JAMA 312:593– 594, 2014.
- Sporea I, Sirli R, Bota S, et al: Comparative study concerning the value of acoustic radiation force impulse elastography (ARFI) in comparison with transient elastography (TE) for the assessment of liver fibrosis in patients with chronic hepatitis B and C. Ultrasound Med Biol 38:1310– 1316, 2012.
- Ferraioli G, Tinelli C, Dal Bello B, et al: Accuracy of real-time shear wave elastography for assessing liver fibrosis in chronic hepatitis C: a pilot study. *Hepatology* 56:2125–2133, 2012.
- Samir AE, Dhyani M, Vij A, et al: Shear-wave elastography for the estimation of liver fibrosis in chronic liver disease: determining accuracy and ideal site for measurement. *Radiology* 274:888–896, 2015.
- 22. Wright TL: Introduction to chronic hepatitis B infection. *Am J Gastroenterol* 101(Suppl 1):S1–S6, 2006.
- Park BK, Park YN, Ahn SH, et al: Long-term outcome of chronic hepatitis B based on histological grade and stage. *J Gastroenterol Hepatol* 22:383–388, 2007.
- 24. Zhang D, Chen M, Wang R, et al: Comparison of acoustic radiation force impulse imaging and transient elastography for non-invasive assessment of liver fibrosis in patients with chronic hepatitis B. Ultrasound Med Biol 41:7–14, 2015.
- 25. Chalasani N, Younossi Z, Lavine JE, et al: The diagnosis and management of nonalcoholic fatty liver disease: practice guideline by the American Gastroenterological Association, American Association for the Study of Liver Diseases, and American College of Gastroenterology. *Gastroenterology* 142:1592–1609, 2012.
- 26. Vernon G, Baranova A, Younossi ZM: Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. *Aliment Pharmacol Ther* 34:274–285, 2011.
- 27. Dhyani M, Anvari A, Samir AE: Ultrasound elastography: liver. *Abdom Imaging* 19:1–11, 2015.
- Dasarathy S, Dasarathy J, Khiyami A, et al: Validity of real time ultrasound in the diagnosis of hepatic steatosis: a prospective study. *J Hepatol* 51:1061–1067, 2009.
- Fierbinteanu-Braticevici C, Sporea I, Panaitescu E, et al: Value of acoustic radiation force impulse imaging elastography for non-invasive evalua-

tion of patients with nonalcoholic fatty liver disease. *Ultrasound Med Biol* 39:1942–1950, 2013.

- Yoneda M, Suzuki K, Kato S, et al: Nonalcoholic fatty liver disease: US-based acoustic radiation force impulse elastography 1. *Radiology* 256:640–647, 2010.
- Palmeri ML, Wang MH, Rouze NC, et al: Noninvasive evaluation of hepatic fibrosis using acoustic radiation force-based shear stiffness in patients with nonalcoholic fatty liver disease. J Hepatol 55:666–672, 2011.
- Merkel C, Montagnese S: Hepatic venous pressure gradient measurement in clinical hepatology. *Dig Liver Dis* 43:762–767, 2011.
- 33. D'Amico G, Garcia-Tsao G, Pagliaro L: Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. *J Hepatol* 44:217–231, 2006.
- 34. Elkrief L, Rautou P-E, Ronot M, et al: Prospective comparison of spleen and liver stiffness by using shear-wave and transient elastography for detection of portal hypertension in cirrhosis. *Radiology* 28:141210, 2014.
- Kim TK, Choi BI, Han JK, et al: Hepatic tumors: contrast agent–enhancement patterns with pulse-inversion harmonic US. *Radiology* 216: 411–417, 2000.
- 36. von Herbay A, Vogt C, Haussinger D: Pulse inversion sonography in the early phase of the sonographic contrast agent Levovist: differentiation between benign and malignant focal liver lesions. J Ultrasound Med 21:1191–1200, 2002.
- Avni FE, Cos T, Cassart M, et al: Evolution of fetal ultrasonography. *Eur Radiol* 17:419–431, 2007.
- Benacerraf BR, Shipp TD, Bromley B: Threedimensional US of the fetus: volume imaging. *Radiology* 238:988–996, 2006.
- Sheiner E, Hackmon R, Shoham-Vardi I, et al: A comparison between acoustic output indices in 2D and 3D/4D ultrasound in obstetrics. *Ultra*sound Obstet Gynecol 29:326–328, 2007.
- Xu HX, Zhang QP, Lu MD, et al: Comparison of two-dimensional and three-dimensional sonography in evaluating fetal malformations. J Clin Ultrasound 30:515–525, 2002.
- Yigiter AB, Kavak ZN: Normal standards of fetal behavior assessed by four-dimensional sonography. J Matern Fetal Neonatal Med 19:707–721, 2006.
- Timor-Tritsch IE, Platt LD: Three-dimensional ultrasound experience in obstetrics. *Curr Opin Obstet Gynecol* 14:569–575, 2002.

# Principles of Computed Tomography Physics, Instrumentation, and Radiation Safety

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# **Computed Tomography Physics**

In the past decade, computed tomography (CT) has undergone tremendous technical advances. In 1992, the first dual-slice CT scanner (CT Twin, formerly Elscint Technologies, Haifa, Israel) was introduced. In 1998, the quad-slice CT scanners were introduced. In 2002, the 16-slice CT scanner became available. With these scanners it became possible to perform coronary CT angiography, multiphasic examinations, and virtual endoscopy studies. In 2004, 64-slice CT scanners were introduced. With 64-slice CT scanners it became possible to acquire submillimeter sections of large body regions, perform high-quality coronary angiography in most patients, and perform perfusion studies.

#### DUAL-ENERGY COMPUTED TOMOGRAPHY

The evolving modality of dual-energy computed tomography (DECT) has specific capacities beyond single-energy CT that can translate into improved abdominal imaging.<sup>1</sup> DECT consists of acquisition of two different image data sets with different kilovoltage peaks, usually 80 and 140 kVp, during the same study. It was first described in 1976, but its clinical applications became possible only recently with the introduction of multi-detector computed tomography (MDCT). Compton scatter and the photoelectric effect are the two primary ways that the x-ray interacts with the materials. The probability of an x-ray undergoing photoelectric effect increases in substances with higher atomic number and at lower energy levels, giving higher attenuation. For example, iodine (Z = 53) has higher attenuation than calcium (Z = 20), which is in turn more attenuating than water.

X-ray attenuation properties at low- and high-energy acquisitions are also used to differentiate materials by mathematically transforming attenuation measurements of an object at low and high kVp as a function of two materials that would be needed to represent the measured attenuation. Besides being used to characterize the composition of the tissue, this information can be mathematically manipulated to generate postprocessed images that can simulate unenhanced data sets, images with the capability to quantify iodine in the tissues, and also virtual images simulating monochromatic energies. In addition, blended images with desired contributions from acquisitions that are of both low and high kilovoltage peak can be processed. By appropriately blending high- and low-energy series, images analogous to those obtained with single-energy 120-kVp acquisition can be obtained.

The dual-source (dsDECT) system consists of two x-ray tubes that acquire data with different energies (low and high kVp) in a DE acquisition. The single-source system (ssDECT) uses a single x-ray tube, which can alternate tube energy (low and high kVp) in less than 0.5 ms, in the same gantry rotation. The single source sandwich detector (sssdDECT) uses a detector with two layers that separate high- and low-energy photons from a single x-ray source from which two image data sets are generated.

The dsDECT approach for material separation uses the three-material decomposition method, which takes into account known x-ray absorption properties of three materials (iodine, soft tissue, and fat) at dual-energy acquisition. Based on different attenuations at a specific location in the CT acquisition at two different tube potentials, the expected amount of each material (selected for the decomposition) is calculated and the density of this point is determined. This process generates iodine images and virtual nonenhanced images (similar to a nonenhanced acquisition).

On ssDECT, by using the material decomposition process for two known selected basis materials, the attenuation measurements from high- and low-energy data can be mathematically transformed into the density (or amount) of the two known materials that would be needed to produce the kilovoltage peaks of low and high attenuation. Usually, water and iodine (a lowand a high-attenuating material, respectively) are selected, resulting in material density pairing—iodine images and water images (latter being similar to a nonenhanced acquisition).

From both DE systems, virtual monochromatic images at desired energy level can be generated through a complex mathematical calculation, enabling the representation of the data as though it came from a monochromatic single energy source.

#### PITCH, NOISE, AND RADIATION DOSE

In a single-slice scanner, the pitch of the helical scan refers to the ratio of the table movement per gantry rotation to the slice width. This definition is not entirely satisfactory when applied to multislice CT scanners. A better definition of pitch in multislice CT is the ratio of table movement to the total x-ray beam collimation. Using this definition, the lengths of volume scanned

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by 64-slice CT scanners, when a pitch of 1 is chosen, range from 58 to 114 mm.

In single-slice CT, the gantry always has to rotate through a specific angle, depending on the reconstruction algorithm used, to acquire the projection information needed to create an axial image. Thus, the number of photons that are used to produce an axial image (the principal determinant of image noise) depends on the tube current/time product and not on the pitch. However, as the pitch increases, the radiation dose reduces, because each part of the scanned volume spends less time in the x-ray beam.

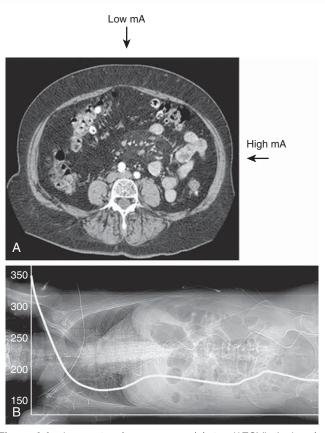
The relationship among pitch, noise, and radiation dose is not the same with current multislice scanners.<sup>2</sup> In the noncardiac mode, as the pitch is increased, 64-slice scanners automatically increase the tube current to maintain a relatively constant noise level. With higher pitch, the larger focal spot may be automatically chosen. These secondary effects negate any reduction of radiation dose that is intuitively expected with an increase in pitch.<sup>3</sup> Therefore, changing the pitch in current multislice CT scanners does not necessarily alter the radiation dose.

# **REDUCING RADIATION DOSE**

CT examination is responsible for approximately 70% of the radiation dose received by the general population from imaging.<sup>4</sup> Modern scanners employ techniques to reduce radiation dose. Automatic tube current modulation (ATCM) changes the tube current to produce an acceptable noise level for each slice. The tube current modulation may be in the radial (x-y) plane (Figure 6-1, A) or in the z-axis (see Figure 6-1, B). Although the modulation techniques work differently in each scanner, in general the milliampere level is altered to maintain a selected noise level throughout the scanned volume. In some scanners, such as Sensation 64 (Siemens Medical Solutions, Malvern, PA), the tube current is constantly varied using dosimetry readings from prior gantry rotations. In others, the localizer image is used to calculate regions requiring higher and lower x-ray tube currents. It is possible on most 64-slice scanners to use simultaneously both radial and z-axis ATCM, leading to an overall reduction in dose of 40% to 60% compared with fixed milliampere scanning. The use of ATCM has been shown to maintain image quality in assessment of structures with high inherent contrast differences, such as in chest CT and CT colonography.<sup>5</sup> However, there is a potential of ATCM to increase noise and adversely affect image quality where the difference in tissue contrast is low.

#### ARTIFACTS OF MULTISLICE SCANNERS

Artifacts caused by beam hardening, photon starvation, and metallic implants occur less commonly in 40- and 64-channel scanners than they did in earlier CT generations. The use of beam-hardening reduction software, adaptive filtration, and ATCM reduces artifacts from dense bone such as in the shoulders and posterior cranial fossa. Adaptive filtration refers to software that smooths the attenuation differences at sites of highly variable attenuation, before reconstruction of source images. Several methods are now available to reduce artifacts from metallic implants, allowing diagnosis of prosthetic malfunction using CT. The use of thin-slice isotropic scanning technique almost completely eliminates stair-step artifacts seen on multiplanar reformatted images. Ring artifacts may be seen



**Figure 6-1** Automatic tube current modulation (ATCM). **A**, Angular (*x-y*) ATCM is depicted as variation in tube current as the gantry rotates round the patient. **B**, Z-axis ATCM. Diagram shows that the tube current is constantly changed through the scan. It is high when scanning through the shoulders, low through the lungs, higher through the abdomen, and even higher through the pelvis. If extremities are scanned, the tube current reduces. The parameters used to alter the tube current vary for each vendor. In general, the tube current alters to maintain noise within a small range.

as a result of poorly functional or incorrectly calibrated detector elements (Figure 6-2).

The wide cone beam required for 40- and 64-slice scanning as well the obligatory reconstruction algorithms result in specific artifacts. These include cone beam, windmill, and zebra artifacts.

#### Cone Beam Artifact

Cone beam artifacts result from approximations in reconstruction algorithms that fail to exactly reconstruct a widely divergent x-ray beam. The artifact may manifest as geometric distortions or a glow around high-contrast objects such as bones (Figure 6-3). The widely divergent cone beam of 64-slice scanners would be expected to show worse cone beam artifact than narrower beams of 4- and 16-slice scanners. However, 64-slice scanners use three-dimensional reconstruction techniques that minimize this artifact.

#### Windmill Artifact

Windmill or splay artifacts occur as a result of inadequate sampling in the z-direction (Figure 6-4). These artifacts are similar to aliasing artifacts seen in Doppler ultrasonography and are unrelated to the cone beam geometry. The appearance of

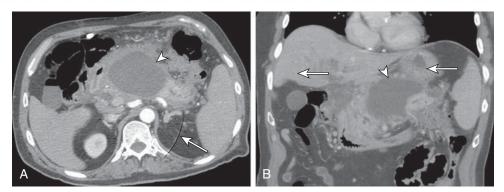
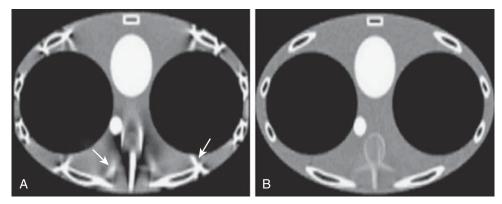
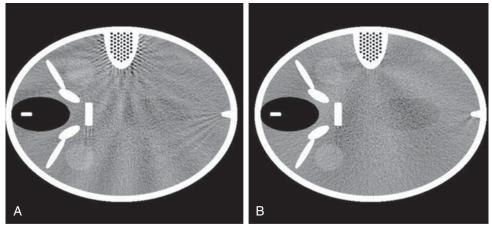


Figure 6-2 Ring artifact. Axial (A) and coronal reformatted images (B) in a 67-year-old man with necrotic pancreatitis. Alternating black and white curves (A) or pixels (B) (arrows) are artifactual and the result of malfunction of a detector element. Note large pseudocyst (arrowheads).



**Figure 6-3** Cone beam artifact. Reconstruction of an anthropomorphic phantom in 40-slice scanner, with standard (180-degree linear interpolation, A) and three-dimensional Feldkamp-based (B) reconstructions. Note that the glow around the "vertebra" and "ribs" (arrows, A) is eliminated by the use of algorithms that take into account the divergence of the x-ray beam in the z-axis.



**Figure 6-4** Windmill (splay) artifact. Windmill pattern of alternating dark and bright fan-like lines is related to undersampling of data, similar in cause to aliasing in Doppler sonography. **A**, Image of anthropomorphic head phantom performed using 16 × 1.5 mm configuration, 1.5 pitch, 2 mm slice width. **B**, Image performed using same parameters except for a 0.5 pitch. Splay artifact is less prominent with lower pitch because of better sampling in the z-axis. The artifact superficially resembles, but is unrelated in cause of, beam-hardening artifacts.

artifacts is determined by the number of detector rows, the detector width, the helical pitch, and the reconstructed slice thickness. For example, splay is more prominent on thin-slice axial images in which the slice thickness is approximately equal to the detector width and they are minimized as the slice thickness is increased. Typically, splay artifact does not occur if the slice thickness is double that of the detector width. The number

of vanes in the windmill artifact is proportional to the pitch; decreasing the pitch also reduces this artifact.

#### Zebra Artifact

Weighting factors used in reconstruction algorithms are associated with inhomogeneity in noise, particularly away from the center of rotation.<sup>6</sup> The variation in noise between different



**Figure 6-5** Zebra artifact. Coronal reformatted images from a 64-slice computed tomography scan shows faintly visible lines best seen over the urinary bladder and gluteal and adductor muscles. These artifacts are due to variation in noise in axial source images that become obvious on images reformatted in the z-axis. Patient had active Crohn's colitis, with thickened colon (arrowhead).

axial slices becomes obvious on images oriented in the z-axis, including nonaxial reformatted images and maximum intensity projection images. The artifact appears as faint stripes of variable density and is termed the *zebra artifact* (Figure 6-5). This artifact is reduced by ATCM techniques that attempt to maintain a constant noise level at different axial locations. Adaptive filtration techniques also can be used to reduce variability of noise between different axial slices. Zebra artifact is not related to beam hardening or the effect of scatter radiation, which may cause a similar-appearing artifact on nonhelical scanners.

# Computed Tomography Instrumentation

The performance of CT, in terms of acquisition time, image quality, and radiation dose, has improved significantly over the past 3 decades. Several breakthroughs in CT hardware and software development have contributed tremendously. The first was the adoption of the slip ring technology in 1980s. This technology allows the x-ray source and the detector assembly to rotate continuously while the power and the data are exchanged between the rotating components and the fixed components. The second revolutionary development was the invention of the spiral scanning mode in the late 1980s. In this scanning mode, the patient table moves at a constant speed through the gantry opening while the x-ray source/detector assembly is rotating continuously. The projections of a volume, not just a slice, are

TABLE	Estimated Effective Doses from Typical
6-1	Abdominal Radiology Examinations

Examination	Dose (mSv)
Abdominal radiograph (AP)	0.2-0.6
Abdominal series (KUB, upright, LLD)	0.6-1.8
Barium enema	5-7
Intravenous pyelogram	8-10*
Small bowel follow-through	4-7†
Abdomen CT	5-7
Pelvis CT	3-5
Abdomen and pelvis CT	8-12

AP, Anteroposterior; CT, computed tomography; KUB, kidney/ureter/ bladder; LLD, left lateral decubitus.

\*Four to five conventional tomograms and six to nine radiographs.

<sup>†</sup>Including fluoroscopy and spot views.

obtained. Any axial slice within the volume can be reconstructed based on the projection data on both sides of the slice using various interpolation algorithms. The third major development wave was marked by the introduction of MDCT in 1998.

# **Radiation Safety**

As CT systems become more sophisticated and more user friendly, the categories of CT applications have expanded rapidly. As a result, the number of CT examinations has increased significantly over the past 20 years.<sup>7</sup> Compared with most x-ray imaging procedures, the patient dose from CT is much higher (Table 6-1). For example, the effective dose for a chest CT is approximately 200 times the effective dose for chest radiography and the effective dose for an abdomen CT is more than 10 times the effective dose for abdominal radiography.<sup>8</sup> Although the number of CT examinations is approximately 12% of total radiology examinations, CT contributes approximately 45% of the collective dose from all medical examinations.<sup>9</sup>

Radiation risks from abdominal CT procedures can be classified into three categories: (1) malfunction of electric medical devices caused by radiation at a high dose rate, (2) deterministic bioeffects when the dose exceeds a threshold, and (3) stochastic bioeffects as a result of low-level radiation exposure.

High-dose CT may cause unintended "shocks" (i.e., stimuli) from neurostimulators, malfunctions of insulin infusion pumps, and transient changes in pacemaker output pulse rate. The U.S. Food and Drug Administration recently issued a public health notification on this problem.<sup>10</sup>

The deterministic bioeffects of radiation will not occur unless a threshold dose is exceeded. For typical one-phase CT scan of abdomen and pelvis, the highest skin dose is under 80 mGy, which is much lower than the threshold for any deterministic effect. However, several special procedures may need attention. These include CT-guided interventional procedures, CT fluoroscopy, CT perfusion, CT biopsy, and so on. In these procedures, the same organ or skin area may be scanned multiple times in a short period and the accumulated skin dose can be more than 2 Gy, which is in the range of the warning level for deterministic skin effects. For instance, the same body section may be scanned up to 40 times in a CT biopsy procedure and the patient skin dose can be up to 3 Gy if improper technique is used.

An important safety issue with CT of the lower abdomen or pelvis of pregnant women is the radiation risk to the fetus. Potential deterministic effects of the x-ray exposure include termination of viability, nonrecoverable growth restriction, small head size, malformation, and mental retardation. The probability of inducing the effect and the severity of radiation risks depends on gestation age and amount of radiation delivered. The most sensitive period for radiation-induced prenatal death is 0 to 8 days after conception. Animal data suggest that radiation-induced prenatal death might occur at the dose of 50 to 100 mGy and higher if delivered before implantation. The critical period for inducing growth restriction occurs during organogenesis, which is between the second and seventh weeks after conception. The fetal doses from abdomen or pelvis scans range from 6.7 to 56 mGy, with an average of 24.8 mGy.<sup>11</sup>

The stochastic effects may occur at any dose level, and the probability of occurrence increases with the dose, according to the linear nonthreshold dose-response model. Stochastic effects include carcinogenesis and the induction of genetic mutations. The cancer induction is the primary risk resulting from CT examinations. The lifetime risk for fatal cancer is approximately 5% per Sievert for the general population.<sup>12</sup> Children are inherently more sensitive to radiation because they have more dividing cells and radiation acts on dividing cells. The lifetime mortality risk is significantly higher when the exposure is received just after birth.

The CT scanning protocols should be optimized in such a way that the quality of images is sufficient for diagnosis and the patient dose is kept as low as reasonably achievable (ALARA). To accomplish the optimization, operators must understand the basic relationship between the dose and image quality and the dependency of the dose on image acquisition parameters.

The quantity volume CT dose index  $(\text{CTDI}_{vol})$  is often used to describe the patient dose.  $\text{CTDI}_{vol}$  represents the average dose in a given scan volume. When a scan is prescribed, the system displays the  $\text{CTDI}_{vol}$  in milligray on the console. However, the dose displayed is not the true dose for the specific patient under examination. Instead, it is the dose value when the patient is replaced with an acrylic phantom while the same image acquisition parameters are used. The body phantom is an acrylic cylinder with a diameter of 32 cm and a height of 15 cm. For neonates, the dose displayed may significantly underestimate the true patient dose.

The effective dose, E, is used to assess the radiation detriment from nonhomogeneous irradiation. The effective dose is a weighted sum of the doses to all exposed tissues.

$$\mathbf{E} = \left[ \sum (\mathbf{w}_{t} \times \mathbf{H}_{t}) \right], \qquad [6-1]$$

where  $H_t$  is the equivalent dose to a specific tissue and  $w_t$  is the weight factor representing the relative radiosensitivity of that tissue. The unit of effective dose is the Sievert (Sv). The effective dose can be estimated by multiplying the dose-length-product (DLP) in a dose report with a conversion factor.<sup>13</sup> For a typical one-phase CT examination of the abdomen, the effective dose is approximately 6.5 mSv.

The patient dose depends on three group factors: equipmentrelated factors, patient-related factors, and application-related factors (Table 6-2 and Box 6-1).

The factors in the first group include the x-ray beam filtration, the x-ray beam collimation, the system geometry, and the detector efficiency. Although users do not have control of most

TABLE 6-2Principles	of Scanning Factors
TUBE CURRENT (mA)	Determines photon fluence Most effective dose-reduction strategy 50% reduction reduces radiation dose by half Decrease in mAs increases image noise
TUBE POTENTIAL (kVp)	Determines x-ray beam energy Dose is approximately proportional to square of kVp Decreasing kVp increases attenuation of iodine Decrease in kVp significantly increases image noise. This needs a compensatory increase in mAs to maintain image quality
GANTRY ROTATION TIME (SECONDS)	Faster gantry rotation reduces photon fluence (mAs) Increase in mA needed to maintain image noise
PITCH AND COLLIMATION (THESE ARE INTERLINKED)	Ratio of table speed to beam collimation (mm) Dose is inversely proportional to pitch Higher pitch increases image noise (if mAs constant) Higher pitch can produce artifacts Wider collimation is more dose efficient
SCANNING LENGTH	Effective dose is proportional to length of scanned volume Scan coverage should be restricted to area of interest Minimize overlap scanning Minimize scan phases
SCANNING MODE	Over-ranging contributes to extra dose Single helical scan volume is more dose-efficient than multiple helical scan volumes to cover a large region

#### BOX 6-1 OTHER DOSE-SAVING FACTORS

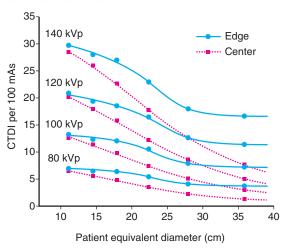
- Low dose scout
- Low dose smart preparation
- Patient positioning
- Noise reductionImproved dose efficiency of scanners
- Over-range shielding

of these factors, it is important to understand that the z-axis dose efficiency is reduced when the total x-ray beam width becomes very small for MDCT owing to the need to keep the beam penumbra out of any detector row. Another dose-related issue with MDCT is overscan. To reconstruct a slice near the end of the prescribed range in the helical mode, the projection data on both sides of the slice are needed for proper interpolation. Therefore, the actual scan range is larger than the prescribed scan range. Some scanners require one additional rotation at each end of the prescribed scan range.

The dose is strongly dependent on patient size, as shown in Figure 6-6 and Box 6-2. If the same technique is used to scan an average adult and a newborn, the dose to the newborn is significantly higher.<sup>14</sup>

Image acquisition parameters such as kilovoltage peak, milliamperes (the product of the tube current and the time in seconds per rotation), and pitch (the table travel per rotation divided by the total x-ray beam width) are selected by the operator. If all other conditions are fixed, the patient dose is

#### 6 Principles of Computed Tomography Physics, Instrumentation, and Radiation Safety 51



**Figure 6-6** Graph shows the volume CT dose index (CTDI) per 100 mAs as a function of patient diameter for four tube voltages, given a 4 × 5-mm transverse acquisition (20-mm nominal collimation). The doses measured in the PMMA phantoms at the edge and at the center are shown. The lines (*solid lines* for edge data, *dotted lines* for center data) represent the computer-fit weighted CTDI values, which were used to interpolate dose values between patient thicknesses. (*From Boone JM, Geraghty EM, Seibert JA: Dose reduction in pediatric CT: a rational approach.* Radiology 228:352–360, 2003.)

#### BOX 6-2 PRACTICAL TIPS FOR COMPUTED TOMOGRAPHY OF OBESE PATIENTS

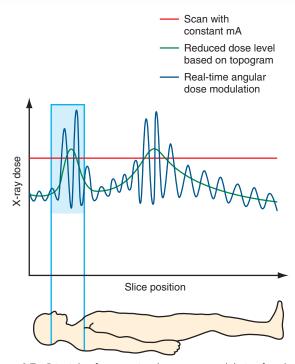
- Kilovoltage peak: 140
- Automatic exposure control (AEC) with maximal current limit of 800 mA
- Rotation time: 0.8 to 1.0 second
- Noise reduction filters
- Increase reconstruction thickness
- Noise-reducing reconstruction algorithms

proportional to the effective milliamperes, which is defined as the milliamperes (milliamperes × seconds per rotation) divided by the helical pitch (Box 6-3). The dependency of the dose to kilovoltage peak is more complicated. In general, the dose increases as a power function of kilovoltage peak (CTDI<sub>vol</sub> ~ kVp<sup>p</sup>) if all other parameters are fixed. The value of p is between 2 and 3 depending on the type of the scanner.<sup>15</sup>

Image quality is closely related to patient dose, and it is characterized by spatial resolution, contrast resolution, image noise, and other quantities. In practice, image noise has been widely used to judge the CT image quality because the detectability of low-contrast objects is strongly dependent on the contrast-to-noise ratio. The standard deviation of a region of interest in the image is usually used to represent the noise. For a given reconstruction kernel and slice thickness, the noise is inversely proportional to the square root of patient dose. To reduce the noise by a factor of 2, the dose must be increased by a factor of 4. In general, image quality is better when the patient dose is increased.

Many dose-reduction methods have been investigated and implemented over the past few years.<sup>16</sup>

The principle of automatic tube current modulation (ATCM) is illustrated in Figure 6-7. The scout images are first obtained to assess the patient size and attenuation properties at each cross



**Figure 6-7** Principle of automatic tube current modulation for a helical scan from shoulder to pelvis. Note the high tube current and strong modulation in shoulder and pelvis and lower tube current and low modulation in abdomen and thorax. (*Redrawn from Siemens SOMATOM Sensation 64 Application Guide.*)

#### BOX 6-3 ADJUSTABLE PARAMETERS FOR DOSE RADIATION

#### DECREASE

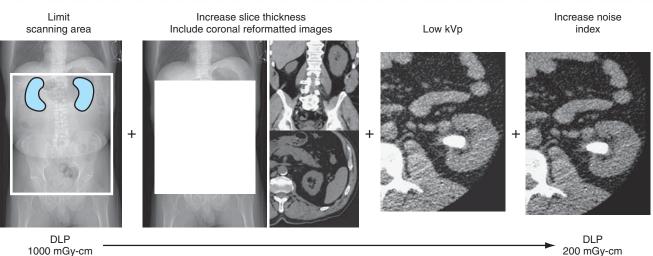
- Tube current
- Tube potential
- Gantry rotation time\*
- Scan length
- Overlap scanning
- Number of scan phases

#### **INCREASE**

- Pitch (table speed)\*
- Beam collimation

\*Provided other scanning factors are kept constant.

section along the z-direction. The current is modulated along the z-direction based on the information collected. The current also may change when the tube moves to a different location in the scan plane. The tube current is generally lower when the x-ray tube is in the anteroposterior direction because the patient thickness is smaller in that direction. It must be pointed out that using the automatic current modulation does not guarantee low patient dose. All current modulation software packages require users to specify the expected image quality. The expected image quality can be specified with an image noise or an image produced using reference milliamperes. It is the user's responsibility to define the proper image quality for a specific imaging task. If the specified image noise is too low, the patient dose may be higher than the dose using a fixed technique (Figure 6-8).



1000 mGy-cm

Total dose reduction by 40% to 70% from standard dose

Figure 6-8 Summary of strategies for dose reduction.

#### SUGGESTED READINGS

Hsieh J: Computed tomography: principles, design, artifacts, and recent advances, Bellingham, WA, 2003, SPIE Press.

Kalender W: Computed tomography: fundamentals, systems technology, image quality, applications, Munich, 2006, Publicis MCD Verlag.

Rruening R, Kuettner A, Flohr T: Protocols for multislice CT, Berlin, 2006, Springer-Verlag.

#### REFERENCES

- 1. Kulkarni NM, Pinho DF, Kambadakone AR, et al: Emerging technologies in CT-radiation dose reduction and dual-energy CT. Semin Roentgenol 48:192-202, 2013.
- 2. Mahesh M, Scatarige JC, Cooper J, et al: Dose and pitch relationship for a particular multislice CT scanner. AJR Am J Roentgenol 177:1273-1275, 2001.
- 3. Theocharopoulos N, Perisinakis K, Damilakis J, et al: Dosimetric characteristics of a 16-slice computed tomography scanner. Eur Radiol 16:2575-2585, 2006.
- 4. Mettler FA, Jr, Wiest PW, Locken JA, et al: CT scanning: patterns of use and dose. J Radiol Prot 20:353-359, 2000.
- 5. Graser A, Wintersperger BJ, Suess C, et al: Dose reduction and image quality in MDCT colonography using tube current modulation. AJR Am J Roentgenol 187:695-701, 2006.
- 6. Hsieh J: Investigation of an image artefact induced by projection noise inhomogeneity in multi-slice helical computed tomography. Phys Med Biol 48:341-356, 2003.

7. IMV 2006 CT Market Summary Report: Des Plains, IL, 2006, IMV Medical Information Division.

- 8. Lee CI, Haims AH, Monico EP, et al: Diagnostic CT scans: assessment of patient, physician, and radiologist awareness of radiation dose and possible risks. Radiology 231:393, 2004.
- 9. Mettler FA, Jr: Magnitude of radiation uses and doses in the United States: NCRP scientific committee 6-2 analysis of medical exposures. Presented at the 43rd annual meeting of the National Council on Radiation and Measurements, Arlington, VA, April 16-17, 2007, рр 9–10.
- U.S. Food and Drug Administration Preliminary 10. Public Health Notification: Possible malfunction of electronic medical devices caused by computed tomography (CT) scanning. 2008. <http://www.fda.gov/MedicalDevices/Safety/ AlertsandNotices/PublicHealthNotifications/ ucm061994.htm>.
- 11. Goldberg-Stein S, Liu B, Hahn P, et al: Body CT in pregnancy: how to best minimize fetal radia-

tion exposure. Presented before the 94th annual meeting of the Radiological Society of North America, Chicago, November 30-December 5, 2008.

- 12. National Council on Radiation Protection: Report 116: Limitation of Exposure to Ionizing Radiation. Bethesda, MD, 1993, National Council on Radiation Protection.
- 13. American Association of Physicists in Medicine: Report 96: The Measurement, Reporting, and Management of Radiation Dose in CT. College Park, MD, 2008, American Association of Physicists in Medicine.
- 14. Boone JM, Geraghty EM, Seibert JA, et al: Dose reduction in pediatric CT: a rational approach. Radiology 228:352-360, 2003.
- Nagal HD: Radiation Exposure in Computed To-15. mography. Hamburg, 2002, CTB Publications.
- McCollough CH, Bruesewitz MR, Kofler JM, Jr: CT dose reduction and dose management tools: overview of available options. Radiographics 26:503-512, 2006.

# **Recent Advances**

AVINASH KAMBADAKONE | KUMARESAN SANDRASEGARAN

For almost 4 decades, computed tomography (CT) has made a remarkable impact on clinical practice. The rapid advances in both CT technology and software have widened the clinical utility of CT of the abdomen and pelvis.<sup>1</sup> The benefits of multidetector CT (MDCT) over single-detector CT include increased temporal and spatial resolution, decreased image noise, and increased anatomic coverage. Better z-axis resolution and larger scan volumes result in improved multiplanar reconstruction in the coronal and sagittal planes. The reduced scanning time achieved by MDCT also helps reduce respiratory and motion artifacts.

Perfusion CT is an exciting CT innovation that allows functional evaluation of tissue vascularity. This technique has many potential applications in abdominopelvic oncologic imaging.<sup>2-4</sup> Dual-energy CT, using either a single source (single x-ray tube) or dual source (dual x-ray tube), is another advance that shows promise for a broad spectrum of abdominal and pelvic applications.<sup>5</sup> Other developments include scanners with 256 or 320 detector rows, superior detector materials (gemstone detector technology), volume or helical shuttle mode techniques, and use of dose reduction iterative reconstruction algorithms.<sup>6-8</sup> In this chapter an overview is provided of the recent advances in CT with emphasis on clinical applications.

# **Technical Aspects**

# ADVANCES IN X-RAY TUBE

Several advances in the x-ray tube in the past few years have enabled CT to broaden its utility in the realm of cardiac imaging and in tissue material differentiation (Table 7-1). One of the best-known advancements has been the introduction of dualsource CT (Somatom Definition, Siemens Medical Solutions, Forchheim, Germany). Dual-source CT contains two sets of x-ray tube and detector arrays, which are arranged in a single gantry perpendicular (90 degrees) to each other in the x-y plane (Figure 7-1, A).<sup>5,9,10</sup> Dual-source CT has three main advantages over the single-source scanners, depending on the mode of scan acquisition. Operating the two tubes at different tube potentials allows dual-energy scanning and thus has applications in tissue differentiation. When the two x-ray tubes are used in unison at equal tube potentials, the resultant increased photon flux permits scanning larger patients with acceptable noise. The third, and most explored, capability of dual-source CT is the improved temporal resolution achieved by the use of two x-ray tubes. By using the two tubes at identical kilovoltage peak levels, it is possible to acquire images using data from only 90 degrees of gantry rotation instead of the conventional 180 degrees of data required for the single-source CT. The resultant temporal resolution of only 83 ms is particularly advantageous in coronary artery imaging. It is possible to obtain diagnostic images at higher heart rates than previously possible and possibly obviate the need for beta-adrenergic blockers.<sup>9</sup>

Dual-energy scanning also can be performed using singlesource CT by rapid voltage and milliampere modulation (see Figure 7-1, *B*).<sup>5</sup> This technique may achieve dual-energy processing using projection data acquired in both axial and helical modes, unlike the image-based dual-energy processing of dual-source CT.<sup>5</sup> Theoretically, this permits accurate material decomposition and monochromatic CT image display, which should potentially facilitate more precise tissue characterization and also substantially decrease image artifacts.<sup>5</sup> Two disadvantages of single-source dual-energy scanning are the unequal noise levels that may result in the data sets owing to the rapid modulation of tube current and the fact that the use of the same filtration for the two energy beams may result in suboptimal spectral separation.<sup>5</sup>

# DUAL-ENERGY COMPUTED TOMOGRAPHY

Owing to their differing electron configurations, the atoms of different elements absorb x-rays with different frequency signatures. This phenomenon can be used, with limitations, to identify the elemental makeup of compounds, including calcium density in bones, to differentiate plaque from contrast-enhanced vessel lumen, to assess tissue fat, and to differentiate calcium and uric acid stones.<sup>11-14</sup> The ability of dual-energy CT to qualitatively and quantitatively assess calcium content has been used to assess urinary stones<sup>15,16</sup> and bone density more reliably than single-energy techniques.<sup>17</sup> The introduction of dual-source CT scanners has facilitated concurrent scanning with two different energy levels, avoiding even small misregistration artifacts.<sup>11,1</sup> The practical utility of DECT is likely to be enhanced by the introduction of rapid kilovoltage switching as another approach for dual-energy scanning.<sup>5,11,14,18</sup> A third approach also exists as an alternative for dual-energy scanning that involves a sandwich detector: the low-energy photons are absorbed in the top layers of the detector, and the higher energy photons are absorbed in the lower levels of the detector.<sup>5</sup>

#### Clinical Applications of Dual-Energy Computed Tomography in the Abdomen

For most clinical applications, dual-energy scanning is performed at the tube potentials of 80 and 140 kVp, which allows for optimum tissue material differentiation because the quality of dual-energy postprocessing is inversely related to the overlap of the spectra, which is least at these two energies.

1. *Virtual unenhanced images*: Reconstruction of the 80 kVp and 140 kVp image data sets allows generation of "virtual unenhanced images" that may preclude the routine need

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TABLE     Technical Details of Current Computed Tomography Technology				
	GE Discovery 750HD	Phillips Brilliance CT	Siemens Flash	Toshiba One
Rows (n $\times$ mm)	64 × 0.625	128 × 0.625 256 × 0.625	$2 \times 64 \times 0.6$	320 × 0.5
Width (cm)	4	8/16	3.8	16
Channels (n)	64	256/512	2 × 128	320
Tube power (kW)	100	120	2 × 100	72
Maximum current (mA	A) 800	950	2 × 850	600
Gantry rotation (ms)	350	270	280	350
Temporal resolution (	ms) 175	135	75	175

From Rubin GD: Cardiac CT technologies: what is important. In Abdominal Radiology Course 2009. Maui, Hawaii, 2009, Society of Gastrointestinal Radiology.

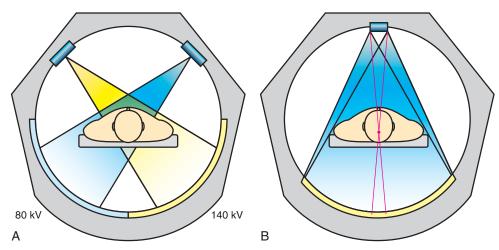


Figure 7-1 Diagrammatic illustration of dual-source computed tomography (CT) (A) with two x-ray tubes and detector assemblies and single-source dual-energy CT (B) with one x-ray tube and detector assembly. (A, Redrawn from art provided courtesy Christianne Leidecker, Siemens Medical Solutions; B, modified from art provided courtesy Mukta Joshi, GE Healthcare.)

for true unenhanced acquisitions.<sup>5,10</sup> Thus, a dual-energy contrast-enhanced acquisition could yield both unenhanced and contrast-enhanced CT images and therefore diminish radiation dose exposure to the patients.

- 2. Determination of stone composition: Dual-energy CT is a robust technique to determine the composition of urinary stones, particularly the differentiation of uric acid from non-uric acid stones, which has implications for treatment (Figure 7-2).<sup>15,16,19</sup> Uric acid stones may be treated with urinary alkalinization as a first-line treatment, whereas non-uric acid stones are usually treated by lithotripsy or surgically.<sup>15,16,19</sup>
- 3. *Evaluation of renal masses:* Dual-energy scanning can be used to generate a color-coded image that shows the distribution of iodine within a particular tissue. These iodine-based maps are sensitive for the detection of subtle enhancement and may be used to differentiate high-density benign cysts from solid renal masses.<sup>5,10</sup>
- 4. *Evaluation of adrenal masses:* In a study performed by Gnannt and associates,<sup>20</sup> good accuracy of virtual unenhanced images generated on dual-source, dual energy CT (dsDECT) was demonstrated in a study evaluating 42 patients with 51 lesions. Using conventional unenhanced

CT as a reference, the sensitivity, specificity, and accuracy for dsDECT virtual unenhanced images for classifying a lesion greater than 1 cm as probably benign were 95, 100, 97%, and 91, 100, 95%, respectively, for two independent readers.

- 5. *Evaluation of the pancreas:* To evaluate pancreatic adenocarcinoma using DECT, Patel and colleagues<sup>21</sup> looked at a group of 65 patients. They compared 70-keV images to contrast-to-noise ratio (CNR)-optimized 45-keV images. The statistically significant increase of lesion contrast at the CNR-optimized kilovoltage was almost double that of the 70-keV image.
- 6. *CT angiography:* Dual-energy techniques may be used for rapid and accurate removal of bony structures and calcified plaques during postprocessing of CT angiographic images. DECT angiography examination reduces radiation dose by 20% to 30%.<sup>5</sup>
- 7. *Other applications:* These include use of iodine maps for liver lesion characterization. Emerging indications for DECT in the gut include improved detection of bowel ischemia, evaluation of alternative contrast agents, and improved methods of electronic cleansing during CT colonography.

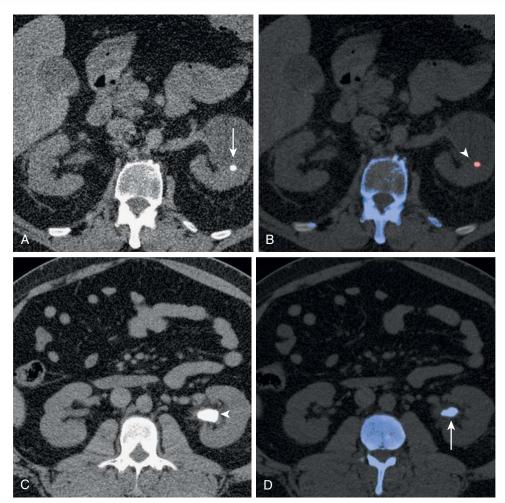


Figure 7-2 A, Axial unenhanced abdominal computed tomography (CT) scan in a 43-year-old man shows a calculus in the left midpole (arrow). B, Corresponding color-coded dual-energy postprocessed image shows the calculus coded as red (arrowhead) indicating a uric acid stone. C, Axial unenhanced abdominal CT scan in a 36-year-old man shows a large calculus in the left renal pelvis (arrow). D, Corresponding color-coded dual-energy image after postprocessing shows the calculus coded as blue (arrowhead), indicating a non–uric acid stone.

#### ADVANCES IN DETECTOR TECHNOLOGY

Currently, 64-slice CT scanners are the preferred MDCT technology. The detector widths in the currently available 64-slice CT scanners range from 2.8 to 4 cm and allow acquisition of slices with widths ranging from 0.5 to 0.625 mm.<sup>22</sup> Reformatting of images in orthogonal planes is possible with isotropic resolution.<sup>22</sup> The craniocaudal coverage of the 64-slice scanners is limited to 3.2 to 4.0 cm, which restricts cine imaging over a wider coverage area.<sup>6,7</sup> Because the value of CT in the realm of functional imaging is gradually increasing, it is desirable to have a wider coverage area for cine imaging. This has led to the emergence of newer CT scanners with wider detector arrays with increasing numbers of rows.<sup>67,22,23</sup>

#### Wide-Area Detector

The latest entrants to the CT arena are scanners with a number of detectors in excess of 100 (128, 256, and 320), which eliminate the need for spiral scanning and has the potential to achieve a "single-shot" scan. The 128-slice scanner has a fluid metalcooled x-ray tube and a 128-row detector array with coverage of 8 cm at 0.625 mm thickness (see Table 7-1).<sup>22</sup> Whereas the spiral scanning option with this CT allows a coverage of 8 cm, operating in the joggle mode (i.e., back-and-forth movements of the two table positions) helps expand the effective coverage for dynamic imaging.<sup>20</sup> The 256-slice CT scanner is able to achieve an isotropic resolution of less than 0.5 mm for a wide craniocaudal coverage in one rotation.<sup>7</sup> The 320-slice dynamic volume CT scanner has a gantry with an aperture of 70 cm and a 70-kW x-ray tube with detector width of 16 cm along the rotational axis of the gantry. The scanner has 320 rows of 0.5-mm-thick detector elements.<sup>24</sup> The wide detector coverage (16 cm) makes it possible to scan the entire heart without table motion and has the potential to allow dynamic imaging over a single heartbeat.<sup>22</sup> This scanner also may allow functional assessment of entire organs or large tumors.<sup>22</sup>

#### New Detector Materials

Another recent innovation in the CT detector systems has been the development of detectors with higher sensitivity to radiation and faster sampling rates. The novel gemstone detector is a garnet-based scintillator that has a fast primary speed (0.03  $\mu$ s) and a short afterglow.<sup>25</sup> This detector material allows the use of rapid kilovoltage switching to acquire dual-energy data with

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almost simultaneous spatial and temporal registration.<sup>2,25</sup> As a result, the resolution is improved and artifacts resulting from beam hardening and metals are reduced.<sup>22,25</sup>

#### Sandwich Detectors

As previously discussed, DECT can be primarily accomplished (1) by scanning with two different energy spectra from two sources operating at different voltages, (2) from a single source by rapid kilovoltage switching, or (3) by analyzing the energy spectrum with a multilayered detector.<sup>22</sup> This third approach is not yet available in clinical practice. The design of this detector assembly consists of a first layer that predominantly receives photons with lower energy and a second, deeper layer that receives photons with higher energy.<sup>22</sup> The signal readout from both detector layers can be used separately for spectral analysis.<sup>22</sup>

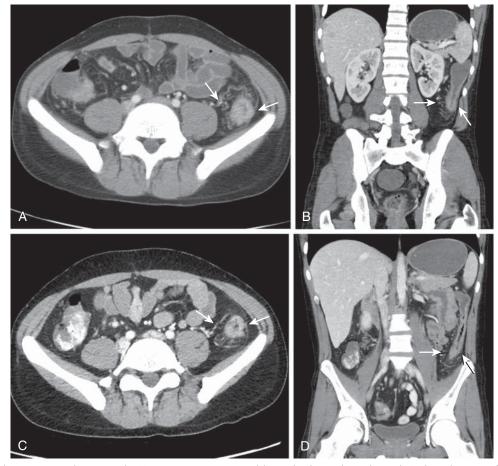
#### NEW RECONSTRUCTION ALGORITHMS

Concern is increasing for the potentially harmful effects of machine-induced radiation.<sup>24</sup> Several approaches have been proposed to reduce radiation doses in CT examinations, such

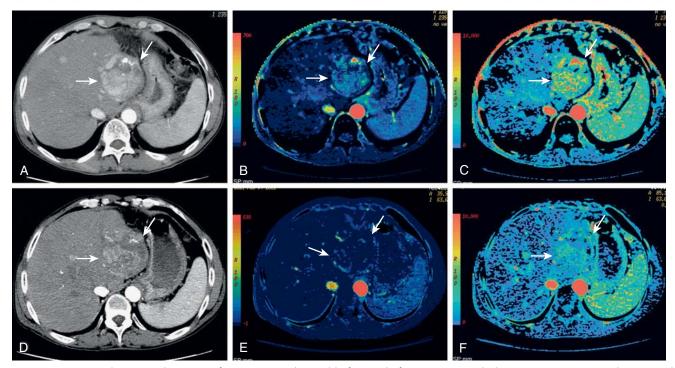
as the use of lower tube current or voltage.<sup>26</sup> An undesirable consequence of most such techniques is the excessive image noise that can deteriorate image quality and diagnostic performance. A step ahead is the emerging use of new image reconstruction techniques, such as full or adaptive statistical iterative reconstruction (ASIR), which have the ability to eliminate image noise and also maintain lesion conspicuity in low-dose CT examinations. The algorithm typically used for reconstruction of CT data is filtered back-projection. Reconstructing CT data with a combined filtered back-projection and ASIR technique can reduce radiation dose by 20% to 80% for various abdominal applications (Figure 7-3).

# PERFUSION COMPUTED TOMOGRAPHY

CT perfusion imaging has been investigated as a functional tool to give information that is complementary or superior to anatomic information of conventional CT.<sup>2-4</sup> Perfusion CT measures the temporal changes in tissue density after intravenous injection of contrast medium bolus using a series of dynamically acquired images.<sup>2</sup> Perfusion imaging has attained significance in the field of oncology owing to the increasing use of



**Figure 7-3** Multiplanar computed tomography (CT) images in a 22-year-old man (body weight, 56 kg) with Crohn's disease with multiple exacerbations. Axial (A) and coronal (B) contrast-enhanced CT images obtained during initial evaluation demonstrate wall thickening and enhancement with increased surrounding perienteric vascularity in the descending colon. Biopsy confirmed Crohn's disease. CT dose for this examination was 11.6 mSv. The patient underwent remission after therapy with corticosteroids. One year later, the patient presented with a relapse. Repeat axial (C) and coronal (D) contrast-enhanced CT scan images were obtained using the adaptive statistical iterative reconstruction technique. The image quality and depiction of enteric and extraenteric changes are comparable to the previous examination. The radiation dose for this CT study was 5.5 mSv (i.e., a radiation dose reduction of 53%).



**Figure 7-4** Computed tomography (CT) perfusion images obtained before and after treatment with the antiangiogenic agent bevacizumab (Avastin) in a 56-year-old man with hepatocellular carcinoma. **A**, Axial contrast-enhanced CT image in the dynamic phase shows the avidly enhancing rounded hepatocellular carcinoma (*arrows*) in the left lobe with corresponding colored perfusion maps demonstrating increased (**B**) blood flow (95 mL/100 g/min) and (**C**) increased blood volume (6.2 mL/100 g). After treatment with bevacizumab, axial contrast-enhanced CT image (**D**) shows reduced enhancement, with corresponding colored perfusion maps demonstrating (**E**) reduction in the blood flow (24 mL/100 g/min) and (**F**) reduced blood volume (1.64 mL/100 g).

targeted therapies such as antiangiogenic drugs targeting tumor vascularity, tumor ablation, and selective internal radiation with yttrium-90 particles. Because these therapies do not cause substantial change in tumor dimensions for several months, functional imaging techniques such as perfusion CT and magnetic resonance imaging have shown promise in better assessing the tumor response long before changes in tumor dimension (Figure 7-4).<sup>2-4,27</sup> The excellent spatial resolution of perfusion CT is an advantage compared with other functional imaging techniques such as positron emission tomography. Another key advantage of perfusion CT is the linear relation between iodine concentration and tissue density changes, which makes quantification of tissue vascularity much simpler and straightforward.<sup>2-4</sup> Moreover, faster scanning times within a short breath-hold that are possible with current-generation MDCT scanners and easy availability of commercial software for perfusion analysis make it a desirable and practical technique for various abdominal applications.

In the realm of oncologic imaging, perfusion CT has been found to be effective to characterize tumor, detect occult tumor, and assess tumor response to therapy and in prognostic evaluation.<sup>4,27</sup> Perfusion CT also has been found to be a useful tool for assessment of tissue perfusion in various nononcologic applications. However, certain limitations remain. The total coverage area over which the perfusion analysis can be performed is limited to 2 to 4 cm depending on the CT technology. Patient movement during dynamic CT data acquisition may degrade image quality, resulting in inaccurate perfusion measurements. Another concern of repeat perfusion CTs is the risk of exposure to ionizing radiation, especially for nononcologic indications.

#### Technique

A limited noncontrast CT scan is performed initially for localization of the tumor or the organ in question. The dynamic CT acquisition is performed after intravenous administration of a contrast bolus of 40 to 70 mL at a rate ranging from 3.5 to 10 mL/s. The dynamic CT acquisition involves a first-pass phase (usually 45 to 60 seconds) followed by a delayed phase (usually 2 to 10 min) for optimal assessment of the tumor perfusion and permeability measurements. The dynamic CT data are then postprocessed with perfusion software to generate colored perfusion maps of blood flow, blood volume, mean transit time, and permeability. The quantitative perfusion parameters are then obtained by drawing the region of interest around the tumor tissue. Perfusion software, the analytical methods employed for postprocessing, and the various quantitative perfusion parameters obtained vary across scanners and among commercial vendors.<sup>2</sup>

#### Abdominopelvic Applications of Perfusion Computed Tomography

**Liver Tumors.** The detection of higher perfusion parameters in metastatic lesions using CT perfusion has been found to be a good prognostic indicator suggesting optimal response to treatment. In hepatocellular carcinoma, perfusion CT has benefits in differential diagnosis, evaluating tumor aggressiveness, and monitoring therapeutic effects.<sup>2,28,29</sup> **Pancreatic Tumors.** On perfusion CT, high blood perfusion was observed in hypervascular tumors such as insulinomas compared with background pancreatic parenchyma.<sup>30</sup>

**Colorectal Cancer.** The predominant application of perfusion CT in colorectal cancer is in diagnosis and in assessing response to treatment.<sup>2,31,32</sup> Perfusion CT has been found to distinguish colonic wall thickening resulting from diverticulitis from colorectal carcinoma based on the high perfusion values in the latter.<sup>33</sup>

**Prostate Cancer.** A potential application of perfusion CT is in the identification of tumor foci within the prostate, thus enabling targeted radiotherapy for the tumor foci with minimal radiation to the surrounding tissues.<sup>34,35</sup>

**Lymphoma.** The data on the utility of the perfusion CT in patients with lymphoma are limited because angiogenesis is not a predominant feature of lymphoma.<sup>36</sup>

#### Nononcologic Applications

Perfusion CT facilitates quantification of organ perfusion in liver, kidney, and pancreas in diverse applications such as renal functional assessment, renal transplant rejection, evaluation of the degree of hepatic fibrosis and cirrhosis, and determination of pancreatic ischemia and necrosis in acute severe pancreatitis.<sup>2</sup>

#### SUGGESTED READINGS

- Fletcher JG, Takahashi N, Hartman R, et al: Dualenergy and dual-source CT: is there a role in the abdomen and pelvis? *Radiol Clin North Am* 47:41–57, 2009.
- Geleijns J, Salvado Artells M, de Bruin PW, et al: Computed tomography dose assessment for a 160 mm wide, 320 detector row, cone beam CT scanner. *Phys Med Biol* 54:3141–3159, 2009.

#### REFERENCES

- Sahani DV, Yaghmai V: Advances in MDCT: preface. Radiol Clin North Am 47:xiii–xiv, 2009.
- Kambadakone AR, Sahani DV: Body perfusion CT: technique, clinical applications, and advances. *Radiol Clin North Am* 47:161–178, 2009.
- 3. Miles KA: Perfusion CT for the assessment of tumour vascularity: which protocol? *Br J Radiol* 76(Spec No 1):S36–S42, 2003.
- 4. Miles KA: Perfusion imaging with computed tomography: brain and beyond. *Eur Radiol* 16(Suppl 7):M37–M43, 2006.
- Fletcher JG, Takahashi N, Hartman R, et al: Dual-energy and dual-source CT: is there a role in the abdomen and pelvis? *Radiol Clin North Am* 47:41–57, 2009.
- Mori S, Endo M, Obata T, et al: Properties of the prototype 256-row (cone beam) CT scanner. *Eur Radiol* 16:2100–2108, 2006.
- Mori S, Endo M, Obata T, et al: Clinical potentials of the prototype 256-detector row CT-scanner. Acad Radiol 12:148–154, 2005.
- Hein PA, Romano VC, Lembcke A, et al: Initial experience with a chest pain protocol using 320slice volume MDCT. *Eur Radiol* 19:1148–1155, 2009.
- Achenbach S, Anders K, Kalender WA: Dualsource cardiac computed tomography: image quality and dose considerations. *Eur Radiol* 18:1188–1198, 2008.
- Graser A, Johnson TR, Chandarana H, et al: Dual energy CT: preliminary observations and potential clinical applications in the abdomen. *Eur Radiol* 19:13–23, 2009.
- 11. Flohr TG, McCollough CH, Bruder H, et al: First performance evaluation of a dual-source CT (DSCT) system. *Eur Radiol* 16:256–268, 2006.
- Raptopoulos V, Karellas A, Bernstein J, et al: Value of dual-energy CT in differentiating focal fatty infiltration of the liver from low-density masses. AJR Am J Roentgenol 157:721–725, 1991.

- Graser A, Johnson TR, Chandarana H, et al: Dual energy CT: preliminary observations and potential clinical applications in the abdomen. *Eur Radiol* 19:13–23, 2009.
- Kambadakone AR, Sahani DV: Body perfusion CT: technique, clinical applications, and advances. *Radiol Clin North Am* 47:161–178, 2009.
- Morgan DE: Dual-energy CT of the abdomen. *Abdom Imaging* 39:108–134, 2014.
- Rogalla P, Kloeters C, Hein PA: CT technology overview: 64-slice and beyond. *Radiol Clin North Am* 47:1–11, 2009.

 Ruzsics B, Lee H, Powers ER, et al: Images in cardiovascular medicine: myocardial ischemia diagnosed by dual-energy computed tomography: correlation with single-photon emission computed tomography. *Circulation* 117:1244– 1245, 2008.

- Ruzsics B, Lee H, Zwerner PL, et al: Dual-energy CT of the heart for diagnosing coronary artery stenosis and myocardial ischemia: initial experience. *Eur Radiol* 18:2414–2424, 2008.
- Graser A, Johnson TR, Bader M, et al: Dual energy CT characterization of urinary calculi: initial in vitro and clinical experience. *Invest Radiol* 43:112–119, 2008.
- 16. Park J, Chandarana H, Macari M, et al: Dual energy computed tomography applications in uroradiology. *Curr Urol Rep* 13:55–62, 2012.
- 17. Laan RF, van Erning LJ, Lemmens JA, et al: Single-versus dual-energy quantitative computed tomography for spinal densitometry in patients with rheumatoid arthritis. *Br J Radiol* 65:901–904, 1992.
- Sosna JST, Mifra A, Amin-Spector S, et al: Improved lesion conspicuity with single source dual energy MDCT. Presented at the scientific assembly and annual meeting program of the Radiological Society of North America. Oak- brook, IL, 2007, Radiological Society of North America, SSC14-09.
- Matlaga BR, Kawamoto S, Fishman E: Dual source computed tomography: a novel technique to determine stone composition. *Urology* 72:1164–1168, 2008.
- Gnannt R, Fischer M, Goetti R, et al: Dualenergy CT for characterization of the incidental adrenal mass: preliminary observations. *AJR Am J Roentegnol* 198:138–144, 2012.
- Patel BN, Thomas JV, Lockhart ME, et al: Single-source dual-energy spectral multidetector CT of pancreatic adenocarcinoma: optimization of energy level viewing significantly

increases lesion contrast. Clin Radiol 68:148-154, 2013.

- Rogalla P, Kloeters C, Hein PA: CT technology overview: 64-slice and beyond. *Radiol Clin North Am* 47:1–11, 2009.
- Geleijns J, Salvado Artells M, de Bruin PW, et al: Computed tomography dose assessment for a 160 mm wide, 320 detector row, cone beam CT scanner. *Phys Med Biol* 54:3141–3159, 2009.
- 24. Rubin GD: Cardiac CT technologies: what is important. In *Abdominal radiology course 2009*, Maui, Hawaii, 2009, Society of Gastrointestinal Radiology.
- Brenner DJ, Hall EJ: Computed tomography: an increasing source of radiation exposure. N Engl J Med 357:2277–2284, 2007.
- Lee CH, Goo JM, Ye HJ, et al: Radiation dose modulation techniques in the multidetector CT era: from basics to practice. *Radiographics* 28:1451–1459, 2008.
- Goh V, Padhani AR: Imaging tumor angiogenesis: functional assessment using MDCT or MRI? *Abdom Imaging* 31:194–199, 2006.
- Sahani DV, Holalkere NS, Mueller PR, et al: Advanced hepatocellular carcinoma: CT perfusion of liver and tumor tissue—initial experience. *Radiology* 243:736–743, 2007.
- 29. Zhu AX, Holalkere NS, Muzikansky A, et al: Early antiangiogenic activity of bevacizumab evaluated by computed tomography perfusion scan in patients with advanced hepatocellular carcinoma. *Oncologist* 13:120–125, 2008.
- Xue HD, Jin ZY, Liu W, et al: [Perfusion characteristics of normal pancreas and insulinoma on multi-slice spiral CT]. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao* 28:68–70, 2006.
- Bellomi M, Petralia G, Sonzogni A, et al: CT perfusion for the monitoring of neoadjuvant chemotherapy and radiation therapy in rectal carcinoma: initial experience. *Radiology* 244: 486–493, 2007.

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- Sahani DV, Kalva SP, Hahn PF: Imaging of rectal cancer. Semin Radiat Oncol 13:389–402, 2003.
- 33. Goh V, Halligan S, Taylor SA, et al: Differentiation between diverticulitis and colorectal cancer: quantitative CT perfusion measurements versus morphologic criteria—initial experience. *Radiology* 242:456–462, 2007.
- Henderson E, Milosevic MF, Haider MA, et al: Functional CT imaging of prostate cancer. *Phys Med Biol* 48:3085–3100, 2003.
- 35. Jeukens CR, van den Berg CA, Donker R, et al: Feasibility and measurement precision of 3D quantitative blood flow mapping of the prostate using dynamic contrast-enhanced multi-slice CT. *Phys Med Biol* 51:4329–4343, 2006.
- 36. Dugdale PE, Miles KA, Bunce I, et al: CT measurement of perfusion and permeability within lymphoma masses and its ability to assess grade, activity, and chemotherapeutic response. *J Comput Assist Tomogr* 23:540–547, 1999.

# **Computed Tomography Contrast Media and Principles** of Contrast Enhancement

SHETAL N. SHAH | RUPAN SANYAL

All radiologic contrast media available for intravascular use depend on iodine for their radiopacity. Ideally, contrast media should be inert in every respect. But unlike other therapeutic medications, contrast media are used in larger quantities and participate in numerous physiologic and pharmacokinetic interactions after intravenous administration. Their interactions not only affect tissue characteristics but also may have significant effects on patient health.

### **Contrast Enhancement Principles**

The principle of contrast enhancement is based on photoelectric interaction of the iodine atom with x-rays. The binding energy of the inner K shell electron of the iodine atom is called its K-edge and is equal to 33.2 keV. The mean energy of diagnostic radiographs is close to this value. When diagnostic radiographs interact with iodine atoms in the body there is increased absorption of the x-rays by the iodine atoms compared with the surrounding soft tissues. The attenuation of the x-ray beam increases with the concentration of iodine in the tissue because of more K shell interactions. This is the fundamental basis of contrast enhancement. There is a linear relation between iodine concentration and attenuation. Every milligram of iodine in a milliliter of blood or cubic centimeter of tissue elevates the attenuation by 25 Hounsfield units (HU).

# **Types of Contrast Media**

All currently used computed tomography (CT) contrast agents are based on the triiodinated benzene ring. Whereas the iodine atom is responsible for the radiopacity of contrast media, the organic carrier is responsible for its other properties, such as osmolality, tonicity, hydrophilicity, and viscosity. The organic carrier is responsible for most of the adverse effects and has received a lot of attention from researchers. Some patients react to small amounts of contrast media, but most of the adverse effects are mediated by the large osmotic load. Thus, over the past few decades researchers have focused on developing contrast media that minimize the osmotic load after contrast agent administration.

Contrast media are classified as ionic or nonionic and as monomers or dimers. Ionic contrast media dissolve in water to dissociate into an iodinated benzene ring containing an iodized carboxyl group and a cation. Nonionic contrast media

are water soluble (hydrophilic) but do not dissociate in solution. Monomers have a single triiodinated benzene ring, whereas dimers have a double benzene ring containing six iodine atoms. Figure 8-1 shows the chemical structure of contrast media molecules.

The most commonly used classification of contrast media is by their osmolality, which is defined as the number of osmotically active particles per kilogram of solvent. This is determined by the size of the contrast media molecule and whether it dissociates in solution. Table 8-1 lists commonly used contrast media.

#### HIGH OSMOLAR CONTRAST MEDIA

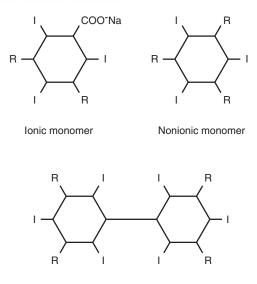
Ionic monomers consisting of a cation (e.g., sodium, meglumine) and an anion (iodine-containing benzoic acid derivative) were developed in the 1950s. These molecules dissociate in solution to give three atoms of iodine for every two particles in solution (iodine atoms to particle in solution ratio of 3:2). The osmolality of these agents ranges from 1500 to 1800 mOsm/kg, whereas that of human plasma is 290 mOsm/kg; thus, they are named high osmolar contrast media. Because of the higher incidence of adverse reactions, these agents are infrequently used today.

#### LOW OSMOLAR CONTRAST MEDIA

Nonionic monomers are widely used today and have better solubility and lower toxicity compared with ionic monomers.<sup>2</sup> Nonionic monomers consist of a benzoic acid derivative containing three iodine atoms per molecule but do not contain an ionizing carboxyl group (iodine atoms to particle in solution ratio of 3:1). These particles do not dissociate in solution. Their osmolality is 600 to 700 mOsm/kg (double that of human plasma). Other than eliminating ionicity and reducing osmolality, newer low osmolar contrast media also have an increased number of, and more evenly distributed, hydroxyl groups. This improves their hydrophilicity by restricting access to the lipophilic areas of the molecule, decreasing affinity for cell membrane and plasma proteins and improving tolerance.

Dimeric ionic contrast media contain six atoms of iodine per molecule. They dissociate in solution into an anion (six-iodine atom double-benzene ring) and a cation, yielding a ratio of iodine atoms to particle in solution of 6:2 or 3:1. The

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#### Nonionic dimer

**Figure 8-1** Diagram showing the molecular structure of ionic monomer, nonionic monomer, and nonionic dimer contrast media molecules.

TABLE 8-1	Classification of Contrast Media				
Classification		lodine per Particle Ratio	Osmolality (mOsm/kg)		
High osmolar contrast media Diatrizoate (Hypaque) Iothalamate (Conray)		3:2	1500-1800		
Nonionic monomer low-osmolar contrast media lohexol (Omnipaque) lomeprol (lomeron) lopamidol (Niopam) lopromide (Ultravist) loversol (Optiray) loxilan (Oxilan) lobitridol (Xenetix)		3:1	600-700		
Ionic dimer Iow-osmolar contrast media Ioxaglate (Hexabrix)		3:1	560		
Nonionic dimer isosmolar contrast media Iodixanol (Visipaque) Iotrolan (Isovist)		6:1	300		

osmolality of ionic dimers is only slightly lower than that of nonionic monomers.

#### ISOSMOLAR CONTRAST MEDIA

Nonionic dimers have been more recently developed. These molecules consist of a double-benzene ring with six iodine atoms. Because they do not dissociate in solution, they have a ratio of iodine atoms to particle in solution of 6:1 and are isosmolar to plasma. The larger molecule size in isosmolar contrast media results in higher viscosity. Nonionic dimers have generally been shown to be less nephrotoxic compared with other compounds, but this is not established.<sup>3</sup>



**Figure 8-2** Axial image arterial-phase computed tomography scan showing hyperenhancing hepatocellular carcinoma.

### **Pharmacokinetics**

All currently used iodinated contrast media have low lipid solubility. Contrast media molecules are not metabolized in the body but are excreted by the kidney via glomerular filtration without tubular reabsorption. They have a half-life of 2 hours in patients with normal renal function, and 75% of the dose is excreted within 4 hours of administration.<sup>2</sup>

# **Factors Affecting Enhancement**

A multitude of factors determine the enhancement of a particular organ or tissue after contrast media administration. Broadly, these can be divided into organ-specific factors, patient-related factors, and injection-related factors.

#### **ORGAN-SPECIFIC FACTORS**

The enhancement patterns of organs vary mainly because of differences in vascular supply. Factors that affect enhancement include vascular anatomy, vascular resistance, and percentage of cardiac output received.

### Liver

Seventy-five percent of the hepatic blood supply is from the portal venous system, and the remaining 25% is from the hepatic arterial circulation. This unique dual blood supply of the liver can be exploited to bring out the differences between normal parenchyma and pathologic lesions. The hepatic arterial phase occurs 20 to 30 seconds after the start of intravenous contrast injection (or 20- to 30-second delay). During this phase, hepatic artery "hypervascular tumors" enhance (Figure 8-2). The normal hepatic parenchyma shows only minimal enhancement during this phase. The hepatic parenchyma enhances only after the contrast media pass through the splanchnic or splenic circulation and reach the portal vein. This phase is known as the *portal venous phase* (60- to 90-second

delay). Hypovascular lesions are relatively hypoattenuating compared with the parenchyma during this phase.

After intravenous injection, the contrast media rapidly diffuse along the concentration gradient into the extravascular (interstitial) space. This redistribution occurs by passive diffusion along the concentration gradient until equilibrium is reached in the equilibrium phase (1.5- to 3-minute delay). Contrast media accumulate in the interstitial spaces of the tumor, reducing the attenuation difference with the hepatic parenchyma. The onset of the equilibrium phase depends on injection duration. Because the attenuation difference between tumor and normal parenchyma is lost in the equilibrium phase, hepatic imaging must be completed before the equilibrium phase.<sup>1,4,5</sup>

#### Pancreas

Although pancreas contrast dynamics are not as well defined as for the liver, the enhancement can be divided into arterial, parenchymal, and portal venous phases. The initial arterial phase (20- to 25-second delay) best opacifies the arterial tree and is followed by the pancreatic phase (40- to 45-second delay) when the parenchymal enhancement is maximum. The portal venous phase (60- to 70-second delay) opacifies the portal veins and is also useful for evaluating hepatic metastatic disease. Pancreatic neuroendocrine tumors are hypervascular and are best seen on arterial phase,<sup>6,7</sup> whereas the peak tumor to parenchymal attenuation difference for hypovascular malignancies (e.g., adenocarcinoma) is best appreciated later during the parenchymal or portal venous phase.<sup>8</sup> Most practices use a biphasic pancreatic protocol, with some variation in the exact timing.

#### Kidneys

The kidney has unique enhancement characteristics because of the greater vascularity of the renal cortex compared with the medulla, which results in greater enhancement of the renal cortex compared with the medulla during the corticomedullary phase (25- to 35-second delay). Small renal tumors can be obscured by this differential enhancement. A more homogeneous enhancement occurs during the nephrographic phase (90- to 110-second delay), which is primarily used to detect renal parenchymal tumors. A more delayed excretory phase (up to 8- to 10-minute delay) is used to opacify the collecting system and ureter and also in CT urography.<sup>9</sup>

#### PATIENT-RELATED FACTORS

In a healthy patient, the only significant factor that determines the amount of iodine required to achieve desired enhancement is body weight. Patient body weight is inversely related to hepatic enhancement, and the total iodine dose needs to increase with increasing body weight to achieve optimal enhancement. Certain comorbid conditions, such as cardiac failure, can alter circulation time and increase the time required to achieve maximal aortic and hepatic enhancement.

#### **INJECTION-RELATED FACTORS**

The total amount of iodine administered per second is obtained by multiplying the injection rate by the iodine concentration and is known as the *iodine flux*. Increasing iodine flux by increasing the rate of injection or iodine concentration results in higher and earlier peak of aortic enhancement.

#### Test Bolus

A fixed delay before start of contrast injection is not advisable for dedicated hepatic or arterial studies. The injection of a small test bolus (15 to 20 mL) followed by nonincremental CT acquisition helps determine the transit time of contrast agent from site of injection to the reference vessel.

#### **Contrast Medium Concentration**

If the total iodine dose is administered using a contrast medium containing a higher concentration of iodine, the total amount of contrast agent and injection duration can be decreased. When this is done, the intravascular iodine concentration increases and the peak aortic enhancement is higher and occurs earlier. The magnitude of enhancement in the hepatic arteries as well as any hypervascular lesion in the arterial phase are also increased. Although the peak hepatic enhancement occurs earlier with increasing contrast agent concentration, the magnitude of hepatic enhancement is unchanged because this depends on the total iodine dose. Thus, whereas 300 to 350 mg/ mL is used for most adult patients for body imaging, a higher concentration (370 to 400 mg/mL) can be used when arteries or hypervascular lesions need to be evaluated. A lower concentration, 240 mg/mL, provides adequate contrast enhancement in thin patients.<sup>1,4</sup>

### **Contrast-Induced Nephropathy**

Contrast-induced nephropathy is defined as an increase of 25% or more or an absolute increase of 0.5 mg/dL or more in serum creatinine concentration from a baseline value at 48 to 72 hours after exposure to intravenous contrast media in absence of any other cause.9ª In 80% of cases, the serum creatinine concentration begins to rise within 24 hours after contrast medium administration. The serum creatinine concentration typically peaks at 3 to 5 days and returns to baseline within 1 to 3 weeks.<sup>10,11</sup> Contrast-induced nephropathy varies from an asymptomatic nonoliguric transient form to severe oliguric acute renal failure requiring dialysis. The extensive use of contrast media in recent years has resulted in an increased incidence of iatrogenic renal function impairment. Contrast-induced nephropathy is now responsible for 11% of cases of hospital-acquired renal impairment. Coronary angiography and percutaneous coronary interventions are associated with higher rates and severity of contrast-induced nephropathy compared with intravenous contrast used in radiologic procedures.

#### **RISK FACTORS**

It is important to identify risk factors for contrast-induced nephropathy in every patient so appropriate measures can be taken before intravenous contrast agent administration.

#### Preexisting Renal Disease

Patients having preexisting renal disease with elevated creatinine concentrations are at highest risk for contrast-induced nephropathy. However, the serum creatinine concentration is not a good indicator of renal function to assess for the risk for contrast-induced nephropathy because it varies with age, muscle mass, physical activity, and gender. The estimated glomerular filtration rate provides a more accurate estimation of renal function. An estimated glomerular filtration rate of 60 mL/min/1.73 m<sup>2</sup> is considered a cutoff for identifying patients at a high risk for contrast-induced nephropathy.<sup>12,13</sup>

#### Diabetes

If patients with diabetes have concomitant diabetic nephropathy, a higher incidence of contrast-induced nephropathy has been noted. However, in the absence of an underlying renal disorder and any other risk factor, the rate of contrast-induced nephropathy in individuals with diabetes is comparable to that in the general population.<sup>14</sup>

#### Age

Older age is an independent risk factor for contrast-induced nephropathy. This is likely multifactorial, including age-related changes in the kidneys and other comorbidities.

#### **Other Risk Factors**

Congestive heart failure, anemia, dehydration, hypotension, myeloma, and recent use of nephrotoxic drugs all increase the risk for contrast-induced nephropathy. The presence of more than one risk factor may have an additive effect.<sup>10</sup>

#### PREVENTION

The pathophysiology of contrast-induced nephropathy is not clearly understood. Altered rheologic properties, renal vasoconstriction, certain paracrine factors, and direct toxic effects on renal epithelial cells all seem to play a role. It has been noted that dehydration increases the risk for contrast-induced nephropathy, so hydrating a patient before contrast agent administration is recommended. Volume supplementation increases renal blood flow, reduces renal vasoconstriction, reduces dwell time of contrast agent within the kidney, dilutes the agent, and avoids tubular obstruction.

Saline supplementation has been established as an inexpensive and effective method of preventing contrast-induced nephropathy in high-risk patients. Intravenous volume supplementation is most effective when isotonic saline is started several hours before the procedure and continued several hours after. Sodium bicarbonate reduces free radical formation and also can be used for volume supplementation. However, it should be kept in mind that a high infusion rate or high total fluid volume may result in volume overload and trigger pulmonary edema in patients with predisposing cardiac conditions.<sup>15</sup> Pharmacologic agents such as N-acetylcysteine have been used to reduce nephrotoxicity through antioxidant and vasodilatory effects. However, there is no conclusive evidence to show that it provides consistent protection against contrastinduced nephropathy.<sup>14</sup>

Low osmolar contrast media have been shown to reduce the incidence of contrast-induced nephropathy in patients with impaired renal function compared with high osmolar contrast media. Whether the newer isosmolar agents have an advantage over low osmolar contrast media in reducing contrast-induced nephropathy is yet to be established.

# **Adverse Effects of Contrast Media**

Adverse reactions to contrast media can be classified as general and organ specific, such as contrast-induced nephropathy, or as cardiovascular, pulmonary, and neurotoxic.

#### **GENERAL ADVERSE REACTIONS**

General adverse reactions can be divided into acute reactions, occurring within 1 hour of contrast agent administration, and delayed reactions occurring between 1 hour and 1 week of administration.

#### Acute Reactions

Acute reactions can be divided into mild, moderate, and severe. Table 8-2 lists the clinical presentation of each subtype. The incidence of general adverse reactions is lower with the use of low osmolar contrast media than with high osmolar contrast media. Mild reactions are seen in 15% of patients given high osmolar contrast media compared with 3% given low osmolar contrast media, whereas very severe reactions are seen in 0.04% of patients given high osmolar contrast media. However, the incidence of fatal reactions (1:170,000) is the same for low and high osmolar contrast media.<sup>2</sup>

There are several predisposing factors to general contrast adverse reactions. These are listed in Box 8-1. The probability of a patient having a general adverse reaction is much higher in patients having these predisposing factors.<sup>16</sup>

#### **Delayed Reactions**

Delayed general adverse reactions occur between 1 hour and 7 days after contrast media administration. They are less common than acute reactions. Delayed reactions usually are mild and include skin manifestations. However, rare cases of more serious delayed effects such as hypotension, dyspnea, and shock can occur. There have been reports of increased delayed reactions with new isosmolar nonionic dimeric agents, resulting in withdrawal of iotrolan for intravenous use.<sup>17</sup>

TABLE 8-2	Clinical Presentation of Acute General Reactions to Contrast Media			
Mild		Moderate	Severe	
Pain Heada	a, vomiting che rticaria	Severe vomiting Extensive urticaria Moderate hypotension Laryngeal edema Bronchospasm	Severe manifestations of moderate symptoms Pulmonary edema Circulatory collapse Cardiac arrhythmia Seizures Unconsciousness	

#### BOX 8-1 PREDISPOSING FACTORS FOR GENERAL ADVERSE REACTIONS

- Asthma
- Prior adverse reaction to contrast media (excluding mild flushing and nausea)
- Atopy
- Cardiac disease
- Preexisting renal disease
- Dehydration
- Anxiety
- Infants and elderly
- Hematologic and metabolic diseases (sickle cell disease, myelomatosis)

#### Pathophysiology of General Adverse Effects

There is no evidence to show that contrast media are allergenic, because no antibodies have been consistently demonstrated. The pathogenesis of general adverse effects is not well understood and is likely multifactorial. Most adverse effects are either pseudoallergic or idiosyncratic. Pseudoallergic reactions are the same as allergic reactions but depend on nonspecific complement system activation and histamine release, mimicking type I allergic reactions. Idiosyncratic reactions are genetically determined, unpredictable reactions that are caused by metabolites and occur after administration of small amount of drugs.

#### Treatment

Mild contrast reactions usually require no treatment other than reassurance. Oral antihistamines can be offered for itching. Intravenous access must be retained in all cases and vital signs closely monitored. Moderate reactions are managed with intravenous or intramuscular antihistamines for urticaria and angioneurotic edema, fluids for hypotension, and salbutamol inhalation and oxygen for bronchospasm. Intravenous hydrocortisone and intravenous or subcutaneous epinephrine may be needed for more severe bronchospasm. Management of more severe allergic reactions is described in Box 8-2.

#### BOX 8-2 TREATMENT OF SEVERE GENERAL **ADVERSE REACTIONS**

#### SEVERE BRONCHOSPASM

- 1. Provide oxygen by mask (6 to 10 L/min).
- Provide salbutamol nebulization (5 mg in 2 mL saline).
   Administer epinephrine injection if bronchospasm is progressive.

#### LARYNGEAL EDEMA

- Provide oxygen by mask (6 to 10 L/min).
- 2. Administer epinephrine (1:1000) 0.5 mL intravenously with electrocardiographic monitoring.
- HYPOTENSION WITHOUT BRADYCARDIA
  - 1. Elevate patient's legs.
  - 2. Provide oxygen by mask (6 to 10 L/min).
  - 3. Administer intravenous fluids (normal saline or lactated Ringer's solution).
  - 4. If unresponsive, give dopamine, 2 to 10  $\mu$ g/kg/min infusion, or epinephrine injection.

#### VAGAL REACTION

- 1. Elevate patient's legs.
- 2. Provide oxygen by mask (6 to 10 L/min).
- 3. Administer intravenous fluids (normal saline or lactated Ringer's solution)
- 4. Inject atropine 0.2 mL/kg of 0.1 mg/mL solution (0.02 mg/kg); repeat if necessary at 3 to 5 minutes up to 3 to 5 mg total.

#### ANAPHYLACTOID GENERALIZED REACTION

- 1. Call for resuscitation team.
- 2. Ensure patent airways.
- 3. Elevate patient's legs.
- 4. Provide oxygen by mask (6 to 10 L/min).
- 5. Administer intravenous fluids (normal saline or lactated Ringer's solution).
- 6. Administer hydrocortisone, 500 mg IV.
- Administer epinephrine IV 5 mg/kg; administer over 1-2 min; maximum of 200 mg with electrocardiographic monitoring.
- From Namasivayam S, Kalra MK, Torres WE: Adverse reactions to intravenous iodinated contrast media: a primer for radiologists. Emerg Radiol 12:210-215, 2006.

#### **ORGAN-SPECIFIC ADVERSE EFFECTS**

The hemodynamic, cardiovascular, neurologic, and subjective effects of contrast media can be explained by the osmolality, tonicity, and viscosity of these agents. After administration of intravascular contrast media there is a sudden increase in intravascular osmolality. This causes a shift of water into the vascular space. The contrast agent does not enter cell membranes, so intracellular water shifts out of red blood cells. This can cause red blood cell desiccation as well as influence cell membrane potential. Also, movement of water from the interstitium into the vascular compartment results in increased intravascular blood volume, increased cardiac output, and decreased peripheral vascular resistance. Peripheral vasodilation after contrast medium injection results in a feeling of warmth and discomfort. Systemic vasodilation leads to hypotension and decreased venous return, possibly leading to cardiac failure.

Contrast media can injure the endothelium, which along with complex effects on platelets and coagulation factors increases the risk for thrombosis. In the central nervous system, contrast media molecules cannot cross the blood-brain barrier. Pathologic increase in the permeability of the blood-brain barrier by infection or neoplasm exposes the brain tissue to the toxic effects of contrast media. All these effects are more common with high osmolar contrast media.

#### Prevention

There is no prophylactic regimen that eliminates the risk for adverse reaction to contrast media. All patients who are considered to be at high risk for contrast reaction should be considered for alternative forms of imaging. If administration of contrast media is necessary, low osmolar contrast media should be used because they significantly reduce the incidence of adverse effects compared with high osmolar contrast media. Oral corticosteroids are relatively safe when given for a brief period and are used for premedication. At our institution 50 mg of oral prednisone is given 13 hours before the scan, followed by a second dose of 50 mg of oral prednisone 7 hours before the scan, followed by a third dose of 50 mg of oral prednisone along with 50 mg of oral diphenhydramine 1 hour before administration of the contrast agent. Because adverse reactions can occur even after premedication, prompt recognition and management are invaluable in preventing life-threatening outcomes.

#### **Key Points**

- A molecule of contrast medium is composed of an iodine atom, which is responsible for radiopacity, and an organic carrier, which is responsible for its other properties and adverse effects.
- Contrast media are classified into high osmolar, low osmolar, and isosmolar agents.
- Knowledge of various phases of enhancement is critical in detecting and characterizing a pathologic process.
- Low-osmolar contrast media have a lower incidence of adverse reactions.
- Contrast-induced nephropathy can be prevented by judicious hydration of at-risk patients with low estimated glomerular filtration rate.
- Patients at high risk for allergic reactions should be premedicated.

#### **SUGGESTED READINGS**

Thomsen HS, Morcos SK, Barrett BJ: Contrastinduced nephropathy: the wheel has turned 360 degrees. *Acta Radiol* 49:646–657, 2008.

REFERENCES

- Herman S: Computed tomography contrast enhancement principles and the use of highconcentration contrast media. J Comput Assist Tomogr 28(Suppl 1):S7–S11, 2004.
- Morcos SK, Thomsen HS: Adverse reactions to iodinated contrast media. *Eur Radiol* 11:1267– 1275, 2001.
- Kuhn MJ, Chen N, Sahani DV, et al: The PREDICT study: a randomized double-blind comparison of contrast-induced nephropathy after low- or isoosmolar contrast agent exposure. AJR Am J Roentgenol 191:151–157, 2008.
- Brink JA: Use of high concentration contrast media (HCCM): principles and rationale body CT. *Eur J Radiol* 45(Suppl 1):S53–S58, 2003.
- Brink JA, Heiken JP, Forman HP, et al: Hepatic spiral CT: reduction of dose of intravenous contrast material. *Radiology* 197:83–88, 1995.
- Fidler JL, Fletcher JG, Reading CC, et al: Preoperative detection of pancreatic insulinomas on multiphasic helical CT. *AJR Am J Roentgenol* 181:775–780, 2003.

- Weisbord SD: Iodinated contrast media and the kidney. *Rev Cardiovasc Med* 9(Suppl 1):S14–S23, 2008.
- Horton KM, Hruban RH, Yeo C, et al: Multidetector row CT of pancreatic islet cell tumors. *Radiographics* 26:453–464, 2006.
- 8. McNulty NJ, Francis IR, Platt JF, et al: Multidetector row helical CT of the pancreas: effect of contrast-enhanced multiphasic imaging on enhancement of the pancreas, peripancreatic vasculature, and pancreatic adenocarcinoma. *Radiology* 220:97–102, 2001.
- 9. Van Der Molen AJ, Cowan NC, Mueller-Lisse UG, et al: CT urography: definition, indications and techniques: a guideline for clinical practice. *Eur Radiol* 18:4–17, 2008.
- Nash K, Hafeez A, Hou S: Hospital-acquired renal insufficiency. *Am J Kidney Dis* 39(5):930– 936, 2002.
- Mehran R, Nikolsky E: Contrast-induced nephropathy: definition, epidemiology, and patients at risk. *Kidney Int Suppl* 100:S11–S15, 2006.
- Katzberg RW, Barrett BJ: Risk of iodinated contrast material-induced nephropathy with intravenous administration. *Radiology* 243:622–628, 2007.

- 12. Swedko PJ, Clark HD, Paramsothy K, et al: Serum creatinine is an inadequate screening test for renal failure in elderly patients. *Arch Intern Med* 163:356–360, 2003.
- Baxmann AC, Ahmed MS, Marques NC, et al: Influence of muscle mass and physical activity on serum and urinary creatinine and serum cystatin C. *Clin J Am Soc Nephrol* 3:348–354, 2008.
- Thomsen HS, Morcos SK, Barrett BJ: Contrastinduced nephropathy: the wheel has turned 360 degrees. *Acta Radiol* 49:646–657, 2008.
- Mueller C: Prevention of contrast-induced nephropathy with volume supplementation. *Kidney Int Suppl* 100:S16–S19, 2006.
- Namasivayam S, Kalra MK, Torres WE, et al: Adverse reactions to intravenous iodinated contrast media: a primer for radiologists. *Emerg Radiol* 12:210–215, 2006.
- Idée JM, Pinès E, Prigent P, et al: Allergy-like reactions to iodinated contrast agents: a critical analysis. *Fundam Clin Pharmacol* 19:263–281, 2005.

9

# **Principles of Magnetic Resonance Imaging Physics**

GARRY CHOY | KOICHI HAYANO

### **Technical Aspects**

The principles of magnetization and physics allow us to create images via magnetic resonance imaging (MRI) noninvasively. In this chapter, an overview is provided on how images are created, illustrating the concepts of protons, radiofrequency (RF) excitation, T1 and T2 relaxation, image acquisition, spatial encoding, and Fourier transform analysis and k-space.

#### MAGNETIZATION AND PROTONS

The nucleus of choice for imaging is hydrogen because the human body consists of an abundance of water as well as hydrogen. Every water molecule contains two hydrogen atoms, and lipids or proteins frequently contain numerous hydrogen atoms. Hydrogen atoms, also referred to as protons, precess at the Larmor frequency (Figure 9-1). The Larmor frequency can be calculated from the gyromagnetic ratio and also the magnetic field strength of the magnet. All the spins comprise the net magnetization as aligned to B0. The Larmor frequency is the frequency at which the RF excitation pulse must be to alter magnetization to generate a signal and, subsequently, images.

#### RADIOFREQUENCY EXCITATION

To use principles of magnetization to generate signals and anatomic information, an excitation RF pulse is generated. The frequency of this pulse will correspond to the center frequency of the system, whether it is a 1.5- or 3.0-Tesla system. The net RF pulse can change the net magnetization from 1 to 180 degrees; this angle is referred to as the *flip angle*.

#### T1 AND T2 RELAXATION

All proton spins reach equilibrium and in the process result in the release of measurable RF signal. In essence, after the RF excitation phase, the net magnetization realigns with the z-axis of the magnet.

There are two types of proton spin relaxations that can be described by the time constants T1 or T2. The T1 relaxation time constant refers to the recovery of longitudinal magnetization. The T2 relaxation time constant refers to the recovery of the transverse magnetization. By enabling the discrimination of anatomic structures via magnetic resonance, each tissue exhibits a different T1 or T2 relaxation time because all protons interact differently in their respective environments depending on whether the tissue is, for example, fat, muscle, or bone. T1 and T2 relaxation times are essentially determinants of tissue contrast (Figures 9-2 and 9-3).

T1 relaxation, also known as spin-lattice relaxation, occurs in the z-axis of the magnet. A hydrogen proton may be bound tightly, in fat, for example, when compared with in water. More tightly bound protons release energy in a shorter period.

On the other hand, T2 relaxation, known as spin-spin relaxation, is an independent process in a perpendicular x-y plane. When the RF excitation pulse is applied, the protons are all spinning in phase. Eventually, protons will return to their outof-phase initial pre-RF excitation state, as measured by the T2 relaxation time. The rate of dephasing is different for each tissue, resulting in further tissue contrast. T2 relaxation also occurs at a much faster rate than T1 relaxation, which can affect the design of sequences in abdominal MRI.

### **Image Acquisition**

The acquisition of images occurs during T1 and T2 relaxation as protons return to equilibrium while energy is released simultaneously. To measure signals in all three orthogonal planes, the receive coil must be present orthogonally located to the main magnetic field B0. The orthogonal positioning enables the induction of measurable electric currents in the coil. The receive coil in many systems is actually the same transmit coil for the initial RF frequency excitation pulse. Many types of coils can be used and are optimized for different body parts.

#### SPATIAL ENCODING

A significant advance that has made MRI possible is the ability to perform three-dimensional (3D) localization. To accomplish this, the location of the signal can be determined using gradient coils that overlay a superimposed magnetic field. This subsequently enables the analysis of amplitude, phase, and frequency of the RF wave associated with proton spins in a specific voxel. The amplitude of an RF wave depends on the amount of proton spins.

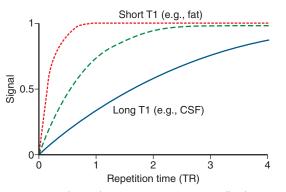
Gradient coils are placed in all three orthogonal axes and allow for the 3D generation of signal. Slice encoding or selection can therefore be accomplished in the z-axis along the bore of the magnet and B0 and can be referred to as the Gz gradient. On each slice, additional spatial localization can be accomplished by utilizing the Gy (phase-encoding gradient) and Gx (frequency-encoding gradient).

#### FOURIER TRANSFORM ANALYSIS AND K-SPACE

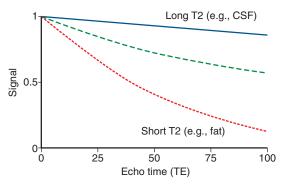
The data acquired before processing and mathematical transformation analysis are known as k-space (Figure 9-4). k-space is best explained and represented by a 2D matrix, often referred

# $\omega_0 = \gamma \times B_0$

Figure 9-1 Equation for Larmor frequency.



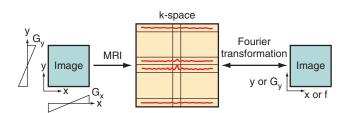
**Figure 9-2** T1 and T2 relaxation times are essentially determinants of tissue contrast. For example, fat has a short T1 relaxation time and cerebrospinal fluid (*CSF*) has a long T1 relaxation time.



**Figure 9-3** T1 and T2 relaxation times are essentially determinants of tissue contrast. For example, cerebrospinal fluid (*CSF*) has a long T2 relaxation time and fat has a short T2 relaxation time.

#### SUGGESTED READINGS

- Edelman ER, Dunkle EE, Wei LI, et al, editors: *Clinical magnetic resonance imaging*, ed 3, Philadelphia, 2006, Saunders.
- Elster AD: *Questions and answers to MRI*, St. Louis, 2000, Mosby.
- Haaga JR, Lanzieri CF, Gilkeson RC: CT and MR imaging of the whole body, St. Louis, 2003, Mosby.
- Martin DR, Brown MA, Semelka RC: *Primer of MR imaging of the abdomen and pelvis*, New York, 2005, Wiley.
- McRobbie DW, Moore EA, Graves MJ, et al: *MRI* from picture to proton, ed 2, New York, 2007, Cambridge University Press.



**Figure 9-4** Illustration of mathematical transformation analysis known as k-space. (From Hashemi RH, Bradley WG, Lisanti CJ, editors: MRI: The basics, ed 2, Philadelphia, 2003, Lippincott Williams & Wilkins, p 153.)

to as the *time domain*. Depending on the frequency of signals, raw data are mapped into k-space. Low-frequency data predominantly include signal and contrast, and high-frequency data include data regarding resolution. In other words, the center of k-space contains values that are responsible for contrast and the periphery of k-space determines resolution. As a map of imaging data, when Fourier transform analysis is applied to k-space, an image of physical space is subsequently generated.

#### **Key Points**

- The nucleus of choice for imaging is hydrogen because the human body consists of an abundance of water as well as hydrogen.
- All proton spins reach equilibrium and in the process result in the release of a measurable radiofrequency signal.
- The data acquired before processing and mathematical transformation analysis are known as k-space.
- As a map of imaging data, when Fourier transform analysis is applied to k-space, an image of physical space is subsequently generated.
  - Mitchell DG, Cohen MS: *MRI principles*, ed 2, Philadelphia, 1999, WB Saunders.
  - Schild HH: *MRI made easy (...well almost)*, Berlin, 1990, Schering AG.

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# Contrast Media and Contrast-Enhanced Magnetic Resonance Imaging

GARRY CHOY | KOICHI HAYANO

# **Technical Aspects**

Contrast agents enhance the visualization of vascular structures as well as pathologic tissues, which appear more prominent against the background of normal tissue. Development of novel contrast agents continues to be an exciting area, with new targeted agents, blood pool agents, and agents based on nanoparticle technologies. This discussion is focused on water-soluble gadolinium chelates used in abdominal and pelvic magnetic resonance imaging (MRI).

#### PRINCIPLE OF RELAXIVITY

The current use of gadolinium is based on paramagnetism. Gadolinium has more orbitals than electron pairs, an odd number, resulting in a net electron spin, and is therefore classified as paramagnetic. Its magnetic moment in addition with unpaired electrons makes gadolinium a useful compound for MRI. Although any agent that alters the local magnetic field can alter both T1 and T2 relaxation, gadolinium predominantly shortens T1 relaxation.

#### CHEMICAL STRUCTURE OF CURRENTLY APPROVED CHELATES OF GADOLINIUM

Gadolinium–diethylenetriamine pentaacetic acid (Gd-DTPA; gadopentetate) was first approved in 1988. Box 10-1 summarizes the currently approved agents for use in Europe and the United States. All of these agents contain a gadolinium ion centrally, an octadentate ligand, and a coordinated water molecule in their chemical structure. The octadentate ligand is responsible primarily for safety because it provides thermodynamic stability. Unchelated gadolinium is severely toxic to human tissues and cells. The coordinated water molecule allows for rapid chemical exchange with other water molecules in the solution that gadolinium is in, resulting in shortening of relaxation time of the water environment.

#### BIODISTRIBUTION

The human body can be divided into extracellular and intracellular compartments. Currently approved gadolinium chelates are extracellular space agents. The extracellular compartment can be simplified into the intravascular and interstitial spaces, which then are linked to the kidneys and liver, where there is hepatobiliary or renal excretion. Agents are initially distributed within the intravascular space and then diffuse into the interstitial space. As an extracellular agent, gadolinium chelates are very hydrophilic and thereby shorten the T1 relaxation time of the molecules around them. Although gadolinium chelates are nonspecific and their distribution is governed by perfusion, tissues that have a larger extracellular or interstitial space, increased capillary breakdown, or increased permeability will also receive a higher concentration of contrast agent, thereby appearing brighter on T1-weighted sequences.

# PHASES OF VASCULAR AND TISSUE ENHANCEMENT

As soon as gadolinium is injected intravenously, the agent is distributed into the pulmonary circulation, aorta, systemic arteries, capillaries, interstitial space, and kidneys for excretion into the urinary collecting system. The phases of enhancement in the vessels and tissues can be divided into arterial, blood pool, and extracellular phases.

The arterial phase is best imaged using fast pulse sequences that allow for capturing the initial arrival of contrast agent into arteries before venous filling. Temporal resolution maximization is critical for good arterial phase imaging. Arterial phase imaging is useful for evaluating arteries and arterially enhancing lesions within the liver or pancreas. Faster techniques such as those using parallel imaging techniques have enabled better quality arterial phase imaging. The best time for arterial phase imaging usually occurs at 20 to 40 seconds after injection.

The blood pool phase, or portal venous phase, follows 60 to 80 seconds after injection and is characterized by contrast agent distributed throughout the vessels. Tumors within the abdomen and pelvis are commonly more prominent during this phase. This is also the phase of highest liver parenchymal enhancement. In many cases, malignancies may be less intense in the portal venous phase. As a result, the portal venous phase is an important component for any evaluation of liver neoplasms.

The extracellular phase follows 120 to 150 seconds after intravenous injection. During this phase, the contrast agent begins to diffuse into the interstitial component of the extracellular space, and pathologic processes such as increased interstitial space or abnormal capillary structure with increased permeability are reflected. It is also during this phase that the contrast agent begins to undergo filtration in the kidneys and accumulates in the collecting system and bladder.

The hepatocyte phase follows 10 to 20 minutes after injection of gadoxetic acid, or 40 to 120 minutes after injection of gadobenate dimeglumine benzyloxy-propionic tetraacetic acid. After injection, these agents have an initial intravascular phase



- Gd-DTPA (Magnevist)
- Gd-DO3A-butrol (Gadovist)
- Gd-DOTA (Dotarem)
- Gd-DTPA-BMA (Omniscan)
- Gd-DTPA-BMEA (OptiMARK)
- Gd-HPDO3A (ProHance)
- Gd-EOB-DTPA (Primovist / Eovist)
- GD-BOPTA (MultiHance)

similar to that of other gadolinium chelates, but they accumulate in the hepatocytes of the liver parenchyma during the later phase. Thus, the lesion-to-liver contrast is increased and these agents aid in the detection of small liver lesions.

# **Pros and Cons**

Contrast agents improve the visualization of vascular structures as well as pathologic tissues, which appear more prominent against the background of normal tissue. Sensitivity and specificity of lesion detection can be improved if these agents are used properly, depending on the clinical indication.

With the emerging risk for nephrogenic systemic fibrosis, gadolinium-based agents should be used only after careful patient screening for renal dysfunction. Many abdominal MRI techniques rely on contrast enhancement with gadolinium; therefore, it is important to understand the risk for administering gadolinium in certain patient populations. Nephrogenic systemic fibrosis is a newly recognized condition that involves widespread cutaneous and systemic fibrosis. Initially termed *nephrogenic fibrosing dermopathy*, this condition is a debilitating disease that has been observed and cited by the U.S. Food and Drug Administration to be associated with gadolinium administration in patients with severely reduced renal function, specifically those who are undergoing dialysis.<sup>1</sup> The true cause of nephrogenic systemic fibrosis is still unclear and is actively being investigated. If patients have stage 4 or 5 chronic renal disease or an estimated glomerular filtration rate of less than 30 mL/min/1.73 m<sup>2</sup>, gadolinium-based contrast studies should be avoided when possible and the clinical decision to administer gadolinium should be discussed with the ordering physician.<sup>2</sup>

#### **Key Points**

- Contrast agents enable the visualization of vascular structures as well as pathologic tissues, which appear more prominent against the background of normal tissue.
- Although any agent that alters the local magnetic field can alter both T1 and T2 relaxation, gadolinium predominantly shortens T1 relaxation.
- Development of novel contrast agents continues to be an exciting area, with new targeted agents, blood pool agents, and agents based on nanoparticle technologies.
- With the emerging risk for nephrogenic systemic fibrosis, gadolinium-based agents should be used only after careful patient screening for renal dysfunction.

#### SUGGESTED READINGS

- Edelman ER, Hesselink JR, Zlatkin, Crues JV, editors: *Clinical magnetic resonance imaging*, Philadelphia, 2006, Elsevier.
- Elster AD: *Questions and answers to MRI*, St. Louis, 2000, Mosby.
- Haaga JR, Lanzieri CF, Gilkeson RC: CT and MR imaging of the whole body, St. Louis, 2003, Mosby. Martin DR, Brown MA, Semelka RC: Primer of MR imaging of the abdomen and pelvis, New York, 2005, Wiley.

McRobbie DW, Moore EA, Graves MJ, Prince MR: *MRI from picture to proton*, ed 2, New York, 2007, Cambridge University Press.

Mitchell DG, Cohen MS: *MRI principles*, ed 2, Philadelphia, 1999, WB Saunders.

#### REFERENCES

- 1. Cowper SE, Rabach M, Girardi M: Clinical and histological findings in nephrogenic systemic fibrosis. *Eur J Radiol* 66:191–199, 2008.
- Kuo PH, Kanal E, Abu-Alfa AK, et al: Gadolinium-based MR contrast agents and nephrogenic systemic fibrosis. *Radiology* 242:647–649, 2007.

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# Advanced Magnetic Resonance Imaging Applications

GARRY CHOY | KOICHI HAYANO

# **Technical Aspects**

Magnetic resonance imaging (MRI) has evolved significantly since its infancy, with major advances in hardware, software, coil developments, sequence development, and contrast agents. Industry and academia continue to advance the field with continued exciting emerging technologies. The discussion in this chapter focuses on the recent emergence of parallel imaging, 3.0-Tesla (T) clinical scanners with high field strength, dedicated contrast agents, perfusion and dynamic contrast-enhanced MRI, and diffusion weighted imaging techniques.

#### PARALLEL IMAGING

Parallel MRI techniques have been introduced by most vendors. Parallel MRI methods allow for faster imaging. In parallel imaging, multiple independent receiver (phase-array) coils placed in a configuration around the subject enable acquisition of fewer data to avoid aliasing to generate an image. In addition to reducing scan time, the advantages of parallel imaging include higher spatial resolution, less motion artifact on singleshot sequences, and reduced specific absorption rate. Parallel imaging techniques can be particularly utilized on higher field strength magnets to reduce the specific absorption rate.

# CLINICAL HIGH FIELD STRENGTH IMAGING WITH 3.0-TESLA IMAGING

In the past few years, there have been numerous installations of the latest 3.0-T clinical scanners with high field strength at various institutions around the world. In addition to research purposes, there has been increasing use of 3.0-T scanners in clinical settings. High field strength imaging with 3.0 T offers significantly higher signal-to-noise ratio in abdominal tissues, particularly when compared with currently widely available 1.5-T scanning.<sup>1,2</sup> In 3.0-T imaging, there is approximately a twofold increase in signal-to-noise ratio.<sup>2,3</sup> Many studies have examined the use of 3.0-T scanners in musculoskeletal and neurologic imaging applications.

Various technical issues are unique to 3.0-T imaging. For example, there is an increased specific absorption rate of approximately four times the radiofrequency deposition compared with 1.5 T. Chemical shift and susceptibility artifacts are also increased significantly. Given that there is increased field strength, the T1 relaxation time is also increased for most tissues. The T2\* relaxation of tissues is shorter, and that of T2 is nearly identical. Studies are still ongoing in body imaging with high field strength and show significant promise.

#### NOVEL TISSUE-SPECIFIC CONTRAST AGENTS

#### Liver-Specific Magnetic Resonance Imaging Contrast Agents

In recent years, liver-specific MRI contrast agents have been developed specifically targeted to hepatocytes or reticuloendothelial cells, providing either positive or negative enhancement after intravenous administration. Hepatocyte-specific contrast agents include mangafodipir trisodium and two gadolinium chelates: gadoxetic acid and gadobenate dimeglumine. Reticuloendothelial cell–specific agents include superparamagnetic iron oxides (SPIOs): ferumoxides and ferucarbon.

Mangafodipir Trisodium. Manganese (mangafodipir trisodium [Mn-DPDP; Teslascan]) is similar to gadolinium and is strongly paramagnetic. Manganese is cleared from the body primarily by biliary or intestinal secretion. It appears to have an affinity for metabolically active tissues, including primarily the liver, and has been marketed with U.S. Food and Drug Administration (FDA) approval for liver lesion characterization. Mangafodipir trisodium contains Mn<sup>2+</sup>, a transitional element that exhibits paramagnetic properties because of five unpaired electrons and shortens the T1 relaxation time. Because of its chemical similarity to vitamin B<sub>6</sub>, it is specifically taken up by hepatocytes. However, evidence exists that metabolic products of this compound are also responsible for selective uptake into liver, pancreas, and cardiac muscle.<sup>4</sup> This compound is administered through slow intravenous infusion over 2 to 5 minutes, and the effect is seen within a few minutes (~15 minutes) and lasts for 24 hours. The adverse events commonly reported include facial flushing and a sensation of heat. The prolonged imaging window makes this agent a good choice for imaging the liver. The signal intensity of normal liver parenchyma is increased, providing high lesion-to-liver contrast. This helps in detecting small liver lesions.<sup>5</sup> This agent may be taken up by well-differentiated hepatocellular carcinoma and thus may mask the tumor. Mangafodipir trisodium is best used for the detection of metastases. During the later phases, it is excreted into bile and provides excellent details of the biliary ducts and aids in the diagnosis of various biliary pathologic processes such as biliary obstruction and bile leaks.

**Gadolinium Chelates.** Two gadolinium chelates exhibit liver specificity owing to their selective uptake by hepatocytes through a carrier-mediated transport across the cell membrane. These include gadoxetic acid (Gd-EOB-DTPA; Primovist/ Eovist) and gadobenate dimeglumine benzyloxy-propionic tetraacetic acid (Gd-BOPTA; MultiHance). These agents are excreted into the bile unaltered and are ultimately excreted through urine and feces. After intravenous administration, these agents have an initial intravascular phase similar to that of other gadolinium chelates and during the later phase they accumulate in the liver parenchyma and increase the signal intensity of the liver. Thus, the lesion-to-liver contrast is increased and these agents aid in the detection of small liver lesions. This phase is the hepatocyte phase, which is 10 to 20 minutes after administration of Gd-EOB-DTPA, or 40 to 120 minutes after administration of Gd-BOPTA. The initial intravascular phase helps in characterization of liver lesions similar to that obtained with any other gadolinium chelate. Similar to mangafodipir trisodium, these agents provide excellent details of the biliary ducts during the delayed phase.

**Ferumoxides.** SPIO nanoparticles are the basis for agents known as ferumoxides (Feridex/Endorem).<sup>6</sup> Ferumoxides are composed of a central iron oxide particle— $Fe_2O_3$ —which is a superparamagnetic compound surrounded by a dextran coating. These agents have a greater magnetic susceptibility than conventional gadolinium-based contrast agents. Their dominant effect is preferentially on T2 and T2\* shortening rather than T1 shortening. Water near these particles therefore becomes dephased by local inhomogeneities, resulting in signal loss and thus acting as a negative contrast agent.

Of note, these agents should be infused slowly over a period of 30 minutes to avoid cardiovascular effects and lumbar pain. Specificity of particles depends on the size of the particle because the amount of contrast depends on the degree of uptake by the Kupffer cells. For instance, SPIOs are preferentially taken up by Kupffer cells in the liver, whereas ultra-small iron oxide particles (USPIOs) are taken up by macrophages in lymph nodes, liver, lung, and spleen. Similar to mangafodipir trisodium, these agents provide prolonged periods for imaging after intravenous infusion, facilitating higher resolution thinsection imaging.

One agent, Feridex, approved by the FDA since 1996, acts as a negative contrast agent when imaging hepatic lesions and may enable detection of smaller lesions.<sup>7,8</sup> Ferumoxtran-10 (Combidex) is another type of investigational SPIO-based agent that aims to differentiate normal lymph nodes from lymph nodes with metastatic cancer involvement.<sup>9</sup> With potential applications for Combidex in breast cancer and prostate cancer, clinical studies have thus far demonstrated that uptake occurs preferentially in normal lymph nodes; as a result, any lymph node with retained signal intensity would be of concern for metastatic disease.

**Ferucarbotran.** Similar to ferumoxides, ferucarbotran (Resovist) contains both a polycrystalline iron oxide core ( $Fe_2O_3$  and  $Fe_2O_4$ ) and a carbodextran coating. Unlike ferumoxides, this agent can be safely injected as a bolus with significantly fewer adverse cardiovascular events or back pain. Ferucarbotran improves focal liver lesion detection on T2- and T2\*-weighted sequences.

#### **Blood-Pool Contrast Agents**

Macromolecular contrast agents, namely, blood pool agents, also are being developed for vascular and perfusion imaging. Another dedicated contrast agent, gadobenate dimeglumine (Gd-BOPTA), is used in the imaging of liver malignancies.<sup>10,11</sup> The structure of gadobenate dimeglumine is similar to that of

the commonly used gadolinium diethylenetriamine pentaacetic acid (Gd-DTPA), with the addition of a benzene ring and short carbon chain, allowing the agent to be preferentially localized to hepatocytes. Gadobenate dimeglumine is typically seen to demonstrate uptake into hepatocytes and excretion into the biliary system at 30 to 120 minutes.

Because gadobenate meglumine circulates in the intravascular space for a longer time, there is a significant reduction in T1 relaxation time of blood containing the agent. Therefore, magnetic resonance angiography has become a useful application for this contrast agent. Although these agents do not diffuse through normal capillary wall, they can diffuse through defective capillaries commonly found in tumor vasculature, possibly playing a role in measuring the permeability of tumor microvasculature. For example, Gadomer-17 is a polymeric compound with a high molecular weight that because of its hydration properties has already demonstrated utility in measuring myocardial perfusion and in tumor imaging. Interestingly, although not yet ready for clinical use, novel agents involving the chelation of ligands such as antibodies to gadolinium for targeted imaging are undergoing active preclinical development.

#### Lymph Node–Specific Magnetic Resonance Imaging Contrast Agents

Lymph node-specific contrast agents also are actively being developed. Although not yet approved, these agents demonstrate significant promise in the evaluation of lymph node involvement in the setting of malignancies. For example, much promise has already been demonstrated in differentiating benign from malignant lymph nodes in prostate cancer using USPIO agents. The smaller size of USPIOs compared with SPIOs as well as their hydrophilic coating result in longer circulation in the intravascular space and rapid accumulation in the reticuloendothelial system. Therefore, as these particles are phagocytosed by macrophages, they accumulate in the lymphatic system, resulting in signal drop on T2\* images in normal lymph node tissue. However, malignant involvement is devoid of macrophages, resulting in a higher signal intensity. Typically, it takes 24 to 36 hours for the contrast agent to accumulate in lymph nodes, and thus postcontrast imaging is usually obtained 24 hours after its administration. The currently available contrast agent in this group for research use is ferumoxtran/AMI-227. Another agent also under investigation is gadofluorine-M.

#### DIFFUSION WEIGHTED IMAGING IN THE ABDOMEN

Diffusion weighted imaging (DWI) has been implemented mainly in brain imaging and has made a significant impact on imaging in stroke patients. Because of its susceptibility to motion, the application of DWI to the abdomen has until recently faced numerous obstacles. However, with the advent of the echoplanar technique minimizing the effect of physiologic motion such as respiration and cardiac movement, DWI has become applicable to the abdomen. DWI has been suggested as a tool to distinguish different tissue compartments and detect changes in cellular tissue structures and viability. DWI has been discussed as a cancer biomarker in a consensus meeting and a publication on consensus and recommendations for DWI as a cancer biomarker has been published recently highlighting the potential of this promising technique in cancer patients.<sup>12</sup>

For example, DWI was applied to differentiate benign from malignant lesions in the liver<sup>13</sup> and was also reported to enable early assessment of treatment response in hepatocellular carcinoma.<sup>14</sup> Malignant liver tumors, probably the result of increased cellular density and altered nuclear-to-cytoplasmic ratios, exhibit restricted water molecule diffusion and therefore reduced apparent diffusion coefficients (ADCs) compared with benign lesions. Because of the variation of sequences available by vendors and the extremely high sensitivity of DWI measurements to motion, this technique is extremely operator dependent.

#### PERFUSION IMAGING AND DYNAMIC CONTRAST-ENHANCED MAGNETIC RESONANCE IMAGING

Whereas standard cross-sectional imaging techniques solely focus on morphology, another technique that moves beyond anatomy and into physiologic or functional assessment includes the use of dynamic contrast-enhanced MRI (DCE-MRI).<sup>15,16</sup> In the literature and various investigations, this technique has been applied to the evaluation of tumor angiogenesis. Kinetic modeling of imaging data plays an important role for DCE-MRI, because quantitative parameters allow for the characterization of physiologic data such as blood volume, vascular permeability, and vessel density. DCE-MRI holds significant promise in monitoring the effect of antiangiogenic agents because morphologic changes in tumor size often lag behind physiologic changes, which can be better characterized by enhancement characteristics.

#### Controversies

In addition to the emerging risk for nephrogenic systemic fibrosis related to gadolinium-based agents, newer contrast agents are not without potential risks. Iron oxide nanoparticles are taken up by macrophages in the reticuloendothelial system involving the liver, spleen, and bone marrow. The long-term effects of nanoparticle presence in the reticuloendothelial system are not completely clear at this time, but preclinical evaluations of SPIOs and USPIOs showed satisfactory and safe clinical profiles according to current pharmacologic and toxicologic tests. Reported symptoms have included, but are not limited to, rash, dyspnea, chest pain, and back pain, but no serious adverse effects have been reported thus far.

#### **Key Points**

- Parallel imaging allows for faster imaging, higher spatial resolution, less motion artifact, and lower specific absorption rate.
- Novel tissue-specific contrast agents serve as new tools to characterize tissues.
- Lymph node-specific contrast agents also are actively being developed. Although not yet approved, these agents demonstrate significant promise in the evaluation of lymph node involvement in malignancy.
- Perfusion and dynamic contrast-enhanced MRI enables physiologic and functional assessment of tissues, such as in monitoring the effects of antiangiogenic agents on tumor vasculature.

#### **SUGGESTED READINGS**

Edelman ER, Dunkle EE, Wei LI, et al, editors: *Clinical magnetic resonance imaging*, ed 3, Philadelphia, 2006, Saunders. Elster AD: *Questions and answers to MRI*, St. Louis, 2000, Mosby.

- Haaga JR, Lanzieri CF, Gilkeson RC: CT and MR imaging of the whole body, St. Louis, 2003, Mosby.
- Martin DR, Brown MA, Semelka RC: Primer of MR imaging of the abdomen and pelvis, New York, 2005, Wiley.

#### **REFERENCES**

- Fenchel M, Nael K, Seeger A, et al: Whole-body magnetic resonance angiography at 3.0 Tesla. *Eur Radiol* 18:1473–1483, 2008.
- Schindera ST, Merkle EM, Dale BM, et al: Abdominal magnetic resonance imaging at 3.0 T: what is the ultimate gain in signal-tonoise ratio? Acad Radiol 13:1236–1243, 2006.
- Merkle EM, Dale BM: Abdominal MRI at 3.0 T: the basics revisited. *AJR Am J Roentgenol* 186: 1524–1532, 2006.
- 4. Toft KG, Hustvedt SO, Grant D, et al: Metabolism of mangafodipir trisodium (MnDPDP), a new contrast medium for magnetic resonance imaging, in beagle dogs. *Eur J Drug Metab Pharmacokinet* 22:65–72, 1997.
- Oudkerk M, Torres CG, Song B, et al: Characterization of liver lesions with mangafodipir trisodium-enhanced MR imaging: multicenter study comparing MR and dual-phase spiral CT. *Radiology* 223:517–524, 2002.
- 6. Saokar A, Braschi M, Harisinghani M: Lymphotrophic nanoparticle enhanced MR imaging

(LNMRI) for lymph node imaging. *Abdom Imaging* 31:660–667, 2006.

- Bluemke DA, Weber TM, Rubin D, et al: Hepatic MR imaging with ferumoxides: multicenter study of safety and effectiveness of direct injection protocol. *Radiology* 228:457–464, 2003.
- Clement O, Siauve N, Cuánod CA, et al: Liver imaging with ferumoxides (Feridex): fundamentals, controversies, and practical aspects. *Top Magn Reson Imaging* 9:167–182, 1998.
- Harisinghani MG, Barentsz J, Hahn PF, et al: Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. *N Engl J Med* 348:2491–2499, 2003.
- Kirchin MA, Pirovano GP, Spinazzi A: Gadobenate dimeglumine (Gd-BOPTA): an overview. *Invest Radiol* 33:798–809, 1998.
- Pavone P, Catalano C, Cademartiri F, et al: Improvement of vascular signal intensity in contrast-enhanced MRA with Gd-BOPTA: comparison with Gd-DTPA. *Acad Radiol* 9(Suppl 1):S134, 2002.

- Padhani AR, Liu G, Kohn DM, et al: Diffusionweighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations. *Neoplasia* 11:102–125, 2009.
- Yoshikawa T, Kawamitsu H, Mitchell DG, et al: ADC measurement of abdominal organs and lesions using parallel imaging technique. *AJR Am J Roentgenol* 187:1521–1530, 2006.
- Schraml C, Schwenzer NF, Martirosian P, et al: Diffusion-weighted MRI of advanced hepatocellular carcinoma during sorafenib treatment: initial results. *AJR Am J Roentgenol* 193:W301– W307, 2009.
- Rosen MA, Schnall MB: Dynamic contrastenhanced magnetic resonance imaging for assessing tumor vascularity and vascular effects of targeted therapies in renal cell carcinoma. *Clin Cancer Res* 13:770s–776s, 2007.
- Taylor JS, Tofts TS, Port R, et al: MR imaging of tumor microcirculation: promise for the new millennium. *J Magn Reson Imaging* 10:903–907, 1999.

12

# Positron Emission Tomography and Computed Tomography Technique and Instrumentation

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# **Technical Aspects**

Positron emission tomography and computed tomography (PET/CT) represents the successful technical combination of multidetector computed tomography (MDCT) and PET into a single scanner. PET with the fluorine-18 (18F)–labeled glucose analog fluorodeoxyglucose (FDG) provides metabolic imaging of tissues, both normal and diseased. FDG-PET provides valuable qualitative and quantitative metabolic information for both diagnosis and management. PET has been shown to be of value in diagnosing and staging malignant tumors as well as in follow-up oncologic imaging after surgical, radiation, or chemotherapeutic treatment.<sup>1</sup> However, the sensitivity of PET in detecting hypermetabolic foci is compromised in large part by the low background FDG uptake when attempting accurate anatomic localization.<sup>2</sup>

CT provides rapidly acquired data sets of high spatial resolution giving multiplanar information regarding the morphologic features and attenuation values of both normal anatomy and pathologic lesions. A major weakness of CT, however, is its dependence on changes in the size, shape, or attenuation values of a structure to detect pathologic processes.

Separate CT and PET scans of the same patient acquired on different scanners certainly can be aligned using a number of available software methods, but the algorithms are often labor intensive and, particularly in the abdomen, may fail to provide a satisfactory overlap. However, combined imaging with PET/ CT allows for the precise structural information provided by CT to accurately locate the hypermetabolic foci identified with PET and thereby improve the overall diagnostic performance (Figure 12-1). The information from combined PET/CT also facilitates identification of physiologic from pathologic uptake and diminishes the false-negative and false-positive interpretations of the individual components. Indeed, it has been shown that PET/CT is more accurate for many oncologic entities than either CT or PET alone.<sup>3</sup> Furthermore, PET has the potential to be used with radiotracers different from FDG to provide other useful biological information, whereas CT provides useful information about the behavior of orally and intravenously administered contrast agents.

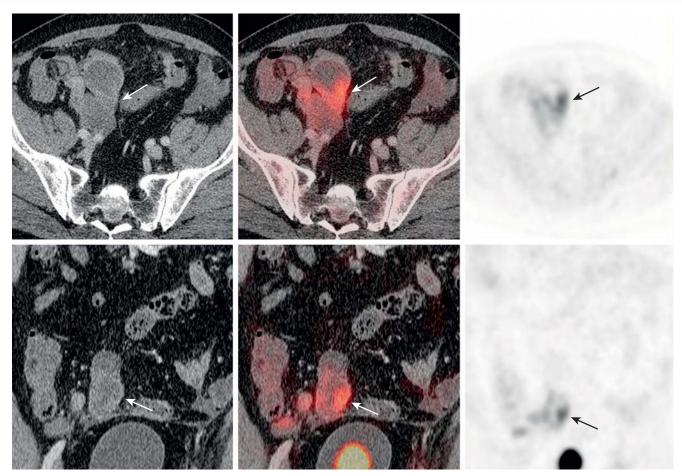
#### INSTRUMENTATION CONSIDERATIONS

The first PET/CT prototype scanner was revealed in 1998.<sup>4</sup> Subsequently, the first clinical scanners appeared in 2001, and by early 2007 more than 800 combined PET/CT scanners had been installed in clinical institutions worldwide. Essentially all new PET machine sales are now as PET/CT scanners.<sup>3</sup>

The automatic and more accurate coregistration of the structural and metabolic data is just one of the inherent advantages of hybrid PET/CT machines. PET-only whole-body scans traditionally required up to 45 to 60 minutes to complete. The transmission scan required for attenuation correction to improve the qualitative and quantitative accuracy of PET is a major contributor to this long scan time.<sup>5</sup> However, CT-based attenuation correction is significantly quicker than traditional PET transmission methods and can provide almost noise-free information and allows for total PET/CT scanning durations of 20 to 30 minutes or less. This greatly reduced scanning time enhances patient comfort and convenience and also allows a greater patient throughput. The current emission PET scan time may now also be decreased by the use of time-of-flight (TOF) technology, which shortens scan time and improves signal-to-noise ratio.6

Feasible TOF now can be applied owing to the newer fast scintillators with high stopping power, such as lutetium oxyorthosilicate (LSO) and LYSO (which is LSO with the addition of a small percentage of yttrium).7 TOF makes use of the ability of the new scanners to measure the arrival time difference between the two positron annihilation-generated photons reaching the detectors to within a certain resolution. Recent detector and scintillator developments allow subnanosecond coincidence timing resolution, which provides a rapid, TOF-based and back-projection-free, three-dimensional (3D) reconstruction algorithm that, combined with real-time data acquisition and a quick detector encoding scheme, permits high-quality images to be obtained in a significantly reduced time, particularly in nonobese patients.8 The stability of these new scanners in practice has yet to be confirmed; and although encouraging and interesting, the precise clinical contribution of TOF PET has yet to be determined. Certainly, high spatial resolution PET detectors appear to optimize the conspicuity of FDG uptake in small lesions.

From the late 1980s until recently, the bismuth germanate (BGO) block detector was the standard for PET. However, the introduction of new faster scintillators with greater light output and shorter decay time than BGO, such as gadolinium oxyor-thosilicate (GSO) and LSO (and LYSO), has recently improved the performance of PET scanners for clinical imaging. The faster scintillators decrease the coincidence timing window and thus the random coincidence rate. The improved light output of the new scintillators makes the energy resolution



**Figure 12-1** Value of precise localization and complementary strengths. Appendiceal adenocarcinoma. Markedly dilated appendix with thick wall and communication with cecum shows increased fluorodeoxyglucose uptake (*arrows*) along its wall. Without the positron emission tomography (PET) findings, the computed tomography (CT) finding might have been overlooked with the dilated appendix mimicking a large bowel loop. Without the CT findings, the PET activity could not have been precisely localized and possibly may have been misinterpreted as physiologic bowel activity.

more accurate by reducing the statistical uncertainty of the measurement. This higher light output also improves the positioning accuracy of a block detector, with potential spatial resolution benefits.

The block design developed by Casey and Nutt has been the basic detector component in all multi-ring PET scanners for the past 2 decades. The first multi-ring PET scanners incorporated septa between the detector rings to shield the detectors from scattered photons out of the transverse plane, thus not allowing 3D reconstruction algorithms. The first multi-ring PET scanners with retractable septa that included the capability to acquire data in either the 2D or 3D mode appeared in the early 1990s. The advantages of 3D imaging for the brain are widely accepted, but 3D imaging for the rest of the body has posed more problems. Recently, however, statistically based reconstruction algorithms, more accurate scatter correction methods,<sup>9</sup> and faster scintillators have significantly improved the achievable whole-body 3D imaging quality. However, 2D imaging still may be more suitable for large patients. Increased axial coverage makes better use of the emitted radiation for a given volume of scintillator. For most PET/CT scanners, axial PET coverage is approximately 15 cm, ranging up to a recently extended 21.6 cm, with resulting imaging advantages.

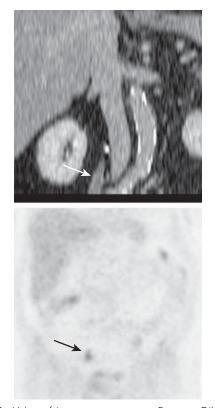
#### **TECHNIQUE CONSIDERATIONS**

PET/CT continues to be an evolving modality, and thus accepted optimal protocols are not yet established. Debate exists, for example, regarding the use of oral and intravenous contrast material and the optimal respiratory phase to scan as well as the most appropriate CT scanning parameters.<sup>10-12</sup> FDG-PET provides quantitative information in the form of the standardized uptake value (SUV). SUV estimation requires attenuation correction to avoid the variability in FDG uptake depending on the tumor depth beneath the skin. As mentioned earlier, CT images are used for attenuation correction of the PET emission data, eliminating the need for a separate lengthy PET transmission scan with much less statistical noise. However, there is also a potential risk for overestimating the true FDG activity with this technique. In normal structures, including bone and soft tissues, this is unlikely to be problematic.<sup>10</sup> However, very dense structures on CT such as metallic prostheses, surgical clips, and devices, as well as high-density oral and intravenous contrast can result in overcorrection with subsequent artifact formation. As a consequence, the corresponding photopenic areas on PET may manifest artifactually as hypermetabolic foci. This usually can be recognized by reviewing the nonattenuation corrected

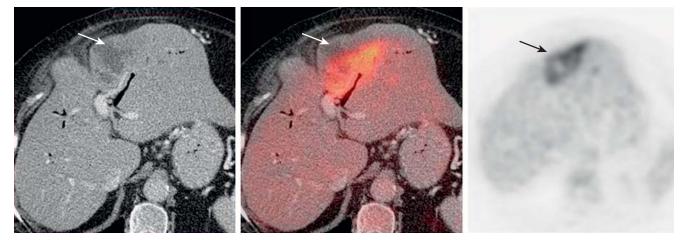
PET images. These artifacts, however, also may obscure true foci of abnormal activity on the attenuation-corrected images, although they are most intense at areas of contrast influx, such as the subclavian vein, outside the abdomen. A saline flush after intravenous injection of a contrast agent may reduce attenuation correction PET artifacts. Recent reports suggested that the changes in attenuation correction wrought by intravenous contrast agents are neither statistically or clinically significant.<sup>11</sup> This is reassuring because intravenous contrast agents are regularly used in CT to augment the contrast between normal and abnormal tissues and thus increase the ease of interpretation. They give useful information about the patency (Figure 12-2), course, and relations of vessels (Figure 12-3) and also dynamic data regarding tissue enhancement, perfusion, and de-enhancement.

Modifications to the basic scaling algorithm<sup>13</sup> have been introduced to distinguish oral contrast enhancement from bone, and strategies have been developed that minimize problems caused by both intravenous and oral contrast material. The modified algorithm also can somewhat reduce artifacts from metallic objects in the patient. Because the attenuation values are energy dependent, the correction factors derived from a CT scan at mean photon energy of 70 keV must be scaled to the PET energy of 511 keV. Scaling algorithms typically use a bilinear function to transform the attenuation values above and below a given threshold with different factors. The scaled CT images are then interpolated from CT to PET spatial resolution, followed by reprojection of the interpolated images. Alternatively, fully optimized contrast-enhanced CT can be performed after initial low-mAs PET/CT without intravenous contrast agent administration for attenuation correction, although this may increase radiation exposure to the patient.

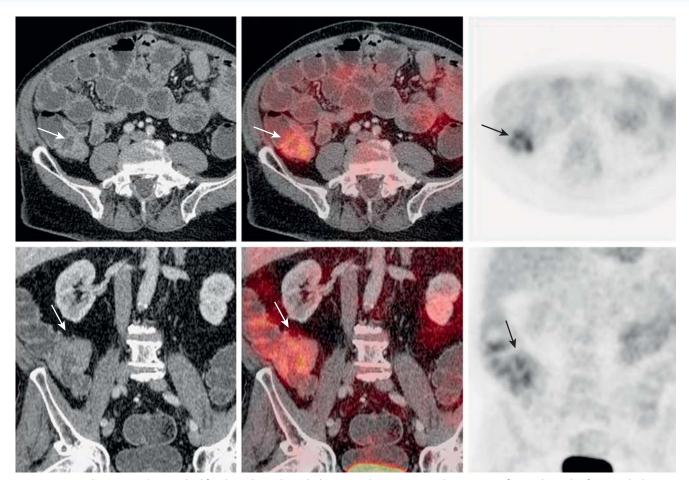
Oral contrast agents are also routinely used in CT to assist the CT diagnosis of both gastrointestinal tract-related and neighboring pathologic conditions. In the past, these were generally positive, dense substances including barium and Gastrografin compounds. This again leads to the potential production of erroneous hypermetabolic foci after CT-based attenuation correction. Furthermore, the distribution of such agents may change position owing to peristalsis between the CT used for attenuation correction and the PET components, a further potential confounding phenomenon. Accordingly, some authors support the use of water-attenuation oral contrast agents<sup>14</sup> or even not using any oral agent at all. However, clearly, oral contrast is helpful for CT interpretation and, as with intravenous contrast agents, there is growing consensus that dilute concentrations of even positive oral contrast agents do not significantly



**Figure 12-2** Value of intravenous contrast: Patency. Dilated nonenhancing gonadal vein (*arrow*) consistent with gonadal vein thrombosis, which may have been overlooked if an intravenous contrast agent had not been given, because there is no corresponding fluorodeoxyglucose (FDG) uptake. *Arrow* indicates ureteric-excreted FDG activity on positron emission tomography alone.



**Figure 12-3** Intravenous contrast value: Vascular relationships. Fluorodeoxyglucose-positive hepatic cholangiocarcinoma with the computed tomography images precisely showing the tumor's relationship to the portal vein and its branches (*arrow*). The positron emission tomography image cannot provide this high spatial resolution information regarding lesion location and the relationships necessary for surgical planning.



**Figure 12-4** Oral contrast value. Marked focal uptake in the right lower quadrant corresponding to circumferential mural soft tissue thickening in the colon because of a colorectal carcinoma (*arrow*). Orally administered contrast agent helps with the identification of the cause of the focal FDG uptake.

alter PET/CT attenuation correction.<sup>15</sup> Optimal PET/CT allows for the ability to delineate the bowel on the CT component and thus differentiate FDG uptake in the colon from that in adjacent tumor sites (Figure 12-4).

Diagnostic CT carries with it a significant radiation dose to patients. When integrating a full-dose CT, with a tube current of 100 to 140 mA, the radiation dose for a scan from the head to the top of the thighs is 15 to 20 mSv. It has been shown that much lower tube currents, with a range of 10 to 40 mA, are adequate for CT-based attenuation correction.<sup>16</sup> Such low-dose scans confer a significantly lower radiation dose, 3 to 4 mSv, to patients, but it is doubtful if such scans are sufficient to allow accurate CT-based interpretation owing to the increased noise level and suboptimal image quality.

As discussed earlier, a major benefit of PET/CT over its individual components is the ability to more accurately localize a focus of hypermetabolic activity. When the individual PET and CT components are superimposed or coregistered on the workstation, there should be appropriate alignment of the two data sets. The advantage of combined imaging is that potential misregistration because of patient motion, bowel motility, and urinary tract distention is minimized by the single examination. However, differing respiratory phases may lead to significant misregistration. Standard diagnostic CT studies are usually performed during a maximal inspiration breath-hold, a technique ideal for chest imaging. Although some patients may not be able to breath-hold sufficiently long for a whole-body CT, resulting in motion artifact in the later scanned body parts, modern multislice CT scanners, including 64-slice machines, are capable of faster whole-body scan times and should allow scan durations within a single breath-hold in the majority of cases. PET studies have average bed acquisition times of 3 to 5 minutes, which are too long for a single breath-hold and are thus acquired with the patient quietly breathing. Employing these two differing techniques usually results in marked misregistration of the diaphragm and adjacent organs. The most prominent respiratory artifact causes a scalloped appearance of the superior hepatic and splenic borders, generating problems of lesion localization in the lung base or liver dome. Respiratory misregistration also can affect the inferior margins of the upper abdominal organs, resulting in lesion misregistration between the inferior margins of the liver, kidney, and spleen and adjacent bowel. Respiratory artifacts can be exacerbated with older scanners that use a slower CT component. Again with faster 16-slice or higher CT units, these artifacts are usually less marked.

The most appropriate CT breathing protocol remains to be agreed upon. During quiet free breathing, the diaphragm is most commonly in the position of end-tidal volume, and it has been shown that performing CT during a suspended end-tidal breath-hold allows for the most accurate image registration.<sup>17</sup> Technologists must instruct and practice with the patient so that breathing instructions are understood before the CT component is performed. However, others, including pulmonary imaging investigators at our institution, have demonstrated that good PET and CT alignment is also possible with mid-suspended breath-hold and quiet breathing, as well as endexpiration, without statistical difference.<sup>18</sup> However, an inspiratory scan is indeed optimal for chest parenchymal evaluation, and manual and mental adjustment of registration is certainly possible during interpretation if the primary scan is obtained during inspiration and, if necessary, additional selected chest images also may be obtained. In addition to respiratory artifacts, misregistration artifacts also can occur in the abdomen as a result of shifting positions of bowel over the course of the PET portion of the study. In the future, respiratory gating software may help to eliminate many of these artifacts.

Having acquired the desired PET and CT data sets, it is then mandatory that the scans be interpreted on a dedicated PET/ CT workstation. An accurate interpretation of the study requires the ability to simultaneously review the CT data, including multiplanar reconstructions with various window settings, together with both the non-attenuation-corrected and attenuationcorrected PET data, as well as with the superimposed coregistered images.

#### **PROTOCOLS IN PRACTICE**

Given the multiple variables to decide on for a protocol for an abdominopelvic PET/CT evaluation, ranging from lowradiation dose nonenhanced CT to a fully diagnostic CT study employing both oral and intravenous contrast, and given the issues and potential artifacts from these various factors, it is apparent why a definitive, standardized protocol has not yet been agreed upon in the literature or practice. In our institution, we combine the two aforementioned approaches.<sup>19</sup> We first acquire a low-radiation dose, nonenhanced CT image mainly to provide attenuation correction for the PET images. Then the PET is performed, followed by a fully diagnostic standard radiation dose, intravenous contrast-enhanced CT with a neutral density oral contrast.<sup>20</sup> We believe that this approach optimizes the diagnostic information from the study and reduces the potential artifact risk.

Patients are kept fasting for a minimum of 6 hours before the test. Because FDG is a glucose analog, its uptake and distribution in tissues are affected by serum glucose and insulin levels such that low levels of both are desirable. An elevated blood glucose level has been shown to decrease FDG uptake within tumors. Water intake is encouraged, however, together with regular bladder voiding, to aid renal tract excretion because FDG, unlike glucose, is excreted by the urinary tract. In addition to fasting, patients with diabetes should not receive regular insulin within the 4-hour period before the study. The serum glucose level should be less than 200 mg/dL, and if it is higher than this level, available options include gentle exercise and then a recheck, administration of subcutaneous insulin and rechecking the serum glucose value after approximately 3 hours, or rescheduling the examination.

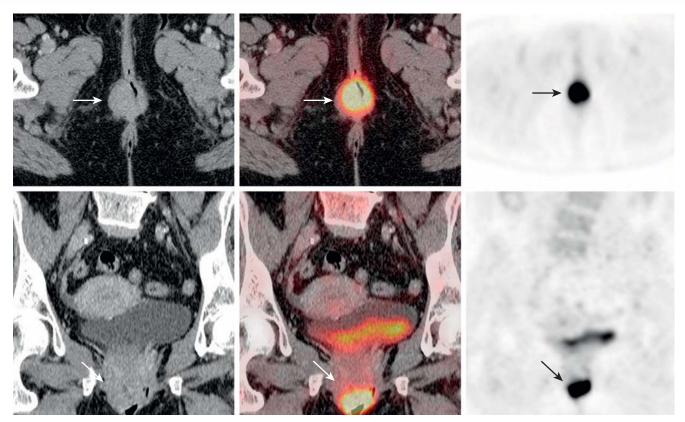
After an appropriate glucose range is confirmed, FDG is administered intravenously at a dose of 140  $\mu$ Ci/kg. Patients are given up to 1350 mL of neutral density oral contrast to drink over 45 minutes.

While waiting the 60 minutes (some centers wait 90 minutes) between FDG administration and subsequent imaging, patients are encouraged to rest and activities including talking, chewing, and walking are discouraged. Then the PET/CT scan is obtained as described earlier with the following additional details. The patient is positioned in the scanner with arms up (except for scanning head and neck cancer patients). If a patient is unable to tolerate the arms-up position for imaging, the arms may then be positioned in front of the body, resting on the thighs or abdomen. Above-head hand grips, as commonly used in radiation therapy practice, can facilitate the arms-up position for PET/CT. These also can help keep the patient immobile and comfortable throughout the scan. The PET scan is performed as a series of acquisitions at discrete bed positions. For highresolution imaging of lung disease, respiratory gating can be applied to the PET scan. The CT scan from the base of the brain to the upper thigh can be acquired in less than 20 seconds, and the PET scan with an extended field of view (FOV) system requires just five bed positions at 2 to 3 minutes per position, depending primarily on patient weight. The practical advantages of an FOV scanner include fewer bed positions needed, reduced scan times, and overall better image quality for larger patients owing to the 78% increase in sensitivity. These faster scanning protocols with extended FOV scanners lead to improved patient compliance with less reported claustrophobia and reduced movement, with the added advantage of increased patient throughput. The extended FOV is particularly beneficial when scanning the entire body, as is desirable when scanning patients with melanoma. This range can be covered in less than 25 minutes and only 11 bed positions with an extended FOV.<sup>21</sup> Injected dose can then be reduced with an up to 50% radiation exposure decrease to the patient.

Specific pelvic imaging–oriented technical details need to address the issues related to physiologic bowel and urinary FDG uptake and their dynamic patterns on both PET and CT. The patient should be well hydrated for the study and have voided completely immediately before starting image acquisition to reduce the FDG/high urinary content as much as possible. The administration of diuretics or placement of Foley catheters is not commonly performed. Particularly in patients with specific clinical pelvis-related questions, the pelvis should be imaged at the beginning of the study to achieve the shortest time interval between the CT and PET components at this level, to best achieve similar bladder size, volume, and shape on both imaging modalities (Figure 12-5).

# Positron Emission Tomography and Magnetic Resonace Imaging

Instruments that combine PET and MR have recently been assembled for use in humans and may have diagnostic performance superior to that of PET/CT.<sup>22</sup> MRI has major strengths compared with CT, including superior soft-tissue contrast resolution, multiplanar image acquisition, and functional imaging capability through specialized techniques such as diffusion-tensor imaging, diffusion weighted (DW) imaging, functional MR imaging, MR elastography, MR spectroscopy, perfusion-weighted imaging, MR imaging with very short echo times, and the availability of some targeted MR imaging contrast agents. The major obstacle to PET in or near an MRI is the presence of the magnetic field, which causes gain changes and spatial distortion in photomultiplier tubes (PMTs), the scintillation light



**Figure 12-5** Pelvic positron emission tomography and computed tomography (PET/CT) considerations. Intense fluorodeoxyglucose uptake (*arrow*) shown in the lower pelvis corresponds to soft tissue mass on CT and PET/CT images in this postmenopausal woman with a vaginal carcinoma. Ideally, the pelvis should be imaged at the beginning of the PET study to achieve the shortest time interval between the noncontrast CT and PET components at this level and to best achieve similar bladder size, volume, and shape on both imaging modalities. On occasion, bladder catheter-ization may be helpful to keep the bladder empty throughout the PET and both the noncontrast and contrast-enhanced CT acquisitions.

detector of choice for PET scanners. The fundamental technical advance that has made simultaneous PET/MR possible for clinical use was the emergence of a new type of solid-stable photon detector (i.e., avalanche photodiode [APD]), which maintains PMT's light sensitivity while insensitive to magnetic fields.<sup>23</sup>

PET/MRI provides distinct challenges and opportunities in contrast to PET/CT. One, attenuation correction, immediately presents itself as a problem for any system without an ionizing radiation source or CT scanner. A second, the capability for dynamic motion correction, presents as a unique opportunity in simultaneous PET/MR systems.<sup>24</sup> Various techniques can be employed to account for these difficulties but are outside the scope of this chapter.

Current MRI technology has reached a certain maturity, but further studies are needed to assess the potential of multiparamentric imaging, for example, using dynamic contrast-enhanced MRI, diffusion weighted imaging, and magnetic resonance spectroscopy conjointly with PET for the assessment of therapy response in malignant disease.

#### **Key Points**

- Combined imaging with PET/CT scanners enables fusion of the CT-acquired morphologic information with the PET-provided functional imaging.
- The recent introduction of new scintillator materials, detector strategies, and electronics has led to overall enhanced PET performance.
- The reduction in rotation time with resulting benefits in speed and resolution has revolutionized CT performance.
- Together, combined PET/CT imaging results in a powerful imaging modality for oncologic patients.
- PET/MRI provides distinct challenges, and opportunities, when compared to PET/CT.

#### SUGGESTED READINGS

- Blodgett TM, Meltzer CC, Townsend DW: PET/CT: form and function. *Radiology* 242:360–385, 2007.
- Carney JP, Townsend DW: CT-based attenuation correction for PET/CT scanners. In von Schulthess G, editor: *Molecular anatomic imaging: PET-CT and SPECT-CT integrated molecular*

#### REFERENCES

- Kapoor V, McCook BM, Torok FS: An introduction to PET-CT imaging. *Radiographics* 24:523– 543, 2004.
- Wahl RL: Why nearly all PET of abdominal and pelvic cancers will be performed as PET/CT. J Nucl Med 45(Suppl 1):82S–95S, 2004.
- Blodgett TM, Meltzer CC, Townsend DW: PET/ CT: form and function. *Radiology* 242:360–385, 2007.
- Beyer T, Townsend DW, Brun T, et al: A combined PET/CT scanner for clinical oncology. *J Nucl Med* 41:1369–1379, 2000.
- Rohren EM, Turkington TG, Coleman RE: Clinical applications of PET in oncology. *Radiology* 231:305–332, 2004.
- Conti M, Bendriem B, Casey M, et al: First experimental results of time-of-flight reconstruction on an LSO PET scanner. *Phys Med Biol* 50:4507–4526, 2005.
- Surti S, Kuhn A, Werner ME, et al: Performance of Philips Gemini TF PET/CT scanner with special consideration for its time-of-flight imaging capabilities. J Nucl Med 48:471–480, 2007.
- Crespo P, Shakirin G, Fiedler F, et al: Direct time-of-flight for quantitative, real-time inbeam PET: a concept and feasibility study. *Phys Med Biol* 52:6795–6811, 2007.
- Watson CC: New, faster image-based scatter correction for 3D PET. *IEEE Trans Nucl Sci* 47: 1567–1594, 2000.

*imaging*, Philadelphia, 2007, Lippincott Williams & Wilkins, pp 55–62.

- Townsend DW: Physics and instrumentation for PET. In Wahl RL, editor: RSNA Syllabus: categorical course in diagnostic radiology: clinical PET and PET/CT imaging, Oak Brook, IL, 2007, Radiological Society of North America.
- Werner MK, Schmidt H, Schwenzer NF: MR/PET: a new challenge in hybrid imaging. *AJR Am J Roentgenol* 199:272–277, 2012.
- Wong TZ, Paulson EK, Nelson RC, et al: Practical approach to diagnostic CT combined with PET. *AJR Am J Roentgenol* 188:622–629, 2007.
- Nakamoto Y, Osman M, Cohade C, et al: PET/CT: comparison of quantitative tracer uptake between germanium and CT transmission attenuation-corrected images. J Nucl Med 43:1137–1143, 2002.
- Antoch G, Freudenberg LS, Beyer T, et al: To enhance or not to enhance? 18F-FDG and CT contrast agents in dual-modality 18F-FDG PET/ CT. J Nucl Med 45(Suppl 1):56S–65S, 2004.
- Wong TZ, Paulson EK, Nelson RC, et al: Practical approach to diagnostic CT combined with PET. AJR Am J Roentgenol 188:622–629, 2007.
- Carney JP, Townsend DW: CT-based attenuation correction for PET/CT scanners. In Von Schulthess G, editor: Molecular anatomic imaging: PET-CT and SPECT-CT integrated molecular imaging, Philadelphia, 2007, Lippincott Williams & Wilkins, pp 55–62.
- Antoch G, Kuehl H, Kanja J, et al: Dual-modality PET/CT scanning with negative oral contrast agent to avoid artifacts: introduction and evaluation. *Radiology* 230:879–885, 2004.
- Cohade C, Osman M, Nakamoto Y, et al: Initial experience with oral contrast in PET/CT: phantom and clinical studies. *J Nucl Med* 44: 412–416, 2003.
- Kamel E, Hany TF, Burger C, et al: CT vs 68Ge attenuation correction in a combined PET/CT system: evaluation of the effect of lowering the CT tube current. *Eur J Nucl Med Mol Imaging* 29:346–350, 2002.

- de Juan R, Seifert B, Berthold T, et al: Clinical evaluation of a breathing protocol for PET/CT. *Eur Radiol* 14:1118–1123, 2004.
- Gilman MD, Fischman AJ, Krishnasetty V, et al: Optimal CT breathing protocol for combined thoracic PET/CT. AJR Am J Roentgenol 187: 1357–1360, 2006.
- Blake MA, Singh A, Setty BN, et al: Pearls and pitfalls in interpretation of abdominal and pelvic PET-CT. *Radiographics* 26:1335–1353, 2006.
- Moore M, Blake MA: PET/CT in abdominal and pelvic malignancies: principles and practices. In Kalra MK, Saini S, Rubin GR, editors: *MDCT from protocols to practice*, New York, 2008, Springer, pp 166–208.
- Townsend DW: Physics and instrumentation for PET. In Wahl RL, editor: RSNA syllabus: categorical course in diagnostic radiology: clinical PET and PET/CT imaging, Oak Brook, IL, 2007, Radiological Society of North America.
- Torigian DA, Zaidi H, Kwee TC, et al: PET/MR imaging: technical aspects and potential clinical applications. *Radiology* 267:26–44, 2013.
- Pichler B, Lorenz E, Mirzoyan R, et al: Performance test of a LSO-APD PET module in a 9.4 Tesla magnet. Paper presented at 1997 IEEE Nuclear Science Symposium; November 9-15, 1997; Albuquerque, NM.
- 24. Catana C, Guimaraes AR, Rosen BR: PET and MR imaging: the odd couple or a match made in heaven? J Nucl Med 54:815–824, 2013.

# 13

# Positron Emission Tomography and Positron Emission Tomography/Computed Tomography Clinical Applications

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The focus of this chapter is on positron emission tomography (PET) and PET and computed tomography (PET/CT) applications specific to the tumors arising in the gastrointestinal tract and female gynecologic organs, excluding systemic malignancies such as lymphoma and melanoma, which can manifest in the abdomen (Figure 13-1), as well as other approved extraabdominal malignancies that can metastasize to the abdomen, such as lung and breast cancers.

# **Imaging of Specific Areas**

### GASTROINTESTINAL TRACT

#### Esophageal Carcinoma

Because it is mainly an intrathoracic organ, the esophagus will not be discussed except to note that the incidence of adenocarcinoma of the distal esophagus and gastroesophageal junction has increased dramatically in recent years, currently accounting for the majority of new cases of esophageal cancer.<sup>1</sup> The Centers for Medicare and Medicaid (CMS) guidelines in the United States approve fluorodeoxyglucose (FDG)-PET, and thus PET/ CT, for the diagnosis, staging, and restaging of patients with esophageal cancer, including both squamous cell carcinoma and adenocarcinoma subtypes (Figure 13-2).

#### Colorectal Carcinoma

Colorectal cancer is the malignant abdominal tumor that has been extensively investigated with FDG-PET and PET/CT. The CMS guidelines in the United States have approved Medicare coverage for FDG-PET, and thus PET/CT, for the diagnosis, staging, and restaging of patients with colorectal cancer.

**Diagnosis.** FDG-PET is sensitive for detecting primary colorectal carcinoma (95% to 100%), but it has unacceptably lower specificity than conventional modalities at initial staging. In practice, FDG-PET is therefore rarely specifically used for the diagnosis of colorectal cancer, although it may incidentally detect such a tumor as PET, and especially PET/CT, becomes more extensively used. At the primary site, however, the positive predictive value of PET is lower than the negative predictive value, owing to the false-positive FDG-PET findings of both physiologic bowel activity and inflammatory processes.<sup>2</sup> **Staging.** In staging patients with colorectal cancer, FDG-PET and PET/CT are mainly used to assess regional lymph node involvement and distant metastases. However, FDG-PET has been shown to have a very low sensitivity of between 22% and 29% for regional lymph node metastases, with CT also demonstrating low values (29%). However, FDG-PET specificity was superior (96% vs. 85%).<sup>3</sup> False-negative findings in regional metastatic lymph nodes on FDG-PET are considered to be due to low sensitivity for microscopic involvement of small lymph nodes or occasionally as a result of increased FDG uptake by the primary tumor, which masks the immediately neighboring structures.

Most patients with colorectal cancer at initial staging have disease limited to the colon or to regional pericolic or mesenteric lymph nodes. For patients with early colorectal cancer, surgery is usually performed with the intention to achieve cure. However, distant metastatic disease may necessitate the surgery for complications, which include hemorrhage, obstruction, and perforation. Given this role of surgery in both regional and advanced disease, surgical and pathologic criteria define the colorectal cancer staging classification.<sup>4</sup>

The standard tumor, node, metastasis (TNM) classification is currently advocated by the American Joint Committee on Cancer. Because of inherent technologic limitations, imaging modalities today are generally unable to match the diagnostic staging information provided by surgical and pathologic findings. PET cannot provide an accurate T-stage determination necessary for TNM nomenclature, in which exact depth of invasion is the primary parameter. PET is usually accurate only in cases of gross serosal penetration and invasion of neighboring structures. CT gives more exact structural information but, unfortunately, usually also cannot adequately resolve the bowel wall layers. N staging necessitates evaluation of mesenteric nodes as well as pericolic nodes, which are frequently small and lie beside the primary tumor. Furthermore, pericolic nodes again are often involved microscopically by tumor, which usually can be diagnosed only by histopathologic evaluation.<sup>5</sup> Despite the clear superiority of surgery and histopathology at TNM staging, preoperative imaging detection of nodal or organ metastases is important in guiding the general management toward palliation or curative tumor resection. Notwithstanding its staging limitations, PET/CT offers combined metabolic and

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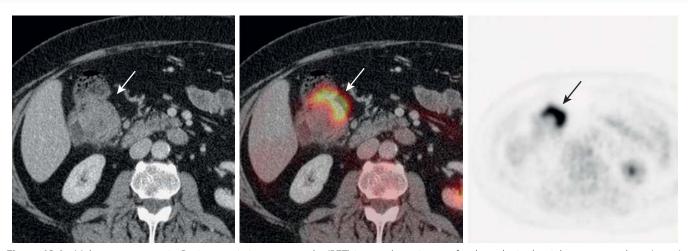


Figure 13-1 Melanoma metastasis. Positron emission tomography (PET) image shows intense focal uptake in the right upper quadrant (arrow), which coregisters to a large colonic soft tissue mass (arrows) on computed tomography (CT) and PET/CT images, representing a melanoma metastasis to the bowel wall.

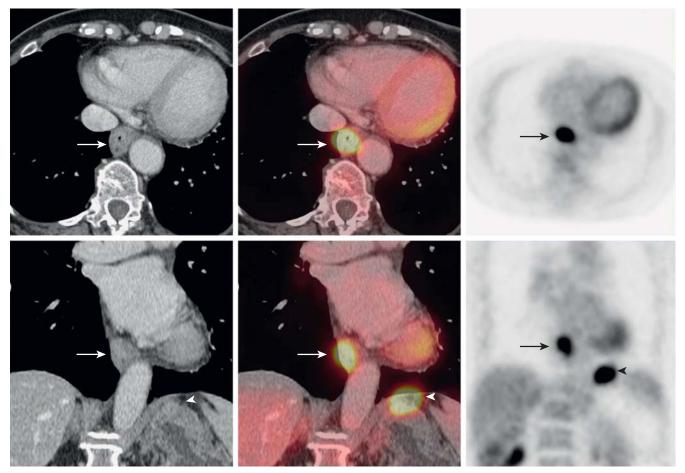


Figure 13-2 Esophageal cancer. Focal fluorodeoxyglucose (FDG) uptake in lower esophagus corresponding to esophageal thickening (arrows), representing an esophageal adenocarcinoma with a left diaphragmatic FDG-avid metastatic lymph node (arrowheads).

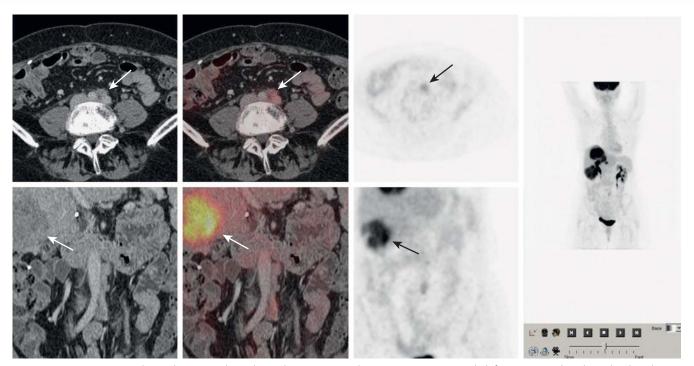


Figure 13-3 Metastatic colorectal cancer. Fluorodeoxyglucose-positive liver masses (arrows) with left para-aortic lymph node also showing increased uptake (arrows) as a result of hepatic metastases and para-aortic metastatic adenopathy.

structural information that is particularly useful in cases of more advanced local disease.

**Metastatic Disease.** Disease spread beyond the regional pericolic or mesenteric lymph nodes represents metastatic disease. Lymphatic spread usually involves internal iliac or retroperitoneal nodes, and hematogenous spread of colorectal cancer usually involves the lungs or liver (Figure 13-3). Metastases to other sites in the absence of pulmonary or hepatic involvement are relatively unusual. A major advantage of PET as well as PET/ CT is the accurate detection of distant metastases.<sup>3</sup>

Liver metastases, if recognized early enough, may be treated by neoadjuvant chemotherapy and resection, which may lengthen survival for patients with colorectal cancer. Both PET and CT are accurate for diagnosis of metastases to the liver. Multidetector row CT following intravenous administration of a contrast agent is a standard primary imaging modality for the assessment of focal liver lesions, with uncertain liver lesions generally evaluated with enhanced MRI. In a meta-analysis performed by Kinkel and colleagues,<sup>6</sup> PET was considered superior to older CT technology for the detection of liver metastases but appears limited in its ability to demonstrate subcentimeter lesions.<sup>7</sup> Sahani and associates<sup>8</sup> showed that gadoliniumenhanced MRI outperformed PET in assessing liver metastases from colorectal and pancreatic cancer, again particularly for small lesions. In addition, PET alone does not provide adequate anatomic information for satisfactory surgical planning regarding the precise localization of metastases according to hepatic segments or with respect to the positioning of lesions in relationship to or involvement of vessels or gallbladder. There are, in general, very few studies comparing PET or PET/CT with modern CT or MRI technique, but a relatively recent study by

Chua and coworkers<sup>9</sup> compared PET/CT with CT with intravenous contrast for the evaluation of patients with hepatic metastases. In patients with colorectal carcinoma, PET/CT had 94% sensitivity and 75% specificity compared with inferior values of 91% and 25%, respectively, for CT. Furthermore, PET/CT may be particularly helpful in patients with fatty liver and hypodense or hypoenhancing liver lesions that are not clearly characterized by CT alone and in patients with an increasing carcinoembryonic antigen (CEA) value in whom CT fails to detect metastases.

The most important role of PET in patients with hepatic metastases is in the diagnosis of extrahepatic metastatic foci that would preclude a curative tumor resection. Several investigators have examined the incremental value of PET as a supplement to CT and found that PET offers significant management information beyond that from CT alone. Investigators have found that when PET is added to CT in preoperative planning for patients with hepatic metastases, additional extrahepatic metastatic foci are identified in 11% to 23% of patients and can result in prolonged patient survival after institution of appropriate patient management. This is often due to a treatment change to a systemic approach with chemotherapy rather than localized therapy.

In patients with elevated CEA levels, FDG-PET can identify metastases previously unrecognized on conventional diagnostic modalities. Valk and coworkers<sup>10</sup> found that an average of \$3003 was saved per patient when PET was added to the preoperative diagnostic workup; FDG scanning was able to differentiate patients with unresectable disease rather than resectable disease, thus avoiding futile operations. This reduction in unnecessary procedures was supported by a study by Park and colleagues.<sup>11</sup> Management was altered in 27 patients based on PET/CT

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results; 9 had intermodality changes, 10 received more extensive surgery, and 8 avoided futile procedures. PET/CT improved the management plan in 24% of patients with primary colorectal cancer.

**Restaging.** As during the initial staging of colorectal cancer, FDG-PET has been reported to be more accurate overall than CT for the presence of metastatic disease. An early study by Hung and colleagues<sup>12</sup> compared FDG-PET, CT, and serum CEA for the evaluation of recurrent colorectal disease. They reported sensitivity and specificity of FDG-PET to be 100% and 83%, respectively, compared with 33% and 86%, respectively, for CEA. Abdominal CT had a lower sensitivity and specificity of 78% and 61% for detecting local recurrence and detected one lymphatic and one hepatic metastasis. They concluded that FDG-PET was more accurate than CT and CEA for the detection of recurrent colorectal cancer. In a recurrent colorectal carcinoma meta-analysis study by Wiering and colleagues,<sup>13</sup> pooled sensitivity and specificity were 88% and 96%, respectively, for FDG-PET in the detection of hepatic metastases compared with lower values of 83% and 84%, respectively, for CT. For extrahepatic disease, pooled sensitivity and specificity for PET were 92% and 95%, respectively, in comparison to 61% and 91% for CT. Clinical management changed in 32% based on the PET findings.

The imaging distinction of postoperative inflammation, scarring, radiation fibrosis, and other sequelae of prior therapy from recurrence is challenging in patients with prior colorectal carcinoma. This is most problematic with rectal tumors, in which presacral scarring and pelvic desmoplastic changes are common findings. With conventional imaging, serial examinations are frequently required before slowly developing malignant changes can be appreciated. When PET is performed more than 6 months after surgery, a time when postsurgical change is not hypermetabolic unless there is a leak causing persistent inflammation, increased FDG uptake in the presacral space generally indicates tumor recurrence.<sup>4</sup> PET/CT at this time has been shown to be highly accurate for differentiation of benign from malignant presacral changes, with reported sensitivity, specificity, and positive and negative predictive values of 100%, 96%, 88%, and 100%, respectively (Figure 13-4).<sup>4</sup> The first published study of PET/CT of colorectal cancer reported that the staging and restaging accuracy improved from 78% with PET alone to 89% with PET/CT. The frequency of equivocal and probable lesion characterization was halved,<sup>14</sup> and the superiority of PET/CT over CT or PET alone has become more established with numerous studies demonstrating improved results.<sup>15,16</sup> Furthermore, PET/CT as a single study is more accurate for recurrent colorectal cancer than coregistration of two separately acquired PET and CT studies.<sup>10</sup>

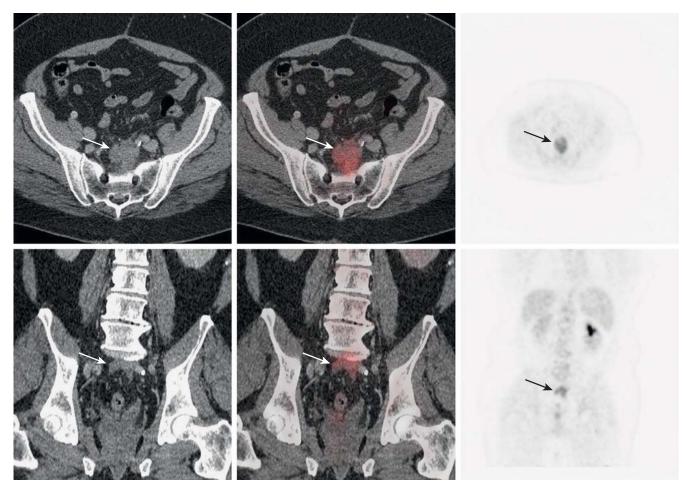


Figure 13-4 Colorectal cancer recurrence. Increased fluorodeoxyglucose uptake (arrows) in presacral soft tissue consistent with recurrent disease in this patient with colorectal cancer.

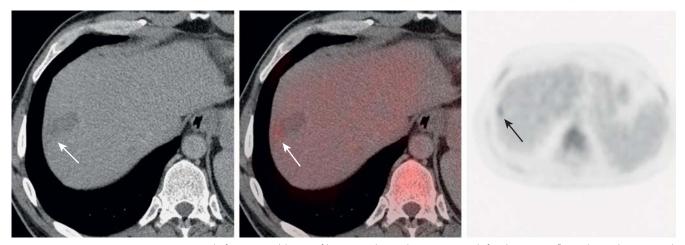


Figure 13-5 Treatment monitoring. Postradiofrequency ablation of hepatic colorectal metastasis with focal posterior fluorodeoxyglucose uptake (arrows) corresponding to an irregularly enhancing focus, consistent with recurrent disease at the edge of the low-density zone of ablation.

**Future Positron Emission Tomography and Computed Tomography Applications for the Patient With Colorectal Disease.** PET/CT will continue to play an important role in determining the resectability status of patients with recurrent rectal carcinoma before surgery and in the planning of aggressive procedures (Figure 13-5) but is limited in defining local invasion of rectal tumors to adjacent tissues. Assessment of neoadjuvant therapy and guidance for radiation therapy are other applications that may be particularly suited to PET/CT. CT colonography (virtual colonoscopy) is a recently approved approach for the evaluation of patients at risk for colon cancer. It is possible combined PET/CT colonography will add specificity by selectively identifying hypermetabolic polyps, likely carrying a higher risk for malignant degeneration.

#### Other Gastrointestinal Malignancies

PET and PET/CT have been used to assess patients with a number of other malignancies associated with the gastrointestinal tract and other abdominal organs. Although many of these are not currently covered by the CMS in the United States, the National Oncologic PET Registry (NOPR) has allowed their use for such diseases if patients are suitably enrolled, and with time many of these malignancies may gain full coverage.<sup>17</sup> Some of these therefore will be briefly discussed here.

**Gastric Cancer.** Early-stage gastric carcinoma has a relatively good prognosis. However, unfortunately patients usually present late with advanced disease and, as a result, it is the second leading cause of cancer death worldwide. Where screening for gastric cancer occurs, the prognosis is better because the malignancy is detected at an earlier stage.

The role of FDG-PET and PET/CT in gastric cancer remains controversial. Despite a positive initial study by Yeung and colleagues,<sup>18</sup> most subsequent studies have demonstrated poorer rates of primary lesion detection, including a study by Shoda and coworkers,<sup>19</sup> which reported just 10% sensitivity and 99% specificity for early gastric cancer. This has led some authors to conclude that FDG-PET is not a suitable first-line diagnostic procedure in the detection of gastric cancer and is not helpful in tumor staging. There are a number of reasons for the relatively poor performance of FDG-PET in gastric cancer. First, normal physiologic FDG uptake in the stomach and gastroesophageal junction is variable and can have a focal appearance, especially if the stomach is empty and collapsed or after partial gastrectomy for malignancy. Benign inflammatory conditions demonstrate increased uptake, which can result in false-positive results. It has been proposed that the sensitivity of PET/CT may be improved upon with the ingestion of water or neutral density contrast to distend the stomach at the time of scanning. Stahl and associates<sup>20</sup> reported variable FDG uptake to be dependent on differing histopathologic findings, which may help explain the variable results for FDG-PET in gastric carcinoma. They reported overall 60% sensitivity for the detection of locally advanced gastric cancers. Within this group, the detection rate was higher for intestinal type at 83% versus just 41% for the diffuse type. The mean standard uptake value was also significantly lower for mucus-containing versus non-mucus-containing tumors (Figure 13-6).

Although unlikely to be highly accurate in local staging of gastric cancer, PET/CT may play a useful role in the detection of distant metastases, such as those of the liver, lungs, adrenal glands, ovaries, and skeleton. FDG-PET also may be helpful in the assessment of chemotherapy, allowing for the identification of early response to treatment. More recently, there has been some interest in PET using different radiotracers. Herrmann and associates<sup>21</sup> reported on a comparison of 3-deoxy-3-18F-fluorothymidine (FLT) with FDG for the detection of gastric cancer and reported 100% sensitivity for FLT and 69% for FDG. Further studies are needed to determine the efficacy of FDG and other novel PET radiotracers in the detection of local nodal metastases and peritoneal dissemination.

#### Tumors of the Small Intestine

Adenocarcinoma, a rare tumor of the small intestine, mostly occurs in the duodenum. The more common small intestinal tumors include neuroendocrine tumors and sarcomas occurring mainly in the jejunum and ileum. Metastases also may occur especially from breast or melanoma and may be detected with PET/CT. PET of neuroendocrine tumors has been successful with the use of FDG and with novel radiotracers such as 6-fluoro-L-dopa (FDOPA) and 68Ga-DOTA-D Phe(1)-Tyr(3)-Octreotide (DOTATOC). FDG-PET also has been useful in the evaluation of both bone and soft tissue sarcomas. Bastiaannet and colleagues<sup>22</sup> reported pooled sensitivity, specificity, and

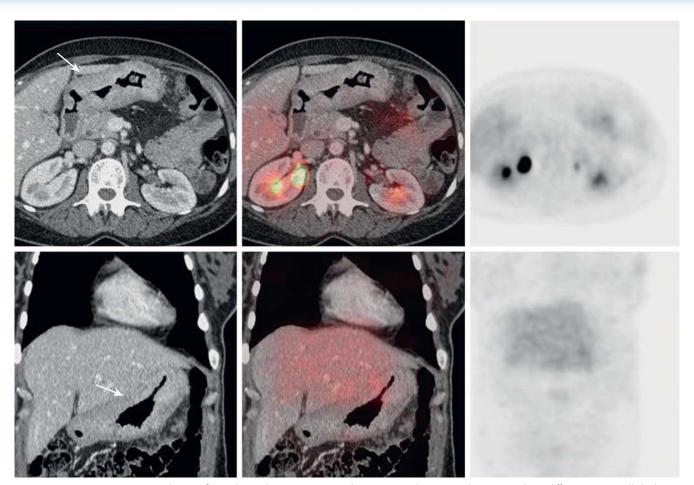


Figure 13-6 Mucinous tumor with poor fluorodeoxyglucose (FDG) uptake. Computed tomography images show diffuse gastric wall thickening (arrows) owing to a mucinous gastric adenocarcinoma that does not show significant FDG uptake.

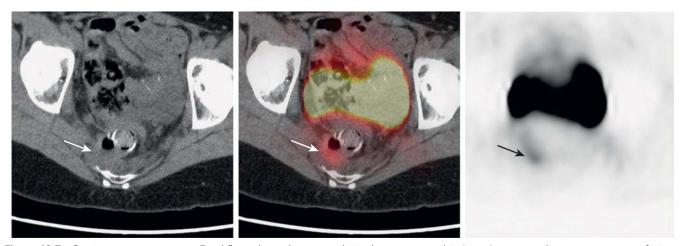
accuracy of 91%, 85%, and 88%, respectively, for PET detection of sarcoma in a meta-analysis. They demonstrated its ability to discriminate between low- and high-grade sarcomas.

**Gastrointestinal Stromal Tumors.** Gastrointestinal stromal tumors (GISTs) are uncommon, accounting for less than 6% of all sarcomas and 3% of all gastrointestinal neoplasms. Most (70% to 80%) GISTs are benign. GISTs originate most commonly in the stomach and small bowel but can arise from anywhere along the gastrointestinal tract. They usually arise in the bowel wall, generally from or between the muscularis mucosa and propria. They also may originate in the mesentery or omentum. Metastatic disease can occur locally by direct invasion of adjacent structures or less typically by involvement of regional lymph nodes. Distant metastatic disease can involve the peritoneum as well as liver, lung, and bones.

There is variable FDG uptake by GISTs. FDG-PET was performed on eight patients, and the primary lesion was identified in just 50% of cases in one study.<sup>23</sup> The false-negative results were in smaller lesions, with a mean diameter of 6 cm and a homogeneous appearance on CT. The PET-positive cases were larger and heterogeneous on CT, and all had metastatic disease. The superior ability of contrast-enhanced CT over FDG-PET in the detection of GIST was confirmed by Goerres and associates,<sup>24</sup> who reported variable FDG uptake and a greater sensitivity for contrast-enhanced CT for lesion detection as compared with PET. The varied reported accuracy of PET at GIST staging may be due to the varied nature of the neoplasm itself. Although the majority of GISTs are benign, there is a histologic continuum between benign and malignant lesions. There is higher FDG uptake in more malignant lesions, and it is possible that this may be used preoperatively to assess malignant potential. Goerres and coworkers<sup>24</sup> concluded that single-stage PET/CT was superior to either PET and/or CT. Comprehensive surgical removal offers the best chance of cure, and the tyrosine kinase inhibitor imatinib has demonstrated good response rates. Heinicke and colleagues<sup>25</sup> reported that FDG-PET can assess the response to imatinib at just 1 week after commencing therapy. In another study, PET/CT was found to be superior to separate PET and CT at tumor response to imatinib treatment characterization, demonstrating 95% accuracy at 1 month and 100% accuracy at 3 and 6-month follow-up.<sup>26</sup> Not only can PET and PET/CT provide information on treatment response but they also have been shown that the degree of FDG uptake at both initial staging and follow-up provides important prognostic information.<sup>2</sup>

#### GYNECOLOGIC MALIGNANCY

CMS guidelines in the United States approve the use of FDG-PET, and thus PET/CT, for use in staging patients with cervical cancer with conventional imaging negative for extrapelvic



**Figure 13-7** Ovarian cancer recurrence. Focal fluorodeoxyglucose uptake in the posterior pelvis (*arrow*) corresponding to asymmetric soft tissue thickening on computed tomography/positron emission tomography images consistent with recurrent disease in this patient status postsurgery for ovarian cancer.

metastatic disease. CMS guidelines also approve the use of PET, and thus PET-CT, for patients with ovarian cancer in certain circumstances. PET and PET/CT have also been used to assess patients with endometrial and prostate cancer.

In premenopausal women, the endometrium demonstrates biphasic FDG uptake peaks during the ovulatory and menstrual phases. In addition, FDG uptake has been demonstrated in uterine fibroids (up to 18% in one series) but only in premenopausal women. Increased ovarian FDG uptake may transiently be seen in premenopausal patients owing to uptake in a corpus luteal cyst. However, ovarian uptake in postmenopausal women is not physiologic and is indicative of malignancy.

#### Cervical Cancer

Cervical cancer, although decreasing, is still estimated to be the third most common gynecologic malignancy in the United States. PET/CT is valuable in the primary staging of untreated advanced cervical cancer, for evaluation of unexplained tumor marker elevation posttreatment, and for restaging of potentially curable recurrent cervical cancer, although it is of limited value in assessing early-stage cervical cancer. PET is approved in the evaluation of asymptomatic patients with cervical tumors with high tumor markers and negative conventional imaging.

A meta-analysis of 15 studies of FDG-PET in cervical cancer reported a pooled sensitivity and specificity of 84% and 95%, respectively, for aortic node metastases and 79% sensitivity and 99% specificity for pelvic node metastases.<sup>27</sup>

In the evaluation of cervical cancer recurrence, PET has been shown to be 90.3% sensitive and 76.1% specific for the detection of disease recurrence in patients with otherwise no evidence of cervical cancer after treatment. The meta-analysis of data from 15 studies on FDG-PET in cervical cancer reported a pooled sensitivity and specificity of 96% and 81%, respectively, for recurrent cervical cancer with clinical suspicion.<sup>27</sup> The results for combined PET/CT in the evaluation of disease recurrence are even better, with one study reporting sensitivity, specificity, and accuracy rates of 90.3%, 81.0%, and 86.5%, respectively.<sup>28</sup>

The use of PET/CT alters patient management, by up to 23% of cases in one study.<sup>28</sup> Assessment of para-aortic lymph node metastases is prognostically important and is related to

progression-free survival in advanced cervical cancer. PET has high sensitivity and specificity and is more sensitive than MRI or CT for the detection of para-aortic lymphadenopathy from advanced cervical cancer.<sup>27</sup>

#### **Ovarian Cancer**

Ovarian cancer is responsible for more than half of gynecologic malignancy–related deaths. The overall 5-year survival for advanced disease is only 17%.

Reports of PET and PET/CT in ovarian cancer demonstrate mixed results. One study demonstrated CT to have a 53% accuracy rate for staging of newly diagnosed ovarian cancer in comparison with surgical staging. When the CT studies were evaluated conjointly with FDG-PET, the accuracy rate for combined imaging was 87%.<sup>29</sup> The overall FDG-PET sensitivity rates for detection of recurrent ovarian cancer range between 45% and 100%, with specificity rates of 40% to 99% (Figure 13-7).<sup>29</sup> Currently, PET is considered to be beneficial for patients with leveled off or increasing abnormal serum CA-125 values and for patients with CT- or MRI-defined localized recurrence for whom biopsy is not possible. Second-look laparotomy or laparoscopy is sometimes performed on patients after treatment who do not have clinical evidence of disease to assess disease response. FDG-PET with second-look laparotomy can decrease unnecessary laparotomies from 70% to 5% and also reduce health care costs. Further studies are needed to clarify the precise role of PET and PET/CT in patients with ovarian cancer.

#### Endometrial Cancer

Endometrial carcinoma is the fourth most common cancer in women and the most common female pelvic malignancy. It is treated and staged with surgery, but, as adjuvant radiation therapy is given in most cases, assessment of nodal involvement is important.

One prospective study assessing preoperative evaluation of patients with endometrial carcinoma reported 96.7% sensitivity for PET (Figure 13-8). However, PET detected none of the five cases of lymph node metastases less than 1 cm in diameter and, excluding retroperitoneal lymph nodes, PET proved to be 83.3% sensitive for the detection of extrauterine lesions.<sup>30</sup>

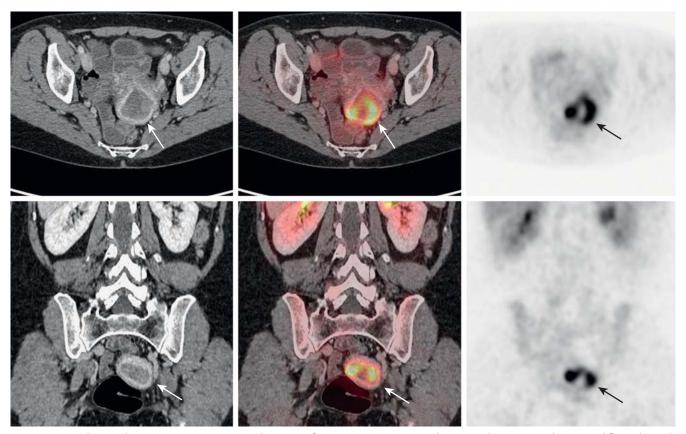


Figure 13-8 Endometrial cancer staging. Large central uterine soft tissue mass on computed tomography (arrows) with increased fluorodeoxyglucose uptake on the positive emission tomography images (arrows) representing endometrial cancer.

Belhocine and colleagues<sup>31</sup> assessed the utility of FDG-PET in the posttherapy surveillance of endometrial cancer and found 96% sensitivity, 78% specificity, and 90% accuracy for the detection of residual or recurrent disease. These results have been supported by other studies. Most of these studies have highlighted that the performance of PET is improved upon when combined with a morphologic imaging modality. Sironi and associates<sup>32</sup> specifically evaluated the role of PET/CT in patients with uterine cancer, either cervical or endometrial, for the detection of tumor recurrence. They reported patient-based sensitivity, specificity, and accuracy for the detection of tumor recurrence of 93%, 100%, and 96%, respectively. The positive and negative predictive values were 100% and 92%.

These results emphasize the benefits of PET and PET/CT in endometrial carcinoma. Early results have shown that addition of PET to CT may have important prognostic capabilities and also may affect patient management in up to a third of cases. PET/CT guides pelvic radiation portals and helps direct intensity-modulated radiotherapy to this area, as well as elsewhere in the body, by defining nodal sites of tumor involvement. This enables tailored radiation doses with sparing of normal tissues.

#### POSITRON EMISSION TOMOGRAPHY MAGNETIC RESONANCE

PET/MR is the newest clinical hybrid imaging modality, though its precise clinical role has yet to be defined. It has a number of advantages over PET/CT.33 First, MRI demonstrates higher soft tissue contrast, even without the use of intravenous contrast. It is therefore beneficial for a number of malignant diseases, in particular liver lesions.<sup>34</sup> Second, MR has an advantage in the assessment of bone/bone marrow. A recent study demonstrated potential improvement in the detection of PET/MRI in extranodal lymphoma, particularly in the bone marrow.<sup>35</sup> The increased sensitivity of MRI for bone marrow involvement has the potential to allow for targeted bone marrow biopsies as well as more aggressive early treatment in patients with disease that would have previously been understaged. Third, MRI has the ability to measure additional parameters that allow further characterization of malignancies and their biologic properties. Additional parameters routinely assessed include tumor vascularity and perfusion properties without the high radiation dose of CT-based perfusion.<sup>36</sup> This would allow evaluation of intravascular treatments such as chemoembolization and selective internal radiotherapy, as well as monitoring treatment effects early after administration.<sup>37</sup> Diffusion weighted imaging in MRI also can be used to assess early tumor response.<sup>38</sup> An additional advantage of whole-body PET/MR relates to radiation dose reduction in children, young adults, and pregnant women.

Disadvantages of PET/MR are in the detection of small pulmonary lesions.<sup>39</sup> Certain contraindications also prevent patients from having an MRI, including most types of cardiac pacemakers and implanted defibrillators as well as certain metallic implants.

#### **Key Points**

- PET/CT has been demonstrated to be the imaging modality of choice for many abdominopelvic malignancies.
- PET/CT plays a particularly important role in the management of patients with colorectal cancer and cervical cancer.
- Current and future results of the National Oncologic PET Registry may provide evidence to further expand approved PET and PET/CT indications and applications.
- Combined PET/CT is superior to later coregistered images for diagnostic accuracy.
- New radiotracers may help to improve the performance of PET/CT in tumors that currently are better imaged with CT or MRI.
- PET/MRI is a new clinical hybrid imaging modality which has a number of advantages over PET/CT.

#### SUGGESTED READINGS

Blodgett TM, Meltzer CC, Townsend DW: PET/CT: form and function. *Radiology* 242:360–385, 2007.

- Chao A, Chang TC, Ng KK, et al: 18F-FDG PET in the management of endometrial cancer. *Eur J*
- the management of endometrial cancer. *Eur J Nucl Med Mol Imaging* 33:36–44, 2006. Fraum TJ, Fowler KJ, McConathy J, et al: PET/MRI
- for the body imager: abdominal and pelvic oncologic applications. *Abdom Imaging* 40:1387–1404, 2015.

#### REFERENCES

- 1. Cerfolio RJ, Bryant AS, Ohja B, et al: The accuracy of endoscopic ultrasonography with fineneedle aspiration, integrated positron emission tomography with computed tomography, and computed tomography in restaging patients with esophageal cancer after neoadjuvant chemoradiotherapy. *J Thorac Cardiovasc Surg* 129:1232–1241, 2005.
- Gutman F, Alberini JL, Wartski M, et al: Incidental colonic focal lesions detected by FDG PET/CT. AJR Am J Roentgenol 185:495–500, 2005.
- Kamel IR, Cohade C, Neyman E, et al: Incremental value of CT in PET/CT of patients with colorectal carcinoma. *Abdom Imaging* 29:663– 668, 2004.
- Even-Sapir E, Parag Y, Lerman H, et al: Detection of recurrence in patients with rectal cancer: PET/CT after abdominoperineal or anterior resection. *Radiology* 232:815–822, 2004.
- Rohren EM, Turkington TG, Coleman RE: Clinical applications of PET in oncology. *Radiology* 231:305–332, 2004.
- Kinkel K, Lu Y, Both M, et al: Detection of hepatic metastases from cancers of the gastrointestinal tract by using noninvasive imaging methods (US, CT, MR imaging, PET): A metaanalysis. *Radiology* 224:748–756, 2002.
- Rohren EM, Paulson EK, Hagge R, et al: The role of F-18-FDG PET in preoperative assessment of the liver in patients being considered for curative resection of hepatic metastases from colorectal cancer. *Clin Nucl Med* 27:550–555, 2002.
- Sahani DV, Kalva SP, Fischman AJ, et al: Detection of liver metastases from adenocarcinoma of colon and pancreas: comparison of mangafodipir trisodium enhanced liver MRI and whole body FDG-PET. *AJR Am J Roentgenol* 185:239– 246, 2005.
- Chua SC, Groves AM, Kayani I, et al: The impact of (18)F-FDG PET/CT in patients with liver metastases. *Eur J Nucl Med Mol Imaging* 34:1906–1914, 2007.
- Valk PE, Abella-Columna E, Haseman MK, et al: Whole-body PET imaging with (18F)fluorode-

Kusmirek J, Robbins J, Allen H, et al: PET/CT and MRI in the imaging assessment of cervical cancer. *Abdom Imaging* 40:2486–2511, 2015.

- Moore M, Blake MA: PET/CT in abdominal and pelvic malignancies: principles and practices. In Kalra MK, Saini S, Rubin GR, editors: *MDCT from protocols to practice*, New York, 2008, Springer, pp 166–208.
- Prabhakar HB, Kraeft JJ, Schorge JO, et al: FDG PET-CT of gynecologic cancers: pearls and pit-falls. *Abdom Imaging* 40:2472–2485, 2015.
- Yen TC, Lai CH: Positron emission tomography in gynecologic cancer. Semin Nucl Med 36:93–104, 2006.

oxyglucose in management of recurrent colorectal cancer. *Arch Surg* 134:503–511, 1999.

- Park IJ, Kim HC, Yu CS, et al: Efficacy of PET/ CT in the accurate evaluation of primary colorectal carcinoma. *Eur J Surg Oncol* 32:941– 947, 2006.
- Hung GU, Shiau YC, Tsai SC, et al: Value of 18F-fluoro-2-deoxyglucose positron emission tomography in the evaluation of recurrent colorectal cancer. *Anticancer Res* 21:1375–1378, 2001.
- 13. Wiering B, Krabbe PF, Jager GJ, et al: The impact of fluoro-18-deoxyglucose-positron emission tomography in the management of colorectal liver metastases. *Cancer* 104:2658–2670, 2005.
- 14. Cohade C, Osman M, Leal J, et al: Direct comparison of (18)F-FDG PET and PET/CT in patients with colorectal carcinoma. *J Nucl Med* 44:1797–1803, 2003.
- Chen LB, Tong JL, Song HZ, et al: (18)F-FDG PET/CT in detection of recurrence and metastasis of colorectal cancer. *World J Gastroenterol* 13:5025–5029, 2007.
- Kim JH, Czernin J, Allen-Auerbach MS, et al: Comparison between 18F-FDG PET, in-line PET/CT, and software fusion for restaging of recurrent colorectal cancer. *J Nucl Med* 46:587– 595, 2005.
- Hillner BE, Liu D, Coleman RE, et al: The National Oncologic PET Registry (NOPR): design and analysis plan. J Nucl Med 48:1901– 1908, 2007.
- Yeung HW, Macapinlac H, Karpeh M, et al: Accuracy of FDG-PET in gastric cancer: preliminary experience. *Clin Positron Imaging* 1:213–221, 1998.
- Shoda H, Kakugawa Y, Saito D, et al: Evaluation of (18)F-2-deoxy-2-fluoro-glucose positron emission tomography for gastric cancer screening in asymptomatic individuals undergoing endoscopy. *Br J Cancer* 97:1493–1498, 2007.
- Stahl A, Ott K, Weber WA, et al: FDG PET imaging of locally advanced gastric carcinomas: correlation with endoscopic and histopathological findings. *Eur J Nucl Med Mol Imaging* 30:288–295, 2003.

- Herrmann K, Ott K, Buck AK, et al: Imaging gastric cancer with PET and the radiotracers 18F-FLT and 18F-FDG: a comparative analysis. *J Nucl Med* 48:1945–1950, 2007.
- 22. Bastiaannet E, Groen H, Jager PL, et al: The value of FDG-PET in the detection, grading and response to therapy of soft tissue and bone sarcomas; a systematic review and meta-analysis. *Cancer Treat Rev* 30:83–101, 2004.
- Hersh MR, Choi J, Garrett C, et al: Imaging gastrointestinal stromal tumors. *Cancer Control* 12:111–115, 2005.
- Goerres GW, Stupp R, Barghouth G, et al: The value of PET, CT and in-line PET/CT in patients with gastrointestinal stromal tumours: longterm outcome of treatment with imatinib mesylate. *Eur J Nucl Med Mol Imaging* 32:153– 162, 2005.
- Heinicke T, Wardelmann E, Sauerbruch T, et al: Very early detection of response to imatinib mesylate therapy of gastrointestinal stromal tumours using 18fluoro-deoxyglucose-positron emission tomography. *Anticancer Res* 25:4591– 4594, 2005.
- 26. Antoch G, Kanja J, Bauer S, et al: Comparison of PET, CT, and dual-modality PET/CT imaging for monitoring of imatinib (STI571) therapy in patients with gastrointestinal stromal tumors. *J Nucl Med* 45:357–365, 2004.
- Havrilesky LJ, Kulasingam SL, Matchar DB, et al: FDG-PET for management of cervical and ovarian cancer. *Gynecol Oncol* 97:183–191, 2005.
- Chung HH, Jo H, Kang WJ, et al: Clinical impact of integrated PET/CT on the management of suspected cervical cancer recurrence. *Gynecol Oncol* 104:529–534, 2007.
- Yoshida Y, Kurokawa T, Kawahara K, et al: Incremental benefits of FDG positron emission tomography over CT alone for the preoperative staging of ovarian cancer. *AJR Am J Roentgenol* 182:227–233, 2004.
- 30. Suzuki R, Miyagi E, Takahashi N, et al: Validity of positron emission tomography using fluoro-2-deoxyglucose for the preoperative evaluation of endometrial cancer. *Int J Gynecol Cancer* 17:890–896, 2007.

#### 13 Positron Emission Tomography and Positron Emission Tomography/Computed Tomography Clinical Applications 91

- Belhocine T, De Barsy C, Hustinx R, et al: Usefulness of (18)F-FDG PET in the post-therapy surveillance of endometrial carcinoma. *Eur J Nucl Med Mol Imaging* 29:1132–1139, 2002.
- 32. Sironi S, Picchio M, Landoni C, et al: Posttherapy surveillance of patients with uterine cancers: value of integrated FDG PET/CT in the detection of recurrence. *Eur J Nucl Med Mol Imaging* 34:472–479, 2007.
- Werner MK, Schmidt H, Schwenzer NF: MR/ PET: a new challenge in hybrid imaging. *AJR Am J Roentgenol* 199:272–277, 2012.
- 34. Floriani I, Torri V, Rulli E, et al: Performance of imaging modalities in diagnosis of liver metas-

tases from colorectal cancer: a systematic review and meta-analysis. *J Magn Reson Imaging* 31:19–31, 2010.

- 35. Heacock L, Weissbrot J, Raad R, et al: PET/MRI for the evaluation of patients with lymphoma: initial observations. *AJR Am J Roentgenol* 204: 842–848, 2015.
- Paldino MJ, Barboriak DP: Fundamentals of quantitative dynamic contrast-enhanced MR imaging. *Magn Reson Imaging Clin N Am* 17: 277–289, 2009.
- 37. Giesel FL, Mehndiratta A, Locklin J, et al: Image fusion using CT, MRI and PET for treatment planning, navigation and follow up in

percutaneous RFA. *Exp Oncol* 31:106–114, 2009.

- Schraml C, Schwenzer NF, Clasen S, et al: Navigator respiratory-triggered diffusion-weighted imaging in the follow-up after hepatic radiofrequency ablation: initial results. J Magn Reson Imaging 29:1308–1316, 2009.
- 39. Sieren JC, Ohno Y, Koyama H, et al: Recent technological and application developments in computed tomography and magnetic resonance imaging for improved pulmonary nodule detection and lung cancer staging. J Magn Reson Imaging 32:1353–1369, 2010.

# 14

# **Ureteral and Kidney Stones**

JORGE A. SOTO

# Etiology

Renal calculi are typically caused by crystallization of supersaturated stone-forming materials in the urine. Calcium, in the form of calcium oxalate, calcium phosphate, and calcium urate, is the most common stone-forming material. Uric acid is the second most common component. Other less common components include xanthine, cystine, struvite, and precipitation of medications such as the protease inhibitor indinavir sulfate in persons infected with human immunodeficiency virus (HIV). Alternatively, renal pathologic processes may initiate crystal formations within the renal tubules that are extruded into the renal collecting system to undergo further growth. Urinary stasis secondary to chronic obstruction or reflux, urinary pH abnormalities, and chronic infections also may contribute to stone formation.

# **Prevalence and Epidemiology**

Nephrolithiasis and ureterolithiasis represent a significant cause of urinary obstruction and abdominal pain. Infections, such as pyelonephritis, pyonephrosis, or renal abscess, may complicate stone disease and may be difficult to differentiate clinically. Imaging evaluation is necessary to confirm the diagnosis of stone disease and detect complications.

The lifetime risk for forming renal stones differs in various parts of the world: it is 1% to 5% in Asia, 5% to 9% in Europe, and 13% in North America. The composition of stones and their location in the urinary tract, bladder, or kidneys also may significantly differ in different countries. Renal stone disease is slightly more common in males than in females and in whites than in blacks. Stones in the upper urinary tract are related to lifestyle and are more frequent among affluent people, those living in developed countries, and in those with diets high in animal protein. A high frequency of stone formation occurs among hypertensive patients and among those with a high body mass index.

# **Clinical Presentation**

Nephrolithiasis and ureterolithiasis often present as severe colicky pain in the region of the flanks that may radiate into the groin. Nausea and vomiting, costovertebral angle tenderness, and hematuria are commonly present with obstruction of a ureter with urinary calculi.

# Pathophysiology

Most patients with symptomatic renal or ureteral stones present because of flank pain caused by acute ureteral obstruction. The most common location of the stone is in one of the three areas of narrowing in the ureter: the ureteropelvic junction, the pelvic brim as the ureter crosses into the pelvis, and the ureterovesical junction.

### Imaging

### RADIOGRAPHY

On abdominal radiographs, nephrolithiasis may be identified as focal calcific densities projecting over the renal shadows.<sup>1</sup> Also, ureteral and bladder calculi may be identified on plain radiographs. In patients with a known history of renal calculi who have undergone lithotripsy, plain radiographs may be used to evaluate for residual renal or ureteral calculi. When multiple ureteral calculi are identified after lithotripsy, this is termed *steinstrasse*, the translation of this German term being "stone street."

Although computed tomography (CT) has replaced the intravenous pyelogram (IVP) in the majority of patients, some institutions still perform IVP. In acute ureteral obstruction, the IVP demonstrates delayed transit of contrast medium through the affected kidney, with delayed images showing the dilated collecting system and the site of the obstructing stone.<sup>1</sup> The main disadvantage of IVP, in addition to requiring iodinated contrast material, is the potential delay in diagnosis from having to wait for the delayed radiographs.

#### COMPUTED TOMOGRAPHY

CT is the preferred imaging technique for renal stone detection in many institutes because of its high sensitivity, specificity, and ability to detect radiolucent stones.<sup>2,3</sup> Typically, renal stone CT protocols are performed without the use of oral or intravenous contrast media, which may obscure the underlying stones. CT has a high diagnostic accuracy in the detection of renal and ureteral calculi and may be used to differentiate among stones of various chemical composition.1-8 Recently, ultralow-dose CT with a radiation dose equivalent to a kidneyureter-bladder radiograph has been shown to be sufficiently diagnostically accurate in evaluating renal and ureteral calculi.<sup>9,10</sup> The most common forms of renal stones are all readily identified by routine CT techniques (Figures 14-1 and 14-2). However, urinary stones formed by crystallized protease inhibitors used for HIV therapy are more difficult to identify on CT (Figure 14-3).

Secondary CT signs of acute ureteral obstruction include enlargement of the kidney, which often demonstrates diffusely decreased attenuation secondary to edema, perinephric stranding, and dilatation of the ureter and collecting system (see

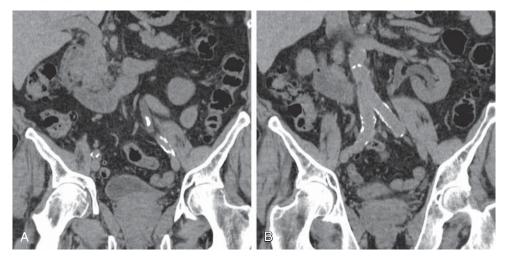
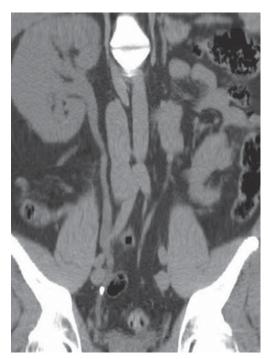


Figure 14-1 A, Coronal reformatted image of axial computed tomography data demonstrates a dense stone within the middle area of the left ureter. B, A slightly more posterior reformatted view than in A shows the dilated collecting system and proximal ureter.



**Figure 14-2** Distal right ureteral stone with hydroureter demonstrated on a coronal reformatted computed tomography image.

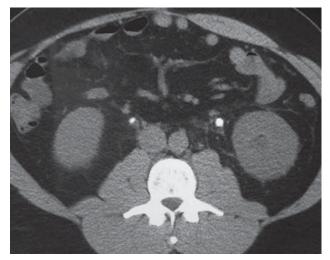
Figures 14-1 and 14-2). Stones are most commonly evident in the three areas of ureteral narrowing: the ureteropelvic junction, the pelvic brim, and the ureterovesical junction. Ureteral stones may demonstrate a "soft tissue rim" sign surrounding the calculus (Figure 14-4), distinguishing a ureteral calculus from adjacent pelvic vein phleboliths. Large intrarenal stones occupying most of the renal pelvis and some of the calyces, known as *staghorn* calculi, also can be seen on CT (Figure 14-5). CT may show renal parenchymal calcifications in cases of nephrocalcinosis (Figure 14-6).

An emerging role for CT is in the differentiation between uric acid (UA) and non–uric acid (NUA) renal stones. A recent



**Figure 14-3** Coronal reformatted computed tomography image shows hydronephrosis and hydroureter on the right side with a distal ureteral stone. The stone is only slightly hyperattenuating relative to the urine-filled ureter. The patient was undergoing therapy with indinavir for human immunodeficiency virus infection.

study using dual-source, dual-energy CT identified 34 patients. A total of 469 stones were identified in dual-source examinations (26 UA and 443 NUA). Overall sensitivity, specificity, and accuracy for identifying UA stones were 73%, 90%, and 89%, respectively. The sensitivity, specificity, and accuracy were 95%, 97%, and 97% for stones 3 mm or greater (n = 341, 19 UA and 322 NUA).<sup>11</sup>



**Figure 14-4** Axial computed tomography image shows bilateral ureteral stones. There is a small crescent of soft tissue partially surrounding the right ureteral stone known as the "soft tissue rim" sign.



**Figure 14-5** Staghorn calculus. The computed tomography image demonstrates a large calculus occupying most of the collecting system of the right kidney.

#### MAGNETIC RESONANCE IMAGING

Occasionally, ureteral or kidney stones may be detected on MRI examinations. On T2-weighted (typically breath-hold half-Fourier acquisition single-shot turbo spin-echo [HASTE]) images, stones typically appear as foci with low signal intensity and partially or completely surrounded by the high signal fluid in the dilated collecting system and/or ureter.<sup>12,13</sup> However, differentiation between an obstructed ureter secondary to a stone and the physiologic dilatation of the ureter and collecting system commonly seen in pregnancy during the second and third trimesters may be difficult.

#### ULTRASONOGRAPHY

Ultrasonography is often employed in patients presenting with acute renal failure. Renal calculi are echogenic foci that typically demonstrate posterior acoustic shadowing.<sup>1,14-16</sup> Also, signs of



**Figure 14-6** Noncontrast computed tomography image demonstrates calcifications within the pyramids of both kidneys. Nephrocalcinosis was secondary to medullary sponge kidney in this patient. Parenchymal calcifications can be associated with ureteral stones.

hydronephrosis and hydroureter may be identified on ultrasound in patients with acute obstruction. In a recent large-scale study, 2759 patients who presented to the emergency department with suspected nephrolithiasis were randomized to ultrasonography or abdominal CT. Initial ultrasonography was associated with lower cumulative radiation exposure than initial CT, without significant differences in high-risk diagnoses with complications, serious adverse events, pain scores, return emergency departments visits, or hospitalizations.<sup>17</sup> Proximal and distal ureteral stones may be clearly identified on ultrasonography; however, bowel gas usually obscures a large part of the ureter; therefore, the sensitivity of ultrasonography for ureteral calculi is significantly less than that of CT. Peristaltic activity of the patent ureter creates ureteral jets in the urinary bladder, and these can be readily identified with color Doppler imaging. The presence of bilateral ureteral jets excludes high-grade ureteral obstruction.

#### IMAGING ALGORITHM

Overall, CT is the preferred method when a diagnosis of ureteral stones is suspected. When a calcification cannot be classified confidently as a ureteral stone, excretory images after intravenous contrast are useful to delineate the stone and the obstructed ureter (Figure 14-7). Ultrasonography is useful as a screening modality because the presence of bilateral jets of urine arising from the ureteral orifices rules out significant obstruction. MRI has little role in the evaluation of ureteral stones. IVP has little role at institutions where rapid access to CT is available (Table 14-1).

#### **Classic Signs**

- Radiography: Calcified stone
- CT: "Soft tissue rim" sign
- Ultrasonography: Intraureteral echogenic focus with hydroureter and hydronephrosis

TABLE Accur	Accuracy, Limitations, and Pitfalls of Modalities Used in Imaging of Ureteral and Renal Stones				
Modality	Accuracy	Limitations	Pitfalls		
Radiography	Sensitivity, 70%	Does not assess degree of obstruction	Calcifications can be confused with phleboliths or gallstones.		
СТ	Sensitivity, 92%-98%	Function not evaluated Radiation exposure	Stones and phleboliths may be difficult to differentiate.		
MRI	Insufficient data	Time consuming Expensive	Interpretation can be difficult.		
Ultrasonograpl	ny Relatively insensitive	Operator dependent	Bowel gas often precludes evaluation of the pelvic region.		



**Figure 14-7** Delayed phase of a contrast-enhanced computed tomography scan (coronal reformatted image) demonstrates the dilated right ureter and a distal obstructing stone.

# **Differential Diagnosis**

Acute ureteral obstruction secondary to an impacted stone should be differentiated from pyelonephritis, acute diverticulitis, and other gastrointestinal causes of acute abdominal pain as well as from acute gynecologic conditions, including ectopic pregnancy and rupture or torsion of ovarian cysts. Depending on the specific clinical presentation, ureteral stones can mimic a ruptured abdominal aortic aneurysm, aortic dissection, renal or splenic infarction, acute cholecystitis, or acute pancreatitis.

If all the signs of acute ureteral obstruction are present, including direct visualization of the stone, the diagnosis can be made with certainty in the majority of cases. On plain radiographs and CT scans, calcifications in the pelvis are very common. Phleboliths typically have a radiolucent center. Calcified atheromas can usually be localized to the wall of an arterial branch. The "soft tissue rim" sign is most useful for making a confident diagnosis of a ureteral stone on CT.

#### Treatment

#### MEDICAL TREATMENT

Obstruction in the absence of infection can be managed with analgesics and hydration. The stone will typically pass if its diameter is smaller than 5 to 6 mm (larger stones are more likely to require surgical measures).

#### SURGICAL TREATMENT

Primary indications for surgical treatment include persistent pain, uncontrolled infection, and persistent obstruction. Extracorporeal shock wave lithotripsy is the least invasive of the surgical methods of stone removal. Approximately 85% of urinary tract calculi that require treatment are currently managed with lithotripsy. Ureteroscopic manipulation of a stone is the next most commonly applied modality. Often, a ureteral stent must be placed after this procedure to prevent obstruction from ureteral spasm and edema. Other options include percutaneous nephrostolithotomy and open extraction.

#### What the Referring Physician Needs to Know

- Where is the stone located?
- How large is the stone?
- Is there associated obstruction?
- Is there associated infection?

#### **Key Points**

- CT is the preferred imaging method for diagnosis of acute ureteral obstruction.
- CT is highly sensitive for urinary calculi.

#### **SUGGESTED READINGS**

- Chen MY, Scharling ES, Zagoria RJ, et al: CT diagnosis of acute flank pain from urolithiasis. *Semin Ultrasound CT MR* 21:2–19, 2000.
- Dalrymple NC, Casford B, Raiken DP, et al: Pearls and pitfalls in the diagnosis of ureterolithiasis with unenhanced helical CT. *Radiographics* 20:439–447, 2000.

#### REFERENCES

- Yilmaz S, Sindel T, Arslan G, et al: Renal colic: comparison of spiral CT, US and IVU in the detection of ureteral calculi. *Eur Radiol* 8:212– 217, 1998.
- Eisner BH, McQuaid JW, Hyams E, et al: Nephrolithiasis: what surgeons need to know. *AJR Am J Roentgenol* 196:1274–1278, 2011.
- Smith RC, Rosenfield AT, Choe KA, et al: Acute flank pain: comparison of non-contrastenhanced CT and intravenous urography. *Radiology* 194:789–794, 1995.
- Smith RC, Verga M, McCarthy S, et al: Diagnosis of acute flank pain: value of unenhanced helical CT. AJR Am J Roentgenol 166:97–101, 1996.
- Preminger GM, Vieweg J, Leder RA, et al: Urolithiasis: detection and management with unenhanced spiral CT: a urologic perspective. *Radiology* 207:308–309, 1998.
- Smith RC, Verga M, Dalrymple N, et al: Acute ureteral obstruction: value of secondary signs of helical unenhanced CT. AJR Am J Roentgenol 167:1109–1113, 1996.
- 7. Boridy IC, Kawashima A, Goldman SM, et al: Acute ureterolithiasis: nonenhanced helical CT

- Goldman SM, Sandler CM: Genitourinary imaging: the past 40 years. *Radiology* 215:313–324, 2000.
- Heidenreich A, Desgrandschamps F, Terrier F: Modern approach of diagnosis and management of acute flank pain: review of all imaging modalities. *Eur Urol* 41:351–362, 2002.

findings of perinephric edema for prediction of degree of ureteral obstruction. *Radiology* 213: 663–667, 1999.

- Boridy IC, Nikolaidis P, Kawashima PA, et al: Ureterolithiasis: value of the tail sign in differentiating phleboliths from ureteral calculi at nonenhanced helical CT. *Radiology* 211:619– 621, 1999.
- Paulson EK, Weaver C, Ho LM, et al: Conventional and reduced radiation dose of 16-MDCT for detection of nephrolithiasis and ureterolithiasis. AJR Am J Roentgenol 190:151–157, 2008.
- Tack D, Sourtzis S, Delpierre I, et al: Low-dose unenhanced multidetector CT of patients with suspected renal colic. *AJR Am J Roentgenol* 180:305–311, 2003.
- Leng S, Shiung M, Ai S, et al: Feasibility of discriminating uric acid from non-uric acid renal stones using consecutive spatially registered low- and high-energy scans obtained on a conventional CT scanner. *AJR Am J Roentgenol* 204:92–97, 2015.
- 12. Regan F, Kuszyk B, Bohlman ME, et al: Acute ureteric calculus obstruction: unenhanced

- Sandhu C, Anson KM, Patel U: Urinary tract stones. I. Role of radiological imaging in diagnosis and treatment planning. *Clin Radiol* 58:415–421, 2003.
- Tamm EP, Silverman PM, Shuman WP: Evaluation of the patient with flank pain and possible ure-teral calculus. *Radiology* 228:319–329, 2003.

spiral CT versus HASTE MR urography and abdominal radiograph. *Br J Radiol* 78:506–511, 2005.

- Sudah M, Vanninen R, Partanen K, et al: Patients with acute flank pain: comparison of MR urography with unenhanced helical CT. *Radiology* 223:98–105, 2002.
- Patlas M, Farkas A, Fisher D, et al: Ultrasound vs CT for the detection of ureteric stones in patients with renal colic. *Br J Radiol* 74:901–904, 2001.
- Sheafor DH, Hertzberg BS, Freed KS, et al: Nonenhanced helical CT and US in the emergency evaluation of patients with renal colic: prospective comparison. *Radiology* 217:792– 797, 2000.
- Fowler KAB, Locken JA, Duchesne JH, et al: US for detecting renal calculi with nonenhanced CT as a reference standard. *Radiology* 222:109–113, 2002.
- 17. Smith-Bindman R, Aubin C, Bailitz J, et al: Ultrasonography versus computed tomography for suspected nephrolithiasis. *N Engl J Med* 371: 1100–1110, 2014.

# **Acute Appendicitis**

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# Etiology

Acute appendicitis results from obstruction of the appendiceal lumen from any cause (most commonly a fecalith), leading to overdistention and superinfection and, if not treated promptly, to perforation and peritonitis.

# **Epidemiology**

Acute appendicitis is a common clinical concern in patients presenting to the emergency department with abdominal pain, with a lifetime risk of 5% to 7%. The mortality rate is less than 1% but may be as high as 20% in certain populations, such as the elderly. In the clinical evaluation and diagnostic investigation of patients with acute right lower quadrant pain, other conditions should be considered in the differential diagnosis. These include right-sided diverticulitis, acute cholecystitis, epiploic appendagitis, renal or ureteral stones, omental infarction, bowel obstruction, and, in females, acute gynecologic conditions.

### **Clinical Presentation**

Patients typically present with gradual onset of anorexia, nausea/vomiting, and nonspecific abdominal pain that worsens progressively and eventually localizes in the right lower quadrant with clinical evidence of peritoneal irritation, leukocytosis, and fever.

### Pathophysiology

The appendiceal orifice is located at the tip of the cecum. However, given the mobility of the cecum itself and the variable length (5 to 12 cm or more) and course of the appendix, the pain can be localized almost anywhere in the abdomen or pelvis.

# Pathology

Initially, the appendiceal lumen occludes secondary to a number of causes, including fecaliths and lymphoid hyperplasia. Once it is occluded, intraluminal fluid continues to accumulate, distending the appendix and eventually increasing the intraluminal and intramural pressures to the point of vascular and lymphatic obstruction. Ineffective venous and lymphatic drainage allows bacterial invasion of the appendiceal wall and lumen. If this bacterial infection is not treated, perforation of the appendix and peritonitis may ensue.

# Imaging

#### RADIOGRAPHY

Abdominal radiographs have very limited clinical utility in patients with suspected appendicitis. A calcified fecalith (appendicolith) may be identified in the right lower quadrant (Figure 15-1), or there may be a focally dilated loop of small bowel ("sentinel loop" sign).

#### COMPUTED TOMOGRAPHY

Computed tomography (CT) is the preferred method for diagnosing appendicitis,<sup>1,2</sup> either after a nonconclusive ultrasound examination or as the first imaging test. On CT, the appendix appears enlarged, often with surrounding inflammatory changes, fascial thickening, and small amounts of free intraperitoneal fluid (Figures 15-2 and 15-3). Appendicoliths are also readily identified on CT (Figure 15-4). There may be edema at the origin of the appendix, as evidenced by thickening of the adjacent cecum, the "arrowhead" sign. There is a wide variation in the diameter of the appendix in normal patients, with sizes ranging up to 1 cm. However, mean values range between 5 and 7 mm. Therefore, when the appendix measures slightly greater than the standard cutoff value of 6 mm, secondary signs of inflammation should be sought to determine if appendicitis is present. Filling of the appendix by orally or rectally introduced positive contrast material is a useful imaging finding in excluding obstruction of the appendix and, therefore, acute appendicitis. However, isolated involvement of the distal segment of the appendix ("tip" appendicitis) is seen occasionally. In patients in whom the appendix is not visualized, this finding, in the absence of right lower quadrant inflammation, carries a high negative predictive value of appendicitis.

The most important complication of acute appendicitis that should be recognized with CT is focal appendiceal rupture. Signs of rupture include periappendiceal abscess (Figure 15-5), extraluminal gas (localized or free), free peritoneal fluid, and focal poor enhancement of the appendiceal wall.<sup>3-6</sup> Other, less common complications include diffuse peritonitis (with free gas in the peritoneal cavity) and portal vein thrombosis.

#### MAGNETIC RESONANCE IMAGING

Pregnant females with abdominal pain often present a diagnostic challenge. As the gravid uterus enlarges, the appendix is displaced from its expected location in the right lower quadrant

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and becomes very difficult to visualize. In those patients with an inconclusive ultrasound examination, both CT and magnetic resonance imaging (MRI) are often employed. Given concerns regarding radiation dose to the fetus, MRI is frequently used to evaluate for suspected appendicitis in pregnant patients.<sup>7-9</sup> MRI offers high diagnostic accuracy and is an excellent modality for excluding appendicitis. The appendix is considered normal when it is 6 mm or less in diameter or filled with air or oral contrast material. As on CT, MRI findings of appendicitis include enlargement of the appendix and associated secondary findings, such as periappendiceal inflammation (Figure 15-6). As the gravid uterus enlarges, the cecum, and therefore

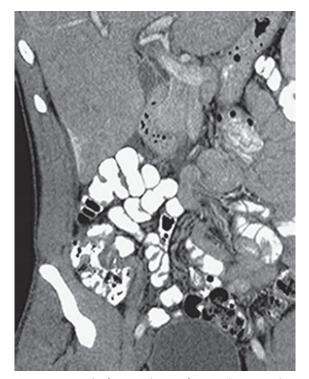


**Figure 15-1** Abdominal radiograph in a patient with acute appendicitis demonstrates a calcification in the right side of the pelvis representing an appendicolith.

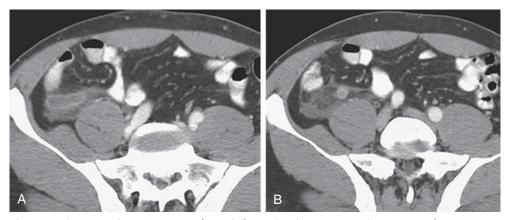
the appendix, may be in atypical locations, displaced superiorly. Therefore, it is helpful to identify the landmarks of the terminal ileum and cecum in attempting to localize the appendix on MRI.

#### ULTRASONOGRAPHY

In the younger population, and especially in females, ultrasonography may be used as an initial imaging evaluation to avoid ionizing radiation.<sup>10</sup> The typical ultrasound findings of appendicitis include the visualization of a noncompressible, blindending tubular structure that is distended with fluid and



**Figure 15-3** Coronal reformatted image from axial computed tomography (CT) data (CT scan performed with oral and intravenous contrast) clearly demonstrates the inflamed appendix in its longitudinal axis.



**Figure 15-2** A, Axial computed tomography (CT) image performed after oral and intravenous administration of contrast agents demonstrates the typical appearance of acute appendicitis: a blind-ending tubular structure with enhancing walls and periappendiceal inflammation. The inflamed appendix is seen in its longitudinal axis. B, CT image at a slightly different level demonstrates a cross section of the inflamed appendix.

measures more than 6 mm in diameter during graded compression (Figure 15-7). Appendicoliths also may be visualized as echogenic, shadowing foci within the lumen of the appendix (Figure 15-8). Color Doppler imaging may demonstrate increased vascularity of the inflamed appendiceal wall. Technical limitations of ultrasonography include difficulties imaging obese patients and the wide variety of locations of the appendix, especially those located more posteriorly within the peritoneal cavity, poses increased difficulty for evaluation.

#### IMAGING ALGORITHM

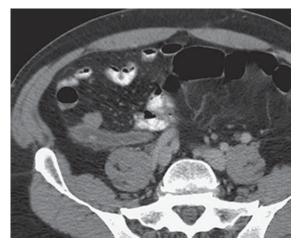
Overall, CT is the preferred method when the diagnosis of acute appendicitis is entertained. Ultrasonography is used mainly in pediatric patients, young women, and patients with small amounts of intraperitoneal fat. MRI is generally reserved for pregnant patients with acute right lower quadrant pain (Table 15-1).

#### Classic Signs

- Radiography: Calcified appendicolith and sentinel loop
- Ultrasonography: Noncompressible blind-ending tubular structure measuring more than 6 mm in diameter
- CT: Distended appendix with adjacent inflammatory changes and thickening of adjacent cecum ("arrowhead" sign)
- MRI: Distended appendix with high T2 signal

## **Differential Diagnosis**

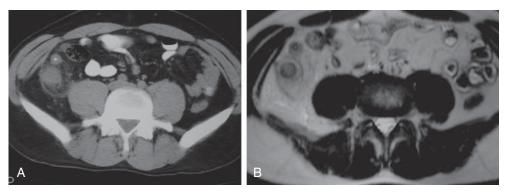
Acute appendicitis should be differentiated from pyelonephritis, acute cholecystitis, diverticulitis of the cecum, and ascending colon and, in females, from ectopic pregnancy and ruptured or torsed ovarian cysts. Epiploic appendagitis can produce similar clinical findings.



**Figure 15-4** Dilated, inflamed appendix with an intraluminal highattenuation focus, representing the appendicolith.



**Figure 15-5** Computed tomography scan after oral and intravenous administration of contrast agents shows acute appendicitis with perforation. The lateral wall of the dilated, inflamed appendix is interrupted, and there is extraluminal gas and fluid, representing the periappendiceal abscess.



**Figure 15-6** A, Axial image of a computed tomography scan performed with oral contrast but without intravenous contrast depicts the dilated appendix with periappendiceal fat inflammation and fascial thickening. These findings are typical of acute appendicitis. B, Axial T2-weighted magnetic resonance image obtained at the same level as in A again shows the dilated appendix and inflammation of the periappendiceal fat.

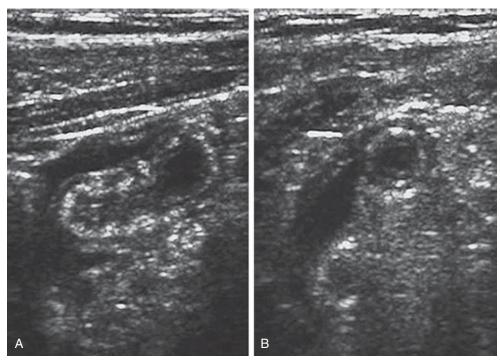
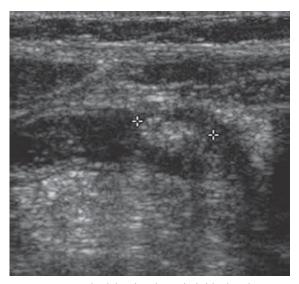


Figure 15-7 Acute appendicitis. A, A longitudinal ultrasound image shows the blind-ending appendix is distended with fluid, and it was not compressible on the real-time examination. There is a small amount of periappendiceal fluid as well. B, On cross section, the inflamed appendix has the typical "target" appearance, with fluid within the lumen and also adjacent to the appendix.



**Figure 15-8** Appendicolith. The distended, blind-ending appendix contains an intraluminal echogenic focus at the tip, with some associated acoustic shadowing. This is the appendicolith.

On ultrasonography the appendix should be differentiated from loops of small bowel. On CT the main difficulty arises when trying to separate a normal appendix from a minimally inflamed one. However, alternative diagnoses are often made with CT and should be readily identified. Epiploic appendagitis is recognized as an ovoid lesion containing fat that abuts the colon and has surrounding inflammatory stranding, often with a central high-attenuation focus representing a thrombosed

TABLE 15-1	Accuracy, Limitations, and Pitfalls of Modalities Used in Imaging the Appendix					
Modality		Accuracy (%)	Limitations	Pitfalls		
Radiography		<10	Appendix not seen	Rarely used in practice		
Computed tomography		92-98	lonizing radiation	Early appendicitis		
Magnetic resonance imaging		95	Time consuming	Difficult study to interpret		
Ultrasonography		80-85	Operator dependent	Appendix may be difficult to find		

vein. In acute diverticulitis, the epicenter of the inflammatory process is an inflamed or perforated diverticulum in the ascending colon or cecum. These may be difficult to differentiate from acute appendicitis, and follow-up imaging may be necessary if the patient does not undergo surgical intervention. Other conditions, such as ureteral stones, acute biliary processes, and gynecologic diseases are discussed elsewhere in this text.

#### Treatment

The vast majority of patients with acute appendicitis are treated with surgery, increasingly performed via a laparoscopic approach.

#### What the Referring Physician Needs to Know

- Is the appendix present and is it inflamed?
- Is there evidence of appendiceal rupture?
- Is there an alternative diagnosis?

### **Key Points**

- CT is the preferred imaging method for diagnosis of acute appendicitis.
- Ultrasonography is preferred in young, thin, and female patients of reproductive age. However, the appendix may be difficult to identify.
- MRI is a good diagnostic alternative for pregnant patients.

#### SUGGESTED READINGS

Birnbaum BA, Wilson SR: Appendicitis at the millennium. *Radiology* 215:337–348, 2000.

- Hayes R: Abdominal pain: general imaging strategies. Eur Radiol 14(Suppl 4):L123–L137, 2004. Kosaka N, Sagoh T, Uematsu H, et al: Difficulties in
- the diagnosis of appendicitis: review of CT and US images. *Emerg Radiol* 14:289–295, 2007.

Pedrosa I, Zeikus EA, Levine D, et al: MR imaging of acute right lower quadrant pain in pregnant

#### REFERENCES

- 1. Rhea JT, Halpern EF, Ptak T, et al: The status of appendiceal CT in an urban medical center 5 years after its introduction: experience with 753 patients. *AJR Am J Roentgenol* 184:1802–1808, 2005.
- Keyzer C, Zalcman M, De Maertelaer V, et al: Comparison of US and unenhanced multidetector row CT in patients suspected of having acute appendicitis. *Radiology* 236:527–534, 2005.
- Oliak D, Sinow R, French S, et al: Computed tomography scanning for the diagnosis of perforated appendicitis. *Am Surg* 65:959–964, 1999.

- and nonpregnant patients. *Radiographics* 27:721–743, discussion 743-753, 2007.
- Kiatpongsan S, Meng L, Eisenberg JD, et al: Imaging for appendicitis: should radiation-induced cancer risks affect modality selection? *Radiology* 273:472–482, 2014.
- Yu J, Fulcher AS, Turner MA, et al: Helical CT evaluation of acute right lower quadrant pain. I.
- Foley TA, Earnest F, Nathan MA, et al: Differentiation of nonperforated from perforated appendicitis: accuracy of CT diagnosis and rela-8.
- stay. *Radiology* 235:89–96, 2005.
  5. Horrow MM, White DS, Horrow JC: Differentiation of perforated from nonperforated appendicitis at CT. *Radiology* 227:46–51, 2003.

tionship of CT findings to length of hospital

- Yeung KW, Chang MS, Hsiao CP: Evaluation of perforated and nonperforated appendicitis with CT. *Clin Imaging* 28:422–427, 2004.
- 7. Birchard KR, Brown MA, Hyslop WB, et al: MRI of acute abdominal and pelvic pain in pregnant

Common mimics of appendicitis. *AJR Am J Roentgenol* 184:1136–1142, 2005.

Yu J, Fulcher AS, Turner MA, et al: Helical CT evaluation of acute right lower quadrant pain. II. Uncommon mimics of appendicitis. *AJR Am J Roentgenol* 184:1143–1149, 2005.

patients. AJR Am J Roentgenol 184:452-458, 2005.

- Pedrosa I, Levine D, Eyvazzadeh AD, et al: MR imaging evaluation of acute appendicitis in pregnancy. *Radiology* 238:891–899, 2006.
- 9. Oto A, Srinivasan PN, Ernst RD, et al: Revisiting MRI for appendix location during pregnancy. *AJR Am J Roentgenol* 186:883–887, 2006.
- Wise SW, Labuski MR, Kasales CJ, et al: Comparative assessment of CT and sonographic techniques for appendiceal imaging. *AJR Am J Roentgenol* 176:933–941, 2001.

## **Hollow Viscus Perforation**

JORGE A. SOTO | STEPHAN W. ANDERSON

## Etiology

16

The presence of extraluminal air in an acutely ill patient with abdominal pain is an ominous sign that usually indicates perforation of a hollow viscus. Common causes include gastroduodenal peptic ulcer disease, perforation of a gastrointestinal neoplasm, acute appendicitis with perforation, and acute colonic or (less often) small bowel diverticulitis, including Meckel's diverticulitis.<sup>1</sup> Other considerations include iatrogenic perforations caused by catheters or endoscopes, perforations caused by foreign bodies, or spontaneous rupture of the distal esophagus (Boerhaave's syndrome), as well as ischemia leading to necrosis and resultant loss of bowel wall integrity.

## **Prevalence and Epidemiology**

The epidemiology of hollow viscus perforation depends on the underlying cause. Although the prevalence of the various causes varies greatly, the morbidity and mortality of hollow viscus perforation are significant in all cases, given the possibility of progression to peritonitis and its resultant complications.

The most common cause of hollow viscus perforation is gastroduodenal peptic ulcer disease. Peptic ulcer disease is exceedingly common, with a lifetime prevalence of approximately 10% in the United States. The incidence of perforation has been reported to be 2% to 5% in patients with peptic ulcer disease.<sup>2</sup> Perforated peptic ulcer disease carries significant morbidity and mortality. Overall postoperative mortality has been reported to be 19% but exceeds 40% in patients older than 79 years of age.<sup>3</sup>

A second common cause of nontraumatic hollow viscus perforation is perforated colonic diverticulitis. The prevalence of diverticulosis is significantly associated with age and is reported to affect 65% of patients older than 65 years of age; 10% to 25% of patients with diverticular disease are reported to develop diverticulitis.<sup>4</sup> Of these, approximately 10% to 15% of patients develop free perforation. Interestingly, the incidence of perforated diverticulitis has been reported to be increasing in certain populations secondary to aging and dietary influences.<sup>5</sup> The mortality of perforated sigmoid diverticulitis has been reported to be approximately 8%.<sup>6</sup>

## **Clinical Presentation**

Because the signs and symptoms of hollow viscus perforation are typically related to the underlying cause, there are a variety of clinical presentations. Initially, symptoms will be localized to the area of disease; for example, patients with peptic ulcers may complain of intermittent or constant epigastric pain, sometimes radiating to the back. Although myriad initial clinical presentations exist, once free perforation into the peritoneal cavity occurs, most patients will have generalized peritonitis with peritoneal guarding, shock, and prostration.

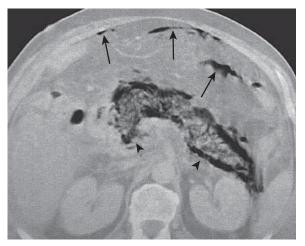
## Pathophysiology

Anatomic considerations depend on the underlying cause of the hollow viscus perforation. Patients with esophageal perforation typically present with pneumomediastinum, which may dissect into the neck, pleural space, or pericardial space, as well as the retroperitoneum and intraperitoneal cavity. The short, intraabdominal portion of the esophagus is within the retroperitoneum. The second and third portions of the duodenum, ascending and descending colon (in most patients), as well as the rectum are considered retroperitoneal structures (Figure 16-1). The remainder of the gastrointestinal tract is considered intraperitoneal. Typically, free air will be found within the abdominal cavity containing the portion of the gastrointestinal tract that is perforated. However, air may track within from the peritoneal cavity into the retroperitoneum and vice versa, as well as caudad into the thorax, including the mediastinum and pleural spaces.

In esophageal rupture secondary to Boerhaave's syndrome there is failure of the cricopharyngeus muscle to relax in coordination with vomiting. The esophageal tears are typically within the posterolateral aspect of the distal esophagus, several centimeters proximal to the gastroesophageal junction. This area has been demonstrated to be an anatomically weak point.<sup>7</sup>

In patients with peptic ulcer disease, the duodenum is more commonly affected than the stomach. Within the duodenum, ulcers are most commonly found within the first portion.<sup>8</sup> Based on preoperative imaging, the sites of gastroduodenal ulcer perforation are typically within the duodenum or are juxtapyloric in location.<sup>9</sup>

In patients with small bowel diverticulosis, the diverticula may be categorized as congenital or acquired.<sup>10</sup> In acquired, or true, diverticula, all three layers of the bowel wall are involved. Like pulsion diverticula elsewhere, acquired diverticula contain protrusions of portions of the bowel wall through an area of focal mural weakness. Meckel's diverticula are true diverticula in that they contain all three layers of the intestinal wall and arise along the antimesenteric border of the small bowel. They are commonly found 40 to 100 cm proximal to the ileocecal valve, and the length of the diverticulum ranges from 1 to 10 cm in 90% of patients.<sup>11</sup> Colonic diverticula represent pulsion diverticula and present as outpouchings of mucosa, muscularis mucosa, or submucosa through focal weaknesses of the colonic wall.



**Figure 16-1** Axial computed tomography image reveals foci of free intraperitoneal air (*arrows*) as well as significant retroperitoneal air, predominantly within the anterior pararenal space around the pancreas (*arrowheads*). At surgery, the patient was found to have perforated ulcers within both the first and third portion of the duodenum, accounting for the intraperitoneal and retroperitoneal air, respectively.

## Pathology

The pathologic findings of hollow viscus perforation depend on the underlying cause. Patients with Boerhaave's syndrome have a failure of the proper timing of cricopharyngeal relaxation with vomiting. This causes a significant increase in the intraluminal pressures of the esophagus, leading to full-thickness rupture.

In patients with peptic ulcer disease, failure of gastroduodenal mucosal mechanisms secondary to *Helicobacter pylori* infection, nonsteroidal antiinflammatory drug use, and hypersecretory states, among others, results in a defect in the muscularis mucosa.<sup>12</sup> If the ulceration continues beyond the muscularis mucosa, free perforation of the stomach or duodenum may occur.

In diverticulitis of the small bowel or colon, once the mucosalined outpouching through the bowel wall is obstructed, distention results secondary to ongoing secretion of mucus and bacterial overgrowth. Vascular compromise of these mucosal outpouchings may occur, leading to perforation. Similar to the pathophysiology of perforated diverticulitis, appendicitis results from obstruction of the appendiceal lumen with subsequent distention from mucosal secretions. Capillary perfusion pressures are outstripped, and venous and lymphatic drainage is obstructed. The influx of bacteria into the appendiceal wall as well as the decreasing arterial flow and tissue necrosis lead to appendiceal perforation.

In patients with colonic perforation secondary to colorectal carcinoma, the perforation may occur proximal to the tumor, related to obstruction and distention, or occur directly at the site of the tumor. In cases of perforation related to obstruction, the pathophysiology is similar to that of the aforementioned examples of increasing luminal distention and decreasing venous return followed by decreasing arterial inflow, resulting in tissue necrosis and loss of mural integrity. In cases of perforation directly at the site of the tumor, transmural tumor invasion and necrosis are underlying mechanisms resulting in loss of mural integrity.

## Imaging

#### RADIOGRAPHY

Plain radiography is useful in the initial evaluation of suspected hollow viscus perforation to detect the secondary signs of extraluminal air (Figure 16-2). However, the precise location and underlying cause of perforation are unlikely to be detected with radiography.

Acquisition of both a supine radiograph of the abdomen and an upright view of the chest is performed to evaluate for free intraperitoneal air. Other options include left lateral decubitus views of the abdomen or lateral chest radiographs. Upright radiographs or left lateral decubitus views should be acquired with the central ray of the x-ray beam at the highest level of the peritoneal cavity to increase the sensitivity of detection of intraperitoneal air.13 Numerous signs of pneumoperitoneum on abdominal radiographs have been described, including Rigler's sign, in which air is seen on both sides of the bowel wall; the falciform ligament sign, in which air outlines the falciform ligament; the football sign, in which air outlines the confines of the peritoneal cavity; the inverted V sign, in which air outlines the medial umbilical folds; and the right upper quadrant air sign, in which a focal, typically triangular, collection of gas is seen in the right upper quadrant.<sup>14</sup> Visualization of air outlining the median subphrenic space, the so-called *cupola sign*, has also been described in a minority of patients with pneumoperitoneum on supine radiographs.

Because esophageal rupture as well as dissection of air from intra-abdominal perforations may lead to pneumomediastinum, chest radiography may be employed for initial evaluation. Various radiographic findings have been described, including the visualization of air superolateral to the heart on the left on an upright chest radiograph, lucent streaks of air outlining the aorta or great vessels, the continuous diaphragm sign with air outlining the superior portions of the diaphragm, and many others.<sup>15</sup>

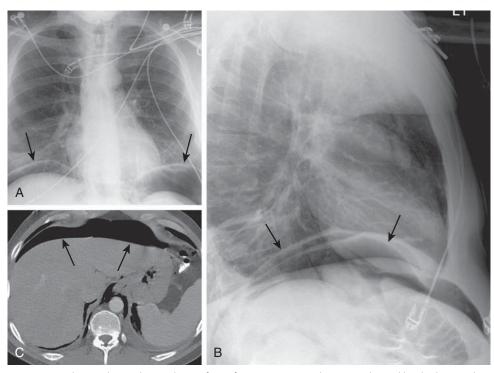
Finally, because hollow viscus perforation may be associated with retroperitoneal air, abdominal radiographs may be useful in the initial diagnosis. Retroperitoneal air may be identified as linear or bubbly lucencies overlying the expected location of the retroperitoneum. Alternatively, air may be seen along fascial planes of known retroperitoneal structures such as the psoas muscles, kidneys and adrenal regions, or muscles of the diaphragm.<sup>16</sup>

#### COMPUTED TOMOGRAPHY

CT is the most sensitive modality in detecting small volumes of extraluminal air. In cases of hollow viscus perforation, CT has been shown to be highly accurate in the localization of the site of perforation, especially when thin collimation images and multiplanar reformatted images are viewed.<sup>17,18</sup> The findings of focal bowel wall thickening, localized air bubbles, and direct visualization of a rent within the wall of the bowel have been shown to be accurate predictors of the site of perforation.<sup>17</sup>

Findings of esophageal rupture on CT include pneumomediastinum, periesophageal fluid, and esophageal thickening, as well as the possibility of direct visualization of the esophageal rent.<sup>19</sup>

CT findings in patients with perforation related to peptic ulcer disease include extraluminal gas as well as extravasation



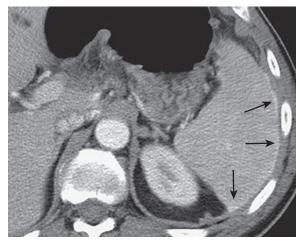
**Figure 16-2** A, Anteroposterior chest radiograph reveals significant free intraperitoneal air as evidenced by the lucency beneath the diaphragms bilaterally (*arrows*). B, Lateral chest radiograph reveals significant free intraperitoneal air, as evidenced by the lucency beneath the diaphragms (*arrows*). C, Axial computed tomography image confirms the presence of significant free intraperitoneal air (*arrows*). Air is also seen tracking into the mediastinum about the aortic hiatus. The patient was diagnosed with perforated diverticulitis at operative exploration.

of oral contrast media (Figures 16-3 and 16-4).<sup>20</sup> In addition, focal thickening of the gastrointestinal tract about the site of perforation as well as inflammatory stranding of the adjacent abdominal structures may be seen.

The CT findings related to perforation of small bowel diverticulitis are typically nonspecific.<sup>21</sup> Pneumoperitoneum as well as an inflammatory phlegmon or associated fluid are typically identified. In most cases of perforation secondary to Meckel's diverticulitis, direct visualization of the inflamed diverticulum is described, in addition to the pneumoperitoneum.<sup>22</sup> On CT, Meckel's diverticulum appears as a blind-ending pouch that is usually several centimeters in length with surrounding inflammatory changes.

In patients with perforated colonic diverticulitis, pneumoperitoneum or retroperitoneal gas as well as extravasation of oral contrast medium is typically identified (Figure 16-5).<sup>23</sup> In addition, the affected segment of colon is typically inflamed and thickened, with diverticula visualized in the area. In the minority of patients with perforated colonic diverticulitis, the defect within the wall of the colon may be directly visualized on CT (Figure 16-6).

In cases of hollow viscus perforation resulting from gastrointestinal obstruction, the pathophysiology involves a component of ischemia. Therefore, in addition to extraluminal gas and dilated loops of bowel, secondary signs of ischemia may be seen. These include pneumatosis intestinalis, air within the portal and mesenteric veins, and decreased enhancement of the affected bowel. Ischemia unrelated to bowel obstruction also may result in perforation. In these cases, the cause of ischemia, such as mesenteric venous or arterial thrombosis, may be directly visualized on CT.

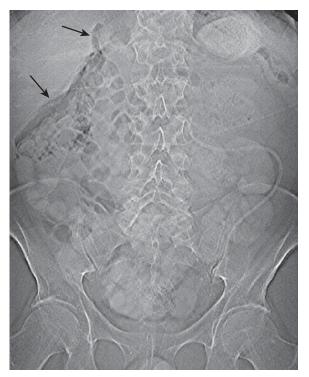


**Figure 16-3** Axial computed tomography image reveals extravasated oral contrast medium within the peritoneal cavity surrounding the spleen (*arrows*). The patient was found to have a perforated gastric ulcer at operative exploration.

Finally, in patients with malignancy as the underlying cause of the hollow viscus perforation, direct visualization of the mass lesion is typically achieved.<sup>24</sup> In these cases, the resultant perforation may be due to transmural extension of tumor with necrosis or obstruction with upstream dilatation and ischemia.



**Figure 16-4** Sagittal reformatted image from axial computed tomography data reveals significant intraperitoneal air along the nondependent aspect of the peritoneal cavity anterior to the liver (*arrows*). The patient was diagnosed with a perforated duodenal ulcer at operative repair.



**Figure 16-5** Frontal scout topogram demonstrates significant free intraperitoneal air about the inferior edge of the liver (*arrows*). The patient had perforated right-sided diverticulitis.



**Figure 16-6** Axial computed tomography image demonstrates multiple foci of free intraperitoneal air (*arrows*) evidence of moderate thickening of the distal transverse colon (*arrowhead*). The patient was successfully treated conservatively for perforated diverticulitis.

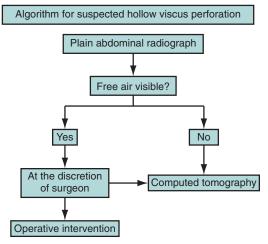


Figure 16-7 Algorithm for suspected hollow viscus perforation.

#### IMAGING ALGORITHM

Initial imaging evaluation in patients with suspected hollow viscus perforation includes plain radiography. If esophageal rupture is suspected, anteroposterior and lateral chest radiographs are commonly acquired. If an intra-abdominal perforation is suspected, supine and upright abdominal radiographs are acquired, possibly with an upright anteroposterior radiograph of the chest for the evaluation of pneumoperitoneum. If there is evidence of hollow viscus perforation based on the initial plain radiographic findings, depending on the clinical status of the patient, the surgical team may decide to proceed directly to operative exploration.

Alternatively, patients with radiographic evidence of hollow viscus perforation may undergo CT evaluation for localization and further characterization of the underlying cause. However, because patients with hollow viscus perforation may present with nonspecific signs and symptoms, CT may be the initial diagnostic evaluation (Figure 16-7 and Table 16-1).

# TABLE<br/>16-1Accuracy, Limitations, and Pitfalls of the<br/>Modalities Used in Imaging of Hollow<br/>Viscus Perforation

Modality	Accuracy (%)	Limitations	Pitfalls
Radiography	<40	Cause, site of perforation not evaluated	Insensitive for small volumes of extraluminal gas
Computed tomography	>95	lonizing radiation	Alternative, benign causes of extraluminal gas (e.g., recent surgery)

#### **Classic Signs**

- Rigler's sign: Air is seen on both sides of the bowel wall (pneumoperitoneum).
- Falciform ligament sign: Air outlines the falciform ligament (pneumoperitoneum).
- Football sign: Air outlines the confines of the peritoneal cavity (pneumoperitoneum).
- Inverted V sign: Air outlines the medial umbilical folds (pneumoperitoneum).
- Right upper quadrant air sign: A focal, typically triangular, collection of gas is seen in the right upper quadrant (pneumoperitoneum).
- Cupola sign: Air outlines the median subphrenic space (pneumoperitoneum).
- Continuous diaphragm sign: Air tracks along the superior layers of the diaphragm; the diaphragm appears continuous across the midline (pneumomediastinum).

## **Differential Diagnosis**

The clinical signs and symptoms of hollow viscus perforation can be nonspecific. Differential diagnostic considerations include other causes of peritonitis, such as spontaneous bacterial peritonitis; systemic infections involving the peritoneum, such as tuberculosis; and sterile irritants of the peritoneal cavity, such as blood, bile, and pancreatic secretions.

In addition to perforation of a hollow viscus, other causes of extraluminal air include iatrogenic causes such as recent surgery. Dissection of air from the thorax in cases of pneumothorax or pneumomediastinum are differential considerations in cases of extraluminal, intra-abdominal gas. In cases of pneumoperitoneum related to prior surgery, one should expect appropriate resolution during the postoperative period. The majority of cases are noted to resolve within 2 days based on radiography,

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but many patients may have small areas of free air for several days and even up to several weeks on postoperative CT scans.

#### Treatment

### MEDICAL TREATMENT

The appropriate therapy in patients with hollow viscus perforation is highly dependent on the underlying cause and typically involves emergent surgical management. However, in a subgroup of patients with perforated diverticulitis, when there is no evidence of gross free intraperitoneal air and fluid, conservative medical management, including intravenous antibiotics, may be indicated. Also, in selected patients with perforated appendicitis, medical management including intravenous antibiotics may be employed before definitive operative management. In patients with hollow viscus perforation managed conservatively, radiology may be a critical facet of nonoperative management via the use of image-guided percutaneous placement of drainage catheters to manage intra-abdominal fluid collections.

#### SURGICAL TREATMENT

Most patients with hollow viscus perforation undergo emergent surgical intervention. The preferred treatment in patients with esophageal perforation has traditionally been surgical intervention, although less invasive interventions are evolving.<sup>25</sup> In patients with perforated peptic ulcer disease, surgical intervention is typically employed, with laparoscopic techniques increasing in prevalence.<sup>26</sup> Patients with severe diverticulitis and gross perforation are typically managed surgically, often employing two-stage procedures.<sup>27</sup> In hollow viscus perforation related to ischemia, surgical intervention is employed, typically with resection of the segments of necrotic bowel. Finally, in patients with perforation secondary to underlying malignancy, surgical intervention with resection of the underlying mass lesion is performed.<sup>28</sup>

#### What the Referring Physician Needs to Know

- Is extraluminal gas visualized? How much?
- Where is the site of perforation?
- What is the underlying cause of the perforation?

#### **Key Points**

- There are many causes of hollow viscus perforation.
- Although plain radiography may be employed initially, CT is the modality of choice for diagnosis and characterization of hollow viscus perforation.
- Generally, hollow viscus perforation represents a surgical emergency; clinical teams should be immediately notified.

#### SUGGESTED READINGS

- Cho KC, Baker SR: Extraluminal air: diagnosis and significance. *Radiol Clin North Am* 32:829–844, 1994.
- Del Gaizo AJ, Lall C, Allen BC, et al: From esophagus to rectum: a comprehensive review of alimentary tract perforations at computed tomography. *Abdom Imaging* 39:802–823, 2014.
- Espinoza R, Rodríguez A: Traumatic and nontraumatic perforation of hollow viscera. *Surg Clin North Am* 77:1291–1304, 1997.
- Furukawa A, Sakoda M, Yamasaki M, et al: Gastrointestinal tract perforation: CT diagnosis of presence, site, and cause. *Abdom Imaging* 30:524–534, 2005.
- Marincek B: Nontraumatic abdominal emergencies: acute abdominal pain—diagnostic strategies. *Eur Radiol* 12:2136–2150, 2002.

#### REFERENCES

- Espinoza R, Rodríguez A: Traumatic and nontraumatic perforation of hollow viscera. Surg Clin North Am 77:1291–1304, 1997.
- 2. Cocks JR: Perforated peptic ulcer: the changing scene. *Dig Dis* 10:10–16, 1992.
- Uccheddu A, Floris G, Altana ML, et al: Surgery for perforated peptic ulcer in the elderly: evaluation of factors influencing prognosis. *Hepato*gastroenterology 50:1956–1958, 2003.
- Comparato G, Pilotto A, Franzè A, et al: Diverticular disease in the elderly. *Dig Dis* 25:151– 159, 2007.
- Mäkelä J, Kiviniemi H, Laitinen S: Prevalence of perforated sigmoid diverticulitis is increasing. *Dis Colon Rectum* 45:955–961, 2002.
- Mäkelä JT, Kiviniemi H, Laitinen S: Prognostic factors of perforated sigmoid diverticulitis in the elderly. *Dig Surg* 22:100–106, 2005.
- Korn O, Oñate JC, López R: Anatomy of the Boerhaave syndrome. *Surgery* 141:222–228, 2007.
- Al-Bahrani ZR, Kassir ZA, Al-Doree W: The location and multiplicity of chronic duodenal ulcer (a study of 1320 patients in Iraq). *Gastro*enterol Jpn 15:539–542, 1980.
- Grassi R, Romano S, Pinto A, et al: Gastroduodenal perforations: conventional plain film, US and CT findings in 166 consecutive patients. *Eur J Radiol* 50:30–36, 2004.
- Pearl MS, Hill MC, Zeman RK: CT findings in duodenal diverticulitis. *AJR Am J Roentgenol* 187:W392–W395, 2006.

- Ludtke FE, Mende V, Kohler H, et al: Incidence and frequency of complications and management of Meckel's diverticulum. *Surg Gynecol Obstet* 169:537–542, 1989.
- 12. Mertz HR, Walsh JH: Peptic ulcer pathophysiology. *Med Clin North Am* 75:799–814, 1991.
- Miller RE, Becker GJ, Slabaugh RD: Detection of pneumoperitoneum: optimum body position and respiratory phase. *AJR Am J Roentgenol* 135:487–490, 1980.
- Levine MS, Scheiner JD, Rubesin SE, et al: Diagnosis of pneumoperitoneum on supine abdominal radiographs. *AJR Am J Roentgenol* 156: 731–735, 1991.
- Bejvan SM, Godwin JD: Pneumomediastinum: old signs and new signs. *AJR Am J Roentgenol* 166:1041–1048, 1996.
- Hill MC, Bieber WP, Koch RL, et al: Extraperitoneal perforations of the gastrointestinal tract. *AJR Am J Roentgenol* 101:315–321, 1967.
- Hainaux B, Agneessens E, Bertinotti R, et al: Accuracy of MDCT in predicting site of gastrointestinal tract perforation. *AJR Am J Roentgenol* 187:1179–1183, 2006.
- Ghekiere O, Lesnik A, Millet I, et al: Direct visualization of perforation sites in patients with a non-traumatic free pneumoperitoneum: added diagnostic value of thin transverse slices and coronal and sagittal reformations for multidetector CT. Eur Radiol 17:2302–2309, 2007.
- 19. De Lutio di Castelguidone E, Pinto A, Merola S, et al: Role of spiral and multislice computed

tomography in the evaluation of traumatic and spontaneous oesophageal perforation: our experience. *Radiol Med (Torino)* 109:252–259, 2005.

- Jacobs JM, Hill MC, Steinberg WM: Peptic ulcer disease: CT evaluation. *Radiology* 178:745–748, 1991.
- Greenstein S, Jones B, Fishman EK, et al: Smallbowel diverticulitis: CT findings. AJR Am J Roentgenol 147:271–274, 1986.
- Bennett GL, Birnbaum BA, Balthazar EJ: CT of Meckel's diverticulitis in 11 patients. AJR Am J Roentgenol 182:625–629, 2004.
- Lohrmann C, Ghanem N, Pache G, et al: CT in acute perforated sigmoid diverticulitis. *Eur J Radiol* 56:78–83, 2005.
- Hulnick DH, Megibow AJ, Balthazar EJ, et al: Perforated colorectal neoplasms: correlation of clinical, contrast enema, and CT examinations. *Radiology* 164:611–615, 1987.
- Wu JT, Mattox KL, Wall MJ, Jr: Esophageal perforations: new perspectives and treatment paradigms. J Trauma 63:1173–1184, 2007.
- Kirshtein B, Bayme M, Mayer T, et al: Laparoscopic treatment of gastroduodenal perforations: comparison with conventional surgery. *Surg Endosc* 19:1487–1490, 2005.
- Floch MH, White JA: Management of diverticular disease is changing. World J Gastroenterol 28(12):3225–3228, 2006.
- Cuffy M, Abir F, Audisio RA, et al: Colorectal cancer presenting as surgical emergencies. *Surg Oncol* 13:149–157, 2004.

## **Acute Gastrointestinal Bleeding**

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## Etiology

The causes of upper gastrointestinal bleeding include esophageal or gastric varices, Mallory-Weiss tears, gastritis, and gastric or duodenal ulcers. Common causes of lower gastrointestinal tract bleeding include colonic diverticulosis, ischemic and infectious colitis, colonic neoplasm, benign anorectal disease, arteriovenous malformations, ischemia, and Meckel's diverticulum.

## **Prevalence and Epidemiology**

Acute gastrointestinal bleeding is classified into upper and lower gastrointestinal regions based on the site of hemorrhage (proximal or distal to the ligament of Treitz). Acute lower gastrointestinal hemorrhage is a common cause of hospital admission, with significant associated morbidity and mortality. Rapid stabilization of and therapy for patients with acute gastrointestinal bleeding is critical. The mortality rate is reported to be up to 20% in cases of upper gastrointestinal hemorrhage, depending on the cause.<sup>1</sup> Mortality in patients with acute lower gastrointestinal bleeding is reported to approach 20%.<sup>2</sup>

### **Clinical Presentation**

Patients with upper gastrointestinal hemorrhage typically present clinically with hematemesis, hematochezia, or melena. Patients with acute lower gastrointestinal hemorrhage can report melena or hematochezia. When severe, gastrointestinal hemorrhage may result in hemodynamic instability and shock. Importantly, the amount of blood passed in vomitus or stool does not serve as a reliable indicator of the severity of the event, because large amounts of blood can be sequestered in the intestines.

In addition to the total amount of blood lost, the rate of bleeding and the overall health of the patient are other factors determining the clinical presentation and the need for emergent intervention. Healthy patients have a tremendous capacity to compensate for acute blood loss. In young individuals with no cardiovascular disease, up to 2 units of blood can be lost with minimal or no hemodynamic changes. Blood flow can be diverted from the skin, splanchnic circulation, and kidneys to maintain perfusion of essential organs such as the brain and heart. Hypotension and tachycardia indicate a larger volume of blood loss, whereas confusion and oliguria develop when bleeding loss reaches 3 to 4 units. Finally, although there is usually a rush to intervene, up to 75% or 80% of the patients will experience spontaneous cessation of bleeding before any therapy is initiated.

## Pathophysiology

The pathophysiology of gastrointestinal hemorrhage depends on the underlying cause. Peptic ulcer disease results in a defect in the gastroduodenal mucosa with eventual exposure and damage to the underlying arteries, including arteritis, aneurysmal dilatation, and eventual rupture and hemorrhage.<sup>3</sup> Mallory-Weiss tears result spontaneously from the marked increase in intraluminal pressures associated with retching and are associated with the presence of a hiatal hernia.<sup>4</sup> Linear tears within the mucosa of the distal esophagus, cardioesophageal junction, or cardia result in injury to the underlying vasculature with subsequent hemorrhage. In patients with varices, increasing hepatic venous pressure results in enlarged varices and the increased risk for rupture and hemorrhage.

Diverticular hemorrhage results from rupture of the vasa recta at the dome of the diverticulum.<sup>5</sup> These vessels have eccentric intimal thickening with asymmetric rupture, suggesting that trauma to these vessels results in intimal proliferation and scarring, leading to subsequent rupture and hemorrhage. Angiodysplasia is typically located within the lower gastrointestinal tract, specifically the right colon. Although the pathophysiology is incompletely understood, angiodysplastic lesions are thought to be acquired degenerative lesions.<sup>6</sup>

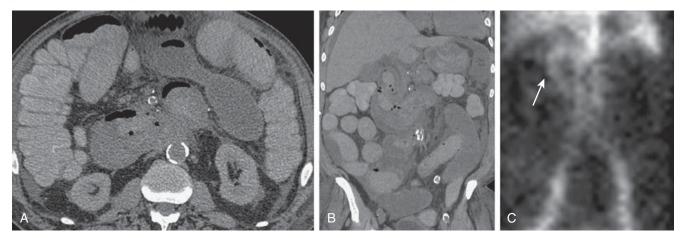
## Imaging

#### RADIOGRAPHY

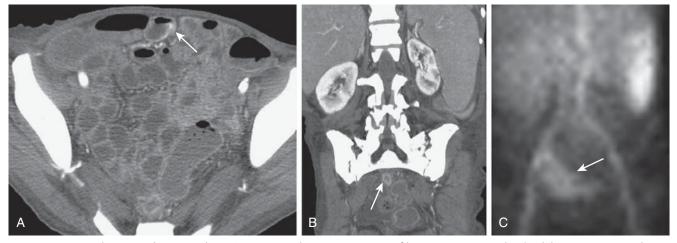
Abdominal radiographs have limited clinical utility in patients with acute gastrointestinal bleeding. Abdominal radiographs have been demonstrated not to affect clinical outcomes or management decisions in patients admitted to an intensive care unit with gastrointestinal hemorrhage.<sup>7</sup>

#### COMPUTED TOMOGRAPHY

Recently, computed tomography (CT) has been shown to have a high diagnostic accuracy in both the detection and the localization of massive gastrointestinal bleeding (Figure 17-1).<sup>8-10</sup> Optimal results necessitate the distention of the bowel with a contrast agent with neutral attenuation, such as water or lowdensity barium suspensions (Figure 17-2). Both unenhanced and arterial-phase intravenous contrast-enhanced acquisitions should be acquired. CT diagnosis relies on the visualization of an area of active arterial contrast extravasation. In the majority of cases, CT may diagnose the underlying cause of acute hemorrhage, such as in the case of small bowel or colonic neoplasms.<sup>8-10</sup> The efficiency and ease of acquisition as well as reported



**Figure 17-1** A, Axial unenhanced computed tomography (CT) image reveals diffuse hyperattenuation throughout the bowel lumen. The lack of intravenous use of a contrast agent precludes the localization of the hemorrhage; however, CT demonstrates its significant volume. B, Coronal reformatted axial CT image reveals the extent of intraluminal hemorrhage as evidenced by hyperattenuation throughout the bowel. C, <sup>9m</sup>Tc-labeled red blood cell scan localizes the area of active hemorrhage to the duodenum (*arrow*). The patient's acute hemorrhage, which was related to underlying peptic ulcer disease, was successfully treated with coil embolization.



**Figure 17-2** A, Axial computed tomography (CT) image reveals a punctuate area of hyperattenuation in the distal ileum consistent with active extravasation (*arrow*). This image demonstrates the importance of adequate oral preparation with a neutral attenuation contrast agent to optimize the contrast between active hemorrhage and the bowel lumen. B, Coronal reformatted axial CT image demonstrates the area of active hemorrhage within the distal ileum (*arrow*). C, <sup>99m</sup>Tc-labeled red blood cell scan reveals ongoing hemorrhage in the distal ileum (*arrow*). The patient underwent digital subtraction angiography twice without evidence of ongoing hemorrhage before undergoing definitive partial small bowel resection.

diagnostic accuracies of multidetector CT in the evaluation of acute gastrointestinal bleeding make this a promising first-line imaging modality.

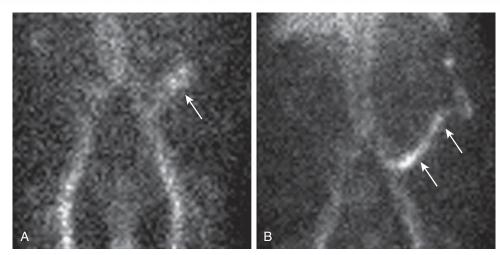
### NUCLEAR MEDICINE

The use of nuclear scintigraphy is sensitive in the detection and accurate in the localization of the source of acute gastrointestinal hemorrhage. Both technetium-99m (<sup>99m</sup>Tc)–labeled red blood cells and <sup>99m</sup>Tc sulfur colloid are applied in the evaluation of acute gastrointestinal hemorrhage.<sup>11</sup> However, <sup>99m</sup>Tc-labeled red blood cells offer the possibility for delayed imaging in cases of intermittent bleeding. The diagnosis of gastrointestinal bleeding on nuclear scintigraphy depends on the visualization of an area of tracer localization that persists and should be seen to move through the lumen of the bowel secondary to peristal-sis. Both antegrade and retrograde transit are observed, but

localization depends on the initial area of visualization (Figure 17-3). The localization of the site of bleeding has been shown to be highly accurate with nuclear scintigraphy and clinically useful in guiding subsequent transcatheter therapies or surgical resection. Single-photon emission computed tomography/ computed tomography erythrocyte scintigraphy has demonstrated superior accuracy and precision over planar scintigraphy in the diagnosis of acute gastrointestinal bleeding.<sup>12</sup>

#### IMAGING ALGORITHM

There is no consensus regarding the initial imaging evaluation of patients presenting with acute gastrointestinal bleeding. Endoscopy, <sup>99m</sup>Tc-labeled red blood cell scintigraphy, CT, and conventional mesenteric angiography are all successfully applied, depending on the scenario (Table 17-1).<sup>8-14</sup> Upper endoscopy is valuable in patients with upper gastrointestinal



**Figure 17-3** A, <sup>99m</sup>Tc-labeled red blood cell scan reveals an initial area of active hemorrhage in the proximal sigmoid colon (*arrow*). B, Note ongoing hemorrhage with retrograde transit within the descending colon (*arrows*). Localization depends on initial visualization and in this case is secondary to sigmoid diverticulosis.

TABLE     Accuracy, Limit	Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Acute Gastrointestinal Bleeding					
Modality	Accuracy (%)	Limitations	Pitfalls			
Computed tomography	>95 for localization	lonizing radiation exposure, intermittent bleeding	Hypervascular gastrointestinal neoplasms			
Nuclear medicine Angiography	>90 for localization >95 for localization	Poor localization of bleeding site Rate of bleeding, intermittent bleeding	Vascular organs interfere with interpretation.			

bleeding to determine the exact source and cause and as a means of therapy. For patients with hematochezia and/or unclear sources of bleeding, nuclear scintigraphy is a valuable technique, although CT enterography also is gaining acceptance in this situation. In cases of severe, massive upper or lower gastrointestinal hemorrhage, catheter angiography of the mesenteric circulation is often necessary as a means for catheter-directed therapy, such as injection of vasopressin and, more currently, for superselective embolization techniques that have been shown to be an effective method of treatment (Figure 17-4). In general, it is believed that a critical rate of hemorrhage of approximately 0.5 mL/min is necessary for a bleeding focus to be detected with angiography, whereas 0.05 mL/min can be detected with state-of-the-art scintigraphic techniques.<sup>15</sup>

An algorithm for the evaluation of acute gastrointestinal bleeding is presented in Figure 17-5.

#### **Classic Signs**

- On CT, the area of gastrointestinal hemorrhage is identified as a contrast blush on the contrast-enhanced images within the lumen of the gastrointestinal tract.
- On nuclear scintigraphy, bleeding is seen as a focus of activity that either increases in intensity or changes in location over time secondary to peristalsis.
- On catheter angiography, active hemorrhage is seen as a focus of active extravasation of contrast-enhanced blood that persists and may grow over time and does not wash out on delayed images.

## **Differential Diagnosis**

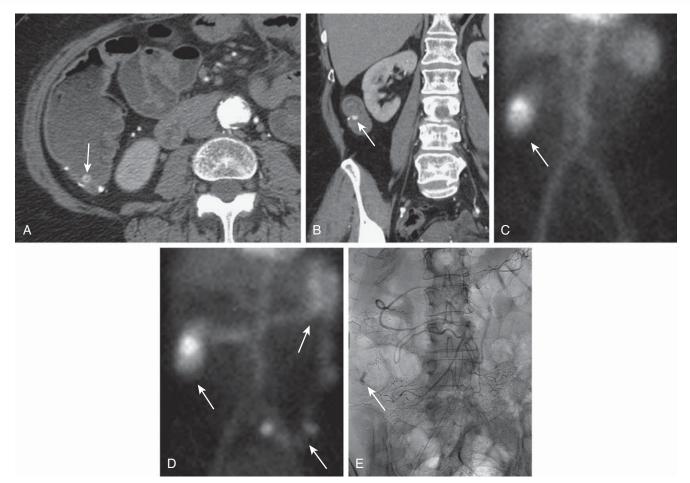
Differential considerations from clinical data depend on the severity of the gastrointestinal bleeding and its underlying cause. In the presence of hematemesis, melena, or hematochezia, gastrointestinal hemorrhage, by definition, is the diagnosis. However, if these signs are not evident and the patient is presenting with syncope or signs of hypotension, myriad differential considerations may be entertained. This would include sources of hemorrhage elsewhere, including intra-abdominal, retroperitoneal, or intramuscular locations. However, patients with acute gastrointestinal bleeding typically present with hematemesis, melena, or hematochezia, allowing for the diagnosis to be made.

Using CT, the differential considerations of a contrast blush within the lumen of the gastrointestinal tract are limited. Potential considerations include small, hypervascular tumors, such as neuroendocrine tumors. A second contrast-enhanced phase of imaging would potentially be useful in differentiating active arterial extravasation from a hypervascular mass lesion. On nuclear scintigraphy, abnormal accumulations of the radio-tracer potentially representing foci of hemorrhage must be differentiated from other sources of activity such as ectopic or accessory spleens, uterine leiomyomas, or a vascular mass lesion, among other potential sources.<sup>16</sup>

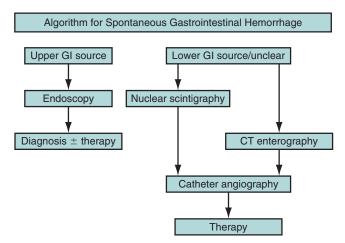
#### Treatment

#### MEDICAL TREATMENT

Patients with acute gastrointestinal hemorrhage should be admitted to the hospital for observation and evaluation. Initial



**Figure 17-4** A, Axial computed tomography (CT) image shows a punctuate area of hyperattenuation in the ascending colon, consistent with active hemorrhage (*arrow*). B, Coronal reformatted axial CT image demonstrates the area of active hemorrhage within the ascending colon (*arrow*). C, <sup>99m</sup>Tc-labeled red blood cell scan reveals active hemorrhage with initial localization to the ascending colon, as on CT (*arrow*). D, Note the ongoing active hemorrhage with antegrade transit into the transverse, descending, and sigmoid colon (*arrows*). E, Digital subtraction angiogram shows an area of active extravasation within the ascending colon (*arrow*) that was subsequently successfully treated with coil embolization.



**Figure 17-5** Algorithm for evaluation of spontaneous gastrointestinal hemorrhage. *CT*, Computed tomography; *GI*, gastrointestinal.

resuscitation includes correction of volume loss with crystalloids and blood products. Continuous monitoring with electrocardiographic lead placement, pulse oximeters, and automatic blood pressure cuffs is advised. Invasive, nonsurgical techniques include transcatheter-directed therapies and endoscopy. Currently, transcatheter-directed embolotherapy is commonly applied in cases of acute gastrointestinal hemorrhage.<sup>16,17</sup> Various forms of therapy are also available with endoscopy, including sclerotherapy, laser coagulation, and banding.<sup>13,18,19</sup>

#### SURGICAL TREATMENT

Although conservative, endoscopic, and transcatheter means of therapy are preferred, emergent surgery is necessary for patients who do not respond or in whom bleeding recurs rapidly after several attempts of control with less-invasive methods. Morbidity and mortality rates are high in these patients.

#### What the Referring Physician Needs to Know

- Is there a source of active bleeding?
- What is the location of the active bleeding?
- What is the cause of bleeding?
- Is the patient a candidate for transcatheter therapy?

#### Key Points

- Sources of acute bleeding should be separated into those affecting the upper and the lower gastrointestinal tract, using the ligament of Treitz as the boundary.
- After initial resuscitation and stabilization, diagnostic methods commonly used include upper and lower endoscopy, nuclear scintigraphy, catheter angiography, and, more recently, CT.
- Many patients can be successfully treated with transcatheter interventional techniques.

#### SUGGESTED READINGS

- Anthony S, Milburn S, Uberoi R: Multi-detector CT: review of its use in acute GI haemorrhage. *Clin Radiol* 62:938–949, 2007.
- Artigas JM, Martí M, Soto JA, et al: Multidetector CT angiography for acute gastrointestinal bleeding: technique and findings. *Radiographics* 33: 1453–1470, 2013.

#### REFERENCES

- Abraldes JG, Bosch J: The treatment of acute variceal bleeding. J Clin Gastroenterol 41(10 Suppl 3):S312–S317, 2007.
- Anthony T, Penta P, Todd RD, et al: Rebleeding and survival after acute lower gastrointestinal bleeding. *Am J Surg* 188:485–490, 2004.
- 3. Swain CP, Storey DW, Bown SG, et al: Nature of the bleeding vessel in recurrently bleeding gastric ulcers. *Gastroenterology* 90:595–608, 1986.
- Knauer CM: Mallory-Weiss syndrome: characterization of 75 Mallory-Weiss lacerations in 528 patients with upper gastrointestinal hemorrhage. *Gastroenterology* 71:5–8, 1976.
- Meyers MA, Alonso DR, Gray GF, et al: Pathogenesis of bleeding colonic diverticulosis. *Gas*troenterology 71:577–583, 1976.
- 6. Foutch PG: Colonic angiodysplasia. Gastroenterologist 5:148–156, 1997.
- Allen TW, Tulchinsky M: Nuclear medicine tests for acute gastrointestinal conditions. *Semin Nucl Med* 43(2):88–101, 2013.
- García-Blázquez V1, Vicente-Bártulos A, Olavarria-Delgado A, et al: EBM-Connect Collaboration. Accuracy of CT angiography in the

- Howarth DM: The role of nuclear medicine in the detection of acute gastrointestinal bleeding. Semin Nucl Med 36:133–146, 2006.
- Laing CJ, Tobias T, Rosenblum DI, et al: Acute gastrointestinal bleeding: emerging role of multidetector CT angiography and review of current

imaging techniques. *Radiographics* 27:1055–1070, 2007.

Soto JA, Park SH, Fletcher JG, et al: Gastrointestinal hemorrhage: evaluation with MDCT. *Abdom Imaging*. 40:993–1009, 2015.

diagnosis of acute gastrointestinal bleeding: systematic review and meta-analysis. *Eur Radiol* 23:1181–1190, 2013.

- Scheffel H, Pfammatter T, Wildi S, et al: Acute gastrointestinal bleeding: detection of source and etiology with multi-detector-row CT. *Eur Radiol* 17:1555–1565, 2007.
- Jaeckle T, Stuber G, Hoffmann MH, et al: Detection and localization of acute upper and lower gastrointestinal (GI) bleeding with arterial phase multi-detector row helical CT. *Eur Radiol* 18:1406–1413, 2008.
- Howarth DM: The role of nuclear medicine in the detection of acute gastrointestinal bleeding. *Semin Nucl Med* 36:133–146, 2006.
- Allen TW, Tulchinsky M: Nuclear medicine tests for acute gastrointestinal conditions. I. See comment in PubMed Commons below Semin Nucl Med 43:88–101, 2013.
- Green BT, Rockey DC: Lower gastrointestinal bleeding: management. *Gastroenterol Clin North* Am 34:665–678, 2005.
- 14. Kuo WT, Lee DE, Saad WE, et al: Superselective microcoil embolization for the treatment of

lower gastrointestinal hemorrhage. J Vasc Interv Radiol 14:1503–1509, 2003.

- 15. Alavi A, Ring EJ: Localization of gastrointestinal bleeding: superiority of 99mTc sulfur colloid compared with angiography. *AJR Am J Roent-genol* 137:741–748, 1981.
- Angelides S, Gibson MG, Kurtovic J, et al: Abdominal wall hematomata and colonic tumor detected on labeled red blood cell scintigraphy: case report. *Ann Nucl Med* 17:399–402, 2003.
- Lee CW, Liu KL, Wang HP, et al: Transcatheter arterial embolization of acute upper gastrointestinal tract bleeding with N-butyl-2cyanoacrylate. J Vasc Interv Radiol 18:209–216, 2007.
- Ramirez FC, Colon VJ, Landan D, et al: The effects of the number of rubber bands placed at each endoscopic session upon variceal outcomes: a prospective, randomized study. *Am J Gastroenterol* 102:1372–1376, 2007.
- Olmos JA, Marcolongo M, Pogorelsky V, et al: Argon plasma coagulation for prevention of recurrent bleeding from GI angiodysplasias. *Gastrointest Endosc* 60:881–886, 2004.

## **Esophageal Imaging**

KOICHI HAYANO | DUSHYANT V. SAHANI

## **Technical Aspects**

#### ANATOMY

18

The esophagus extends from the pharynx to the cardiac portion of the stomach. The length of the esophagus is approximately 25 to 30 cm, and it has cervical, thoracic, and abdominal portions. The cervical portion extends from the cricopharyngeus to the suprasternal notch behind the trachea. The thoracic portion extends from the suprasternal notch to the diaphragm behind first the trachea and then the left atrium. The abdominal portion extends from the diaphragm to the cardiac portion of the stomach.

## Imaging

Imaging of the esophagus is challenging because of the location surrounded by many vital organs and poor distensibility of the esophagus. However, recent advancements of multidetector computed tomography (MDCT) and workstation and postprocessing techniques have amplified clinical application of computed tomography (CT) in the evaluation of esophageal diseases. These techniques enable coverage of a large volume in a very short scan time. Single breath-hold acquisition with thin collimation and isotropic voxels allows imaging of the entire esophagus with high-quality multiplanar reformation (MPR) and three-dimensional reconstruction.<sup>1</sup> Generally, on CT, the esophagus appears as a well-delineated circular or oval shape of soft-tissue with a thin wall, which is less than 3 mm in a dilated esophagus, but can be thicker in a contracted esophagus.<sup>2,3</sup> Thus, proper distention of the esophagus (by oral administration of effervescent granules and water) and optimal timing of administration of intravenous contrast material are necessary to detect and characterize esophageal diseases. Compared to endoscopy and double-contrast examination, CT esophagography can provide information on the esophageal wall and the extramural extent of disease.<sup>4,5</sup> Specifically, MDCT plays a robust role in preoperative staging of esophageal malignant neoplasms. Furthermore, various benign conditions of the esophagus, including rupture, achalasia, esophagitis, diverticula, and varices can be visualized and detected in MDCT.

Magnetic resonance imaging (MRI) for esophageal imaging has been technically challenging because of the deep location of the esophagus and the degree of movement related to cardiac motion, peristalsis, and respiration, combined with the relatively slow acquisition time of MRI, which affect image quality. However, recent MRI technology has improved the achievable signal-to-noise ratio, and provides detailed information of the esophagus and the posterior mediastinum with high spatial resolution.<sup>6</sup> High-resolution T2-weighted fast spin echo technique with phased array surface coil can visualize the individual components of the esophageal wall.<sup>6, 7</sup> Cine MRI technique, which can visualize peristalsis of the esophagus, can help staging of esophageal cancer, because interruption of peristalsis reflects impaired muscle function caused by stage T3 or T4 esophageal cancer.<sup>8</sup>

## **Pathologic Conditions**

Esophageal tumors include various types of pathologic conditions. We summarized esophageal tumors in Box 18-1, classifying them into mucosal and submucosal tumors, because these differences closely associate with imaging features of the tumors. For example, typical submucosal tumors appear as a mass with smooth margins on CT and double-contrast examination. Benign esophageal tumors are not common, but sometimes it is difficult to differentiate benign from malignant tumors. Given the high mortality of esophageal cancer, pretreatment diagnosis for esophageal tumors is quite important.

#### **BENIGN ESOPHAGEAL TUMORS**

Benign esophageal tumors are not common, representing 20% of esophageal neoplasms at autopsy.<sup>9</sup> Most benign tumors are small and asymptomatic lesions, but some patients may present with dysphagia, bleeding, weight loss, or other symptoms. Benign esophageal tumors are grouped into mucosal and submucosal tumors according to the site of origin. The majority of benign esophageal tumors are located in the middle and lower thirds of the thoracic esophagus, but only fibrovascular polyps arise from the cervical esophagus.<sup>11</sup>

#### **Mucosal Tumors**

Squamous papillomas and adenomas are benign esophageal tumors arising from the esophageal mucosa. Squamous papillomas typically occur as solitary polyps in the esophagus and are sometimes difficult to differentiate from early esophageal cancer. The size of the tumors is relatively small, ranging from 0.5 to 1.5 cm, and most patients are asymptomatic. Adenomas are rare polyps in the esophagus, because the mucosa of the esophagus is composed of squamous rather than columnar epithelium. However, esophageal adenomas can arise in metaplastic columnar epithelium associated with Barrett esophagus. Because adenomas have the risk for malignant transformation, endoscopic or surgical resection is necessary. Generally, these tumors are too small to be detected on CT and MRI, but they can appear as small polyps with a smooth or slightly lobulated shape on double-contrast examination.

#### SUBMUCOSAL TUMORS

In esophageal benign submucosal tumors, leiomyomas are the most common, followed by esophageal cysts.

### BOX 18-1 ESOPHAGEAL TUMORS

## MUCOSAL

#### Benign

- Adenoma
- Squamous papilloma

#### Malignant

- Squamous cell carcinoma (SCC)
  - SCC variant
    - Spindle cell carcinoma
  - Basaloid squamous carcinoma
  - Verrucous carcinoma
  - Adenocarcinoma
  - Adenosquamous carcinoma
  - Neuroendocrine tumor

#### SUBMUCOSAL

#### Benign

- Leiomyoma
- Cyst
- Fibrovascular polyp
- Granular cell tumor
- Hemangioma
- Schwannoma
- Lipoma

#### Malignant

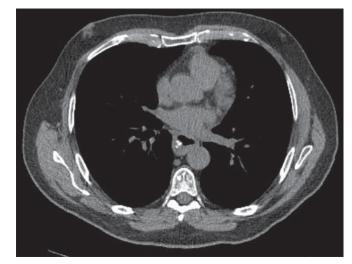
- Gastrointestinal stromal tumor
- Sarcoma (leiomyosarcoma)
- Lymphoma
- Malignant melanoma

#### Leiomyoma

Leiomyomas account for more than 50% of benign esophageal tumors.<sup>10,11</sup> The tumors are present more often in male patients (2:1) at a median age of 30 to 35 years. These tumors arise from smooth muscle and usually are located in the lower two thirds of the esophagus because of the abundance of smooth muscle at this location. Basically, these tumors are slow growing and have a low risk for turning into cancerous tumors. Most of esophageal leiomyomas occur as solitary lesions, but 3% to 4 % of patients are reported to have multiple lesions. Clinically, if the tumor size increases, dysphagia or pain may occur, but most patients are asymptomatic. Treatment options for esophageal leiomyoma may include observation for small tumors that are not causing symptoms and endoscopic or surgical resection. On the double-contrast examination, these appear as a smooth, rounded filling defect forming an obtuse angle with the esophageal wall. On CT, these appear as an intraluminal mass or a wall thickening with smooth peripheral margin, homogenous soft tissue attenuation, and occasional coarse calcification. Sometimes it is difficult to differentiate leiomyoma from esophageal cancer, but leiomyoma is the only tumor that may contain calcification (Figure 18-1). Additionally, absence of imaging features indicating the invasive nature of cancer such as infiltration of the esophageal wall or typical circumferential growth enables differentiation from esophageal cancer.<sup>1</sup>

#### Esophageal Cyst

Esophageal cysts are the second most common type of benign esophageal tumors. Duplication cysts are more common than inclusion cysts. Duplication cysts usually arise from the lower



**Figure 18-1** Leiomyoma of the esophagus on computed tomography. The tumor appears as wall thickening with smooth peripheral margins, homogenous soft tissue attenuation, and calcification.

third of the esophagus, and most of these cysts are located in the right posterior inferior mediastinum and detected in infants or children.<sup>12</sup> Duplication cysts share a muscular wall with the native esophagus and are attached to the esophagus in a paraesophageal or intramural fashion. Duplication cysts are commonly lined by gastric mucosa, and gastric acid produced by this ectopic mucosa may cause complications such as ulceration, hemorrhage, and perforation. Because of these possible complications, surgical removal or enucleation is generally advisable. On the double-contrast examination, the cysts appear as extrinsic or intramural compression because of close contact with the esophagus. On CT, the cysts showed the well-defined, thick-walled structure with fluid, and on MRI these are appreciated as low to intermediate signal intensity on T1-weighted images and high signal intensity on T2-weighted images (Figure 18-2). Their appearance on CT or MRI is identical to that of bronchogenic cysts; however, the thicker wall and the more intimate contact with the esophagus may be helpful for diagnosis.<sup>13,14</sup> Technetium-99m sodium pertechnetate scan may be helpful in pediatric patients, in whom 50% of the cysts contain ectopic gastric mucosa.15

#### Fibrovascular Polyp

Fibrovascular polyp is a rare benign submucosal tumor of the esophagus composed of varying amounts of fibrous, adipose, and vascular tissues, accounting for 1% to 2% of benign esophageal tumors. It usually arises from the cervical esophagus and sometimes prolapses into the mouth. It can be a very large tumor with a vascularized thick stalk; thus, surgical resection is the treatment of choice.<sup>16</sup> On CT, attenuation of a fibrovascular polyp shows a wide spectrum, depending on the amount of fibrous and adipose tissue in the tumor. If it predominantly contains adipose tissue, it appears as low (fat) attenuation, which is the typical CT sign of fibrovascular polyp (Figure 18-3). Because of the excellent soft tissue components of the tumor. On T1-weighted imaging, it is appreciated as an intraluminal tumor with high signal intensity, because of its lipid

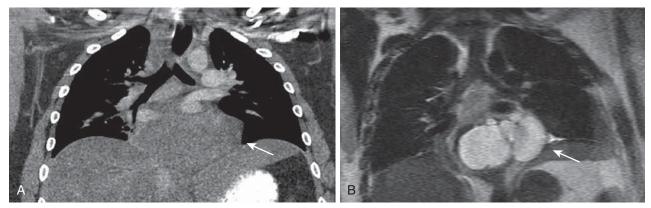
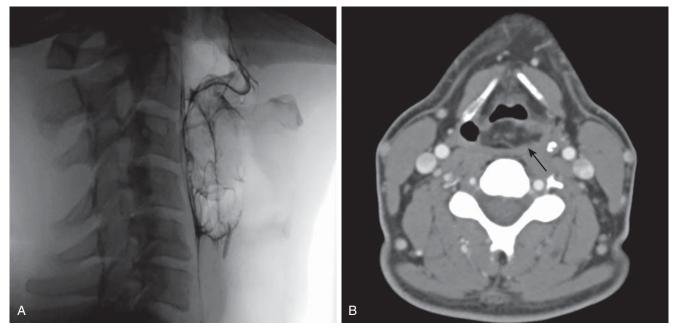


Figure 18-2 Duplication cyst of the esophagus on computed tomography (CT) (A) and T2-weighted magnetic resonance imaging (MRI) (B). On CT, the cyst appears as a low-attenuation lesion (*arrow*), and on MRI, it shows high signal intensity (*arrow*) on T2-weighted image because of fluid in the cyst.



**Figure 18-3** Fibrovascular polyp of the esophagus on double-contrast examination (A) and computed tomography (CT) (B). It usually arises from the cervical esophagus, and sometimes can be a very large tumor. On CT, a fibrovascular polyp (*arrow*) typically appears low in attenuation (fat) if it contains predominantly adipose tissue.

content; it is appreciated as a tumor with low signal intensity on T2-weighted images. Multiplanar MRI also plays an important role in defining the spatial location of the mass.

#### MALIGNANT ESOPHAGEAL TUMORS

#### Esophageal Cancer

Approximately 80% of esophageal tumors are malignant, and more than 90% of those tumors are squamous cell carcinomas or adenocarcinomas. Precise clinical staging is quite important in the management of esophageal cancer, because it allows for the prognostic stratification of patients and appropriate treatment planning. Imaging techniques such as CT and MRI have served as useful modalities for staging, and the tumor, node, metastasis (TNM) staging system maintained by the American Joint Committee on Cancer and the Union for International Cancer Control has been commonly used. In terms of tumor resectability, precise assessments for aortic invasion, tracheal invasion, and distant metastases are necessary. The following sections address how imaging modalities are used for TNM staging in esophageal cancer (Table 18-1).

#### **Tumor Classification**

Invasion of primary tumor is represented by the T classification. CT is a commonly used imaging modality to assess staging of esophageal cancer because of its wide availability. T1 or T2 tumor may be seen as just an asymmetric thickening of the esophageal wall, but CT cannot evaluate the extent of the tumor

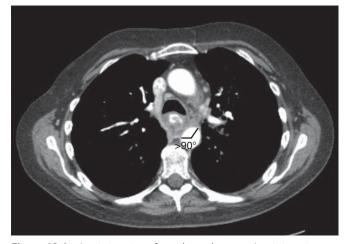
TABLE 18-1	Esophageal Cancer		
Stage	Description		
PRIMARY (T)			
TIS T1	High-grade dysplasia T1a; invasion of lamina propria or muscularis mucosa T1b; invasion of submucosa		
T2	T2 musclaris propria		
Т3	Invasion of adventitia		
Τ4	T4a; invasion of pleura, pericardium, or diaphragm (resectable) T4b; invasion of other adjacent structures (unresectable)		
NODE			
N0	No regional lymph node metastasis		
N1	1 to 2 regional lymph node metastases		
N2	3 to 6 regional lymph node metastases		
N3	≥7 regional lymph node metastases		
METASTASIS			
MO	No distant metastasis		
M1	Distant metastasis		

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in the esophageal wall. For assessment of T1 and T2 tumors, endoscopic ultrasonography is more reliable. T3 tumor can be seen at CT as definite wall thickening or mass. Even though adventitial penetration by the tumor may appear as ill-defined abnormal soft tissue around the tumor, if the fat planes between the tumor and adjacent structures are preserved, this finding can be classified as T3. T4 tumors are those that invade adjacent structures such as pleura-peritoneum, pericardium, diaphragm, aorta, carotid vessels, azygos vein, trachea, main bronchus, or vertebral body. Generally, CT criteria for local invasion include the loss of the fat layer between tumor and adjacent structures. But pericardial invasion, especially of the left atrium, is still difficult to evaluate because of pulsation artifacts. Pericardial thickening, pericardial effusion, or indentation of the heart with a concave deformity may help diagnose pericardial invasion. Regarding aortic invasion, Picus and associates<sup>17</sup> reported that aortic invasion could be diagnosed if the contact area between the tumor and the aorta created an arc of more than 90 degrees with an accuracy of more than 90% (Figure 18-4). Tracheobronchial invasion of the tumor, which sometimes results in fistula or airway obstruction, is suspected if there is discrete indentation on the posterior wall or displacement of the trachea or bronchus by the tumor.<sup>18</sup> Previous reports demonstrated that diagnostic accuracy for tracheobronchial invasion ranges from 88% to 97%.<sup>19</sup>

#### Node Classification

Lymph node status is one of the important prognostic factors in esophageal cancer.<sup>20</sup> Therefore, precise N classification is very important. On CT, regional lymph nodes are commonly considered metastatic when the short-axis diameter is 10 mm or greater; other criteria for metastatic lymph nodes are a nearly round shape (longitudinal-transverse diameter ratio = 1.5), a fatty hilum that is eccentric or missing, and marked or



**Figure 18-4** Aortic invasion of esophageal cancer. Aortic invasion can be diagnosed if the contact area between the tumor and the aorta creates an arc of more than 90 degrees.

heterogeneous enhancement.<sup>1,21,22</sup> There also have been several reports regarding the efficacy of 18-fluorodeoxyglucose (FDG) positron emission tomography (PET) in the preoperative evaluation of esophageal cancer. Commonly, a lymph node with focally prominent FDG uptake in comparison with background mediastinal activity is considered to be metastatic.<sup>23</sup> However, both CT and FDG-PET may not be accurate enough for evaluation of metastatic lymph nodes. The accuracy of CT has been reported to range from 45% to 96%, and that of FDG-PET has been reported to range from 37% to 90%.<sup>23</sup> It may be because these imaging modalities essentially have difficulty in detection of smaller metastatic lymph nodes or microscopic metastases in lymph nodes.

#### Metastasis Classification

Metastasis to a distant organ defines the M classification. Esophageal cancer most commonly spreads to the liver (35%) but also can spread to the lungs (20%), bones (9%), adrenal gland (5%), and, rarely, brain and peritoneum. CT has played an important role in detecting distant metastases. Liver metastases appear as hypoattenuating lesions with irregular and undefined borders. Lung metastases are typically round with well-defined borders and no calcification. FDG-PET is also one of the modalities to depict distant metastases, and it has the advantage of allowing whole-body coverage. Previous studies reported that PET with CT is superior to CT for depicting distant metastases.<sup>24,25</sup>

#### Neuroendocrine Tumors

Neuroendocrine carcinomas (NECs) represent approximately 1% of esophageal cancers. According to the World Health Organization, neuroendocrine tumors (NETs) are classified into three groups—low grade (G1) (carcinoid), intermediate grade (G2), and high grade (G3) (NEC; small cell and large cell subtypes)—and NEC is considered most aggressive.<sup>26</sup> Therefore, early detection and accurate diagnosis may help improve clinical outcome. At barium study, NEC appears as a mass with smooth margins and central ulceration in the mid-esophagus. Because of their abundant blood supply, NETs and their metastases usually show moderate to avid arterial enhancement (Figure 18-5).<sup>27</sup>



Figure 18-5 Neuroendocrine tumor of the esophagus. It shows moderate enhancement (arrow) on contrast-enhanced computed tomography.

#### OTHER MALIGNANT ESOPHAGEAL TUMORS

Esophageal lymphoma is rare, like other types of gastrointestinal lymphoma. On CT, it appears as irregular esophageal wall thickening, which is sometimes accompanied by ulceration. CT is also useful to assess mediastinal involvement of lymphoma. It is rare, but the diagnosis should be considered in patients who have risk factors such as human immunodeficiency virus infection and chronic immunosuppression.<sup>28</sup>

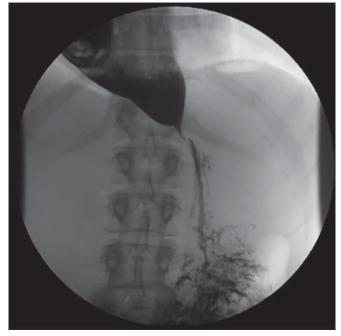
Gastrointestinal stromal tumors (GISTs) derive from interstitial cells of Cajal and may develop all along the digestive tract, but rarely in the esophagus. On CT, they appear as a hyperenhancing extraluminal or intraluminal mass with well-defined borders, and larger tumors frequently have central necrosis, hemorrhage, or cystic degeneration. The most common site of metastasis is the liver.<sup>29</sup>

Leiomyosarcoma of the esophagus is quite rare, accounting for less than 1% of all malignant esophageal tumors. On CT, a bulky and nonobstructing soft tissue mass with a large exophytic component can be considered a leiomyosarcoma. On MRI, the tumor can be appreciated as a mass with a signal intensity similar to that of skeletal muscle on T1-weighted images and high signal intensity on T2-weighted images.

#### OTHER ESOPHAGEAL DISEASES

#### Achalasia

Achalasia is an esophageal motor disorder caused by the absence of normal relaxation of the lower esophageal sphincter. It is caused by degeneration of ganglion cells in the myenteric plexus of the esophageal body and the lower esophageal sphincter.<sup>30</sup> Idiopathic achalasia is rare, with an incidence of 0.3 to 1.63 per 100,000 people per year in adults, and 0.18 per 100,000 people per year in children younger than 16 years.<sup>31</sup> The diagnosis of achalasia is usually made based on esophagography, manometry, and endoscopy. Esophagography often shows a narrow esophagogastric junction with a dilated esophagus, which is called the "bird-beak" appearance (Figure 18-6). To assess emptying of the esophagus, a timed barium esophagogram (TBE) can be done. In TBE, the height of the barium column 5 minutes after inges-



**Figure 18-6** Achalasia. On esophagography, it appears as a narrow esophagogastric junction with a dilated esophagus, which is called the "bird-beak" appearance.

tion of diluted barium is a measure of emptying, and TBE can provide objective assessment after treatment. Regarding association with malignancy, the risk for esophageal cancer (especially squamous cell carcinoma) is substantially increased in patients with long-standing achalasia. When patients who have a long history of achalasia show rapid worsening of symptoms, the possibility of esophageal cancer should be considered.

#### **Esophageal Varices**

Esophageal varices are typically caused by portal hypertension and obstruction of the superior vena cava. Portal hypertension increases portal venous pressure, which leads to hepatofugal venous flow through the coronary vein into a plexus of dilated esophageal and periesophageal veins. Obstruction of superior vena cava results in reversal of flow into the cervical and upper thoracic esophagus via the superior intercostal vein, inferior thyroid vein, and other mediastinal collateral vessels. On contrast-enhanced CT or MRI, esophageal varices appear as dilated veins in the esophageal wall (Figure 18-7). The diagnosis of esophageal varices is important because variceal rupture and bleeding are sometimes fatal. It is also important to check the portal venous system, superior vena cava, and surrounding collateral vessels if esophageal varices are discovered.

#### Esophageal Perforation

Esophageal perforation or rupture can result in a mediastinal infection, which may be fatal. Spontaneous esophageal perforation, which is called *Boerhaave's syndrome*, may occur as a result of sudden, rapid increase in intraesophageal pressure. Other possible causes of esophageal perforation include foreign body impaction, infectious esophagitis, Barrett's syndrome, esophageal cancer, and aortic rupture.<sup>32</sup>

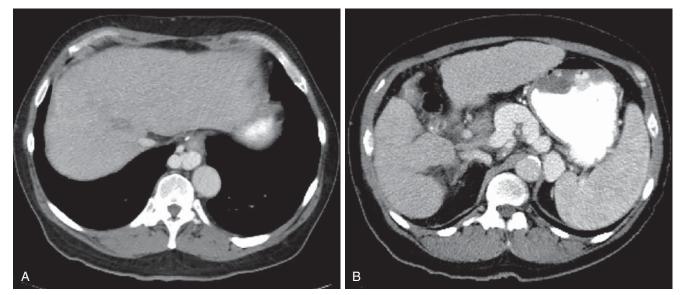


Figure 18-7 Esophageal varices on contrast-enhanced computed tomography. Dilated veins are appreciated in the esophageal wall (A) secondary to portal hypertension from liver cirrhosis (B).

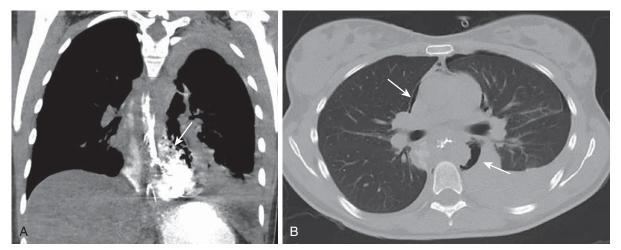


Figure 18-8 Esophageal perforation. A, Extravasation of contrast material and fluid collections (arrow) resulting from perforation. B, Mediastinal air and pleural effusion (arrow) secondary to perforation.

Because esophageal perforation usually occurs with sudden onset of severe chest or back pain, CT plays an important role in the diagnosis. On CT, esophageal perforation may appear as wall thickening, periesophageal gas and fluid collections, extravasation of contrast material, mediastinal inflammation, focal wall defect, and pleural effusion (Figure 18-8). Regarding the site of perforation, the distal left posterior wall is the most common site of spontaneous rupture, which causes pneumomediastinum and left pleural effusion. Perforation of the cervical esophagus typically causes cervical subcutaneous emphysema or a superior mediastinal fluid collection.

#### **Key Points**

- On CT, the esophagus appears as a well-delineated circular or oval soft tissue structure with a thin wall, which is less than 3 mm in a dilated esophagus.
- MDCT plays a robust role in preoperative staging of esophageal malignant neoplasms as well as in detection of various benign conditions of the esophagus, such as rupture, achalasia, esophagitis, and varices.
- Recent MRI technology has improved the achievable signal-to-noise ratio and provides detailed information of

the esophagus and the posterior mediastinum with high spatial resolution.

- Benign esophageal tumors are rare, and the majority of them are located in the middle and lower thirds of the thoracic esophagus. Fibrovascular polyps arise from the cervical esophagus.
- Approximately 80% of esophageal tumors are malignant, and more than 90% of those tumors are squamous cell carcinomas or adenocarcinomas.

#### **SUGGESTED READINGS**

Edge S, Bryd DR, Compton CC, et al, editors: Esophagus and Esophagogastric Junction. In *AJCC cancer staging manual*, ed 7, New York, 2009, Springer.

Gore RM, Levine MA: *Textbook of gastrointestinal* radiology: expert consult, St. Louis, 2015, Elsevier.

Haaga JR: Computed tomography & magnetic resonance imaging of the whole body (vol 2), Philadelphia, 2008, Elsevier.

#### REFERENCES

- Ba-Ssalamah A, Zacherl J, Noebauer-Huhmann IM, et al: Dedicated multi-detector CT of the esophagus: spectrum of diseases. *Abdom Imaging* 34:3–18, 2009.
- Schmalfuss IM, Mancuso AA, Tart RP: Postcricoid region and cervical esophagus: normal appearance at CT and MR imaging. *Radiology* 214:237–246, 2000.
- Xia F, Mao J, Ding J, et al: Observation of normal appearance and wall thickness of esophagus on CT images. *Eur J Radiol* 72:406–411, 2009.
- Kim SH, Kim YJ, Lee JM, et al: Esophageal varices in patients with cirrhosis: multidetector CT esophagography—comparison with endoscopy. *Radiology* 242:759–768, 2007.
- Kim SH, Lee JM, Han JK, et al: Threedimensional MDCT imaging and CT esophagography for evaluation of esophageal tumors: preliminary study. *Eur Radiol* 16:2418–2426, 2006.
- Riddell AM, Davies DC, Allum WH, et al: Highresolution MRI in evaluation of the surgical anatomy of the esophagus and posterior mediastinum. *AJR Am J Roentgenol* 188:W37–W43, 2007.
- Riddell AM, Allum WH, Thompson JN, et al: The appearances of oesophageal carcinoma demonstrated on high-resolution, T2-weighted MRI, with histopathological correlation. *Eur Radiol* 17:391–399, 2007.
- Koyama T, Umeoka S, Saga T, et al: Evaluation of esophageal peristalsis in patients with esophageal tumors: initial experience with cine MR imaging. *Magn Reson Med Sci* 4:109–114, 2005.
- 9. Lewis RB, Mehrotra AK, Rodriguez P, et al: From the radiologic pathology archives: esophageal neoplasms—radiologic-pathologic correlation. *Radiographics* 33:1083–1108, 2013.
- Choong CK, Meyers BF: Benign esophageal tumors: introduction, incidence, classification, and clinical features. *Semin Thorac Cardiovasc Surg* 15:3–8, 2003.

- 11. Seremetis MG, Lyons WS, deGuzman VC, et al: Leiomyomata of the esophagus: an analysis of 838 cases. *Cancer* 38:2166–2177, 1976.
- Liu R, Adler DG: Duplication cysts: diagnosis, management, and the role of endoscopic ultrasound. *Endosc Ultrasound* 3:152–160, 2014.
- Kuhlman JE, Fishman EK, Wang KP, et al: Esophageal duplication cyst: CT and transesophageal needle aspiration. *AJR Am J Roent*genol 145:531–532, 1985.
- LeBlanc J, Guttentag AR, Shepard JA, et al: Imaging of mediastinal foregut cysts. *Can Assoc Radiol J* 45:381–386, 1994.
- Ferguson CC, Young LN, Sutherland JB, et al: Intrathoracic gastrogenic cyst: preoperative diagnosis by technetium pertechnetate scan. *J Pediatr Surg* 8:827–828, 1973.
- Vagli P, Solito B, Neri E, et al: Giant fibrovascular polyp of the esophagus-imaging techniques for proper treatment planning: report of two cases. *Abdom Imaging* 37:512–518, 2012.
- Picus D, Balfe DM, Koehler RE, et al: Computed tomography in the staging of esophageal carcinoma. *Radiology* 146:433–438, 1983.
- Kumbasar B: Carcinoma of esophagus: radiologic diagnosis and staging. *Eur J Radiol* 42:170– 180, 2002.
- 19. Holscher AH, Dittler HJ, Siewert JR: Staging of squamous esophageal cancer: accuracy and value. *World J Surg* 18:312–320, 1994.
- 20. Eloubeidi MA, Desmond R, Arguedas MR, et al: Prognostic factors for the survival of patients with esophageal carcinoma in the U.S.: the importance of tumor length and lymph node status. *Cancer* 95:1434–1443, 2002.
- Panebianco V, Grazhdani H, Iafrate F, et al: 3D CT protocol in the assessment of the esophageal neoplastic lesions: can it improve TNM staging? *Eur Radiol* 16:414–421, 2006.
- Mazzeo S, Caramella D, Gennai A, et al: Multidetector CT and virtual endoscopy in the evaluation of the esophagus. *Abdom Imaging* 29:2–8, 2004.

- Yoon YC, Lee KS, Shim YM, et al: Metastasis to regional lymph nodes in patients with esophageal squamous cell carcinoma: CT versus FDG PET for presurgical detection prospective study. *Radiology* 227:764–770, 2003.
- Kato H, Kuwano H, Nakajima M, et al: Comparison between positron emission tomography and computed tomography in the use of the assessment of esophageal carcinoma. *Cancer* 94:921–928, 2002.
- Flamen P, Lerut A, Van Cutsem E, et al: Utility of positron emission tomography for the staging of patients with potentially operable esophageal carcinoma. J Clin Oncol 18:3202–3210, 2000.
- Kloppel G: Classification and pathology of gastroenteropancreatic neuroendocrine neoplasms. *Endocr Relat Cancer* 18(Suppl 1):S1–S16, 2011.
- Wang D, Zhang GB, Yan L, et al: CT and enhanced CT in diagnosis of gastrointestinal neuroendocrine carcinomas. *Abdom Imaging* 37:738–745, 2012.
- Gloghini A, Dolcetti R, Carbone A: Lymphomas occurring specifically in HIV-infected patients: from pathogenesis to pathology. *Semin Cancer Biol* 23:457–467, 2013.
- Hong X, Choi H, Loyer EM, et al: Gastrointestinal stromal tumor: role of CT in diagnosis and in response evaluation and surveillance after treatment with imatinib. *Radiographics* 26:481– 495, 2006.
- Vaezi MF, Pandolfino JE, Vela MF: ACG clinical guideline: diagnosis and management of achalasia. *Am J Gastroenterol* 108:1238–1249, quiz 1250, 2013.
- 31. Boeckxstaens GE, Zaninotto G, Richter JE: Achalasia. *Lancet* 383:83–93, 2014.
- Young CA, Menias CO, Bhalla S, et al: CT features of esophageal emergencies. *Radiographics* 28:1541–1553, 2008.

## Imaging of the Stomach and Duodenum

NIALL POWER

SUKANYA GHOSH | ABRAHAM C. THOMAS | SUJIT VAIDYA |

## **Technical Aspects**

#### **TECHNIQUE**

The patient is given sodium bicarbonate/dimethicone granules (Carbex), a gas-producing agent, to swallow and then drinks the E-Z HD 250% weight/volume 60 mL barium. Spot views of the esophagus are taken at the beginning (anteroposterior and right anterior oblique positions) while barium is being swallowed (if clinically indicated), and then the patient is asked to lie down on the left side (thus preventing the barium reaching the distal duodenum too quickly and obscuring views of the greater curvature and antrum of the stomach). The patient then is asked to lie slightly on the right so that the barium is against the gastroesophageal junction to check for reflux while screening. If reflux is not elicited, the patient may be asked to cough, swallow water, or tip the head down while being observed fluoroscopically and spot films are taken.<sup>1,2</sup>

#### Stomach Views

- Antrum and greater curvature: Right anterior oblique (Figure 19-1)
- Body and antrum: Supine (Figure 19-2)
- Lesser curvature en face: Left anterior oblique (Figure 19-3)
- Left lateral: With head tilted up at 45 degrees

Throughout this procedure it is vital to ensure the barium does not flood into the duodenum, and thus the patient is asked to roll onto the left side as soon as the fundus view has been taken.

#### **Duodenum Views**

- *Duodenal loop:* The patient lies prone on the compression pad to prevent barium flooding into the duodenum (additional views of the anterior wall of the duodenal loop can be taken in the right anterior oblique position).
- Duodenal bulb: The following spot views can help: prone, right anterior oblique, supine, and left anterior oblique (occasionally tilting the head up and allowing the air bubble to rise into the coated duodenal cap) (Figure 19-4). The appearance of the duodenum varies according to the patient's body habitus, and the gallbladder often indents the duodenal cap.

Erect views of the fundus can be taken at the end of the study.

#### Single-Contrast Examination

A single-contrast examination can emphasize mucosal relief, compression, and barium filling. This includes spot views of the barium-filled stomach with the patient recumbent: prone, left posterior oblique, right lateral, and right anterior oblique.

Mucosal relief radiographs are performed by giving the patient 60 to 90 mL of barium to drink, and then prone and supine spot views are taken to correctly demonstrate the gastric fold pattern. The anterior gastric wall is better seen on the singlecontrast study than the double-contrast examination. Compression views require compression of the stomach, which is moderately distended with a small amount of barium to spread on the rugal folds. Overdistention makes it impossible to penetrate the barium radiographically, and the amount of barium used can be controlled by patient rotation or tilting the table. The views seen vary according to patient body habitus, and compression can be performed only below the rib cage; hence, often only the distal stomach can be identified. The compression view often demonstrates ulcers and masses, although small flat lesions can be missed and wall rigidity may occur from scarring or infiltration.

### **Normal Anatomy**

When fully distended the stomach forms a J-shaped configuration and is divided into cardia, fundus, body, pyloric antrum, and pylorus (Figure 19-5). The stomach has two surfaces: anterosuperior and posteroinferior, bounded by two borders, the lesser and greater curvatures, respectively. This hollow organ is completely covered by peritoneum, which passes as a double layer from the lesser curve (as the lesser omentum) and from the greater curve (as the greater omentum).<sup>3</sup> The stomach is composed of four layers: the outer serosa layer, muscularis externa, submucosa, and mucosa. The outer serosal layer consists of layers of connective tissue continuous with the peritoneum. The muscularis externa consists of three layers: the inner oblique layer (thicker at the antrum to perform forceful contractions); a middle circular layer that is thickest at the pylorus, forming a pyloric sphincter; and an outer longitudinal layer. The stomach is lined by columnar cells (for acid protection), unlike the esophagus, which is lined with squamous cells.

The duodenum has a C-shaped configuration and is divided into four parts. The first (superior) portion extends from the pylorus to the neck of the gallbladder and consists primarily of the duodenal bulb. The second part (Figure 19-6) lies to the right of the second/third lumbar vertebrae, running inferiorly lateral to the head of the pancreas and medial to the hilum of the right kidney. Posteromedially at the junction of the upper two thirds and the lower third of the duodenum lies the opening of the duodenal papilla or ampulla of Vater (opening of the bile and pancreatic ducts).

The third part runs from right to left below the lower margin of the head of the pancreas, whereas the fourth portion is 4 cm

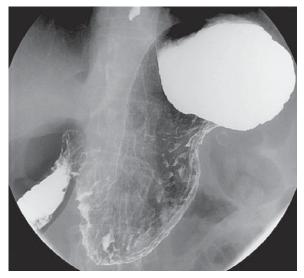


Figure 19-1 Right anterior oblique view.

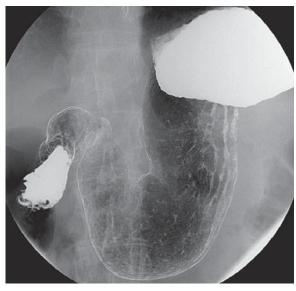


Figure 19-2 Supine view.

and runs craniad and lies medial to the left psoas muscle, fixed by the ligament of Treitz (a peritoneal fold that ascends to the right crus of the diaphragm). This is an important landmark when distinguishing malrotation of the small intestine in children. The first part of the duodenum is the only part that is intraperitoneal, whereas the rest are retroperitoneal structures, again an important point for localizing a pathologic process.

## Patterns and Appearances on Barium Studies

### GASTRIC ULCERS

The detection of gastric ulcers and the decision regarding whether these represent benign or malignant processes are a major part of the barium meal study.

Helicobacter is a gram-negative bacteria that is recognized as an important cause of 70% of peptic ulcer disease and 95% of

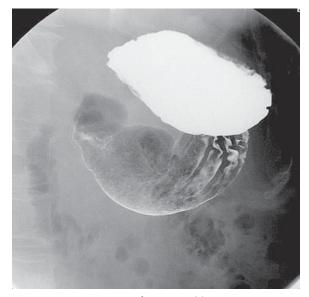


Figure 19-3 Left anterior oblique view.

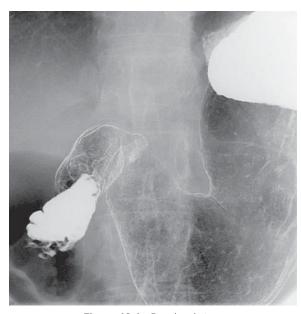


Figure 19-4 Duodenal view.

duodenal ulcers in the United States.<sup>4</sup> Patients infected with *Helicobacter pylori* have a six times risk for developing gastric carcinoma and a 90% association with mucosal-associated lymphoid tissue. Other causes of infectious gastritis include tuber-culosis, histoplasmosis, and syphilis.

Ulcers are best identified on double-contrast studies. Often they are common on the posterior wall of the stomach and least common on the fundus.<sup>1,2</sup> Ulcers secondary to nonsteroidal antiinflammatory drugs and alcohol are often seen on the greater curvature of the antrum, possibly owing to the direct toxic effects.<sup>5</sup>

The en face radiologic signs of gastric ulcers are best seen on double-contrast studies. Primarily, the signs include pooling of barium within the ulcer crater (on the dependent wall). A thin radiolucent line is often seen separating the barium in the

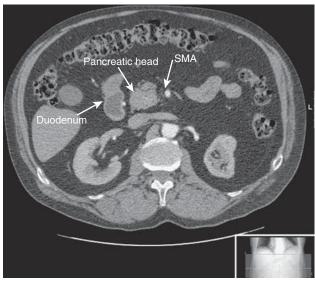
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**Figure 19-5** Computed tomography with air contrast within the stomach demonstrating the axial configuration (*arrows*).



**Figure 19-7** Note the irregular edge of a benign gastric ulcer on the lesser curvature (*arrow*).



**Figure 19-6** Axial computed tomography through the second part of the duodenum. *SMA*, Superior mesenteric artery.

lumen from that in the crater and is referred to as Hampton's line. If the ulcer is on the nondependent wall, the barium coats the "rim," causing a ring-like effect. The patient can be turned prone or supine to fill the middle part of the crater. Often a small mound of edema is seen surrounding the crater, causing a circular filling defect. The folds radiating from this should be smooth and symmetric with normal areae gastricae, suggesting benignity. Classically, benign ulcers are seen on the lesser curvature (Figure 19-7). Giant ulcers ( $\geq$ 3 cm) are virtually almost always benign. A healed ulcer is identified when folds converge to the site of the ulcer, whereas incomplete healing, irregularity of the folds, residual mass, or loss of mucosal pattern suggests malignancy.

Carman's meniscus sign is diagnostic of a specific type of ulcerated neoplasm. When examined in profile with compression, the ulcer has a semicircular (meniscoid) configuration.



**Figure 19-8** Note that the biliary tree is opacified, suggesting fistulation with a duodenal ulcer.

The combination of this characteristic type of barium-filled ulcer and a radiolucent shadow of the elevated ridge of neoplastic tissue surrounding it is called the Carman-Kirklin complex. The inner margin of the barium trapped in the ulcer is usually irregular. It is always convex toward the lumen, in contrast to the "crescent sign" of a benign gastric ulcer in which the inner margin is concave toward the lumen.<sup>6</sup>

An abrupt transition between the normal mucosa and the abnormal tissue surrounding a gastric ulcer is characteristic of a neoplastic lesion, in contrast to the diffuse, almost imperceptible transition between the mound of edema surrounding a benign ulcer and normal gastric mucosa. Nodularity, clubbing, and amputation of normal radiating folds also suggest a malignant lesion.

#### DUODENAL ULCERS

Duodenal ulcers also can be identified by double-contrast studies, and sometimes complications are seen—for example, formation of a fistula with the biliary tree (Figure 19-8).

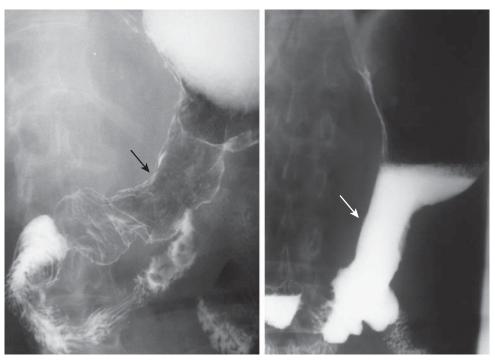


Figure 19-9 Linitis plastica pattern. Note the marked narrowing of the body and antrum of the stomach as a result of lymphatic infiltration (arrows).

## NARROWING OF THE STOMACH (LINITIS PLASTICA PATTERN)

A linitis plastica pattern refers to any condition in which marked thickening of the gastric wall causes the stomach to resemble a rigid tube. The most common cause is scirrhous carcinoma of the stomach (Figure 19-9). The tumor invades the gastric wall, resulting in a desmoplastic reaction that leads to diffuse thickening and fixation of the stomach wall. At fluoroscopy, peristalsis does not pass the tumor.

Other lesions that can mimic this appearance are lymphoma, Kaposi's sarcoma, and metastases. Sometimes benign causes such as ulcer disease, Crohn's disease, sarcoidosis, and tuberculosis can cause this appearance.

#### FILLING DEFECTS IN THE STOMACH

Areae gastricae are normal anatomic features of the gastric mucosa. On a double-contrast study they appear as a fine reticular pattern surrounded by barium-filled grooves. This appearance simulates multiple filling defects.

Hyperplastic polyps are the most common causes of discrete gastric filling defects, accounting for up to 90% of all gastric polyps. Most hyperplastic polyps appear as sharply defined, round or oval filling defects measuring less than 1 cm. They have smooth contours and no evidence of contrast material within them. They tend to be multiple and are clustered in the fundus or body of the stomach.

An adenomatous polyp is a true neoplasm; it shows a tendency to malignant transformation and is therefore vital to identify. Characteristic features include size greater than 1 cm, lobulated or pedunculated shape, and a variation in size over time. Other lesions that can present as filling defects include lymphoma, carcinoid tumor, and metastases.

#### THICKENING OF GASTRIC FOLDS

Longitudinal folds traverse the stomach in the direction of its long axis. Folds in the fundus are thicker and more tortuous than distally. Folds in the antrum measuring more than 5 mm are considered abnormal. These folds may appear prominent in a nondistended stomach.

#### EXTRINSIC LESIONS

Lesions outside the gastric walls could indent on the stomach and cause extrinsic impressions or apparent filling defects. Cysts arising from the kidney, spleen, and pancreas can produce these appearances.

#### WIDENING OF THE DUODENAL C LOOP

Although widening of the duodenal C loop is often taken to represent pancreatic malignancy, benign conditions such as pseudocyst also may cause such an appearance. It is advisable to resort to cross-sectional imaging to resolve (Figure 19-10).

## Computed Tomography of the Stomach

#### GASTRIC ULCER

A gastric ulcer is a common cause of upper gastrointestinal tract symptoms and is amenable to reliable radiologic detection. An upper gastrointestinal study with barium contrast is a reliable,



**Figure 19-10** Widening of the duodenal loop secondary to a large pancreatic head tumor.

noninvasive investigation used to identify ulcers and early mucosal lesions in the stomach.<sup>7</sup> CT findings of gastritis include the following<sup>8</sup>:

- Thickened gastric folds
- Focal wall thickening, particularly at the antrum
- A three-layered wall appearance that may enhance during the arterial phase secondary to hyperemia. Maintenance of normal wall layering may distinguish benign and malignant conditions.
- Life-threatening emphysematous gastritis, which, although rare, is characterized by air within the stomach wall secondary to invasion by gas-producing organisms (*Escherichia coli*).

A gastric ulcer may be suggested on CT by a focal area of wall thickening with an associated mucosal defect. Submucosal edema also may be seen. Although the sensitivity of CT for detecting gastritis and ulceration is less than that of the upper gastrointestinal study with barium contrast, it is excellent at identifying complications such as bleeding or perforation secondary to gastric antral or duodenal ulcers. CT signs of perforation include tiny locules of fluid (Figures 19-11 to 19-13) and/ or air (Figure 19-14) around the organ concerned. Giant gastric ulcers are almost always greater than 3 cm and benign but have a higher rate of complications.

#### GENERALIZED GASTRIC WALL THICKENING

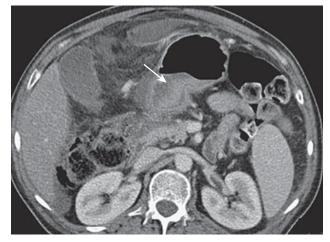
Thickening of the stomach, including the gastroesophageal junction, is often difficult to interpret. It is an important but nonspecific sign. On CT, the gastric wall can appear "thickened" because the mucosal folds are collapsed. It gives the appearance of "pseudo thickening," which can often be mistaken for tumor infiltration.

Pseudotumor at the gastroesophageal junction in patients with hiatal hernia or apparent thickening resulting from underdistention of the stomach needs to be excluded. It is essential to ensure aggressive gastric and gastroesophageal junction distention with water or air contrast.

Focal or diffuse thickening of the gastric wall (with adequate distention of the stomach) that exceeds 5 mm suggests the following differential diagnosis: carcinoma, lymphoma, gastric



**Figure 19-11** On this computed tomography image note the secondary sign of periantral fluid (*arrow*) most likely secondary to the perforated peptic ulcer.



**Figure 19-12** Axial computed tomography slice through the gastric antrum with high density within it (*arrow*) demonstrating active extravasation of blood from a peptic ulcer.

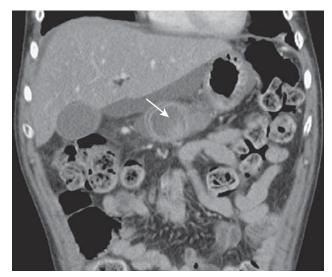


Figure 19-13 Coronal computed tomography image of active bleeding peptic ulcer (arrow).



Figure 19-14 The small locule of air (arrow) is a secondary computed tomography sign of perforated peptic ulcer.

inflammation (peptic ulcer/Crohn's disease), perigastric inflammation (e.g., pancreatitis), and radiation.<sup>9-11</sup>

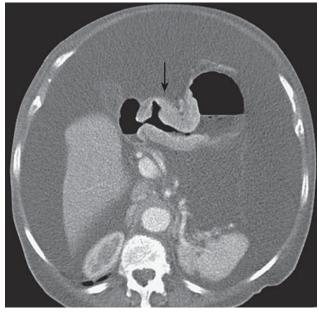
Gastric wall thickening is commonly focal and in the antrum. Often, the mucosal wall may enhance avidly during the arterial phase of scanning because of hyperemia, causing a three-layered wall appearance suggesting possible malignant change. It may help to identify secondary signs such as stranding at the gastroesophageal junction or around the stomach, celiac axis lymphadenopathy, and metastasis to other organs such as the liver.

#### PRIMARY MALIGNANT NEOPLASMS

Ninety-five percent of gastric carcinoma is adenocarcinoma.<sup>12</sup> The remainder includes lymphoma, sarcoma (malignant gastrointestinal stromal tumors [GISTs]), carcinoid, and metastasis. Most early gastric carcinomas manifest on CT as focal, nodular, or irregular segmental thickening of the gastric wall or as a polypoid intraluminal mass. Diffuse thickening with narrowing of the lumen suggests appearances of scirrhous carcinoma (linitis plastica) (Figure 19-15). It has been proved that in a well-distended stomach, a wall thickness of more than 1 cm that is focal, eccentric, and enhancing after intravenous contrast administration has a sensitivity of 100% and a specificity of 98% in detecting a malignant or potentially malignant lesion, warranting further investigation by upper gastrointestinal study with barium contrast or endoscopy.<sup>13</sup> Perigastric fat involvement is nearly always present when the wall thickness is more than 2 cm. Blurring of the serosal surfaces, fat stranding, and peritoneal deposits are often seen. Perigastric lymph nodes with a short-axis diameter greater than 6 mm, particularly near the tumor and the celiac axis or gastrohepatic ligament, are suggestive of malignant infiltration (Figures 19-16 and 19-17). Nodal involvement is likely if the nodes are heterogeneous or enhance markedly after administration of a contrast agent.

Advanced tumors frequently manifest as large, irregular masses that may ulcerate (Figure 19-18). There may be transgastric spread, occasionally with direct invasion of adjacent structures (namely, liver, spleen, pancreas, transverse colon); hematogenous spread to liver, lung, adrenal glands, kidneys, bones and brain; or diffuse intraperitoneal spread.

The following CT features are therefore important if resection is considered:



**Figure 19-15** On this computed tomography image note the diffuse fibrotic thickening of the gastric antrum causing luminal narrowing (*arrow*).

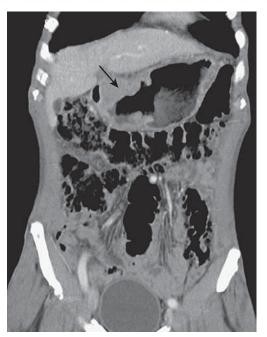


**Figure 19-16** The gross antral thickening greater than 1 cm on this computed tomography image suggests malignancy (*long arrow*). There also is a small periantral node (*short arrow*).

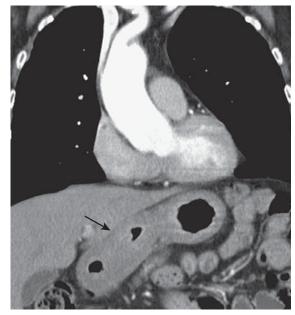
- Site and size of tumor
- Involvement of serosa
- Lymph node spread
- Metastasis

#### GASTRIC LYMPHOMA

The most frequent site of lymphoma in the gastrointestinal tract is the stomach (Figure 19-19),<sup>14</sup> and 90% to 95% are non-Hodgkin's lymphoma. Gastric lymphoma can manifest as diffuse wall infiltration that involves at least 50% of the length of the stomach, as segmental focal or nodular thickened folds,



**Figure 19-17** Coronal computed tomography image of antral thickening suggesting malignancy (*arrow*).



**Figure 19-19** Markedly diffuse thickening of the gastric wall is seen on this computed tomography image of a patient with lymphoma (*arrow*).



**Figure 19-18** Note the gastric wall thickening with thin linear pocket of air suggesting possible ulceration (*arrow*) on this computed tomography image.

or as a polypoid mass associated with an ulcer. Additionally, widespread lymphadenopathy may be present. The CT features that favor a diagnosis of lymphoma rather than carcinoma include marked gastric wall thickening, often more than 4- to 5-cm, bulkier nodes that may extend below the renal hilum, and involvement of more than one region of the gastrointestinal tract.<sup>15</sup> Whereas carcinoma typically causes luminal narrowing, in lymphoma the lumen is preserved and may be dilated.

#### SUBMUCOSAL LESIONS

#### Gastrointestinal Stromal Tumors

GISTs are the most common nonepithelial tumors of the gastrointestinal tract, with full evaluation in Chapter 21.

#### Leiomyosarcoma

Leiomyosarcoma is an uncommon tumor, accounting for 1% of gastric lesions. However, it is the second most common type of polypoid lesion in the stomach after hyperplastic polyps. It is a smooth muscle tumor arising from the muscularis propria, and growth is often exophytic and exogastric or dumbbell shaped. The tumor is usually larger than 5 cm at presentation. These lesions can be submucosal and thus often not seen by endoscopy. Therefore, CT is important to detect and characterize the mass and evaluate spread. Leiomyosarcoma is often heterogeneous with areas of low attenuation suggestive of necrosis and with primarily exophytic growth.<sup>16</sup> Complications include ulceration (suggested by the presence of air within the lesion) and perforation. Another cause of air within the lesion may be superinfection of the necrotic tumor (Figure 19-20). Leiomyosarcoma can invade adjacent organs directly (e.g., the left lobe of the liver, spleen, lesser sac, pancreas, and kidney) or metastasize hematogenously to the liver or lung.

#### **METASTASIS**

The most common primary tumors metastasizing to the stomach are breast cancer, malignant melanoma, and lung cancer. Hematogenous spread to the stomach may manifest as submucosal masses that may appear nonspecific. Breast cancer metastasis can manifest as a linitis plastica–like appearance, indistinguishable from primary gastric cancer.

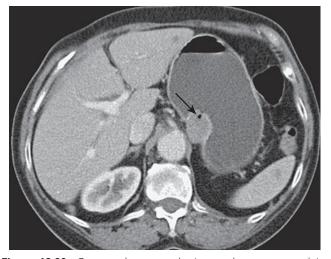
#### MISCELLANEOUS DISORDERS

#### Gastric Varices

Gastric varices are often seen secondary to portal hypertension or splenic vein thrombosis. CT findings include clusters of round and/or tubular structures in or adjacent to the stomach. The risk for gastrointestinal hemorrhage is increased in the presence of varices (Figure 19-21).<sup>17</sup> Other signs of liver disease are frequently seen, including a nodular heterogeneous appearance of the liver suggestive of cirrhosis, splenomegaly, and splenic varices. Splenic vein thrombosis often manifests as gastric varices without esophageal varices.

#### **Gastric Distention**

Gastric distention can be seen secondary to diabetic neuropathy or secondary to gastric outlet obstruction, causes of which

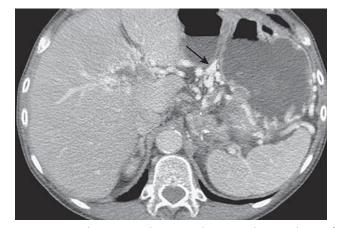


**Figure 19-20** Computed tomography image demonstrates a leiomyoma with a pocket of air (*arrow*), possibly representing superinfection or perforation.

include pyloric gastritis with scarring, gastric or duodenal tumors, or extrinsic compression (Figure 19-22).

## Computed Tomography of the Duodenum

It is important to identify and recognize the pancreaticoduodenal groove because multiple disease processes may affect this region. For example, inflammatory processes such as pancreatitis can affect the surrounding peripancreatic fat and the second, third, and fourth parts of the duodenum, resulting in an associated duodenitis.



**Figure 19-21** This computed tomography image shows a cluster of collateral vessels around the lesser curvature (*arrow*) and splenomegaly secondary to splenic vein thrombosis.

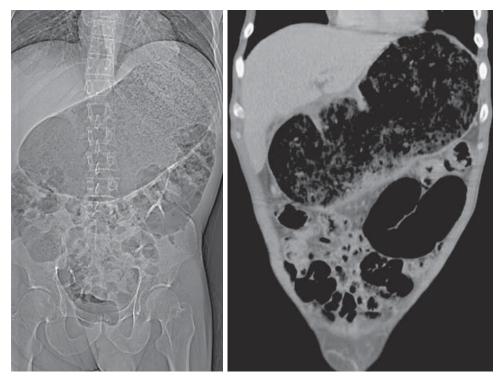


Figure 19-22 Gastric distention in scanogram (left) and coronal computed tomography scan (right).

Tumors of the pancreatic head can grow and invade the surrounding structures, namely, the second and/or third parts of the duodenum. Duodenal tumors, too, can be aggressive, such as leiomyosarcoma (although this tumor accounts for only 10% of duodenal tumors). These tumors tend to infiltrate adjacent structures such as the pancreas. Hence when reviewing a CT, it is essential to inspect the pancreaticoduodenal groove to assess involvement and spread of disease processes.<sup>18</sup>

#### INFLAMMATORY CONDITIONS

As in the stomach, *H. pylori* is the most common cause of peptic duodenal ulcer. There are weak associations of duodenal ulcers with smoking and alcohol intake. Most patients with peptic ulcers can be investigated endoscopically; however, the upper gastrointestinal study with barium contrast is excellent at demonstrating duodenal ulcers. CT helps distinguish complications, such as perforation (Figure 19-23).

Giant duodenal ulcers are defined as a benign ulcer crater of more than 2 cm in diameter and have a tendency to bleed.

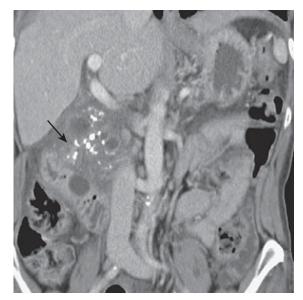
Pancreatitis is the most common cause of inflammatory change in the duodenum (Figures 19-24 and 19-25). In pancreatitis, there is typically periduodenal retroperitoneal fat stranding. Peripancreatic fluid collections may be seen. The release of the pancreatic enzymes causes reactive edema of the duodenum, the extent of which may be severe enough to cause gastric outlet obstruction. Disruption of the intramural vasculature by the digestive pancreatic enzyme elastase can result in intramural hematoma.

Severe cholecystitis can result in inflammation of the duodenum, and, if this is of long standing, it can result in a gallstone eroding through the gallbladder wall into the duodenum, eventually causing gallstone ileus. Bouveret's syndrome is gastric outlet obstruction from a gallstone.

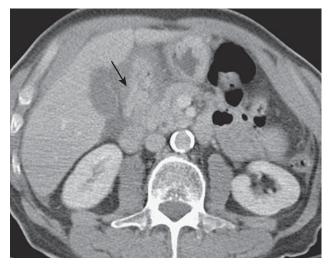
#### DUODENAL DIVERTICULUM

The incidental finding of a duodenal diverticulum is frequent on CT. These lesions are typically seen in the second part of the duodenum, with 85% arising from the medial surface (Figures 19-26 and 19-27).<sup>19</sup> They are lined with intestinal epithelium, the majority causing no symptoms. However, occasionally a diverticulum can be lined by aberrant pancreatic, gastric, or other functioning mucosa and can be the site of ulceration or perforation. Retention of food or a foreign body occasionally can cause symptoms. Aberrant insertion of the common bile duct into a duodenal diverticulum may cause cholangitis or pancreatitis.<sup>20</sup>

CT features of duodenal diverticulum include saccular outpouching, which may resemble a masslike structure between the duodenum and the pancreas containing air, air/fluid level, contrast material, or debris. However, the features of duodenal diverticulitis are similar to those seen in the colon, with wall thickening and retroperitoneal fat stranding. Perforation is a rare complication.<sup>21</sup>



**Figure 19-24** Gross calcification of pancreatitis involving the first, second, and third part of the duodenum (*arrow*) can be seen on this computed tomography image.



**Figure 19-23** Computed tomography image of perforated duodenal ulcer with free fluid around the duodenal wall (*arrow*).



**Figure 19-25** Axial CT image of pancreatitis and duodenitis. Note the duodenal wall thickening (*arrow*), fat stranding, and extensive inflammatory change.



**Figure 19-26** Axial computed tomography image through the second part of the duodenum demonstrating two air-filled, saccular diverticula (*arrows*).



**Figure 19-28** Small enhancing soft tissue within the duodenal lumen (*arrow*) is evident on this computed tomography image. Histologic evaluation confirmed adenocarcinoma.

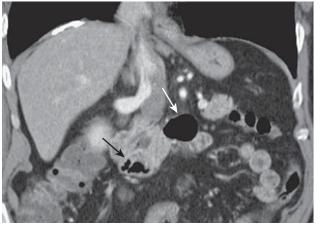


Figure 19-27 The most common region for a diverticulum is the medial aspect of the second part of the duodenum (arrows).

### NEOPLASM

#### Malignant Tumors

Malignant tumors of the duodenum are uncommon, the most common being primary adenocarcinoma (Figure 19-28) or tumor of the papilla of Vater (Figure 19-29). Presentation of these tumors can vary and include obstruction or the appearance of peptic ulcer disease. CT often demonstrates a mass within the duodenum, causing obstruction proximally (Figure 19-30); or if it is at the ampulla of Vater there may biliary or pancreatic ductal dilatation.

#### Secondary Involvement

The most common tumors involving the duodenum include gastric carcinoma and lymphoma; in both cases, duodenal involvement is typically secondary to direct spread across the pylorus. Carcinoma of the head of the pancreas often involves the duodenum. Owing to its close proximity to the duodenum, the tumor may cause widening of the C shape of the duodenal loop. It may manifest as bleeding, perforation, or duodenal obstruction.

Metastatic deposits to the duodenum may arise from primary tumors of the colon, kidney, uterus, or breast or from malignant melanoma.



Figure 19-29 Small, enhancing papillary carcinoma (arrow).

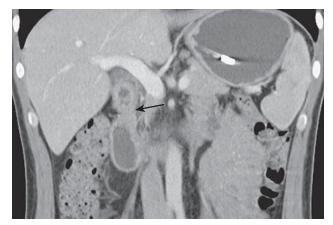


Figure 19-30 Circumferential duodenal tumor (*arrow*) causing gastric outlet obstruction.

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#### **Key Points**

- Endoscopy is the gold standard in evaluating the upper gastrointestinal tract, and the role of the barium examination is diminishing.
- A double-contrast study can help detect and characterize ulcers.
- A malignant ulcer does not protrude beyond the gastric outline, demonstrates the meniscus sign, and shows focal nodularity and distortion of adjacent areae gastricae with amputated folds.
- The best modality to identify peptic and duodenal ulcers is the upper gastrointestinal study with barium contrast,

whereas CT demonstrates complications such as perforation.

- Gastric cancer and lymphoma can be difficult to distinguish.
- Staging of gastric carcinoma by CT is useful for planning treatment.
- GISTs are often large and exophytic but can respond dramatically to therapy.
- Duodenal trauma is a surgical emergency and is identified by secondary signs of small pockets of air or fluid adjacent to the duodenum.

#### REFERENCES

- Stevenson GW, Somers S, Virjee J: Routine double-contrast barium meal: appearance of normal duodenal papillae. *Diagn Imaging* 49:6– 14, 1980.
- Chapman S, Nakielny R: A guide to radiological procedures, ed 4, London, 2001, Saunders, pp 57–59.
- Robbins SE, Virjee J: The gastrointestinal tract. In Butler P, Mitchell AWM, Ellis H, editors: *Applied radiological anatomy*, 1999, Cambridge University Press, pp 211–214.
- Nolan DJ: The duodenum. In Grainger RG, Allison D, Adam D, et al, editors: Grainger and allison's diagnostic radiology: A textbook of medical imaging, ed 4, New York, 2001, Churchill Livingstone, pp 1063–1073.
- 5. Kottler RE, Tuft RJ: Benign greater curve gastric ulcer: the sump-ulcer. *Br J Radiol* 54:651–654, 1981.
- Eisenberg RL: Clinical imaging: an atlas of differential diagnosis, ed 4, Philadelphia, 2003, Lippincott Williams and Wilkins, p 326.
- Shirakabe H, et al: Atlas of the X-ray diagnosis of early gastric cancer, Tokyo, 1966, Igaku Shoin.

- Webb R, Brant W, Major N: *Fundamentals of body CT*, ed 3, Philadelphia, 2006, WB Saunders, pp 324–328.
- Desai RK, Tagliabue JR, Wegryn SA, et al: CT evaluation of wall thickening in the alimentary tract. *Radiographics* 11:771–783, 1991.
- Gossios KJ, Tsianos EV, Demou LL, et al: Use of water or air as oral contrast media for computed tomographic study of the gastric wall: comparison of the two techniques. *Gastrointest Radiol* 16:293–297, 1991.
- 11. Scatarige JC: CT of the stomach and duodenum. *Radiol Clin North Am* 27:687–706, 1989.
- Howson CP, Hiyama T, Wynder EL: The decline in gastric cancer: epidemiology of an unplanned triumph. *Epidemiol Rev* 8:1–27, 1986.
- Insko EK, Levine MS, Birnbaum BA, et al: Benign and malignant lesions of the stomach: evaluation of CT criteria for differentiation. *Radiology* 228:166–171, 2003.
- Enhlich AN: Gastrointestinal manifestations of malignant lymphoma. *Gastroenterology* 54: 1115–1121, 1968.

- Megibow AJ: Gastrointestinal lymphoma: the role of CT in diagnosis of gastric lymphoma. *AJR Am J Roentgenol* 138:859–865, 1982.
- Pannu HK, Hruban RH, Fishman EK: CT of gastric leiomyosarcoma: patterns of involvement. AJR Am J Roentgenol 173:369–373, 1999.
- Chang D, Levine MS, Ginsberg GG, et al: Portal hypertensive gastropathy: radiographic findings in eight patients. *AJR Am J Roentgenol* 175:1609– 1612, 2000.
- Gore RM, Levine SL: *Textbook of gastrointestinal radiology*, ed 2, Philadelphia, 2000, WB Saunders, pp 546–657.
- 19. Levene G: The clinical significance of duodenal diverticula. *Am J Dig Dis* 7:877–885, 1962.
- Rose PG: Clinical and radiological features of aberrant insertion of the common bile duct. *Clin Radiol* 26:121–127, 1975.
- Pearl MS, Hill MC, Zeman R: CT findings in duodenal diverticulitis. *AJR Am J Roentgenol* 187:W392–W395, 2006.

## Mucosal Diseases of the Stomach: Differentiating Benign from Malignant

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## **Malignant Mucosal Processes**

#### **ETIOLOGY**

A wide range of benign disease processes can affect the mucosa of the stomach, including inflammatory, infectious, hereditary, and autoimmune processes. What these processes have in common is that they affect one of the primary defenses of the stomach wall—the mucosal layer.

In considering the radiologic appearance of these entities, it is helpful to divide them into their primary mucosal manifestations—ulcers, polyps and masses, and diffuse mucosal processes. Some of the more common processes include the following:

- Ulcers: Infections (Helicobacter pylori, cytomegalovirus), erosive gastritis (nonsteroidal antiinflammatory drugs [NSAIDs], alcohol, stress, radiation, direct trauma), Crohn's disease, autoimmune (Behçet's) disease, sarcoidosis<sup>1</sup>
- *Polyps and masses:* Hyperplastic and adenomatous polyps (also seen in Cronkhite-Canada syndrome and familial polyposis of the colon), hamartomas (Peutz-Jeghers syndrome, Cowden's disease), heterotopic pancreatic tissue, lymphoid hyperplasia<sup>2</sup>
- *Diffuse mucosal processes:* Acute gastritis, atrophic gastritis, eosinophilic and lymphocytic gastritis, Zollinger-Ellison syndrome, Ménétrier's disease, and those that cause a linitis plastica appearance (corrosives, radiation, Crohn's disease, tuberculosis, sarcoidosis, syphilis)<sup>2</sup>

In this chapter, the discussion is tailored to each of these categories, with a description of the most common entities.

#### PREVALENCE AND EPIDEMIOLOGY

#### Benign Diseases Causing Mucosal Ulcerations

The most common benign cause of mucosal ulcerations is peptic ulcer disease. Although decreasing in overall incidence with the routine use of histamine-2 (H<sub>2</sub>) blockers, the overall death rate from peptic ulcer disease has remained stable. The vast majority of cases of gastric ulcers (70% to 90%) and duodenal ulcers (up to 90%) are due to *H. pylori* infection.<sup>3</sup>

Other causes of gastric ulcers include NSAIDs and aspirin.<sup>4</sup> Chronic NSAID users have a prevalence of peptic ulcer disease of 25%. Less common causes of benign gastric mucosal ulcers include stress ulcers in burn patients (Curling's ulcers) and head trauma patients (Cushing's ulcer), crack cocaine and alcohol abuse,<sup>1</sup> Crohn's disease,<sup>5,6</sup> sarcoidosis,<sup>7</sup> cytomegalovirus infection, and Behçet's disease.

#### Benign Diseases Causing Polyps and Masses

Polypoid lesions of the stomach include hyperplastic (regenerative), adenomatous, hamartomatous, and inflammatory polyps, as well as heterotopic pancreatic tissue. The most common benign polyps are hyperplastic polyps, which can commonly occur in the setting of gastritis. Unlike adenomatous polyps, which can degenerate in a fashion similar to that of colonic adenomas, hyperplastic polyps have almost no malignant potential.<sup>2</sup>

Hamartomatous polyposis syndromes are rare and include Peutz-Jeghers syndrome, multiple hamartoma/Cowden's disease,<sup>8</sup> juvenile polyposis, Cronkhite-Canada syndrome, and Bannayan-Riley-Ruvalcaba syndrome. Whereas hamartomatous polyps are themselves without malignant potential, they are frequently associated with adenomatous polyps. More importantly, these syndromes can be associated with extraintestinal malignancies, and diagnosis is essential so the patient can be undergo screening.<sup>9</sup>

#### Benign Diseases Causing Diffuse Mucosal Abnormalities

The most common diseases that affect the gastric mucosa diffusely are acute gastritis and chronic and atrophic gastritis. Acute gastritis, most commonly secondary to *H. pylori* infection, can progress to a chronic state if left untreated. Other causes of acute gastritis include NSAID-induced gastritis, caustic ingestion,<sup>1</sup> and granulomatous disease (sarcoidosis,<sup>7</sup> tuberculosis), as well as less common causes such as cytomegalovirus infection, herpesvirus infection, and syphilis.<sup>10</sup>

Chronic gastritis can progress to atrophic gastritis, which is characterized by loss of the normal mucosal glands and is categorized by the portion of the stomach involved. Type A chronic and atrophic gastritis, which affects predominantly the fundus and body, has been termed *autoimmune gastritis* and is the least common of the two types. This form is associated with pernicious anemia, caused by destruction of the parietal cells and loss of intrinsic factor, which leads to vitamin B<sub>12</sub> deficiency and megaloblastic anemia. More common is type B chronic/atrophic gastritis, which affects predominantly the antrum and is associated with chronic *H. pylori* infection.<sup>1</sup>

Other causes of gastritis are less common. Eosinophilic gastritis is characterized by blood eosinophilia and eosinophilic gastric wall infiltrates. The antrum is predominantly involved,

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and mucosal fold thickening can become severe enough to cause gastric outlet obstruction.<sup>11</sup> Bowel involvement can occur and is termed *eosinophilic gastroenteritis*.<sup>1</sup>

Diffuse gastric fold thickening can occur as a result of inflammation or infiltration. In Ménétrier's disease there is hypertrophy of the mucus-producing cells of the stomach mucosa, causing marked fold thickening. This rare disorder is of unknown cause and can mimic malignancy as well as severe gastritis or an infiltrative process.<sup>2</sup> In addition to the usual clinical presentation of pain, weight loss, and occasional bleeding, the disorder is characterized by hypoalbuminemia secondary to loss of proteins.<sup>1</sup>

#### PATHOLOGY

In general, entities that affect the stomach mucosa can be divided into a few broad categories: infectious, inflammatory, infiltrative, autoimmune, and hereditary. Those processes causing ulcers can fall into any of these categories, but polypoid lesions tend to represent either inflammatory or hereditary causes.<sup>2</sup>

Infectious causes, including most commonly *H. pylori*, all begin by circumventing the stomach mucosa's natural defenses. Because of its highly acidic environment, the stomach is able to withstand infection from a wide range of ingested bacteria. However, in *H. pylori*, the bacteria have adapted mechanisms to neutralize the acidic environment by creating sodium bicarbonate and ammonia from the enzyme urease. Once it has colonized the stomach, *H. pylori* causes an increase in gastric acid production through a variety of mechanisms, including inhibition of the production of somatostatin by the antral D cells. Because somatostatin is a potent inhibitor of antral G cell gastrin production, this leads to an overall increase in acid secretion. This acid hypersecretion is thought to be the primary mechanism for *H. pylori*—induced gastritis and ulcer formation.<sup>2</sup>

Other infectious agents, including herpesvirus and cytomegalovirus, involve direct viral infection of the mucosal cells. Clinically, these affect immunocompromised patients. Cytomegalovirus infection is characterized by intranuclear inclusions seen on biopsy.<sup>1</sup> Syphilitic involvement of the stomach is rare but has been seen with increasing frequency in immunocompromised patients. In early disease, gastritis is characterized pathologically by perivascular and mucosal mononuclear infiltration. In later stages of the disease, gummatous involvement of the stomach can occur, as well as scarring and stricture.<sup>10</sup>

Inflammatory causes of gastritis include NSAID-induced gastritis, as well as caustic ingestion. The most common of these disorders is NSAID-induced gastritis. NSAIDs cause a decrease in stomach mucus and bicarbonate production by inhibiting prostaglandins. This leads to a breakdown in the defensive barrier of the stomach lining to gastric acid, which in turn leads to gastritis and ulcer disease.<sup>1</sup>

Infiltrative causes tend to result in a diffuse abnormality of the stomach mucosa. These include eosinophilic and lymphocytic gastritis, Ménétrier's disease, sarcoidosis, and tuberculosis. The pathologic hallmark is infiltration of mucosa or submucosa with abnormally increased cells (in the case of eosinophilic and lymphocytic gastritis, as well as Ménétrier's disease) or reactive tissue (in the case of granulomas of sarcoidosis and tuberculosis).<sup>11</sup>

Benign polypoid and mucosal mass lesions of the stomach are most commonly hyperplastic and seen in the setting of gastritis. These have a low potential for malignancy.<sup>12</sup> Adenomatous polyps, which can be seen in the setting of polyposis syndromes mentioned previously, have a higher potential for malignancy and can be either tubular or villous.<sup>13</sup> Finally, hamartomatous polyps, also seen in the setting of polyposis syndromes, are the least common of the subtypes.<sup>14</sup>

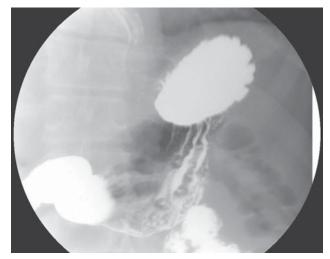
#### IMAGING

#### Ulcers

Gastric ulcer disease typically manifests as symptoms of epigastric or abdominal pain, which is worse with eating. These clinical symptoms are nonspecific and can be seen in a variety of abdominal pathologic processes, not just referable to the stomach.<sup>15</sup> Magnetic resonance imaging (MRI), ultrasonography, and positron emission and computed tomography (PET/ CT) are not generally useful in the diagnosis.

**Radiography.** Evaluation of mucosal disease is best seen with double-contrast barium evaluation. Gastric ulcers appear as abnormal accumulations of contrast media that persist on different views. Within the stomach, these collections are most often round, as opposed to in the esophagus, where they can also appear as linear defects. In benign ulcers, the ulcer crater projects outside the gastric lumen. Additionally, mucosal folds are typically thin and extend to the margin of the ulcer (this is not seen with malignant ulcers or ulcerated masses).<sup>16</sup> The pattern of mucosal ulcerations also can be useful. In the case of erosive gastritis caused by NSAID use, small ulcers are aligned along thickened folds (Figure 20-1).<sup>4</sup> Peptic ulcers tend to be solitary or few, but aphthous ulcers of Behçet's disease and Crohn's disease are often multiple.<sup>6</sup>

**Computed Tomography.** Studies have shown that multidetector CT with virtual gastroscopy is a useful way to distinguish benign from malignant gastric ulcers. Using criteria such as ulcer shape and margin (regular vs. irregular), gastric fold



**Figure 20-1** Double-contrast barium upper gastrointestinal examination of the stomach reveals thickened gastric folds with multiple ulcers lined along the gastric folds. Endoscopic sampling revealed gastritis, negative for *Helicobacter pylori*. This case was thought to be most likely secondary to use of nonsteroidal antiinflammatory drugs.

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changes, and enhancement of the ulcer base, Lee and colleagues reported 80% to 90% sensitivity and 77% to 78% specificity for the differentiation of benign from malignant ulcers.<sup>17</sup>

More commonly, CT is used generally to evaluate patients with abdominal pain. In these cases, gastric wall thickening or edema can be seen at the site of ulcers. Importantly, some of the complications of gastric ulcers can be readily detected by CT, including perforation (Figure 20-2) and gastric outlet obstruction. Bleeding ulcers are less likely to be detected with CT.<sup>2</sup>

#### Polyps and Masses

Gastric polyps and benign masses are generally clinically occult unless they cause bleeding or gastric outlet obstruction. These are typically incidentally detected with endoscopy or barium



**Figure 20-2** Axial computed tomography scan performed with intravenous and oral contrast media demonstrates a defect in the gastric wall, with oral contrast medium entering the peritoneal cavity. At surgery this was found to be a perforated gastric ulcer.

radiography. MRI, ultrasonography, nuclear medicine studies, and PET/CT are not generally useful in diagnosis.

**Radiography.** The radiographic evaluation of benign mucosal polyps and masses again rests on the double-contrast barium upper gastrointestinal evaluation. Gastric polyps appear as filling defects on barium studies and can be pedunculated or tubular (Figure 20-3) or villous. When numerous, the possibility of a polyposis syndrome is raised. Additionally, mucosal masses such as heterotopic pancreatic rests can have a characteristic appearance, typically with a centrally umbilicated mass in the pylorus.<sup>18-20</sup>

**Computed Tomography.** CT is not generally useful when imaging mucosal lesions unless there is a large mass or a complication such as gastric outlet obstruction.<sup>21</sup>

#### Diffuse Mucosal Disease

Again, abdominal pain is the most common manifesting symptom in these cases and is nonspecific. If a patient has scarring or fibrosis, early satiety may be a symptom that would prompt evaluation of the stomach. Additionally, patients with Ménétrier's disease present with hypoalbuminemia, which may prompt a search for an underlying cause.<sup>22</sup>

**Radiography.** Double-contrast barium radiography may be ordered in the patient with early satiety to evaluate for underlying neoplasm or mass. Barium studies may show gastric non-distensibility, or segmental scarring, such as in Crohn's disease. The differential considerations for this appearance are wide, and close evaluation of the patient's history may narrow the diagnostic possibilities.<sup>5</sup>

**Computed Tomography.** CT is generally not useful without a distended stomach. Wall thickening of the stomach can be simulated by underdistention.

**Positron Emission Tomography With Computed Tomography.** PET/CT is not useful in the diagnosis of diffuse gastric

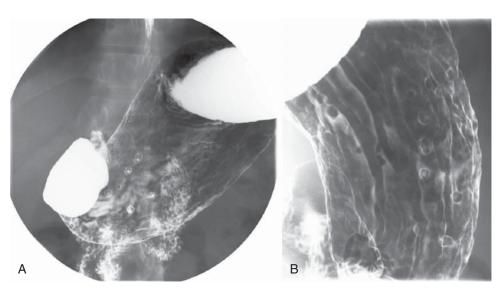


Figure 20-3 A, Double-contrast barium upper gastrointestinal examination of the stomach reveals multiple polypoid lesions. B, Endoscopic biopsy revealed hyperplastic polyps, the most common type.

mucosal disease. In patients who have PET/CT for other reasons, incidental detection of inflammatory processes such as gastritis may be seen with increased fluorodeoxyglucose uptake.<sup>23</sup>

**Imaging Algorithm.** In patients presenting with abdominal pain, the first-line imaging study is typically CT. If CT does not yield a diagnosis, the patient should proceed to double-contrast barium upper gastrointestinal study or endoscopy for further evaluation. The choice of these two procedures most often depends on the patient's clinical status and pretest likelihood of disease.

#### **Classic Signs**

- Hampton's line (benign ulcer): Thin straight line at the base of the ulcer seen in profile indicating thin rim of undermined mucosa<sup>16</sup>
- Ram's horn sign (Crohn's disease): Deformity, nondistensibility, narrowing, and poor peristalsis of the stomach antrum, leading to configuration similar to a ram's horn<sup>5</sup>
- Linear and serpiginous gastric ulcers: Aspirin/NSAIDinduced erosive gastritis)<sup>4</sup>
- Heterotopic pancreatic rests: A centrally umbilicated mass located in the pylorus<sup>19-21</sup>

# DIFFERENTIAL DIAGNOSIS

Abdominal and epigastric pain are classic symptoms of gastritis and ulcer disease. These are nonspecific symptoms and may prompt evaluation of the stomach only with the appropriate clinical history (e.g., NSAID use, history of Crohn's disease or sarcoidosis).<sup>15,22</sup>

As discussed previously, the differential diagnosis rests on categorizing mucosal diseases into their primary manifestations: ulcers, polyp and masses, and diffuse processes.

# **Malignant Mucosal Processes**

# ETIOLOGY

Malignant mucosal processes can have manifestations similar to those of benign disease, and it is helpful to categorize them according to their most common presentations. Overall, there is considerable overlap in the presentation of malignant gastric diseases because the major diseases—gastric adenocarcinoma, lymphoma, and metastatic disease—can manifest as any of the radiologic manifestations described here. Classifying these processes by their different mucosal manifestations—ulcer, polyp or mass, and diffuse mucosal processes—yields the following causes:

- *Ulcers:* Malignant gastric ulcer secondary to gastric adenocarcinoma, lymphoma, carcinoid, metastatic disease from melanoma, lung, adenocarcinoma, Kaposi's sarcoma
- Polyps and masses: Gastric carcinoma, carcinoid
- Diffuse mucosal processes: Linitis plastica (gastric carcinoma, lymphoma, metastatic disease especially from breast cancer), Ménétrier's disease with associated adenocarcinoma

# PREVALENCE AND EPIDEMIOLOGY

Both primary and metastatic malignancy can affect the stomach. Primary malignancies include adenocarcinoma (95%), lymphoma (4%), and gastrointestinal stromal tumors (GISTs) (1%). Of metastatic malignancies, direct invasion from adjacent tumors of the pancreas or colon is more common than hematogenous metastases such as those from carcinoma of the breast and melanoma. Of these, malignancies that affect the gastric mucosa include adenocarcinoma, lymphoma, and hematogenous metastases.<sup>2</sup>

Overall, gastric malignancy incidence has decreased over the past century. In the early 1900s, gastric cancer was the leading cause of death in men in the United States, whereas today it is not in the top 10. However, while the incidence has decreased in the West, gastric cancer is still relatively common in Asia and Eastern Europe, representing the second most common cancer. The highest prevalence occurs in Costa Rica, Japan, and the republics of the former Soviet Union, whereas the lowest prevalence is in the United States and parts of Africa and Southeast Asia.<sup>2</sup> Overall, prognosis is poor, with 5-year survival at 22%, a statistic that has not changed significantly in the past 30 years.<sup>2,24</sup>

Causes of gastric adenocarcinoma are unclear, but epidemiologic studies have pointed to diet (low in fruits and vegetables, high in nitrates and salt) as a factor. Additionally, *H. pylori* infection has been implicated in the increased risk for both adenocarcinoma and lymphoma. Genetic mutations, including those seen with Li-Fraumeni syndrome and hereditary nonpolyposis colorectal cancer, increase the risk for gastric malignancy.<sup>2,24,25</sup>

Unlike adenocarcinoma, the incidence of gastric lymphoma has been increasing. Similar to adenocarcinoma, infection with *H. pylori* is a risk factor and there can be significant regression of lymphomatous involvement with antibiotic treatment. Staging for gastric lymphoma, which is almost always the B-cell non-Hodgkin's type, is the same as for non-Hodgkin's lymphoma.<sup>2</sup>

# PATHOLOGY

Gastric adenocarcinoma, which accounts for 95% of gastric malignancies, is generally divided into two broad categories: type I (intestinal) and type II (diffuse). Type I adenocarcinoma is generally well differentiated, contains distinct glandular elements, is typically found in older male patients, and carries a better prognosis. Type II adenocarcinoma is poorly differentiated, is infiltrative, is found in younger and female patients, and carries a worse prognosis.<sup>24</sup>

Gastric lymphoma, although less common, is the most common extranodal site for lymphomatous involvement. Almost all cases of gastric lymphoma are B-cell non-Hodgkin's type. These can include both well-differentiated superficial mucosa-associated lymphoid tissue lymphoma and high-grade large cell lymphoma.<sup>25</sup>

# IMAGING

#### Malignant Mucosal Disease

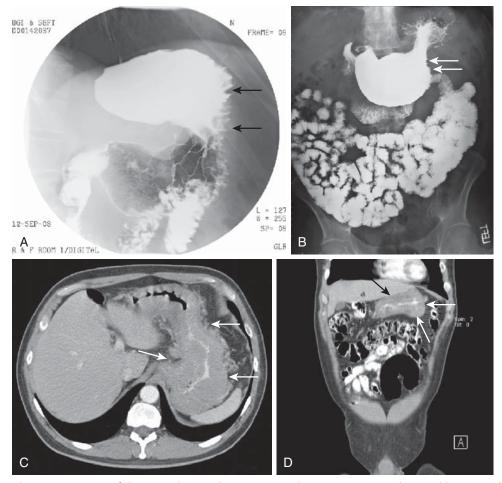
There is considerable overlap in the clinical presentation of benign and malignant gastric mucosal processes, including epigastric pain, weight loss, food avoidance, and anemia. Generally, because it is easier and less invasive to perform double-contrast barium radiography, this is often the initial test ordered.<sup>22,25</sup>

**Radiography.** Double-contrast barium radiography is often recommended as the first method of evaluation for patients presenting with a wide variety of epigastric or abdominal complaints. When mucosal abnormalities are present, they generally fall into one of three main categories: ulcers, polyps or masses, or diffuse mucosal disease. These three categories include numerous benign and malignant causes, and most often the patient must undergo endoscopic evaluation and biopsy for definitive diagnosis. There are, however, classically described findings in benign and malignant ulcers that may suggest a cause.

The goal of double-contrast barium radiography in the evaluation of mucosal ulcerations is to distinguish benign from malignant ulcers. Benign ulcers have been classically described as round, with thin mucosal folds radiating to the crater surface as well as projecting outside the gastric lumen. In contrast, malignant ulcers have nodular, irregular radiating folds that do not extend to the ulcer crater (ulcerated mass) and lie within the stomach wall. Using these criteria, those ulcers that clearly fall within the benign category do not need endoscopic confirmation according to the radiology literature.<sup>16,26</sup> However, it is recommended in the internal medicine literature that all ulcers undergo endoscopic evaluation to confirm benignity.<sup>22,25</sup>

In patients with mucosal polyps or masses seen on doublecontrast barium radiography, the majority are benign hyperplastic or inflammatory polyps. However, because a percentage of these polyps are adenomatous and cannot be distinguished from hyperplastic polyps, endoscopic removal is recommended to exclude premalignant lesions. Villous polyps have a higher rate of malignancy (55%) and are removed endoscopically or surgically when found.<sup>13</sup>

Thickened gastric folds and other diffuse mucosal presentations can have a variety of causes. In general, thickened, irregular, tortuous folds invoke an infiltrative cause, such as adenocarcinoma (Figure 20-4), lymphoma, or metastatic disease. However, there is overlap with other conditions such as Ménétrier's disease, which can be benign or associated with other malignancies (Figure 20-5). Nondistensibility of the stomach is not helpful because it can be seen with scirrhous carcinoma and metastatic disease as well as benign causes such as Crohn's disease and syphilis. When these findings are seen at double-contrast barium radiography, they should trigger further evaluation for the underlying cause.<sup>27-29</sup>



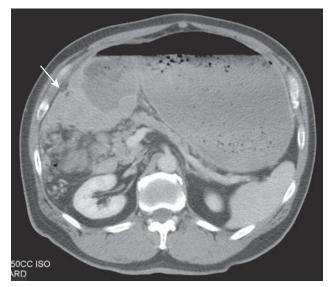
**Figure 20-4** Linitis plastica appearance of the stomach secondary to gastric adenocarcinoma. A and B, Double-contrast barium radiography demonstrates limited distensibility and thickened gastric folds (*arrows*). C and D, Axial and coronal computed tomography images enhanced with intravenous and oral contrast agents show marked gastric wall thickening (*arrows*) with limited gastric distensibility.

**Computed Tomography.** Although most useful in the staging and follow-up for gastric malignancy, multidetector CT with virtual gastroscopy has been used to differentiate benign from malignant ulcers. Using ulcer shape, wall thickness, and enhancement as criteria, in conjunction with multiplanar reconstruction images, Chen and colleagues<sup>17</sup> were able to demonstrate 80% sensitivity and 100% specificity in differentiating benign from malignant ulcers.

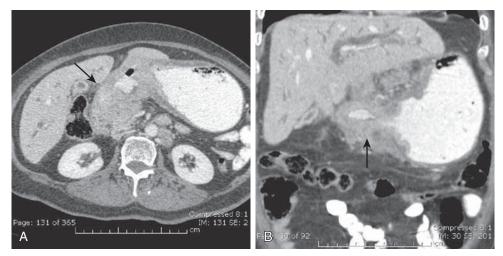


**Figure 20-5** Ménétrier's disease associated with nongastric adenocarcinoma. Coronal computed tomography image enhanced with intravenous and oral contrast agents shows marked gastric wall thickening and associated enhancing soft tissues masses (*arrows*) in the left upper quadrant. Biopsy revealed gastric changes consistent with Ménétrier's disease, and the adjacent mass was consistent with adenocarcinoma.

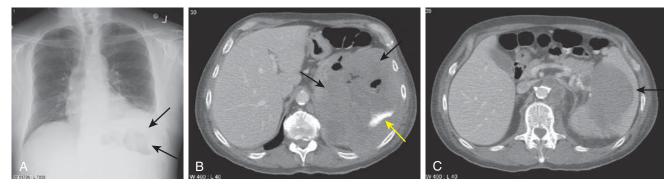
More commonly, CT is used in the staging of known gastric malignancy or evaluation of complications. When a patient presents acutely with abdominal pain, CT is often the first test ordered. In these cases, patients who demonstrate perforation, obstruction (Figures 20-6 and 20-7), or hemorrhage are surgically treated and the underlying cause (malignant or benign) can be determined. In patients with diffuse disease, such as extensive gastric wall thickening, the presence of extragastric disease will point to a malignant cause over a benign one (Figure 20-8).<sup>30-32</sup> Additionally, when the primary gastric cancer is not evident, multidetector CT can be useful in excluding advanced disease and allow for consideration of a less invasive treatment.<sup>33</sup>



**Figure 20-7** Gastric lymphoma causing gastric outlet obstruction. Axial computed tomography image enhanced with intravenous and oral contrast agents shows distal gastric wall thickening (*arrow*) with gastric outlet obstruction. This case is not easily distinguishable from that in Figure 34-3 and demonstrates the importance of biopsy.



**Figure 20-6** Gastric adenocarcinoma causing gastric outlet obstruction. A and B, Axial and coronal computed tomography images enhanced with intravenous and oral contrast agents show marked gastric wall thickening of the distal stomach (*arrows*), with distention of the proximal stomach, consistent with gastric outlet obstruction. Currently, malignancy is the most common cause of gastric outlet obstruction.



**Figure 20-8** Gastric lymphoma invading the spleen. A, Posteroanterior view of the chest shows nodular gastric wall thickening (arrows). B and C, Axial computed tomography images enhanced with intravenous and oral contrast show marked gastric wall thickening, with invasion of the spleen (arrows). Note the small amount of oral contrast agent within the stomach lumen, which is grossly distorted (yellow arrow).

# **Key Points**

- The most useful imaging technique for the diagnosis of gastric mucosal disease is the double-contrast barium upper gastrointestinal study.
- CT can be useful in further evaluating known ulcers as well as in imaging the acute complications such as perforation and gastric outlet obstruction.
- The double-contrast barium upper gastrointestinal series may be the initial test in patients presenting with epigastric pain.
- Once a gastric mucosal process is diagnosed, the patient should undergo endoscopic evaluation/biopsy because malignant mucosal disease can mimic benign causes.

#### REFERENCES

- 1. Valle JD: Peptic ulcer disease and related disorders. In Fauci AS, Braunwald E, Kasper DL, et al, editors: *Harrison's principles of internal medicine*, ed 17, New York, 2008, McGraw-Hill.
- Dempsey DT: Stomach. In Brunicardi FC, Andersen DK, Billiar TR, et al, editors: *Schwartz's principles of surgery*, ed 8, New York, 2008, McGraw-Hill.
- 3. Cello JP: *Helicobacter pylori* and peptic ulcer disease. *AJR Am J Roentgenol* 164:283–286, 1995.
- Levine MS, Verstandig A, Laufer I: Serpiginous gastric erosions caused by aspirin and other nonsteroidal antiinflammatory drugs. AJR Am J Roentgenol 146:31–34, 1986.
- Farman J, Faegenburg D, Dallemand S, et al: Crohn's disease of the stomach: the "ram's horn" sign. Am J Roentgenol Radium Ther Nucl Med 123:242–251, 1975.
- Nelson SW: Some interesting and unusual manifestations of Crohn's disease ("regional enteritis") of the stomach, duodenum and small intestine. Am J Roentgenol Radium Ther Nucl Med 107:86–101, 1969.
- Levine MS, Ekberg O, Rubesin SE, et al: Gastrointestinal sarcoidosis: radiographic findings. AJR Am J Roentgenol 153:293–295, 1989.
- Gold BM, Bagla S, Zarrabi MH: Radiologic manifestations of Cowden disease. AJR Am J Roentgenol 135:385–387, 1980.
- Harned RK, Buck JL, Sobin LH: The hamartomatous polyposis syndromes: clinical and radiologic features. AJR Am J Roentgenol 164: 565–571, 1995.
- Jones BV, Lichtenstein JE: Gastric syphilis: radiologic findings. AJR Am J Roentgenol 160: 59–61, 1993.

- 11. Burhenne HJ, Carbone JV: Eosinophilic (allergic) gastroenteritis. *Am J Roentgenol Radium Ther Nucl Med* 96:332–338, 1966.
- Joffe N, Antonioli DA: Atypical appearances of benign hyperplastic gastric polyps. AJR Am J Roentgenol 131:147–152, 1978.
- Miller JH, Gisvold JJ, Weiland LH, et al: Upper gastrointestinal tract: villous tumors. AJR Am J Roentgenol 134:933–936, 1980.
- Wong-Kee-Song L, Topazian M: Gastrointestinal endoscopy. In Fauci AS, Braunwald E, Kasper DL, et al, editors: *Harrison's principles of internal medicine*, ed 17, New York, 2008, McGraw-Hill, pp 1836–1846.
- Spiller RC: ABC of the upper gastrointestinal tract: anorexia, nausea, vomiting, and pain. *BMJ* 323:1354–1357, 2001.
- Thompson G, Somers S, Stevenson GW: Benign gastric ulcer: a reliable radiologic diagnosis? AJR Am J Roentgenol 141:331–333, 1983.
- Chen CY, Wu DC, Kuo YT, et al: MDCT for differentiation of category T1 and T2 malignant lesions from benign gastric ulcers. *AJR Am J Roentgenol* 190:1505–1511, 2008.
- Stone DD, Riddervold HO, Keats TE: An unusual case of aberrant pancreas in the stomach: a roentgenographic and gastrophotographic demonstration. *Am J Roentgenol Radium Ther Nucl Med* 113:125–128, 1971.
- Rohrmann CA, Jr, Delaney JH, Jr, Protell RL: Heterotopic pancreas diagnosed by cannulation and duct study. *AJR Am J Roentgenol* 128:1044– 1045, 1977.
- Besemann EF, Auerbach SH, Wolfe WW: The importance of roentgenologic diagnosis of aberrant pancreatic tissue in the gastrointestinal

tract. Am J Roentgenol Radium Ther Nucl Med 107:71-76, 1969.

- Cherukuri R, Levine MS, Furth EE, et al: Giant hyperplastic polyps in the stomach: radiographic findings in seven patients. *AJR Am J Roentgenol* 175:1445–1448, 2000.
- 22. Hasler WL, Owyang C: Approach to the patient with gastrointestinal disease. In Fauci AS, Braunwald E, Kasper DL, et al, editors: *Harrison's principles of internal medicine*, ed 17, New York, 2008, McGraw-Hill, pp 1847–1854.
- Prabhakar HB, Sahani DV, Fischman AJ, et al: Bowel hot spots at PET-CT. *Radiographics* 27: 145–159, 2007.
- Phan AT, Yao JC, Allam SR, et al: Carcinoma of the esophagus and gastric carcinoma. In Kantarjian HM, Wolff RA, Koller CA, editors: *MD* anderson manual of medical oncology, New York, 2006, McGraw-Hill.
- Mayer RJ: Gastrointestinal tract cancer. In Fauci AS, Braunwald E, Kasper DL, et al, editors: *Harrison's principles of internal medicine*, ed 17, New York, 2008, McGraw-Hill, pp 570–579.
- Low VH, Levine MS, Rubesin SE, et al: Diagnosis of gastric carcinoma: sensitivity of doublecontrast barium studies. *AJR Am J Roentgenol* 162:329–334, 1994.
- Balthazar EJ, Davidian MM: Hyperrugosity in gastric carcinoma: radiographic, endoscopic, and pathologic features. *AJR Am J Roentgenol* 136:531–535, 1981.
- Bragg DG, Seaman WB, Lattes R: Roentgenologic and pathologic aspects of superficial spreading carcinoma of the stomach. *Am J Roentgenol Radium Ther Nucl Med* 101:437–446, 1967.

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- Rourke JA, Tomchik FS: Diffuse gastric abnormality: benign or malignant? Am J Roentgenol Radium Ther Nucl Med 96:400–407, 1966.
- Balthazar EJ, Siegel SE, Megibow AJ, et al: CT in patients with scirrhous carcinoma of the GI tract: imaging findings and value for tumor detection and staging. *AJR Am J Roentgenol* 165: 839–845, 1995.
- Buy JN, Moss AA: Computed tomography of gastric lymphoma. AJR Am J Roentgenol 138: 859–865, 1982.
- 32. Park MS, Kim KW, Yu JS, et al: Radiographic findings of primary B-cell lymphoma of the stomach: low-grade versus high-grade malignancy in relation to the mucosa-associated lym-
- phoid tissue concept. *AJR Am J Roentgenol* 179: 1297–1304, 2002.
- 33.Yu JS, Choi SH, Choi WH, et al: Value of nonvisualized primary lesions of gastric cancer on preoperative MDCT. *AJR Am J Roentgenol* 189: W315–W319, 2007.

# **Gastric Stromal Tumors**

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Stromal tumors of the stomach are rare tumors that arise from the mesenchyma, the connective tissue and blood vessels that support an organ. The parenchyma, on the other hand, represents the functional tissue of the organ. Within the stomach, the parenchyma includes the epithelial glandular tissue within the mucosa and the mesenchyma consists of the supporting tissues, or stroma. The components of the stroma include smooth muscle cells, nerve cells, lipocytes, vascular structures, and epithelioid cells. Gastric stromal tumors arise from these cell types.

# **Prevalence and Epidemiology**

The prevalence of gastric stromal tumors varies by type. The most common is the gastrointestinal stromal tumor (GIST), with 10 to 20 cases per million persons, representing 5000 to 6000 cases in the United States annually. GISTs make up 2% to 3% of all gastric tumors.<sup>1</sup> Lipomas represent 2% to 3% of benign gastric tumors, neurogenic tumors account for 4%, and vascular tumors comprise 2%. The remainder of the gastric stromal tumors are exceedingly rare.

There is an increased risk for GIST with neurofibromatosis, Carney's syndrome, and germline mutations of KIT.<sup>1</sup>

# **Clinical Presentation**

Gastrointestinal bleeding (33%) and abdominal pain (19%) are the most common presenting symptoms associated with GIST.<sup>2</sup> Anemia, hematochezia, hematemesis, bloating, abdominal pain, palpable mass, and abdominal distention are additional features.

# Pathology

Historically, GISTs were referred to as leiomyoma, leiomyosarcoma, epithelioid leiomyosarcoma, and leiomyoblastomas, based on the thought that the tumors arise from smooth muscle cells.<sup>1</sup> However, it is now felt that GISTs arise from the interstitial cell of Cajal, which is a primitive gut stem cell in the muscularis propria that expresses KIT, a tyrosine kinase receptor. Distinguishing GIST from other stromal tumors is by the expression of KIT, and 95% of GISTs express KIT. CD117 immunohistochemistry stains are positive for KIT and are diagnostic of GIST.<sup>1</sup> The expression of KIT in GIST is the premise behind medical therapy.

GISTs can be benign or malignant. The determination of a benign or malignant GIST is based on the number of mitoses observed per high-power field. Malignant GISTs can recur and metastasize to the liver and peritoneal surface, with distant metastasis being rare. Metastatic GISTs do not manifest with lymphadenopathy.<sup>1</sup> Therefore, if lymphadenopathy is present, other malignant tumors, such as adenocarcinoma and lymphoma, should be considered.

Other gastric stromal tumors are diagnosed histologically. Schwannomas stain positive for S-100 protein.<sup>3</sup> True leiomyomas and leiomyosarcomas arise from smooth muscle cells and are rare in the stomach.<sup>1</sup>

# Imaging

Seventy percent of GISTs are found in the stomach (Figure 21-1), and 75% of these are found in the body. GISTs also can be found anywhere from the esophagus to the anus and can arise from the mesentery, retroperitoneum, and omentum. The second most common site of presentation is within the small bowel, representing 20% to 30% of cases.<sup>1</sup> Other stromal tumors mimic the appearance of GIST and should be considered in the differential diagnosis.

# COMPUTED TOMOGRAPHY

On CT, GISTs are usually peripherally contrast enhancing and often will have extragastric and intragastric components. Given their size, it is often difficult to determine which portion of the bowel the GIST arises from, but subtle bowel wall thickening can be a clue. Cavitation and calcification are uncommon findings (Figure 21-2).<sup>1</sup>

No definite imaging criteria have been established to distinguish benign from malignant GIST. Initially, it was found that besides evidence of metastatic disease, only size greater than 5 cm was predictive of malignancy.<sup>4</sup> Recently, however, it has been suggested that heterogeneous enhancement and a cysticnecrotic component can be found with a GIST with malignant potential.<sup>5</sup> Metastatic disease from GISTs are often confined to the liver and mesentery, with predominantly hypervascular metastasis.<sup>5</sup>

Gastric adenocarcinoma and lymphoma do not often have extragastric components, and that can be used as a clue for diagnosis. Other benign stromal tumors are much rarer, and imaging characteristics are nonspecific but are also in the differential diagnosis. However, gastric schwannomas, for example, may be suspected if there is homogenous enhancement of a well-circumscribed mass.<sup>3</sup> A smooth, well-circumscribed mass measuring -70 to -120 Hounsfield units is diagnostic of gastric lipoma.<sup>6</sup>

# MAGNETIC RESONANCE IMAGING

The magnetic resonance imaging (MRI) appearance of GISTs mimics that of CT. The lesions usually will have increased T1 signal in the solid areas and increased T2 signal in the cystic

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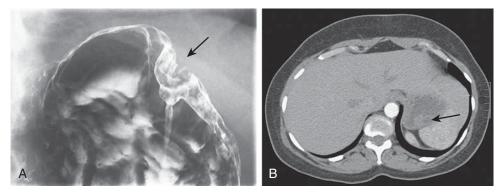
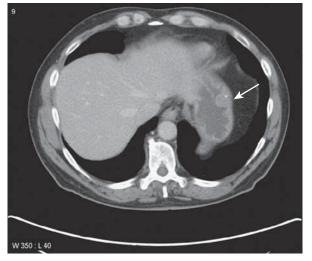


Figure 21-1 A, Selected image from a double-contrast upper gastrointestinal study shows an intraluminal filling defect (arrow). B, Contrastenhanced computed tomography image shows the corresponding mass (arrow) later found to be a gastrointestinal stromal tumor.



**Figure 21-2** Contrast-enhanced computed tomography shows an intraluminal stomach mass with a punctate focus of calcification (*arrow*), later determined to be a gastrointestinal stromal tumor.

areas. The mass can be heterogeneous because of the presence of hemorrhage. GISTs usually enhance and also demonstrate hypervascular metastases.<sup>7</sup>

Uniformly high T1 signal in a submucosal mass is consistent with a lipoma.<sup>8</sup> Only a single case of MRI of gastric schwannoma has been reported, which described uniform enhancement of a lobulated, low-T1 signal, high-T2 signal well-circumscribed mass.<sup>9</sup>

# POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

GISTs and metastases generally demonstrate high fluorodeoxyglucose (FDG) activity.<sup>10</sup> PET has been used for both staging and follow-up for treatment of GIST (Figure 21-3).<sup>10</sup> PET is especially helpful in monitoring the response to imatinib (Gleevac). In patients treated with imatinib, marked decrease in FDG activity has been observed shortly after treatment is initiated, which is further described in the medical treatment section.

# Treatment

# MEDICAL TREATMENT

Historically, the medical treatment for metastatic or unresectable GIST involved cytotoxic chemotherapy. However, results generally have been poor. Currently, the mainstay of medical therapy is with imatinib. Imatinib is a tyrosine kinase inhibitor that selectively inhibits KIT, as well as certain other tyrosine kinases. Because many GISTs overexpress KIT, targeted medical therapy with imatinib is now being used. This drug has been shown to cause significant tumor regression with only mild to moderate side effects.<sup>11</sup> Imatinib is indicated in patients with KIT and GISTs that are metastatic or surgically unresectable.<sup>12</sup> Imatinib is used in the adjuvant setting in patients who are at high risk for recurrence, with studies having shown decreased disease recurrence.<sup>13,14</sup> In patients who are intolerant or refractory to imatinib, another tyrosine kinase inhibitor—sunitinib (Sutent)—has been approved for treatment.<sup>15</sup>

After treatment with imatinib, primary tumor and metastatic lesions can become cystic.<sup>16,17</sup> On follow-up CT examinations, enhancing nodules or peripheral thickening, even without an increase in size, can represent progression and may suggest lack of response to imatinib.<sup>18</sup> PET/CT shows a marked reduction in activity of primary and malignant GISTs even after one dose of imatinib, months before CT changes are detected. Response even has been shown on PET/CT after 24 hours of a single dose.<sup>19-21</sup> A lack of decrease in activity suggests that the tumors are resistant to imatinib.<sup>10</sup>

#### SURGICAL TREATMENT

Despite the medical therapy advances, the main treatment of GIST continues to be surgery, especially in localized, resectable cases.<sup>22</sup> Complete surgical resection can be accomplished in 40% to 60% of patients. The location of the tumor often determines the surgical approach. Tumors near the gastric cardia or pylorus are treated with open surgical resection, whereas tumors from other areas of the stomach are often treated with laparoscopic resection. CT gastrography may help in defining the location of the tumor.<sup>23</sup> Neoadjuvant therapy with imatinib can be considered in patients in whom reducing the size of the tumor would improve surgical morbidity.<sup>24</sup> Adjuvant therapy with imatinib is used in patients with high-grade tumors. Patients should be observed at regular intervals to detect

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**Figure 21-3** Gastric mass. A 67-year-old man presented with an incidentally detected gastric mass on upper endoscopic evaluation for a guaiacpositive stool. Axial computed tomography (A), axial fused positron emission tomography with computed tomography (PET/CT) (B), and axial PET (C) images show increased fluorodeoxyglucose uptake corresponding to a proximal soft tissue gastric mass seen on CT (*arrows*). Biopsy of the mass revealed a gastrointestinal stromal tumor.

recurrence. Current research is aimed at stratifying patients into surgical and medical treatment based on tumor status and new targeted agents.

#### What the Referring Physician Needs to Know

 Radiologic staging of GIST may have an impact on the surgical and medical management, especially in metastatic disease.

#### **Key Points**

- GISTs are exophytic masses that may occur anywhere from the esophagus to the anus and predominantly arise from the stomach.
- Surgery is the usual treatment modality, with adjuvant imatinib therapy if indicated. Follow-up imaging with PET/CT and CT is helpful for determining response to therapy.

# REFERENCES

- Levy AD, Remotti HE, Thompson WM, et al: Gastrointestinal stromal tumors: radiologic features with pathologic correlation. *Radiographics* 23:283–304, 2003.
- Scarpa M, Bertin M, Ruffolo C, et al: A systematic review on the clinical diagnosis of gastrointestinal stromal tumors. *J Surg Oncol* 98:384–392, 2008.
- Levy AD, Quiles AM, Miettinen M, et al: Gastrointestinal schwannomas: CT features with clinicopathologic correlation. *AJR Am J Roentgenol* 184:797–802, 2005.
- 4. Kim HC, Lee JM, Kim KW, et al: Gastrointestinal stromal tumors of the stomach: CT findings and prediction of malignancy. *AJR Am J Roentgenol* 183:893–898, 2004.
- Ulusan S, Koc Z, Kayaselcuk F: Gastrointestinal stromal tumours: CT findings. Br J Radiol 81: 618–623, 2008.
- Thompson WM, Kende AI, Levy AD: Imaging characteristics of gastric lipomas in 16 adult and pediatric patients. *AJR Am J Roentgenol* 181:981–985, 2003.
- Sandrasegaran K, Rajesh A, Rushing DA, et al: Gastrointestinal stromal tumors: CT and MRI findings. *Eur Radiol* 15:1407–1414, 2005.
- Regge D, Lo Bello G, Martincich L, et al: A case of bleeding gastric lipoma: US, CT and MR findings. *Eur Radiol* 9:256–258, 1999.
- 9. Yang M, Martin DR, Karabulut N: Gastric schwannoma: MRI findings. *Br J Radiol* 75:624–626, 2002.

- Van den Abbeele AD, Annick D: The lessons of GIST-PET and PET/CT: a new paradigm for imaging. Oncologist 13:8–13, 2008.
- Pisters PWT, Patel SR: Gastrointestinal stromal tumors. J Surg Oncol 102:530–538, 2010.
- Demetri GD, Von Mehren M, Blanke CD, et al: Efficacy and safety of imatinib mesylate in advanced gastrointestinal stromal tumors. *N Engl J Med* 347:472–480, 2002.
- Dematteo RP, Ballman KV, Antonescu CR, et al: Adjuvant imatinib mesylate after resection of localised, primary gastrointestinal stromal tumour: a randomised, double-blind, placebocontrolled trial. *Lancet* 373:1097–1104, 2009.
- Nilsson B, Sjölund K, Kindblom LG, et al: Adjuvant imatinib treatment improves recurrencefree survival in patients with high-risk gastrointestinal stromal tumours (GIST). Br J Cancer 96:1656–1658, 2007.
- 15. Demetri GD, Van Oosterom AT, Garrett CR: Efficacy and safety of sunitinib in patients with advanced gastrointestinal stromal tumour after failure of imatinib: a randomised controlled trial. *Lancet* 368:1329–1338, 2006.
- Chen MY, Bechtold RE, Savage PD: Cystic changes in hepatic metastases from gastrointestinal stromal tumors (GISTs) treated with Gleevec (imatinib mesylate). AJR Am J Roentgenol 179:1059–1062, 2002.
- Gong JS, Zuo M, Yang P, et al: Value of CT in the diagnosis and follow-up of gastrointestinal stromal tumors. *Clin Imaging* 32:172–177, 2008.

- Mabille M, Vanel D, Albiter M, et al: Follow-up of hepatic and peritoneal metastases of gastrointestinal tumors (GIST) under imatinib therapy requires different criteria of radiological evaluation (size is not everything!!!). *Eur J Radiol* 69:204–208, 2009.
- Holdsworth CH, Badawi RD, Manola JB, et al: CT and PET: early prognostic indicators of response to imatinib mesylate in patients with gastrointestinal stromal tumor. *AJR Am J Roentgenol* 189:W324–W330, 2007.
- Shinto A, Nair N, Dutt A, et al: Early response assessment in gastrointestinal stromal tumors with FDG PET scan 24 hours after a single dose of imatinib. *Clin Nucl Med* 33:486–487, 2008.
- Van den Abbeele AD, Badawi RD, Tetrault RJ, et al: FDG-PET as a surrogate marker for response to Gleevec (imatinib mesylate) in patients with advanced gastrointestinal stromal tumors (GIST). J Nucl Med 44(Suppl):24P, 2003.
- Hueman MT, Schulick RD: Management of gastrointestinal stromal tumors. Surg Clin North Am 88:599–614, 2008.
- Lee MW, Kim SH, Kim YJ, et al: Gastrointestinal stromal tumor of the stomach: preliminary results of preoperative evaluation with CT gastrography. *Abdom Imaging* 33:255–261, 2008.
- Eisenberg BL, Judson I: Surgery and imatinib in the management of GIST: emerging approaches to adjuvant and neoadjuvant therapy. *Ann Surg Oncol* 11:465–475, 2004.

# **Gastric Outlet Obstruction**

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# Etiology

Gastric outlet obstruction is an uncommon clinical consequence with a wide range of causes. Benign and malignant as well as gastric and extragastric causes have been described. It was once relatively common to see patients present with gastric outlet obstruction secondary to inflammation or scarring from peptic ulcer disease (up to 12%).<sup>1</sup> Although it is difficult to define with certainty the incidence of gastric outlet obstruction, it is thought to have likely declined as treatments have improved for gastritis and peptic ulcer disease. Since the introduction of histamine-2 (H<sub>2</sub>) blockers, malignant causes now represent the most common cause of gastric outlet obstruction overall.<sup>2</sup>

Peptic ulcer disease remains the most common benign cause of gastric outlet obstruction.<sup>3</sup> Other benign causes include gastric and gastroduodenal bezoars,<sup>4,5</sup> Crohn's disease, hyperplastic<sup>6</sup> or eosinophilic gastroenteritis,<sup>7</sup> heterotopic pancreatic tissue within the antrum or duodenal bulb,<sup>8</sup> gastric volvulus, obstructing gallstone (also known as Bouveret's syndrome),<sup>9-11</sup> and pancreatitis and pancreatic pseudocysts.<sup>12</sup> Unusual benign causes that have been described in the literature include Brunner's gland hyperplasia (Figure 22-1),<sup>13</sup> gastroduodenal tuberculosis,<sup>14,15</sup> and neurofibromatosis.<sup>16</sup> Gastric outlet obstruction is rare in the pediatric population and includes such benign causes as antral and pyloric atresia, antral and pyloric webs,<sup>17</sup> gastric and gastroduodenal lactobezoars,<sup>18</sup> and pyloric duplication cysts.<sup>1</sup>

Malignant causes now represent the most common cause of gastric outlet obstruction in the adult population.<sup>2</sup> Neoplasms that can cause gastric outlet obstruction include gastric adenocarcinoma, lymphoma, pancreatic adenocarcinoma,<sup>19</sup> and gallbladder carcinoma.<sup>20</sup> In these cases, gastric outlet obstruction may be a presenting manifestation of the disease or may be caused by inflammation or scarring from treatments such as radiation therapy.<sup>20</sup>

The role of imaging and interventional radiology in the diagnosis and treatment of gastric outlet obstruction depends on the underlying cause. Most commonly, when a patient presents with symptoms of gastric outlet obstruction, including intractable vomiting, "food fear," and cachexia,<sup>21</sup> some of the first diagnostic studies are abdominal radiography and CT. It is relatively straightforward to make a diagnosis of gastric outlet obstruction using these modalities, but the more difficult task remains in determining what may be the culprit in any individual patient. Some of the causes have classic imaging findings on CT (e.g., gastric bezoar<sup>4</sup>), and some will likely be easy to diagnose (e.g., advanced pancreatic neoplasm). However, it is also likely that the underlying causes may not be readily ascertained by the initial imaging study (e.g., as in the case of gastric lymphoma). For this reason, it is important to keep in mind not only the different causes of gastric outlet obstruction but also

the epidemiology of these entities to better tailor a differential diagnosis.

# **Prevalence and Epidemiology**

The overall prevalence of gastric outlet obstruction is difficult to determine secondary to the wide variety of underlying causes. It may be easier to consider how often each of the possible causes, both benign and malignant, manifest as gastric outlet obstruction.

In the adult population, malignant causes are the most common, followed by benign peptic ulcer disease. Studies have indicated that the incidence of people presenting with advanced peptic ulcer disease has decreased with the advances in treatment, including  $H_2$  blockers. Presumably, as this once-common entity and presentation has become rarer, the overall incidence of gastric outlet obstruction also has likely decreased. This, however, has not been studied in the literature.<sup>22</sup>

Currently, the most common causes of gastric outlet obstruction in the adult are malignant.<sup>2</sup> Up to 35% of patients with gastric cancer present with gastric outlet obstruction, but the incidence of this is thought to be decreasing in the developed world. Of patients with pancreatic cancer, 15% to 25% present with gastric outlet obstruction and typically these patients also will have signs and symptoms of biliary obstruction.<sup>23</sup>

In the pediatric population, malignant causes are unlikely. Benign causes that may be seen in younger patients include congenital causes (pyloric stenosis, antral webs, and duplication cysts),<sup>17</sup> inflammatory processes (pancreatitis and pancreatic pseudocyst), and acquired obstruction (foreign body, bezoar).<sup>18</sup>

# **Clinical Presentation**

The hallmark of gastric outlet obstruction is nausea and intractable vomiting. Typically, the vomiting is nonbilious and may contain undigested food particles.<sup>1</sup> Depending on the underlying cause, the patient may present with pain, particularly in peptic ulcer disease,<sup>22</sup> pancreatitis,<sup>12</sup> or Bouveret's syndrome.<sup>10</sup> In patients with malignancy as the cause for gastric outlet obstruction, early satiety and weight loss are frequent symptoms.<sup>19</sup> These also can be seen in patients with chronic causes such as gastric bezoars.

With severe gastric outlet obstruction, the abdomen may be distended with a tympanic left upper quadrant. Depending on the underlying cause, physical examination may yield additional clues. Patients with underlying progressive malignancies may be cachectic or jaundiced in the case of pancreatic and biliary malignancies. In patients with peptic ulcer disease, pancreatitis, or obstruction caused by gallstones, there will be associated pain to palpation. In the infant with pyloric stenosis, the classically described physical examination finding is an "olive"

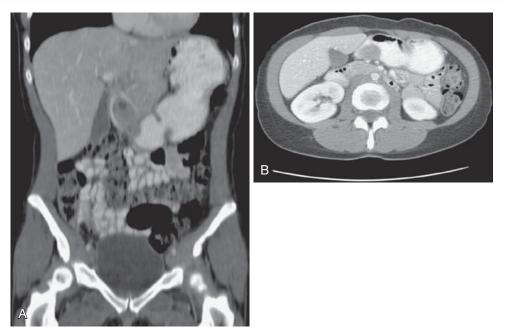


Figure 22-1 A, Coronal computed tomography (CT) reconstructed image after intravenous and oral contrast agent administration demonstrates a markedly distended stomach. B, Axial CT image shows a mass in the distal stomach and antrum. Biopsy of this lesion demonstrated Brunner's gland hyperplasia to be the cause of the gastric outlet obstruction.

in the upper abdomen. Finally, in patients with trichobezoars, hair loss from constant pulling may be found.<sup>24</sup>

Abnormal laboratory values may be associated with gastric outlet obstruction if the patient has had long-standing vomiting causing dehydration or malnutrition. Vomiting causes loss of hydrochloric acid and can lead to metabolic alkalosis. Additionally, if the patient has progressed to dehydration, abnormalities of blood urea nitrogen and creatinine may be present. Finally, any laboratory abnormalities associated with the underlying cause of the gastric outlet obstruction also may be seen. These include a positive test for *Helicobacter pylori* in cases of peptic ulcer disease, elevated amylase and lipase levels in pancreatitis, an elevated bilirubin level in cases of obstructive jaundice secondary to pancreatic neoplasm, and anemia in patients with bleeding peptic ulcer disease, underlying malignancy, or chronic disease such as Crohn's disease or tuberculosis.<sup>1,12,22</sup>

# Imaging

The general manifestations of gastric outlet obstruction are nausea and intractable vomiting. In more severe or chronic cases, cachexia and food aversion may be seen. Differential considerations for this broad spectrum of symptoms can be narrowed with evaluation of patient age, physical examination, laboratory data, diagnostic imaging, and endoscopic evaluation if necessary.<sup>25</sup>

# RADIOGRAPHY

Abdominal radiography may show a dilated stomach, which can displace bowel inferiorly (see Figure 22-1). Barium upper gastrointestinal studies may show the site of obstruction. Narrowing of the distal portion of the stomach can help differentiate gastric outlet obstruction from functional gastroparesis or delayed gastric emptying. In the acute setting, barium upper gastrointestinal studies are rarely performed. In more chronic cases, if a double-contrast barium study is performed, an ulcer or intrinsic mass that is large enough to cause gastric outlet obstruction should be readily seen.

#### Computed Tomography

CT is the most useful imaging modality for both the diagnosis of gastric outlet obstruction and the differentiation of its many underlying causes. On CT, gastric outlet obstruction is seen as a large dilated stomach.<sup>4,11</sup> If an oral contrast agent has been administered, little of it will have progressed past the site of obstruction.

More useful is CT's role in differentiating the underlying causes of gastric outlet obstruction. Malignant processes such as pancreatic cancer can be diagnosed using CT, particularly if it progressed enough to cause gastric outlet obstruction (Figure 22-2). Benign causes such as pancreatitis and pancreatic pseudocyst (Figure 22-3), bezoar,<sup>4</sup> and Bouveret's syndrome<sup>11</sup> can also be differentiated.

# Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is of limited utility in the diagnosis of gastric outlet obstruction. Although some of the previously described entities can be seen, including pancreatic neoplasm, pancreatitis and pancreatic pseudocyst, and gastric cancer, MRI is rarely used for the initial diagnosis in cases that have progressed to gastric outlet obstruction.

# Ultrasonography

In the pediatric population, ultrasonography is often the first imaging modalities to be used, because of the absence of ionizing radiation. Ultrasound evaluation is useful in the diagnosis of pyloric stenosis, in which the criteria for the thickness and

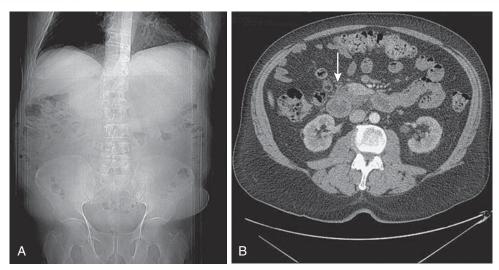


Figure 22-2 A, Preliminary scout image from a computed tomography (CT) scan demonstrates marked distention of the stomach, which displaces the transverse colon inferiorly. B, CT scan performed after intravenous contrast agent administration shows a hypodense mass at the head of the pancreas, which causes gastroduodenal obstruction (*arrow*).



**Figure 22-3** Axial noncontrast computed tomography demonstrates a dilated stomach consistent with gastric outlet obstruction. Stranding is seen in the region of the pancreatic head, with a small focus of calcification, consistent with pancreatitis.

length of the pylorus are well described. Additionally, the ultrasonographic findings of obstructing bezoars have been described and include an intraluminal mass with a hyperechoic surface and marked posterior acoustic shadowing.<sup>4</sup> Ultrasonography can show pancreatic pseudocysts, but if the size of the cyst is large enough to cause gastric outlet obstruction it may be difficult to clearly determine the origin of the cystic lesion.

# Nuclear Medicine

Although not generally used in the diagnosis of acute gastric outlet obstruction, patients with more chronic cases may obtain a nuclear medicine gastric emptying study to evaluate for gastroparesis.<sup>26</sup>

# Positron Emission Tomography With Computed Tomography

Positron emission tomography with computed tomography (PET/CT) is useful in the staging of gastric cancer and lymphoma but not typically used for the initial diagnosis of gastric outlet obstruction. In patients with a chronic gastric outlet obstruction secondary to a known malignancy, PET/CT may demonstrate these findings.

### Imaging Algorithm

If abdominal radiographs demonstrate the presence of gastric dilatation, CT imaging should be performed to further evaluate for an underlying cause (Table 22-1).

#### **Classic Signs**

- Bouveret's syndrome: Calcified gallstone in the distal stomach/duodenum with air in the gallbladder from cholecystoduodenal fistula (seen on CT)<sup>11</sup>
- Obstructing gastric bezoar: Well-defined intraluminal mass with air within the interstices (seen on CT)<sup>4</sup>
- Pyloric stenosis in the infant: Shoulder sign (collection of barium in the dilated antrum on upper gastrointestinal study); on ultrasonography, pyloric muscle thickness greater than 4 mm and a length greater than 16 mm
- Crohn's disease of the stomach: Ram's horn sign, a tubular narrowing, and deformity of the antrum, with poor distensibility<sup>27</sup>

# **Differential Diagnosis**

Based on the clinical presentation of nausea, vomiting, anorexia, and pain, the differential considerations are broad. Most importantly, the clinician needs to take into account the patient's age to come to a more focused differential list. In fact, given the relatively low incidence of gastric outlet obstruction, it is likely not to be one of the differential considerations. The likelihood of an underlying pathologic process rises with age, with fewer

TABLE 22-1	Accuracy	y, Limitations, and Pitfalls of the Modalities Used in Imaging of Gastric Outlet Obstruction		
Modal	ity	Accuracy	Limitations	Pitfalls
Radiography		Depends on the severity of the obstruction	Generally cannot differentiate underlying causes	
СТ		High, excellent for differentiating most underlying causes	Difficult to differentiate benign and malignant gastroduodenal inflammation and thickening	Difficult to differentiate benign versus malignant gastric ulcers and inflammation
MRI		Not generally used for diagnosis; may be useful for staging underlying gastric or pancreatic neoplasm	Difficult to differentiate inflammation from malignancy in the acute setting	Gadolinium enhancement can be seen in both benign and malignant causes
Ultrasc	onography	Modality of choice for imaging pyloric stenosis in the infant; can see large masses and cysts causing obstruction	Limited utility in the diagnosis of other causes; will generally need CT to define extent of underlying disease or obstruction	Excessive gas from bowel obstruction will limit utility of this modality.
PET/C	Т	Not used in primary diagnosis; useful in the secondary staging of gastric cancer and lymphoma	Not used in primary diagnosis	

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

than half of patients younger than the age of 40 having an organic cause for their symptoms.<sup>25</sup>

The most common differential considerations based on clinical presentation include functional dyspepsia, gallstones, gastric and duodenal ulcer (not necessarily causing gastric outlet obstruction), irritable bowel syndrome, gastroesophageal reflux, and gastric cancer. These can be further narrowed based on patient characteristics. Gallstones are more common in women, whereas the incidence of ulcer disease and gastric cancer is higher in men. If the patient presents with painless jaundice, nausea, vomiting and anorexia, pancreatic cancer becomes higher in the differential diagnosis and gastric outlet obstruction may be the manifesting symptom.<sup>25</sup>

In summary, there is nothing specific in the typical clinical presentation that will point exclusively to gastric outlet obstruction. However, when considered in conjunction with demographic clues, physical examination, and laboratory values, an underlying cause for gastric outlet may be suggested.

Based on imaging studies, gastric outlet obstruction is a relatively straightforward diagnosis to make. More importantly, using imaging techniques can help the gastroenterologist or surgeon narrow the differential diagnosis and allow for the appropriate treatment methods, either medical or surgical management.

# Treatment

# MEDICAL TREATMENT

In the acute setting, patients presenting with gastric outlet obstruction should be treated symptomatically. A nasogastric tube should be inserted to decompress the stomach, and the patient should receive intravenous fluids and supplemental nutrition if dehydration and malnutrition are issues.<sup>21</sup>

Once the acute symptoms have lessened, medical treatment consists of treating the underlying cause. In patients with malignant causes of gastric outlet obstruction, a palliative stent can be placed by endoscopy or under fluoroscopic guidance.<sup>28</sup> In patients with peptic ulcer disease, medical treatment can be

used if it is thought that the obstruction was caused by inflammation rather than scarring.<sup>22</sup> Endoscopic balloon dilatation can be used in patients with benign pyloric stenosis from a variety of causes.<sup>3</sup>

# SURGICAL TREATMENT

Traditionally, the palliative treatment of malignant gastric outlet obstruction was gastrojejunostomy; however, stenting is now more commonly used because there is less associated morbidity. Surgical treatment may be used in patients with peptic ulcers (vagotomy and antrectomy or distal gastrectomy), pyloric stenosis (pyloroplasty), and pancreatitis and pancreatic pseudocyst (débridement as necessary). Additionally, if the patient fails stenting in cases of malignant causes, gastrojejunostomy can be considered.<sup>1</sup>

#### What the Referring Physician Needs to Know

- Gastric outlet obstruction has both benign and malignant causes.
- In patients with gastric outlet obstruction, a search for an underlying cause should begin once the acute presentation has been stabilized.

# **Key Points**

- Gastric outlet obstruction is a clinical manifestation of a wide range of benign and malignant causes.
- The most common cause in adults is malignancy (gastric and pancreatic).
- The most common benign cause in adults is peptic ulcer disease.
- Once gastric outlet obstruction is diagnosed, CT can be helpful to determine an underlying cause.

### REFERENCES

- Dempsey DT: Stomach. In Brunicardi FC, et al, editors: *Schwartz's principles of surgery*, 8th ed, New York, 2005, McGraw-Hill, pp 933–995.
- Shone DN, Nikoomanesh P, Smith-Meek MM, et al: Malignancy is the most common cause of gastric outlet obstruction in the era of H2 blockers. Am J Gastroenterol 90:1769–1770, 1995.
- Yusuf TE, Brugge WR: Endoscopic therapy of benign pyloric stenosis and gastric outlet obstruction. *Curr Opin Gastroenterol* 22:570– 573, 2006.
- Ripolles T, Garcia-Aguayo J, Martinez MJ, et al: Gastrointestinal bezoars: sonographic and CT characteristics. *AJR Am J Roentgenol* 177:65–69, 2001.
- Sodhi KS, Khandelwal N, Khandelwal S, et al: Gastric bezoar: an uncommon yet important cause of abdominal pain. *J Emerg Med* 28:467– 468, 2005.
- Dean PG, Davis PM, Nascimento AG, et al: Hyperplastic gastric polyp causing progressive gastric outlet obstruction. *Mayo Clin Proc* 73: 964–967, 1998.
- Burhenne HJ, Carbone JV: Eosinophilic (allergic) gastroenteritis. Am J Roentgenol Radium Ther Nucl Med 96:332–338, 1966.
- Haj M, Shiller M, Loberant N, et al: Obstructing gastric heterotopic pancreas: case report and literature review. *Clin Imaging* 26:267–269, 2002.
- Cappell MS, Davis M: Characterization of Bouveret's syndrome: a comprehensive review of 128 cases. Am J Gastroenterol 101:2139–2146, 2006.
- 10. Kaushik N, Moser AJ, Slivka A, et al: Gastric outlet obstruction caused by gallstones: case

report and review of the literature. *Dig Dis Sci* 50:470–473, 2005.

- Tuney D, Cimsit C: Bouveret's syndrome: CT findings. Eur Radiol 10:1711–1712, 2000.
- 12. Greenberger N, Toskes P: Acute and chronic pancreatitis. In Fauci A, Braunwald E, Kasper D, et al, editors: *Harrison's principles of internal medicine*, 17th ed, New York, 2008, McGraw-Hill.
- Krishnamurthy P, Junaid O, Moezzi J, et al: Gastric outlet obstruction caused by Brunner's gland hyperplasia: case report and review of literature. *Gastrointest Endosc* 64:464–467, 2006.
- Rao YG, Pande GK, Sahni P, et al: Gastroduodenal tuberculosis management guidelines, based on a large experience and a review of the literature. *Can J Surg* 47:364–368, 2004.
- Amarapurkar DN, Patel ND, Amarapurkar AD: Primary gastric tuberculosis: report of 5 cases. BMC Gastroenterol 3:6, 2003.
- Bakker JR, Haber MM, Garcia FU: Gastrointestinal neurofibromatosis: an unusual cause of gastric outlet obstruction. *Am Surg* 71:100–105, 2005.
- Brandon FM, Weidner WA: Antral mucosal membrane: a congenital obstructing lesion of the stomach. Am J Roentgenol Radium Ther Nucl Med 114:386–389, 1972.
- DuBose TM, Southgate WM, Hill JG: Lactobezoars: a patient series and literature review. *Clin Pediatr* 40:603–606, 2001.
- Molinari M, Helton WS, Espat NJ: Palliative strategies for locally advanced unresectable and metastatic pancreatic cancer. *Surg Clin North Am* 81:651–666, 2001.

- 20. Mogavero GT, Jones B, Cameron JL, et al: Gastric and duodenal obstruction in patients with cholangiocarcinoma in the porta hepatis: increased prevalence after radiation therapy. *AJR Am J Roentgenol* 159:1001–1003, 1992.
- Hasler WL, Owyang C: Approach to the patient with gastrointestinal disease. In Fauci A, Braunwald E, Kasper D, et al, editors: *Harrison's principles of internal medicine*, 17th ed, New York, 2008, McGraw-Hill.
- Valle JD: Peptic ulcer disease and related disorders. In Fauci AS, Braunwald E, Kasper D, et al, editors: *Harrison's principles of internal medicine*, 17th ed, New York, 2008, McGraw-Hill.
- 23. Chua YJ, Cunningham D: Pancreatic cancer. In Fauci AS, Braunwald E, Kasper D, et al, editors: *Harrison's principles of internal medicine*, 17th ed, New York, 2008, McGraw-Hill.
- 24. Carr JR, Sholevar EH, Baron DA: Trichotillomania and trichobezoar: a clinical practice insight with report of illustrative case. *J Am Osteopath Assoc* 106:647–652, 2006.
- 25. Spiller RC: ABC of the upper gastrointestinal tract: anorexia, nausea, vomiting, and pain. *BMJ* 323:1354–1357, 2001.
- 26. Thrall JH, Zeissman HA: Nuclear medicine: The requisites, St. Louis, 2001, Mosby.
- Farman J, Faegenburg D, Dallemand S, et al: Crohn's disease of the stomach: the "ram's horn" sign. Am J Roentgenol Radium Ther Nucl Med 123:242–251, 1975.
- 28.Lopera JE, Brazzini A, Gonzales A, et al: Gastroduodenal stent placement: current status. *Radiographics* 24:1561–1573, 2004.

# Gastric Function Imaging: Technique and Applications

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# **Technical Aspects**

Radionuclide gastric emptying studies (scintigraphy) remain the most widely used method for evaluation of gastric function.

# RADIOPHARMACEUTICALS

Gastric emptying scintigraphy is most commonly performed with technetium-99m (<sup>99m</sup>Tc) sulfur colloid dispersed in a solid and/or liquid bolus.

To be a gastric function tracer, a radioactive marker must meet certain criteria. The criteria for a good liquid-phase marker includes the ability to equilibrate rapidly and be nonabsorbable. <sup>99m</sup>Tc sulfur colloid in water meets these criteria. The solid-phase radioactive marker for evaluation of solid gastric emptying requires the ability to bind tightly to the solid food particle. The reason is that liquids empty faster than solids, thereby producing an erroneously shortened solid emptying time. The most wellaccepted in-vitro methods for radioactive labeling involves frying eggs with <sup>99m</sup>Tc sulfur colloid, resulting in binding to the egg albumin and administering as an egg sandwich.<sup>1,2</sup>

In dual (solid/liquid) phase studies, indium-111–labeled diethylenetriaminepentaacetic acid (<sup>111</sup>In-DTPA) is the liquid marker and <sup>99m</sup>Tc sulfur colloid is the solid marker.

# TECHNIQUE

Gastric emptying scintigraphy requires the patient to be fasting for 8 to 12 hours.<sup>3,4</sup> Medications that affect gastric motility should be stopped, if possible. These include calcium channel blockers, anticholinergics, antidepressants, narcotics, gastric acid suppressants, and aluminum-containing antacids. Alcohol consumption and use of tobacco products should be stopped for a minimum of 24 hours.

On the morning of the study, the radiolabeled meal is prepared (Table 23-1). <sup>99m</sup>Tc sulfur colloid (1 millicurie) is added to solidifying scrambling eggs and mixed until solidified and then placed between two pieces of toasted bread. Once prepared, the <sup>99m</sup>Tc sulfur colloid radiolabeled egg should be consumed within 5 to 10 minutes. Promptly after ingestion, a continuous data acquisition with a frame rate of 30 to 60 seconds per image is performed for 90 minutes ( $64 \times 64$  pixels) with the patient positioned in the supine position. Additional imaging at 3 and 4 hours can be performed to identify patients with delayed emptying.<sup>5</sup>

A region of interest is drawn over the stomach, and the percent of gastric emptying is determined. The radioactive counts increase as the food travels from the fundus, a posterior structure, to the antrum, an anterior structure. The attenuation effect is therefore one of the technical factors that can cause underestimation of gastric emptying and, therefore, a falsepositive result. This is most commonly corrected with the accepted gold standard for correcting attenuation, the geometric mean measure.<sup>6</sup> Frequent image acquisition increases accuracy in determining gastric emptying. An alternative method to decrease false-positive results is to acquire images in the left anterior oblique position.

# **Pros and Cons**

Radionuclide gastric emptying studies have become the gold standard for evaluation of gastric function, reflected by the test's accuracy, sensitivity, both qualitative and quantitative abilities, and ease of performance (Table 23-2).

The major disadvantage is radiation exposure. It is also time consuming and has poor interlaboratory standardization. Each laboratory has its standardization values that take into account both whether a liquid or solid substance is used as well as the type of food particle binding agent. It is because of this that competing nonradionuclide techniques have surged and investigative efforts have intensified.<sup>7</sup>

# Normal Gastric Analysis Curves and Image

Liquids empty immediately in an exponential fashion, with no initial delay (lag phase). The dual-phase meal demonstrates exponential emptying as well, although a slower rate relative to a liquid-only phase. In contrast, solid emptying demonstrates an initial lag phase, followed by a constant linear rate of gastric emptying (Figure 23-1).<sup>8-10</sup>

# Pathophysiology

Causes of delayed gastric emptying can be divided into mechanical and functional causes. Mechanical causes of delayed gastric emptying include obstruction by tumor or pyloric ulcer. Functional causes of gastroparesis include acute dysfunction such as from acute gastroenteritis and metabolic derangements or, more commonly, chronic dysfunction, such as from diabetes mellitus.<sup>10-12</sup>

# FACTORS AFFECTING GASTRIC EMPTYING

There are multiple physiologic and technical factors that affect gastric emptying. The meal content is a primary factor. Large food volumes, weight, particle size, and caloric density slow the rate of gastric emptying. Solid food empties the slowest, followed by semisolid food, which empties slower than nutrient liquids. Clear liquids empty faster than nutrient liquids.

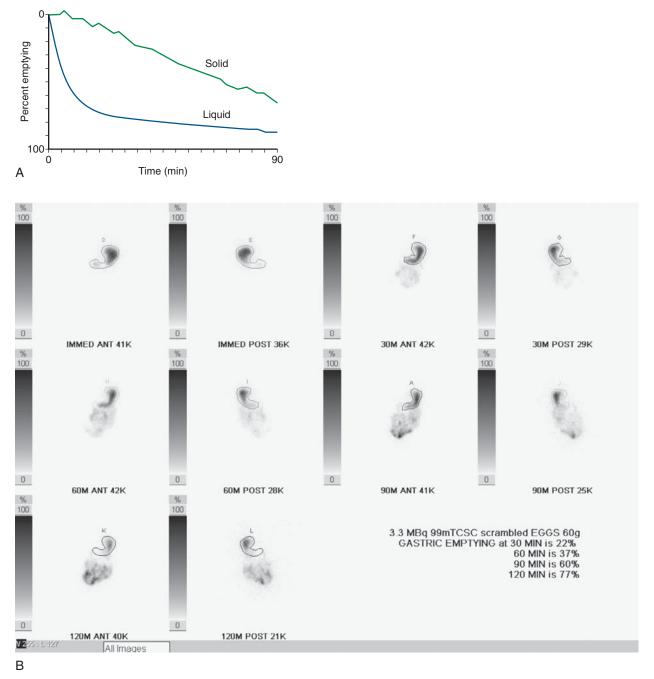


Figure 23-1 A, Normal gastric function. Liquids empty immediately in an exponential fashion. The solid emptying demonstrates an initial lag phase, followed by a constant linear rate of gastric emptying. B, Normal gastric function. There is more than 50% gastric emptying at 60 minutes. (Values are standardized in each laboratory.) (A courtesy Alexander A. Ree, MD; B courtesy of Ruth Lim, MD.)

TABLE 23-1	Adult Dosimetry for Gastric Function	
Phase	Adult Dosimetry for Gastric Scintigraphy	
Liquid Solid	0.5-1 mCi <sup>99m</sup> Tc sulfur colloid 0.5-1 mCi <sup>99m</sup> Tc sulfur colloid ovalbumin 0.5-1 mCi <sup>99m</sup> Tc sulfur colloid chicken liver	

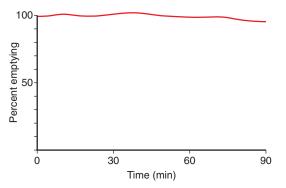
Therefore, solid-phase analysis is more sensitive than liquid emptying to determine early abnormal gastric emptying.<sup>10</sup>

# MECHANICAL DELAYED GASTRIC EMPTYING

Mechanical obstruction can cause delayed gastric emptying (Figure 23-2).

Accuracy, Limitations, and Pitfalls of Gastric Function Imaging Modalities			
Modality	Accuracy	Limitations	Pitfalls
Scintigraphy	Most accurate to assess gastric function	Radiation exposure Time consuming Poor interlaboratory standardization	Cannot always determine the cause of delayed gastric emptying
MRI (echoplanar)	Correlates well with scintigraphy in both solid and liquid phase	Investigational Time consuming Patient-limiting factors: Breath-holding, claustrophobia, pacemakers	
Ultrasonography		Patient-limiting factors: Large body habitus and bowel gas	
Breath test		Patient-limiting factors: Results can be altered by liver, pancreatic, pulmonary, and small intestinal disease	
Gastric intubation		Invasive Requires serial aspirations Patient discomfort	
Marker dilution		Invasive Patient discomfort Tubing can alter emptying	
SPECT	Investigational	Measures only gastric accommodation	

*MRI*, Magnetic resonance imaging; *SPECT*, single-photon emission computed tomography.



**Figure 23-2** Mechanical obstruction. Complete pyloric obstruction secondary to an antral/pyloric gastric carcinoma. Preoperative radionuclide gastric emptying study demonstrates no gastric emptying. (*Courtesy Alexander A. Ree, MD.*)

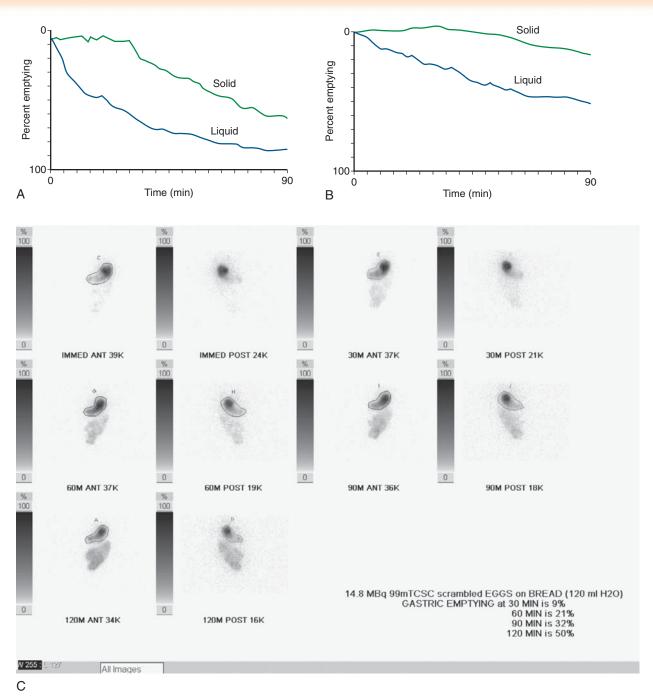
#### FUNCTIONAL DELAYED GASTRIC EMPTYING

The most common clinical cause of chronic delayed gastric emptying is diabetes mellitus, which most commonly affects patients with type 1 insulin-dependent diabetes and may be due to vagal neuropathy (Figure 23-3).<sup>11,12</sup> Uncontrolled hyperglycemia alone also can delay gastric emptying.

# **Key Points**

- <sup>99m</sup>Tc sulfur colloid–radiolabeled egg sandwich is the most widely used radiolabeled meal for gastric emptying studies. Geometric mean measurement or acquisition in the left anterior oblique projection must be obtained to decrease false-positive results.
- Standardization protocols and value references must be obtained in each laboratory for reproducible results.
- Liquids empty immediately in an exponential fashion.
- Solid emptying demonstrates an initial lag phase, followed by a constant linear rate of gastric emptying.
- The most common cause of delayed gastric emptying is functional from diabetic gastroparesis.





**Figure 23-3** Chronic functional gastroparesis. **A**, A patient presented with a history of insulin-dependent diabetes for 20 years. Radionuclide gastric emptying study demonstrates delayed solid emptying but normal liquid emptying consistent with early gastroparesis. **B**, Same patient 10 years later. Radionuclide gastric emptying study demonstrates delayed solid and liquid emptying consistent with more severe gastroparesis. **C**, Same patient 5 years later. Radionuclide gastric emptying study with <sup>99m</sup>Tc sulfur colloid mixed in a scrambled egg sandwich demonstrates delayed solid emptying consistent with gastroparesis. (**A** and **B** courtesy Alexander A. Ree, MD; **C** courtesy Ruth Lim, MD.)

# REFERENCES

- Knight LC, Malmud LS: Tc-99m ovalbumin labeled eggs: comparison with other solid food markers in vitro. J Nucl Med 22:28–33, 1981.
- Saremi F, Jadvar H, Siegel ME: Pharmacological interventions in nuclear radiology: indications, imaging protocols, and clinical results. *Radiographics* 22:477–490, 2002.
- Donohue KJ, Maurer AH, Ziessman HA, et al: Society of Nuclear Medicine Procedure Guideline for Gastric Emptying and Motility, version 2.0, Reston, VA, 2004, Society of Nuclear Medicine.
- Zeissman HA, Fahey FH, Atkins FB, et al: Standardization and quantification of radionuclide solid gastric-emptying studies. J Nucl Med 45:760–764, 2004.
- 5. Zeissman HA, Bonta DV, Goetz S, et al: Experience of a simplified, standardized 4-hour

gastric-emptying protocol. J Nucl Med 48:568-572, 2007.

- Ford PV, Kennedy RL, Vogel JM: Comparison of left anterior oblique, anterior and geometric mean methods for determining gastric emptying times. *J Nucl Med* 33:127–130, 1992.
- Brattern J, Jones MP: New direction in the assessment of gastric function: clinical applications of physiologic measurements. *Dig Dis* 24:252–259, 2006.
- Abell TL, Camiller M, Donohoe K, et al: Consensus recommendations for gastric emptying scintigraphy: a joint report of the American Neurogastric and Motility Society and the Society of Nuclear Medicine. *Am J Gastroenterol* 103:753–763, 2008.
- Lartigue S, Bizais Y, Des Varannes SB, et al: Inter- and intrasubject variability of solid and liquid gastric emptying parameters: a scintigraphic study in healthy patients and diabetic patients. *Dig Dis Sci* 39:109–115, 1994.
- Matolo NM, Stadalnik RC: Assessment of gastric motility using meal labeled with technetium-99m sulfur colloid. *Am J Surg* 146: 823–826, 1983.
- Rothstein RD, Alavi A: The evaluation of the patient with gastroparesis secondary to insulindependent diabetes mellitus. J Nucl Med 33: 1707–1709, 1992.
- Urbain JL, Vekemans MC, Bouillon R, et al: Characterization of gastric antral motility disturbances in diabetes using a scintigraphic technique. J Nucl Med 34:576–581, 1993.

# 24

# Imaging the Small Bowel

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Traditional evaluation of the small bowel involved small bowel follow-though (SBFT) or enteroclysis, which provide excellent survey of the small bowel but are insensitive for subtle bowel pathologic processes and extraluminal abdominal findings. Within the last decade, as a result of significant advances in technology there has been a paradigm shift in the imaging evaluation of the gastrointestinal tract. With the advent of multidetector computed tomography (MDCT) and advances in abdominal magnetic resonance imaging (MRI) along with administration of oral contrast media, it is now possible to effectively evaluate bowel wall thickening, enhancement, and extraluminal findings to detect and characterize small bowel pathologic processes. Although used less frequently in small bowel evaluation, ultrasound and nuclear medicine techniques have utility in the diagnosis of small bowel pathologic processes. A comparison of the various imaging modalities available for imaging the small bowel is presented in Table 24-1.

# Fluoroscopic Small Bowel Imaging Techniques

# SMALL BOWEL FOLLOW-THROUGH

An SBFT examination involves ingestion of approximately 600 to 1200 mL of a low-density barium solution (30% to 50% weight/volume [w/v]). Patient preparation usually involves the patient having a nothing by mouth (NPO) status after midnight. After ingestion of the barium solution, overhead spot images of the abdomen (Figure 24-1) are obtained at intervals of 15 to 60 minutes depending on small bowel motility.<sup>1,2</sup> Fluoroscopic evaluation of the small bowel is performed to evaluate any potential pathologic processes identified on spot images or to delineate superimposed bowel loops. Particular fluoroscopic attention is paid to the terminal ileum (Figure 24-2), a location at which numerous infectious and inflammatory conditions often manifest. The examination concludes when the contrast reaches the ascending colon. Small bowel transit time-the time it takes to reach the ascending colon after ingestion of contrastshould be reported, because it is a useful clinical indicator. For normal patients, typical transit times range from 1 to 3 hours, although in patients with ileus or bowel obstruction transit times can be significantly longer.

### FLUOROSCOPIC ENTEROCLYSIS

Fluoroscopic small bowel enteroclysis involves nasojejunal intubation followed by balloon inflation and brisk instillation of low-density barium (20% to 40% w/v) at an initial rate of 75 mL/min for a total volume of 600 to 1200 mL. Subsequently, water is instilled until the terminal ileum is reached (Figure 24-3). Enteroclysis often allows excellent bowel distention

because of the brisk rate of contrast instillation, although the procedure can be poorly tolerated by patients secondary to discomfort from nasojejunal tube placement, abdominal discomfort, distention from balloon inflation, and contrast instillation. The patient is made NPO after midnight before the examination with a clear liquid diet and/or osmotic cathartic the day before the examination.<sup>3-5</sup> Metoclopramide is often administered 30 to 60 minutes (if administered orally) or 1 to 3 minutes (if administered intravenously) before the examination to relax the pyloric sphincter and increase duodenal contractions to ease the 8 to 13 French nasojejunal tube placement.<sup>6</sup>

# Small Bowel Computed Tomography Techniques ABDOMINAL AND PELVIC

# COMPUTED TOMOGRAPHY

Typical routine CT abdomen and pelvis protocols are optimized to evaluate both solid organs and bowel using positive oral contrast media. The technique can evaluate areas of bowel dilatation or narrowing and is especially helpful in distinguishing partial and complete small bowel obstructions, in which no distal oral contrast is identified in complete small bowel obstructions.<sup>7,8</sup> Often, the transition point can be determined by change in bowel caliber coupled with distal bowel decompression in high-grade partial small bowel obstructions. The small bowel transit time is often increased in partial small bowel obstructions with associated dilutional effects in loops of bowel distal to the obstruction, secondary to mixing with increased fluid accumulated proximal to the obstruction. Thus, it may be helpful to increase the standard postingestion delay of 1 to 2 hours, to more accurately evaluate the entire small bowel in patients with clinical concern for bowel obstruction.

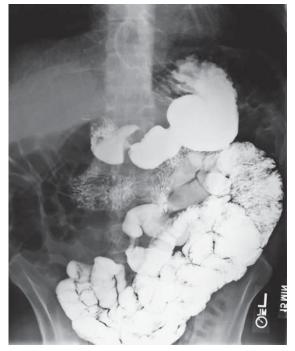
Although positive oral contrast media have the ability to readily distinguish bowel from adjacent structures, the inherent high density of the media makes it difficult to identify subtle bowel pathologic processes. Thus, the media rely on the structural changes in bowel, to recognize abnormalities. In addition, poor mixing of positive oral contrast and enteric debris can result in fillings defects that can manifests pseudolesions.

### COMPUTED TOMOGRAPHY ENTEROGRAPHY

Neutral oral contrast is used in CT enterography, which is becoming the default modality for initial evaluation of the small bowel (Figure 24-4).<sup>9</sup> The technique allows for appreciation of bowel mucosal changes and ulceration, which are not readily appreciated on positive oral contrast examinations (Figure 24-5). To optimally evaluate the bowel mucosal changes, the

TABLE 24-1Comparison of \$	Small Bowel Imaging Methods	
Modality	Pros	Cons
Small bowel follow through	<ul> <li>Real-time evaluation of small bowel peristalsis</li> <li>High spatial resolution evaluation of mucosal abnormalities</li> </ul>	<ul> <li>Insensitive for extramural findings</li> <li>Time intensive</li> <li>High relative radiation level</li> </ul>
Fluoroscopic enteroclysis	<ul> <li>Real-time evaluation of small bowel</li> <li>Consistent, excellent bowel distention</li> <li>Excellent evaluation for mucosal abnormalities</li> </ul>	<ul> <li>Poorly tolerated because of bowel preparation and nasojejunal intubation</li> <li>Time intensive</li> <li>High relative radiation level</li> </ul>
Abdomen/pelvis CT	<ul><li> Evaluation of mural and extramural abnormalities affecting small bowel</li><li> Fast and reproducible</li></ul>	<ul> <li>Insensitive for abnormal mucosal enhancement</li> <li>Iodinated contrast allergies</li> <li>High relative radiation level</li> </ul>
CT enterography	<ul> <li>Excellent evaluation for abnormal small bowel wall thickening and enhancement</li> <li>Evaluation of sequelae of small bowel pathology, including abscess and fistula</li> <li>Fast and reproducible</li> </ul>	<ul> <li>High relative radiation level</li> <li>Requires patient compliance to drink a relatively large volume of oral contrast in the allotted time</li> <li>Iodinated contrast allergies</li> </ul>
CT enteroclysis	<ul> <li>Gold standard for CT evaluation of small bowel because of reproducible bowel distention</li> <li>Evaluation of sequelae of small bowel pathologic processes, including abscess and fistula</li> </ul>	<ul> <li>Time intensive</li> <li>Poorly tolerated because of bowel preparation and nasojejunal intubation</li> <li>Iodinated contrast allergies</li> <li>High relative radiation level</li> </ul>
MR enterography	<ul> <li>Evaluation of sequelae of small bowel pathologic processes, including abscess and fistula</li> <li>Can evaluate real-time bowel peristalsis with cine images</li> </ul>	<ul> <li>Some patient intolerant to MRI</li> <li>Time intensive</li> <li>Gadolinium contrast allergies (less frequent than iodinated contrast)</li> <li>Requires patient compliance to drink a relatively large volume of oral contrast in the allotted time</li> <li>No ionizing radiation</li> </ul>
MR enteroclysis	<ul> <li>Gold standard for MR evaluation of small bowel because of reproducible bowel distention</li> <li>Evaluation of sequelae of small bowel pathologic processes, including abscess and fistula</li> <li>Can evaluate real-time bowel peristalsis with cine images</li> </ul>	<ul> <li>Poorly tolerated because of bowel preparation, nasojejunal intubation, and MRI</li> <li>Time intensive</li> <li>Gadolinium contrast allergies (less frequent than iodinated contrast)</li> <li>No ionizing radiation</li> </ul>

CT, Computed tomography; MR, magnetic resonance; MRI, magnetic resonance imaging.



**Figure 24-1** Fifteen-minute overhead radiograph of normal small bowel follow-through examination.



 $\label{eq:Figure 24-2} \mbox{ Figure 24-2 } \mbox{ Spot fluoroscopic image of normal terminal ileum with manual compression.}$ 

technique requires optimal bowel distention, neutral oral contrast, and appropriate phase(s) of contrast. Optimal bowel distention is achieved through slow administration of a large volume of a neutral oral contrast agent (1 to 2 L), including a 0.1% w/v barium sulfate solution (VoLumen, Bracco, Milan, Italy), water-methyl-cellulose solution, or polyethylene glycol. An optimal technique would require patients to abstain from solid foods for 4 hours before the examination, to prevent mistaking food debris from intraluminal pathologic processes. Many protocols split up the contrast bolus into thirds at 15- to 20-minute intervals with an additional 200 to 300 mL of water or neutral contrast ingested immediately before imaging. The bowel is imaged in the "enteric" phase at 45 to 50 seconds

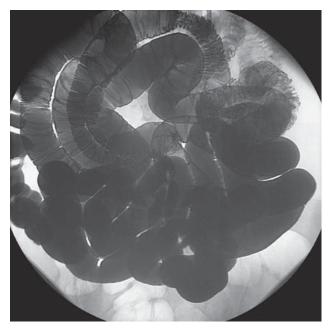


Figure 24-3 Normal findings of small bowel enteroclysis.

postcontrast with high-volume flow rate of intravenous iodinated contrast at 4 mL per second.<sup>10</sup>

CT enterography can be performed as a single-phase or multiphase examination, depending on the indication. Single-phase examinations are often performed for evaluation of inflammatory bowel disease (IBD) at initial presentation and for acute exacerbations of IBD symptoms. Patients with IBD often present at a young age in the second or third decades of life and require multiple follow-up imaging examinations for evaluation of disease involvement, treatment response, acute or chronic symptoms, and complications. Thus, radiation dose is an important consideration for a population that often will be imaged early in life and continue to have numerous imaging examinations. Multiphasic CT enterography protocols often involve evaluation for mesenteric ischemia or occult gastrointestinal bleeding, both of which occur more often in older populations during acute events, for which multiple subsequent imaging evaluations are not often required. Mesenteric ischemia protocols are often performed in the arterial (25- to 30-second delay) and portal venous (65- to 70-second delay) phases, to evaluate the small bowel mesentery arterial and portal venous vasculature, respectively. Occult gastrointestinal bleeding protocols often image the bowel using a noncontrast phase to evaluate for hyperdense enteric contents that could be mistaken for blood products, followed by arterial, portal venous, and delayed (3 to 5 minutes postcontrast) phases, evaluation for intraluminal contrast that accumulates on delayed images.

# COMPUTED TOMOGRAPHY ENTEROCLYSIS

CT enteroclysis is the gold standard in CT of the small bowel. There are many indications, including low-grade small bowel obstruction, IBD, obscure gastrointestinal bleeding, and small bowel tumors.<sup>11,12</sup> After nasojejunal intubation, a large volume of neutral enteric contrast medium is rapidly infused directly into the proximal jejunum by an infusion pump, followed by thin-section CT with intravenous contrast material.<sup>12</sup> Compared with routine CT and CT enterography, the strength of this technique is the enteral volume challenge by nasojejunal intubation, which allows controlled rapid infusion of large

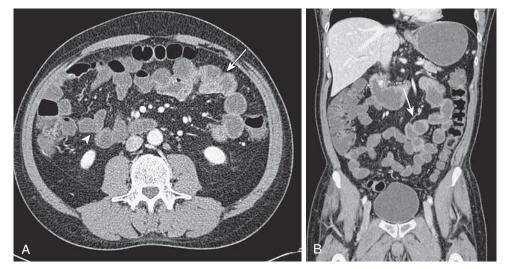


Figure 24-4 Axial (A) and coronal (B) images of normal computed tomography enterography. Enhancement of normal jejunal loops (arrows) is greater than that of normal ileal loops (arrowhead).

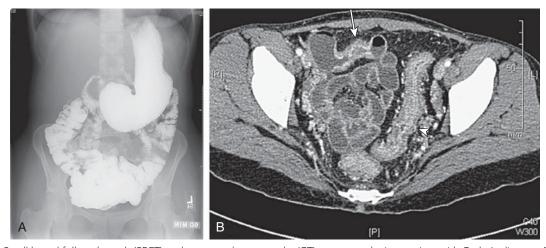


Figure 24-5 Small bowel follow-through (SBFT) and computed tomography (CT) enterography in a patient with Crohn's disease. A, SBFT cannot evaluate the colon or overlapping small bowel loops in the pelvis. B, CT enterography in the same patient performed after SBFT shows segmental mural thickening and hyperenhancement of an ileal loop (arrow) and acute colonic inflammation (arrowhead).

volumes of enteric contrast material, thereby optimizing the degree and extent of small bowel distention (Figure 24-6). It is also advantageous compared with capsule endoscopy because it allows evaluation of the entire abdomen and is not affected by small bowel obstruction, which is an absolute contraindication in capsule endoscopy. Because of the invasive nature of this examination, patients may require sedation. In addition to patient discomfort, there is a risk for bowel perforation with intubation, as well as the inherent risks of sedation. CT enteroclysis remains highly operator dependent and not widely available.

# Small Bowel Magnetic Resonance Imaging Techniques

# MAGNETIC RESONANCE ENTEROGRAPHY

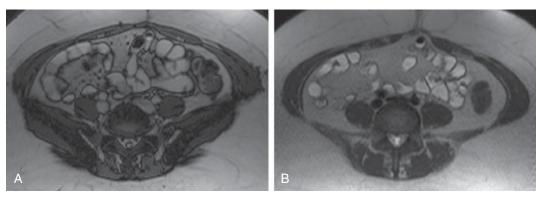
MR enterography is an MRI technique optimized to evaluate the small bowel (Figure 24-7). The patient preparation for MR enterography is similar to that for CT enterography, in which the patient is asked to not ingest solid food 4 hours before the examination and slowly ingests a large volume of contrast (often 900 to 1250 mL) 30 to 60 minutes before the examination. Optimally, the patient ingests "biphasic" oral contrast that is hypointense on T1-weighted images and hyperintense on T2-weighted images. Biphasic agents allow distinction of the hypointense bowel wall from the hyperintense luminal contents on T2-weighted images while allowing distinction between the enhancing bowel wall on postcontrast images from the hypointense luminal contents on T1-weighted images (Figure 24-8).<sup>13</sup> Neutral oral contrast agents commonly used for CT enterography, including barium sulfate (VoLumen), polyethylene glycol, and mannitol, all have the imaging characteristics of biphasic contrast agents. Many centers use glucagon intramuscular or intravenous injection before the examination to decrease bowel peristalsis and improve image quality, although the administration can affect blood glucose levels in diabetic patients and is contraindicated in patient with pheochromocytoma, because it can result in catecholamine release.<sup>14</sup>

Pulse sequences for MR enterography are designed to highlight differences between the bowel wall and luminal contents,



**Figure 24-6** Computed tomography enteroclysis with intravenous and neutral enteric contrast material in a patient with Crohn's disease. There is segmental mural thickening and hyperenhancement in the ileum (*black arrow*) with engorgement of the vasa recta (*white arrow-head*). Proximal ileal dilation (*white arrow*) indicates luminal stricture. Also note intrahepatic biliary dilation secondary to primary sclerosing cholangitis, which is an extraintestinal complication of Crohn's disease. (*Courtesy Kumar Sandrasegaran, MD.*)

to assess for wall thickening or enhancement while being performed quickly to minimize effects of patient motion and peristalsis (Figure 24-9). Typically the abdomen and pelvis will be assessed first on single-shot fast (or turbo) spin echo (SSFSE) T2-weighted images and steady-state free precession (SSFP)



**Figure 24-7** Axial true fast imaging with steady-state precession (FISP) (A) and axial T2-weighted half-Fourier acquisition single-shot turbo spinecho (HASTE) (B) images demonstrate normal small bowel with normal wall thickness ( $\leq$ 3 mm) and signal. In this patient, 1000 mL of dilute barium sulfate was administered over 1 hour just before the examination to achieve adequate bowel distention.



**Figure 24-8** Coronal postgadolinium, T1-weighted, gradient-recalledecho fat-saturation image demonstrates an abnormal segment of distal ileum in the right lower quadrant with mural thickening and hyperenhancement (*thick arrow*). Prominent perienteric vascularity is seen surrounding this segment. Adequate bowel distention allows for confident evaluation of the distal small bowel. This is in distinction to the jejunal loops in the left upper abdomen, which show apparent wall thickening because of lack of distention (*thin arrow*).

gradient recalled echo images to survey the gastrointestinal tract (Figure 24-10). The SSFSE and SSFP images can be obtained quickly within a single breath-hold while minimizing the effects of patient and respiratory motion.<sup>15</sup> Diffusion weighted images of the abdomen with associated apparent diffusion coefficient maps can identify areas of inflammatory disease involvement. Fat-suppressed T2-weighted images of the abdomen and pelvis can help distinguish acute inflammation from chronic bowel changes, because chronic fibrosis tends to impart a hypointense T2-weighted signal within the bowel wall, whereas more acute changes tend to have hyperintense T2-weighted signal secondary to edema. Finally, precontrast and dynamic postcontrast spoiled gradient recalled echo T1-weighted images with delayed postcontrast images up to 7 minutes after injection can help identify areas of acute and

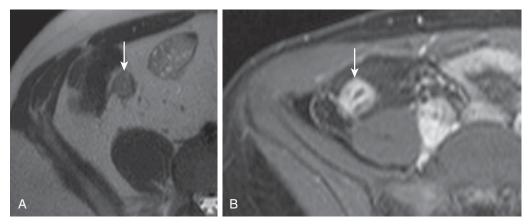
chronic disease involvement, because acutely inflamed segments will display enhancement in the enteric phase, whereas areas of chronic fibrosis will demonstrate enhancement on delayed postcontrast images. It is possible to have acute inflammatory changes superimposed on chronic fibrosis.<sup>16,17</sup>

# MAGNETIC RESONANCE ENTEROCLYSIS

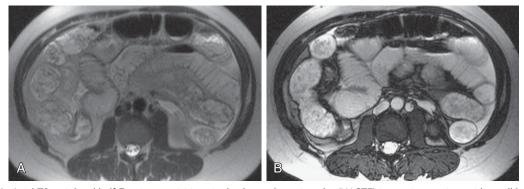
MR enteroclysis combines the advantages of fluoroscopic enteroclysis with those of cross-sectional imaging and reliably achieves optimal small bowel distention (Figure 24-11). However, it requires nasojejunal intubation, resulting in patient discomfort. The intubation is typically performed under fluoroscopic guidance, resulting in a longer procedure. The patient then can be transported to the MRI suite, and the small bowel may be filled after the patient is placed on the scanner.<sup>18</sup> Patients are imaged in the prone position to achieve abdominal autocompression.<sup>19</sup> Then 1500 to 2000 mL of hyperosmotic water solution (polyethylene glycol [PEG]) is administered via the nasojejunal tube with an MR-compatible pump. If this pump is not available, either manual-injection or hand-held infusion pumps may be used.<sup>18</sup> Typically, the contrast agent is administered in two phases. Initially, a flow rate of 80 to 120 mL/min is used until the agent reaches the terminal ileum. The flow rate can then be increased to 300 mL/min to create reflex atony.<sup>20</sup> Small bowel filling may be monitored by use of MR fluoroscopy or intermittent imaging with a thick-slab half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequence. Alternatively, the small bowel may be filled outside the scanner; however, less optimal distention may be attained without constant infusion.

# Ultrasound Evaluation of Small Bowel

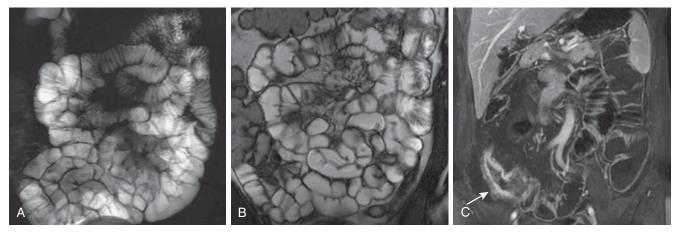
Ultrasonography can reveal important small bowel abnormalities that can have a profound impact on patient management. It is paramount for the sonographer and radiologist to be familiar with the normal location and appearance of the small bowel, so that alterations can be recognized. Many pathologic processes that affect the small bowel are amenable to ultrasound imaging. Infection, inflammatory diseases, neoplastic processes, and small bowel obstruction are all potential indications for ultrasonography.<sup>21</sup> These pathologic processes



**Figure 24-9** A, Axial T2-weighted half-Fourier acquisition single-shot turbo spin-echo (HASTE) image shows concentric wall thickening with the characteristic appearance known as the target sign (*arrow*). This implies acute inflammation in this patient with active Crohn's disease. B, Axial, postgadolinium, T1-weighted, gradient-recalled-echo, fat-saturation image in a different patient with active Crohn's disease again shows the characteristic target sign (*arrow*). Note the hyperenhancement of the mucosa and the decreased enhancement of the submucosa and muscularis layers due to edema.



**Figure 24-10** A, Axial T2-weighted half-Fourier acquisition single-shot turbo spin-echo (HASTE) image in a patient with small bowel obstruction. Oral contrast was not administered. There is distention of the bowel by intrinsic enteric contents. Bowel is normal thickness and signal. However, note the apparent intraluminal filling defects confirmed to be artifactual on true fast imaging with steady-state precession (FISP) images. B, Axial true FISP image in the same patient again demonstrates fluid-filled, dilated loops of small bowel with more homogeneous intraluminal opacification lacking the apparent flow voids seen on the HASTE image. Additionally, black boundary artifact is also present and characterized by the *black line* along the external surface of the bowel wall. This artifact is frequently seen on true FISP sequences.



**Figure 24-11** A, Coronal thick single-shot fast spin echo image in a patient with normal small bowel demonstrates the great degree of distention of the jejunal and ileal loops achieved with magnetic resonance enteroclysis using a hyperosmotic polyethylene glycol water solution. B, Coronal fast imaging employing steady-state acquisition (FIESTA) sequence on the same patient shows the normal appearance of the intraluminal folds, the bowel wall, and mesentery. Visualization of increased anatomic detail is aided by the significant degree of distention afforded by magnetic resonance enteroclysis. C, Coronal postgadolinium T1-weighted image in a patient with Crohn's disease who underwent magnetic resonance enterography shows the abnormal terminal ileum with mural thickening and hyperenhancement of the mucosal and serosal surfaces and corresponding low signal intensity in muscularis and submucosa layers (arrow). Such a stratified pattern of enhancement to the bowel wall is indicative of active disease. This appearance results from hyperenhancement of the mucosa, with decreased enhancement of the submucosa and muscularis layers secondary to edema. (All magnetic resonance enteroclysis images courtesy Dr. Gabriele Masselli, Umberto I Hospital, La Sapienza University, Rome, Italy.)

manifest as luminal narrowing, thickened bowel wall, and abnormal peristaltic activity. Familiarity with the ultrasound appearance and distribution of abnormalities may allow for a specific diagnosis.

Graded compression, first described by Puylaert,<sup>22</sup> is a technique using ultrasound-guided palpation. It is performed by applying uniform sustained gentle pressure with the transducer. When used appropriately, graded compression will displace normal gas-containing bowel away from narrowed, thickened, or fluid-filled small bowel. A fixed and noncompressible small bowel is the key to finding and characterizing a pathologic process. If, despite compression, gas continues to hinder the examination, the transducer can be placed at the mid or posterior axillary line so that ventrally located gas can be avoided. Decubitus or occasionally upright positioning also may be helpful.

It is beneficial to examine the small bowel with it in the resting state. Food and water can adversely affect the examination, so fasting by the patient before the evaluation is preferred. The choice of transducer for small bowel assessment largely depends on the patient's body habitus and the distance between the probe and the object of study. A 2.0- to 5.0-MHz curvilinear probe is used for a large patient. A 7.0- to 12.0-MHz linear transducer, which facilitates high-resolution ultrasonography, is used for an average-size or thin patient and for assessment of superficial abnormalities. A multifrequency transducer allows for optimal visualization of a pathologic process, using the highest frequency possible for better resolution. The field of view should be optimized so that all of the abdominal contents are included. The focal zone should be adjusted during the examination when looking for a bowel pathologic process or for finding normal landmarks.<sup>21</sup>

Color Doppler imaging can be used to differentiate edema or intramural hemorrhage from acute inflammation or infection.<sup>24</sup> Thus, mural thickening in conjunction with hyperemia of the small bowel seen on color or power Doppler imaging strongly suggests vasodilatation related to an infectious or inflammatory process.<sup>25</sup> However, the specificity of color Doppler imaging is unknown.

# Imaging

# NORMAL APPEARANCE

The multilayered ultrasonographic appearance of the wall of the stomach, small bowel, and colon is due to alternating hypoechoic and echogenic layers. These correspond to the histologic appearance of the bowel. There are five concentric rings (Figure 24-12): the mucosa (most inner layer), submucosa, and serosal layers are echogenic; and the muscularis mucosa and the muscularis propria are hypoechoic. Although the lumen of the small bowel can vary in diameter, in normal patients the small bowel wall is 3 mm or less in thickness.

Small bowel peristalsis is a normal event. Peristalsis is also an important factor in diagnosing a small bowel pathologic process. The frequency of peristalsis and the amount of fluid or solid material within the small bowel lumen should be assessed. In patients with bowel obstruction or gastroenteritis there is increased peristaltic activity and also a large amount of luminal fluid that makes the examination much easier to interpret. Normally, there is forward peristaltic movement. To-and-fro or reversed directional activity is always abnormal. Alternatively,



**Figure 24-12** Longitudinal ultrasound image of the small bowel, which is surrounded by ascites, shows the normal multilayered appearance (*arrow*).

in patients with paralytic ileus there may be no peristaltic activity.

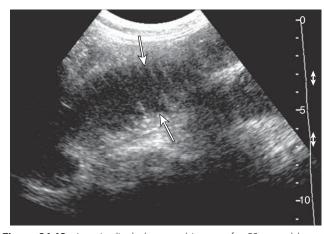
# THE ABNORMAL SMALL BOWEL

Small bowel pathologic processes will manifest as wall thickening, mass, luminal narrowing, abnormal peristalsis, or soft tissue abnormalities in the adjacent mesentery or peritoneum (Figure 24-13).<sup>26</sup> As a general rule, preservation of the bowel layers on ultrasonography suggests an infectious or inflammatory process (Figure 24-14). Conversely, absence of such layering is more supportive of a neoplastic cause. When examining the small bowel with ultrasound, it is imperative to note the thickness and length of the involved segment because that aids in differentiating the pathologic entities. Echogenic mesenteric fat adjacent to the abnormal bowel loops is an important finding and is secondary to mesenteric edema or neoplastic infiltration.<sup>27-31</sup>

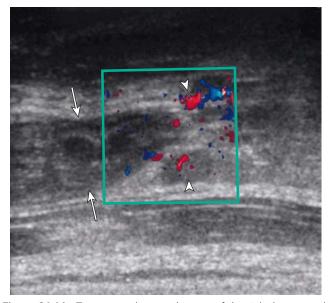
The obvious advantages of ultrasonography in the assessment of the small bowel are lack of ionizing radiation, lack of need for intravenously administered contrast material, and its cost-effectiveness. However, in clinical practice, ultrasonography usually is not the favored modality, owing to inherent limitations, which include operator dependency, obscuration of pathologic bowel by gas, and abdominal pain that may limit the ability to perform graded compression. The sensitivity of ultrasonography to detect perforation, fistulas, abscesses, or the activity of the disease compared with the latest generation of CT and MR scanners is unknown.

# Nuclear Medicine Evaluation of Small Bowel

Although a variety of imaging and nonimaging nuclear medicine tests are available to evaluate anatomic and functional



**Figure 24-13** Longitudinal ultrasound image of a 28-year-old pregnant patient with a small bowel obstruction from adhesions. The valvulae conniventes (*arrows*) are well demonstrated projecting into the fluid-filled small bowel.

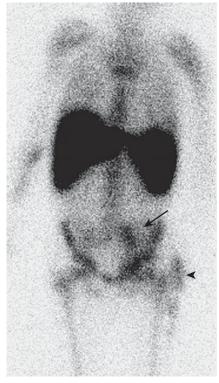


**Figure 24-14** Transverse ultrasound image of the right lower quadrant of a 22-year-old woman with mesenteric adenitis. There is a thickened loop of ileum with a loss of normal stratification (*arrows*). Adjacent to the thickened bowel are slightly enlarged mesenteric lymph nodes showing hyperemia on color Doppler imaging (*arrowheads*). Although these findings are nonspecific, the patient recovered 2 days later.

small bowel abnormalities, the most commonly used indications for imaging small bowel pathologic processes are described in the following section. The tests that will be described include imaging of tagged white blood cells (RBCs), Meckel's diverticula, tagged red blood cells (RBCs), and carcinoid tumors.

# IMAGING OF INFLAMMATION AND INFECTION

Assessment of disease extent in IBD is very important for treatment planning, particularly when surgery is being considered. The true extent of the inflammation of the small bowel is



**Figure 24-15** Leukocyte scintiscan labeled with indium-111. Abnormal activity in left psoas abscess (*arrow*) and left gluteal inflammation (*arrowhead*) in a patient with methicillin-resistant *Staphylococcus aureus* (MRSA) septicemia.

difficult to assess in Crohn's disease and is often underestimated by conventional techniques.

Labeled leukocyte imaging is a noninvasive technique for the detection of occult inflammation and infection. Because leukocytes can be separated and labeled without significant loss of function, they can be used to image small bowel inflammation and disease complications, such as abscess and possibly fistula.<sup>32</sup>

# Principle

WBCs accumulate at the site of inflammation and mount a physiologic response. The labeled leukocytes marginate and then migrate to the inflamed lesion. Several studies have examined the role of labeled leukocyte scintigraphy in the assessment of disease extent in patients with established inflammatory bowel disease.<sup>33</sup>

Scintigraphy is particularly useful in children<sup>34</sup> and very sick patients. Another advantage includes evaluation of the entire small and large bowel at the same time. The technique has the potential for verifying the presence of intraabdominal and extraabdominal abscesses and, possibly, fistulas.<sup>32</sup>

#### Image Interpretation

In WBCs, normal examination demonstrates activity in the spleen, liver, and bone marrow. Uptake in the spleen is most intense because of physiologic cell pooling. With technetium-99m exametazime (<sup>99</sup>Tc-HMPAO), there is urinary excretion and low-grade lung activity may be seen. Activity outside the normal expected distribution suggests infection (Figure 24-15).

Activity equal to that of the liver is considered clinically important. Uptake greater than that of the liver is typical for abscess. Activity less than marrow suggests a low-level inflammatory response.

Leukocyte scintigraphy has a high sensitivity for the detection of suspected IBD and to assess disease activity in patients with known IBD.

#### Pros and Cons

Because of its low specificity, this technique may not be able to distinguish between infective enteritis and inflammatory or ischemic bowel conditions. Also, activity within the abdomen may be due to causes other than inflammation and has the potential for misinterpretation.

# IMAGING OF MECKEL'S DIVERTICULUM

Meckel's diverticulum occurs in approximately 2% of the population. It results from failure of closure of the omphalomesenteric duct. Almost 96% of Meckel's diverticula remains asymptomatic. Rarely, complications such as bleeding, intussusception, ulceration, obstruction, or torsion can occur. Heterotopic gastric mucosa is present in 10% to 30% of patients with Meckel's diverticula, in approximately 60% of symptomatic patients, and in 98% of those who bleed.

#### Principle

The principle of <sup>99m</sup>Tc-pertechnetate scintigraphy is that the pertechnetate anion is selectively taken up by the surface mucus-secreting cells that line the gastric mucosa whether it is located in the stomach or is ectopic.<sup>35,36</sup>

# Image Interpretation

Meckel's diverticulum appears as a focal area of increased activity commonly in the right lower quadrant. The activity can be seen 5 to 10 minutes after tracer injection, increasing over time at a rate similar to gastric mucosa (Figure 24-16). Pertechnetate scintigraphy has a sensitivity of 80% to 90%, a specificity of 95%, and an accuracy of 90% in children.<sup>37</sup> In adults, the study is less reliable, with a sensitivity of 62.5%, a specificity of 9%, and an accuracy of 46%.<sup>38</sup>

### IMAGING FOR GASTROINTESTINAL BLEEDING

<sup>99m</sup>Tc RBC scintigraphy plays an important role in the evaluation of lower gastrointestinal bleeding owing to the limited sensitivity of endoscopy and intermittent bleeding. Radionuclide studies have typically been used as a screening examination to identify patients who require targeted angiography or surgery.

Lower gastrointestinal tract bleeding is more frequent in the colon as opposed to the small bowel. The most common causes of colonic bleeding include mucosal vascular malformations such as angiodysplasia, diverticulum, adenomatous neoplasms, and polyps. Colonoscopy performed within 24 hours of hospital admission will confirm a colonic bleeding site in 68% to 77% of cases. However, many patients may not be good candidates for colonoscopy.

Angiography will locate gastrointestinal bleeding sites in up to 65% of cases when hemorrhage occurs at a rate greater than 1 mL/min. The majority of gastrointestinal bleeding, however, is intermittent, and bleeding may not be occurring during contrast injection (20 to 30 seconds). Repeated angiographic studies are not practical. However, with <sup>99m</sup>Tc-labeled RBC, imaging can be performed over prolonged periods, which can be extremely useful in the setting of intermittent gastrointestinal bleeding. Also, a <sup>99m</sup>Tc RBC study can detect a bleeding rate of 0.04 mL/min.<sup>39</sup>

# Principle

The principle of radionuclide gastrointestinal bleeding studies is that the blood pool agent normally remains confined in the vascular system. During active bleeding the radionuclide extravasates into the bowel lumen.

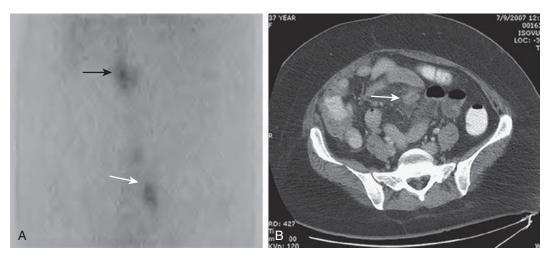
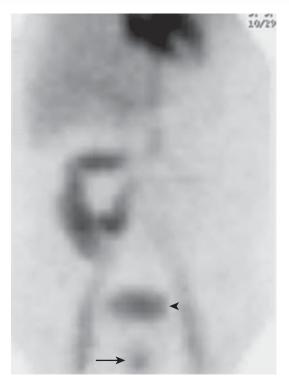
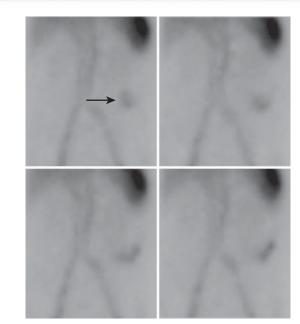


Figure 24-16 Technetium-99m pertechnetate scintiscan. A, Select anterior image shows abnormal activity left of the midline in the lower abdomen (*white arrow*), appearing in the same temporal fashion as the stomach (*black arrow*). B, Computed tomography scan in the same patient in the mid-abdomen demonstrates an inflamed Meckel's diverticulum (*arrow*).



**Figure 24-17** Accumulation of technetium-99m–labeled red blood cells in the expected location of the terminal ileum and colon in a patient with Crohn's disease. Physiologic activity is seen in the urinary bladder (*arrowhead*) and genitalia (*arrow*).



**Figure 24-18** Selected serial images from a cine sequence of a technetium-99m–labeled red blood cell study demonstrating a focus of active small bowel bleeding as progressive tracer accumulation in the left lower quadrant (*arrow*).

#### Image Interpretation

A normal scintiscan shows activity confined to the blood pool, with activity in the heart, aorta, inferior vena cava, liver, and spleen. Activity is also seen in the genitalia, and there is some urinary excretion of free pertechnetate.

Gastrointestinal hemorrhage appears as a focal activity, not in the expected location of blood pool or urinary excretion. The activity should progressively increase over time and conform to an intestinal anatomy and show peristalsis, either antegrade or retrograde (Figure 24-17).

Because of bowel peristalsis the hemorrhage may move antegrade or retrograde; therefore, it is important to review the 1-minute dynamic acquisition frames to accurately determine the site of bleeding (Figure 24-18).

<sup>99m</sup>Tc RBC scintigraphy is 93% sensitive and 95% specific for detecting a bleeding site with active arterial or venous bleeding rates as low as 0.04 mL/min<sup>39</sup> anywhere within the gastrointestinal tract.

The role of <sup>99m</sup>Tc RBC scintigraphy is limited in the evaluation of upper gastrointestinal bleeding owing to the widespread use of upper endoscopy as a first-line modality. Endoscopy of the upper gastrointestinal tract is reported to have an overall diagnostic accuracy of more than 90% in identifying duodenal and gastric ulcers, gastric erosions, varices, and Mallory-Weiss tears. However, <sup>99m</sup>Tc RBC scintigraphy can be useful when endoscopy is not readily available or in patients in whom endoscopy is difficult or impossible.

# SOMATOSTATIN IMAGING

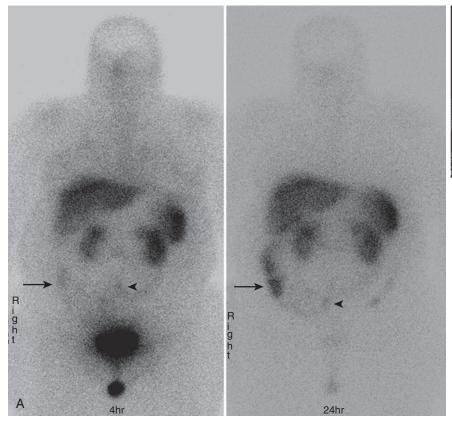
### Principle

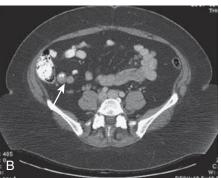
Somatostatin is a neuropeptide that is secreted and released by endocrine and nerve cells, especially by the hypothalamus. Somatostatin inhibits the release of growth hormone, insulin, glucagon, gastrin, serotonin, and calcitonin. Because carcinoid tumor is of neuroendocrine origin, a high density of somatostatin receptors is present. Therefore, a radiolabeled somatostatin analog—that is, indium-111–labeled pentetreotide (octreotide)—can be used for imaging these tumors.

# Image Interpretation

In a normal scintiscan the activity is identified in the blood pool, thyroid gland, liver, gallbladder, spleen, kidneys, and bladder. As the somatostatin is excreted by the kidneys, significant activity is seen in the kidneys on the delayed images. Also, on the delayed images, activity can be normally seen in the bowel. Tumor is seen as a focal area of increased uptake that persists on the delayed scintiscans. Of tumors, 80% to 90% are visible by 4 hours. The conspicuity increases on the delayed images owing to background clearance (Figure 24-19).

Octreotide scintigraphy serves as an efficient screening tool in patients with suspected carcinoid. It is useful in imaging of multifocal lesions and distant metastasis. For carcinoids the sensitivity of the octreotide scintiscan is 85% to 95%.<sup>40</sup> Other neuroendocrine tumors, such as gastrinoma, pheochromocytoma, and neuroblastoma, which also have somatostatin receptors, also can be imaged with radiolabeled somatostatin analogs.





**Figure 24-19** A, Four-hour and 24-hour anterior indium-111 pentetreotide images of the abdomen show normal activity in the liver, kidneys, and spleen. Some bowel activity is seen on the 24-hour image. However, an abnormal focus of activity is seen in the right lower quadrant (*arrow*) and in the mesentery in the midline (*arrowhead*). These become more intense on the 24-hour delayed images. **B**, Computed tomography scan in the same patient in the mid-abdomen demonstrating thickening of the terminal ileum (*arrow*) and an adjacent lymph node.

#### **Key Points**

- The major advantage of SBFT over enteroclysis is that it avoids intubation. Long segments of abnormal bowel are easy to see as long as frequent fluoroscopy is performed. As a result, diseases involving long segments of small bowel, such as Crohn's disease, ischemia, or radiation changes, are easily detected on SBFT.
- Enteroclysis has important advantages over SBFT, including improved luminal distention. Short lesions such as tumors or skip lesions of Crohn's disease are better demonstrated by enteroclysis because the lumen is overdistended, making subtle areas of focal narrowing more conspicuous. The small bowel folds are also better evaluated by enteroclysis because the folds are straightened.
- CT has a major advantage over barium studies in that it does not rely on barium reaching the site of obstruction but can use intraluminal fluid to outline the transition zone.
- MDCT has made cross-sectional imaging of the small bowel possible.
- Routine CT of the abdomen and pelvis uses positive enteric contrast material with or without intravenous contrast material and is most useful for evaluation of small bowel obstruction.

- CT enterography is a noninvasive technique using intravenous contrast and neutral enteric contrast material to visualize intrinsic small bowel abnormalities, as well as associated extraenteric pathologic processes.
- Indications for CT include IBD, acute gastrointestinal bleeding, obscure gastrointestinal bleeding, mesenteric ischemia, small bowel tumors, and pre-capsule endoscopy workup.
- Neutral enteric contrast material allows visualization of abnormal mucosal and mural enhancement, mucosal and submucosal small bowel masses, small bowel vascular malformations, and extravasation of intravenous contrast material into the bowel lumen.
- Multiplanar reformatted images are an integral part of all imaging protocols, improving visualization of both normal structures and pathologic processes, as well as increasing diagnostic accuracy.
- With the advent of MDCT, imaging of the small bowel is complementary to endoscopic techniques, allowing identification of transmural or perienteric abnormalities and extraenteric complications.
- CT enteroclysis uses intravenous contrast material and nasojejunal intubation to volume-challenge the small bowel with neutral enteric contrast material.

Continued

#### Key Points-cont'd

- Indications for CT enteroclysis include low-grade small bowel obstruction, IBD, obscure gastrointestinal bleeding, and small bowel tumors.
- In mechanical small bowel obstruction there is a dilated, fluid-filled hyperactive small bowel with to-and-fro or reversed peristalsis. This is readily determined when the bowel contains a substantial fluid quantity. In a patient with a paralytic ileus there is no peristaltic activity.
- Adequate bowel distention is a crucial component of MRI of the small bowel and necessary in evaluating for mucosal abnormalities. Inadequate distention can mask subtle areas of bowel wall thickening or may falsely mimic wall thickening.
- MR enteroclysis results in reliable bowel distention but is invasive and time consuming.
- Fast and ultrafast breath-hold sequences including HASTE and true fast imaging with steady-state precession are commonly used T2-weighted sequences in evaluating the small bowel. These sequences limit respiratory and

motion artifact and provide excellent-quality images. However, poor soft tissue resolution may limit characterization of lesions.

- Pregadolinium and postgadolinium T1-weighted fast low-angled shot (FLASH) with fat suppression provides superior soft tissue contrast, allowing for assessment of bowel wall enhancement and lesion characterization based on enhancement pattern. The mesentery also can be accurately assessed.
- Inflammation and infection evaluation detects intraabdominal and extraabdominal clinically occult inflammation and infection.
- Meckel's diverticulum scintigraphy has a sensitivity of 80% to 90%, a specificity of 95%, and an accuracy of 90% in children (less in adults).
- <sup>99m</sup>Tc-RBC gastrointestinal bleeding studies can detect a bleeding rate of 0.04 mL/min. The majority of gastrointestinal bleeding is intermittent.
- In neoplasm evaluation, octreotide scintigraphy has an 85% to 95% sensitivity for carcinoids.

# ACKNOWLEDGMENTS

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# REFERENCES

- Rubesin SE: Barium examinations of the small intestine. In Gore RM, editor: *Textbook of gastrointestinal radiology*, Philadelphia, 2008, WB Saunders, pp 735–754.
- Laufer I, Hreseel HY: Principles of double contrast diagnosis. In Levine MS, editor: *Double contrast gastrointestinal radiology*, Philadelphia, 2000, WB Saunders, pp 8–46.
- Maglinte DDT, Lappas JC, Heitkamp DE, et al: Technical refinements in enteroclysis. *Radiol Clin North Am* 41:213–229, 2003.
- Herlinger H, Maglinte DDT, Tsuneyosi Y: Enteroclysis: technique and variations. In Herlinger H, editor: *Clinical imaging of the small intestine*, New York, 1999, Springer-Verlag, pp 95–124.
- Nolan DJ, Cadman PJ: The small bowel enema made easy. *Clin Radiol* 38:295–301, 1987.
- 6. Herlinger H: A modified technique for the double contrast small bowel enema. *Gastrointest Radiol* 3:201–207, 1978.
- Nicolaou S, Kai B, Ho S, et al: Imaging of acute small-bowel obstruction. AJR Am J Roentgenol 185:1036–1044, 2005.
- Qalbani A, Paushter D, Dachman AH: Multidetector row CT of small bowel obstruction. *Radiol Clin North Am* 45:499–512, 2007.
- 9. Huprich JE, Bree RL, Foley WD, et al: *Expert panel on gastrointestinal imaging. Crohn's disease [online publication]*, Reston, VA, 2005, American College of Radiology (ACR).
- Schindera S, Nelson RC, DeLong DM, et al: Multi-detector row CT of the small bowel: peak enhancement temporal window—initial experience. *Radiology* 243:438–444, 2007.

- Maglinte DD, Sandrasegaran K, Lappas JC: CT enteroclysis: techniques and applications. *Radiol Clin North Am* 45:289–301, 2007.
- 12. Maglinte DD, Sandrasegaran K, Lappas JC, et al: CT enteroclysis. *Radiology* 245:661–671, 2007.
- Kavaliauskiene G, Ziech MLW, Nio CY, et al: Small bowel MRI in adult patients: not just Crohn's disease—a tutorial. *Insights Imaging* 2: 501–513, 2011.
- Hosseinnezhad A, Black RM, Aeddula NR, et al: Glucagon-induced pheochromocytoma crisis. *Endocr Pract* 17:e51–e54, 2011.
- Leyendecker JR, Bloomfeld RS, DiSantis DJ, et al: MR enterography in the management of patients with Crohn disease. *Radiographics* 6:1827–1846, 2009.
- Umschaden HW, Gasser J: MR enteroclysis. Magn Reson Imaging Clin North Am 12:669–687, 2004.
- Low R: Magnetic resonance imaging of the hollow viscera. In Gore R, Levine M, editors: *Textbook of gastrointestinal radiology*, Philadelphia, 2008, Saunders, pp 91–106.
- Fidler J: MR imaging of small bowel. Radiol Clin North Am 45:317–331, 2007.
- 19. Masselli G, Casciani E, Polettini E, et al: Comparison of MR enteroclysis with MR enterography and conventional enteroclysis in patients with Crohn's disease. *Eur Radiol* 18:438–447, 2008.
- Gourtsoyiannis N, Papanikolaou N: Magnetic resonance enteroclysis of the small bowel. In Gore R, Levine M, editors: *Textbook of gastrointestinal radiology*, Philadelphia, 2008, Saunders, pp 765–774.

- Puylaert J, van der Zant FM, Rijke AM: Sonography and the acute abdomen: practical. *AJR Am J Roentgenol* 168:179–186, 1997.
- Puylaert JB: Acute appendicitis: US evaluation using graded compression. *Radiology* 158:355– 360, 1986.
- Chaubal N, Manjiri D, Shah M, et al: Sonography of the gastrointestinal tract. J Ultrasound Med 25:87–97, 2006.
- Frisoli JK, Desser TS, Jeffrey RB: Thickened submucosal layer: a sonographic sign of acute gastrointestinal abnormality representing submucosal edema or hemorrhage. AJR Am J Roentgenol 175:1595–1599, 2000.
- Hata J, Kamada T, Haruma K, et al: Evaluation of bowel ischemia with contrast-enhanced US: initial experience. *Radiology* 236:712–715, 2005.
- Hanbidge AE, Lynch D, Wilson SR: US of the peritoneum. *Radiographics* 23:663–685, 2003.
- Rosch T, Classen M: Gastroenterologic endosonography, New York, 1992, Thieme Medical Publishers, p 36.
- Kimmey MB, Martin RW, Hagitt RC, et al: Histologic correlates of gastrointestinal ultrasound images. *Gastroenterology* 96:433–441, 1989.
- Niclaou S, Kai B, Ho S, et al: Imaging of acute small-bowel obstruction. AJR Am J Roentgenol 185:1038–1044, 2005.
- 30. Retterbacher T, Hollerweger A, Macheiner P, et al: Abdominal wall hernias. *AJR Am J Roent-genol* 177:1061–1066, 2001.
- Sarratiz J, Wilson SR: Manifestations of Crohn disease at US. *Radiographics* 16:499–520, 1996.
- Charron M, Di LC, Kocoshis S: CT and 99mTc-WBC vs. colonoscopy in the evaluation of

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inflammation and complications of inflammatory bowel diseases. *J Gastroenterol* 37:23–28, 2002.

- Giaffer MH: Labeled leucocyte scintigraphy in inflammatory bowel disease: clinical applications. *Gut* 38:1–5, 1996.
- 34. Alberini JL, Badran A, Freneaux E, et al: Technetium-99m HMPAO–labeled leukocyte imaging compared with endoscopy, ultrasonography, and contrast radiology in children with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr* 32:278–286, 2001.
- Marsden DS, Alexander C, Yeung P, et al: Autoradiographic explanation for the uses of 99mTc in gastric scintigraphy. J Nucl Med 14: 632, 1973.
- Conway JJ: Radionuclide diagnosis of Meckel's diverticulum. *Gastrointest Radiol* 5:209–213, 1980.
- Sfakianakis GN, Anderson GF, King DR: The effect of intestinal hormones of the Tc-99m pertechnetate imaging of ectopic gastric mucosa in experimental Meckel's diverticulum. J Nucl Med 22:678–683, 1981.
- Schwartz MJ, Lewis JH: Meckel's diverticulum: pitfalls in the scintigraphic detection in the adult. Am J Gastroenterol 79:611–618, 1984.
- Zuckier LS: Acute gastrointestinal bleeding. Semin Nucl Med 33:297–311, 2003.
- 40.Kwekkeboom DJ, Krenning EP: Somatostatin receptor imaging. *Semin Nucl Med* 32:84–91, 2002.

# **Small Bowel Obstruction**

ZARINE K. SHAH | WILLIAM F. BENNETT

# Small Bowel Obstruction: General Considerations

# ETIOLOGY

Small bowel obstruction (SBO) is a common manifestation, and appropriate management continues to be a clinical challenge. The morbidity and mortality associated with acute SBO continue to be significant; however, there has been a decline in mortality from SBO in the last 50 to 60 years from 25% to 5%.<sup>1</sup> The goal of treatment is to recognize the complications of ischemia early and develop an appropriate clinical plan. SBO can be caused by a variety of lesions, and the cause can be broadly classified based on their location. Intraluminal, intramural, and extraluminal causes have been described. The causes of SBO by age are listed in Table 25-1.

# **Prevalence and Epidemiology**

The leading cause of SBO in the United States is adhesions occurring after surgical procedures such as appendectomy, colorectal surgery, and gynecologic and upper gastrointestinal procedures. Other common causes are Crohn's disease, neoplasm, and hernia.

SBOs can be classified based on the completeness into partial or complete (high grade vs. low grade) and based on complications as nonstrangulated or strangulated. If left untreated, strangulated obstructions cause death in 100% of patients. Mortality decreases to 8% if surgery is performed within 36 hours and to 25% if the surgery is postponed beyond 36 hours.<sup>2,3</sup> The prevalence of SBO by cause is summarized in Box 25-1. Numbers vary across studies.<sup>2,3</sup>

# **CLINICAL PRESENTATION**

The diagnostic approach should focus on recognizing an obstruction, distinguishing partial from complete SBO, distinguishing simple from strangulated SBO, and identifying the underlying cause. Patients with SBO usually present with a variable period of abdominal pain, often accompanied by nausea and vomiting. Colicky pain is more often associated in patients with simple obstruction and increases in severity. It can be continuous or interspersed with pain-free intervals. Strangulated obstructions commonly manifest as constant pain. The presence of vomiting is another feature of SBO. In more proximal obstructions, vomiting is an early finding, with or without significant distention of the abdomen. In more distal obstruction, abdominal distention is marked and vomiting is delayed as the bowel takes time to fill. Patients can have constipation or diarrhea, which is caused by secondary increased peristalsis distal to an obstruction. Whereas patients with partial obstruction might have diarrhea and can still pass flatus, patients with complete obstruction tend to have complete obstipation. Fever, hypotension, tachycardia, and leukocytosis are suggestive of strangulation.

On physical examination, patients will show abdominal distention. The degree of distention often depends on the level of obstruction. Bowel sounds can be hyperactive in an early stage of obstruction or hypoactive late in the course as well as with strangulated lesions. Strangulated SBO also is often associated with peritoneal signs. Peritonitis and perforation present as a silent tender abdomen and are late signs.<sup>3,4</sup> The most important clinical findings in patients with SBO are shown in Box 25-2.

# ANATOMY

The small bowel is a complex organ with multiple functions. It measures approximately 120 cm in length from the pylorus to the ileocecal valve. The potential surface area available for digestion is increased approximately 600 times by the presence of the circular folds, villous mucosa, and microvillar surface of the epithelium. The jejunum and ileum receive their blood supply from the superior mesenteric artery and its vascular arcades. Venous drainage is by the superior mesenteric vein, which joins the splenic vein posterior to the pancreas to form the portal vein. Small bowel loops are suspended by a mobile mesentery and covered by a lining of peritoneum that extends over the serosal surface of the bowel. Lymphatic drainage of the small bowel is into the regional lymph nodes, which follow the vascular arcades and drain into the cisterna chili. Loops of jejunum are mostly located in the left hypochondrium in an individual with normal gut rotation. The ileum is mostly in the midline of the pelvis. The terminal ileum is the narrowest part of the small bowel. Knowing the normal bowel gas pattern on abdominal radiographs is important because this determines the ability to detect deviation from the normal pattern and classify this further.<sup>3-5</sup> The various bowel gas patterns are discussed in detail later in the section on radiographic imaging.

# PATHOLOGY

Obstruction of the small bowel leads to proximal dilatation of the intestine secondary to accumulation of gastrointestinal secretions and swallowed air. This bowel dilatation stimulates cell secretory activity, resulting in more fluid accumulation. This leads to increased peristalsis both above and below the obstruction with frequent loose stools and flatus early in its course. Vomiting occurs if the level of obstruction is proximal. Increasing small bowel distention leads to increased intraluminal pressures. This can cause compression of mucosal lymphatics, leading to bowel wall lymphedema. With even higher intraluminal hydrostatic pressures, increased hydrostatic pressure in

TABLE 25-1	Causes of Small Bowel Obstruction by Age			
Cause		Neonates and Infants <2 Years	Children and Young Adults	Adults and the Elderly
Intralu	minal	Meconium ileus Foreign bodies	Foreign bodies Ascaris lumbricoides	Foreign bodies Gallstones Food bolus
Intram	ural	Intussusception Congenital atresias and stenoses Henoch-Schönlein purpura	Crohn's disease Benign and malignant neoplasms Tuberculosis	Crohn's disease Benign and malignant neoplasm Radiation strictures Surgical anastomoses
Extram	nural	Midgut volvulus Inguinal hernia Congenital bands Postoperative adhesion	Inguinal hernia Adhesions Midgut volvulus	Adhesions (postoperative and inflammatory) Hernia Neoplasia

#### BOX 25-1 PREVALENCE OF SMALL BOWEL OBSTRUCTION BY CAUSE

- Adhesions: 67% to 74%
- Neoplasms: 5% to 13%
- Inflammatory bowel disease: 4% to 7%
  Hernia: 2% to 8%
- Miscellaneous: 4% to 12%

#### BOX 25-2 CLINICAL FINDINGS IN PATIENTS WITH SMALL BOWEL OBSTRUCTION

- Abdominal pain
- Nausea and vomiting
- Abdominal distention
- Diarrhea or constipation; obstipation in complete small bowel obstruction
- Bowel sounds are hyperactive in early stages or hypoactive in late stages

the capillary beds results in massive third spacing of fluid, electrolytes, and proteins into the intestinal lumen. The fluid loss and dehydration that ensue may be severe and contribute to increased morbidity and mortality.<sup>3</sup> Strangulated SBOs are most commonly associated with adhesions and occur when a loop of distended bowel twists on its mesenteric pedicle. The arterial occlusion leads to bowel ischemia and necrosis. If left untreated, this progresses to perforation, peritonitis, and death. Proximal to the obstruction, bacteria proliferate in the gut. Microvascular changes in the bowel wall allow translocation to the mesenteric lymph nodes. This is associated with an increase in incidence of bacteremia due to *Escherichia coli*.<sup>6</sup>

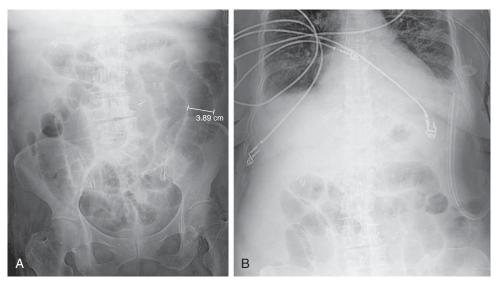
# IMAGING

SBO is a common clinical condition, and its diagnosis can be established if there is the classic triad of good clinical history, focused clinical examination, and targeted imaging and laboratory evaluation. The challenge is making the diagnosis of SBO, which is uncomplicated and can potentially be managed conservatively, from complicated SBO, in which bowel ischemia and strangulation are the concern. Vomiting, abdominal distention, and colicky or constant abdominal pain (individually or as a combination) are often the manifesting complaints. Imaging plays a very important role in making the diagnosis of this condition, and abdominal radiography, although not very sensitive or specific, is the first imaging test because of its widespread availability and low cost. Subsequent use of imaging modalities depends on the findings on radiographs and the level of clinical concern. Evaluation can be done using luminal contrast-enhanced studies or cross-sectional imaging. The goal of advanced imaging is three-fold: confirm the diagnosis, identify the cause, and evaluate for associated complications.

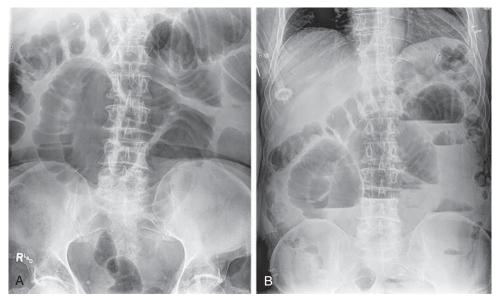
# Radiography

Abdominal Radiography. Conventional abdominal radiography remains the preferred method of initial radiologic examination of symptomatic patients suspected of SBO.7-12 The normal bowel gas pattern is either absence of small bowel gas or small amounts of gas within up to four variably shaped nondistended (<2.5 cm) loops of small bowel. A normal gas distribution and presence of stool in the large bowel should be recognized. A normal but nonspecific gas pattern describes a pattern of at least one loop of borderline or mildly distended small bowel (2.5 to 3 cm) with three or more air/fluid levels on upright or lateral decubitus radiographs. The colonic gas and stool pattern is either normal or has a similar degree of borderline distention. This kind of pattern can result from many conditions, such as low-grade obstruction, functional ileus, and medication-induced hypoperistalsis. The probable SBO pattern consists of multiple gas or fluid-filled loops of dilated small bowel with a moderate amount of colonic gas. The presence of colonic gas can indicate early complete SBO, incomplete SBO, or a nonobstructive ileus. A definite SBO pattern shows dilated gas or fluid-filled loops of small bowel in the setting of a gasless colon (Figure 25-1). These findings are diagnostic of SBO.<sup>3,10,11</sup> It is important to distinguish complete from partial SBO, because management is different. On plain radiographs, the presence of residual colonic gas after 6 to 12 hours is suggestive of partial SBO (Figure 25-2). Despite the description of the various gas patterns that can be seen on radiographs, these are diagnostic in only 50% to 60% of cases.<sup>1</sup> Box 25-3 lists common manifestations of SBO on plain radiography.

**Intraluminal Contrast Radiography.** Barium can be safely used in the adynamic gut because it does not typically inspissate within it.<sup>8</sup> Evaluation of the small bowel using barium can be done by either nonintubation techniques or intubation and



**Figure 25-1** Complete small bowel obstruction. **A**, Erect radiograph from an acute abdominal series of a 76-year-old woman shows multiple dilated loops of small bowel with air/fluid levels up to 3.9 cm in width. There is relative paucity of air in the colon, which suggests that the obstruction is complete. This patient has had multiple prior abdominal surgeries, as noted by the clips and mesh repair coils on the radiograph. **B**, Supine radiograph of the same patient confirms the findings. There is no free intraperitoneal air.



**Figure 25-2** Partial small bowel obstruction. Acute abdominal series in a 38-year-old woman with abdominal distention and vomiting. **A**, Supine radiograph shows multiple air-filled dilated loops of small bowel with gas in the colon. **B**, Erect radiograph shows multiple air/fluid levels wider than 3 cm, each suggestive of small bowel obstruction. Presence of air in the colon suggests that the obstruction is not complete.

#### BOX 25-3 MANIFESTATIONS OF SMALL BOWEL OBSTRUCTION ON PLAIN RADIOGRAPHY

- Loops of distended small bowel (>3 cm)
- Dilated bowel loops proximal and collapsed bowel loops distal to obstruction
- Gas and fluid levels (>3 air/fluid levels on an erect radiograph measuring >3 cm)
- Increased distance between valvulae conniventes ("stretch" sign)
- Trapped gas between valvulae conniventes ("string-of-pearls" sign)

insufflations.<sup>9</sup> Nonintubation techniques include small bowel follow-through (SBFT) or per-enterostomy (colostomy or ileostomy) small bowel enemas. SBFT has limitations in the setting of SBO. The presence of significant bowel distention in patients with SBO can result in dilution of the ingested barium, resulting in incomplete opacification and poor mucosal detail. Also, in patients with bowel obstruction there is a prolonged transit time of the oral contrast agent that can be a limiting factor. The nonintubation techniques are unable to assess intestinal distensibility and fixity of bowel loops, which is another drawback. Despite these limitations, the SBFT technique is a viable alternative to enteroclysis in settings in which intubation is not possible because of technical or patient-related factors.<sup>10-13</sup> Common manifestations of SBO on barium follow-through are listed in Box 25-4.

**Barium Enteroclysis.** Enteroclysis is not practiced widely because it requires conscious sedation, nasointestinal intubation, and constant radiologist involvement. This technique involves the intubation of small bowel to a point beyond the pylorus and often beyond the duodenojejunal flexure, with infusion of nondiluted contrast medium. Based on findings of enteroclysis, SBO has been graded. This grading is being used for the characterization of bowel obstruction on modalities such as CT. In Table 25-2 the causes of SBO are classified on the basis of the findings of enteroclysis.

Enteroclysis has a diagnostic value in patients in whom the diagnosis of low-grade SBO is clinically uncertain. Its ability to distinguish low-grade obstruction from normal bowel makes it important in assisting diagnosis.<sup>14,15</sup> Enteroclysis challenges the distensibility of small bowel and exaggerates the effect of mild or subclinical mechanical obstruction. The infusion technique promotes flow of contrast agent toward the site of obstruction despite diminished peristalsis. This distention facilitates evaluation of fixed and nondistensible bowel segments. Studies have shown that this technique can predict the presence of obstruction in 100%, the absence of obstruction in 88%, the level of obstruction in 89%, and the cause of obstruction in 86% of patients.<sup>16</sup> SBO is excluded when unimpeded flow of contrast agent is seen in normal-caliber loops from the duodenojejunal junction to the right colon. Mechanical SBO is confirmed when a transition point is demonstrated. By enteroclysis criteria, 3 cm is the upper limit of normal for jejunal caliber and 2.5 cm is the upper limit for the ileum.<sup>14</sup>

The level of obstruction is identified during the singlecontrast phase of the study; the cause of obstruction is best evaluated during double-contrast evaluation in which mucosal

#### BOX 25-4 MOST COMMON MANIFESTATIONS OF SMALL BOWEL OBSTRUCTION ON BARIUM FOLLOW-THROUGH

- Small amount of contrast agent through narrow lumen at the site of obstruction ("beak" sign)
- Increased peristalsis to overcome obstruction leading to bulbous shape proximal to obstruction (snakehead appearance)
- Stretched mucosal folds
- Dilution of ingested barium in massively distended loops of small bowel (drawback of small bowel follow-through)

# TABLEClassification of Small Bowel Obstruction on<br/>the Basis of Enteroclysis Findings

Type of Obstruction	Description
Low grade	Sufficient contrast agent flow through obstruction to define mucosal folds distal to obstruction.
High grade	Delayed passage of contrast agent leads to dilution by intestinal fluid. Minimal flow does not enable definition of mucosal folds.
Complete	No contrast agent passes the obstruction.

detail is well appreciated. In partial SBO, enteroclysis has been almost 85% accurate in distinguishing adhesions from metas-tases, tumor recurrence, and radiation damage.<sup>17</sup>

Enteroclysis can also gauge the severity of intestinal obstruction, an advantage over other modalities. In low-grade partial SBO there is no delay in contrast medium arriving at the point of obstruction, and adequate contrast medium passes distally such that the fold patterns of the distal bowel are well visualized. High-grade partial SBO is diagnosed when retained bowel fluid dilutes the barium and results in inadequate contrast density above the site of obstruction, allowing only small amounts of contrast medium to pass through the obstruction into the collapsed distal loops. Complete obstruction is diagnosed when there is no passage of contrast medium beyond the point of obstruction, as shown on delayed radiographs obtained up to 24 hours after the start of the examination.

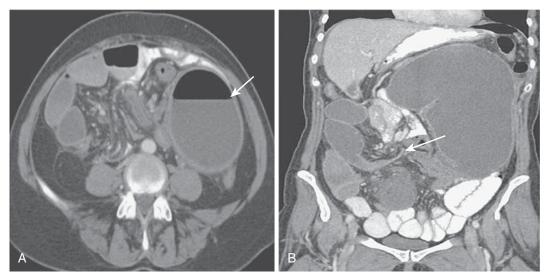
Despite all its advantages, it is often impractical to perform this as an outpatient procedure. In the acute setting when time is limited, CT is often the initial method of examination.

# Computed Tomography

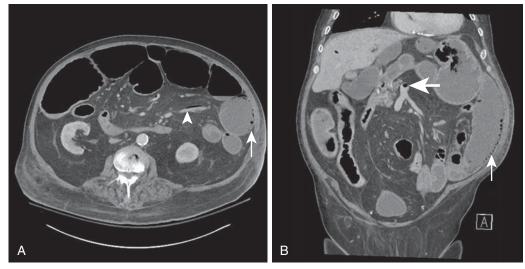
CT is a valuable tool in the evaluation of patients with suspected SBO. A low overall sensitivity (63%) of CT for all grades of SBO has been reported. Sensitivity increases with high-grade SBO (81% to 100%) and conversely worsens with low-grade SBO (48%).<sup>17-19</sup> CT can identify the location and severity of an SBO and detects the cause of the obstruction in 93% to 95% of cases. Complications such as closed-loop obstructions and strangulation are recognized, which would prompt immediate surgical intervention.<sup>17-19</sup> Strangulation of bowel and ischemia occur as a complication of intussusception, volvulus (Figure 25-3), torsion, hernia, or other types of closed-loop obstruction in which there is compromise of the mesenteric vascular pedicle. The presence of pneumatosis intestinalis on CT is an indicator of strangulation and bowel ischemia (Figure 25-4). Decreased enhancement of a segment of bowel wall in the arterial phase with increased enhancement in the venous phase seems to be highly specific for bowel ischemia. Evaluation of the course of vascular arcades around the involved loops of bowel on CT helps identify patients who are at risk for the life-threatening complications of strangulation and ischemia. This is one of the major advantages of CT over other modalities for the diagnosis of this condition. CT is also useful in distinguishing high-grade obstruction from an ileus pattern with reported sensitivities up to 100% compared with 46% with plain radiographs.<sup>18</sup>

The speed of multidetector CT (MDCT) and the isotropic data available with the newer generation scanners have revolutionized abdominal imaging. The widespread use of MDCT scanners and their availability has enabled rapid acquisition of scan data and has added significantly to CT diagnosis and evaluation of SBO.<sup>20</sup> Multiplanar reformats can be used to identify the transition point of SBO more reliably and to assess adjacent structures, as well as the mural and extramural extent of small bowel lesions. This aids planning for surgical resection.<sup>21,22</sup>

CT can be performed using barium and water as enteral contrast agents assist in visualization of mucosal detail. An intravenous contrast agent is used routinely in the absence of contraindications because it assists in the evaluation of bowel wall and mucosa, possible associated inflammatory or neoplastic processes, and mesenteric vasculature. In patients suspected of having ischemic bowel, scans should be performed in the arterial and venous phases to search for occluded arteries and



**Figure 25-3** Volvulus secondary to adhesions. **A**, Axial contrast-enhanced CT of a 53-year-old woman demonstrates a massively dilated loop of bowel in the left mid-abdomen (*arrow*). Loops of small bowel proximal to this are dilated, confirming the diagnosis of small bowel obstruction. **B**, Coronal contrast-enhanced image shows the mesenteric "swirling" (*arrow*) and tapering of a small bowel loop at the transition point of the obstruction. Other images (*not shown*) showed the appendix next to the massively dilated loop of bowel, confirming that this was the cecum and aiding in the diagnosis of cecal volvulus. These findings were confirmed at surgery.



**Figure 25-4** Pneumatosis of the small bowel with mesenteric venous gas. A 78-year-old man presented with severe abdominal pain and distention. He had a history of ulcerative colitis with prior subtotal colectomy with a J-pouch anastomosis. **A**, Axial nonenhanced CT image of the abdomen reveals dilated small bowel loops with multiple air/fluid levels. There is intramural air in a small bowel loop in the left mid-abdomen (*arrow*) with air also noted within branches of the superior mesenteric vein (*arrowhead*). Pneumatosis (air in the bowel wall) raised concern for mesenteric is chemia. **B**, Coronal reconstructed image demonstrates the extent of the pneumatosis (*thick arrow*). The extent of air in the mesenteric vasculature is noted (*thin arrow*), and air is also within the intrahepatic portal venous branches. The patient was taken to surgery, and extensive adhesiolysis was performed. Segments of bowel with evidence of ischemia were resected, and a temporizing diverting ileostomy was created.

veins, to depict vascular anatomy, and to assess bowel wall perfusion.  $^{\rm 20}$ 

Controversy exists about what oral contrast agent should be used in the setting of a suspected SBO, and practices vary by institution. Some authors use a positive oral contrast medium in this setting as tolerated by the patient because it is helpful in determining if an obstruction is complete.

Analysis of dilution effects on CT can be particularly helpful in patients whose plain radiographs did not show any gas-filled dilated loops (so-called *gasless abdomen*). It also can help in localizing the point of obstruction because the small bowel loops containing more dilute contrast medium are distal relative to those with more dense oral contrast.<sup>20</sup>

Other investigators have deemed oral contrast unnecessary if SBO is evident on plain radiographs, because the contrast agent is unlikely to reach the obstruction and may make evaluation of bowel wall thickening difficult if it does reach the obstruction. If ischemia is suspected, water is used as the enteric contrast agent because positive contrast media interfere with vascular three-dimensional (3D) reconstructions. In general,

#### BOX 25-5 MOST COMMON MANIFESTATIONS OF SMALL BOWEL OBSTRUCTION ON COMPUTED TOMOGRAPHY

- Dilated proximal bowel loop (>2.5 cm) and collapsed distal loop (<1 cm)
- Passage of contrast agent into collapsed segment indicating partial obstruction
- Accumulation of feces and gas proximal to obstruction (feces sign) indicating mechanical obstruction
- Bowel wall thickening, portal venous gas, and pneumatosis indicating strangulation

water is better tolerated than positive contrast media in patients with SBO.<sup>1,23</sup> The most common manifestations of SBO on CT are shown in Box 25-5.

# Magnetic Resonance Imaging

Although magnetic resonance imaging (MRI) can be used for evaluation of the small bowel, its role is somewhat limited in the acute setting. Advantages of MRI are the high soft tissue contrast and the acquisition of multiplanar images without exposing patients to ionizing radiation. This is especially important for young patients who are undergoing multiple evaluations (e.g., those with Crohn's disease) pregnant patients.

For imaging of SBO, the major advantage of MRI is the direct visualization of the small bowel wall. Fast sequences enable acquisition of T1- and T2-weighted images within a single breath-hold. For T2-weighted images half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequences with a fast acquisition time of approximately 1 second per image are used.<sup>24</sup> For T1-weighted images, 2D or 3D spoiled gradient recalled echo (SPGR) before and after intravenous administration of a contrast agent are used. These ultrafast sequences have the disadvantage of being prone to chemical shift artifacts but are especially useful in patients who are unable to hold their breath. The use of parallel imaging techniques is another option to minimize scan time, by reducing the number of phase encoding steps per repetition time. This allows even shorter scan times by maintaining spatial resolution or alternatively allowing higher spatial resolution by maintaining short acquisition time.

For both T1- and T2-weighted sequences the addition of fat-saturated pulses has been shown to increase contrast between bowel and surrounding fat tissue.

The major problem of the described MRI methods is flow artifacts that are generated by peristaltic motion that could imitate intraluminal lesions. This can be reduced by antiperistaltic medication.<sup>25,26</sup> Placing the patient in the prone position also can aid in reduction of artifact from abdominal wall motion and respiration. MRI of the small bowel is performed with oral contrast agents. Positive oral contrast agents, such as gadolinium chelates and ferrous and manganese ions are paramagnetic and reduce mainly T1 relaxation time. However, the use of positive contrast agents is limited because a hyperintense lumen often obscures pathologic processes of the bowel wall. Negative contrast agents, such as iron oxides, perfluoroocytl bromide, and barium sulfate produce low signal intensity on T1-wighted as well as T2-weighted images. T2 effects are predominant and caused by spin dephasing, which leads to a loss of signal intensity. One disadvantage of negative contrast agents are magnetic

#### BOX 25-6 MOST COMMON MANIFESTATIONS OF SMALL BOWEL OBSTRUCTION ON ULTRASONOGRAPHY

- Luminal diameter greater than 2.0 to 2.5 cm in jejunum and greater than 1.5 to 2.0 cm in ileum
- Dilated segment longer than 10 cm
- Increased peristalsis in dilated loops
- Collapsed colon

susceptibility artifacts by ferrous oxide on gradient-echo sequences.<sup>25,26</sup>

Biphasic contrast agents show different signal characteristics in different sequences. Manganese and gadolinium chelates at high concentrations lead to hyperintensity on T1-weighted images and hypointensity on T2-weighted images, whereas water, mannitol-based solutions, polyethylene glycol, and barium sulfate create hypointensity on T1-weighted images and hyperintensity on T2-weighted images. Disadvantages of these contrast agents are the intestinal absorption of water and unwanted intestinal side effects of mannitol solutions.<sup>26,27</sup>

MRI of the small bowel requires distention, because collapsed bowel loops can hide pathologic findings. There are two main approaches: imaging after administration of an oral contrast agent (MR follow-through) and imaging with distention by nasojejunal contrast application (MR enteroclysis).

For MR SBFT, image acquisition is preceded by oral ingestion of 600 to 1000 mL of contrast agent 20 minutes before the examination. A spasmolytic agent is added intravenously immediately before imaging is performed. T2-weighted and T1/T2 hybrid sequences are acquired in axial and coronal planes, until the terminal ileum is completely distended.

With the MR enteroclysis technique a biphasic contrast agent is given through a nasojejunal tube. The volume of contrast agent depends on the subject and varies between 1500 and 2000 mL. It is preferably applied using a peristaltic pump with an infusion rate between 80 and 150 mL. The main advantages of MR enteroclysis are improved intestinal distention and real-time imaging with ultrafast sequences. In the evaluation of SBO, MRI can be especially useful for distinction of nonobstructive or partially obstructive lesions using real-time evaluation with MR enteroclysis.<sup>28</sup>

# Ultrasonography

Ultrasonography is widely used in the assessment of acute abdominal pain. However, its use in the evaluation of SBO obstruction is limited. It is important to be aware of the findings of bowel obstruction on ultrasonography because this may be an incidental finding in a patient who is being evaluated for abdominal pain. In SBO, fluid accumulates in the bowel lumen. When there is no gas in the bowel lumen, fluid-filled bowel loops might be difficult to detect on plain radiographs. Contrast ultrasonography can be very useful to visualize SBO, because the intraluminal fluid is a natural contrast medium and helps demonstrate the origin of the obstruction. It can accurately detect the location of the obstruction. Characteristic features are rounded distended bowel loops with loss of definition and prominent valvulae conniventes. Ultrasonography is also able to assess the peristalsis and movements of intraluminal content.<sup>29-31</sup> Box 25-6 shows the most common manifestations of SBO seen on ultrasound evaluation.

TABLE 25-3	Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Small Bowel Obstruction			
Modal	ity	Accuracy (%)	Limitations	Pitfalls
Radiog	graphy	Sensitivity: 75 Specificity: 53	Barium studies cannot be performed in patients with perforation or complete SBO Extended transit time in SBFT	Diagnosis might be missed if no gas present in the small bowel
СТ		Accuracy: 94 Sensitivity: 92 Specificity: 96	lonizing radiation Risk for contrast reaction	Low sensitivity for low-grade, partial, or incomplete SBO
MRI		Accuracy: 88 Sensitivity: 90 Specificity: 86	Expensive Time consuming Not available everywhere	Patient factors: Claustrophobia, pacemakers, metal implants
Ultrasc	onography	Accuracy: 84 Sensitivity: 83 Specificity: 100	Air can obscure the field of view Difficult in obese patients	Operator dependent
Nuclea	ar medicine	Sensitivity: 79 Specificity: 98	Poor spatial resolution	Activity can be observed with other causes of inflammation.
PET/C	Т	Data not available	lonizing radiation High cost	Differentiation of benign from borderline neoplasms can be difficult.
MRI Ultrasc Nuclea	ar medicine	Sensitivity: 92 Specificity: 96 Accuracy: 88 Sensitivity: 90 Specificity: 86 Accuracy: 84 Sensitivity: 83 Specificity: 100 Sensitivity: 79 Specificity: 98	Ionizing radiation Risk for contrast reaction Expensive Time consuming Not available everywhere Air can obscure the field of view Difficult in obese patients Poor spatial resolution Ionizing radiation	incomplete SBO Patient factors: Claustrophobia, pacemake metal implants Operator dependent Activity can be observed with other cause of inflammation. Differentiation of benign from borderline

MRI, Magnetic resonance imaging; PET/CT, positron emission tomography with computed tomography; SBFT, small bowel follow-through.

# Imaging Algorithm

No single, generally accepted approach exists to evaluate patients with SBO. Plain radiography remains the initial modality of choice. However, radiographs may be diagnostic in only 45% to 60% of cases.<sup>15</sup> The decision to use additional diagnostic imaging methods should be based on clinical presentation and findings on plain radiography. The definitive presence of SBO on plain radiograph confirms the diagnosis. Based on the clinical condition of the patient, if conservative management is initiated or if there are doubts about the diagnosis, standard CT has emerged as the imaging modality of choice for further evaluation of SBO (Table 25-3). CT enteroclysis may be performed only if conventional CT is nondiagnostic. Ultrasonography and MRI can occasionally be useful in the diagnosis of SBO and evaluation of possible causes. However, CT is superior to these imaging modalities because it is more comprehensive and not limited by intraluminal air. Nuclear medicine studies and positron emission tomography with CT (PET/CT) do not play a role in the diagnosis of acute SBO and are reserved for assessment of underlying causes of SBO. An imaging algorithm is provided in Figure 25-20.

# DIFFERENTIAL DIAGNOSIS

A number of medical conditions can cause symptoms similar to those of SBO. Abdominal distention, vomiting, and constipation can be seen in patients with electrolyte disorders, uremia, diabetic ketoacidosis, and thyroid disorders, as well as intoxication with anticholinergics or tricyclic antidepressants. Peritonitis of any cause can mimic the symptoms of SBO.

Any condition resulting in small bowel dilatation or abdominal distention can be confused with SBO before clinical and radiographic investigations are completed and integrated. Obstruction typically results in distention that may include the colon in addition to small bowel. A concurrent inflammatory process, recent surgery, gastrointestinal infection, and electrolyte disturbances are predisposing factors for SBO, and appreciation of these comorbidities is important in scan interpretation. Cecal volvulus causes more proximal colonic obstruction and typically secondary small bowel dilatation, as well. Recognition of the distended cecum is the key to differentiating volvulus from an isolated SBO. Shock bowel can manifest as dilated loops of small bowel, but involvement of the colon and history should help differentiate the MDCT findings from SBO. Frank ischemia also can cause marked small bowel distention and simulate the appearance of obstruction. Ancillary findings of bowel wall thickening, segmental bowel perfusion abnormalities, and proof of arterial atherosclerotic disease provide evidence for an ischemic cause of the dilatation, however. Although Crohn's disease may cause SBO because of stricture formation, stenotic-phase disease, or superimposed acute disease, it also may result in areas of dilatation and narrowing without a true obstruction.<sup>20</sup>

# TREATMENT

# Medical Treatment

Initial nonsurgical management includes fluid administration, bowel decompression using nasogastric tubes, analgesics, antiemetics, and antibiotics, which should cover gram-negative and anaerobic organisms. Based on clinical features, laboratory and radiologic findings, nonoperative trial, and conservative management may be used for partial or simple obstruction. Resolution of the obstruction can occur in patients with these lesions in up to 72 hours.<sup>4,5</sup> Surveillance using imaging techniques and regular clinical monitoring is done for these patients on conservative treatment, to detect any change that indicates complications.

#### Surgical Treatment

A strangulated SBO is a surgical emergency. In patients in whom the SBO is complete, the risk for strangulation is high and early surgical intervention is necessary. Patients with simple complete obstructions in whom nonoperative trials fail also need surgical treatment but experience no apparent disadvantage from delayed surgery.<sup>32</sup>

# What the Referring Physician Needs to Know: General Considerations of Small Bowel Obstruction

- Recognize SBO: Clinical presentation and plain radiography (diagnostic in 45% to 60%).
- Determine the site of obstruction.
- Discriminate partial from complete obstruction.
- Discriminate simple from strangulated obstruction.
- Determine the cause (is there a cause that can be removed?).
- Detect and treat associated complications.

# Benign Causes of Small Bowel Obstruction

# ETIOLOGY

The leading cause of benign SBO in the United States is postsurgical adhesions.<sup>2</sup> Single-band adhesions were most commonly found in cases with strangulating obstruction, whereas nonstrangulated obstructions were more commonly associated with multiple adhesions. Other common causes of SBO are inflammatory bowel diseases, hernias, gallstone ileus, Crohn's disease, hernia, and radiation injury or a combination of these findings.<sup>1,31</sup> Rare causes of nonmalignant SBO include phytobezoar after previous gastric surgery,<sup>33</sup> familial Mediterranean fever causing recurrent attacks of febrile inflammation of the peritoneum,<sup>34</sup> swallowed foreign bodies, parasites, tuberculosis, intraabdominal abscess, and intramural hematoma. In pediatric patients, causes of SBO are intussusception, congenital intestinal atresia, malrotation of bowel with midgut volvulus, and necrotizing enterocolitis.

The varying incidence of etiologic factors in different studies can be attributed to the evaluation practices used and referral patterns in institutions. There also has been a change in the cause of SBO during this century, with hernia as the leading cause at the beginning of the 20th century. Elective treatment of groin hernias caused the decrease of strangulated hernia to only 2% to 5%.<sup>2</sup> Hernia is still the leading cause of SBO in developing countries, owing to a lack of access for elective repair.<sup>35</sup> Demographic factors also seem to play a role in the cause of SBO, especially in diseases with a hereditary component such as Crohn's disease.

# PREVALENCE AND EPIDEMIOLOGY

Benign causes account for 70% to 80% of all reasons for admission for SBO. Numbers vary in the literature, but the leading causes are adhesions (67% to 74%), inflammatory bowel diseases (7% to 10%), and hernia (2% to 8%).<sup>2</sup> Adhesions are due to previous surgery, most commonly appendectomy, colorectal resection, and gynecologic procedures. The terminology used in describing SBOs is presented in Box 25-7.

# **CLINICAL PRESENTATION**

Patients present with abdominal pain, accompanied by nausea and vomiting. SBO can be associated with constipation or diarrhea. Physical examination reveals abdominal distention and initially hyperactive bowel sounds, followed by hypoactive

# BOX 25-7 TERMINOLOGY IN BOWEL OBSTRUCTION

- Simple obstruction: Small bowel obstruction with intact blood supply
- Strangulated obstruction: Small bowel obstruction with bowel ischemia
- Partial obstruction: Narrowed lumen with conserved passage of gas and intestinal contents
- Complete obstruction: Total luminal occlusion with lack of gas and fecal material in colon or nondistended small bowel
- Closed loop obstruction: Bowel segment occluded at two points that are adjacent to each other

bowel sounds in later stages. The early diagnosis of SBO is crucial to prevent bowel ischemia or perforation.

# PATHOPHYSIOLOGY

Lower abdominal and pelvic operations are more likely to cause subsequent SBO than upper gastrointestinal procedures. The bowel is fixed at the root of the mesentery; therefore, the cranial part of the bowel is less mobile. In the pelvis, where the intestine is more mobile, it is more likely to undergo a torsion, leading to SBO.

# PATHOLOGY

Postoperative adhesions can manifest as early SBO within 4 weeks of surgery (Figure 25-5) or as delayed SBO years after a surgical procedure. Hernias account for 2% to 8% of all SBO cases in the United States.<sup>2</sup> They include inguinal, umbilical (Figure 25-6), ventral wall (Figure 25-7), femoral, obturator, and internal hernias (Figure 25-8). A loop of small bowel can enter any form of hernia and become obstructed at the narrow neck of the hernia. This leads to a compromise of venous return of the entrapped bowel segment with congestion and edema, eventually resulting in ischemia, necrosis, and perforation in some cases. Inflammatory bowel diseases, such as Crohn's disease, are increasingly recognized as leading causes of SBO and account for approximately 10% of all cases. Patients most likely present with intermittent subacute or chronic forms of partial bowel obstruction. Gallstone ileus is a rare complication of cholelithiasis; it has a high morbidity and mortality and most commonly manifests in patients older than 65 years of age.<sup>2</sup> It accounts for 1% to 4% of all mechanical SBO and is caused by impaction of a gallstone in the intestinal lumen.

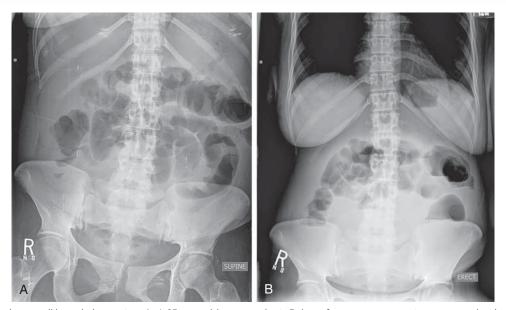
# IMAGING

CT has established its role for imaging SBO, with a reported accuracy of 90% to 95%.<sup>17,18</sup>

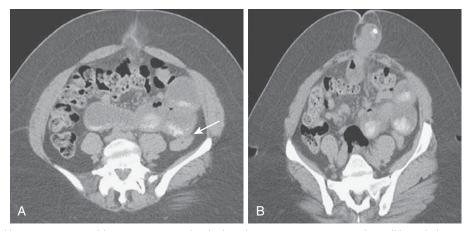
### Radiography

The most common general radiologic features of SBO that are seen on plain radiography were described earlier. Less common findings can be associated with specific circumstances or causes of SBO. However, certain specific findings on plain radiographs can help in diagnosing the cause of SBO. Presence of intramural gas secondary to ischemia, which can be appreciated on plain radiograph, is considered a poor prognostic sign. In a closedloop obstruction a bowel segment is not decompressed by the

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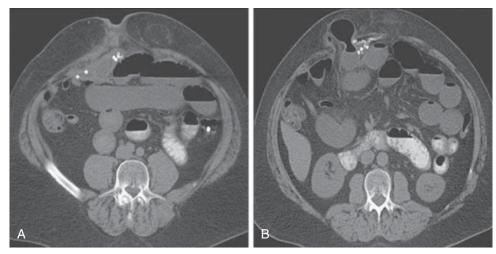
**Figure 25-5** Complete small bowel obstruction. **A**, A 25-year-old woman who is 5 days after a cesarean section presented with vomiting and lower abdominal pain. Supine radiograph taken as a part of the acute abdominal series reveals multiple dilated air-filled loops of small bowel. The colon is gasless. **B**, Erect radiograph confirms small bowel obstruction. There is no free gas under the domes of the diaphragm. Presence of a smooth extrinsic mass effect on the small bowel loops as a result of the postpartum uterus is noted.



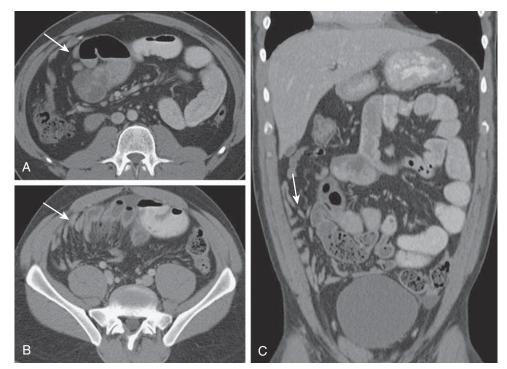
**Figure 25-6** Umbilical hernia. A 62-year-old woman presented with clinical symptoms consistent with small bowel obstruction. There was a vague fullness in the periumbilical region. **A**, Axial contrast-enhanced image demonstrates multiple dilated small bowel loops without dilatation of the colon (*arrow*), confirming the clinical suspicion of small bowel obstruction. **B**, Axial image at the level of the umbilicus is diagnostic for an umbilical hernia causing the bowel obstruction. The narrow neck of the hernial sac was compressing the loop of bowel reentering the peritoneal cavity. The hernia was surgically reduced.

caudal passage of gas and fluid. It is important to distinguish paralytic ileus (Figure 25-9, *A*) from mechanical obstruction. Paralytic ileus can develop when an insult is not of the occlusive type or as expression of a worsening of a mechanical obstruction. Unlike in mechanical obstruction, the patency of the intestinal lumen is maintained. Characteristic radiographic findings of paralytic ileus are multiple air/fluid levels with a reduced fluid component, increased diameter of bowel loops with decreased tone, thickened appearance of the intestinal wall, horizontal side-by-side placement of distended bowel loops, and absence of gas in the colon.<sup>36</sup> On enteroclysis, the contrast medium should reach the cecum within 4 hours with paralytic ileus. If it remains stationary for longer than 4 hours, mechani-

cal obstruction is suggested. If radiographic examination does not prove diagnostic, CT examination should be undertaken (see Figure 25-9, *B* and *C*). In cases of gallstone ileus the triad of SBO, ectopic gallstones, and pneumobilia is considered pathognomonic; however, these imaging findings are seen in only 30% to 35% of abdominal plain radiographs and is more easily demonstrated on CT.<sup>37</sup> However, these specific findings are not always present. The overall reported rate of diagnosed causes of SBO on plain radiography is only 2% to 7%.<sup>30</sup> In Crohn's disease, aphthoid ulcers develop into linear ulcers and fissures to produce an ulceronodular or "cobblestone" appearance. The bowel wall is thickened by a combination of fibrosis and inflammatory infiltrates.<sup>38</sup> SBFT (Figure 25-10) is part of



**Figure 25-7** Ventral wall hernia. **A**, Axial contrast-enhanced computed tomography image in a 52-year-old woman shows multiple dilated loops of small bowel with air/fluid levels. There is a small amount of fluid in the colon with some air, suggesting that the obstruction is not complete. This patient has a history of bowel surgery. **B**, Another axial contrast-enhanced image confirms that a ventral wall hernia through the surgical scar is the cause of the obstruction.



**Figure 25-8** Pericecal hernia. A 32-year-old man presented with acute abdominal pain and vomiting. A, Axial contrast-enhanced CT image shows multiple dilated loops of small bowel with a sudden abrupt change in caliber in the right lower quadrant (*arrow*). B, Nondilated loops of bowel are present in a nonanatomic location lateral to the cecum (*arrow*), which is confirmed by the coronal reformatted image (*arrow*, C). This was diagnosed as a case of pericecal hernia secondary to a congenital defect in the cecal mesentery. Internal hernias are uncommon, and recognizing the normal location of the bowel is very important for diagnosis.

the standard radiologic approach to the investigation of Crohn's disease. It shows the entire small bowel but has limitations for Crohn's disease.

# Computed Tomography

Because of the very high resolution and the presence of intravenous contrast enhancement, CT can not only diagnose the presence of SBO but also possibly determine the cause and the complications of the condition. The identification of a site of transition in the small bowel and detection of change in caliber from dilated to nondilated bowel is important in identifying the cause of obstruction.<sup>30,31</sup> Studies have found that coronal and sagittal reformatted images are of benefit in determining the site and cause of obstruction and that the presence of these images



**Figure 25-9** Ileus. A, Supine radiograph of the abdomen in a 52-year-old woman shows diffuse dilatation of small and large bowel loops. This patient had a history of constipation. The findings are diagnostic of functional ileus pattern of the bowel. B, Axial computed tomography image shows fluid-filled dilated small and large bowel loops. C, Coronal image confirms the findings of ileus. No transition point in the bowel and a proportionate dilatation of small and large bowel loops are diagnostic of ileus.



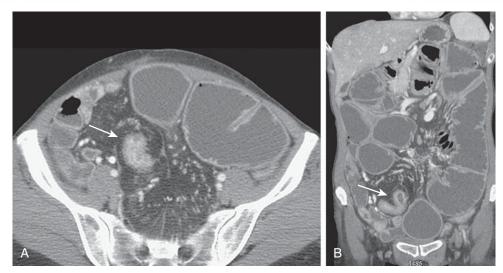
**Figure 25-10** Small bowel follow-through in Crohn's disease. Note the presence of massively dilated loops of small bowel filled with barium. There is a narrowed loop of small bowel in the left lower quadrant that is involved with Crohn's disease that was proved by computed tomography.

improves reader confidence in diagnosis.<sup>21,22</sup> There are, however, certain drawbacks for the coronal reformatted images, such as difficulties in determination of conditions involving the ventral abdominal wall because this is often not included when reformatted images are generated. Reformatted images should be

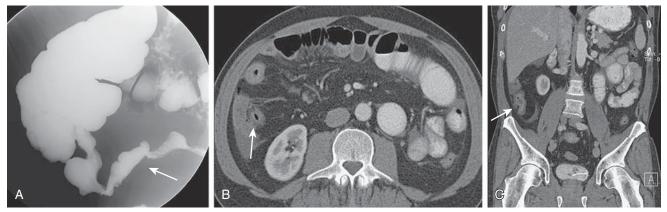
used as an adjunct and not as a replacement for conventional axial imaging.  $^{\rm 21,22}$ 

The presence of intravenous contrast medium is especially useful in conditions in which an intramural pathologic process is causing SBO (e.g., Crohn's disease or infective or inflammatory enteritis). Evaluation of the wall thickness, pattern of attenuation, degree of enhancement, and length of involvement is helpful to make the diagnosis. CT of Crohn's disease shows bowel wall thickening and mural stratification as a target or double-halo appearance during acute inflammation. Inflamed mucosa and serosa enhance after contrast agent administration, and the intensity of contrast agent enhancement correlates with disease activity (Figures 25-11 and 25-12). The stenosis and prestenotic dilatation as well as skip lesions can be identified. In chronic disease, mural stratification disappears and transmural fibrosis is seen. Mesenteric changes manifest as fibrofatty proliferation, lymphadenopathy, and hypervascularity of the vasa recta ("comb" sign). CT also can detect complications of Crohn's disease, such as fistulas, abscesses, strictures, and secondary tumors.38,3

CT cannot identify a bowel adhesion itself. The diagnosis is made by the presence of an abruptly changing caliber of the small bowel lumen in the absence of another obstructing cause (Figure 25-13). CT is superior to plain radiography in the diagnosis of a hernia, because anatomic relationships as well as complications can be determined. Especially in obturator hernias, which are difficult to detect clinically and are associated with bowel ischemia and high mortality, CT can establish a fast diagnosis followed by surgical intervention.<sup>30,31</sup> When SBO is caused by diverticulitis, CT findings consist of mural thickening, submucosal edema in small bowel adjacent to the diverticulitis, mesenteric inflammation, and typical signs of colonic diverticulitis, such as diverticula, colonic wall thickening, and abscess formation (Figure 25-14).<sup>40</sup> Most adult intussusceptions in the small bowel are transient. However, intussusceptions that lead to SBO are usually secondary to benign lesions, such as lipoma, leiomyoma, hemangioma, or neurofibroma. Of lesions



**Figure 25-11** Crohn's disease. A, Axial contrast-enhanced CT in a 68-year-old woman shows multiple significantly dilated loops of small bowel. There is a loop of ileum in the right lower quadrant that is thick walled and inflamed (*arrow*). The patient has symptoms of inflammatory bowel disease, and this appearance is consistent with Crohn's ileitis with small bowel obstruction. **B**, Coronal reconstructed image in the same patient clearly demonstrates the dilated fluid-filled loops of small bowel with the inflamed ileal loop in the right lower quadrant (*arrow*).

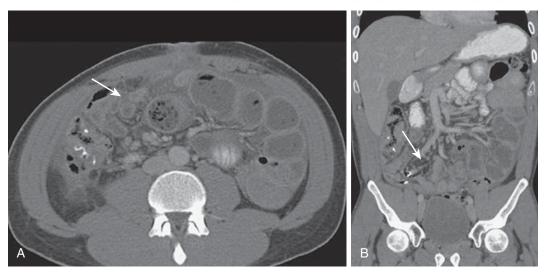


**Figure 25-12** Crohn's disease small bowel follow-through (SBFT). A 36-year-old man presented with a known history of Crohn's disease. A, SBFT image at the level of the ileocecal junction shows nodularity of the terminal ileum. There were multiple dilated loops of small bowel proximal to the ileocecal junction (*arrow*). Delayed transit of barium to the ileocecal junction was noted. **B**, Axial contrast-enhanced computed tomography image shows the dilated obstructed small bowel loops with a narrowed ileum at the ileocecal junction with inflammatory thickening of the wall of this loop of bowel (*arrow*). **C**, Coronal image at this level confirms the findings of Crohn's stricture with active inflammation (*arrow*). There were no complications of the disease diagnosed at this time.

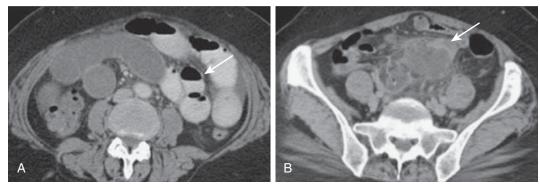
causing small bowel intussusception in adults, 15% are malignant and most often are metastases. Adult intussusception appears as a complex soft tissue mass and can manifest as either a target-shaped lesion with concentric alternating layers of high and low attenuation or as a sausage-shaped mass (Figure 25-15).<sup>41</sup> With intramural hematoma, CT findings are often nonspecific and depend on the age of the hematoma. In early stages the hemorrhage is hypodense, but it becomes hyperdense as time passes. Once lysis of the clot begins, the hemorrhage manifests as decreased density (Figure 25-16). CT is more reliable in detecting gallstone ileus than radiographs alone. On CT, the gallstone is more reliably identified, as is gas within the gallbladder and pneumobilia secondary to biliary-enteric fistula.<sup>37</sup> CT also demonstrates a bezoar as a mass in the obstructed bowel segment. The mass may be mottled because of air trapped in the proximal bowel loop.

# Magnetic Resonance Imaging

MRI with fast sequences (HASTE) uses the intrinsic intestinal fluid as contrast medium and avoids the time-consuming administration of oral contrast agents as needed for CT. Images are created rapidly during one breath-hold. The technique has been shown useful in finding the cause for SBO for some underlying pathologic processes.<sup>24</sup> Adhesions can manifest on MRI as sharply angled loops of dilated bowel and multiple transition points. With strictures, a focal narrowing of the bowel with abrupt change in caliber without a surrounding mass can be seen. Obstructing tumor masses cause increased signal intensity at the transition point, but further differentiation of the mass is not possible. The cause can be correctly identified in approximately 50% of cases.<sup>26</sup> MRI also has the advantage over CT of getting a semifunctional assessment of bowel peristalsis when



**Figure 25-13** Adhesions with small bowel obstruction. A 48-year-old man with multiple prior bowel surgeries presented to the emergency department with a 3-day history of constipation and recent onset of vomiting. Computed tomography (CT) scan of the abdomen was performed with a high index of suspicion for bowel obstruction. **A**, Axial contrast-enhanced CT confirms small bowel obstruction up to the transition point at the right lower quadrant (*arrow*) very close to the site of prior bowel surgery. **B**, Coronal reformatted image shows the extent of the bowel obstruction and confirms the site of transition (*arrow*). Adhesions from prior bowel surgery were the cause for the obstruction. Conservative management was successfully performed in this patient.



**Figure 25-14** Diverticular abscess. **A**, Axial contrast-enhanced CT image of a 72-year-old woman shows dilated fluid-filled loops of small bowel with multiple air/fluid levels (*arrow*). There is the presence of air and some fluid in the colon. These features are suggestive of partial small bowel obstruction. **B**, Image in the pelvis demonstrates diverticulitis with a diverticular abscess (*arrow*). The small bowel obstruction is the result of the inflammation adjacent to the abscess.

using dynamic sequences acquired through the abdomen and pelvis. Evaluation of strictures or areas of subtle narrowing can be done with this technique.

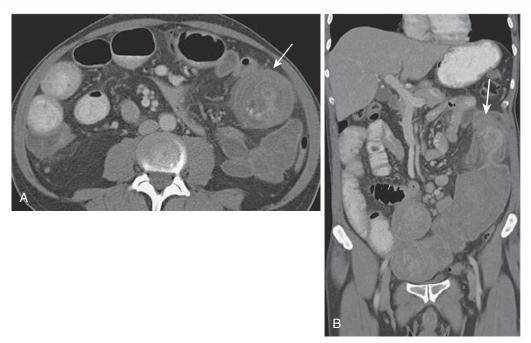
MR enteroclysis is an emerging technique that combines the advantages of conventional enteroclysis with cross-sectional imaging. It can effectively determine the level and presence of SBO. MR enteroclysis shows a wide spectrum of imaging findings of Crohn's disease, including early nonspecific changes such as mucosal nodularity or aphthous-type ulcers, longitudinal or fissure ulcers, cobblestoning, intramural tracts, wall thickening, luminal narrowing and prestenotic dilatation, fibrofatty proliferation, mesenteric hypervascularity, the comb sign, associated mesenteric lymphadenopathy, and/or complications such as fistula formation, phlegmon, or abscess and can provide pictorial evidence of disease activity. In one study, MR enteroclysis showed 100% sensitivity in the diagnosis of lumen stenosis and demonstration of associated prestenotic dilatation.42 However, this technique is user dependent and not widely practiced.

# Ultrasonography

Ultrasonography can be used to locate dilated loops as well as to assess peristalsis and thus differentiate a mechanical obstruction from paralytic ileus. Its use is limited however, owing to the inherent inability of sound waves to penetrate gaseous loops. The presence of free peritoneal fluid is a nonspecific finding of SBO. Intussusception can appear as a mass of concentric rings of alternating hyperechoic and hypoechoic layers, often referred to as a "target" or "doughnut" shape. Doppler ultrasonography is useful to assess the vascular flow to the intestine, with an absence of blood flow suggestive of necrosis. It is also used to demonstrate congenital abnormalities such as meconium ileus or jejunoileal atresia. In meconium ileus, bowel loops contain highly echogenic material.<sup>29,30</sup>

#### Nuclear Medicine

Nuclear medicine techniques do not play an important role in diagnosing benign SBO. One application is white blood



**Figure 25-15** Intussusception. A 62-year-old man presented to the emergency department with nausea, vomiting, and abdominal pain for 2 days. He had tenderness in the abdomen and hyperactive bowel sounds. **A**, Axial contrast-enhanced computed tomography image demonstrates a whorled appearance of a loop of small bowel in the left mid-abdomen (*arrow*) with dilated small bowel loops proximally. **B**, Coronal image clearly demonstrates the intussusceptions (*arrow*) and the proximal small bowel obstruction. This patient was taken to surgery, and a leiomyoma causing the intussusception was resected.

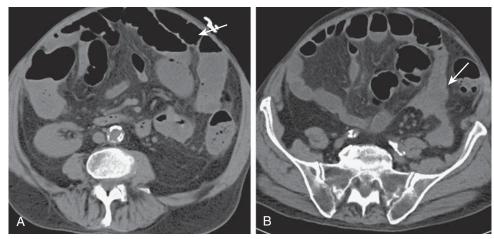


Figure 25-16 Bowel wall hemorrhage. A 73-year-old man had a history of trauma. The patient was known to be on anticoagulants for the treatment of a prior pulmonary embolism. Computed tomography of the abdomen (A) and pelvis (B) was performed, and axial images displayed dilated loops of small bowel with obstruction at the site of bowel hematoma. This was seen as an area of bowel wall thickening and presence of stranding around the loops of small bowel (*arrows*).

cell scanning to localize inflammatory disease underlying the obstruction. Technetium-99m–hexamethylpropyleneamine oxime (HMPO) scanning has been shown useful in assessment of disease activity in patients with Crohn's disease and can distinguish it from other causes of mural thickening.<sup>43</sup>

# Imaging Algorithm

An imaging algorithm is provided in Figure 25-20.

# Classic Signs: Benign Causes of Small Bowel Obstruction

- Dilated small bowel loops with air/fluid levels
- Absent or minimal gas in the colon
- Localized transition zone
- Collapsed small bowel loops distal to the obstruction
- Small bowel feces sign

# TREATMENT

#### Medical Treatment

General options for medical and surgical management were discussed earlier in this chapter. Management of specific causes depends on etiologic factors. Patients with SBO secondary to Crohn's disease can be managed nonsurgically with tube decompression in combination with treatment of the underlying inflammatory process. Parenteral nutrition should be provided for periods of prolonged bowel rest. Patients with partial SBO can be managed nonoperatively, and in 60% to 85% of these patients the obstruction will resolve without the need for surgical intervention. Parenteral nutrition should be provided for a prolonged period with bowel rest.<sup>4,5</sup>

# Surgical Treatment

Patients who present with SBO from adhesions usually benefit from early operative lysis by simple laparotomy or laparoscopy. When SBO is caused by a hernia, manual reduction of the obstruction can be tried for inguinal, umbilical, incisional, and incarcerated hernias, followed by close observation of the patient. Elective repair of the hernia should be performed to prevent recurrence and strangulation. Irreducible hernias have to be managed by a primary operative approach.<sup>32</sup>

#### What the Referring Physician Needs to Know: Small Bowel Obstruction from Benign Causes

- In patients with symptoms and nonspecific plain radiographs, CT after oral administration of a contrast agent is recommended.
- When CT is not diagnostic, CT or MR enteroclysis can be performed.
- When nonsurgical management is considered, CT can exclude strangulated obstruction.
- CT is the most comprehensive method to determine the cause of SBO.

# Malignant Causes of Small Bowel Obstruction

# ETIOLOGY

Primary tumors of the small bowel are uncommon and constitute only 2% to 3% of all tumors of the gastrointestinal tract. However, small intestinal involvement from metastatic cancer is common. As cancer patients live longer with improved therapy, secondary tumors of the small bowel are becoming more likely.<sup>44</sup> The most common cause of SBO secondary to malignancy is secondary peritoneal implants, typically from intraabdominal tumors of ovaries, pancreas, stomach, or colon. Lymphatic spread rarely causes masses large enough to obstruct the small bowel. Hematogenous spread from distant sites is rare and is mainly caused by breast and lung cancer. Obstruction by a tumor can be caused by either direct invasion or extrinsic compression.

# PREVALENCE AND EPIDEMIOLOGY

Although the small bowel makes up 75% of the total length and more than 90% of the mucosal surface of the gastrointestinal tract, less than 2% of malignant neoplasms of the entire tract are primary small bowel neoplasms.<sup>45</sup> Malignant tumors account for 7% to 25% of cases of SBO.<sup>2</sup> Histologic evaluations of primary tumors showed lymphoma to be the most common tumor, followed by adenocarcinoma, carcinoid, and gastrointestinal stromal tumors (GISTs).<sup>46</sup> The incidence of metastatic cancer of the small bowel varies among different malignancies. Diffuse peritoneal carcinomatosis has been reported in up to 5% to 10% of patients with breast cancer and malignant melanoma. Other causes for peritoneal carcinomatosis are primary appendiceal mucinous tumors, peritoneal mesothelioma, and metastasis from ovarian malignancy.<sup>44</sup>

# CLINICAL PRESENTATION

Patients with SBO secondary to malignant neoplasm most frequently present with nonspecific symptoms of abdominal pain, associated with nausea and/or vomiting. Weight loss can be present because of the underlying malignancy. Clinical findings include abdominal distention with or without guarding and rigidity. A palpable abdominal mass can be present. Metastatic carcinoid tumors can manifest as flushing and diarrhea. GISTs are slow-growing tumors and are associated with a long period of symptoms. Patients are often anemic as a result of recurrent melena arising from ulcerated component. The time interval from diagnosis of the primary tumor to the development of SBO secondary to metastases varies widely and can be the initial manifestation of the tumor. Symptoms are related to tumor size, location within the small bowel, blood supply, and tendency to undergo ulceration and necrosis. In a patient with a known history of malignancy, obstructive symptoms, or bleeding from the gastrointestinal tract, a metastatic lesion must be considered.4

# PATHOPHYSIOLOGY

Malignant tumors can be found in any part of the small bowel. Primary neoplasms are most often located in the jejunum (41%), followed by ileum (33%) and duodenum (22%). In 4%, tumors could be found in multiple sites of the small bowel.<sup>47</sup> The duodenum is the most frequent location of small bowel adenocarcinoma. Most carcinoid tumors of the small bowel occur in the appendix and distal ileum, which is also the most common site of clinically significant carcinoid tumors. Lymphoma occurs most commonly in the distal and terminal ileum, whereas GISTs are mostly found in ileum and jejunum.<sup>45</sup>

# PATHOLOGY

Adenocarcinoma, carcinoid tumor, lymphoma, and GIST are primary malignant tumors of the small bowel. Adenocarcinomas of the duodenum are polypoid, ulcerated, or infiltrative. In the jejunum and ileum, adenocarcinomas are mostly annular, constricting, and particularly ulcerated; the remainder are polypoid and fungating.<sup>45</sup>

Most of the non-Hodgkin's lymphomas are of B-cell type, except for the sprue-related T-cell lymphoma.<sup>48</sup> Hodgkin's disease accounts for only approximately 1% of all malignant lymphomas of the gastrointestinal tract. In adults, the most common lymphoma is histiocytic, whereas in children it is the well-differentiated lymphocytic type. A poor prognosis is associated with large tumor size, ulceration, multicentric origin, and presence of involved lymph nodes. Small bowel carcinoids are usually submucosal-intramural tumors that bulge slightly into the lumen. They can become polypoid and cause intussusceptions or obstruction as they enlarge. More often, carcinoid-related obstructions are of lower grade and result from desmoplastic response rather than the mass effect of the tumor. GISTs arise from the muscular coats of the bowel wall and are most frequently subserosal and exoenteric. However, they may grow toward the bowel lumen and become polypoid. They assume a round or oval shape and frequently have a central area of mucosal ulceration that causes a high incidence of intestinal bleeding.<sup>45,49</sup>

#### IMAGING

The diagnosis of malignant tumors as a cause of SBO is difficult. Because they are very rare, the index of suspicion is generally low. Symptoms are usually nonspecific and might be the same as symptoms caused by more common causes of SBO, such as adhesions. The workup should be the same as the general diagnostic workup for SBO, regardless of the underlying cause.<sup>44</sup>

# Radiography

Contrast radiography remains the cornerstone of diagnosis for small bowel tumors. Enteroclysis has been considered a very useful diagnostic method for the detection of small bowel tumors. The bowel obstruction resulting from malignant tumors manifests with the same radiologic signs as do benign causes and was described previously. Additional findings are present on radiography and can be nonspecific, as in the form of diffuse thickening of mucosal folds with or without nodular filling. More specific findings depend on the underlying tumor.

Lymphoma is characterized by the presence of a narrowed segment of small bowel with nodular filling defects, aneurysmal dilatation of a bowel loop, and a polypoid or excavated mass. A large mass with necrosis and ulcerations, resulting in irregular cavities filled with barium as well as excavation and fistula formation, is suggestive of a GIST.<sup>49</sup> Primary adenocarcinomas of the small bowel most often manifest as solitary lesions located in the jejunum and are characterized on radiography by a polypoid mass with annular stricture and filling defects. On barium examination, the usual radiologic abnormality of a small bowel primary adenocarcinoma is the "apple core" lesion.<sup>50</sup> This is a short, annular, circumferentially narrowed segment with features of mucosal destruction. It is frequently ulcerated and separated from the normal bowel wall above and below it by overhanging edges. The malignant stricture is usually central in position, rigid, and without change of shape during compression. The ulcerating form of adenocarcinoma appears as a short, narrow lesion usually with an inconspicuous and mostly central ulcer. A polypoid mass that intussuscepts is also a rare manifestation of adenocarcinoma.45

Carcinoid tumors of the small bowel are commonly found in the distal ileum. They are associated with a broader spectrum of radiologic appearances, such as filling defects, strictures, kinking, stretching, thickening of the valvulae conniventes, and fixation of the bowel loops.<sup>45,49</sup>

In metastases, the mechanism of tumor spread influences its radiographic appearance. Metastasis through intraperitoneal seeding is most commonly observed in pelvic small bowel loops and in the ileocecal region. When metastases are deposited on the serosal surface of a small bowel segment, rounded protrusions toward the lumen of lesions at least 1 cm in diameter can be demonstrated by a carefully performed contrast-enhanced examination. Metastatic infiltration and fixation of folds at the affected bowel edge are accentuated by a divergence of folds toward the unaffected side. An associated fibrous reaction may lead to angulation and tethering of folds.<sup>49</sup> The neoplastic implants (e.g., gastrointestinal, ovarian, and uterine) typically grow in relation to the concave or mesenteric border of bowel loops and can incite fibrosis. The early radiologic changes in hematogenous metastases to the small bowel are usually multiple nodules, seen mostly along the antimesenteric border, where the vasa rectae arborize into a rich submucosal plexus. Metastases can be seen generally as polypoid masses, which tend to be large and multiple and have a worse prognosis. Infiltrating ulcerative lesions may be seen as well. Early melanoma metastases to the small bowel usually exhibit smooth, rounded polypoid lesions of different sizes. The demonstration on barium examination of a nonobstructing, fairly large intraluminal mass favors the diagnosis of melanoma metastasis. This is due to the softness of the highly cellular mass, which contains little stroma. Metastases from lung cancer to the small bowel may be shown as single or multiple discrete intraluminal lesions, either flat or polypoid, that are frequently ulcerated.45,49

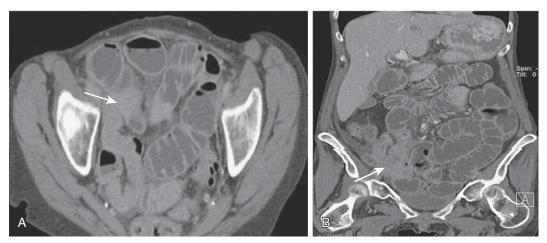
#### Computed Tomography

CT can directly depict tumors of the bowel wall as well as adjacent structures, which can all be involved in malignant neoplastic processes and cause SBO by external compression. CT is useful to assess the local extent and screen for distant metastases. The sign suggestive of malignancy is a mass larger than 2 cm with soft tissue density that extends from the lumen to the serous surface. Other manifestations are eccentric or asymmetric mural thickening with compression of the lumen with proximally dilated and distally collapsed bowel and lobulated borders.

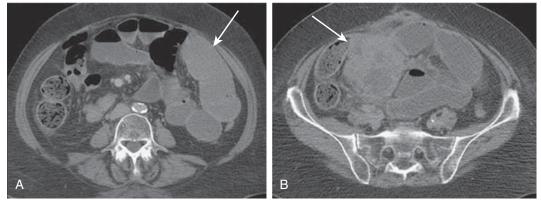
In their CT presentation, adenocarcinomas are solitary soft tissue masses causing lumen narrowing and obstruction. The lesions may be heterogeneous in attenuation and show moderate enhancement after intravenous contrast medium administration. Mesenteric extension should be suggested in patients with large mesenteric masses with heterogeneous attenuation and associated asymmetric narrowing of the small bowel wall. Regional lymph nodes, liver, peritoneal surfaces (Figure 25-17), and ovaries may be involved by mesenteric spread.<sup>49</sup>

Lymphoma usually appears as a hypodense wall thickening that may be associated with nodal enlargement (Figure 25-18). In contrast to adenocarcinoma and leiomyosarcoma, which tend to produce a focal or segmental lesion, lymphoma of the small bowel originates at multiple sites and extends along the axis of the small bowel. The principal radiologic manifestation of small bowel lymphoma is circumferential segmental infiltration, endoenteric or exoenteric disease with cavitation, aneurysmal dilatation, polypoid lesions, mesenteric nodal lymphoma with secondary infiltration of the small bowel, and the possible transformation of diffuse nodular lymphoid hyperplasia into lymphoma (see Figure 25-18). The infiltrating form generally displays moderate lumen widening and is the most common radiologic appearance, closely followed by the cavitary form.<sup>45,49</sup>

CT is extremely valuable in showing the extent of spread of a carcinoid tumor, which typically appears as a hypervascular mass with homogeneous attenuation in the root of the mesentery (Figure 25-19). Desmoplastic response is associated with the mass in a characteristic pattern. More often, carcinoidrelated obstructions are of lower grade and result from fibrosis



**Figure 25-17** Omental metastasis from endometrial cancer. A 67-year-old woman with a known history of endometrial cancer treated with total abdominal hysterectomy with bilateral salpingo-oophorectomy presented with signs of bowel obstruction. She had been followed for nearly 5 years after surgery, during which remained asymptomatic. **A**, Axial computed tomography image demonstrates dilated fluid-filled small bowel with nodular deposits of enhancing tissue at the serosal surface in the pelvis. There is obstruction (*arrow*) to the loops because of these deposits, which is convincingly demonstrated on the coronal reformatted image (*arrow*, **B**). This patient had metastatic endometrial cancer with peritoneal and serosal implants causing bowel obstruction.



**Figure 25-18** Lymphoma. A 53-year-old woman presented with small bowel obstruction. There was a recent history of treated lymphoma. A, Axial contrast-enhanced computed tomography image shows dilated loops of small bowel with air/fluid levels (*arrow*) up to a heterogeneously enhancing mass in the right lower quadrant (*arrow*, **B**). The loops of small bowel in close proximity to this mass are tethered to it, resulting in obstruction. This was diagnosed as a case of lymphomatous involvement of the small bowel.

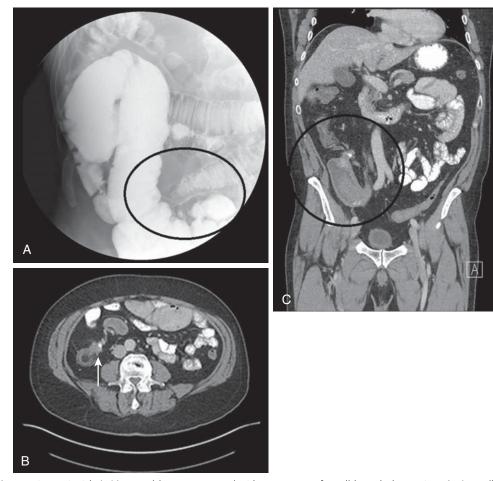
rather than the mass effect of the tumor. Local serotonin output produces hypertrophy of the muscularis and fibrosis with crowding of folds and kinking of the lumen. This fibrosis is responsible for the fixation, kinking, and angulation seen on the small bowel series and the stellate soft tissue density mass on CT scan examinations.<sup>45</sup>

Among all primary malignant tumors of the small bowel, GISTs account for 9% of the cases. Benign leiomyomas and GISTs cannot be differentiated radiographically. Usually, smooth muscle cell tumors that are large or show significant ulceration are malignant. GISTs usually appear as an extrinsic mass displacing small bowel loops, owing to the predominant extraluminal growth pattern. Flattening, stretching, and possible ulceration of the mucosa can be seen. Adjacent loops may adhere to the mass as a result of infiltration or tethering by the considerable saprophytic blood supply.<sup>49</sup> The characteristic CT pattern of a GIST is that of a bulky lesion, growing exoenterically. The soft tissue component of the tumor usually shows significant enhancement after intravenous contrast agent

administration. Liposarcoma, angiosarcoma, and fibrosarcoma of the small bowel are rare tumors and are radiologically indistinguishable from GISTs.<sup>45,49</sup>

# Magnetic Resonance Imaging

The role of MRI in small bowel tumors has not been fully evaluated; however, the technique is able to provide information on morphologic characteristics and internal constituents of tumors with benefits of direct multiplanar capability, excellent soft tissue contrast, and increased capability for assessing the biochemical changes.<sup>26</sup> Also, high contrast between a tumor and the adjacent bowel or surrounding fat enables MRI to depict the extent of lesions, especially with combined use of nonsuppressed T1-weighted and gadolinium-enhanced fat-suppressed T1-weighted images. Small bowel adenocarcinoma may appear on MRI as either a focal rounded mass with extraluminal growth or as an annular constricting lesion narrowing the bowel lumen. Lymphoma typically demonstrates asymmetric but circumferential wall thickening, often associated with



**Figure 25-19** Mesenteric carcinoid. A 64-year-old man presented with symptoms of small bowel obstruction. **A**, A small bowel follow-through (SBFT) performed at another hospital raised concern for a point of transition in the right lower quadrant. An image from the SBFT shows dilated bowel loops that appear tethered together. On retrospective evaluation, a very faint calcific density was noted on the radiograph done before administration of oral contrast. **B**, Axial contrast enhanced computed tomography images demonstrate dilated small bowel with a change in caliber at the level of a small partially calcified soft tissue mass abutting the wall of the distal ileum (*arrow*). **C**, Coronal reformatted images show thickened loops of ileum just proximal to the anastomosis, suggestive of desmoplastic response to the carcinoid tumor and a puckered appearance of the mesentery locally. The patient was taken to the operating room, and resection of the ileal carcinoid was performed.

marked luminal dilatation and mesenteric lymphadenopathy, and a homogeneous, slightly increased signal intensity on T2-weighted images combined with moderate gadolinium enhancement. Carcinoid tumors typically appear as an ill-defined homogeneous mass that displaces bowel loops and may exhibit very low signal intensity on T2-weighted images and strong gadolinium enhancement.<sup>51</sup>

# Ultrasonography

Ultrasonography has limited utility for the diagnosis of neoplasms; however, if used, it may be able to locate intraluminal, intramural, and extraluminal growth patterns, as well as those tumors with "dumbbell" shapes. It also detected metastases, particularly those with necrotic centers. In lymphomas of the small bowel a "sandwich" sign has been described, caused by mural lymphomatous infiltrates and dilation of the bowel lumen. Lymphomatous infiltrates are usually anechoic.<sup>52</sup>

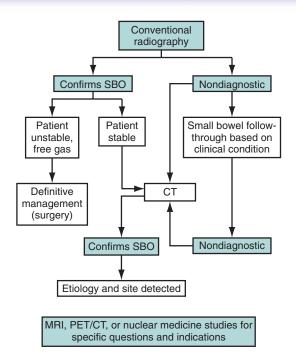
### Nuclear Medicine

Scintigraphy with indium-111 octreotide or <sup>99m</sup>Tc-octreotate is the gold standard for detection of somatostatin receptor-

positive tumors such as carcinoid tumors of the small bowel. Despite the wide spectrum of imaging methods, carcinoid tumors can remain hidden before surgery. CT and MRI are efficient in the detection of larger primary tumors (>1 cm) and liver and lymph node metastases. The efficiency of scintigraphy in the detection of carcinoids is 75% to 80%, and the efficiency of scintigraphy followed by radio-guided surgery exceeds 90%.<sup>53</sup> Small intestine carcinoids with a relatively high malignant potential can cause serious challenges in visualization. CT, MRI, and endoscopic capsules are insufficient, especially for the detection of small submucosal lesions.<sup>54</sup>

# Positron Emission Tomography With Computed Tomography

In SBO caused by primary tumors or metastatic disease, PET images can detect focal fluorodeoxyglucose (FDG) activity in the abdomen. Coregistration of FDG-PET with CT images enables detection and localization of malignant lesions in the small bowel. The diagnosis of SBO by malignant tumor can be made by identification of an FDG-active point in combination with typical CT signs for SBO.<sup>55</sup> However, it can be difficult to



**Figure 25-20** Imaging algorithm for suspected small bowel obstruction. *CT*, Computed tomography; *MRI*, magnetic resonance imaging; *PET*, positron emission tomography; *SBO*, small bowel obstruction.

differentiate nodal from intestinal disease based on the pattern of FDG uptake. Apparent accumulation of FDG in the small bowel may be a spurious finding resulting from a combination of normal peristaltic activity, gastrointestinal lymphoid tissue, and excreted radiotracer within the bowel lumen. Although such bowel activity can be intense, it tends to be diffuse rather than focal or multifocal.<sup>56</sup>

# Imaging Algorithm

An imaging algorithm is provided in Figure 25-20.

#### Classic Signs: Malignant Causes of Small Bowel Obstruction

- Lymphoma: Aneurysmal dilation and polypoid mass
- GIST: Mass with necrosis and ulcerations with excavations and fistula
- Adenocarcinoma: "Apple core" lesion
- Carcinoid tumor: Mass with radiating fibrous strands

# TREATMENT

# Medical Treatment

Patients with SBO caused by a malignant tumor are initially managed like patients with SBO from adhesions to remove the acute obstruction, followed by resection of the underlying malignancy. The most challenging situation is found in patients who have been treated for a malignant tumor or patients with peritoneal carcinomatosis.<sup>4,5</sup>

# Surgical Treatment

The indication for laparotomy remains clinical, depending on the patient's symptoms. It also depends on the patient's ability to undergo surgery as well as on the extent of the primary tumor or metastatic spread. Retrospective analysis showed that approximately 35% of patients with cancer were diagnosed with complete SBO and that 96% of these patients required surgery. Approximately half of the patients with partial SBO can be successfully managed without surgery. The entire bowel must be examined during surgery to exclude multiple lesions. Operative treatment has a better outcome than nonoperative management in terms of symptom-free interval and reobstruction rates. However, it is marked by high postoperative morbidity. After a short trial of nasogastric decompression, patients with obstruction secondary to malignant disease should be operated on if clinical factors indicate that they will survive the operation.<sup>32,57</sup>

# What the Referring Physician Needs to Know: Malignant Causes of Small Bowel Obstruction

- Metastatic conditions causing SBO should be suspected in patients with known primary tumors.
- Clinical symptoms are nonspecific, and a high index of suspicion coupled with images is essential for diagnosis.
- CT is the mainstay in imaging evaluation because it is capable of identifying the cause and most often the site and severity of SBO and associated complications if present.
- Scintigraphy has a role in diagnosis of carcinoid tumors, which are often evasive.
- PET/CT can be used to detect the presence of malignant involvement of bowel if there is a diagnostic dilemma.

#### Key Points

# **General Considerations**

- Adhesions, Crohn's disease, neoplasia, and hernia are the most common causes of SBO.
- Conventional abdominal radiography is used for initial evaluation.
- Partial obstructions benefit from extended nonsurgical management.
- Most patients with complete SBO are managed after initial resuscitation because of risk for strangulation.

# **Benign Causes**

- Benign causes comprise 70% to 80% of all cases of SBO.
- CT can reliably detect the severity and location of SBO, as well as complications and causes.
- MRI, ultrasonography, and other methods are used for disease- or patient-specific indications.

#### Malignant Causes

- Primary tumors of the small bowel are rare and constitute only 2% to 3% of gastrointestinal tract tumors.
- The most common cause of malignant SBO is a peritoneal implant from an intraabdominal tumor.
- Hematogenous spread from the small bowel is mainly from breast and lung carcinoma.
- Treatment is directed at removing the acute obstruction, followed by removal of the underlying tumor.

# REFERENCES

- Zielinski MD, Eiken PW, Bannon MP, et al: Small bowel obstruction: who needs an operation? A multivariate prediction model. *World J* Surg 34:910–919, 2010.
- Miller G, Boman J, Shrier I, et al: Etiology of small bowel obstruction. Am J Surg 180:33–36, 2000.
- Herlinger H, Maglinte DDT: Small bowel obstruction. In Herlinger H, Maglinte DDT, editors: *Clinical radiology of the small intestine*, Philadelphia, 1989, WB Saunders, pp 479–507.
- Hayanga AJ, Bass-Wilkins K, Bulkley GB: Current management of small bowel obstruction. Adv Surg 39:1–33, 2005.
- Bass KN, Jones B, Bulkley GB: Current management of small-bowel obstruction. Adv Surg 31:1–34, 1997.
- Alexander JW, Boyce ST, Babcock GF, et al: The process of microbial translocation. *Ann Surg* 212:496–510, 1990.
- 7. Maglinte DD, Reyes BL, Harmon BH, et al: Reliability and role of plain film radiography and CT in the diagnosis of small bowel obstruction. *AJR Am J Roentgenol* 167:1451–1455, 1996.
- Nolan DJ, Marks CG: The barium infusion in small intestinal obstruction. *Clin Radiol* 32:651– 655, 1981.
- Maglinte DDT, Miller RE: Intubation infusion method: reliability in diagnosis of mechanical partial small-bowel obstruction. *Mt Sinai J Med* 51:372–377, 1984.
- Ericksen AS, Krasna MJ, Mast BA, et al: Use of gastrointestinal contrast studies in obstruction of the small and large bowel. *Dis Colon Rectum* 33:56–64, 1990.
- 11. Maglinte DD, Kelvin FM, O'Connor K, et al: Current status of small bowel radiography. *Abdom Imaging* 21:247–257, 1996.
- Maglinte DDT, Lappas JC, Kelvin FM, et al: Small bowel radiography: how, when and why? *Radiology* 163:297–305, 1987.
- Taverne PP, van der Jagt EJ: Small bowel radiography: a prospective comparative study of three techniques in 200 patients. *Rofo* 143:293–297, 1985.
- Maglinte DDT, Peterson LA, Vahey TN, et al: Enteroclysis in partial small-bowel obstruction. *Am J Surg* 147:325–329, 1984.
- Shrake PD, Rex DK, Lappas JC, et al: Radiographic evaluation of suspected small-bowel obstruction. Am J Gastroenterol 86:175–178, 1991.
- Maglinte DD, Balthazar EJ, Kelvin FM, et al: The role of radiology in the diagnosis of small bowel obstruction. *AJR Am J Roentgenol* 168:1171– 1180, 1997.
- Megibow AJ, Balthazar EJ, Cho KC, et al: Bowel obstruction: evaluation with CT. *Radiology* 180:313–318, 1991.
- Fukuya T, Hawes DR, Lu CC, et al: CT diagnosis of small-bowel obstruction: efficacy in 60 patients. *AJR Am J Roentgenol* 158:765–769, 1992.
- Maglinte DDT, Gage SN, Harmon BH, et al: Obstruction of the small intestine: accuracy and role of CT in diagnosis. *Radiology* 186:61–64, 1993.
- Qalbani A, Paushter D, Dachman AH: Multidetector row CT of small bowel obstruction. *Radiol Clin North Am* 45:499–512, 2007.

- Jaffe TA, Martin LC, Miller CM, et al: Abdominal pain: coronal reformations from isotropic voxels with 16-section CT—reader lesion detection and interpretation time. *Radiology* 242: 175–181, 2007.
- 22. Shah ZK, Uppot RN, Wargo JA, et al: Small bowel obstruction: the value of coronal reformatted images from 16-multidetector computed tomography—a clinicoradiological perspective. J Comput Assist Tomogr 32:23–31, 2008.
- Gulati K, Shah ZK, Sainani N, et al: Gastrointestinal labeling for MDCT of abdomen: comparison of low density barium and low density barium in combination with water. *Eur Radiol* 18:868–873, 2008.
- Lee JK, Marcos HB, Semelka RC: MR imaging of the small bowel using the HASTE sequence. AJR Am J Roentgenol 170:1457–1463, 1998.
- Chou CK, Liu GC, Chen LT, et al: The use of MRI in bowel obstruction. *Abdom Imaging* 18:131–135, 1993.
- 26. Regan F, Beall DP, Bohlam ME, et al: Fast MR imaging and the detection of small bowel obstruction. *AJR Am J Roentgenol* 170:1465–1469, 1998.
- Laghi A, Carbone I, Paolantonio P, et al: Polyethylene glycol solution as an oral contrast agent for MR imaging of the small bowel. *Acad Radiol* 9:S355–S356, 2002.
- Umschaden HW, Szolar D, Gasser J, et al: Small bowel disease: comparison of MR enteroclysis images with conventional enteroclysis and surgical findings. *Radiology* 215:717–725, 2000.
- Schmutz GR, Benko A, Fournier L, et al: Small bowel obstruction: role and contribution of sonography. *Eur Radiol* 7:1054–1058, 1997.
- 30. Suri S, Gupta S, Sudhakar PJ, et al: Comparative evaluation of plain films, ultrasound and CT in the diagnosis of intestinal obstruction. *Acta Radiol* 40:422–428, 1999.
- Burkill G, Bell J, Healy J: Small bowel obstruction: the role of computed tomography in its diagnosis and management with reference to other imaging modalities. *Clin Radiol* 56:350– 359, 2001.
- Williams SB, Greenspon J, Young HA, et al: Small bowel obstruction: conservative vs. surgical management. *Dis Colon Rectum* 48:1140– 1146, 2005.
- Lo CY, Lau PWK: Small bowel phytobezoars: an uncommon cause of small bowel obstruction. *Aust N Z J Med* 64:187–189, 1994.
- Ciftci AO, Tanyel FC, Buyukpamukcu N, et al: Adhesive small bowel obstruction caused by familial Mediterranean fever: the incidence and outcome. J Pediatr Surg 30:577–579, 1995.
- Chiedozi LC, Aboh IO, Piserchia NE: Mechanical bowel obstruction: review of 316 cases in Benin City. *Am J Surg* 139:389–393, 1980.
- 36. Grassi R, Di Mizio R, Pinto A, et al: Serial plain abdominal film findings in the assessment of acute abdomen: spastic ileus, hypotonic ileus, mechanical ileus and paralytic ileus. *Radiol Med* 108:56–70, 2004.
- Delabrousse E, Bartholomot B, Sohm O, et al: Gallstone ileus: CT findings. *Eur Radiol* 10:938– 940, 2000.

- Furukawa A, Saotome T, Yamasaki M, et al: Cross-sectional imaging in Crohn disease. *Radiographics* 24:689–702, 2004.
- Gore RM, Balthazar EJ, Ghahremani GG, et al: CT features of ulcerative colitis and Crohn's disease. AJR Am J Roentgenol 167:3–15, 1996.
- Kim AY, Bennett GL, Bashist B, et al: Small bowel obstruction associated with sigmoid diverticulitis: CT evaluation in 16 patients. *AJR Am J Roentgenol* 170:1311–1313, 1998.
- Gayer G, Zissin R, Apter S, et al: Adult intussusceptions: a CT diagnosis. *Br J Radiol* 75:185– 190, 2002.
- Gourtsoyiannis N, Papanikolaou N, Grammatikakis J, et al: MR enteroclysis: technical considerations and clinical applications. *Eur Radiol* 12:2651–2658, 2002.
- 43. Madsen SM, Thomsen HS, Munkholm P, et al: Inflammatory bowel disease evaluated by lowfield magnetic resonance imaging: comparison with endoscopy, 99mTc-HMPAO leucocyte scintigraphy, conventional radiography and surgery. Scand J Gastroenterol 37:307–316, 2002.
- Idelevich E, Kashtan H, Mavor E, et al: Small bowel obstruction caused by secondary tumors. *Surg Oncol* 15:19–32, 2006.
- Korman MU: Radiologic evaluation and staging of small intestine neoplasms. *Eur J Radiol* 42:193–205, 2002.
- Nagi B, Verma V, Vaiphei K, et al: Primary small bowel tumors: a radiologic-pathologic correlation. *Abdom Imaging* 26:474–480, 2001.
- Garcia Marcilla JA, Sanchez Bueno F, Aguilar J, et al: Primary small bowel malignant tumors. *Eur J Surg Oncol* 20:630–634, 1994.
- Kojima M, Nakamura S, Kurayabashi Y, et al: Primary malignant lymphoma of the intestine: clinicopathologic and immunohistochemical studies of 39 cases. *Pathol Int* 45:123–130, 1995.
- Maglinte DDT, Herlinger H: Small bowel neoplasms. In Maglinte DDT, Herlinger H, Birnbaum BA, editors: *Clinical imaging of the small intestine*, ed 2, New York, 1999, Springer, pp 377–438.
- Maglinte DDT, Reyes BL: Small bowel cancer: radiologic diagnosis. *Radiol Clin North Am* 35:361–380, 1997.
- 51. Kim KW, Ha HK: MRI for small bowel diseases. Semin Ultrasound CT MR 24:387–404, 2003.
- Miller JH, Hindman BW, Lam AH: Ultrasound in the evaluation of small bowel lymphoma in children. *Radiology* 135:409–414, 1980.
- Benjegård SA, Forssell-Aronsson E, Wängberg B, et al: Intraoperative tumour detection using 111In DTPA-d-Phe-octreotide and a scintillation detector. *Eur J Nucl Med* 28:1456–1462, 2001.
- 54. Caplin ME, Buscombe JR, Hilson AJ, et al: Carcinoid tumour. *Lancet* 352:799–805, 1998.
- Strobel K, Skalsky J, Hany TF, et al: Small bowel invagination caused by intestinal melanoma metastasis: unsuspected diagnosis by FDG-PET/ CT imaging. *Clin Nucl Med* 32:213–214, 2007.
- Sam JW, Levine MS, Farner MC, et al: Detection of small bowel involvement by mantle cell lymphoma on F-18 FDG positron emission tomography. *Clin Nucl Med* 27:330–333, 2002.
- Miller G, Boman J, Shrier I, et al: Small-bowel obstruction secondary to malignant disease: an 11-year audit. *Can J Surg* 43:353–358, 2000.

# Acute and Chronic Small Bowel Ischemia

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# **Etiology**

Acute mesenteric ischemia of the small bowel has four major causes: (1) arterial embolism, (2) arterial thrombosis, (3) non-occlusive mesenteric ischemia, and (4) mesenteric venous thrombosis (Table 26-1). Less common causes include aortic dissection, spontaneous dissection of the celiac or superior mesenteric artery (SMA), and vasculitis.<sup>1,2</sup> The common end result is an acute reduction in splanchnic blood flow that can lead to bowel necrosis.

# PREVALENCE AND EPIDEMIOLOGY

Acute mesenteric ischemia affects approximately 1% of patients with acute abdomen and increases in incidence with age.<sup>2-5</sup> Mortality rates exceed 60%, exacerbated by delays in diagnosis.

Arterial embolism, the most frequent cause of acute mesenteric ischemia, is implicated in up to 50% of cases<sup>6</sup> and most often involves the SMA. The embolus is usually of cardiac origin; hence, myocardial infarction, arrhythmia, valvular disease, and ventricular aneurysm are important risk factors.<sup>6</sup>

Acute SMA thrombosis is the second most common cause of acute mesenteric ischemia, accounting for 25% of cases,<sup>6</sup> usually in the setting of severe atherosclerosis. Hypercoagulability is another important risk factor.

Nonocclusive mesenteric ischemia, implicated in 20% of patients with acute mesenteric ischemia, has a mortality rate as high as 70%.<sup>7</sup> It is most often seen in patients older than age 50 years with reduced cardiac output, hypovolemia, or hypotension. A low-flow state results in diffuse mesenteric vasoconstriction, which may be exacerbated in patients on vasopressor therapy.<sup>6</sup> The incidence of nonocclusive mesenteric ischemia is declining, presumably owing to advances in critical care medicine, including the use of vasodilator therapy.

Mesenteric venous thrombosis accounts for approximately 18% of cases of acute mesenteric ischemia.<sup>6</sup> It has a poor prognosis with a long-term survival of 30% to 40%. Mesenteric venous thrombosis is considered acute when symptoms are present for less than 4 weeks. Risk factors include recent surgery, trauma, inflammatory disorders such as pancreatitis, and hypercoagulable states.

# **CLINICAL PRESENTATION**

The clinical presentation of acute mesenteric ischemia is nonspecific and may mimic other common disease processes such as small bowel obstruction or pancreatitis. The presentation is also a function of the specific pathologic process that is compromising splanchnic blood flow—SMA embolism or thrombosis, nonocclusive mesenteric ischemia, or mesenteric venous thrombosis (see Table 26-1). Because of the nonspecificity of manifestation, delays in diagnosis are common and many cases progress to bowel infarction.

Acute mesenteric ischemia classically manifests as acute abdominal pain that is disproportional to the findings on physical examination.<sup>1</sup> Other findings may include dehydration, tachycardia, and altered mental status. Nonspecific laboratory findings such as an elevated serum lactate level and leukocytosis may be found with all major causes of acute mesenteric ischemia.

Both SMA occlusion and thrombosis may manifest acutely. Patients with SMA thrombosis, however, may report an antecedent history of postprandial pain, weight loss, and aversion to food. Because these symptoms are associated with chronic mesenteric ischemia secondary to atherosclerosis,<sup>6</sup> there may be an "acute on chronic" manifestation, in which there may be a better developed collateral circulation than in patients with SMA embolism.<sup>1</sup>

Patients with nonocclusive mesenteric ischemia are usually older, critically ill, intubated, or on vasopressor or digitalis therapy and may be unable to communicate symptoms.<sup>6</sup> Clinicians must have a high index of suspicion, particularly in patients with unexplained failure to thrive.

Patients with acute mesenteric venous thrombosis are more typically symptomatic than patients with chronic mesenteric venous thrombosis and may present with slowly progressive diffuse abdominal pain and distention.<sup>8,9</sup> Bloody ascites, dehydration, hemoccult-positive stool, and hypotension may be associated findings.<sup>6</sup>

# ANATOMY AND PATHOPHYSIOLOGY

The arterial supply of the small bowel is predominantly from the celiac axis and SMA. The inferior mesenteric artery and the internal iliac arteries may become important contributors in the setting of arterial disease.

The celiac artery gives origin to the left gastric artery, and then it bifurcates into the splenic and common hepatic arteries (Figure 26-1). The gastroduodenal artery is a branch of the common hepatic artery and gives off, among other vessels, the superior pancreaticoduodenal arteries.

The SMA arises from the anterior aspect of the aorta at the level of the L1 vertebral body (Figure 26-2) and supplies the duodenum, small bowel, and colon proximal to the splenic flexure. The inferior pancreaticoduodenal artery arises from the SMA as the first branch and anastomoses with the superior

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pancreaticoduodenal artery, forming the pancreaticoduodenal arcades (Figure 26-3). The middle colic artery may arise from the right side of the SMA to supply the transverse colon. It bifurcates into a right branch, which anastomoses with the right colic artery, and a left branch, which anastomoses with the ascending branch of the left colic artery (Figure 26-4). Multiple jejunal and ileal arteries as well as the right colic artery supplying the ascending colon arise from the SMA. More distally, the SMA terminates in the ileocolic artery, which supplies the terminal ileum, cecum, and ascending colon.

The inferior mesenteric artery arises from the left aspect of the aorta at the level of the L3 vertebral body (see Figure 26-4). It divides into the left colic, sigmoid, and superior hemorrhoidal arteries, which supply the descending colon, sigmoid

TABLE 26-1	Clinical Features of Acute Small Bowel Ischemia			
Cause		Onset of Presentation	Associated Features	
SMA embolism		Acute	Myocardial infarction, arrhythmia, ventricular aneurysm, valvular disease, prior embolic event	
SMA thrombosis		Acute or acute on chronic	Atherosclerotic disease, hypercoagulable state	
Nonocclusive mesenteric ischemia		Acute, failure to thrive	Critical illness, hypotension, myocardial infarction, sepsis, disseminated intravascular coagulation, vasopressors	
Mesenteric venous thrombosis		Acute (<4 wk) Chronic (≥4 wk)	Recent surgery, hypercoagulable state, oral contraceptive use	

SMA, Superior mesenteric artery.

colon, and rectum, respectively. The ascending branch of the left colic artery anastomoses with the left branch of the middle colic artery, a branch of the SMA. The superior hemorrhoidal artery anastomoses with branches of the anterior division of the internal iliac arteries.

The marginal artery, defined as the artery closest to and parallel with the mesenteric margin of the intestine, gives off the vasa rectae, which are small vessels that supply the bowel wall.<sup>10</sup> In the colon, this artery is termed the *marginal artery of Drummond* (see Figure 26-4). The middle colic artery may serve as the marginal artery for much of its distribution.<sup>10</sup>

The rich arterial supply of the bowel provides ample opportunity for collateral development in the setting of mesenteric arterial stenosis or occlusion (Figure 26-5). The superior and inferior pancreaticoduodenal arteries can provide important collaterals between the celiac axis and the SMA (see Figure 26-3). In addition, a persistent fetal arterial communication between the celiac axis and the SMA (often referred to as the arc of Buehler) may exist in up to 2% of patients. Collateral pathways between the superior and inferior mesenteric arteries primarily involve communication between the left and middle colic arteries via the arc of Riolan (Figure 26-6), located centrally in the mesentery, and the marginal artery of Drummond, located peripherally.<sup>11</sup> The internal iliac arteries also may provide collateral circulation to the principal mesenteric vessels.

The superior mesenteric vein is usually a single vessel that drains the small intestine and the ascending and transverse colon. Within the mesentery, the superior mesenteric vein courses anteriorly and to the right of the SMA (Figure 26-7) and joins the splenic vein to form the main portal vein. The inferior mesenteric vein, which drains the left colic, sigmoid, and superior hemorrhoidal veins, usually terminates in the splenic vein or the superior mesenteric vein. Portal-to-portal collaterals may develop in the setting of chronic superior mesenteric vein occlusion; these are often submucosal and are prone to bleeding.<sup>12</sup> Portal-to-systemic collaterals (varices) also may develop in portal hypertension.

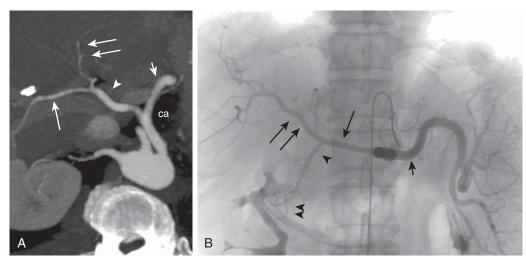


Figure 26-1 A, Maximum intensity projection from computed tomography angiogram of the abdomen demonstrates the celiac artery (ca), splenic artery (short arrow), common hepatic artery/hepatic artery proper (arrowhead), right hepatic artery (single long arrow), and left hepatic artery (double long arrows). The gastroduodenal artery is not shown. B, Selective contrast injection of the celiac artery demonstrates the splenic artery (short arrow), common hepatic artery (single long arrow), right hepatic artery (double long arrows), gastroduodenal artery (single arrowhead), and superior pancreaticoduodenal arcade (double arrowheads).

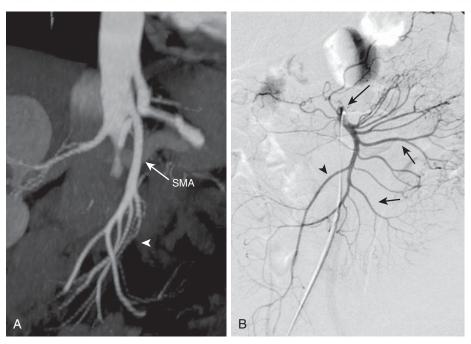
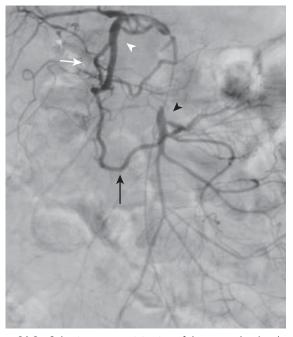


Figure 26-2 A, Maximum intensity projection from computed tomography angiogram of the abdomen demonstrates the superior mesenteric artery (SMA, long arrow) as well as jejunal and ileal branches (arrowhead). B, Selective contrast injection of the superior mesenteric artery (long arrow) demonstrates multiple jejunal and ileal branches (short arrows) as well as the ileocolic artery (arrowhead).



**Figure 26-3** Selective contrast injection of the gastroduodenal artery (*white arrowhead*) demonstrates the superior pancreaticoduodenal arteries (*white arrow*), which anastomose with the inferior pancreatico-duodenal arteries (*black arrow*) derived from the superior mesenteric artery (*black arrowhead*).

# PATHOLOGY

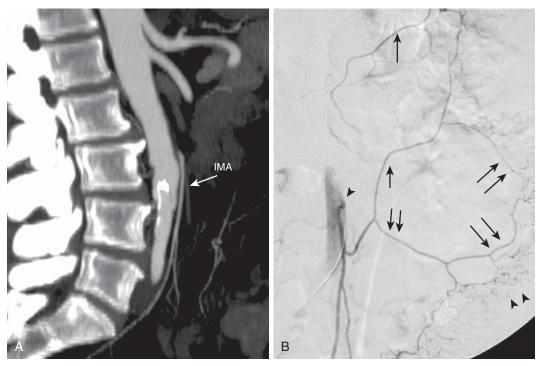
Mesenteric blood flow is regulated by perfusion pressure, oxygen demand, alpha- and beta-adrenergic stimulation, and humoral factors such as vasopressin.<sup>6</sup> At baseline, 20% to 25% of mesenteric capillaries may be open with considerable reserve

against changes in blood flow.<sup>11,13</sup> Although the bowel can tolerate a considerable reduction in mesenteric perfusion, when there is a prolonged mismatch between demand and supply, ischemia will ensue. Prolonged ischemia may result in tissue damage secondary to reperfusion injury, resulting in increased microvascular permeability.<sup>6,14</sup> Ultimately, compromise of the intestinal mucosal barrier may occur, mediated by oxygen free radicals.<sup>6,15</sup>

SMA emboli are most often of cardiac origin, with approximately one third of patients having a history of embolic events.<sup>6</sup> Arterial emboli typically involve the SMA because of the oblique angle of its origin, with approximately 15% occluding the origin. A majority of emboli, however, will lodge distally in the SMA at branch points, and the distribution of ischemic bowel in many cases will therefore involve the distal jejunum and ileum, while sparing the proximal jejunum. Large emboli that initially occlude the SMA origin may propagate distally and potentially obstruct collateral flow from the celiac artery and inferior mesenteric artery. The clinical presentation is acute, with insufficient time to develop a collateral perfusion.

The most common site of arterial thrombosis is the origin of the SMA. Because of progressive atherosclerotic disease, collateral circulation may have developed and thus symptoms occur only when there is disease of multiple mesenteric arteries and major collateral vessels or when thrombosis occurs with insufficient collateral support. Acute hemodynamic compromise, dehydration, or hypercoagulability in the setting of visceral artery stenosis may prompt the thrombotic event. In SMA thrombosis, a greater length of bowel may become ischemic or progress to infarction than with SMA embolus.

In nonocclusive mesenteric ischemia, diminished mesenteric arterial flow results from reduced perfusion pressure or vasoconstriction rather than from a physical impediment to blood flow. This reduced perfusion pressure resulting from various



**Figure 26-4** A, Maximum intensity projection from a computed tomography angiogram of the abdomen demonstrates the inferior mesenteric artery (*IMA, arrow*). B, Selective contrast injection of the inferior mesenteric artery (*single arrowhead*) demonstrates the ascending (*single short arrow*) and descending (*double short arrows*) branches of the left colic artery. The ascending branch anastomoses with the left branch of the middle colic artery (*single long arrow*), which is derived from the superior mesenteric artery. The marginal artery of Drummond (*double long arrows*) gives off arborizing vasa rectae (*double arrowheads*) to colon.

causes such as heart failure, hypotension, sepsis, disseminated intravascular coagulation, vasoconstrictive medications, and/or major surgery, eventually causes diffuse mesenteric vasoconstriction via autoregulatory mechanisms.

Mesenteric vein thrombosis, which is often associated with recent surgery, hypercoagulable state, or inflammatory disorders, usually begins in the venous arcades and can propagate to the superior mesenteric vein and portal vein. The inferior mesenteric vein is less frequently affected. Venous obstruction results in hypovolemia and hemoconcentration, arteriolar vasoconstriction, and reduced arterial inflow, ultimately leading to hemorrhagic bowel infarction. Infarcted bowel is segmental, and the transition between normal and ischemic bowel is typically more gradual compared with other causes of acute mesenteric ischemia.

# IMAGING

# Superior Mesenteric Artery Embolism

Because acute mesenteric ischemia may rapidly progress to bowel infarction, patients with peritoneal signs should proceed to emergent laparotomy. Nevertheless, imaging can play an important role in the diagnosis of SMA embolism and operative planning.

**Radiography.** Plain radiography is nonspecific in all causes of acute mesenteric ischemia and may be normal in one fourth of cases. Plain radiographs may demonstrate dilated fluid-filled bowel loops, suggesting a nonspecific ileus, thumbprinting from focal submucosal hemorrhage, or separation of bowel

loops as a result of mesenteric thickening. Pneumatosis (Figure 26-8), mesenteric or portal venous gas (Figure 26-9), and pneumoperitoneum indicate bowel infarction. Plain radiography may help exclude some other causes of abdominal pain such as bowel obstruction.

**Computed Tomography.** CT may demonstrate nonspecific fluid-filled dilated bowel with wall thickening, ascites, and mesenteric edema. CT also may demonstrate a water-halo sign, in which two concentric rings of different attenuation are seen in the bowel wall: either a high-attenuation outer ring with gray attenuation inner ring or vice versa.<sup>16</sup> Similarly, a target sign (Figure 26-10) may be seen, in which a central ring of gray attenuation is interposed between two rings of higher attenuation.<sup>16</sup> Inflammatory bowel disease may produce a similar appearance.

More specific findings include lack of bowel wall enhancement and infarcts of other visceral organs such as the kidney (Figure 26-11). CT angiography (CTA) increases the accuracy of the detection of an SMA embolus and should include initial noncontrast images for evaluation of vascular calcifications. CTA will demonstrate a filling defect within or nonopacification of the SMA (Figures 26-11 to 26-13), although sensitivity diminishes with more distal emboli. Few to no collateral vessels are demonstrated.

Late-stage findings such as pneumatosis (Figure 26-14), pneumoperitoneum, and mesenteric and portal venous gas factors (Figure 26-15) are markers of bowel infarction and necrosis.<sup>17</sup> CT is helpful to evaluate other causes of abdominal pain as well.

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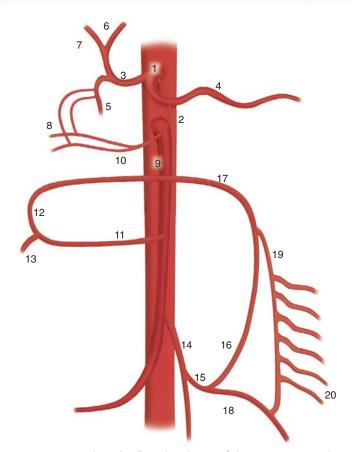


Figure 26-5 Selected collateral pathways of the mesenteric circulation. The celiac artery (1) gives off the common hepatic artery (3), splenic artery (4), and ultimately the gastroduodenal artery (5); the left (6) and right (7) hepatic arteries; and superior pancreaticoduodenal arteries (8). The superior mesenteric artery (9) gives off the inferior pancreaticoduodenal arteries (10) as well as the middle colic (11) artery, which gives off left (12) and right (13) branches. Collateral circulation between the celiac axis and superior mesenteric artery may occur via a persistent direct fetal communication known as the arc of Buehler (2) or via the pancreaticoduodenal arcades, formed by communication of the superior (8) and inferior (10) pancreaticoduodenal arteries. The inferior mesenteric artery (14) gives off the left colic artery (15), which divides into ascending (16) and descending (18) branches. Collateral circulation between the superior and inferior mesenteric arteries may occur through the arc of Riolan (17) or the marginal artery of Drummond (19). Jejunal and ileal branches (20) are also demonstrated.

**Magnetic Resonance Imaging.** Gadolinium-enhanced MR angiography (MRA) can be used to demonstrate SMA emboli<sup>1</sup> but is not the first-choice imaging modality in acute mesenteric ischemia, given long examination times that can delay treatment.

**Ultrasonography.** Although duplex sonography may detect occlusion at the origin of the SMA, more distal emboli may be missed. An occluded vessel will appear dilated and may contain echogenic debris with absent Doppler flow. Linear echogenic foci of intramural or portal venous gas may be detected and are signs of bowel infarction.<sup>3</sup> Ultrasonography is operator dependent and can be limited by bowel gas, body habitus, and patient noncooperation.



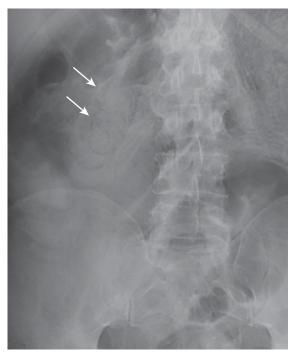
**Figure 26-6** Selective contrast injection of the inferior mesenteric artery (*arrowhead*) demonstrates a prominent arc of Riolan (*short arrow*). The arc of Riolan bridges the inferior and superior mesenteric arteries (*long arrow*).



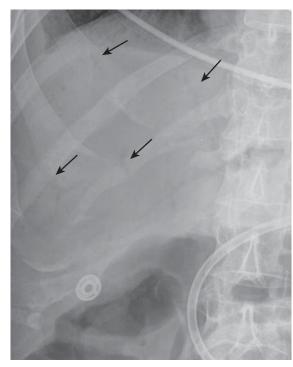
**Figure 26-7** Magnetic resonance angiogram demonstrates the superior mesenteric vein (*long arrow*) joining the splenic vein (*arrowhead*) to become the portal vein (*short arrow*).

**Nuclear Medicine.** There is no role for scintigraphy in the evaluation of SMA embolism.

**Positron Emission Tomography With Computed Tomography.** There is no role for positron emission tomography with



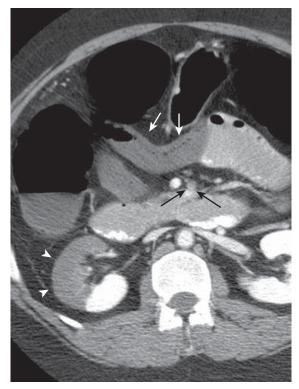
**Figure 26-8** Plain radiograph of the abdomen demonstrates curvilinear lucencies (*arrows*) within the bowel wall, consistent with pneumatosis.



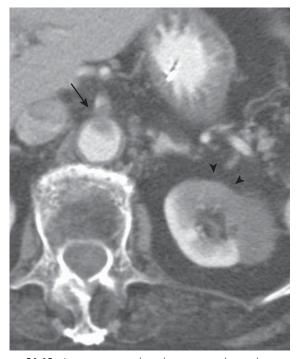
**Figure 26-9** Plain radiograph of the abdomen demonstrates branching linear lucencies (*arrows*) coursing to the periphery of the liver, consistent with portal venous gas.



**Figure 26-10** Intravenous and oral contrast-enhanced computed tomography scan of the abdomen and pelvis in a man with acute mesenteric ischemia of small bowel secondary to superior mesenteric artery embolism (not shown). A target sign (arrows) is characterized by an outer and inner hyperattenuating and middle hypoattenuating layer.



**Figure 26-11** Intravenous and oral contrast-enhanced computed tomography scan of the abdomen and pelvis demonstrates wedgeshaped areas of nonenhancement in the right kidney (*arrowheads*) consistent with infarct in a patient with superior mesenteric artery embolism (*black arrows*). Nonenhancement of bowel wall (*white arrows*) is also a sign of ischemia.



**Figure 26-12** Intravenous and oral contrast-enhanced computed tomography scan of the abdomen and pelvis demonstrates a filling defect (*arrow*) within the origin of the superior mesenteric artery, consistent with embolus. Focal nonenhancement in the left kidney (*arrow*-*heads*) is consistent with infarct and is further evidence of embolic phenomena.



**Figure 26-14** Intravenous and oral contrast-enhanced computed tomography of the abdomen and pelvis demonstrates linear foci of gas (*arrows*) within the wall of small bowel, consistent with pneumatosis intestinalis.

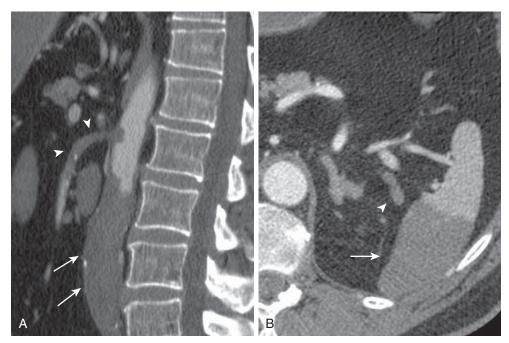
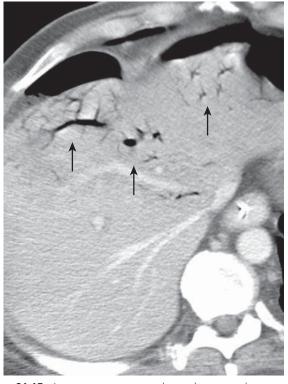


Figure 26-13 A, Intravenous contrast-enhanced computed tomography of the abdomen demonstrates embolic occlusion of the proximal superior mesenteric artery (arrowheads) as well as distal aorta (arrows). B, A wedge-shaped area of hypoattenuation in the spleen (arrow) is consistent with infarct from splenic artery embolism (arrowhead).



**Figure 26-15** Intravenous contrast-enhanced computed tomography of the abdomen and pelvis demonstrates branching foci of air attenuation (*arrows*) extending into the periphery of the liver, consistent with portal venous gas.

computed tomography (PET/CT) in the evaluation of SMA embolism.

**Angiography.** Angiography is the gold standard for the detection of SMA embolism, with sensitivity exceeding 90%.<sup>18</sup> Lateral aortography is used to evaluate the origins of the artery and celiac axis (Figure 26-16). Anteroposterior aortography is useful to assess the aorta, renal arteries, and distal mesenteric vessels. The angiographic diagnosis of acute embolus is made when a filling defect is demonstrated that at least partially obstructs the artery, with absence of collateral vessels.<sup>12</sup> Selective arteriography of the SMA can be performed in the absence of disease at its origin to assess for distal occlusion and may be accompanied by catheter-directed intervention, if appropriate.

Angiography, however, is invasive and time consuming and is associated with potential nephrotoxicity and other procedurerelated morbidities.

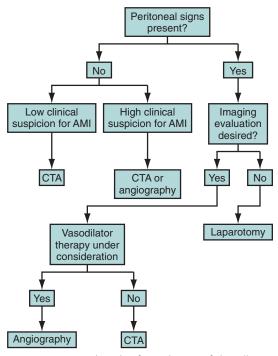
**Imaging Algorithm.** An imaging algorithm is provided in Figure 26-17. See also Table 26-2.

#### **Classic Signs: Superior Mesenteric Artery Embolism**

- Abdominal pain out of proportion to physical findings
- Filling defect within the SMA
- Lack of bowel wall enhancement
- Infarcts of other visceral organs
- Late findings: Pneumatosis, portomesenteric venous gas, pneumoperitoneum



**Figure 26-16** Lateral aortogram demonstrates a normal celiac artery (*arrow*) and origin of the superior mesenteric artery (*arrowhead*).



**Figure 26-17** Imaging algorithm for evaluation of clinically suspected occlusive acute mesenteric ischemia (*AMI*) of small bowel. The presence of peritoneal signs will prompt emergent laparotomy, although depending on the clinical situation, surgeon preference, and capacity to perform imaging quickly, imaging may be performed first. Patients with a high clinical suspicion for occlusive AMI who are not presenting with peritoneal signs may undergo imaging first to confirm the diagnosis; angiography may be preferred over computed tomography angiography fi transcatheter therapy is considered, although this may delay surgical therapy.

TABLE 26-2	Accuracy,	Limitations, and Pitfalls of Modalities Used	l in Imaging of Superior	Mesenteric Artery Embolism
Modal	ity	Accuracy	Limitations	Pitfalls
Radiog	graphy	Poor	Sensitivity 30% Nonspecific	May not suggest disease until late stage of bowel infarction/perforation
СТ		Sensitivity 64%-82%	Radiation	Distal emboli may be missed.
MRI		Although sufficient comparative data are lacking, sensitivity and specificity may be comparable to that for CT for vessel findings but less accurate for bowel findings.	Long examination times High cost	Suboptimal evaluation of stented vessels Tailored examination less able to assess abdomen for other pathologic process compared with CT
Ultrasc	onography	Accuracy diminishes with more distal emboli and is operator dependent.	Patient body habitus Bowel gas Patient cooperation	Distal emboli may be missed.
Nuclea	ar medicine	No role in the evaluation of acute mesenteric ischemia	Poor spatial resolution	
PET/C	Т	No role in the evaluation of acute mesenteric ischemia	Radiation High cost	
Angiog	graphy	Sensitivity 90%	Radiation Invasive	

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

#### Superior Mesenteric Artery Thrombosis

SMA thrombosis may manifest as "acute on chronic" symptoms. Atherosclerotic disease may affect several mesenteric vessels, with thrombotic occlusion of the SMA precipitating the acute clinical event.

**Radiography.** Plain radiography of the abdomen is nonspecific in all major causes of acute mesenteric ischemia.

**Computed Tomography.** CT and CTA are useful in the evaluation of SMA thrombosis. Bowel findings overlap with that of SMA embolism. As previously noted, CTA should initially include noncontrast images so as to evaluate for vascular calcifications that may otherwise be obscured. Stenosis or occlusion may be demonstrated in the origin of the superior mesenteric, inferior mesenteric, or celiac arteries and collateral vessels may be identified. Thrombosis of a previously stented mesenteric artery also may cause acute mesenteric ischemia (Figure 26-18). Three-dimensional (3D) image postprocessing can be useful in diagnosis and in planning revascularization.

**Magnetic Resonance Imaging.** Contrast-enhanced MRA may similarly demonstrate narrowing or cutoff of the SMA. Collateral vessels may be demonstrated. However, MRA is not advocated for the evaluation of acute mesenteric ischemia because long examination times can delay treatment.

**Ultrasonography.** Duplex sonography may demonstrate elevated peak systolic velocities in the proximal SMA, indicating stenosis, or lack of flow, suggesting occlusion. As with SMA embolism, ultrasonography is not advocated in the evaluation of acute mesenteric ischemia.

**Nuclear Medicine.** There is no role for scintigraphy in the evaluation of SMA thrombosis.

**Positron Emission Tomography With Computed Tomography.** There is no role for PET/CT in the evaluation of SMA thrombosis.



**Figure 26-18** Computed tomography angiogram in patient presenting with worsening abdominal pain demonstrates nonopacification of the superior mesenteric artery at the level of a stent (*arrow*) previously placed to treat chronic mesenteric ischemia. This is consistent with thrombosis that extends into the artery just distal (*arrowhead*) to the stent.

**Angiography.** Angiography can delineate important anatomic information, outline collateral vessels, and demonstrate visceral arterial stenoses and occlusions. The salient findings are non-opacification of the origin of the SMA and reduced bowel opacification. Although time consuming and invasive, it can enable therapeutic intervention through thromboaspiration, thrombolysis, and vasodilator therapy.

TABLE Accuracy	, Limitations, and Pitfalls of Modalities Us	ed in Imaging of Super	ior Mesenteric Artery Thrombosis
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Sensitivity 30% Nonspecific	May not suggest disease until late stage of bowel infarction/perforation
CT	Sensitivity 64%-82%	Radiation	
MRI	Although sufficient comparative data are lacking, sensitivity and specificity may be comparable to CT for vessel findings but less accurate for bowel findings.	Long examination times High cost	Suboptimal evaluation of calcifications and stented vessels Tailored examination less able to assess abdomen for other pathologic processes compared with CT
Ultrasonography	Accuracy dependent on ability to visualize proximal superior mesenteric artery.	Patient body habitus Bowel gas Patient cooperation	Atherosclerotic disease burden may be underestimated because of incomplete visualization of mesenteric vessels.
Nuclear medicine	No role in the evaluation of acute mesenteric ischemia	Poor spatial resolution	
PET/CT	No role in the evaluation of acute mesenteric ischemia	Radiation High cost	
Angiography	Sensitivity 90%	Radiation Invasive	

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

**Imaging Algorithm.** An imaging algorithm is provided in Figure 26-17. See also Table 26-3.

#### **Classic Signs: Superior Mesenteric Artery Thrombosis**

- Abdominal pain out of proportion to physical findings
- Nonopacification and/or narrowing of the SMA origin
- Severe atherosclerotic disease
- Late findings: Pneumatosis, portomesenteric venous gas, pneumoperitoneum

# Nonocclusive Mesenteric Ischemia

Except for the absence of occlusive lesion within visceral arteries, the radiologic features of nonocclusive mesenteric ischemia may be identical to other forms of acute mesenteric ischemia.

**Radiography.** Plain radiography of the abdomen is nonspecific in all major causes of acute mesenteric ischemia.

**Computed Tomography.** CT may demonstrate bowel findings seen in other forms of acute mesenteric ischemia. Bowel wall that uniformly enhances greater than venous enhancement may be seen in shock bowel—a form of nonocclusive mesenteric ischemia seen in hypotensive and hypovolemic patients.<sup>16</sup> CTA may be used to exclude a lesion of the SMA. Late findings such as pneumatosis or pneumoperitoneum may be noted.

**Magnetic Resonance Imaging.** Although gadoliniumenhanced MRA may demonstrate absence of an SMA lesion, the long examination times should preclude the use of MRI in critically ill patients in whom nonocclusive mesenteric ischemia is suspected.

**Ultrasonography.** There is no role for ultrasonography in the assessment of nonocclusive mesenteric ischemia.

**Nuclear Medicine.** There is no role for scintigraphy in the evaluation of nonocclusive mesenteric ischemia.

**Positron Emission Tomography With Computed Tomography.** There is no role for PET/CT in the evaluation of nonocclusive mesenteric ischemia.

**Angiography.** Patients suspected of having nonocclusive mesenteric ischemia should be promptly referred for angiography. There is diffuse vasoconstriction (Figure 26-19) with reduced bowel parenchymal opacification.<sup>3</sup> Major branches of the SMA may demonstrate segmental constrictions, producing a "string of sausages" sign.<sup>6</sup> Contrast material may reflux back into the aorta. The venous phase of mesenteric angiography is normal. Angiography also provides a tool for catheter intervention through the infusion of vasodilators directly in the SMA.

**Imaging Algorithm.** Angiography is recommended in clinically suspected nonocclusive mesenteric ischemia (Table 26-4). CT may be performed first to exclude other pathologic processes.

#### **Classic Signs: Nonocclusive Mesenteric Ischemia**

- Critically ill patient, failure to thrive
- Vasopressor therapy, digitalis
- Lack of intraluminal filling defect within visceral vessels
- Diffuse narrowing of vessels with reduced opacification of bowel parenchyma on angiography
- "String of sausages" sign on angiography

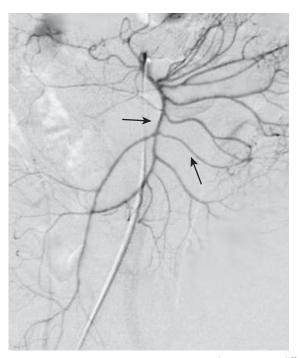
#### Mesenteric Venous Thrombosis

Mesenteric venous thrombosis can be easily demonstrated on cross-sectional imaging with CT or MRI. It is not uncommon to identify incidental mesenteric venous thrombosis in asymptomatic patients undergoing CT and MRI for other reasons.

**Radiography.** Plain radiography of the abdomen is nonspecific in all major causes of acute mesenteric ischemia.

**Computed Tomography.** CT/CTA is the test of choice for the evaluation of mesenteric thrombosis, with sensitivity exceeding

Document téléchargé de ClinicalKey.fr par Faculte de Medecine de Tunis août 30, 2016. Pour un usage personnel seulement. Aucune autre utilisation n'est autorisée. Copyright ©2016. Elsevier Inc. Tous droits réservés. 90%.<sup>8,9</sup> The most common CT finding is bowel wall thickening, typically associated with a target sign.<sup>8,16</sup> Small bowel dilatation, nonenhancement of the bowel wall, pneumatosis, portomesenteric gas, and pneumoperitoneum are findings that overlap with other forms of acute mesenteric ischemia. The most specific finding is a central focus of low attenuation within the venous lumen such as the superior mesenteric vein (Figure 26-20) that is persistent on multiple phases of enhancement and may be



**Figure 26-19** Superior mesenteric arteriogram demonstrates diffuse and segmental narrowing of the arterial branches (*arrows*) in a patient with nonocclusive mesenteric ischemia. Compare with Figure 26-2, *B*.

surrounded by a rim-enhancing venous wall.<sup>8</sup> This finding, when coupled with bowel wall thickening and intraperitoneal fluid, is associated with a higher risk for bowel infarction compared with cases without intraperitoneal fluid.<sup>8</sup> Thrombus within multiple mesenteric veins is common.

**Magnetic Resonance Imaging.** Gadolinium-enhanced MRA is an excellent modality to evaluate mesenteric venous thrombosis. Lack of signal in the central superior mesenteric vein may be seen (Figure 26-21). Image postprocessing can greatly facilitate the diagnosis. The lack of radiation is an advantage over CT, although images may be degraded as a result of turbulent flow. MRI examination times are significantly longer than those for CT and may be inappropriate in the evaluation of a patient with acute symptoms.

**Ultrasonography.** Duplex ultrasonography may be useful in assessing mesenteric venous thrombosis by demonstrating a lack of portomesenteric blood flow and intraluminal echogenic debris. However, evaluation is limited by bowel gas, patient body habitus, and patient noncooperation. Collateral vessels may be incompletely imaged or may be mistaken for patent central veins.<sup>8</sup>

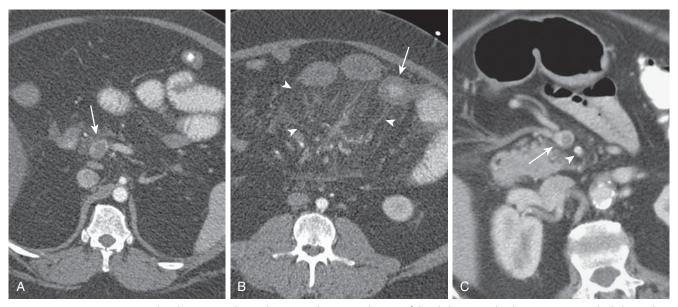
**Nuclear Medicine.** There is no role for scintigraphy in the evaluation of mesenteric venous thrombosis.

**Positron Emission Tomography With Computed Tomogra-phy.** There is no role for scintigraphy in the evaluation of mesenteric venous thrombosis.

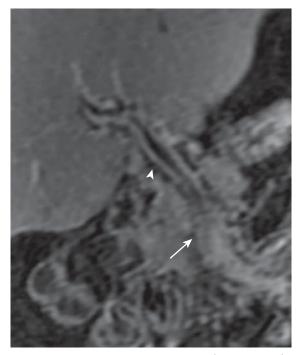
**Angiography.** Mesenteric venous thrombosis may be evaluated angiographically by direct portography, such as transhepatic or transjugular portography or splenoportography. Such techniques also provide an avenue for endovascular intervention such as angioplasty. Alternatively, mesenteric arteriography with delayed-phase imaging can be performed (so-called

Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive Nonspecific	May not suggest disease until late stage of bowel infarction/perforation
СТ	Poor Can help exclude occlusive disease	Radiation Diffuse mesenteric arterial narrowing not as well discerned as on angiography	
MRI	Poor Can help exclude occlusive disease	Long examination times High cost Diffuse mesenteric arterial narrowing not as well discerned as on angiography	Suboptimal evaluation of stented vessels Tailored examination less able to assess abdomen for other pathologic processes compared with CT
Ultrasonography	Poor	Patient body habitus Bowel gas Patient cooperation	
Nuclear medicine	No role in the evaluation of acute mesenteric ischemia	Poor spatial resolution	
PET/CT	No role in the evaluation of acute mesenteric ischemia	Radiation High cost	
Angiography	Imaging test of choice as best demonstrates diffuse vessel narrowing	Radiation Invasive	

PET/CT, Positron emission tomography/computed tomography.



**Figure 26-20** A, Intravenous and oral contrast-enhanced computed tomography (CT) of the abdomen and pelvis in a patient with abdominal pain demonstrates a filling defect within the superior mesenteric vein (*arrow*). B, Multiple loops of small bowel demonstrate wall thickening (*arrow*) with adjacent hazy attenuation of mesentery (*arrowheads*) consistent with venous congestion. C, In a different patient, CT demonstrates a filling defect within the superior mesenteric vein (*arrow*), which is located anterior and to the left of the superior mesenteric artery (*arrowhead*). The superior mesenteric artery demonstrates vascular calcifications, which are partially obscured by intraluminal contrast.



**Figure 26-21** Magnetic resonance angiogram demonstrates absence of enhancement of the superior mesenteric vein (*arrow*) and portal vein (*arrowhead*), consistent with thrombosis.

*arterioportography*). In addition to reduced arterial inflow and reflux of contrast back into the SMA, such indirect portography may demonstrate segments of nonopacified mesenteric and portal venous tributaries on delayed-phase images, signifying occlusions (Figure 26-22). Portal-to-portal and portal-to-system collateral vessels may also be demonstrated.

**Imaging Algorithm.** An imaging algorithm is provided in Figure 26-17. See also Table 26-5.

#### **Classic Signs: Mesenteric Venous Thrombosis**

- Recent surgery, hypercoagulable state
- CT or MRI: Central well-defined filling defect within mesenteric vein; multiple veins may be affected
- Angiography: Segmental nonopacification of portomesenteric veins, slow arterial flow

#### DIFFERENTIAL DIAGNOSIS

The clinical presentation of acute mesenteric ischemia can be vague. A high index of suspicion is needed to facilitate early diagnosis and intervention and should be prompted when peritoneal signs are present. Clinicians may consider acute inflammatory disorders such as pancreatitis, cholecystitis, or inflammatory bowel disease, although pain may be more localized compared with acute mesenteric ischemia. Small bowel obstruction is also a consideration. Acute mesenteric ischemia should be considered strongly in patients with prior embolic events or cardiac disease or who are critically ill or are on vasopressor therapy. Patients with a primary clotting disorder may prompt consideration of mesenteric venous thrombosis.

A bowel target sign on CT is nonspecific and may be attributed to mesenteric ischemia, inflammatory bowel disease, or infection. Pneumatosis intestinalis is more specific for ischemia, although infection and trauma are other possible causes.

A filling defect at a branch point of the SMA in the absence of prominent collateral vessels in a patient with a history of cardiac disease or prior embolic event favors embolism.

Nonopacification of the SMA particularly at its origin, severe atherosclerotic disease, presence of collateral vessels, and

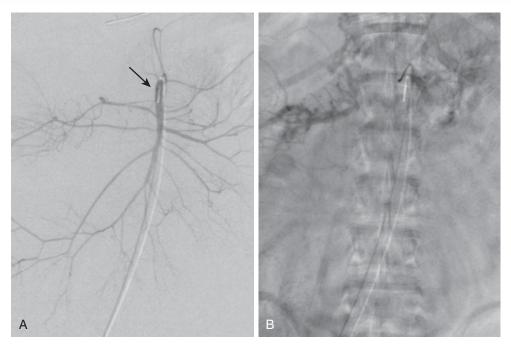


Figure 26-22 A, Selective contrast injection of the superior mesenteric artery (arrow) demonstrates a normal arteriogram. B, Delayed venous phase of the arteriogram demonstrates nonopacification of the superior mesenteric vein and its tributaries, consistent with thrombosis.

TABLE Accuracy	Accuracy Limitations and Rittalls of Modalitios Llood in Imaging of Mocontoris Vonous Thrombosis			
Modality	Accuracy	Limitations	Pitfalls	
Radiography	Poor	Insensitive Nonspecific	May not suggest disease until late stage of bowel infarction/perforation	
СТ	High accuracy with multiphasic imaging	Radiation		
MRI	Comparable to CT	Long examination times High cost	Suboptimal evaluation of calcifications and stented vessels Tailored examination less able to assess abdomen for other pathologic processes compared to CT	
Ultrasonography	Accuracy diminishes for evaluation of peripheral mesenteric veins Accuracy may be greater for portal compared to mesenteric vein thrombus	Patient body habitus Bowel gas Patient cooperation	Collaterals may be missed or mistaken for patent mesenteric veins.	
Nuclear medicine	No role in the evaluation of acute mesenteric ischemia	Poor spatial resolution		
PET/CT	No role in the evaluation of acute mesenteric ischemia	Radiation High cost		
Angiography	High	Radiation Invasive		

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

antecedent history of postprandial abdominal pain and weight loss favor thrombosis of the SMA.

Diffuse mesenteric arterial narrowing on angiography without evidence of occlusion suggests nonocclusive mesenteric ischemia, although vasculitis also may be considered.

Filling defects within mesenteric veins are diagnostic of mesenteric venous thrombosis and are often easily distinguished from extrinsic compression by tumor such as by pancreatic malignancy.

# TREATMENT

# **Medical Treatment**

Prompt treatment is imperative once the diagnosis of acute mesenteric ischemia is established. Medical therapy should begin with fluid resuscitation and, if there is no contraindication, anticoagulation. Broad-spectrum antibiotics should be administered early. Nasogastric tube decompression is indicated. When possible, vasoconstricting agents should be avoided.<sup>18</sup>

Therapy for nonocclusive mesenteric ischemia is primarily directed at reversing the offending stimulus (e.g., stopping digoxin). Catheter infusion of papaverine into the SMA may be helpful, but the primary stimulus must be addressed.

Similarly, mesenteric venous thrombosis may be treated medically unless there is evidence of bowel infarction, in which case laparotomy is mandated. Anticoagulation is the mainstay of therapy, and some patients recover spontaneously.<sup>6</sup> Long-term anticoagulation may be needed if a primary clotting disorder is discovered.

# Surgical Treatment

Peritoneal signs should prompt laparotomy. Nonviable bowel is resected. Revascularization is pursued in SMA embolism and thrombosis and, in some cases, mesenteric venous thrombosis. Because vasospasm of otherwise unaffected mesenteric vessels may occur after revascularization, angiography and intraarterial catheter infusion of a vasodilator such as papaverine may be performed before surgery unless reperfusion is established within 3 hours of onset.<sup>18</sup> Revascularization for SMA embolism may be performed via a transverse arteriotomy and embolectomy of the artery, which limits the potential iatrogenic reduction in arterial lumen diameter.<sup>2.6</sup>

Revascularization in the setting of SMA thrombosis may involve a longitudinal arteriotomy and thrombectomy of the artery, with subsequent patch angioplasty to preserve luminal diameter. If, however, a bypass graft is necessary to augment flow after thrombectomy, the arteriotomy site may serve as the distal anastomosis.<sup>6</sup> Bypass grafting is often necessary in severe atherosclerotic disease. Autologous vein grafts are mandated when there is intraperitoneal contamination from bowel perforation.

Thrombectomy is sometimes employed in cases of focal, acute mesenteric venous thrombosis within the proximal superior mesenteric vein.<sup>8</sup> Surgical thrombectomy is less feasible when there are numerous inaccessible thrombi. Intraportomesenteric or intra–superior mesenteric arterial catheter infusion of thrombolytic agents is better suited in such cases.<sup>8</sup>

In select patients, percutaneous treatment of SMA obstruction such as by mechanical thrombectomy may be successful.<sup>19,20</sup> Many patients will require laparotomy, regardless, because of nonviable bowel. Further studies are required comparing percutaneous with surgical revascularization. Intraarterial vasodilator therapy may be helpful in acute mesenteric ischemia to prevent or treat vasospasm.

# **Chronic Small Bowel Ischemia**

Atherosclerotic disease is the primary cause of chronic mesenteric ischemia, accounting for more than 95% of cases.<sup>3,21</sup> Because of the rich arterial supply of the small bowel and the capability to develop collaterals, chronic mesenteric ischemia occurs only when there is disease of at least two of the three major mesenteric arteries: the celiac axis, SMA, and/or inferior mesenteric artery.

#### PREVALENCE AND EPIDEMIOLOGY

Chronic mesenteric ischemia occurs in patients older than 50 years of age, and its prevalence increases with age.<sup>21</sup> Females are more commonly affected, with a female-to-male ratio of 3:1. Approximately 18% of people older than 65 years

may have a mesenteric arterial stenosis exceeding 50%, but only a small percentage will have symptoms.<sup>22,23</sup> Up to 50% of patients with this disorder have had surgery for atherosclerotic disease.<sup>19</sup> Other risk factors include hypertension, smoking, and diabetes.

# **CLINICAL PRESENTATION**

The classic presentation is intestinal angina, defined as recurrent postprandial abdominal pain subsiding in 1 to 2 hours with associated weight loss and aversion to food.<sup>3</sup> Because intestinal angina is rare, diagnosis is delayed and patients may have symptoms for months or years before presentation.

# PATHOPHYSIOLOGY

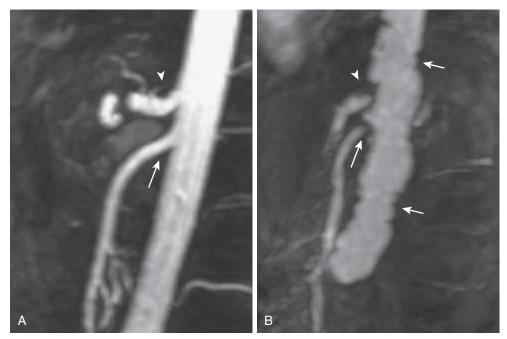
An understanding of the anatomy and common collateral pathways of the mesenteric vasculature is critical to the imaging evaluation of patients with chronic mesenteric ischemia. Please refer to the discussion of mesenteric vessel anatomy in the previous chapter on acute small bowel ischemia.

#### PATHOLOGY

The predominant cause of chronic mesenteric ischemia is atherosclerotic disease affecting the proximal or ostial segments of the mesenteric arteries. As mentioned earlier, symptomatic patients have stenosis or occlusion of at least two mesenteric arteries (Figures 26-23 and 26-24). In rare cases, only one vessel is involved and distal disease predominates, thus circumventing proximal collateral flow. The postprandial nature of the



**Figure 26-23** Maximum intensity projection of a computed tomography angiogram of the abdominal aorta demonstrates severe narrowing and calcification at the origin of the celiac artery (*arrowhead*). A severe stenosis is also demonstrated at the origin of the superior mesenteric artery (*arrow*).



**Figure 26-24** A, Maximum intensity projection from a magnetic resonance (MR) angiogram demonstrates a normal celiac artery (*arrowhead*) and the origin of the superior mesenteric artery (*arrow*). B, MR angiogram in a different patient with chronic mesenteric ischemia demonstrates diffuse wall irregularity (*short arrows*) of the aorta, consistent with atherosclerotic disease. Loss of signal at the celiac artery (*arrowhead*) and origin of the superior mesenteric artery (*long arrow*) is consistent with severe stenosis.

abdominal pain is consistent with an underlying mismatch between oxygen demand and supply that is exacerbated by food challenge.

Because most patients with mesenteric vascular disease are asymptomatic, its presence is not diagnostic of chronic mesenteric ischemia. In the setting of severe stenosis or occlusion of at least two mesenteric vessels, the diagnosis may be suggested by clinical findings in the absence of evidence of an alternative pathologic process.

# IMAGING

Imaging is useful in the evaluation of chronic mesenteric ischemia because it can both accurately assess the atherosclerotic disease burden of the mesenteric vasculature and exclude other potential pathologic processes.

# Radiography

Plain radiography is insensitive and nonspecific and is relegated to excluding other disorders, such as small bowel obstruction. A lateral abdominal radiograph may show calcified plaques at the origins of the mesenteric arteries.

# Computed Tomography

Contrast-enhanced CT and CTA are the mainstays of evaluation. CT can evaluate inflammatory and neoplastic causes of abdominal pain. Findings of bowel wall thickening, target sign, pneumatosis, and portomesenteric gas indicate an acute process and are absent in chronic mesenteric ischemia. CTA is sensitive for detecting stenosis and occlusion (see Figure 26-23) and may demonstrate collateral vessels; a noncontrast examination should be included, however, to assess for the presence of vascular calcifications.

#### Magnetic Resonance Imaging

Gadolinium-enhanced MRA provides an accurate evaluation of the mesenteric vasculature (see Figure 26-24)<sup>24</sup> but may not be as sensitive as CT in screening for other abdominal pathologic processes. 3D imaging techniques and postprocessing such as maximum intensity projections and volume rendering can facilitate diagnosis and operative planning. Limitations include susceptibility artifact from stents or poor demonstration of calcifications, with potential overestimation of severity of arterial stenoses.<sup>3</sup>

Other MR techniques to evaluate physiologic parameters of the mesenteric vasculature are performed before and after food challenge. Cine phase-contrast imaging assesses superior mesenteric vein flow, whereas MR oximetry evaluates the oxygenation of the blood of this vein.<sup>27</sup> Because mesenteric blood flow increases after food challenge,<sup>11,25</sup> a blunted superior mesenteric vein flow response implies chronic mesenteric ischemia on phase-contrast imaging.<sup>11</sup> MR oximetry takes advantage of the increased oxygen extraction of mesenteric blood in chronic mesenteric ischemia, given the inability to increase blood flow. Increased oxygen extraction reduces oxygen saturation and, consequently, the T2 value of the blood in the superior mesenteric vein.<sup>11</sup> Postprandial reduction of the T2 value of this blood has been demonstrated in patients with symptomatic chronic mesenteric ischemia, in contrast to a rise in T2 in asymptomatic patients.<sup>11</sup>

#### Ultrasonography

Duplex ultrasonography may be used to assess proximal SMA stenosis or occlusion (Figure 26-25). A peak systolic velocity of greater than 275 cm/s correlates with a stenosis of at least 70%,<sup>3,21</sup> whereas lack of flow is consistent with occlusion.

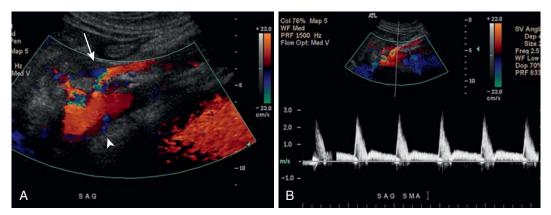


Figure 26-25 A, Color Doppler image of the abdominal aorta (arrowhead) demonstrates the takeoff of the superior mesenteric artery (SMA) (arrow). B, Duplex ultrasonography of the proximal SMA demonstrates an elevated peak systolic velocity approaching 300 cm/s, suggestive of a stenosis greater than 70%.

Ultrasonography, however, is limited by the patient's body habitus and overlying bowel gas. In addition, sonographic evidence of stenosis may suggest atherosclerotic disease but does not necessarily imply chronic mesenteric ischemia. Evaluation of the inferior mesenteric artery as well as more distal portions of the mesenteric vessels is limited.

#### Nuclear Medicine

There is no role for scintigraphy in the evaluation of chronic mesenteric ischemia.

### Positron Emission Tomography With Computed Tomogra-

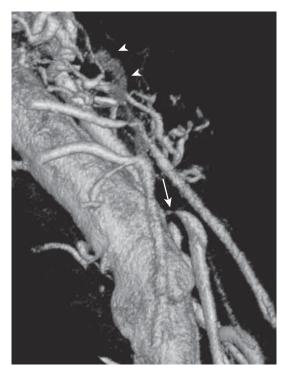
**phy.** There is no role for PET/CT in the evaluation of chronic mesenteric ischemia.

#### Angiography

Angiography is the gold standard in evaluating the mesenteric vasculature. Lateral aortography is used to assess the origins of the celiac axis and SMA. The presence of collateral vessels such as the arc of Riolan (Figures 26-26 and 26-27) may indicate a proximal mesenteric arterial stenosis or occlusion. Anteroposterior aortography and selective mesenteric angiography are used to assess distal disease as well as to demonstrate collateral vessels. Although invasive, costly, and associated with morbidities, angiography may be combined with interventions such as angioplasty and stenting (Figure 26-28) to treat any identified pathologic process.

# Imaging Algorithms

CT/CTA is the mainstay of evaluation of chronic mesenteric ischemia. In addition to demonstrating the mesenteric arteries, CT can exclude other abdominal pathologic processes. Although MRA can assess the mesenteric arteries, it may overestimate stenoses and is limited when evaluating stented vessels. More specific physiologic parameters can be assessed with phasecontrast MR and MR oximetry, but these techniques are neither standardized nor widely available. Conventional angiography may be useful for problem solving and intervention. Duplex ultrasonography avoids the radiation associated with CT or conventional angiography and is sensitive in evaluating the proximal SMA but is limited in evaluating other mesenteric vessels and collateral pathways.



**Figure 26-26** Three-dimensional image obtained from a conventional aortogram demonstrates thrombosis of the superior mesenteric artery (*arrowheads*) and severe stenosis of the proximal inferior mesenteric artery (*arrow*).

# Classic Signs: Chronic Small Bowel Ischemia

- Postprandial abdominal pain associated with food aversion and weight loss
- Narrowing of origin or proximal aspect of at least two of the following vessels: celiac artery, SMA, and inferior mesenteric artery
- Prominent collateral vessels
- Peak systolic velocity greater than 275 cm/s in the proximal SMA on ultrasonography



**Figure 26-27** Selective contrast injection of the inferior mesenteric artery (*single long arrow*) in the same patient as in Figure 26-26 demonstrates a prominent arc of Riolan (*single short arrow*), which reconstitutes the superior mesenteric artery (*double short arrows*). Severe stenosis of the origin of the inferior mesenteric artery, as shown in Figure 26-26, results in reflux of contrast (*single arrowhead*) into the aorta. There is a poorly developed marginal artery of Drummond (*double arrowheads*).

# DIFFERENTIAL DIAGNOSIS

The clinical manifestation of chronic mesenteric ischemia is nonspecific. New-onset or recent worsening of symptoms should prompt evaluation for acute mesenteric ischemia. Postprandial pain can be seen with gastroduodenal ulcers, which should be excluded by endoscopy. Weight loss is a nonspecific complaint that should prompt evaluation for malignancy.<sup>21</sup> Female patients in their third or fourth decade presenting with weight loss and epigastric pain that worsens with expiration suggests median arcuate ligament syndrome. Similarly, the finding in young female patients of abdominal pain and a history of hypertension may suggest fibromuscular dysplasia.

CT findings of target sign, bowel wall thickening, pneumatosis, or portomesenteric venous gas should prompt evaluation for acute ischemia. CT can assess numerous other causes of abdominal pain and weight loss, particularly malignancies such as pancreatic adenocarcinoma or lymphoma.

Angiographic demonstration of extrinsic narrowing of the celiac origin that worsens with expiration is compatible with median arcuate ligament syndrome.<sup>1,21,26,</sup> Hemodynamically significant compression may cause enlargement of the gastro-duodenal artery with SMA collateralization via the pancreati-coduodenal arcade.<sup>9</sup> Imaging that demonstrates beading of mesenteric arteries in a young female patient suggests fibro-muscular dysplasia, whereas diffuse stenosis, aneurysms, vessel wall thickening, and enhancement may suggest vasculitis.<sup>1,27</sup>

# TREATMENT

The traditional treatment for chronic mesenteric ischemia is surgical revascularization, which may consist of endarterectomy, reimplantation of the SMA, or bypass grafting.<sup>2</sup> Although

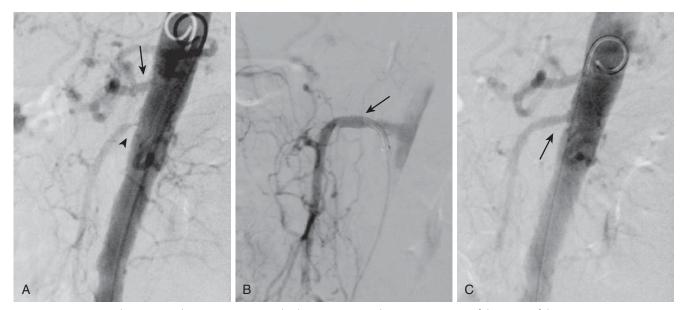


Figure 26-28 A, Lateral aortogram demonstrates a normal celiac origin (arrow) but severe stenosis of the origin of the superior mesenteric artery (SMA) (arrowhead). B, Subsequently, angioplasty and stent placement (arrow) were performed. C, Repeat lateral aortogram demonstrates normal luminal diameter of the origin of the SMA (arrow).

multiple vessels may be diseased, in most instances revascularization of one vessel is needed, usually the SMA. Surgery has high long-term patency rates (70% to 93%) but may be associated with a morbidity of 29% and mortality of 7%,<sup>28</sup> with complication rates exacerbated by cardiovascular comorbidities, which are common in this patient population.

Endovascular therapies (e.g., angioplasty and stents) have been employed in treating stenotic mesenteric vessels since

#### What the Referring Physician Needs to Know

- CT and conventional angiography are the mainstays of imaging in acute manifestations of mesenteric ischemia; MRI is the second choice owing to long examination times.
- Vessel anatomy and collateral mapping are helpful in operative planning.
- Angiography is extremely useful for both diagnosis and treatment; in some patients with peritoneal signs, emergent angiography before laparotomy may be performed to prevent posttreatment vasospasm.
- Bowel infarction and intraperitoneal contamination may prompt use of autologous veins for bypass grafting, if necessary.

### **Key Points**

- Peritoneal signs should prompt emergent laparotomy.
- Bowel wall findings are more specific in late stages of acute mesenteric ischemia.
- Superior mesenteric artery emboli prefer to lodge at branch points.
- Infarcts in other visceral organs may suggest SMA embolism.
- SMA thrombosis preferentially occurs at the origin of the artery.
- Collateral vessels are more typically seen in SMA thrombosis than embolism.
- Nonocclusive mesenteric ischemia typically occurs in critically ill patients or patients on vasopressors.

- 1980,<sup>29-31</sup> but there are limited prospective trials comparing them with surgery. Although further studies are required, angioplasty and stenting have high technical success rates; restenoses may be re-treated percutaneously.<sup>30</sup> Although reported patency rates after percutaneous treatments are lower than with surgery, new techniques and devices are expected to close these gaps. Percutaneous revascularization may be preferred in patients who are high-risk surgical candidates.
- Surgery may not be necessary in nonocclusive mesenteric ischemia unless there is bowel infarction.
- Thrombosis of multiple mesenteric veins precludes surgical revascularization.
- Atherosclerosis is responsible for over 95% of cases of chronic mesenteric ischemia.
- Percutaneous therapies are an important alternative to surgical revascularization, particularly in high-risk surgical candidates.
- Recent surgery or hypercoagulable state is associated with mesenteric venous thrombosis.
- Chronic mesenteric ischemia is rare despite the high prevalence of atherosclerotic disease of mesenteric arteries.
- CT/CTA is the mainstay in evaluation of suspected chronic mesenteric ischemia.
- Stenosis or occlusion of the origin or proximal segments of at least two mesenteric arteries is typical.
- Chronic mesenteric ischemia suspected in young female patients should suggest fibromuscular dysplasia or median arcuate ligament syndrome.

#### REFERENCES

- Shi MP, Hagspiel KD: CTA and MRA in mesenteric ischemia. I. Role in diagnosis and differential diagnosis. *AJR Am J Roentgenol* 188:452–461, 2007.
- 2. Milner R, Velazquez OC: Mesenteric ischemia and intestinal vascular disorders. In Lichtenstein GR, Wu GD, editors: *Requisites in gastroenterology: small and large intestine* (vol 2), St. Louis, 2004, Mosby, pp 217–241.
- Kim AY, Ha HK: Evaluation of suspected mesenteric ischemia: efficacy of radiologic studies. *Radiol Clin North Am* 41:327–342, 2003.
- Kaleya RN, Sammartano RJ, Boley SJ: Aggressive approach to mesenteric ischemia. Surg Clin North Am 72:157–181, 1992.
- Moore WM, Hollier LH: Mesenteric artery occlusive disease. Cardiol Clin 9:535–541, 1991.
- 6. Oldenburg WA, Lau LL, Rodenberg TJ, et al: Acute mesenteric ischemia: a clinical review. *Arch Intern Med* 164:1054–1062, 2004.
- Bassiouny HS: Nonocclusive mesenteric ischemia. Surg Clin North Am 77:319–326, 1997.

- Bradbury MS, Kavanagh PV, Bechtold RE, et al: Mesenteric venous thrombosis: diagnosis and noninvasive imaging. *Radiographics* 22:527– 541, 2002.
- 9. Rhee RY, Gloviczki P: Mesenteric venous thrombosis. *Surg Clin North Am* 77:327–338, 1997.
- Horton KM, Fishman EK: Volume-rendered 3D CT of the mesenteric vasculature: normal anatomy, anatomic variants, and pathologic conditions. *Radiographics* 22:161–172, 2002.
- Chow LC, Chan FP, Li KCP: A comprehensive approach to MR imaging of mesenteric ischemia. *Abdom Imaging* 27:507–516, 2002.
- 12. Kaufman JA, Lee MJ: Vascular and interventional radiology: the requisites, St. Louis, 2004, Mosby.
- 13. Schneider TA, Longo WE, Ure T, et al: Mesenteric ischemia: acute arterial syndromes. *Dis Colon Rectum* 37:1163–1174, 1994.
- Schoenberg MH, Beger HG: Reperfusion injury after intestinal ischemia. *Crit Care Med* 21:1376– 1386, 1993.

- Zimmerman BJ, Grisham MB, Granger DN: Role of oxidants in ischemia/reperfusioninduced granulocyte infiltration. *Am J Physiol* 258:G185–G190, 1990.
- Wittenberg J, Harisinghani MG, Jhaveri K, et al: Algorithmic approach to CT diagnosis of the abnormal bowel wall. *Radiographics* 22:1093– 1109, 2002.
- Sebastia C, Quiroga S, Espin E, et al: Portomesenteric vein gas: pathologic mechanisms, CT findings, and prognosis. *Radiographics* 20:1213– 1224, 2000.
- Martinez JP, Hogan GJ: Mesenteric ischemia. Emerg Med Clin North Am 22:909–928, 2004.
- Hirsch AT, Haskal ZJ, Hertzer NR, et al: ACC/ AHA 2005 practice guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aorta). *Circulation* 113:e463–e654, 2006.
- 20. Demirpolat G, Oran I, Tamsel S, et al: Acute mesenteric ischemia: endovascular therapy. *Abdom Imaging* 32:299–303, 2007.

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- Cognet F, Ben Salem D, Dranssart M, et al: Chronic mesenteric ischemia: imaging and percutaneous treatment. *Radiographics* 22:863–880, 2002.
- 22. Cademartiri F, Raajimakers RH, Kuiper JW, et al: Multi-detector row CT angiography in patients with abdominal angina. *Radiographics* 24:969–984, 2004.
- Roobottom CA, Dubbins PA: Significant disease of the celiac and superior mesenteric arteries in asymptomatic patients: predictive value of Doppler sonography. *AJR Am J Roentgenol* 161: 985–988, 1993.
- 24. Gilfeather M, Holland GA, Siegelman ES, et al: Gadolinium-enhanced ultrafast threedimensional spoiled gradient-echo MR imaging

of the abdominal aorta and visceral and iliac vessels. *Radiographics* 17:423–432, 1997.

- Burkart DJ, Johnson CD, Ehman RL: Correlation of arterial and venous blood flow in the mesenteric system based on MR findings. *AJR Am J Roentgenol* 161:1279–1282, 1993.
- Horton KM, Talamini MA, Fishman EK: Median arcuate ligament syndrome: evaluation with CT angiography. *Radiographics* 25:1177–1182, 2005.
- 27. Ha HK, Lee SH, Rha SE, et al: Radiologic features of vasculitis involving the gastrointestinal tract. *Radiographics* 20:779–794, 2000.
- 28. Schaefer PJ, Schaefer FKW, Mueller-Huelsbeck S, et al: Chronic mesenteric ischemia: stenting

of mesenteric arteries. *Abdom Imaging* 32:304–309, 2007.

- Matsumoto AH, Tegtmeyer CJ, Fitzcharles EK, et al: Percutaneous transluminal angioplasty of visceral arterial stenosis: results and long-term clinical follow-up. J Vasc Interv Radiol 6:165– 174, 1995.
- Nyman O, Ivancey K, Lindle M, et al: Endovascular treatment of chronic mesenteric ischemia: report of five cases. *Cardiovasc Intervent Radiol* 21:305–313, 1998.
- Maleux G, Wilms G, Stockx L, et al: Percutaneous recanalization and stent placement in chronic proximal superior mesenteric artery occlusion. *Eur Radiol* 7:1228–1230, 1997.

27

# Benign Neoplasms and Wall Thickening of the Small Bowel

STEPHEN THOMAS | ABRAHAM H. DACHMAN | ARUNAS E. GASPARAITIS | AYTEKIN OTO

Normal intestinal wall thickness depends on the degree of bowel distention and the imaging modality. The normal jejunum wall thickness measures approximately 2 mm and the ileum 1 mm on enteroclysis.<sup>1</sup> On computed tomography (CT), 3 mm is accepted as the upper limit of normal when the bowel is completely distended.<sup>1</sup>

The hallmark of benign wall thickening is homogenous or stratified wall thickening. The appearance is due to low attenuation of the submucosa from edema, inflammation, or fat deposition and is also referred to as a "target" sign. In this chapter, benign causes of small bowel wall thickening (Box 27-1) and benign small bowel neoplasms (Table 27-1) are discussed.

# **Crohn's Disease**

# ETIOLOGY

Crohn's disease is an idiopathic, transmural inflammatory process that can affect the entire gastrointestinal tract, with a tendency toward segmental distribution. Environmental factors, microbial influences along with immunologic dysregulation, and genetic factors have been implicated as the cause of this disease.<sup>2</sup>

# PREVALENCE AND EPIDEMIOLOGY

Crohn's disease is more common in northern Europe and North America, and its incidence has increased in recent years and then reached a plateau.<sup>3</sup> The disease most commonly affects young adults between 15 and 25 years of age. A second peak in the elderly is thought to be caused by unrecognized ischemic colitis. Crohn's is two to four times more common in the Jewish population. The prevalence of disease is increased in the relatives of those who have the disease. For patients who have Crohn's disease, the occurrence of disease in their offspring is 9.2%.<sup>4</sup> However, classic mendelian inheritance patterns are not seen and Crohn's disease cannot be linked to a single gene locus.<sup>2</sup>

# **CLINICAL PRESENTATION**

The typical manifestation is recurrent episodes of abdominal pain, diarrhea, and low-grade fever. The pain is usually in the right lower quadrant and steady. Cramping abdominal pain can suggest intestinal obstruction. If there is colonic involvement, rectal bleeding and perianal fistulas may develop. During the advanced stages of the disease, stricture formation and partial small bowel obstruction are common. Free perforation of the small bowel into the peritoneal cavity is rare, but small, sealedoff perforations are characteristic of the disease and may lead to fistula formation. The risk for colorectal cancer is 4 to 20 times higher than that of the general population.<sup>5</sup>

Extraintestinal manifestations are more common in Crohn's disease than in ulcerative colitis. Biliary complications are the most common and include cholelithiasis and sclerosing cholangitis. Urolithiasis, sacroiliitis, peripheral arthritis, and ocular and skin manifestations are the other systemic complications, which can be seen in 20% to 30% of the patients.

# ANATOMY

Crohn's disease can involve any part of the gastrointestinal tract in a discontinuous fashion, with the terminal ileum and colon most frequently affected. Isolated small bowel involvement can occur in one third of patients. The jejunum and ileum (sparing the terminal ileum) are affected by the disease in 3% to 10% of the patients.<sup>6</sup>

# PATHOLOGY

The classic gross description of Crohn's disease is segmental, transmural inflammation of the bowel wall with skip lesions.<sup>7</sup> The mucosa shows multiple aphthous or linear ulcers, and the intervening normal mucosa has the appearance of pseudopolyps. Noncaseating granulomas are not pathognomonic but are very suggestive of the disease; they are found only in up to two thirds of biopsy specimens.<sup>7</sup> Fissures and fistula tracts are common, and the serosal surface may show transmural inflammation associated with a thickened layer of surrounding fat that is also referred to as fibrofatty proliferation.

# IMAGING

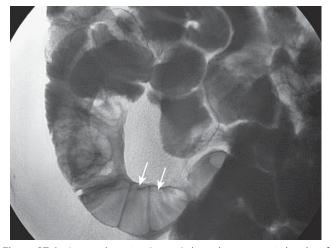
# Radiography

Plain radiographs of the abdomen are obtained in patients with acute presentation to evaluate for intestinal obstruction or perforation. Incidental findings may include gallstones and urinary stones. In cases of severe disease, wall thickening of the bowel segments also may be apparent on plain radiographs.

In a prospective trial, Lee and colleagues<sup>8</sup> showed that CT and magnetic resonance (MR) enterography and small bowel follow-through (SBFT) are equally accurate in detecting inflammation in the small intestine. The sensitivity values of CT enterography (89%) and MR enterography (83%) were slightly higher than those of SBFT (67% to 72%).<sup>8</sup> CT and MR were more accurate in depicting extraintestinal complications such

#### BOX 27-1 COMMON CAUSES OF BENIGN SMALL BOWEL WALL THICKENING

- Inflammatory bowel disease (Crohn's disease, ulcerative colitis [backwash ileitis])
- Infectious causesVascular causes
- Miscellaneous causes (eosinophilic enteritis, Whipple's disease, amyloidosis, graft-versus-host disease, intestinal lymphangiectasia)
- Benign neoplasms of small bowel

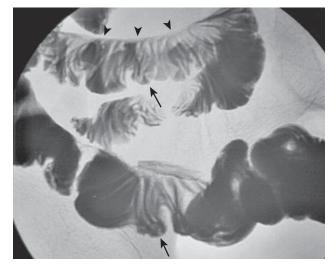


**Figure 27-1** Linear ulceration (*arrows*) along the mesenteric border of a segment of ileum. These ulcers usually run parallel to the mesenteric border and can exceed 15 cm in length.

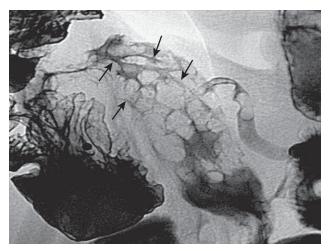
as sinus tracts, fistulas, and abscesses.<sup>8-10</sup> The addition of peroral pneumocolon to the SBFT allows better evaluation of the terminal ileum.<sup>11</sup> A wireless video capsule endoscopy is superior in the detection of early nonstricturing small bowel Crohn's disease but is contraindicated in stricturing disease.<sup>12</sup>

Coarsening of the villous pattern and thickening of the intestinal folds secondary to edema and inflammation can be seen in early disease. Ulcerations can be aphthous or linear. Aphthous ulcers are punctuate, shallow, discrete depressions surrounded by a halo. Linear ulcers can be long and run parallel to the mesenteric border (Figure 27-1). Together with mesenteric border shortening and antimesenteric sacculations, these ulcers are very characteristic for Crohn's disease (Figure 27-2). Linear ulcers may penetrate the entire wall of the bowel. Islands of intervening normal mucosa surrounded by denuded mucosa can give the appearance of pseudopolyps, and multiple polypoid elevations can produce the "cobblestoning" appearance (Figure 27-3).

Stenosis of the small intestine in Crohn's disease can be a combination of fibrosis, inflammation, and spasm. The "string" sign represents intense spasm of the bowel and indicates transmural inflammation (Figure 27-4). This needs to be differentiated from strictures secondary to fibrosis that are not distensible and cause obstruction (Figure 27-5). Asymmetric and discontinuous involvement of the bowel wall are the other hallmarks of Crohn's disease. Complications such as sinus tracts, fistulas, and abscesses either ending blindly or penetrating the colon or



**Figure 27-2** Asymmetric wall involvement in Crohn's disease. Mesenteric border of the small bowel segments is shortened and straightened (*arrowheads*), and there is redundancy and ulcerations (*arrows*) in the antimesenteric border. The combination of these findings is pathognomonic for Crohn's disease.



**Figure 27-3** Classic cobblestone appearance. Multiple linear ulcerations (*arrows*) separating islands of normal mucosa.

another organ can be visualized by SBFT or enteroclysis (Figures 27-6 and 27-7).

# Computed Tomography

CT can be used to diagnose, monitor therapy, and evaluate complications related to Crohn's disease. When performed with neutral oral contrast agents, it allows mucosal evaluation. CT features of active small bowel Crohn's disease are bowel wall thickening, mural hyperenhancement, and mural stratification (Figure 27-8).<sup>13</sup> Narrowing of the lumen is another common finding, which can be fixed (as a result of fibrosis) or reversible (inflammation or spasm) (Figure 27-9). Enlarged vasa recta and increased amount of fat surrounding the involved bowel segments are common findings (Figure 27-10). Fistulas between the small bowel and colon or other organs can be seen as enhancing tracts (Figure 27-11). Multiplanar reformatted views may better assist in depiction of fistulous tracts. Positive oral

se	Additional Findings	If associated with syndromes	Extraintestinal manifestations such as sclerosing cholangitis, joint involvement, etc.		Atherosclerotic disease
sowel Disea		ur sy	Ey intent	diffuse ement J It	el ant
ammatory E	Enhancement Pattern	Variable	Fibrofatty proliferation, variable enhancement	Variable, diffuse enhancement of the involved bowel segment	Decreased or sometimes increased enhancement of the bowel wall
all Bowel and Inflé	Distinguishing Imaging Findings	Lipomas are fat-containing lesions. GISTs are exophytic masses with hemorrhage, necrosis, and calcification.	Asymmetric and discontinuous involvement Coarsening of villous pattern and wall stratification Linear/aphthous ulcers Cobblestoning String sign secondary to inflammation and spasm Sinus tracts/fistulas and abscess formation	Nonspecific findings; usually terminal ileum and right colon are involved.	Thrombus in the mesenteric vessels Intestinal wall thickening, "thumbrinting"
ious Lesions of the Sma	Imaging Modality of Choice	Enteroclysis, wireless capsule endoscopy, CT enterography	Enteroclysis and wireless capsule endoscopy for subtle mucosal involvement CT or MR enterography for extent of the disease and complications	Usually none; in chronic cases or immunocompromised patients CT may be helpful.	CT; CT or MR angiography
Imaging Characteristics of Benign Neoplasms, Vascular Lesions, and Infectious Lesions of the Small Bowel and Inflammatory Bowel Disease	Distinguishing Clinical Presentation	Associated as a spectrum of polyposis syndromes or, if large, can manifest as small bowel obstruction, intussusception, palpable mass. Rarely perforation is noted.	Perianal fistula formation, extraintestinal manifestations	Diarrhea, acute or chronic manifestation, fever, abdominal pain	Abdominal pain, acute abdomen, gastrointestinal bleeding
	Distinguishing Clinical History	Could be incidental on imaging	Right lower quadrant pain, intermittent diarrhea, weight loss, rectal bleeding	Immune suppression, recent history of travel or living in endemic places	History of atherosclerotic disease, blood dyscrasia, abdominal surgery or infortion
	Sex	ц Е Д	M = F, four times more common in Ashkenazi Jews	M = F, endemic in some places	μ = Σ
g Characteristics	Age	5th-óth decade	15-25 yr	Any age, more common in pediatric patients	More common in elderly patients
TABLE Imaging	Lesion	Benign neoplasms or neoplasm- like lesions	Inflammatory bowel disease	Infectious diseases	Vascular diseases

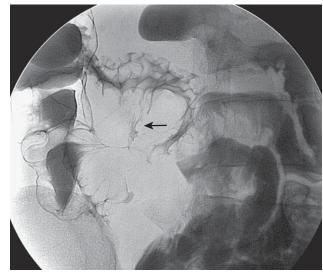
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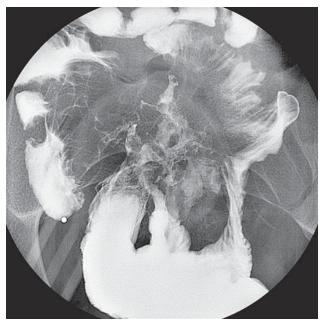
CT, Computed tomography; F, female; G/STs, gastrointestinal stromal tumors; M, male.



**Figure 27-4** String sign (*arrows*). Decrease in the caliber is associated with spasm, and the most common site is the terminal ileum.



**Figure 27-6** Ileoileal fistula. Peroral pneumocolon study demonstrates the linear connection (*arrow*) between the terminal ileum and a distal segment of ileum representing the fistulous tract.





**Figure 27-5** Linear ulcers and fissure tracts. Multiple linear ulcers are seen in the strictured terminal ileum. Linear extensions of barium outside the bowel wall *(arrowheads)* represent fissure tracts. Some of these may evolve into fistulas or abscesses.

**Figure 27-7** Extensive fistula formation involving the small bowel and colon segments in Crohn's disease.

contrast agents may be preferred if a fistula is clinically suspected.<sup>14</sup> In a prospective study by Hara and colleagues,<sup>15</sup> Crohn's disease was depicted by CT enterography in 53%, ileoscopy in 65%, SBFT in 24%, and capsule endoscopy in 71% of the patients.<sup>15</sup>

#### Magnetic Resonance Imaging

MR enterography can provide a systematic evaluation of the entire small bowel and the mesentery without exposing the patients to ionizing radiation. In a study by Schreyer and colleagues,<sup>16</sup> all pathologic findings seen on conventional enteroclysis were seen on MR enterography or MR enteroclysis.<sup>16</sup>

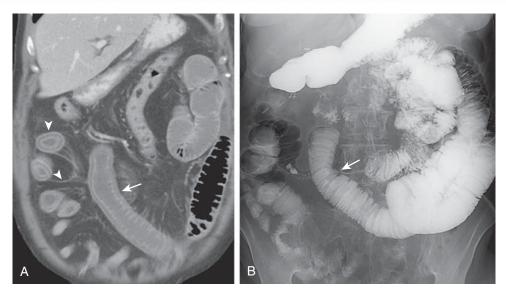
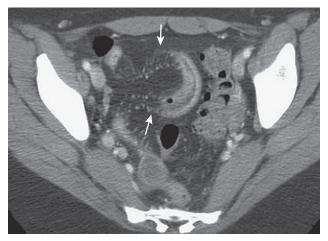


Figure 27-8 Computed tomography enterography after administration of a neutral oral contrast agent (A) shows thick-walled jejunal (arrow) and ileal segments (arrowheads) with mural hyperenhancement and stratification. Small bowel follow-through study (B) demonstrates the thickened, edematous folds in the involved jejunal segment (arrow).



**Figure 27-9** Axial computed tomography image shows an inflamed, thick-walled distal ileum segment (*arrow*) causing dilatation of the proximal small bowel segments (*arrowheads*), representing bowel obstruction.



**Figure 27-10** "Comb" sign and fibrofatty proliferation. Mesenteric vessels are prominent (*arrows*), and there is a focal increase in the amount of fat around the inflamed small bowel segment.

Some reports have shown greater than 90% sensitivity and specificity with MRI in detection of Crohn's disease.<sup>17</sup> Increased enhancement and thickness of the bowel wall suggest active inflammation (Figure 27-12). The inflamed segments have increased perfusion and show restricted diffusion.<sup>18</sup>

High signal intensity in the bowel wall on T2-weighted images also indicates active disease, and low signal on T2-weighted images with homogenous, cordlike enhancement is suggestive of chronic Crohn's disease.<sup>17,18</sup>

#### Ultrasonography

During the past decade, advances in the resolution of ultrasound technology with development of high-frequency probes, harmonic imaging, and improved temporal resolution have led to better imaging of the bowel wall. Common ultrasonographic findings of Crohn's disease are thickened bowel wall and decreased peristalsis.<sup>19</sup> Wall thickness in the range of 3.5 to 15 mm is considered pathologic, with amount of thickening influencing the sensitivity and specificity of detecting inflammation, ranging from 75% to 94% and 67% to 100%, respectively.<sup>20</sup>

Despite the high sensitivity of ultrasonography in the diagnosis of Crohn's disease, ultrasonography underestimates the extent of involvement.<sup>19,21</sup> Use of oral and intravenous contrast agents may further increase the diagnostic capability of ultrasonography.

#### Nuclear Medicine

Labeled white blood cell scans (indium-111 tropolone or technetium-99m hexamethyl propylene amine oxime [<sup>99m</sup>Tc-HMPAO]) and granulocyte scintigraphy with labeled antibodies have been reported to detect the inflammation in Crohn's

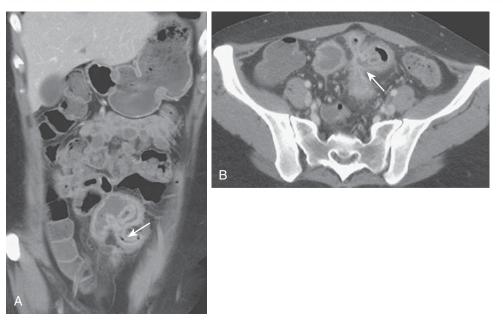


Figure 27-11 Ileosigmoid fistula. Coronal (A) and axial (B) computed tomography enterography images demonstrate the fistulous communication (arrows) between the inflamed ileum and sigmoid colon segments. Exact localization of these fistulas is important for surgical planning.

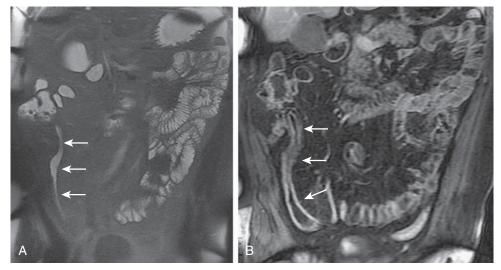


Figure 27-12 Magnetic resonance (MR) enterography. Coronal fat-saturated T2-weighted.W single-shot fast spin echo (A) and contrast-enhanced T1-weighted (B) MR images show the asymmetric stricture involving a long segment of the terminal ileum (*arrows*). Note the increased fat around the terminal ileum.

disease. Reported sensitivities vary between 5% and 70%, and they have been suggested to be more useful in reassessments rather than the initial diagnosis.<sup>22</sup>

#### Positive Emission Tomography With Computed Tomography

Recently, fluorodeoxyglucose (FDG)-labeled positron emission tomography (PET) combined with CT (PET/CT) has been shown to be a reliable tool for detection of active disease in both the small and large bowel (Figure 27-13). In a study comparing PET, MR enterography, and granulocyte scintigraphy with labeled antibodies, FDG-PET showed significantly higher sensitivity (85.4%) compared with the other imaging tools for the detection of inflamed bowel segments.<sup>23</sup>

#### Imaging Algorithm

In patients with suspected Crohn's disease, enteroclysis, SBFT, and CT or MR enterography can be the initial test, depending on the experience of the radiologist. Capsule endoscopy can be used in patients without stricturing small bowel Crohn's disease. Radiologic tests also can be helpful to exclude stenosis before the capsule endoscopy and provide more accurate localization of the pathologic process after the capsule endoscopy. Currently, CT enterography is the initial test for patients with acute



**Figure 27-13** Acute inflammation on positron emission tomography with computed tomography (PET/CT). Coronal PET/CT image shows increased fluorodeoxyglucose uptake in the small and large bowel segments (*arrows*). Acute inflammation was confirmed by colonoscopy in this patient.

presentation and suspected obstruction, fistula, or abscess (Table 27-2; see also Figure 27-28).

#### Classic Signs: Crohn's Disease

- Cobblestoning: Radiographic appearance caused by islands of normal mucosa (appearing as pseudopolyps) surrounded by denuded affected mucosa
- "String" sign: Stenosis of the bowel caused by inflammation and spasm
- Fibrofatty proliferation: Increased amount of fat around the involved bowel segments
- Wall stratification: Low density between mucosal and serosal enhancement representing fat or inflammation

#### DIFFERENTIAL DIAGNOSIS

The early symptoms of Crohn's disease are mild and nonspecific. Infectious enteritis can radiologically mimic Crohn's disease. Irritable bowel syndrome and lactose intolerance can have similar clinical presentation. In patients without small bowel involvement, differentiation from ulcerative colitis may be difficult. In elderly patients, ischemic enteritis should be differentiated from Crohn's disease. Other differential diagnoses include ischemia, neoplasm (lymphoma and, rarely, adenocarcinoma), ulcerative colitis, radiation therapy, vasculitis, and, in children, lymphoid hyperplasia.

		ns and Pitfalls of the Moda maging of Crohn's Disease	
Modal	lity	Limitations	Pitfalls
Radiog	graphy	Extraintestinal findings, detection of disease activity, radiation	
СТ		Radiation, insensitive to early mucosal findings	Undistended bowel
MRI		Expensive, duration of the test, motion artifacts	Undistended bowel
Ultrasc	onography	Unable to image the entire bowel	Nonspecific findings
Nuclea	ar medicine	Radiation, poor spatial resolution	Normal bowel uptake
PET/C	Т	Expensive, radiation, relatively less data available	Normal bowel uptake

*MRI*, Magnetic resonance imaging; *PET/CT*, positron emission tomography with computed tomography.

#### TREATMENT

#### Medical Treatment

Medical therapy is usually individualized and requires a combination of different drugs to achieve sustained response. The choice of drugs varies according to the severity of the disease, which is based on clinical, biochemical, endoscopic, and histologic findings. The Crohn's Disease Activity Index (CDAI) score is commonly used to determine the severity of the disease. Different drugs used for Crohn's disease range from sulfasalazine, to antibiotics in mild cases, to oral corticosteroids, azathioprine, methotrexate, and anti–tumor necrosis factor (TNF) antibody in moderate and severe cases.<sup>20</sup> The use of anti-TNF antibody has revolutionized the therapy of severe Crohn's disease.<sup>20</sup>

#### Surgical Treatment

Failure to respond to medical management, development of complications (obstruction, abscess, fistula, or stricture), and inability to tolerate effective therapy are the most common indications for surgical therapy.

#### What the Referring Physician Needs to Know: Crohn's Disease

- Differentiation of Crohn's disease from other causes of enteritis
- Differentiation between active and chronic Crohn's disease
- Recognition of complications
- Monitoring of therapy

#### **Infectious Causes**

Infectious diseases of the small bowel can be caused by various organisms, including bacteria, viruses, parasites, and fungi. Radiologic signs are often nonspecific, and bowel wall thickening is a common finding. Clinical information such as stool culture, the immune status, and geographic location is helpful for a specific diagnosis.

#### ETIOLOGY

Common bacterial causes of community-acquired infectious enterocolitis in the United States are *Campylobacter jejuni*, *Salmonella*, *Shigella*, *Escherichia coli*, and *Yersinia*.<sup>24</sup> Rotavirus and Norwalk virus are the most common pathogens in the children. Adenovirus and cytomegalovirus (CMV) should be considered in immunocompromised patients. *Giardia lamblia* is the most frequent cause of parasitic enteritis in the United States.<sup>25</sup> Other common parasitic infections that can affect the small intestine are *Ancylostoma*, *Ascaris*, *Cryptosporidium*, and *Taenia*. *Cryptosporidium* is a particularly common pathogen in the immunocompromised hosts. With the increasing population of immunocompromised patients (e.g., those with acquired immunodeficiency syndrome), the incidence of *Mycobacterium tuberculosis* and *Mycobacterium avium* complex (MAC) has increased during the past 2 decades.

#### PREVALENCE AND EPIDEMIOLOGY

Acute diarrhea is one of the most common diagnoses in general practice. Immune status, clinical setting, and geographic location are important factors in disease expression and treatment.<sup>26</sup> Acute enteritis causes 3 to 6 million deaths (mostly of children) worldwide.<sup>24</sup> Each year in the United States tens of millions of people acquire gastrointestinal infections with thousands of hospitalizations and deaths.<sup>27</sup> Chronic enteritis occurs less frequently and can be seen with parasites and, less commonly, with bacteria. Immunosuppressed individuals cannot clear pathogens effectively and can develop chronic diarrhea. *Campylobacter* and *Salmonella* can cause persistent diarrhea in patients with human immunodeficiency virus infection.<sup>28</sup>

Acute infectious diarrhea is acquired mostly through the fecal-oral route or ingestion of contaminated food and water. In developing countries, infectious enteritis can be endemic; and in most parts of the world, seasonality is recognized in the incidence of acute diarrhea.<sup>26</sup>

#### **CLINICAL PRESENTATION**

Patients may present with abdominal pain, diarrhea (with or without blood), and fever. If the host is a child, elderly, or immunocompromised, dehydration may be frequently encountered. Enteropathogens may involve the entire small bowel, although certain pathogens are more likely to colonize at certain segments. For example, *M. tuberculosis* tends to involve the terminal ileum and ileocecal valve and *Giardia* primarily causes duodenal and proximal jejunal disease.

#### PATHOLOGY

In most cases, a pathogen enters and colonizes in an area of intestine. However, ingestion of the toxin alone can cause infection (*Staphylococcus aureus, Clostridium botulinum*). Most bacteria disrupt mucosal integrity through cytotoxic mediators. *Shigella* and enteroinvasive *E. coli* can cause significant tissue invasion and destruction of the bowel mucosa. Rotavirus may disrupt the mucosa and produce villous atrophy. CMV produces characteristic nuclear and cytoplasmic inclusions that can be recognized on light microscopic examination. Whereas most infections elicit an inflammatory response, parasites such as *Giardia* or *Cryptosporidium* cause minimal

mucosal response, and it may be difficult to localize these organisms in the villi.<sup>29</sup>

MAC includes two related organisms. *M. avium* and *Mycoplasma intracellulare* enter into the intestinal mucosa and are phagocytosed by histiocytes, which are unable to digest them. Acid-fast bacilli within the histiocytes or in the stool samples can be identified. The pathologic findings resemble those of Whipple's disease, but the intestinal biopsy samples contain non–acid-fast granules and histiocytes are typically foamy.<sup>29</sup> Pathologic findings of infection with *M. tuberculosis* is similar to that of MAC, with the addition of caseation granulomas in the wall or in the mesentery of the bowel.

Endoscopic findings in infectious enteritis range from normal intestine (mostly viral infections) to inflammation, atrophic or blunted villi, erosions, and ulcers.

#### IMAGING

#### Radiography

Plain radiographic findings are often normal or nonspecific, showing mild ileus. Barium studies are rarely indicated for acute disease. If the course is prolonged, it is important to differentiate an infectious cause from inflammatory, neoplastic, and vascular causes. The diagnosis depends on the findings of biopsy, stool examination, and culture.

The terminal ileum is most severely affected in infections with *Campylobacter* and *Yersinia*, and demonstrates wall thickening with nodular folds and sometimes aphthous ulcers.<sup>30,31</sup> In *Yersinia* infection, the bowel mostly retains its normal caliber. These changes also can extend to the cecum and ascending colon. In salmonellosis, barium studies are rarely indicated, and findings are nonspecific with aphthous ulcers and wall thickening most commonly in the region of the terminal ileum.<sup>32</sup> Shigellosis, on the other hand, predominantly colonizes the colon and affects the small intestine by its enterotoxin.<sup>32</sup>

*M. tuberculosis* causes transaxial ulcerations, polyps, and thickening of the folds mostly in the ileocecal region in the early phase.<sup>33,34</sup> Involvement is more prominent in the cecum compared with the terminal ileum, and strictures may develop during the course of the disease. Strictures are usually short and have an hourglass configuration and sometimes cause small bowel obstruction. The cecum and ileocecal valve may be unrecognizable, with cephalad retraction of the cecum and straightening of the ileocecal angle.<sup>34</sup> Differentiation of ileocecal tuberculosis from Crohn's disease is difficult.

In the immunocompromised host, MAC, *Cryptosporidium*, and CMV are the most common infective agents causing enteritis. On barium studies, a diffuse granular pattern secondary to nodular thickening of mucosal folds is a common finding in MAC infection.<sup>35</sup> Ulcers are typical findings of CMV enterocolitis and can be large.<sup>36</sup> The ileocecal region is the most commonly involved area, and changes can extend into the cecum and the rest of the colon (Figure 27-14). The barium study findings of cryptosporidiosis are nonspecific fold thickening and increase in intraluminal fluid.

#### Computed Tomography

CT is usually not indicated in the evaluation of immunocompetent patients with acute enteritis, but it is important to know the CT findings to be able to consider acute enteritis in the differential diagnosis when these findings are incidentally encountered. Nonspecific wall thickening, mild ileus secondary to altered mobility of the involved small bowel segments, and mesenteric adenopathy are the common, nonspecific CT findings of acute enteritis.

CT can demonstrate the extent of the disease in patients with *M. tuberculosis* infection. CT findings include significant wall thickening mostly involving the ileocecal area, mesenteric adenopathy, and inflammatory masslike lesions in the right lower quadrant.<sup>37</sup> CT also can show ascites and peritoneal and omental soft tissue densities representing peritonitis and may mimic peritoneal carcinomatosis (Figure 27-15).

In the immunocompromised host, CT can help in differentiation of typhlitis (which requires medical treatment) from acute appendicitis and save the patient from unnecessary surgery.<sup>38</sup> CT features of typhlitis include segmental bowel wall thickening involving the terminal ileum, appendix, cecum and ascending colon, pneumatosis coli, and pericolonic fat stranding (Figure 27-16). The extent of the colonic involvement is more substantial in typhlitis, and the presence of known risk factors favors the diagnosis of typhlitis (neutropenic colitis).<sup>39</sup> In patients with MAC infection, detection of mesenteric adenopathy with low attenuation centers indicating necrosis is very suggestive of the cause (Figure 27-17). Similar lymph nodes can be seen in patients with Whipple's disease in the immunocompetent host.



**Figure 27-14** Cytomegalovirus colitis. Note significant, concentric wall thickening of the terminal ileum (*arrow*).

#### Magnetic Resonance Imaging

Limited experience is available on the MRI findings of infectious enteritis, and the role of MRI in the diagnosis of small bowel infections has not yet been established.

#### Ultrasonography

Acute infectious ileitis may show thickening of the ileal wall and mesenteric adenopathy.<sup>29</sup> An involved segment is usually aperistaltic, and the inflammation also can involve the cecum. Demonstration of the normal appendix on ultrasonography can rule out appendicitis.

#### Nuclear Medicine and Positron Emission Tomography With Computed Tomography

The roles of nuclear medicine and PET/CT have not yet been established in the diagnosis of small bowel diseases.

#### Imaging Algorithm

Imaging usually is not indicated in immunocompetent patients with acute enteritis (see Figure 27-28). Clinical and laboratory



**Figure 27-15** Tuberculous peritonitis. Axial computed tomography image shows peritoneal soft tissue nodules (*arrows*) with small amount of ascites. Small bowel wall thickening is also noted (*arrowheads*).

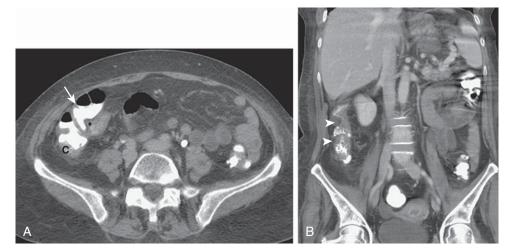


Figure 27-16 Typhlitis in a neutropenic patient. Axial (A) and coronal (B) computed tomography images demonstrate wall thickening of the terminal ileum (arrow, A), cecum (C), and ascending colon (arrowheads, B).

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evaluation with stool examination with or without cultures is usually enough to make the diagnosis or at least decide about the management. CT may be helpful to rule out a surgical diagnosis or complication of an infectious process. CT is also commonly used for the evaluation of immunocompromised patients with suspected enteritis to identify the cause and the extent of the disease as well as to exclude complications or neoplastic cause (Table 27-3). SBFT and enteroclysis can be obtained in chronic cases. Specific radiologic findings, location, and extent of the disease can help in the accurate diagnosis when evaluated together with the clinical and laboratory information.

#### DIFFERENTIAL DIAGNOSIS

The clinical diagnosis of infectious enteritis is usually not difficult, although the specific pathogen cannot be determined in all cases. When the inflammation causes ileus, clinical presentation may mimic bowel obstruction. When the course of the infection is chronic, inflammatory, neoplastic, and vascular causes also should be considered in the differential diagnosis.

When there is involvement of the ileocecal area, the differential diagnosis includes Crohn's disease, radiation enteritis, neoplasm (lymphoma, adenocarcinoma, carcinoid), or extrinsic inflammatory masses such as abscess/phlegmon from acute appendicitis. When the folds are thickened without narrowing and the history is more acute, infection with *Yersinia, Salmonella*, or *Campylobacter* is the most likely cause. Luminal narrowing and mesenteric border ulcers are suggestive of Crohn's



**Figure 27-17** Mycobacterium avium complex (MAC) infection. Multiple enlarged retroperitoneal lymph nodes with central low densities (*arrow*) representing necrosis are typical for MAC infection in this patient with known human immunodeficiency virus infection. There is also a retroperitoneal abscess on the left side (*a*).

disease. Tuberculosis can mimic Crohn's disease with skip lesions but affects the right colon more than the terminal ileum. In tuberculosis, the ileocecal valve is patulous. Behçet's disease also has predilection for the terminal ileum, and the presence of other clinical manifestations helps make the diagnosis.

When the involvement is more proximal (jejunum and proximal ileum), ulcerative jejunoileitis, eosinophilic enteritis, lymphoma, and abetalipoproteinemia can be considered in the differential diagnosis. Ulcerative jejunoileitis is a rare complication of celiac disease and may manifest as ulcer formation, which may eventually lead to stricture formation. Radiologically, it may be impossible to differentiate it from lymphoma. In the immunocompromised host, the main differential considerations are neoplasm (lymphoma, Kaposi's sarcoma) and graft-versus-host disease (GVHD).

#### TREATMENT

#### Medical Treatment

The treatment of infectious enteritis depends on the causative agent. Treatment is mostly hydration and diet alterations because most cases of community-acquired infectious enteritis are self-limiting in the immunocompetent host. In contrast, microorganisms such as most parasites, *M. tuberculosis*, and *Shigella* are treated with the appropriate antibiotics.<sup>24</sup> Agent-specific antimicrobial therapy is more aggressively pursued in the immunocompromised host.

#### Surgical Treatment

Surgical therapy is rarely indicated. It is performed mostly for the complications of intestinal tuberculosis such as perforation, obstruction, or massive hemorrhage.<sup>40</sup>

### What the Referring Physician Needs to Know: Infectious Causes of Small Bowel Disease

- CT can exclude abdominal acute inflammatory conditions that may mimic infectious enteritis and that will require surgery or drainage.
- When the clinical and laboratory information does not allow a definite diagnosis, radiologic information can help exclude an ischemic, neoplastic, or inflammatory cause or in some cases suggest a specific infectious agent.

### Miscellaneous Causes of Benign Small Bowel Wall Thickening

In this section, we will review the imaging findings of the relatively rare causes of benign small bowel wall thickening, including eosinophilic enteritis, GVHD, amyloidosis, Whipple's disease, and intestinal lymphangiectasia. Radiologic findings

TABLE 27-3	Accuracy and Limitations of the Modalities	Jsed in Imaging of Infectious Causes of Small Bowel Disease
Moda	ity Accuracy	Limitations
Radiography		Nonspecific findings and cannot evaluate the extramural disease
Comp	uted tomography Very helpful in evaluation of acut	ely Nonspecific findings and cannot evaluate the mucosal disease

presenting immunocompromised patients

are mostly nonspecific in these diseases, and biopsy is usually required for definitive diagnosis.

### Etiology

Eosinophilic enteritis is a rare inflammatory condition of unknown cause characterized by focal or diffuse eosinophilic infiltration of the intestinal tract. Graft-versus-host disease occurs after bone marrow transplant when immunologically competent T lymphocytes are introduced into the immunocompromised host and may affect the skin, intestine, and liver. Amyloidosis is a rare systemic condition characterized by extracellular deposition of insoluble protein-mucopolysaccharide complex and involves the gastrointestinal tract in more than 70% of patients with generalized amyloidosis. Primary amyloidosis is associated with multiple myeloma or Waldenström's macroglobulinemia, and secondary amyloidosis is associated with chronic inflammatory diseases such as rheumatoid arthritis or familial Mediterranean fever. Lymphangiectasia can occur as a result of congenital hypoplasia of lymphatics in the bowel wall (primary) or obstruction of the lymphatics by retroperitoneal or mesenteric abnormalities (secondary). Primary lymphangiectasia is a rare disease, and patients are usually young adults.

#### **CLINICAL PRESENTATION**

Eosinophilic enteritis is a disease of young adults and children. The symptoms vary depending on the location of eosinophilic infiltration within the digestive system and layers of the digestive system infiltrated with eosinophils.<sup>41</sup> Patients with predominantly mucosal disease may present with diarrhea, abdominal pain, and symptoms of malabsorption or protein-losing enteropathy. If the disease primarily affects the muscularis propria, partial obstruction can be seen. Ascites is common when serosa is the predominantly affected layer. Peripheral eosinophilia is present in most patients with eosinophilic enteritis.

Acute GVHD disease manifests within the first 100 days of allogenic bone marrow transplantation. After marrow grafting, subacute disease can develop within 1 to 4 months and chronic GVHD may occur within 3 to 12 months. Severe diarrhea, abdominal pain, rash, dry mouth, and elevated liver enzymes are common findings.

Clinical manifestation of small bowel amyloidosis depends on the involved bowel segment. Symptoms may include diarrhea, bleeding, malabsorption, hemorrhage, intestinal infarction, or even perforation. Biopsy of the small bowel is diagnostic.

Whipple's disease manifests as abdominal pain, diarrhea, intestinal bleeding, loss of appetite, weight loss, fatigue, and weakness.<sup>42</sup> Mesenteric adenopathy may cause intestinal lymphangiectasia, leading to protein-losing enteropathy. Definitive diagnosis requires small bowel biopsy.

Primary lymphangiectasia manifests with protein-losing enteropathy, ascites, pleural effusions, and asymmetric edema of the extremities. The main findings are reduced serum concentrations of albumin, and gamma globulins (IgA, IgG, and IgM).

Malabsorption, hypoalbuminemia, and lymphocytopenia can be seen secondary to development of lymphoenteric fistulas. Hypogammaglobulinemia, mainly affecting IgG and IgA, is also a common finding.

#### PATHOLOGY

Any segment of the gastrointestinal tract can be involved in eosinophilic enteritis. Most commonly involved areas are gastric antrum and proximal small bowel.<sup>43</sup> Eosinophilic infiltration of the submucosa is the hallmark of the disease. Infiltration may involve the mucosa, muscularis propria, and serosa.

Histologic analysis of GVHD shows varying degrees of epithelial cell apoptosis, crypt cell dropout, and mucosal inflammation.<sup>41</sup> Lymphocytic infiltration may be present in the thickened bowel wall.

Gastrointestinal system involvement is more common in primary amyloidosis. Primary amyloidosis is often referred to as light amyloidosis because the amyloid is made up of the light chains of immunoglobulins.<sup>44</sup> Amyloid is deposited in the submucosa and muscular layers of the bowel wall.

The mucosa and submucosa of the intestinal wall are diffusely infiltrated by foamy macrophages in Whipple's disease containing material that is positive for periodic acid–Schiff stain. The short, curved, rodlike Whipple bacillus can be identified within the cytoplasm.

In patients with intestinal lymphangiectasia, pathologic study shows dilated lacteals and lymphatics in the villi and edematous submucosa, which can be focal or diffuse.

#### IMAGING

See Table 27-4 and Figure 27-28.

#### Radiography

In eosinophilic enteritis, barium studies of the small bowel show thickening of the small bowel folds and gastric antrum. Nodularity may be present. When the disease predominantly affects the muscularis propria, narrowing of bowel lumen can be detected.

In acute GVHD, barium studies may show thickened or effaced mucosal folds, decreased transit time, and shallow or deep ulcerations (Figure 27-18).<sup>45</sup> Barium coating may persist over the mucosa for a few days. Rapid progression to luminal narrowing and to ribbon-like small bowel segments may be observed. Increased wall thickening, nodularity, and stenosis may be seen in subacute and chronic phases.

The radiologic findings in amyloidosis are not specific. Barium studies can be normal or demonstrate nonspecific fold thickening with or without nodular pattern (Figure 27-19). Delayed contrast transit times have been reported owing to altered motility.<sup>46</sup>

In Whipple's disease, barium studies show diffuse thickening of the folds and sometimes a micronodular pattern with normal

TABLE <b>27-4</b>	Used ir	ions and Pitfalls of the I Imaging for Miscella Wall Thickening	
Modal	ity	Limitations	Pitfalls
Radiog	graphy	Nonspecific findings	Can be normal in mild disease
Compo tomo	uted ography	Nonspecific findings, relatively insensitive to mucosal disease	Nondistended small bowel may mimic wall thickening

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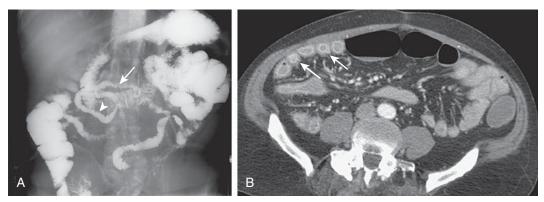


Figure 27-18 Chronic graft-versus-host disease. A, Small bowel follow-through shows thickened folds in the proximal jejunum (arrow) and fold effacement (arrowhead) and luminal narrowing in the ileum segments. Wide separation of the bowel segments is also noted. B, Axial computed tomography image demonstrates the wall thickening involving the ileal segments with a mural stratification pattern and increased enhancement of the mucosa (arrows).



**Figure 27-19** Amyloidosis. Numerous nodules in the jejunum associated with thickening of the folds. Biopsy demonstrated amyloid deposition in the mucosa and submucosa.

fold thickening.<sup>47</sup> Nodules measuring 1 to 2 mm may be diffuse or patchy in distribution.

In addition to nonspecific changes in barium studies, including mild fold thickening, dilatation, and increased fluid, enteroclysis can show a micronodular surface pattern produced by dilatation of the lacteals in the villi in patients with lymphangiectasia.<sup>48</sup>

#### Computed Tomography

CT features of eosinophilic enteritis are nonspecific and have been recently described by Zheng and colleagues.<sup>41</sup> Small bowel wall thickening with or without a "halo" sign (specifying submucosal edema and benign cause) and luminal narrowing can be demonstrated on CT.

Bowel wall thickening with or without proximal dilatation, engorgement of the vasa recta, mesenteric fat stranding, and mucosal and serosal enhancement are the described CT findings for GVHD (see Figure 27-18).<sup>49</sup> Ascites, biliary abnormalities, and wall thickening involving other segments of the gastrointestinal tract also can be detected on CT.

CT findings of amyloidosis are normal or nonspecific in most cases. Bowel wall thickening is usually symmetric and may resemble ischemia.<sup>49</sup>

The presence of enlarged low-density mesenteric lymph nodes associated with small bowel wall thickening is highly suggestive of Whipple's disease.<sup>50</sup> Hepatomegaly and ascites also can be present.

In patients with intestinal lymphangiectasia, CT may show diffuse wall thickening of the small bowel. The halo sign, characterized by an inner ring of low CT attenuation surrounded by a higher attenuation outer ring, was described for intestinal lymphangiectasia.<sup>51</sup> However, this sign is not specific and also can be seen in patients with Crohn's disease, ulcerative colitis, radiation enteritis, ischemic colitis, and pseudomembranous colitis.<sup>46</sup> CT also can demonstrate the cause of secondary lymphangiectasia.

#### Nuclear Medicine

Lymphoscintigraphy using <sup>99m</sup>Tc-dextran can be used to localize the bowel segment with intestinal lymphangiectasia.<sup>52</sup> Protein-losing enteropathies can be diagnosed by the rapid appearance of <sup>99m</sup>Tc-labeled albumin within the bowel after intravenous injection.

### Classic Sign: Miscellaneous Causes of Bowel Wall Thickening

 Halo sign: Nonspecific sign characterized by an inner ring of low CT attenuation surrounded by a higher attenuation outer ring in the small bowel wall. This sign may be seen in patients with intestinal lymphangiectasia as well as another colitis or enteritis.

#### DIFFERENTIAL DIAGNOSIS

Clinical manifestation of these diseases is usually nonspecific and does not allow a definite diagnosis. GVHD is seen in a highly selective subgroup of patients, and the differential diagnosis for acute GVHD includes gastrointestinal infections,

Document téléchargé de ClinicalKey.fr par Faculte de Medecine de Tunis août 30, 2016. Pour un usage personnel seulement. Aucune autre utilisation n'est autorisée. Copyright ©2016. Elsevier Inc. Tous droits réservés. neutropenic enterocolitis, radiation changes, and chemotherapy side effects.

The differential diagnosis list is long and includes inflammatory bowel disease, infectious enteritis, neoplasms, and connective tissue diseases. Definitive diagnosis usually requires endoscopic biopsies.

Common radiographic findings of these diseases are bowel wall thickening and micronodularity. Additional radiographic differential diagnosis includes infectious enteritis, Crohn's disease, radiation changes, intestinal ischemia, vasculitis, and submucosal hemorrhage (especially when the involvement is focal). The presence of micronodular pattern is more suggestive of Whipple's disease and lymphangiectasia. CT can help in the differential diagnosis in some cases by demonstrating extraintestinal findings such as low-density lymph nodes seen in patients with Whipple's disease.

#### TREATMENT

#### Medical Treatment

Medications are used for prevention of attacks or relief of acute symptoms in patients with eosinophilic enteritis. Corticosteroids are the most commonly used drugs. Azathioprine and other immunomodulators have been used with some success.

Intensive prophylaxis with immunosuppressive drugs, selective depletion of T lymphocytes from the donor graft, using umbilical cord blood as the source of donor cells, and choosing more closely matched human leukocyte antigen donors have decreased the incidence and severity of GVHD.<sup>51</sup> Steroids in combination with cyclosporine is usually administered in patients with acute GVHD.

Treatment of small intestine amyloidosis is supportive until the development of rare complications such as bleeding, ischemia, or obstruction. In secondary amyloidosis, treatment of the underlying cause (neoplasm or chronic infection) is the main focus.

Whipple's disease is treated with antibiotics, usually a combination of penicillin, streptomycin, and trimethoprimsulfamethoxazole. Depending on the seriousness of the disease, treatment also may include fluid and electrolyte replacement, iron, folate, vitamin D, calcium, and magnesium. Relapses are common during the course of the disease.

Treatment of intestinal lymphangiectasia first starts with the treatment of the underlying cause, which can be inflammation or neoplasm. Supportive therapy includes a low-fat diet rich in medium-chain triglycerides and diuretics.

#### Surgical Treatment

Surgery is usually not indicated in the treatment of the diseases discussed in this section.

#### What the Referring Physician Needs to Know: Miscellaneous Causes of Bowel Wall Thickening

- The location and extent of the involved small bowel segments
- Any radiologic findings (intestinal or extraintestinal) that can help make a more specific diagnosis
- Development of complications such as strictures
- Exclusion of neoplasm and acute events requiring surgery

## Benign Neoplasms of the Small Bowel

#### **ETIOLOGY**

The cause of most small bowel lesions is unknown. Most are acquired in adulthood, but there are some notable exceptions. There are lesions of congenital origin that may remain asymptomatic until adulthood. These include heterotopic pancreas, heterotopic gastric mucosa, duplication cysts, and myoepithelial hamartoma.

#### PREVALENCE AND EPIDEMIOLOGY

Between 2% and 5% of all gastrointestinal tumors originate in the small bowel.38,53-56 The duodenum is more commonly involved than the remainder of the small bowel. Carcinoid, which can be benign or malignant, is probably the most common of the small bowel tumors, constituting 25% to 40% of the small bowel neoplasms. Gastrointestinal stromal tumors (GISTs) can be either benign or malignant and account for 9% of small bowel tumors and are found in both the jejunum and ileum.<sup>57</sup> Of the benign-only tumors, lipomas are the second most common and most are ileal in location. Excluding the malignant neuroendocrine tumors, benign tumors of neural origin are rare.58 Most are gangliocytic paragangliomas, found in patients with neurofibromatosis type 1 and, when present, are most commonly located in the duodenum. Other rare tumors include hemangiomas, lymphangiomas, hyperplastic polyps, inflammatory fibroid polyps, and hamartomatous polyps associated with Peutz-Jeghers syndrome.<sup>59,6</sup>

Some lesions are associated with syndromes, such as neural tumors in neurofibromatosis type 1, adenomas in polyposis syndromes (e.g., Gardner's syndrome), and hamartomas in Peutz-Jeghers syndrome or generalized juvenile polyposis.

#### **CLINICAL PRESENTATION**

Excluding neurofibromatosis type 1 and congenital lesions that are also present in childhood (e.g., duodenal duplications or ectopic pancreatic rests), the average age of presentation is the 5th to 6th decades. Most benign tumors are clinically silent and may be discovered incidentally; however, large or soft lesions may act as a lead point for an intussusception and cause bowel obstruction. This can occur in up to one third of benign tumors and cause symptoms such as early satiety, nausea, vomiting, constipation, abdominal distention, and a palpable mass. Large tumors may erode the overlying mucosa and cause bleeding (melena, gastrointestinal hemorrhage, pain, and, rarely, perforation). In fact, bleeding as a manifesting sign is reported in almost 40% of benign small bowel tumors. Large hemangiomas, for example, can present with life-threatening hemorrhage. Other nonspecific symptoms may occur, such as anorexia and anemia. For patients with symptoms, diagnosis is usually made in 6 to 12 months from the onset of symptoms.

#### Peutz-Jeghers Syndrome

This autosomal dominant syndrome that occurs equally in men and women of all races and is usually diagnosed in the teens or early 20s with frequently a known family history. The incidence in the United States is 1 in 60,000 to 300,000 live births. The disease has characteristic mucocutaneous lesions with patches

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of hyperpigmentation found on the mouth, hands, and feet. The hamartomatous intestinal polyps can cause acute intestinal obstruction secondary to intussusception in approximately 40% of patients. Other manifestations include abdominal pain, gastrointestinal bleeding, and prolapse of a rectal polyp. Less common clinical findings include precocious puberty, gynecomastia in males when associated with a Sertoli cell testicular tumor, and irregular menses in females as a result of hyperestrogenism from a sex cord tumor). Approximately half of the patients die in their 50s from cancer of the gastrointestinal tract or elsewhere (see section on Pathology).

#### ANATOMY

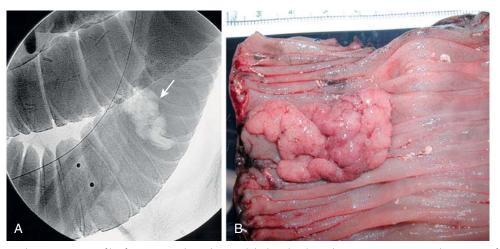
It is important to recognize the differences in the normal fold pattern in different parts of the small intestine, because some causes of benign small bowel disease can affect the fold pattern. The valvulae conniventes or small bowel folds are deeper and more prominent in the jejunum. In the ileum, the folds are more shallow, farther apart, and more effaceable with distention or compression.

#### PATHOLOGY

#### Benign Neoplasms

**Adenoma.** Small bowel adenomas are neoplastic growths from the mucosa that may be histologically tubular (most common), villous, or mixed tubulovillous with varying degrees of differentiation. Villous adenomas are rare in the small intestine (Figure 27-20), and approximately 85% of adenomas occur in the duodenum and 10% in the jejunum. Small bowel adenomas are usually solitary but can be multiple. They may occur in association with familial polyposis or Gardner's syndrome and are more likely than tubular adenomas to undergo malignant degeneration.<sup>61</sup> Any adenoma is more likely to be malignant if large. Additionally, a unique adenoma occurring in the duodenal bulb (often near the apex of the bulb and always proximal to the ampulla of Vater) is the Brunner gland adenoma, also classified by some as a hamartoma, which may actually contain some ductal or stromal elements as well (Figure 27-21).<sup>62,63</sup>

**Lipoma.** Lipomas are most common in the colon, and only 5% to 10% of gastrointestinal lipomas occur in the small



**Figure 27-20** Villous adenoma. A, Spot film from enteroclysis shows a lobulated polypoid mass projecting into the contrast-filled lumen (*arrow*). The surface features are well outlined by the graded compression of the loop, showing a frondlike appearance that corresponds well to the surgical specimen (B). This surface feature is characteristic of villous tumors.

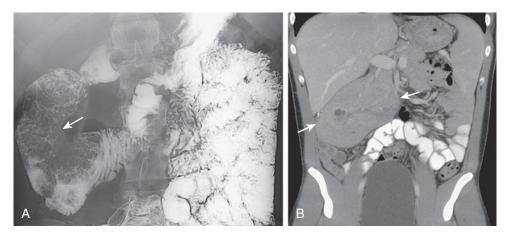


Figure 27-21 Duodenal hamartoma. A, Spot film from small bowel follow-through demonstrates a large intraluminal polypoid mass (arrow) in the duodenum. B, Coronal computed tomography image shows a large, well-defined, homogeneous, soft tissue mass (arrows) in the region of the duodenum. Histopathologic study revealed the diagnosis as hamartoma.

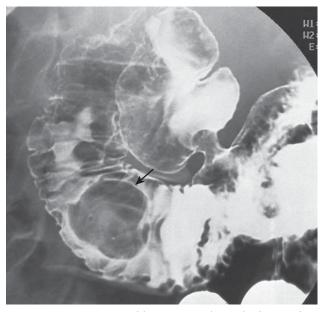


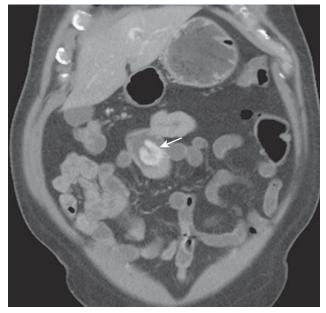
Figure 27-22 Lipoma. Double-contrast radiograph shows a large, well-defined, compressible, polypoid mass (arrow) in the duodenum.

intestine.<sup>64,65</sup> These are always benign submucosal lesions of mesenchymal origin that begin as sessile lesions but owing to their soft nature may become pedunculated when repeatedly stretched by peristalsis (Figure 27-22). If that occurs, the lipoma can then serve as a lead point for intussusception. There is a variable amount of fibrous tissue in some lipomas; thus there is a spectrum from pure lipoma to fibrolipoma and fibroma.

**Neural Tumors.** Neural tumors originate in the submucosa, are usually solitary, and are varied in histologic category. Most are gangliocytic paragangliomas found in neurofibromatosis type 1 and, when present, are most commonly found in the duodenum, often near the ampulla of Vater. Malignant degeneration is rare.

**Vascular Tumors.** These account for 5% to 10% of small bowel tumors and are submucosal lesions that come in three main types: capillary, cavernous (most common), and mixed.<sup>66</sup> They may be solitary or multiple and when multiple may rarely be part of a systemic hemangiomatosis involving multiple organs. The endoluminal shape may be that of a sessile polyp or a carpet lesion. When left untreated, the hemangiomas may develop phleboliths in veinlike channels and may undergo fibrosis. When not fibrotic, the gross appearance will be red and/or blue, suggesting the vascular nature of the lesions. However, when fibrosed, the lesion will be white and mimic other small bowel masses, in which case, if seen by endoscopy, it could be confused for a malignant mucosal lesion. If sampled, these lesions will bleed profusely.

**Leiomyoma and Gastrointestinal Stromal Tumors.** Stromal tumors are composed of nests of spindle-shaped cells usually located between the muscularis propria and muscularis mucosa. GISTs display immunochemical characteristics that are distinctive and express the CD117, CD34 antigen, or both.<sup>67</sup> One third of GISTs occur in the small intestine. Because the overlying mucosa is grossly intact, these have radiologic and pathologic



**Figure 27-23** Benign gastrointestinal stromal tumor (GIST). Coronal computed tomography enterography image shows an enhancing small mass (*arrow*) within a mid-jejunal segment. No associated adenopathy, mass, or ascites is present. Surgery confirmed the diagnosis of a benign GIST.

features of a submucosal lesion (Figure 27-23). Malignant features are assessed by judging the number of mitotic cells per high-power field. Nearly all lesions previously classified as leiomyomas and leiomyosarcomas now fall into the classification of GISTs. Rare variants such as leiomyoblastomas may occur.

The gross pattern of growth can be endoluminal, exophytic or both ("dumbbell"). They are often silent clinically and therefore can be large at the time of diagnosis. Large lesions often undergo necrosis and ulcerate.

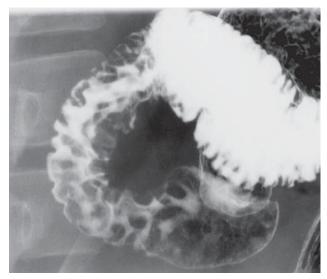
Polyposis and Polyposis Syndromes. The most common polyposis syndrome to involve the small intestine is Peutz-Jeghers syndrome.<sup>60</sup> This is an inherited autosomal dominant disease (but some sporadic mutations occur) caused by a mutation in the STK11 gene. The disease is characterized by hamartomatous polyps with smooth muscle radiating within the polyp (in distinction from the hamartomas of Cronkite-Canada syndrome, which are characterized by cystic dilatation of glands). The polyps nearly always involve the small intestine, but fewer polyps are commonly found in the stomach or colon. Mucocutaneous melanotic macules are seen on the hands, face, and lips that involve buccal and sometimes anal mucosa. The presence of mucosal melanotic macules is essentially diagnostic. The hamartomas have no malignant potential, but sometimes a few adenomas or carcinomas may occur in the gastrointestinal tract (or elsewhere, including the esophagus, stomach, small intestine, colon, pancreas, lung, breast, uterus, and ovary). There is an association with a mutation on the STK11 and CDK7 genes.

#### Tumor-Like Benign Conditions

**Heterotopic Pancreas.** Congenital pancreatic tissue is known by several names: pancreatic rests, ectopic pancreas, accessory pancreas, and aberrant pancreas.<sup>68</sup> These tissues are distinct by location and vascular supply from the main body of the pancreas. They are surprisingly common in autopsy series but are asymptomatic. Approximately 75% are located in the upper gastrointestinal tract, in which case they can become symptomatic. Symptoms include pain, gastrointestinal bleeding, and other obstructive symptoms. More commonly, it is an incidental finding on endoscopy or upper gastrointestinal series in an infant or child. Small 2- to 5-mm submucosal nodule(s) are typically found on the greater curvature of the antrum or first portion of the duodenum, characterized by central umbilication. This characteristic central umbilication is thought to be an aborted form of a pancreatic duct. Biopsy will reveal pancreatic tissue and confirm the diagnosis. If symptomatic, surgical resection is curative.

**Hyperplasia of Brunner Gland.** Brunner glands are mucosal and submucosal alkaline-secreting glands, most commonly found in the first and proximal second parts of the duodenum.<sup>69</sup> They are usually solitary and small but can be multiple.<sup>70</sup> Brunner gland lesions have been classified as hamartomas or hyperplasia and by some as adenomas (Figure 27-24). When multiple, they will produce a cobblestone pattern that should be distinguished from polyps, lymphoid hyperplasia, carcinoid, or metastases. Solitary lesions rarely can be large or pedunculated and thus can cause obstruction or bleeding and be seen on upper gastrointestinal series or CT scans as a smooth intraluminal mass. They constitute 5% of all duodenal masses and are important to differentiate from other duodenal lesions.

**Endometriosis.** The association of gynecologic complaints and gastrointestinal symptoms in a premenopausal woman should raise the suspicion for endometriosis.<sup>70</sup> Endometriosis can implant on any peritoneal surface, although the cul-de-sac and sigmoid colon are the most common. When the small bowel is involved, the terminal ileum is the most common site (Figure 27-25).<sup>71</sup> The endometrial implants behave similar to any other process with serosal implantation. They may cause distortion of loops, angulation, crenulation, or frank mechanical obstruction on small bowel series or CT.<sup>71</sup> As a submucosal mass, they can form a lead point for intussusception.



**Figure 27-24** Brunner gland hyperplasia. Thickening and nodularity of the duodenal folds. Most cases are associated with peptic duodenitis.

**Inflammatory Fibroid Polyp.** These are rare benign submucosal lesions that occur in the small intestine and are of unknown cause, although some familial cases have been reported.<sup>72</sup> More often, they are located in the stomach or terminal ileum, but they can occur anywhere in the gastrointestinal tract. Approximately 70% are pedunculated and therefore may act as a lead point for intussusception, causing pain, but other presentations, including bleeding, weight loss, diarrhea, or anemia, are reported. Most are found incidentally. When these polyps are symptomatic, polypectomy or resection is curative.

**Heterotopic Gastric Mucosa.** Heterotopic gastric mucosa can occur in a variety of locations, including the esophagus, duodenum, and colon or within a Meckel diverticulum, the gallbladder, and elsewhere.<sup>73,74</sup> The involved mucosa has an appearance similar to that of normal areae gastricae, as seen in the stomach on a double-contrast upper gastrointestinal series (Figure 27-26). Unlike lymphoid hyperplasia, these lesions are usually angulated. The abnormality often can be seen to be contiguous with the pyloric channel, extending to involve the duodenal bulb for a variable distance. The appearance is essentially pathognomonic.

**Lymphoid Hyperplasia.** Lymphoid follicles are a normal feature in the small bowel mucosa. When prominent, the term *nodular lymphoid hyperplasia* applies. Nodular lymphoid hyperplasia can be a normal variant, particularly in the terminal ileum in children. In adults, small bowel lymphoid follicles can become abnormally prominent secondary to inflammation or other reasons, such as common variable immunodeficiency, food hypersensitivity, bacterial overgrowth, lymphoma, and other lymphoid malignancies and near a carcinoma (Figure 27-27). When symptomatic, this variant may be associated with



**Figure 27-25** Endometriosis. Spot film from a dedicated small bowel follow-through shows multifocal sites of angulation and tenting consistent with adhesions. At least three distinct sites of eccentric nodular luminal deformity (*arrows*) were present, each with a crenulated concave mural margin. These appeared to be caused by a discrete extraluminal soft tissue process.

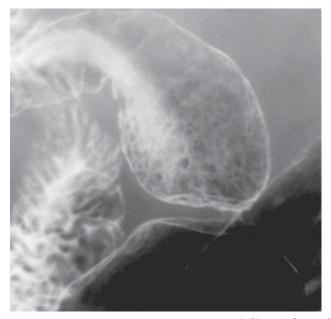
diarrhea, weight loss, and pain.<sup>75</sup> In the duodenal bulb it can become prominent as well, for similar reasons.<sup>73</sup>

**Mimics.** An inverted Meckel diverticulum can appear as an elongated intraluminal "polyp" on fluoroscopic studies or CT, as can an inverted solitary diverticulum of any type.

#### IMAGING

#### Solitary Benign Tumors

In addition to the radiographic studies listed in the following section, gastroenterologists may use wireless capsule endoscopy (Figure 27-28), which can show video images of the small bowel



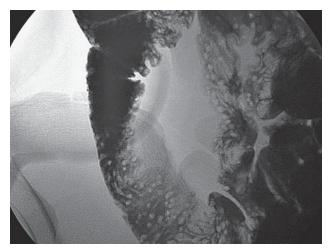
**Figure 27-26** Heterotopic gastric mucosa. Small filling defects of various sizes are shown on a double-contrast radiograph of the duodenal bulb.

and demonstrate the shape and color of lesions. This can be helpful in characterizing vascular lesions such as hemangiomas or varices, which will have a blue or reddish color or characteristic shape.

**Radiography.** If the lesions are large or cause intussusception, plain radiography may show dilated small bowel with a partial small bowel obstruction. Sometimes, complete mechanical obstruction may be present secondary to an intussusception.

Rarely, bowel gas may outline polyps or masses that project intraluminally, but this is more likely to be a retrospective observation than a prospective diagnostic feature. When the polyp contour is outlined by gas or on barium studies, the submucosal lesions have a smooth surface with acute angles except for lesions that are ulcerated. The adenomas have features of a mucosal lesion, irregular surface (especially for villous tumors), and acute angles.

Selective angiography of the gastroduodenal artery, superior mesenteric artery, or mesenteric branches can help reveal sites



**Figure 27-27** Lymphoid hyperplasia. Multiple small, nodular filling defects are evenly distributed through several loops of small bowel.

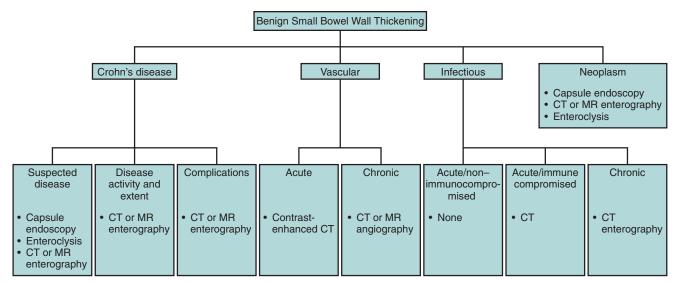


Figure 27-28 Imaging algorithm for benign small bowel wall thickening. CT, Computed tomography; MR, magnetic resonance.

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of active bleeding and also help control bleeding by direct arterial embolization techniques.

**Computed Tomography.** Partial or complete obstruction sites can be identified on CT and help with surgical planning. The size, shape, and density of the mass can be seen if the mass is large enough. CT is better than fluoroscopy in the determining lesion size and can better characterize the lesion. The size of a GIST is an important factor in predicting its clinical behavior; larger lesions are more likely to be malignant. Lipomas are seen as fatty masses, which is a diagnostic factor. Most masses are hypodense and show some enhancement on portal venous phase imaging.

Patients with active bleeding can undergo a three-phase (noncontrast, arterial and portal venous phase) CT enterography technique to identify active extravasation of a contrast agent.

Necrosis of large masses such as GISTs can be seen as areas of heterogeneity and nonenhancement. Tumors with exophytic growth such as GISTs will also exert a mass effect on surrounding structures.

**Magnetic Resonance Imaging.** Similar to CT, MRI can show signs of bowel obstruction, mass size, and location and enhancement characteristics. Most soft tissue tumors, especially GISTs, tend to be isointense relative to skeletal muscle on T1-weighted imaging and hyperintense on T2-weighted imaging. Fatty tumors and those with hemorrhage can be best depicted on nonenhanced, non-fat-suppressed T1-weighted spoiled gradient recalled echo images.

**Ultrasonography.** Except in children, ultrasonography is usually not performed in the evaluation of the small bowel.

**Nuclear Medicine.** In patients who present with signs of brisk gastrointestinal bleeding, a tagged red blood cell scan can help identify the site of bleeding.

**Positron Emission Tomography With Computed Tomography.** PET/CT is not applicable unless malignancy or a neuroendocrine tumor is suspected.

#### Peutz-Jeghers Syndrome

**Radiography.** Barium studies show small bowel polyps that are too numerous to count and some gastric and colonic polyps. Both sessile and pedunculated lesions may be seen. Typically, some segments of the small bowel are spared but short segments with carpeting of polyps can be seen. Polyps may cause intussusception or obstruction.

**Computed Tomography.** CT can show polyps and sites of intussusception or obstruction. Malignancies complicating the syndrome can be diagnosed and staged with CT.

**Magnetic Resonance Imaging.** Similar features to those of CT can be seen on MRI enteroclysis.

**Ultrasonography.** Ultrasonography can have a potential role for surveillance of the testes for males with the syndrome, surveillance of the pancreas for tumors, and surveillance of the ovaries for tumors.

**Positron Emission Tomography With Computed Tomography.** Some rare malignancies, such as pancreatic cancer, can be staged with PET/CT.

**Imaging Algorithm.** Patients known to have Peutz-Jeghers syndrome should undergo surveillance for malignancy of the gastrointestinal tract, breasts, and testes. Imaging is used for initial diagnosis and for the evaluation of complications (Table 27-5).

#### DIFFERENTIAL DIAGNOSIS

The clinical differential diagnosis for partial or complete small bowel obstruction is extensive. In an adult with no prior surgery and no evidence of a primary malignancy, infection, or ischemia, a small bowel tumor should be included in the differential diagnosis.

For patients with a gastrointestinal hemorrhage, the differential diagnosis is also vast. A small bowel tumor may be

	Vei		
Modality	Accuracy	Limitations	Pitfalls
Radiography	Small bowel series or enteroclysis is best to detect small polyps and masses. Angiography can be done to detect bleeding sites or embolize active bleeding sites.	Limited evaluation of exophytic and extraluminal components of disease	Magnification factor will make lesion measurements less accurate than those with CT.
СТ	Good for large masses, but if done as CT enterography, can be as good as a small bowel series or better	Not as good as barium studies in showing mucosal detail and small lesions or ulcerations within lesions	
MRI	Similar to CT	Spatial resolution not as good as CT	
Ultrasonography	Not generally done. May have a role in children		
Nuclear medicine	Not done for detection but can help localize bleeding		
PET/CT	Not applicable for benign lesions, except neuroendocrine lesions		

### TABLE Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging for Benign Neoplasms of the 27-5 Small Bowel

CT, Computed tomography; MRI, magnetic resonance imaging; PET/CT, positron emission tomography with computed tomography.

discovered if CT or a small bowel series or nuclear scintigraphy is used to search for a cause of the bleeding.

#### TREATMENT

#### Medical Treatment

Partial or complete small bowel obstruction is treated with decompression. Patients with anemia and active gastrointestinal bleeding are referred for diagnostic and therapeutic triage.

#### Surgical Treatment

High-grade obstruction (e.g., small bowel tumor causing intussusception) or a localized active bleeding site not amenable to minimally invasive angiographic embolization may require surgery. Large tumors causing symptoms that might also be malignant may be evaluated for elective resection.

#### What the Referring Physician Needs to Know: Benign Neoplasms of the Small Bowel

- Ninety percent of benign small bowel tumors are adenomas, GISTs, lipomas, or hemangiomas.
- Lesion location is important for suggesting some uncommon lesions. Myoepithelial hamartoma occurs in the stomach or duodenum; Brunner gland polyps are in the first or second portion of the duodenum; inflammatory fibroid polyps occur in the terminal ileum (as can solitary carcinoid); and gangliocytic paragangliomas are found near the ampulla of Vater.
- CT is the study of choice for the patient with a partial or complete small bowel obstruction.
- When there is strong indication of a small bowel lesion (e.g., a history of gastrointestinal bleeding in a patient with normal upper and lower bowel studies), consider wireless capsule endoscopy, dedicated small bowel series, or CT enterography (see Figure 27-28).
- Incidental small lesions seen on CT should be evaluated in the clinical context. In most patients with no known underlying disease, a solitary soft tissue lesion is usually a GIST.
- Fatty lesions are "leave me alone" lesions consistent with lipoma.

#### **Key Points**

#### Crohn's Disease

- Crohn's disease is a chronic disease affecting the entire gastrointestinal system.
- It causes transmural inflammation with discontinuous bowel involvement.
- The aims of imaging in Crohn's disease are early, noninvasive diagnosis, differentiation between active and chronic disease, determination of extent and activity of the disease, and recognition of complications.
- CT and MR enterography and enteroclysis have emerged as effective cross-sectional imaging methods, allowing the detection of intestinal and extraintestinal disease manifestations.

#### Infectious Causes of Small Bowel Disease

- Imaging is usually not indicated in immunocompetent patients with acute enteritis. The diagnosis depends on the findings of biopsy, stool examination, and culture.
- Terminal ileum is most severely affected in Campylobacter, Yersinia, and Mycobacterium infections.
- M. tuberculosis causes transaxial ulcerations, polyps, and thickening of the folds, mostly in the ileocecal region in the early phase.
- In the immunocompromised host, M. avium complex, Cryptosporidium, and CMV are the most common infective agents causing enteritis.
- Ulcers are typical findings of CMV enterocolitis, and they can be large.
- CT features of typhlitis include segmental bowel wall thickening involving the terminal ileum, appendix, cecum, and ascending colon, pneumatosis coli, and pericolonic fat stranding.

#### Miscellaneous Causes of Bowel Wall Thickening

- Eosinophilic enteritis most commonly involves the stomach and proximal small bowel and is associated with peripheral eosinophilia.
- Acute GVHD develops within the first 100 days of allogenic bone marrow transplantation.
- CT can show low-density mesenteric lymph nodes in patients with Whipple's disease.
- Thrombocytopenia and low IgA levels are suggestive of intestinal lymphangiectasia in patients with diarrhea and steatorrhea.
- Gastrointestinal system involvement is more common in secondary amyloidosis.
- Small bowel and/or rectal biopsy is required for the definitive diagnosis of these diseases in most patients.

#### Benign Neoplasms of the Small Bowel

- Small bowel series and CT enterography are excellent studies to detect small bowel polyps and masses.
- The differential diagnosis can be tailored to the location of the lesions and their appearance.
- When numerous small bowel lesions are seen, consider polyposis syndromes or metastatic disease.
- If a lesion is soft enough to change size and shape, it is likely a lipoma, a diagnosis that can be made without biopsy based on CT features of gross fat content. Duplication cysts also can be soft and deformable.
- Demonstration of a phlebolith(s) in a lesion is diagnostic of a hemangioma.
- Tumor size is the best factor to predict benign versus malignant behavior of a GIST tumor and is most accurately measured by CT or MRI.

#### REFERENCES

- 1. Balthazar EJ: CT of the gastrointestinal tract: principles and interpretation. *AJR Am J Roent-genol* 156:23–32, 1991.
- Thoreson R, Cullen JJ: Pathophysiology of inflammatory bowel disease: an overview. Surg Clin N Am 87:575–585, 2007.
- Crohn BB, Ginzburg L, Oppenheimer GD: Regional ileitis: a pathologic and clinical entity. *Am J Med* 13:583–590, 1952.
- Orholm M, Fonager K, Sorensen HT: Risk of ulcerative colitis and Crohn's disease among offspring of patients with chronic inflammatory bowel disease. *Am J Gastroenterol* 94:3236–3238, 1999.
- Fichera A, Michelassi F: Surgical treatment of Crohn's disease. J Gastrointest Surg 11:791–803, 2007.
- Michelassi F, Balestracci T, Chappell R, et al: Primary and recurrent Crohn's disease: experience with 1379 patients. *Ann Surg* 214:230–238, discussion 8–40, 1991.
- Yantiss RK, Odze RD: Diagnostic difficulties in inflammatory bowel disease pathology. *Histopathology* 48:116–132, 2006.
- Lee SS, Kim AY, Yang S-K, et al: Crohn disease of the small bowel: comparison of CT enterography, MR enterography, and small-bowel follow-through as diagnostic techniques. *Radiology* 251:751–761, 2009.
- Fleckenstein P, Pedersen G: The value of the duodenal intubation method (Sellink modification) for the radiological visualization of the small bowel. *Scand J Gastroenterol* 10:423–425, 1975.
- Carlson HC: Perspective: the small bowel examination in the diagnosis of Crohn's disease. *AJR Am J Roentgenol* 147:63–65, 1986.
- 11. Kelvin FM, Gedgaudas RK, Thompson WM, et al: The peroral pneumocolon: its role in evaluating the terminal ileum. *AJR Am J Roentgenol* 139:115–121, 1982.
- Triester SL, Leighton JA, Leontiadis GI, et al: A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. Am J Gastroenterol 101:954– 964, 2006.
- Al-Hawary MM, Kaza RK, Platt JF: CT enterography: concepts and advances in Crohn's disease imaging. *Radiol Clin North Am* 51:1–16, 2013.
- Paulsen SR, Huprich JE, Hara AK: CT enterography: noninvasive evaluation of Crohn's disease and obscure gastrointestinal bleed. *Radiol Clin North Am* 45:303–315, 2007.
- Hara AK, Leighton JA, Heigh RI, et al: Crohn disease of the small bowel: preliminary comparison among CT enterography, capsule endoscopy, small-bowel follow-through, and ileoscopy. *Radiology* 238:128–134, 2006.
- Schreyer AG, Geissler A, Albrich H, et al: Abdominal MRI after enteroclysis or with oral contrast in patients with suspected or proven Crohn's disease. *Clin Gastroenterol Hepatol* 2:491–497, 2004.
- 17. Fidler J: MR imaging of the small bowel. *Radiol Clin North Am* 45:317–331, 2007.
- Oto A, Kayhan A, Williams JT, et al: Active Crohn's disease in the small bowel: evaluation by diffusion weighted imaging and quantitative dynamic contrast enhanced MR imaging. *J Magn Reson Imaging* 33:615–624, 2011.
- 19. Parente F, Greco S, Molteni M, et al: Imaging inflammatory bowel disease using bowel ultra-

sound. *Eur J Gastroenterol Hepatol* 17:283–291, 2005.

- Novak KL, Wilson SR: The role of ultrasound in the evaluation of inflammatory bowel disease. Semin Roentgenol 48:224–233, 2013.
- Pradel JA, David XR, Taourel P, et al: Sonographic assessment of the normal and abnormal bowel wall in nondiverticular ileitis and colitis. *Abdom Imaging* 22:167–172, 1997.
- Sayfan J, Wilson DA, Allan A, et al: Recurrence after strictureplasty or resection for Crohn's disease. Br J Surg 76:335–338, 1989.
- 23. Neurath MF, Vehling D, Schunk K, et al: Noninvasive assessment of Crohn's disease activity: a comparison of 18F-fluorodeoxyglucose positron emission tomography, hydromagnetic resonance imaging, and granulocyte scintigraphy with labeled antibodies. *Am J Gastroenterol* 97: 1978–1985, 2002.
- Procop GW: Gastrointestinal infections. Infect Dis Clin North Am 15:1073–1108, 2001.
- Addiss DG, Davis JP, Roberts JM, et al: Epidemiology of giardiasis in Wisconsin: increasing incidence of reported cases and unexplained seasonal trends. *Am J Trop Med Hyg* 47:13–19, 1992.
- Ilnyckyj A: Clinical evaluation and management of acute infectious diarrhea in adults. *Gastroen*terol Clin North Am 30:599–609, 2001.
- Altekruse SF, Cohen ML, Swerdlow DL: Emerging foodborne diseases. *Emerg Infect Dis* 3:285– 293, 1997.
- Lee SD, Surawicz CM: Infectious causes of chronic diarrhea. *Gastroenterol Clin North Am* 30:679–692, viii, 2001.
- Puylaert JB, Van der Zant FM, Mutsaers JA: Infectious ileocecitis caused by Yersinia, Campylobacter, and Salmonella: clinical, radiological and US findings. *Eur Radiol* 7:3–9, 1997.
- Ekberg O, Sjöström B, Brahme F: Radiological findings in Yersinia ileitis. *Radiology* 123:15–19, 1977.
- Brodey PA, Fertig S, Aron JM: Campylobacter enterocolitis: radiographic features. AJR Am J Roentgenol 139:1199–1201, 1982.
- Speelman P, Kabir I, Islam M: Distribution and spread of colonic lesions in shigellosis: a colonoscopic study. J Infect Dis 150:899–903, 1984.
- 33. Kalra N, Agrawal P, Mittal V, et al: Spectrum of imaging findings on MDCT enterography in patients with small bowel tuberculosis. *Clin Radiol* 69:315–322, 2014.
- 34. Pulimood AB, Amarapurkar DN, Ghoshal U, et al: Differentiation of Crohn's disease from intestinal tuberculosis in India in 2010. World J Gastroenterol 17:433–443, 2011.
- 35. Poorman JC, Katon RM: Small bowel involvement by *Mycobacterium avium* complex in a patient with AIDS: endoscopic, histologic, and radiographic similarities to Whipple's disease. *Gastrointest Endosc* 40:753–759, 1994.
- Balthazar EJ, Martino JM: Giant ulcers in the ileum and colon caused by cytomegalovirus in patients with AIDS. AJR Am J Roentgenol 166: 1275–1276, 1996.
- Ha HK, Ko GY, Yu ES, et al: Intestinal tuberculosis with abdominal complications: radiologic and pathologic features. *Abdom Imaging* 24:32– 38, 1999.
- Hoeffel C, Crema MD, Belkacem A, et al: Multidetector row CT: spectrum of diseases involving the ileocecal area. *Radiographics* 26:1373–1390, 2006.

- Yu J, Fulcher AS, Turner MA, et al: Helical CT evaluation of acute right lower quadrant pain. II. Uncommon mimics of appendicitis. *AJR Am J Roentgenol* 184:1143–1149, 2005.
- Hassan I, Brilakis ES, Thompson RL, et al: Surgical management of abdominal tuberculosis. *J Gastrointest Surg* 6:862–867, 2002.
- Zheng X, Cheng J, Pan K, et al: Eosinophilic enteritis: CT features. *Abdom Imaging* 33:191– 195, 2008.
- Maizel H, Ruffin JM, Dobbins WO, 3rd.: Whipple's disease: a review of 19 patients from one hospital and a review of the literature since 1950. *Medicine* 49:175–205, 1970.
- Schulman A, Morton PC, Dietrich BE: Eosinophilic gastroenteritis. *Clin Radiol* 31:101–104, 1980.
- Kala Z, Valek V, Kysela P: Amyloidosis of the small intestine. *Eur J Radiol* 63:105–109, 2007.
- Jones B, Kramer SS, Saral R, et al: Gastrointestinal inflammation after bone marrow transplantation: graft-versus-host disease or opportunistic infection? *AJR Am J Roentgenol* 150:277–281, 1988.
- Horton KM, Corl FM, Fishman EK: CT of nonneoplastic diseases of the small bowel: spectrum of disease. J Comput Assist Tomogr 23:417–428, 1999.
- Herlinger H: Radiology in malabsorption. *Clin Radiol* 45:73–78, 1992.
- Aoyagi K, Iida M, Yao T, et al: Intestinal lymphangiectasia: value of double-contrast radiographic study. *Clin Radiol* 49:814–819, 1994.
- Kalantari BN, Mortele KJ, Cantisani V, et al: CT features with pathologic correlation of acute gastrointestinal graft-versus-host disease after bone marrow transplantation in adults. AJR Am J Roentgenol 181:1621–1625, 2003.
- Rijke AM, Falke TH, de Vries RR: Computed tomography in Whipple disease. J Comput Assist Tomogr 7:1101–1102, 1983.
- Cutler C, Kim HT, Hochberg E, et al: Sirolimus and tacrolimus without methotrexate as graftversus-host disease prophylaxis after matched related donor peripheral blood stem cell transplantation. *Biol Blood Marrow Transplant* 10: 328–336, 2004.
- Puri AS, Aggarwal R, Gupta RK, et al: Intestinal lymphangiectasia: evaluation by CT and scintigraphy. *Gastrointest Radiol* 17:119–121, 1992.
- Ramachandran I, Sinha R, Rajesh A, et al: Multidetector row CT of small bowel tumours. *Clin Radiol* 62:607–614, 2007.
- Horton KM, Fishman EK: MDCT of the duodenum: technique and clinical applications. *Crit Rev Comput Tomogr* 45:309–334, 2004.
- Wittenberg J, Harisinghani MG, Jhaveri K, et al: Algorithmic approach to CT diagnosis of the abnormal bowel wall. *Radiographics* 22:1093– 1107, discussion 107–109, 2002.
- Blanchard DK, Budde JM, Hatch GF, 3rd, et al: Tumors of the small intestine. *World J Surg* 24:421–429, 2000.
- McGarrity TJ, Kulin HE, Zaino RJ: Peutz-Jeghers syndrome. Am J Gastroenterol 95:596– 604, 2000.
- Sathe PA, Kulkarni VM, Raut AA, et al: Ileal polyposis as manifestation of neurofibromatosis syndrome. *Indian J Gastroenterol* 25:159–160, 2006.
- 59. Hirasaki S, Matsubara M, Ikeda F, et al: Inflammatory fibroid polyp occurring in the transverse

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colon diagnosed by endoscopic biopsy. *World J Gastroenterol* 13:3765–3766, 2007.

- Burton MJ, Seery JP, Taylor-Robinson SD, et al: Jejunal intussusception secondary to Peutz-Jeghers type hamartoma diagnosed on angiography. *Clin Radiol* 54:476–478, 1999.
- Taylor SA, Halligan S, Moore L, et al: Multidetector-row CT duodenography in familial adenomatous polyposis: a pilot study. *Clin Radiol* 59:939–945, 2004.
- 62. Chappuis VS, Vernez M, Denys A, et al: Brunner gland hamartoma: a challenging diagnosis. *Pancreas* 33:202–203, 2006.
- 63. Merine D, Jones B, Ghahremani GG, et al: Hyperplasia of Brunner glands: the spectrum of its radiographic manifestations. *Gastrointest Radiol* 16:104–108, 1991.
- Oyen TL, Wolthuis AM, Tollens T, et al: Ileo-ileal intussusception secondary to a lipoma: a literature review. *Acta Chir Belg* 107:60–63, 2007.

- 65. Bentama K, Chemlal I, Benabbou M, et al: Acute intussusception secondary to a lipoma of the small intestine: about a case and review of the literature. *Pan African Med J* 12:98, 2012.
- Boyle L, Lack EE: Solitary cavernous hemangioma of small intestine: case report and literature review. Arch Pathol Lab Med 117:939–941, 1993.
- He LJ, Wang BS, Chen CC: Smooth muscle tumours of the digestive tract: report of 160 cases. Br J Surg 75:184–186, 1988.
- Gurbulak B, Kabul E, Dural C, et al: Heterotopic pancreas as a leading point for small-bowel intussusception in a pregnant woman. J Pancreas 8:584–587, 2007.
- Patel ND, Levy AD, Mehrotra AK, et al: Brunner's gland hyperplasia and hamartoma: imaging features with clinicopathologic correlation. *AJR Am J Roentgenol* 187:715–722, 2006.
- Scarmato VJ, Levine MS, Herlinger H, et al: Ileal endometriosis: radiographic findings in five cases. *Radiology* 214:509–512, 2000.

- Attar A, Lagorce C: Small bowel obstruction caused by endometriosis. *Clin Gastroenterol Hepatol* 5:A30, 2007.
- Wysocki AP, Taylor G, Windsor JA: Inflammatory fibroid polyps of the duodenum: a review of the literature. *Dig Surg* 24:162–168, 2007.
- Glick SN, Gohel VK, Laufer I: Mucosal surface patterns of the duodenal bulb: subject review. *Radiology* 150:317–322, 1984.
- Langkemper R, Hoek AC, Dekker W, et al: Elevated lesions in the duodenal bulb caused by heterotopic gastric mucosa. *Radiology* 137:621– 624, 1980.
- Rubio-Tapia A, Hernandez-Calleros J, Trinidad-Hernandez S, et al: Clinical characteristics of a group of adults with nodular lymphoid hyperplasia: a single center experience. World J Gastroenterol 12:1945–1948, 2006.

## Malignant Neoplasms and Wall Thickening of the Small Bowel

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Small bowel neoplasms remain a diagnostic challenge for radiologists and clinicians. The small bowel represents 75% of the total length of the gastrointestinal tract and more than 90% of the mucosal surface, but less than 2% of all gastrointestinal malignancies originate in the small bowel.<sup>1</sup> Malignant tumors of the small bowel may arise from the mucosal epithelium, lymphoid tissue, blood vessels, nerves, and muscle. Secondary involvement of the small bowel is more common than primary malignancies. Considerable delay in the diagnosis of small bowel malignancies leads to low survival rates. Increased awareness of the small intestine as a potential source of nonspecific abdominal complaints or chronic anemia and the selection of the most accurate diagnostic tests would lead to improvement of a patient's prognosis.<sup>2</sup>

In this chapter both secondary and primary malignancies of the small bowel are reviewed, with an emphasis on their imaging findings (Table 28-1).

## Secondary Malignancies of the Small Bowel

#### ETIOLOGY

Metastatic disease to the bowel is more common than primary malignancies. Mechanisms of metastatic seeding to the small bowel include intraperitoneal seeding, direct extension along the fascia or mesenteric attachments, hematogenous spread, and lymphatic extension.<sup>3</sup> The mechanism of spread determines the radiologic appearance. Intraperitoneal spread is the most common mechanism and usually occurs as a result of spread via ascitic fluid. The primary neoplasms are usually gastrointestinal in men and ovarian in women.<sup>4</sup> Direct invasion of the small intestine is seen from primary colon, pancreas, biliary, ovarian, renal, and adrenal malignancies. Hematogenous spread of primary neoplasms to the small bowel is rare. Melanoma, lung, breast, kidney, and gynecologic cancers are the most common tumors with embolic spread to the small bowel.

Lymphatic dissemination to the small bowel plays a small role. A typical example is spread of cecal carcinoma to the terminal ileum by retrograde lymphatic flow after occlusion of the pericecal lymphatic vessels.<sup>5</sup> Melanoma is the extraintestinal malignancy with the greatest predilection to bowel metastasis, and the small bowel is the most common part of the gastrointestinal tract to be affected by metastatic melanoma.<sup>6</sup>

#### **CLINICAL PRESENTATION**

The primary tumor is known in most cases, and patients present with nonspecific signs such as abdominal pain, weight loss, anemia, gastrointestinal bleeding, or obstruction. The interval between the diagnosis of malignancy and intestinal obstruction caused by the metastatic disease can vary widely.<sup>7</sup> Intermittent obstruction and anemia can be caused by intussusception, with metastatic lesions serving as a lead point. It is important to consider the possibility of metastatic small bowel lesions in the setting of nonspecific abdominal complaints or chronic unexplained iron deficiency anemia in patients with known malignancies.

#### PATHOPHYSIOLOGY

When the mechanism of spread is direct invasion, the localization of an involved small bowel segment depends on the primary tumor. The infiltration involves a larger segment of small bowel in patients with ovarian cancer but shorter segments in the case of primary colon carcinoma.<sup>8</sup> Pancreatic tumors and hepatic flexure tumors infiltrate the duodenum, whereas cecal tumors invade the terminal ileum.

Peritoneal fluid has a continuous flow within the anatomic pathways of peritoneal recesses and mesenteric reflections.<sup>9</sup> A primary neoplasm or metastatic lymph node can break into the peritoneal cavity and initiate the peritoneal spread.<sup>10</sup> The most common sites for the lodging and growth of peritoneal spread are the pouch of Douglas, right paracolic gutter, superior aspect of the sigmoid mesocolon, and terminal portion of the mesentery in the right lower quadrant.<sup>9</sup> The negative pressure under the diaphragm and increased capillary forces make the dome of the liver a common site for peritoneal deposits. Peritoneal deposits on serosal surfaces adhere through fibrinous exudation and may incite a desmoplastic response.

#### PATHOLOGY

Hematogenous metastases can be solitary or multiple and tend to be submucosal.<sup>11</sup> The masses are usually on the antimesenteric border where the vasa recta end in a rich submucosal plexus and can demonstrate central ulceration because of their limited blood supply.

Lymphatic blockage by the primary tumor can cause retrograde lymphatic flow and spread of tumor cells into the small

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TABLE <b>28-1</b>	Characte	eristics of	Maligna	Characteristics of Malignant Neoplasms of th	ne Small Bowel				
Lesion		Age	Sex	Distinguishing Clinical History	Distinguishing Clinical Presentation	Imaging Modality of Choice	Distinguishing Imaging Findings	Enhancement Pattern	Additional Findings
Adeno	Adenocarcinoma	6th-7th decades	ц = >	No specific symptoms, high level of suspicion is recommended in patients with long-standing disease, vague gastrointestinal symptoms, and weight loss	Abdominal pain (60%) Obstruction (40%) Gastrointestinal hemorrhage (24%)	Enteroclysis, CT enterography	Partial or complete small bowel obstruction or intussusception on plain film Barium studies: Apple core lesion, asymmetric wall thickening or infiltrative pattern More in proximal small bowel	Heterogeneous enhancement (hemorrhage, necrosis, or ulceration in 40% of cases)	Local extension, regional abdominal lymphadenopathy, distant metastases
Carcinoid	þic	6th-7th decades	∟ ■ ≥	Asymptomatic or present with carcinoid syndrome (cutaneous flushing, sweating, bronchospasm, abdominal pain, and diarrhea)	Classic carcinoid syndrome	Abdominal CT, CT enterography, nuclear scan	Intussusception on plain film Mesenteric mass on CT scan	Spiculated margins, low attenuation Mass with fat stranding and minimal enhancement Hypervascular liver metastases	"Spokewheel" or "sunburst" appearance on CT Encasement of mesenteric vessels leading to ischemia of affected bowel loops Octreoscan study is more sensitive in localizing carcinoids and metastatic disease compared with CT, MRI, or endoscopy.
Lymphoma	oma	Bimodal, <10, >50	⊥ ∧ ≥	Chronic anemia, weight loss	Abdominal pain, diarrhea, steatorrhea	Abdominal CT or CT enterography	Four patterns of involvement: (1) multiple nodules at multiple sites; (2) single large mass, triggering point for intussusception; (3) infiltrative pattern, presents as asymmetric wall thickening or aneurysmal dilatation of bowel loop; (4) exophytic mass	Low-attenuation soft tissue mass with minimal enhancement	Enlarged lymph nodes in the chest, abdomen, or pelvis Aneurysmal dilatation of the involved bowel loop without obstruction
GIST		5th-6th decades	⊥ ∧ ≥	Incidental finding on imaging	Bleeding and abdominal pain; directly correlates with size of tumor	CT enterography or small bowel series	Intramural exophytic mass with or without internal calcifications and necrosis Submucosal lesion with smooth surface and acute angle	Circumscribed exophytic low- attenuation mass with heterogeneous enhancement depending on hemorrhage, necrosis	Liver metastases can be hypervascular.
Metastatic disease	atic ase	After the 5th decade	L = Z	History of a primary neoplasm, especially melaroma or gastrointestinal, pancreatic, or ovarian in origin	Gastrointestinal bleeding, increased abdominal pain, bowel obstruction in patients with known neoplasms	Abdominal CT	Diffuse or nodular peritoneal and intestinal wall thickening "Bull's eye" appearance on barium studies Intussusception	Variable	Primary tumor and other metastatic disease

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CT, Computed tomography; GIST, gastrointestinal stromal tumor; MRI, magnetic resonance imaging.

bowel with the terminal ileum and proximal jejunum being the most common sites of involvement.

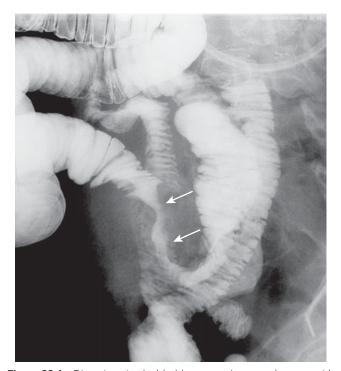
#### IMAGING

#### Radiography

Direct invasion from another primary tumor usually produces mucosal destruction and narrowing of the lumen without the shouldering of the margins, which is a characteristic of a primary neoplasm (Figure 28-1).<sup>10</sup> Chronic radiation changes need to be differentiated from secondary invasion. The duode-num is a common segment for secondary invasion and can be invaded by pancreatic, colon, renal, and adrenal tumors.

Peritoneal deposits may be seen as rounded protrusions toward the lumen of the small bowel. Discrete separation of ileal loops, often with a parallel configuration, angulated tethering of mucosal folds on their mesenteric border, and narrowing of loops are suggestive of peritoneal seeding associated with some desmoplastic reaction.<sup>9</sup> Striking angulation and marked fixation of small bowel loops can be seen in primary cancers, causing a significant desmoplastic reaction, such as pancreatic or gastric carcinoma.<sup>9</sup>

Multiple, round, polypoid nodules mostly seen along the antimesenteric border of the small bowel are the most common radiologic finding for hematogenous metastases, especially from a primary or malignant melanoma (Figure 28-2). The metastatic nodules tend to ulcerate centrally, and, when the lesions are small, ulcerations appear as target lesions ("bull's eye" lesions) with collection of barium at the central ulcers.<sup>12</sup> These nodules can act as a lead point for intussusception. Larger masses may have large ulcers or cavitations outlined with barium and may have a mass effect on the surrounding small bowel segments.<sup>8</sup> Breast cancer metastases are rare but described

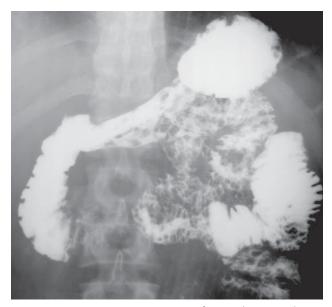


**Figure 28-1** Direct invasion by bladder cancer. Intramural masses with loop fixation and mucosal tethering of an ileum segment (*arrow*) are causing mild small bowel obstruction.

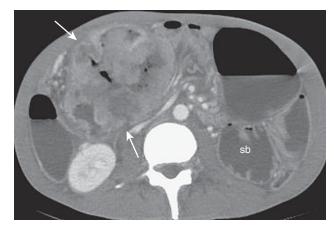
as spreading through the submucosa, causing multiple strictures and intestinal obstruction.<sup>13</sup> Metastases from lung or renal cell carcinoma are usually seen as solid or multiple large mesenteric masses with frequent ulcerations.<sup>14</sup>

#### Computed Tomography

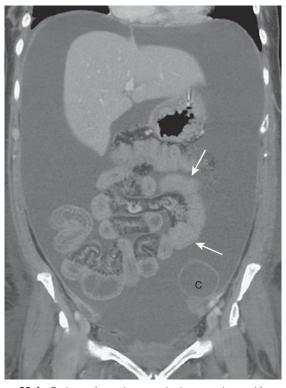
Computed tomography (CT) can show the metastatic lesions in the small bowel wall, mesentery, peritoneal surfaces, and lymph nodes and therefore can give a better idea about the size and extent of the disease. CT also can depict the extension of disease to the surrounding organs. Another advantage of CT is its ability to identify the primary tumor (Figure 28-3). Intestinal bowel wall or peritoneal thickening (either nodular or plaquelike), mesenteric or omental nodules, and/or fat stranding are the common CT findings in patients with metastases to small



**Figure 28-2** Hematogenous metastasis from malignant melanoma. Multiple nodular filling defects throughout the stomach and jejunal segments are seen on small bowel follow-through. Some of these nodules demonstrate central ulcerations.



**Figure 28-3** Primary colon cancer arising from hepatic flexure invading small bowel segments. Axial computed image shows large, heterogeneous mass (*arrows*) invading the small bowel segments in the right upper quadrant. Small bowel segments in the left upper quadrant (*sb*) are dilated, representing obstruction.



**Figure 28-4** Peritoneal carcinomatosis in a patient with ovarian cancer. Coronal computed tomography image shows significant malignant ascites and diffuse wall thickening of the small bowel segments (*arrows*) secondary to peritoneal carcinomatosis. Additional cystic peritoneal metastatic mass (*C*) is seen in the left lower quadrant.

bowel segments (Figure 28-4). Metastases from melanoma manifest as enhancing mural nodules or focal thickening of the intestinal wall (Figure 28-5).<sup>15</sup>

#### Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) can provide a sensitive and accurate depiction of tumor involving the peritoneum and bowel serosa. Fat-suppressed, gadolinium-enhanced MRI is preferred for detection of small peritoneal or mesenteric tumors.<sup>16</sup> Peritoneal tumors are found to be more conspicuous on delayed MR images obtained 5 to 10 minutes after intravenous injection of gadolinium. Even small implants can be depicted on delayed, fat-suppressed, gadolinium-enhanced gradient echo images.<sup>16</sup> Diffusion weighted imaging in combination with conventional MRI is more accurate in detecting peritoneal metastasis.<sup>17</sup>

#### Ultrasonography

Ultrasonography can be sensitive for detection of serosal, and superficial neoplastic deposits when performed with a high-frequency probe. However, it is limited in evaluating deposits between the loops or along the posterior wall.<sup>18</sup> The focal thickened wall of the small bowel shows the nonspecific "pseudo-kidney" sign, which can be seen in both benign and malignant diseases.

#### Positron Emission Tomography With Computed Tomography

Peritoneal metastatic deposits can demonstrate uptake of fluorodeoxyglucose (FDG), and PET/CT may be a useful diagnostic



**Figure 28-5** Malignant melanoma metastasis. Coronal computed tomography image shows multiple soft tissue masses in the small bowel wall and mesentery (*arrows*).

tool when peritoneal biopsy is either unavailable or inappropriate (Figure 28-6).<sup>19</sup> However, further studies are needed to better determine the role of FDG-PET for evaluation of peritoneal carcinomatosis.

#### Imaging Algorithm

SBFT is noninvasive but relatively insensitive for detection of small intramural deposits and is completely blind to extraintestinal disease.

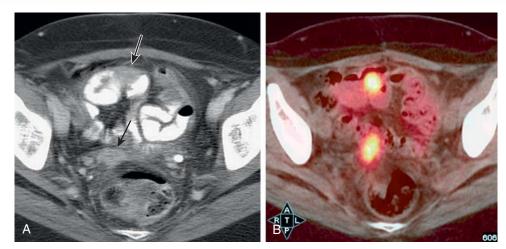
Enteroclysis can detect small intestinal metastases earlier than CT, but it is an invasive test. With the advances of CT technology, new techniques such as CT enterography or CT enteroclysis have emerged and can evaluate both intestinal and extraintestinal disease (Table 28-2).<sup>20</sup> Therefore, CT is often used as an initial tool for evaluation of abdominal symptoms in patients with known cancer. In cases complicated with bowel obstruction, CT should be the diagnostic test of choice (see Figure 28-18).

#### Classic Sign: Secondary Malignancies of the Small Bowel

 Target lesion (bull's eye): Central ulceration of the hematogenous metastases, most common in the malignant melanoma metastases

#### DIFFERENTIAL DIAGNOSIS

Symptoms of metastatic disease to the small bowel are very nonspecific; therefore, the clinical differential diagnosis is very wide. Complications related to the treatment (irradiation or



**Figure 28-6** Peritoneal metastasis from colon cancer on positron emission tomography with computed tomography (PET/CT). Subtle, peritoneal soft tissue deposits invading small bowel walls on axial CT image (*arrows,* **A**) are more obvious on the PET/CT image (**B**), demonstrating increased FDG uptake.

### TABLEAccuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Secondary Malignancies28-2of the Small Bowel

Modality	Accuracy	Limitations	Pitfalls
Radiography	Enteroclysis is very accurate in detecting smaller lesions involving the small bowel wall	Cannot show mesenteric, peritoneal disease or primary tumor	Radiation enteritis
СТ	Very accurate in the detection of relatively larger intestinal lesions and extraintestinal disease	Limited sensitivity in detection of small mucosal or intramural lesions	Undistended bowel
MRI	Slightly more sensitive in depiction of small peritoneal lesions	Limited experience, longer study time, less spatial resolution compared with CT	

CT, Computed tomography; MRI, magnetic resonance imaging.

chemotherapy) of the primary cancer, bowel ischemia, infection, inflammation, paraneoplastic syndromes, primary gastrointestinal tumors, and other causes of abdominal pain must be considered.

The primary tumor is usually known and helps in determining the diagnosis. Adhesions, metastases, and radiation enteritis are considered in the differential diagnosis of small bowel obstruction in patients with known malignancies. Adhesions usually cause linear compression of the lumen with straight margins. Ileocecal metastatic disease may resemble Crohn's disease. Endometriosis can mimic multiple, small hematogenous metastases. Abdominal tuberculosis can cause peritoneal thickening, mesenteric fat stranding, bowel wall thickening, and adenopathy mimicking metastatic disease. Radiologic differentiation from neoplastic disease may be difficult.

#### TREATMENT

#### Medical Treatment

Medical treatment is aimed specifically against the primary tumor and may consist of hormone therapy, chemotherapy, and targeted biological therapy. There is a large variability in the expected effectiveness of the treatment, as well as in the prognosis of patients.<sup>6,7</sup> Obstruction may be relieved, and the symptoms may resolve after chemotherapy in patients with breast carcinoma.

#### Surgical Treatment

Surgical treatment of secondary intestinal malignancies aims to relieve the intestinal obstruction and/or control the metastatic disease.<sup>7</sup> Radiologic demonstration of noninvolved small bowel segments significantly contributes to the achievement of both of these targets. An accurate preoperative understanding of the extent of the disease is crucial for surgical planning. The specific anticancer therapy is almost always considered after surgery.

#### What the Referring Physician Needs to Know: Secondary Malignancies of the Small Bowel

- Knowing if small bowel metastases are present changes the staging, and their presence may cause complications such as intussusception, bleeding, or obstruction.
- Knowing the extent of disease is important for surgical planning and to decide between medical versus surgical treatment.
- Any complications related to metastatic disease should be considered.
- Abnormalities that may have a similar clinical presentation should be excluded.

# Primary Malignancies of the Small Bowel

#### ETIOLOGY

The most common malignant primary small bowel neoplasms are small bowel adenocarcinoma, carcinoid, lymphoma, and gastrointestinal stromal tumors (GISTs). Small bowel adenocarcinoma is a rare neoplasm, and the most important risk factor in the development of adenocarcinoma is Crohn's disease. Higher incidence of small bowel adenocarcinoma is also associated with adenomatous polyps, villous adenomas, familial adenomatous polyposis, hereditary nonpolyposis colorectal cancer, celiac sprue, cystic fibrosis, and peptic ulcer disease.<sup>8,21</sup>

Carcinoid tumors originate from the diffuse endocrine system outside the pancreas and thyroid and most frequently occur in the gastrointestinal tract (66.9%), followed by the tracheobronchial system (24.5%).<sup>8</sup> They are frequently associated with specific syndromes such as Zollinger-Ellison syndrome, multiple endocrine neoplasia type 1, carcinoid syndrome, or neurofibromatosis type 1.

The exact cause of small bowel lymphoma is unknown. Various predisposing factors have been postulated to be responsible for small bowel lymphoma. A few of the predisposing factors include celiac disease, previous extraintestinal lymphoma, immunosuppressed conditions such as human immunodeficiency virus infection and acquired immunodeficiency syndrome, long-standing systemic lupus erythematosus, Crohn's disease, and postchemotherapy conditions.

GISTs are CD117-positive mesenchymal tumors thought to originate from interstitial cells of Cajal that are normally part of the autonomic nervous system of the gastrointestinal tract.<sup>22</sup>

#### PREVALENCE AND EPIDEMIOLOGY

Primary adenocarcinoma of the small intestine accounts for less than 1% of all primary gastrointestinal tumors, with an estimated annual incidence of 0.25 to 0.4 per 100,000 population.<sup>8,21</sup> It predominantly affects the duodenum and jejunum in 42% and 43% of cases, respectively. The ileum is involved in less than 15% of the patients, except in Crohn's disease.<sup>8</sup> The peak incidence is in the sixth and seventh decades of life.

Carcinoid is the second most common small bowel malignancy, representing approximately 25% of all primary small bowel tumors, and most commonly affects the ileum. In the past 30 years there has been an increase in the incidence of carcinoid tumors, with 41.8% of gastrointestinal carcinoids occurring in the small intestine, followed by the rectum (27.4%), appendix (24.1%), and stomach (8.7%).<sup>8</sup> The appendix was thought to be the most common location for gastrointestinal carcinoids, but several authors have noted a decreased incidence of appendiceal carcinoids. This observation is probably due to the decreasing rate of appendectomies related to the increasing accuracy of diagnosing inflammatory appendicitis preoperatively.<sup>23</sup>

The mean age at the time of diagnosis for all carcinoids is 61.4 years, and the disease occurs equally in men and women. Synchronous or metachronous malignancies occur in 29% of patients with small intestinal carcinoids.

Small bowel lymphoma is the third most common small bowel malignancy, representing 10% to 15% of small bowel malignancies. It can involve any portion of the gastrointestinal tract and predominantly targets the lymphoid follicles. It is most common in the ileum, and most manifest as intermediate- to high-grade non-Hodgkin's lymphoma; T-cell variants are more often associated with celiac disease. Mediterranean abdominal lymphoma is a variant associated with immunoproliferative small intestinal disease and consists of diffuse lymphomatous infiltration of mucosa and submucosa in long segments of the small intestine.

There is a slight male predominance with bimodal age distribution, with peaks in those younger than the age of 10 and older than the age of 50. Small bowel lymphoma is multifocal in 15% of cases. Increased incidence of small bowel lymphoma was reported among patients with celiac disease.<sup>24</sup>

GIST is the fourth most common small bowel neoplasm. It constitutes 9% of all small bowel malignant tumors.<sup>25</sup> GISTs rarely involve the duodenum. They occur in the fifth and sixth decades and are more common in males. It is difficult to distinguish benign from malignant GISTs based on radiographic appearance alone.

#### **CLINICAL PRESENTATION**

There is a significant overlap among the clinical presentations of small bowel neoplasms. The clinical presentation and diagnosis of small bowel adenocarcinoma are usually delayed by 6 to 8 months primarily because small bowel carcinomas are not amenable to endoscopic examination when they are distal to the duodenum. Clinical presentation includes abdominal pain in 66%, obstruction in 40%, and gross intestinal hemorrhage in 24% of patients.<sup>21</sup> Especially in patients with long-standing bowel diseases, malignancy should be considered.

Patients with carcinoid tumor can be completely asymptomatic or may present with carcinoid syndrome (cutaneous flushing, sweating, bronchospasm, abdominal pain, and diarrhea) in less than 10% of cases.<sup>26</sup> The syndrome most commonly occurs in patients with ileal carcinoids and hepatic or retroperitoneal metastases.

Patients with small bowel lymphoma can present with chronic anemia, weight loss, fatigue, diarrhea, steatorrhea, or vague dull abdominal pain. A palpable mass can be present in one third of cases. Acute gastrointestinal bleeding is less common than in small bowel adenocarcinoma, but the risk for perforation is higher.

When small, GISTs can be incidental on medical imaging. As they increase in size, the most common manifesting symptom is gastrointestinal bleeding and abdominal pain. Less common symptoms are bowel obstruction and a palpable mass.

#### PATHOPHYSIOLOGY

Small bowel adenocarcinoma occurs most frequently in the duodenum. Carcinoid tumors are submucosal, are more common in the ileum, and produce a characteristic mesenteric mass through lymphatic spread. Lymphoma of the small bowel could be either a primary small bowel tumor or a manifestation of lymphomatous disease. In cases with primary small bowel lymphoma there is less evidence of mediastinal or peripheral lymphadenopathy or splenomegaly. The mesenteric lymph node involvement is limited to the region of involved bowel. Lymphoma can occur anywhere in the gastrointestinal tract but is more common in the distal small bowel. GISTs are more common in the jejunum and ileum and can be bulky, causing mass effect on adjacent organs with ulceration or necrosis.

#### PATHOLOGY

Grossly, small bowel adenocarcinomas present as solitary, infiltrative, polypoid, or annular obstructing lesions. Single or multiple ulcers can be associated with an infiltrative pattern. Histologically, they are most commonly mucin-secreting adenocarcinomas.

On gross pathologic study, carcinoids are white, yellow, or gray firm nodules that rarely exceed 3.5 cm in the intestinal wall. They can typically manifest as multiple nodules (30% of cases), exophytic masses, or intramural masses. They may protrude into the lumen as polypoid nodules or classically manifest as infiltrative fibrous lesions. These are typically slow-growing tumors that may cause superficial ulcerations and hemorrhage. The metastatic deposits of carcinoid in the lymph nodes, mesentery, and liver vary in size and gross morphology. Extensive involvement of the subserosa and adjacent mesentery stimulates local release of serotonin, which is responsible for the development of desmoplastic reaction. Mesenteric arteries and veins located both near and far from the tumor may be thickened and may result in intestinal ischemia.<sup>27,28</sup>

Small bowel lymphoma is confined to a small bowel segment with regional lymphadenopathy. There is no evidence of hepatic or splenic involvement except by direct tumor extension and mediastinal lymphadenopathy. The peripheral blood smear and bone marrow biopsy could be normal. Small bowel lymphomas are usually diffuse and poorly differentiated and a common site of non-Hodgkin's lymphoma in children.

GISTs can manifest as exophytic large masses arising from the stromal layer with signs of central necrosis, hemorrhage, and ulceration. They can be characterized as benign, borderline, of low malignant potential, or malignant based on the pathologic appearance.

#### IMAGING

The diagnosis of small bowel neoplasms can be challenging because these tumors are often small, infrequent, and difficult to detect radiographically. Currently, small bowel series and enteroclysis are used for evaluation of small bowel tumors in detecting small lesions. CT is now considered an important modality that helps in detection and staging of disease. Improvement in CT technology, including the introduction of multidetector-row CT (MDCT) scanners and advanced threedimensional (3D) imaging capabilities have improved interest in using CT routinely to evaluate small bowel neoplasms and evaluate a source of gastrointestinal bleeding or suspected obstruction, especially if the small bowel series or enteroclysis was negative. MDCT enteroclysis has an overall accuracy of 84.7% for depiction of small bowel neoplasms.<sup>29</sup> Gastroenterologists are routinely using wireless capsule endoscopy to capture video images of the small bowel, which is otherwise difficult to visualize by routine endoscopic procedures. These studies are gaining popularity in recent years and have complemented other radiographic modalities such as CT and MRI. It is routinely performed in patients with gastrointestinal hemorrhage of unknown cause, anemia of chronic disease, and an obvious mass on CT scan.

#### Radiography

Plain films of the abdomen are helpful in evaluating partial or complete small bowel obstruction or intussusception as seen



**Figure 28-7** Adenocarcinoma. "Apple core" lesion with concentric irregular narrowing of the lumen. *Arrowheads* indicate the overhanging edges (shouldering) at both ends of the lesion.

in cases of small bowel adenocarcinoma. Contrast radiographic studies are essential in the initial evaluation of small bowel diseases. Barium studies can demonstrate a wide spectrum of findings from "apple core" lesions, asymmetric wall thickening, to a more infiltrative process leading to a malignant stricture subsequently causing small bowel obstruction (Figure 28-7).

Carcinoids can appear as trigger points leading to intussusception. Small bowel series are helpful in evaluating small polypoid and multifocal nodular appearances of carcinoid (Figures 28-8 and 28-9). Ulcerations can be well appreciated on small bowel series as barium-filled craters on the surface of the lesion.<sup>30</sup>

In evaluating small bowel lymphoma, small bowel series can show luminal narrowing of the involved segment with loss of mucosal pattern, thickening of the folds, and intraluminal filling defects, possibly with dilatation of the involved segment (Figures 28-10 and 28-11). Small bowel obstruction is seldom seen. Nodular lesions can vary in size and are irregularly distributed. Widening of the lumen rather than narrowing is noted from circumferential involvement and destruction of the myenteric plexus leading to aneurysmal dilatation (see Figure 28-11).

SBFT and CT are commonly used to adequately make the diagnosis of GISTs. Small GISTs appear as intramural masses; and when they increase in size, they grow outward from the bowel. Internal calcifications and necrosis, creating a central hypodense cavity that can eventually ulcerate into the lumen of the bowel, may be seen (Figure 28-12). GISTs can sometimes manifest with partial or complete small bowel obstruction. The submucosal lesions have a smooth surface with acute angles. The exophytic lesions can cause significant mass effect on the adjacent bowel loops that can be evident on the plain film. The tumor can directly invade adjacent structures in the abdomen and, if metastatic, can spread to the liver and peritoneum.

#### Computed Tomography

CT analysis of small bowel diseases requires adequate bowel distention because specific attention should be paid to the thickness of the intestinal wall, character of the wall, enhancement patterns, and alterations in the surrounding mesenteric fat and vasculature. Intravenous administration of a contrast

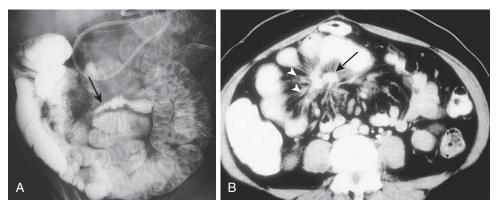
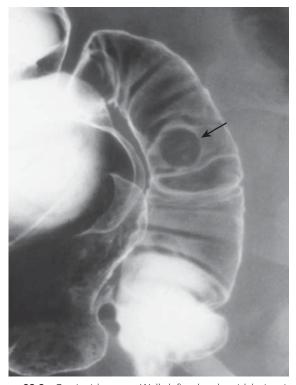


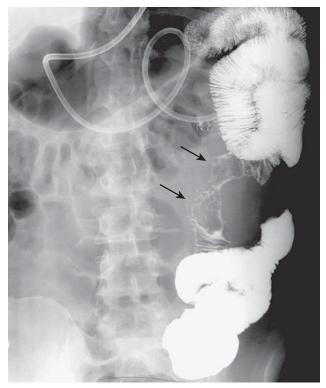
Figure 28-8 Carcinoid tumor. A, Spot film from enteroclysis reveals irregular narrowing of an ileal segment (*arrow*) with kinking of the lumen and fixation of the loops. B, Mesenteric spiculated mass (*arrow*) and desmoplastic reaction in the small bowel mesentery (*arrowheads*) tethering adjacent small bowel loops are better demonstrated on the axial computed tomography image.



**Figure 28-9** Carcinoid tumor. Well-defined polypoid lesion in the terminal ileum (*arrow*) is incidentally noted on the peroral pneumocolon study. Surgery confirmed carcinoid tumor.

agent is essential for a comprehensive CT examination of the small bowel and mesentery, especially when a small bowel neoplasm is suspected.

CT enterography with a negative contrast agent is routinely used to delineate detailed mucosal abnormalities. The highdensity oral contrast agents can mix unevenly with gastric and intestinal fluid, resulting in pseudotumors, and also obscure the enhancing bowel wall or enhancing tumors such as carcinoid when the intravenous contrast agent is administered rapidly. Also, if 3D imaging of the small bowel or mesenteric vessels is planned, the use of high-density oral agents will hinder the postprocessing protocol. Therefore, the value of low-density agents as oral contrast for CT is gaining more popularity.



**Figure 28-10** Small bowel lymphoma. Circumferentially infiltrated lymphoma causing irregular narrowing of a jejunum segment (*arrows*).

CT features of malignant small bowel neoplasms include a focal area of wall thickening causing malignant stricture, polypoid intraluminal masses, and "apple core" or infiltrative lesions (Figure 28-13). Partial or complete small bowel obstruction may be noted. These tumors can demonstrate signs of necrosis, hemorrhage, and, occasionally, ulceration, as seen in 40% of cases.<sup>8</sup> CT staging of small bowel adenocarcinoma is extremely important and is determined by local extension beyond the bowel wall involving adjacent fat or structures, abdominal lymphadenopathy, or distant metastasis in the liver.

Small carcinoids frequently escape radiologic detection, but larger, polypoid lesions may be identified easily by CT.

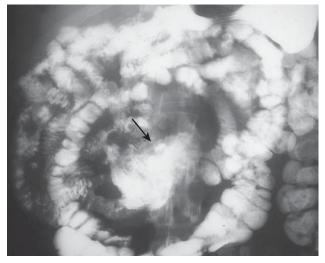


Figure 28-11 Small bowel lymphoma. Dilated ileum segment with irregular contours (arrow), typical for lymphoma involvement.

The submucosal carcinoid tumor is seldom identified on CT. Thirty percent of carcinoid tumors are multicentric and can manifest as multiple nodules and eventually extend into the adjacent mesentery.<sup>31</sup> The CT appearance is characteristically demonstrated as a soft tissue density mesenteric mass, with calcification seen in up to 70% of cases. The mass has spiculated margins, low attenuation, and adjacent fat stranding and occasionally causes encasement of mesenteric vessels, leading to ischemia of the affected bowel loops. Fibrosis in the mesentery may create a "spokewheel" or "sunburst" appearance of mesenteric vessels. Infiltrative tumors can manifest as asymmetric mural thickening, producing fibrosis and subsequent malignant stricture. At the time of diagnosis, 58% to 64% of patients with small intestinal carcinoids have disease that has spread beyond the intestine to regional lymph nodes or the liver.8 Carcinoid metastasis to the liver is commonly hypervascular and best seen on the arterial phase imaging (Figure 28-14).

CT appearance of intestinal lymphoma can be variable.<sup>8</sup> Multiple nodules may be seen within the small bowel at

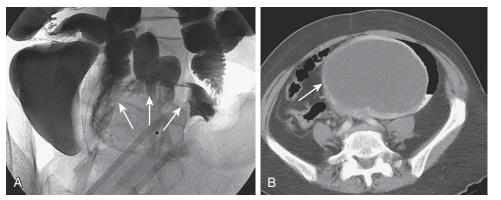


Figure 28-12 Malignant gastrointestinal stromal tumor. A, Spot film from small bowel follow-through shows large excavated mass (arrows) displacing the adjacent small bowel loops. B, Axial computed tomography image demonstrates the large mass (arrow) with homogeneously hypodense center.

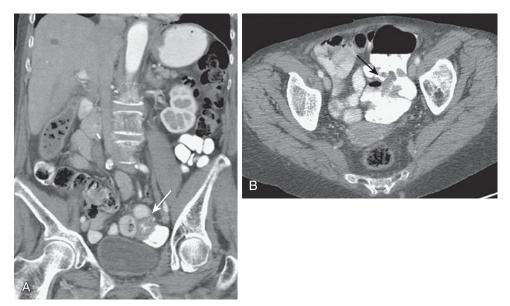


Figure 28-13 Adenocarcinoma. Coronal (A) and axial (B) computed tomography images reveal focal irregular narrowing and concentric wall thickening in an ileum segment (arrows) representing adenocarcinoma, which was later confirmed by surgery.

multiple sites. This pattern is better appreciated on small bowel series.<sup>21</sup> A single large mass of varying size may act as a trigger point for intussusception but less likely is due to the soft nature of these tumors.<sup>22</sup> An infiltrative pattern may manifest as asymmetric small bowel wall thickening. The tumor infiltrates the muscular layer of the wall and may develop aneurysmal dilatation of bowel loops.<sup>32</sup> An exophytic mass may cause a significant mass effect on the surrounding bowel and visceral structures based on its location. This pattern can simulate adenocarcinoma or GIST (Figure 28-15). Small bowel lymphoma spreads through direct extension into adjacent organs or hematoge-

nously to the liver. Non-Hodgkin's lymphoma can develop within the small bowel mesentery and encase the mesenteric vessels, seldom causing ischemia of the affected bowel loops owing to the soft nature of the mass. Peritoneal metastasis may also be seen.

Small GISTs (<2 cm) are rarely symptomatic and usually benign; they are often detected incidentally on imaging studies. Large GISTs ( $\geq 2$  cm) usually manifest as exophytic, well-defined tumors, with necrosis or hemorrhage causing a low-density center (Figure 28-16).<sup>33</sup> Liver metastasis can appear of lowdensity or hypovascular on triple-phase imaging studies.

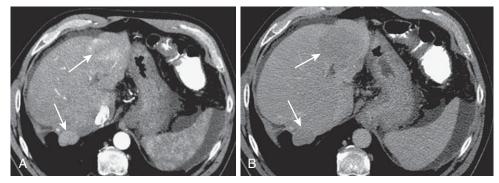
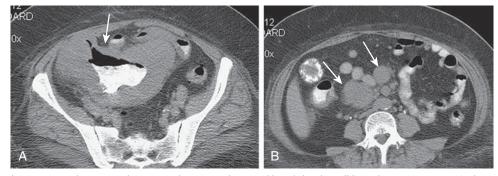


Figure 28-14 Carcinoid metastasis in the liver. Focal lesions in the liver (*arrows*) enhancing on the arterial phase image (A) and washing out on the delayed phase image (B) with residual rim enhancement. These computed tomography findings are consistent with metastatic disease in a patient with known carcinoid tumor.



**Figure 28-15** Lymphoma. **A**, Axial computed tomography image shows a dilated distal small bowel segment (*arrow*) with concentric wall thickening without causing any proximal bowel obstruction. **B**, Another axial image through the abdomen demonstrates multiple enlarged mesenteric lymph nodes (*arrows*).

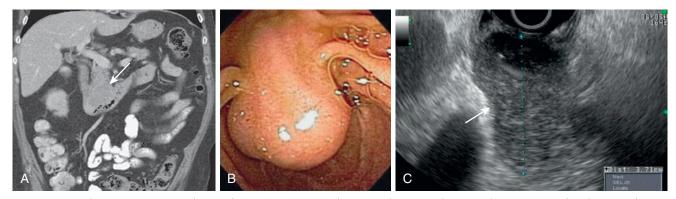


Figure 28-16 Malignant gastrointestinal stromal tumor (GIST). Coronal computed tomography (A), endoscopic (B), and endoscopic ultrasound (C) images show a well-defined, submucosal mass (arrows) in the second portion of the duodenum. Endoscopy confirms the normal mucosa. Surgery confirmed the diagnosis of a malignant GIST.

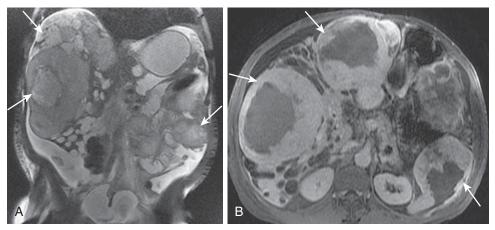


Figure 28-17 Peritoneal spread from a malignant gastrointestinal stromal tumor. Coronal T2-weighted (A) and contrast-enhanced axial T1-weighted (B) magnetic resonance images show multiple large, peritoneal-based masses (*arrows*) and ascites. On the postcontrast images, the center of the mass lesions do not enhance, indicating necrosis.

#### Magnetic Resonance Imaging

MRI is not commonly used for detection and staging of malignant small bowel neoplasms. However, MR enterography and MR enteroclysis are capable of detecting even small intraluminal neoplasms. MRI also can show peritoneal spread, liver metastasis, and metastatic lymph nodes (Figure 28-17).

#### Ultrasonography

Ultrasonography is not routinely performed for small bowel lesions. It can be a good screening tool to look for liver metastases, abdominal lymphadenopathy, or ascites but is less sensitive than CT or MRI.

#### Nuclear Medicine

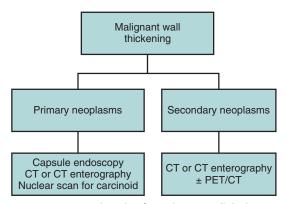
A tagged red blood cell scan is helpful in cases of acute gastrointestinal bleeding as a manifesting symptom of small bowel adenocarcinoma. Localization of the primary tumor to facilitate surgery is better performed using octreoscan in patients with carcinoid tumors. Data have shown that an octreoscan study was positive in 94% of patients with metastatic disease compared with CT, MRI, and endoscopic procedures.<sup>27</sup> Furthermore, primary carcinoid tumors and metastatic lesions of the small intestine were revealed in 16% and 33% of patients, respectively, and were missed on other imaging procedures (e.g., CT and MRI).<sup>27</sup>

### Positron Emission Tomography With Computed Tomography

PET may play a role in cases with widespread abdominal lymphadenopathy and liver metastases.

#### Imaging Algorithm

The current radiologic practice considers CT enterography to be the initial test in acute clinical settings such as suspected small bowel obstruction or gastrointestinal bleeding (Table 28-3). In patients with highly suspected small bowel neoplasm, SBFT and enteroclysis are reliable tools to come to a preliminary diagnosis (Figure 28-18). Wireless capsule endoscopy is considered an adequate initial diagnostic test for suspected cases of small bowel neoplasm that cannot be evaluated by routine endoscopy. Radiologic tests also can be helpful to exclude



**Figure 28-18** Imaging algorithm for malignant wall thickening of the small bowel. *CT*, Computed tomography; *PET*, positron emission tomography.

stenosis before the capsule endoscopy and assist in appropriate localization of the lesion after the procedure. MDCT is essential for disease staging. MR enterography is gaining attention because it is beneficial for surgical planning and ionizing radiation is not involved.

### Classic Signs: Primary Malignant Neoplasms of the Small Bowel

- Carcinoid tumors manifest with a fairly characteristic mesenteric mass on CT that can demonstrate spiculated margins, calcifications, hemorrhage, or necrosis (70%).
- Characteristic desmoplastic changes in the mesentery can cause a "spokewheel" appearance of the mesenteric vessels.
- Small bowel lymphoma can cause dilatation of the small bowel, resulting in aneurysmal dilatation.
- The mesenteric lymph nodes in small bowel lymphoma encase the mesenteric vessels without invading them, leading to the "sandwich" sign.

TABLE 28-3	Accuracy,	Limitations, and Pitfalls of the M	odalities Used in Imaging of Prima	ary Neoplasms of the Small Bowel
Modal	ity	Accuracy	Limitations	Pitfalls
Radiog	graphy		Small lesion cannot be diagnosed. Metastatic disease cannot be evaluated.	Undistended bowel Uncooperative patient
СТ			Small mucosal irregularities can be missed.	Acute setting; patient cannot drink oral contrast agent Compromised renal function; intravenous contrast agent cannot be administered
MRI		Better delineation of size, location, extent of disease; functionality of the bowel seen	Small mucosal irregularities can be missed.	Long scan time, cost, respiratory motion
Ultrasc	onography		Bowel lesions cannot be well demonstrated.	Low sensitivity and specificity
Nuclea	ar medicine	Surgical planning in carcinoids; metastatic disease evaluation	Can be used in localization and confirmation for the diagnosis of carcinoid tumors	
PET/C	Т		Mostly used for metastatic disease	
OT O			DET IN THE I	

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

#### DIFFERENTIAL DIAGNOSIS

Clinical symptoms of malignant small bowel neoplasms are nonspecific and include abdominal pain, gastrointestinal bleeding, and weight loss. It is important to consider small bowel malignancies as a potential cause of these symptoms and to have a high level of suspicion for catching them at an early stage. The clinical differential diagnosis is vast and includes ischemic, infectious, and inflammatory causes and other primary malignancies. Carcinoid tumors may have more specific clinical presentation at later stages when they are metastatic.

Small bowel lymphoma and adenocarcinoma can manifest as small bowel obstruction or intussusception. Both are difficult to differentiate based on radiologic findings. Focal amyloidomas of the small bowel may have the appearance of an ulcerated annular mass on CT, and small bowel series and can mimic small bowel adenocarcinoma.34 Bulky mesenteric lymphadenopathy favors lymphoma, whereas a metastatic liver lesion favors small bowel adenocarcinoma. The differential diagnosis of lymphoma can include tuberculosis and inflammatory small bowel disease. A mesenteric mass on CT is a characteristic feature of carcinoid tumor. The differential diagnosis includes lymphoma, desmoid tumor, metastases, and mesenteric lymphadenopathy. GISTs are typically extraluminal, causing a mass effect on adjacent structures. Size criteria greater than 2 cm can suggest a malignant GIST over a benign GIST. Frank invasion of mass into adjacent structures is more suggestive of malignant GIST

#### TREATMENT

Surgical removal is the first line of treatment of small bowel adenocarcinoma. Five-year survival rates range from 10% to 60%, with a median of approximately 30%.<sup>35</sup>

Factors associated with poor prognosis are age greater than 75 years, lack of surgical resection, advanced stage, and tumor arising in the duodenum.

Carcinoid tumors with metastatic disease have a positive octreoscan study. This test is helpful in treatment planning and can predict the response to somatostatin analogs. Patients with positive octreoscan findings are treated with somatostatin analogs, which results in control of symptoms (75%), stabilization of tumor growth (71%), or tumor shrinkage (9%).<sup>27</sup> Interferon-alfa can be added to the regimen in patients with no predictable response to maximum somatostatin analogs alone. Surgical excision is the treatment of choice in nonmetastatic carcinoid tumors. Transarterial chemoembolization is the procedure of choice for management of inoperable carcinoid liver metastases and shows promising results with partial response in at least 50% of patients and a mortality rate of 5%.<sup>36</sup>

Guidelines for the treatment of small bowel lymphoma are based on histology and staging of small bowel lymphoma. The treatment may range from resection followed by chemotherapy for local tumor to only chemotherapy in advanced tumors. The chemotherapy regimen depends on the histologic subtype of non-Hodgkin's lymphoma. Radiation therapy is the treatment of choice for initially bulky tumor sites, treatment of residual disease after chemotherapy, or serious local problems.

Current guidelines for the treatment of GISTs are surgery (first line), targeted therapy with imatinib mesylate (Gleevac), a tyrosine kinase inhibitor, or a combination of targeted therapy followed by surgery. The most important factors that decide mode of treatment are small bowel tumor size and cell division rate. Multiple clinical trials with imatinib have demonstrated significant shrinkage in the size of the tumor in more than 50% of cases with locally recurrent or metastatic GISTs. An additional 28% of cases demonstrated disease stabilization on imatinib.<sup>37</sup>

What the Referring Physician Needs to Know: Primary Malignant Neoplasms of the Small Bowel

- Acute presentation: Is there obstruction, perforation, or intussusception?
- Are the lesions synchronous or metachronous?
- After staging of the cancer, is the patient a surgical candidate?
- Is there association with Crohn's disease or a polyposis syndrome?
- What follow-up studies have been done?

#### **Key Points**

#### Secondary Malignant Neoplasms

- There are four different ways of metastatic spread to small bowel: direct extension, peritoneal seeding, hematogenous spread, and lymphatic extension.
- The radiologic appearance changes with the mechanism of spread.
- Ovarian cancer in women and gastrointestinal cancer in men are the most common causes of peritoneal spread.
- Malignant melanoma commonly spreads hematogenously to the small bowel.
- Multiple round masses in the small bowel with central ulcerations are very suggestive of hematogenous metastatic spread.

#### Primary Malignant Neoplasms

- Small Bowel Adenocarcinoma
- Predominantly affects the duodenum and jejunum
- More common in Crohn's disease
- Can manifest as small bowel obstruction, acute gastrointestinal bleeding, or intussusception Carcinoid
- Appears more commonly in the ileum; 30% have multifocal disease

#### REFERENCES

- 1. Barclay TH, Schapira DV: Malignant tumors of the small intestine. *Cancer* 51:878–881, 1983.
- 2. Fenoglio-Preiser CMPRR, Perzin KH: *Tumors of the intestines*, Washington, DC, 1990, Armed Force Institute of Pathology.
- 3. Meyers MA: *Dynamic radiology of the abdomen: normal and pathologic anatomy*, New York, 1976, Springer.
- Meyers MA: Clinical involvement of mesenteric and antimesenteric borders of small bowel loops. II. Radiologic interpretation of pathologic alterations. *Gastrointest Radiol* 1:49–58, 1976.
- Moffat RE, Gourley WK: Ileal lymphatic metastases from cecal carcinoma. *Radiology* 135:55– 58, 1980.
- Gill SS, Heuman DM, Mihas AA: Small intestinal neoplasms. J Clin Gastroenterol 33:267–282, 2001.
- Idelevich E, Kashtan H, Mavor E, et al: Small bowel obstruction caused by secondary tumors. *Surg Oncol* 15:29–32, 2006.
- Nolan D: Secondary neoplasms. In Gourtsoyiannis NC, Nolan DJ, editors: *Imaging of small intestinal tumours*, Amsterdam, 1997, Elsevier, pp 193–211.
- Meyers MA: Metastatic seeding along the small bowel mesentery: roentgen features. AJR Am J Roentgenol 123:67–73, 1975.
- Meyers MA: Intraperitoneal spread of malignancies and its effect on the bowel. *Clin Radiol* 32:129–146, 1981.
- 11. Nelson RL, Nyhus LM: Surgery of the small intestine, Norwalk, Conn, 1987, Appleton & Lange.
- Ollila DW, Essner R, Wanek LA, et al: Surgical resection for melanoma metastatic to the gastrointestinal tract. *Arch Surg* 131:975–979, 979– 980, 1996.
- Rees BI, Okwonga W, Jenkins IL: Intestinal metastases from carcinoma of the breast. *Clin Oncol* 2:113–119, 1976.
- McNeill PM, Wagman LD, Neifeld JP: Small bowel metastases from primary carcinoma of the lung. *Cancer* 59:1486–1489, 1987.
- 15. Kawashima A, Fishman EK, Kuhlman JE, et al: CT of malignant melanoma: patterns of small

- Submucosal location, hypervascular tumor
- Synchronous or metachronous malignancies in 29% of patients with small intestinal carcinoids
- Mesenteric mass seen on CT
- "Spokewheel" appearance of mesenteric desmoplastic reaction caused by local release of serotonin
   Small Bowel Lymphoma
- Second most frequent site of gastrointestinal tract involvement by lymphoma
- Most common in the ileum, rare in the duodenum
- Most cases result from non-Hodgkin's lymphoma
- Risk factors: Celiac disease, immunocompromised state, chronic lymphocytic leukemia
- Polypoid lesions can cause intussusception
- Infiltrative lesions can cause aneurysmal dilatation along the antimesenteric segment of the bowel
- GISTs
- Rarely involve the duodenum
- Extraluminal mass; size 2 cm or greater considered malignant
- Internal calcification; necrosis seen in 70% of cases
- Metastasize to peritoneum and liver but rarely to lymph nodes
- bowel and mesenteric involvement. J Comput Assist Tomogr 15:570–574, 1991.
- Low RN: MR imaging of the peritoneal spread of malignancy. *Abdom Imaging* 32:267–283, 2007.
- Low RN, Sebrechts CP, Barone RM, et al: Diffusion-weighted MRI of peritoneal tumors: comparison with conventional MRI and surgical and histopathologic findings—a feasibility study. AJR Am J Roentgenol 193:461–470, 2009.
- Maccioni F, Rossi P, Gourtsoyiannis N, et al: US and CT findings of small bowel neoplasms. *Eur Radiol* 7:1398–1409, 1997.
- Turlakow A, Yeung HW, Salmon AS, et al: Peritoneal carcinomatosis: role of (18)F-FDG PET. J Nucl Med 44:1407–1412, 2003.
- 20. Paulsen SR, Huprich JE, Fletcher JG, et al: CT enterography as a diagnostic tool in evaluating small bowel disorders: review of clinical experience with over 700 cases. *Radiographics* 26:641– 657, discussion 657-662, 2006.
- Dabaja BS, Suki D, Pro B, et al: Adenocarcinoma of the small bowel: presentation, prognostic factors, and outcome of 217 patients. *Cancer* 101:518–526, 2004.
- Sanders KM, Koh SD, Ward SM: Interstitial cells of Cajal as pacemakers in the gastrointestinal tract. *Annu Rev Physiol* 68:307–343, 2006.
- Modlin IM, Latich I, Zikusoka M, et al: Gastrointestinal carcinoids: the evolution of diagnostic strategies. *J Clin Gastroenterol* 40:572–582, 2006.
- Johnston SD, Watson RG: Small bowel lymphoma in unrecognized coeliac disease: a cause for concern? *Eur J Gastroenterol Hepatol* 12:645– 648, 2000.
- Horton KM, Fishman EK: Multidetector-row computed tomography and 3-dimensional computed tomography imaging of small bowel neoplasms: current concept in diagnosis. *J Comput Assist Tomogr* 28:106–116, 2004.
- Song T, Shen J, Guo HC, et al: [Imaging and pathological features of gastrointestinal stromal tumors]. *Zhonghua Zhong Liu Za Zhi* 29:386– 390, 2007.

- Nikou GC, Lygidakis NJ, Toubanakis C, et al: Current diagnosis and treatment of gastrointestinal carcinoids in a series of 101 patients: the significance of serum chromogranin-A, somatostatin receptor scintigraphy and somatostatin analogues. *Hepatogastroenterology* 52:731–741, 2005.
- Oberg K: Neuroendocrine gastrointestinal tumours. Ann Oncol 7:453–463, 1996.
- Pilleul F, Penigaud M, Milot L, et al: Possible small-bowel neoplasms: contrast-enhanced and water-enhanced multidetector CT enteroclysis. *Radiology* 241:796–801, 2006.
- Levy AD, Sobin LH: From the archives of the AFIP: gastrointestinal carcinoids: imaging features with clinicopathologic comparison. *Radiographics* 27:237–257, 2007.
- Modlin IM, Lye KD, Kidd M: A 5-decade analysis of 13,715 carcinoid tumors. *Cancer* 97:934– 959, 2003.
- Gourtsoyiannis NC: Diseases of the small intestine. In Gourtsoyiannis NC, editor: *Radiologic imaging of the small intestine*, New York, 2002, Springer-Verlag.
- Sandrasegaran K, Rajesh A, Rushing DA, et al: Gastrointestinal stromal tumors: CT and MRI findings. *Eur Radiol* 15:1407–1414, 2005.
- Saindane AM, Losada M, Macari M: Focal amyloidoma of the small bowel mimicking adenocarcinoma on CT. AJR Am J Roentgenol 185:1187–1189, 2005.
- 35. Howe JR, Karnell LH, Menck HR, et al: American College of Surgeons Commission on Cancer and the American Cancer Society. Adenocarcinoma of the small bowel: review of the National Cancer Data Base, 1985-1995. *Cancer* 86:2693– 2706, 1999.
- Wallace S, Ajani JA, Charnsangavej C, et al: Carcinoid tumors: imaging procedures and interventional radiology. *World J Surg* 20:147–156, 1996.
- Demetri GD, von Mehren M, Blanke CD, et al: Efficacy and safety of imatinib mesylate in advanced gastrointestinal stromal tumors. *N Engl J Med* 347:472–480, 2002.

29

### Colon Imaging: Conventional Imaging and Computed Tomography

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### **Conventional Imaging**

#### TECHNICAL ASPECTS

Before cross-sectional imaging, the double-contrast enema was the foremost radiologic method for detection of colonic mucosal lesions and precancerous polyps. Diagnostic highquality double-contrast barium enema examination is an art, requiring skillful maneuvering of the patient and barium pool while optimally using fluoroscopy. With the advent of computed tomography (CT), intramural as well as extraluminal extension of colonic diseases can be detected. This chapter discusses the principles and techniques for safe and accurate barium enema and review technical considerations for the performance of colorectal CT.

#### Barium Enema Examination

Single-contrast examination is preferred in immobile, elderly, or incontinent patients.<sup>1</sup> The single-contrast examination is less sensitive than the double-contrast examination for detection of small polypoid lesions and evaluation of inflammatory bowel disease (Figure 29-1).<sup>2</sup> Double-contrast barium enema should be performed 1 week after a recent polypectomy, mucosal cautery, or large forceps biopsy to avoid the risk for colonic perforation.<sup>3,4</sup>

**Bowel Preparation.** Rigorous colonic cleansing is necessary for an optimal barium enema examination. Several colon cleansing regimens have been described.<sup>5-7</sup>

A standard bowel preparation is outlined in Box 29-1. Contraindications for the standard bowel preparation include bedridden patients, postoperative patients, patients with diabetes and hypothyroidism, and patients taking opiates.

**Procedure.** Before starting the study, compliance with the bowel preparation should be confirmed. A preliminary abdominal radiograph can assess bowel preparation adequacy.<sup>8</sup> The procedure may need to be rescheduled if there is significant colonic residue.

**Rectal Catheter Insertion.** The patient lies in a recumbent, left side down position. Lubricant is applied on the external anal surface and the rectal catheter tip,<sup>9</sup> and the catheter is gently inserted into the anal canal. Balloon insufflation is performed only in patients who are leaking barium or air out of the anal canal.

#### **Technique Tips**

- Rectal balloon inflation should be performed only after outlining the rectum with barium.
- Contraindications for inflating rectal balloons include suspected colitis, a history of pelvic radiation or colitis, suspected rectovaginal fistula, and Crohn's disease.<sup>10</sup>

#### BARIUM INSTILLATION

The patient is placed prone and barium is slowly instilled. Once a full column has reached the descending colon, fully open the tube. The radiologist turns the patient 360 degrees to coat the colon. The patient is turned prone to advance the barium into the mid-transverse colon. The distal rectum is then drained by dropping the barium bag to the floor to avoid bubbles when air is insufflated.

#### **Technique Tip**

 Rapid distention of the rectum will cause sphincteric spasm at the rectosigmoid junction and increase the patient's urge to defecate.

#### AIR INSUFFLATION

Air is used to aid barium across the transverse colon into the ascending colon. The patient is turned right side down to fill the proximal transverse colon and then turned into the supine position to fill the posteriorly located hepatic flexure.

The enema tip can then be removed, providing physical relief to the patient and allowing better evaluation of the distal rectum. The enema tip may need to be left in place in patients expelling gas and who may need additional air to visualize the terminal ileum (e.g., patients with Crohn's disease).

#### **Technique Tips**

- Perform air insufflation only after barium has passed the splenic flexure.
- Avoid rapid air insufflations and always turn the patient in different obliguities to redistribute air.



Figure 29-1 Single-contrast barium enema: normal findings.

#### BOX 29-1 SUGGESTED OUTLINE FOR BOWEL PREPARATION

On the day before the study:

- 1. Twenty-four hours of clear liquids for breakfast, lunch, and dinner
- 2. Plenty of liquids or water between meals to maintain hydration
- 3. Sixteen ounces of magnesium citrate at 5 PM
- 4. Four bisacodyl tablets at 8 PM
- On the day of the examination: Nothing by mouth

#### RADIOGRAPHIC DOCUMENTATION: SPOT FILMS AND OVERHEAD VIEWS

Complementary radiologic projections evaluate the colon. Twelve to 14 spot films and 4 to 5 overhead films are obtained.<sup>11</sup> A routine sequence obtained in a double-contrast barium enema study is suggested in Table 29-1 (Figure 29-2).

#### **Technique Tips**

- Sigmoid colon spot films are obtained before barium reaches the ascending colon. If barium refluxes through the ileocecal valve, the sigmoid colon may be partly obscured.
- Obtain views without the enema tip to avoid missing distal rectal lesions.
- Anterior cecal masses may need to be evaluated by spot films with the patient prone.
- Applying compression in either the erect or recumbent, left posterior oblique position can aid visualization of the appendix and terminal ileum.
- Postevacuation fluoroscopic films may be obtained with suspected fistulas or extraluminal diverticular collections.

#### TABLE Sequence of Images Obtained in a Double-Contrast Barium Enema Evaluation

Spot Radiograph	Patient Position
Rectum (enema tip in)	Prone, left lateral
Rectum with air (enema tip out)	Supine, right lateral view
Proximal sigmoid colon	Left posterior oblique, prone
Distal sigmoid colon	Right posterior oblique, supine
Proximal descending colon	Erect
Distal descending colon	Recumbent right posterior oblique
Splenic flexure	Erect right posterior oblique
Hepatic flexure	Erect left posterior oblique
Proximal ascending colon	Prone or Trendelenburg left posterior oblique
Lateral wall of cecum	Supine, left posterior oblique
Medial wall of cecum	Supine, right posterior oblique
Remaining colonic segments	Supine
Overhead Radiograph	View
Rectosigmoid junction	Prone angled
Rectum	Left and right lateral decubitus cross-table view with horizontal beam
Rectum	Prone cross-table lateral views

#### BOX 29-2 PROS AND CONS OF A BARIUM ENEMA STUDY

#### PROS

- Inexpensive
- Very useful in small centers
- Adequate mucosal surface information

#### CONS

- Replaced in larger centers by colonoscopy and cross-sectional studies
- Lacks information of the mucosal, submucosal layers and the mesentery
- No extracolonic information
- Results depend on technical expertise of operator
- Residual barium in colon as a result of previous studies can pose difficulties in performance of future CT and MRI examinations

Some technical challenges during a double-contrast barium enema examination and plausible solutions are summarized in Box 29-2.

### **Technical Modifications**

#### WATER-SOLUBLE CONTRAST ENEMA

In patients with suspected colonic perforation or in postoperative patients, a water-soluble contrast agent can be used to look for fistulas or perforations (Figure 29-3).<sup>12</sup>

In cystic fibrosis patients, a hyperosmolar water-soluble molar contrast agent can liquefy the viscous stool by drawing fluid into the bowel.

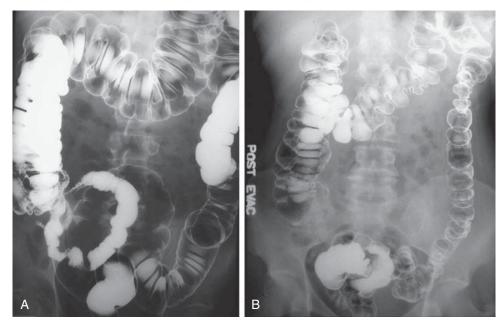
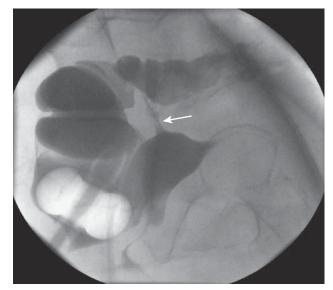


Figure 29-2 A, Upright radiograph of a double-contrast barium enema (normal study). B, Postevacuation film is important to detect lesions obscured by the barium pool.

TABLE



**Figure 29-3** Barium enema with water-soluble contrast in a postoperative patient demonstrates a fistulous tract (*arrow*).

29-2	Barium	Enema Study	
Proble	em	Implication	Solution
Poor b prep	oowel paration	Simulates inflammatory bowel disease	Horizontal beam upright and lateral decubitus views; repeat study with preparation
Fecal r	residue	Simulates polyps	Found on dependent surface
Sigmo dive	id rticulosis	Difficult to detect polyps	Single-contrast examination of sigmoid
Patient inco	t ntinence	Leakage of air and barium	Intravenous glucagon prevents spasm; inflation of retention balloon
Nonfill right	ing of t colon	Missed lesions	Postevacuation films; single-contrast study of right colon

**Technical Challenges During Double-Contrast** 

#### COMPLICATIONS

The most serious complication is colonic perforation, which can be both intraperitoneal and extraperitoneal and is usually seen in a diseased rectum secondary to inflation of rectal balloon.<sup>13</sup> Air insufflations can cause abdominal discomfort and can be minimized by the use of carbon dioxide. Allergic reactions may be observed to barium, glucagon, or latex in gloves and rectal catheters. Transient bacteremia and septicemia are very rare complications of barium enema. Barium impaction can cause delayed complications with varying degrees of constipation and/or abdominal pain. Venous intravasation may result from barium breaching the colonic mucosa and is a feared complication because of its high mortality rate.<sup>14</sup>

#### COLOSTOMY ENEMA

Double-contrast examinations can be performed through a colostomy.

#### PROS AND CONS

The pros and cons of a barium enema study are outlined in Table 29-2.

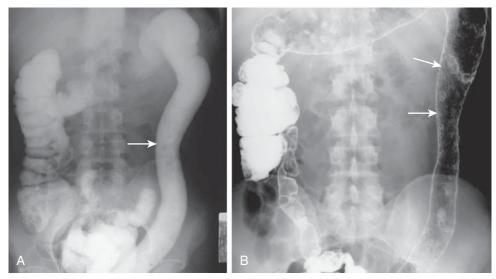


Figure 29-4 Ulcerative colitis. A, The left hemicolon is diffusely mildly narrowed with loss of haustral markings (arrow). B, Double-contrast enema shows left-sided ulcerative colitis. Deep "collar stud" ulcers (arrows) are present on a background of abnormal mucosa.

#### CONTROVERSIES

The continued use of the double-contrast barium enema for detecting colorectal polyps is controversial. Although the procedure is reimbursed by Medicare for colon screening, two large prospective clinical trials show the sensitivity of double-contrast barium enema examinations is approximately 50% for polyps measuring at least 10 mm in diameter.<sup>15,16</sup>

#### NORMAL ANATOMY

The goal of the double-contrast barium enema is uniform coating of the mucosal surface with barium without formation of barium pools, which can obscure pathologic processes. It is important to be well versed with normal appearances and variations on a double-contrast study.

#### Luminal Distention

When the lumen is optimally distended, the normal mucosal folds are just effaced. Inadequate distention may conceal lesions, but overdistention can obscure lesions such as shallow ulcers.

#### Mucosal Surface Variations

The normal mucosal surface usually has a smooth, featureless appearance. En face, the mucosal surface fades from the white line of the contour to a smooth, gray-white surface. Potential anatomic features include the following:

- *Innominate grooves or areae colonicae:* Seen as a fine network of lines and should not be mistaken for superficial ulceration
- *Transverse striations:* Transient, secondary to contraction of the muscularis mucosa
- *Lymphoid follicles*: May appear as a pattern of fine 1- to 3-mm nodules on the mucosal surface. Enlargement of these follicles may represent Crohn's disease, inflammation, and lymphoma.

#### IMAGING OF SPECIFIC LESIONS

#### **Ulcerative** Colitis

Confluent diffuse involvement affecting primarily the mucosa and submucosa of the colon is seen (Figure 29-4).

#### **Early Changes**

- *Fine granular pattern:* Early mucosal hyperemia and edema
- *Mucosal stippling:* Secondary to barium adhering to the superficial ulcers
- *"Collar button" ulcers:* Deeper ulcerations of thickened edematous mucosa with crypt abscesses
- Coarse granular pattern: Results from replacement of diffusely ulcerated mucosa with granulation tissue

#### Late Changes

- *Pseudo polyps:* Mucosal remnants in areas of extensive ulceration
- Inflammatory polyps: Small islands of inflamed mucosa
- *Postinflammatory polyps:* Mucosal tags seen in quiescent phases of the disease
- Filiform polyps: Postinflammatory polyps having a wormlike appearance

#### **Crohn's Disease**

- Predominant right colon disease, discontinuous involvement with intervening regions of normal bowel, early aphthous ulcers (Figure 29-5)
- Deep ulcerations in later stage
- Strictures, fistulas, and sinus formation
- Pseudodiverticula of the colon secondary to asymmetric fibrosis on one side of the lumen, causing saccular outpouching on the other side

#### Diverticulitis

Barium enema examination is considered safe, except when signs of free intraperitoneal perforation or sepsis are present.

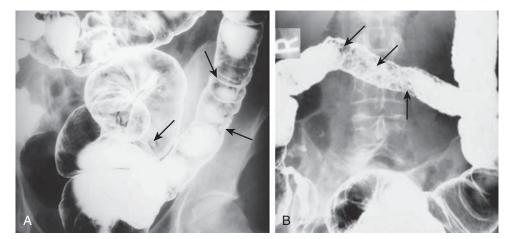


Figure 29-5 Crohn's colitis. A, Discrete aphthoid ulcers are seen on double-contrast barium enema surrounded by normal mucosa (arrows). B, Note severe involvement of transverse colon with cobblestoning and ulceration (arrows).

Deformed diverticular sacs are seen, along with demonstration of abscess, and extravasation of barium outside the colon lumen (Figure 29-6).

## Lipoma

Lipomas are the most common colonic submucosal tumor and occur most frequently in the cecum and ascending colon. Barium studies demonstrate a smooth, well-defined, elliptical filling defect, usually 1 to 3 cm in diameter (Figure 29-7). Tumors are soft and change shape with compression.

#### **Extrinsic Masses**

Extrinsic masses commonly cause mass effect on the colon that may simulate intrinsic disease (Figure 29-8). Defects are sharply defined and can compress but do not usually encircle the lumen. Benign pelvic masses such as ovarian cysts and uterine fibroids produce smooth extrinsic mass impressions on the colonic wall.

#### Colorectal Carcinoma

The rectum and sigmoid regions are the most common sites for carcinoma. Annular constricting lesions are the most common manifestation and are seen as short "apple core" segments of narrowing with destruction of the mucosal pattern (Figure 29-9). Other manifestations include polypoid lesions, which are fungating and intraluminal plaque-like lesions with submucosal spread and ulcerating tumors. Occasionally, colonic carcinoma may manifest as localized or free perforation.

## PATHOLOGY

The interpretation of double-contrast barium studies requires excellent images and understanding of the basic tenets of pathology and pathophysiology of the underlying lesions.<sup>17</sup>

## Dependent and Nondependent Surfaces

The appearance of various lesions is based on their location on the dependent or nondependent surfaces, as summarized in Table 29-3.<sup>18,19</sup>

• *Dependent surface:* The coating of barium is thicker, and a barium pool is formed in any depression.



**Figure 29-6** Sigmoid diverticulitis. Multiple barium-filled outpouchings (*arrows*) are noted in the sigmoid colon with spasm, mural thickening, and lack of distensibility of a focal segment of sigmoid colon.

• *Nondependent surface:* It has a thin coating of barium, because all the free barium moves onto the dependent surface.

## Artifacts

Structures anterior or posterior to the bowel may project over the bowel and simulate lesions arising from the bowel. Flaking of barium produces an appearance suggestive of inflammatory bowel disease. Inadequate distention leads to apposition of the anterior and posterior colonic walls, causing a "kissing" artifact that may resemble mass lesions. Air bubbles rise to the highest point of a column of contrast agent (the "carpenter's level" sign), but fecal material usually remains dependent. Plaques are flat lesions that barely rise above the mucosal surface.

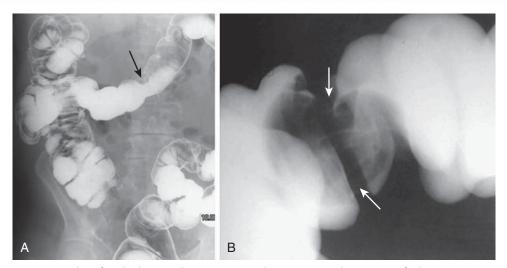


Figure 29-7 Lipoma. A, A smooth-surfaced submucosal mass is seen in the transverse colon. B, Magnified spot image in another patient demonstrates a smooth-contoured lesion that proved to have fat density on computed tomography.



**Figure 29-8** Extrinsic mass effect on the rectosigmoid due to a large ovarian cyst. Note the smooth contour of the mass effect (*arrow*) without any signs of invasive disease.

## **Computed Tomography Imaging**

## **TECHNICAL ASPECTS**

CT can demonstrate intramural disease and extraluminal extension of colonic diseases. In the remainder of this chapter, we review technical considerations for the performance of colorectal CT with emphasis on distinctive CT patterns that may help distinguish specific diseases of the colon and rectum.

#### Imaging Protocol

The conventional CT technique consists of scanning the abdomen after the oral and intravenous administration of contrast material. A suggested protocol for scanning the colon and



**Figure 29-9** Colon carcinoma. Annular constricting lesion seen as a short "apple core" segment (*arrows*) of narrowing with destruction of the mucosal pattern in the transverse colon.

rectum is outlined in Table 29-4 (Figure 29-10). Intravenous administration of contrast material helps detect subtle bowel wall abnormalities. Delayed scans or decubitus views can clarify subtle bowel findings, such as colonic leak or perforation, pneumatosis, fistulas, and sinus tracts.<sup>20</sup>

Multiplanar reconstruction or three-dimensional imaging can aid in visualizing a tumor in adjacent organs. They also provide information on strictures and the exact location of bowel obstruction (Figure 29-11).<sup>21</sup>

#### Contrast Agents

**Intravenous Contrast Agents.** Intravenous contrast material is critical for enabling detection of subtle bowel wall abnormalities. The portal venous phase usually is sufficient for

### 256 PART 4 Small Bowel and Colon

29-3 Dependent a					
Lesion	Cause	Dependent Surface	Nondependent Surface		
Protrusions	Mucosal folds or polyps (see Figure 29-10)	Radiolucent filling defect because it displaces barium from the barium pool	Coated with barium, appears to be "etched in white"		
Plaque-like lesions	Flat polyps	Best visualized in presence of a shallow barium pool	Difficult to visualize because it is faintly outlined with barium		
Stalactite phenomenon	Barium droplet	Not seen	Transient, always seen on the nondependent surface as a protrusion		
"Mexican hat" sign	Pedunculated polyp Associated with polyps only		Hanging from the nondependent surface Outer ring: Head of the polyp Inner ring: Stalk seen end-on through the head		
"Bowler hat" sign	Polyp	Dome of the "hat" points inward to	ward the long axis of the bowel		
	Diverticulum	Dome of the "hat" points outward fr	rom the long axis of the bowel		
Depressed lesions	Ulcers or diverticula	Focal barium collections as a result of accumulation of barium	Devoid of barium or appear as a ring shadow if there is adequate coating of the sides		
Barium pool	Any lesion	Best seen with a very shallow barium pool	Lesion seen if totally devoid of barium		

## TABLESuggested Protocol for Scanning the Colon29-4and Rectum

Position/Landmark	Head first or feet first supine; xiphoid
Topogram direction	Craniocaudal
Scan type	Helical
Scan start/end locations	1 cm superior to diaphragm up to symphysis pubis
Dual field of view	38 cm
КVр	120 kV
mA	Smart mA (100-750) with noise index of 30
Rotation time (sec)	0.8
Pitch	1.375:1
Speed (mm/rotation)	55.00 mm
Detector width $\times$ rows	0.625 mm × 64
Slice thickness/spacing	Thin abdomen/pelvis: 0.6 mm × 0.6 mm for multiplanar reconstructions
Algorithm	Abdomen/pelvis: 5 mm × 5 mm for picture archiving and communications system
Intravenous contrast	130-150 mL at 3 mL/s
Scan delay (sec)	80

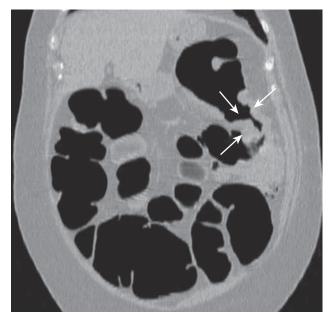
Figure 29-10 Polyp (arrow) seen as a well-defined radiolucent filling defect in the transverse colon.

KVp, kilovoltage peak; mA, milliamps.

demonstrating mesenteric arteries and mesenteric veins. Administration of intravenous contrast material is also essential for complete staging of colorectal cancer. In patients with known Crohn's disease, a shorter delay (such as 45 seconds) may be beneficial to optimize mural enhancement in the small and large bowel.<sup>22</sup>

**Luminal Contrast Agents.** Luminal distention is essential for optimal assessment of the bowel wall. Both positive and neutral contrast material can be used. However, nonopaque fluid distention may reveal luminally oriented features possibly obscured by positive oral contrast material.

**Positive Contrast Opacification.** Positive contrast opacification is accomplished by ingesting iodinated water-soluble agents. Commercial preparations with low percentages of barium are designed specifically for CT. The patient is instructed to ingest oral contrast 60 to 90 minutes before the CT study. In urgent cases, positive contrast agents can be administered via rectum. Rectal contrast material distends the rectum and colon and helps differentiate between collapsed bowel wall and mural



**Figure 29-11** Coronal multiplanar reformatted image demonstrates splenic flexure stricture (*arrows*) with irregular nodular walls that was pathologically proved cancer.

thickening secondary to inflammation. If necessary, a fistulous tract can be catheterized and rectal contrast material can be administered and a noncontrast CT performed.

**Neutral Contrast Opacification.** Neutral agents such as water<sup>23</sup> or negative agents such as air or carbon dioxide<sup>24</sup> also can be easily administered via a rectal tube and provide excellent contrast to detect polyps and small masses. Rectal water should not be used when a colonic perforation or postoperative leak is suspected.

Volumen is an alternative that achieves the advantages of neutral-contrast distention over a longer period owing to the rapid reabsorption of water.

## PROS AND CONS

CT has several advantages. It is widely available and accurately depicts the bowel wall, pericolonic soft tissues, and adjacent structures. CT and its reconstructions can assess inflammatory conditions and accurately stage abdominal neoplasms as well as detect pneumoperitoneum and extravasation of oral contrast agent at the site of perforation.

Limitations include failure to depict early and superficial mucosal changes of inflammatory bowel disease. Tumor invasion depth through the colonic wall cannot be accurately determined with CT.

## NORMAL ANATOMY

## Characteristic Features of the Colon

The colon is located in the periphery of the abdomen and outlined by fat. It can be distinguished from the small intestine on the basis of appearance, caliber, and location.

Taeniae coli are three longitudinal bands approximately 8 mm wide that run the length of the colon. Haustra are prominent sacculations formed in the spaces between the taeniae. The prominence of the haustra depends on the contraction of the taeniae. The appendices epiploicae are small packets of fat that run along the taeniae and vary in size.

The normal transverse diameter of the colon varies. The cecum has the greatest diameter and is usually less than 9 cm. The transverse colon is usually less than 6 cm in diameter, and the descending colon and sigmoid colon are usually slightly smaller in caliber. The caliber of the rectum can vary significantly in normal individuals. In general, the normal colonic wall thickness is 1 to 2 mm<sup>25</sup> if well distended with contrast or air. When the lumen is collapsed, the normal thickness can reach 3 to 4 mm.

### Variations in Colon Anatomy

Redundancy of the sigmoid colon and cecum can lead to anomalous location and, at times, to volvulus or obstruction. If the colon is located between the anterior abdominal wall and the liver, this anatomic variant is called the Chilaiditi sign. The Chilaiditi syndrome can occasionally develop, causing right upper quadrant pain, probably owing to colonic distention. However, colonic obstruction or volvulus as a complication of Chilaiditi syndrome is very rare.<sup>26</sup>

## **CLINICAL PRESENTATION**

A careful assessment of clinical features is beneficial in achieving a definitive diagnosis. The salient clinical features of different disease entities are summarized in Table 29-5.

The sites of involvement also provide clues for the diagnosis of the disease in question.

## IMAGING OF SPECIFIC AREAS

There is considerable overlap in the imaging features of inflammatory and neoplastic conditions of the bowel. In addition to the algorithmic approach based on bowel wall attenuation proposed by Wittenberg and colleagues (see later discussion), there are other features that can help narrow the differential diagnosis.

## Bowel Wall Thickening

The presence of isolated bowel wall thickening has limited value as the degree of luminal distention must be taken into consideration.<sup>27</sup>

## Morphology of Fat

In chronic ulcerative colitis, proliferation of perirectal fat is frequently present. In Crohn's, this represents the body's attempt to contain the inflammatory process. CT demonstrates an increase in higher attenuation (20 to 60 Hounsfield units [HU]) mesenteric fat because of edema and inflammatory cell infiltrates.<sup>28</sup>

In epiploic appendagitis, CT reveals a well-defined oval or round pericolic area of fat with an enhancing rim immediately adjacent to the colon (Figure 29-12).<sup>29</sup> A central high attenuation dot within the inflamed appendage represents a thrombosed vein.<sup>30</sup>

#### Ascites

Ascites is not a specific sign and is associated with benign and malignant conditions. It is often present in infectious colitis and

## TABLEFive Salient Clinical Features of Different29-5Disease Entities of the Colon and Rectum

Disease Entity	Clinical Features
Ulcerative colitis and Crohn's disease	Abdominal pain, tenesmus (rectal urgency), bright red rectal bleeding, small-volume stools
Crohn's disease	Extraintestinal manifestations of erythema nodosum, large-joint nondestructive arthritis, and spondylitis
Amebic colitis	Colonic diarrhea with small volume of bloody stools
Pseudomembranous colitis	History of use of broad-spectrum antibiotics, watery diarrhea, and abdominal cramps
Neutropenic colitis	In patients with leukemia or acquired immunodeficiency syndrome and after transplantation or chemotherapy
lschemic colitis	Age >70, history of myocardial infarction, arrhythmia, embolus, thrombosis, shock, or trauma; abdominal pain and rectal bleeding
Radiation colitis	Sigmoid colon and rectum
Diverticulitis	Abdominal pain, cramping, diarrhea and constipation, rare gross bleeding or iron-deficiency anemia
Epiploic appendagitis	Right lower quadrant abdominal pain, low-grade fever, obstipation, and, rarely, elevated white blood cell count
Appendicitis	Right lower quadrant pain, obstipation, low-grade fever, and paraumbilical pain, diarrhea, and elevated white blood cell count



**Figure 29-12** Right-sided epiploic appendagitis. Inflamed epiploic appendage (*arrow*) is seen as an ovoid fat density surrounded by a thickened rim of visceral peritoneum that shows as high attenuation and is in continuity with the ascending colon.

usually absent in inflammatory bowel disease. The presence of ascites in pseudomembranous colitis is one of the features that distinguishes it from Crohn's disease, in which ascites is very rare.<sup>31</sup> The presence of fluid in the root of the sigmoid mesentery and engorgement of adjacent sigmoid mesenteric vasculature favors the diagnosis of diverticulitis.

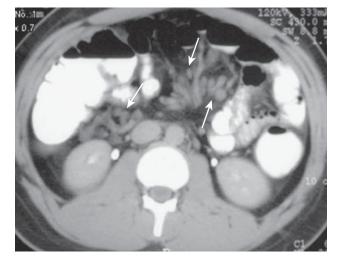


Figure 29-13 Mesenteric adenitis. Multiple enlarged mesenteric nodes (arrows) are noted in a patient with Crohn's disease.

## Lymphadenopathy

Mesenteric lymphadenopathy is often seen in Crohn's disease (Figure 29-13). However, lymphoma risk is increased in patients with Crohn's disease, and mesenteric lymph nodes larger than 1 cm should be investigated further.<sup>32</sup> Pericolonic lymph nodes suggest colon cancer rather than diverticulitis. In developing countries, if peritoneal thickening, ascites, abdominal lymphadenopathy, and thickened intestinal walls are seen, abdominal tuberculosis should be considered.<sup>33</sup>

## Complications

CT is useful in the identification of complications such as toxic megacolon, phlegmon, abscesses, fistula, and perforation; and timely management is vital in life-threatening conditions.

Rectal and colon cancer metastasis occurs via the portal vein to the liver. However, lower rectal cancers can drain into the pelvic veins and directly into the inferior vena cava to produce isolated pulmonary metastases.

## Descriptive Computed Tomography Signs

Some signs have been used to describe typical imaging features; however, these signs are not specific and are seen in several inflammatory conditions.

**"Comb" Sign.** Mesenteric hypervascularity with vascular dilatation, tortuosity, and spacing of the vasa recta, produces the "comb" sign (Figure 29-14).<sup>34</sup> This can be seen in active Crohn's disease or any moderate to severe acute inflammatory condition of the bowel. The "comb" sign may be used to differentiate active inflammatory bowel disease from lymphoma and metastatic carcinoma, which tend to be hypovascular.

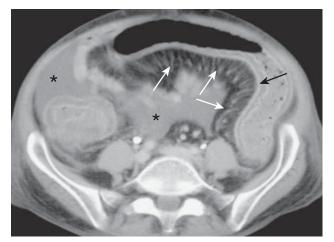
## Imaging Algorithm

Wittenberg and associates<sup>35</sup> have proposed an algorithm incorporating enhancement and attenuation of the bowel wall after intravenous contrast to aid in the differential diagnosis. The spectrum of mural attenuation patterns includes white (avid contrast material enhancement), gray, "water halo" sign, "fat halo" sign, and black (pneumatosis). A single disease may simultaneously demonstrate multiple attenuation patterns in contiguous segments of bowel as a result of coexistent pathophysiology.

White Attenuation. White attenuation represents intense enhancement of the thickened bowel wall. The relative attenuation is the same as, or greater than, venous opacification seen in the same scan. It is best discerned in bowel loops devoid of luminal contrast. Pericolonic vessels may appear prominent.

- *Pathophysiology*: Vasodilation and/or injury to intramural vessels with accompanying interstitial leakage
- *Representative example:* Shock bowel—diffuse ischemia of the small bowel in hypotensive adults as a result of blunt trauma<sup>36</sup>
- *Differential diagnosis:* Acute inflammatory bowel diseases—acute ulcerative colitis and Crohn's disease (Figure 29-15), vascular disorders; uncommon diagnosis: malignancy
- *Pitfalls:* Assessment is subjective, and there is no cutoff Hounsfield unit for designating white attenuation.

**Gray Attenuation.** Gray attenuation is the least specific of, and is common in, both benign and malignant diseases and is thickened bowel wall that shows attenuation comparable to that of



**Figure 29-14** "Comb" sign. Engorged vasa rectae (*white arrows*) are seen supplying a thickened bowel segment (*black arrow*) in a patient with Crohn's disease. Ascites is also noted (*asterisks*).

enhanced muscle. A common cause of false-positive diagnosis is incomplete luminal distention.

**"Water Halo" Pattern.** The "water halo" sign is a strong indicator of acute bowel wall injury (Figure 29-16).

- *Double halo:* A halo sign with two layers composed of either a higher-attenuation outer annular ring (muscularis propria) surrounding a second, luminally oriented annular ring of gray attenuation or a higher attenuation inner layer and an outer ring of gray attenuation.<sup>37</sup>
- *Target sign:* This is composed of three rings—outer highattenuation muscularis propria, a middle ring of gray attenuation, and a luminally oriented ring of high attenuation.<sup>38</sup>
- *Pathophysiology:* The lower-attenuation (gray) layer of the water halo sign is believed to represent submucosal edema. The inner and outer rings of the target sign can be regarded as the mucosa and muscularis propria respectively, with the higher attenuation being the consequence of preferential enhancement.
- *Differential diagnosis:* Idiopathic inflammatory bowel diseases, vascular disorders, infectious diseases, radiation damage; uncommon diagnosis: malignancy



**Figure 29-15** White attenuation. Contrast enhancement in the diseased ileal loop (*white arrow*) is almost equal to inferior venal caval opacification (*black arrow*) in a patient with acute inflammatory Crohn's disease.

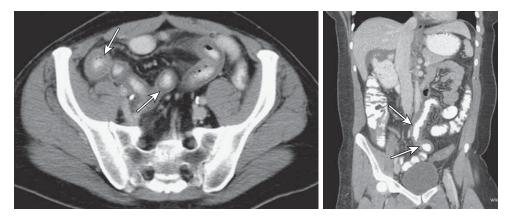


Figure 29-16 "Water halo" pattern (arrows) secondary to angioedema seen in a patient on angiotensin-converting enzyme inhibitors, representing submucosal edema as a dominant component.

• *Pitfalls:* A positive Hounsfield unit value rather than the negative Hounsfield unit value of fat helps confirm the finding.

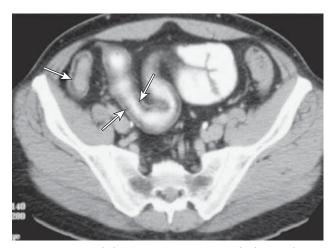
**Fat Halo Pattern.** The fat halo pattern refers to a three-layered target sign of thickened bowel in which the middle or submucosal layer has the attenuation of intramural fat (Figure 29-17). If the attenuation of the dark ring is measured in Hounsfield units, the numbers will largely be below 10 HU. However, the attenuation is seldom that of mesenteric or retroperitoneal fat owing to either partial volume effect or coexistent edema.<sup>39</sup>

- *Differential diagnosis:* Ulcerative colitis, Crohn's disease in the colon; uncommon diagnoses: cytoreductive therapy exposure, chronic radiation enteritis
- *Pitfalls:* Intramural fat may exist in the colon as a normal variant in normal patients. The normal intramural fat layer is generally very thin, with the muscularis propria also being uniformly thin, rarely exceeding 1 mm in thickness with no surrounding mesenteric abnormalities. The

observation of the normal fat halo sign is most frequently made in undistended or poorly distended bowel loops. The clinical history must be considered in the final diagnosis.

**Black Attenuation.** Black attenuation is the equivalent of pneumatosis and usually represents acute injury to the bowel, other than the rare, large cystic collections. Gas within intramural or extramural vessels is also diagnostic of pneumatosis (Figure 29-18).<sup>40</sup>

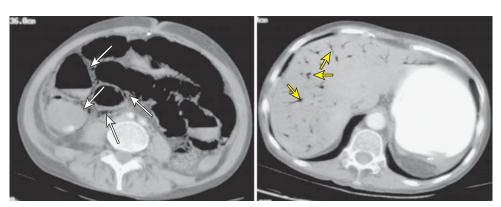
- Pathophysiology: Represents acute injury to the bowel.
- Representative example: Pneumatosis.
- *Differential diagnosis:* Ischemia, infection, and trauma; uncommon diagnosis: iatrogenic injury.
- *Pitfalls*: Intraluminal gas collections clinging to the mucosa can cause false-positive results. Differentiating dependently located gas bubbles in the cecum and ascending colonic wall from trapped gas can be confirmed by rescanning in decubitus position.



**Figure 29-17** "Fat halo" pattern in a patient with chronic ulcerative colitis demonstrating multiple thickened bowel segments with a central band of fat attenuation (*arrows*).

## Key Points

- Performance of a diagnostic high-quality double-contrast barium enema is an art form.
- Rigorous colonic cleansing plays a vital role in the performance of an optimal diagnostic barium enema examination.
- Technical tips can help circumvent potential challenges.
- Optical and virtual colonoscopies have resulted in the steady decline of the number of barium enema examinations performed.
- Multidetector CT is the initial diagnostic test for the evaluation of inflammatory and infectious diseases.
- CT can accurately depict the degree of bowel thickening, extent and location of the disease, and associated complications.
- Bowel attenuation and wall enhancement patterns can aid in narrowing the differential diagnosis.



**Figure 29-18** Black attenuation pattern. The presence of intramural gas or pneumatosis (*white arrows*) is suggestive of acute injury to the bowel. Computed tomography of the liver shows gas in the portal vein (*yellow arrows*).

Wilkins.

## **SUGGESTED READINGS**

- Adam A, Dixon AK, editors: Grainger & Allison's diagnostic radiology, ed 5, London, 2008, Elsevier. Brant WE, Helms CA, editors: Fundamentals of diag-
- nostic radiology, ed 3, Philadelphia, 2006, Lippincott Williams & Wilkins.
- Eisenberg RL: Gastrointestinal radiology: a pattern approach, ed 4, Philadelphia, 2003, Lippincott Williams & Wilkins.

### REFERENCES

- Frederick MG, Ott DJ, Gelfand DW, et al: Gastrointestinal fluoroscopy in difficult patients. *Appl Radiol* 26:12–22, 1997.
- 2. Ott DJ: Accuracy of double-contrast barium enema in diagnosing colorectal polyps and cancer. *Semin Roentgenol* 35:333–341, 2000.
- 3. Harned RK, Consigny PM, Cooper NB: Barium enema examination following biopsy of the rectum or colon. *Radiology* 145:11–16, 1982.
- 4. Maglinte DDT, Strong RC, Strate RW, et al: Barium enema after colorectal biopsies: experimental data. *AJR Am J Roentgenol* 139:693–697, 1982.
- Dodds WJ, Scanlon GT, Shaw DK, et al: An evaluation of colon cleansing regimens. *AJR Am J Roentgenol* 128:57–59, 1977.
- Fork F-T, Ekberg O, Nilsson G, et al: Coloncleansing regimens: a clinical study in 1200 patients. *Gastrointest Radiol* 7:383–389, 1982.
- Gelfand DW, Chen YM, Ott DJ: Preparing the colon for the barium enema examination. *Radiology* 178:609–613, 1991.
- Eisenberg RL, Hedgcock MW: Preliminary radiograph for barium enema examination: is it necessary? *AJR Am J Roentgenol* 136:115–116, 1981.
- 9. Miller RE: A new enema tip. *Radiology* 92:1492, 1969.
- Dodds WJ, Stewart ET, Nelson JA: Rectal balloon catheters and the barium enema examination. *Gastrointest Radiol* 5:227–234, 1989.
- 11. Rubesin SE, Maglinte DD: Double-contrast barium enema technique. *Radiol Clin North Am* 41:365–376, 2003.
- 12. Shorthouse AJ, Bartram CI, Eyers AA, et al: The water-soluble contrast enema after rectal anastomosis. *Br J Surg* 69:714–717, 1982.
- Blakeborough A, Sheridan MB, Chapman AH: Complications of barium enema examinations: a survey of UK consultant radiologists, 1992 to 1994. *Clin Radiol* 52:142–148, 1997.
- Rosenberg LS, Fine A: Fatal venous intravasation of barium during a barium enema. *Radiol*ogy 73:771–773, 1959.
- Winawer SJ, Stewart ET, Zauber AG, et al: A comparison of colonoscopy and doublecontrast barium enema for surveillance after

- Gelfand D: The colon. *Curr Opin Radiol* 2:407–412, 1990.
- Wolff BG, Fleshman JW, Beck DE, et al, editors: *The ASCRS textbook of colon and rectal surgery*, New York, 2007, Springer.
- Ros PR, Mortele KJ, Lee S, et al, editors: *CT and MRI* of the abdomen and pelvis: a teaching file, ed 2,

polypectomy. National Polyp Study Work

Rockey DC, Paulson E, Niedzwiecki D, et al:

Analysis of air contrast barium enema, com-

puted tomographic colonography, and colo-

noscopy: prospective comparison. Lancet 365:

contrast diagnosis. In Gore RM, Levine MS,

Laufer I, editors: Textbook of gastrointestinal

radiology, Philadelphia, 1994, WB Saunders,

trast diagnosis. In Laufer I, Levine MS, editors:

Double contrast gastrointestinal radiology, Phila-

morphology on double-contrast barium enema:

its pathologic predictive value. AJR Am J Roent-

spiral CT pneumocolon for suspected colonic

tidetector CT of bowel obstruction: value of

post-processing. Eur Radiol 15:2323-2329,

Crohn disease: CT findings and interobserver

agreement for enteric phase CT enterography.

carcinoma: CT staging with water as contrast

puted tomographic air enema technique to

demonstrate colonic neoplasms. Gastrointest

computed tomography. J Comput Assist Tomogr

and associated Chilaiditi's syndrome: case

report and literature review. Am J Gastroenterol

17. Laufer I: Barium studies: principles of double-

18. Laufer I, Kressel HY: Principles of double con-

19. Ott DJ, Gelfand DW, Wu WC, et al: Colon polyp

20. Amin Z, Boulos PB, Lees WR: Technical report:

21. Aufort S, Charra L, Lesnik A, et al: Mul-

22. Booya F, Fletcher JG, Huprich JE, et al: Active

23. Angelelli G, Macarini L, Lupo L, et al: Rectal

24. Solomon A, Michowitz M, Papo J, et al: Com-

25. Fisher JK: Abnormal colonic wall thickening on

26. Plorde JJ, Raker EJ: Transverse colon volvulus

27. Thoeni RF, Cello JP: CT imaging of colitis. Radi-

medium. Radiology 177:511-514, 1990.

neoplasms. Clin Radiol 51:56-61, 1996.

delphia, 1992, WB Saunders, pp 9-54.

genol 141:965-970, 1983.

Radiology 241:787-795, 2006.

Radiol 11:194-196, 1986.

7:90–97, 1983.

91:2613-2616, 1996.

ology 240:623-638, 2006.

Group. N Engl J Med 342:1766-1772, 2000.

16.

305-311, 2005.

pp 38-49.

2005.

 Philpotts LE, Heiken JP, Westcott MA, et al: Colitis: use of CT findings in differential diagnosis. *Radiology* 190:445–449, 1994.

Philadelphia, 2006, Lippincott Williams &

- Rao PM, Wittenberg J, Lawrason JN: Primary epiploic appendagitis: evolutionary changes in CT appearance. *Radiology* 204:713–717, 1997.
- Rao PM, Novelline RA: Case 6: primary epiploic appendagitis. *Radiology* 210:145–148, 1999.
- Markose G, Ng CS, Freeman AH: The impact of helical computed tomography on the diagnosis of unsuspected inflammatory bowel disease in the large bowel. *Eur Radiol* 13:107–113, 2003.
- Friedman S: Cancer in Crohn's disease. Gastroenterol Clin North Am 35:621–639, 2006.
- Pereira JM, Madureira AJ, Vieira A, et al: Abdominal tuberculosis: imaging features. *Eur J Radiol* 55:173–180, 2005.
- 34. Madureira AJ: The comb sign. *Radiology* 230: 783–784, 2004.
- Wittenberg J, Harisinghani MG, Jhaveri K, et al: Algorithmic approach to CT diagnosis of the abnormal bowel wall. *Radiographics* 22:1093– 1107, 2002.
- Mirvis SE, Shanmuganathan K, Erb R: Diffuse small-bowel ischemia in hypotensive adults after blunt trauma (shock bowel): CT findings and clinical significance. *AJR Am J Roentgenol* 163:1375–1379, 1994.
- Frager DH, Goldman M, Beneventano TC: Computed tomography in Crohn disease. J Comput Assist Tomogr 7:819–824, 1983.
- Balthazar EJ, Hulnick D, Megibow AJ, et al: Computed tomography of intramural intestinal hemorrhage and bowel ischemia. J Comput Assist Tomogr 11:67–72, 1987.
- Jones B, Fishman EK, Hamilton SR, et al: Submucosal accumulation of fat in inflammatory bowel disease: CT/pathologic correlation. *J Comput Assist Tomogr* 10:759–763, 1986.
- Connor R, Jones B, Fishman EK, et al: Pneumatosis intestinalis: role of computed tomography in diagnosis and management. J Comput Assist Tomogr 8:269–275, 1984.

## **Computed Tomographic** Colonography

SUNIT SEBASTIAN | WILLIAM SMALL | NICOLE D. HORST

## **Technical Aspects**

Colorectal cancer is the second cause of cancer deaths in the United States,<sup>1</sup> second only to lung cancer in men and breast cancer in women. Colorectal cancer screening can be used to identify adenomatous polyps, the precursor lesion to colon cancer for screening symptomatic patients.<sup>2</sup> Computed tomographic (CT) colonography can be simply defined as a highly sophisticated technique that employs rigorous bowel preparation (cleansing) followed by distention of the bowel with air or carbon dioxide (CO<sub>2</sub>). Multidetector CT (MDCT) is used to acquire volumetric data, and specialized software is used for postprocessing the data sets to generate two-dimensional (2D) multiplanar images or 3D images of the colon. A detailed description of the various techniques and protocols essential for an optimal CT colonography is provided here. In addition, various methods of visualization, interpretation guidelines, and common pitfalls associated with the procedure are discussed.

## **TECHNIQUE**

Successful CT colonography examination involves the following:

- 1. Colonic cleansing with tagging of residual stool and luminal fluid
- 2. Colonic distention
- 3. Data acquisition
- 4. Visualization of CT colonography with 2D and 3D techniques

The examination can be entirely performed by a technologist after adequate training with minimal assistance from a radiologist. However, the presence of an onsite radiologist is preferred for consultation in difficult cases.

## COLONIC CLEANSING

The presence of residual fluid or stool will result in a suboptimal CT colonography because it can obscure polyps or neoplasms or make differentiation between polyps and stool difficult.<sup>3</sup> Hence, a robust colonic preparation is perhaps the most important step of the entire study. Colonic cleansing is achieved by combining four basic components: dietary restriction, administration of a cathartic agent, tagging of residual stool, and tagging of residual luminal fluid.

The patient is instructed to consume a clear liquid diet the day before the examination. The main bowel cleansing agents include cathartics such as magnesium citrate and sodium phosphate and gut lavage solutions such as polyethylene glycol (PEG). The two popular commercial preparation kits are the

24-hour Fleet 1 Preparation (Fleet Pharmaceuticals, Lynchburg, VA) and the LoSo Preparation (EZ-EM, Westbury, NY). A time outline for bowel preparation is suggested in Table 30-1.

Sodium phosphate is an oral saline cathartic and is referred to as a "dry prep" because it leaves behind little residual fluid in the colon.<sup>4</sup> Magnesium citrate is also a saline cathartic that causes fluid to accumulate in the bowel because of its osmotic effects and promotes peristaltic activity and bowel emptying.

PEG is an effective agent for cleansing the bowel, but it often results in excessive fluid retention in the colon. It is considered a "wet prep" and is not the ideal bowel cleansing agent for virtual colonoscopy. The PEG preparation is associated with the poorest compliance because of its consistency and large volume of ingestion. In a study comparing PEG and sodium phosphate, the majority of the subjects were unable to complete the PEG regimen, whereas 84% of the patients found sodium phosphate to be tolerable compared with only 33% of patients receiving PEG.<sup>5</sup> There is no significant difference between oral sodium phosphate and PEG electrolyte solution in the quality of bowel cleansing.<sup>6</sup> Magnesium citrate can be used in conjunction with a decreased volume (2 L) of PEG lavage solution to reduce preparation time and improve patient tolerance.<sup>7</sup> The advantages and disadvantages of using a dry or wet bowel cleansing agent are illustrated in Table 30-2.

## Contraindications for Bowel Cleansing Agents

The use of a particular laxative is governed by the health status of the individual. Sodium phosphate can cause electrolyte disturbances leading to hyperphosphatemia, hypocalcemia, and hypernatremia. Hence it should not be used in patients with renal, cardiac, or hepatic insufficiency and preexisting electrolyte abnormalities.8 Sodium phosphate also should be avoided in elderly hypertensive patients who are taking angiotensinconverting enzyme inhibitors. Although magnesium citrate has been reported to cause electrolyte imbalances, these changes are less pronounced than those seen with sodium phosphate. Magnesium citrate should not be used in patients with renal failure.<sup>9</sup>

## **RESIDUAL STOOL AND LUMINAL** FLUID TAGGING

Dual-positive oral contrast agents are used for tagging of the residual stool and luminal fluid after catharsis.<sup>10</sup> Barium and/ or iodine solutions are ingested with meals, usually in conjunction with the oral cathartics, 24 to 48 hours before imaging to allow adequate incorporation of the positive contrast material with colonic contents. Tagged stool and residual fluid demonstrate higher attenuation and are easily discernible from the homogeneous soft tissue density of polyps and colonic folds.

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TABLE 30-1	Suggested Protocol for Bowel Preparation				
Prepa	ration	Day Before Examination	Morning of CT Colonography	Additional Instructions	
Sodiur	n phosphate	6 PM: 45 mL of sodium phosphate diluted in 4 oz of water orally	10-mg bisacodyl suppository approximately 1 hr before the examination	Refrain from eating solids and maintain adequate hydration	
		9 PM: Four bisacodyl tablets (5-mg each) orally		with clear liquids	
Magne	esium citrate	4 PM: 200-300 mL (10 oz) of magnesium citrate orally	10-mg bisacodyl suppository approximately 1 hr before the examination		
		6 PM: Four bisacodyl tablets are taken orally with 8 oz of water			

CT, Computed tomography.

TABLE <b>30-2</b>	Advantages and Disadvantages of Dry and Wet Preparation			
Prepa	ration	Advantages	Disadvantages	
	ep: Sodium phosphate agnesium citrate	Less fluid to obscure colonic walls Better patient compliance More tolerable for consumption	More solid debris along the colonic wall makes three- dimensional endoluminal view more time consuming.	
Wet prep: Polyethylene glycol		Less debris along the wall Minimizes solid stool Preferred preparation for inpatients and elderly who cannot tolerate even moderate fluid or electrolyte shifts	<ul> <li>More fluid can obscure colonic wall without stool subtraction.</li> <li>Patient compliance is poor because of large volume of ingestion.</li> <li>Abdominal discomfort, bloating, and nausea and vomiting occur.</li> </ul>	

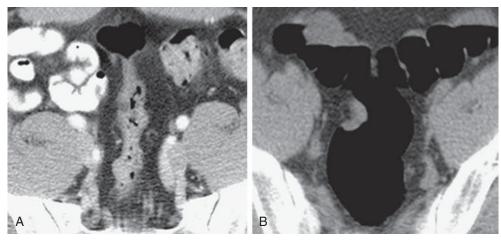


Figure 30-1 A, The collapsed segment of the rectum does not reveal any pathologic process even on careful inspection. B, Well-distended segment in the supine image revealed a 2-cm polyp within the rectum.

Either dilute 2% CT barium or 30% to 40% barium can be used for residual stool tagging; 30% to 40% barium can be very dense and cause artifacts and is also less well tolerated by patients.

Diatrizoate meglumine and diatrizoate sodium solution are used for uniform opacification of the residual luminal fluid, and their added secondary cathartic effects eliminate a significant amount of adherent solid debris. The tagged residual stool and fluid are then eliminated by electronic subtraction of the high-density material. Pickhardt and colleagues<sup>11</sup> demonstrated that patients who underwent residual stool and fluid tagging with electronic subtraction for a CT colonographic study demonstrated higher sensitivity for detection of adenomatous polyps measuring 8 mm or more than with conventional colonoscopy. The use of stool and fluid tagging provides a window of opportunity for possible elimination or significant decrease in the amount of laxative to be consumed by the patient. At present, the American College of Radiology (ACR) practice guideline for performing virtual colonoscopy in adults recommends using oral contrast for labeling stool or fluid when possible.<sup>12</sup>

## COLONIC DISTENTION

Inadequately distended segments of the colon can make polyp and cancer detection difficult, compromising the sensitivity and specificity of the examination (Figure 30-1). Room air or  $CO_2$  may be used for colonic distention for the virtual colonoscopic examination. CT technologists after adequate training and experience could easily manage to perform the introduction of the rectal catheter. The need for radiologist intervention can be reserved for difficult situations or very apprehensive patients.

## ROOM AIR

Advantages of room air include ease of use, ready availability, and lack of additional cost and because it provides good colonic distention. However, because room air is composed predominantly of nitrogen it is poorly absorbed through the colonic wall and patients can experience abdominal discomfort and pain after the CT colonography until the air is totally expelled distally by peristalsis. In addition, significant time may be required to teach patients to self-insufflate with room air, leading to increased operator dependence.

## CARBON DIOXIDE

The patient is advised to evacuate just before the start of the study. Automatic  $CO_2$  insufflation can be a useful alternative to room air for colonic distention. A commercially available electronic insufflation device provides a constant flow of  $CO_2$  into the colon per rectum at a relatively low level of preset pressure to reduce the risk for colonic perforation.  $CO_2$  is absorbed rapidly through the colonic wall and exhaled through the lungs. Shinners and associates<sup>13</sup> have observed decreased postprocedural discomfort and improved colonic distention using automated  $CO_2$  compared with patient-controlled room air. The automated  $CO_2$  procedure is fairly easy to explain to the patient. The automated  $CO_2$  technique can decrease operator dependence. The risk for perforation with automated  $CO_2$  technique or patient-controlled distention methods probably approaches zero for screening CT colonography.<sup>13</sup>

## Technique

**Room Air.** The patient is advised to evacuate just before the start of the study. With the patient in the left lateral decubitus position a small rubber catheter is used to insufflate the colon with a hand-held bulb syringe. Using an insufflation bulb, 50 to 70 puffs or 2 L of room air is administered until the patient experiences fullness or mild discomfort, which signals that the colon is well distended.

Automated Carbon Dioxide Technique. In the automated CO<sub>2</sub> technique a small-caliber, flexible rectal catheter is placed with the patient in the left lateral decubitus position and 1.0 to 1.5 L CO<sub>2</sub> is delivered by the automated device at equilibrium pressure of approximately 20 mm Hg. The patient is moved into the right lateral decubitus position until approximately 2.5 L of  $CO_2$  has been introduced. The total volume of  $CO_2$  used in the procedure can vary from 2 to 10 L owing to individual differences in colonic volume, colonic resorption, and reflux through the ileocecal valve. Finally, a scout image of the abdomen and pelvis is obtained with the patient in the supine position. The colonic distention can be checked on the CT scout image or on the review of the 2D transverse images during the examination. Adequate colonic distention will reveal an almost complete column of gas from the rectum to the cecum. Additional  $CO_2$  may be administered with the patient in the prone position if the colon is suboptimally distended. The virtual colonoscopy scan then is repeated in the prone position after a

second scout localizing image. Scans performed with the patient in both the supine and prone positions provide improved colonic distention, particularly of the transverse and sigmoid colon compared with supine or prone imaging alone.<sup>14</sup> Although dual-position scanning increases the radiation dose, it facilitates optimal bowel distention and differentiation of fecal material from polyps. Furthermore, persistent segments of focal collapse may need to be scanned with the patient in the right lateral decubitus position.

## USE OF SPASMOLYTIC AGENTS

### Glucagon

Glucagon causes relaxation of the smooth muscle in the gastrointestinal tract, including the colon, presumably improving patient comfort and colonic distention. The ACR practice guideline suggests that the use of antispasmotics is not necessary for routine examination and no benefit is seen with glucagon.

## Hyoscine Butylbromide

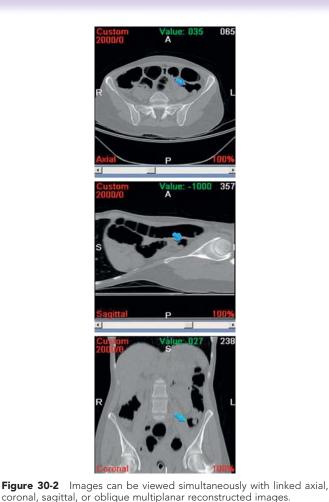
This anticholinergic drug is administered intravenously and acts by blocking parasympathetic ganglia, causing relaxation of smooth muscle. Hyoscine butylbromide has been reported to be more effective than glucagon in distending the colon for barium enema examinations.<sup>15</sup> Adverse effects include blurring of vision, dry mouth, tachycardia, and acute urinary retention. Contraindications to the use of hyoscine butylbromide include glaucoma, obstructive uropathy, and myasthenia gravis. It is not approved for use in the United States but has been used widely in Europe and Asia.

The parenteral administration of spasmolytic agents, given their potential adverse reactions, can create added patient anxiety and thereby increase the duration and cost of the examination.

## MULTIDETECTOR COMPUTED TOMOGRAPHY PROTOCOL FOR COMPUTED TOMOGRAPHIC COLONOGRAPHY

After air or CO<sub>2</sub> insufflation, CT colonography is performed first in the supine position in a cephalocaudad direction encompassing the entire colon and rectum. The patient is then placed in the prone position, and the scan is repeated over the same z-axis range. An optimal study can be performed using 4-, 8-, or 16-channel MDCT scanners with 1.25-mm collimation. The 16- and 64-slice MDCT scanners have considerably decreased scanning times, leading to virtual elimination of motion artifacts from peristalsis and respiration. The 64-slice scanners are generally not necessary because submillimeter collimation results in increased radiation dose. Screening CT colonography is a noncontrast study, and intravenous contrast material is not administered routinely. Oral contrast tagging and 3D polyp detection have a high diagnostic accuracy, making the use of intravenous contrast unnecessary for screening. Disadvantages of the use of intravenous contrast include the possibility of contrast reactions, higher radiation dose, increased interpretation times, and higher cost. Intravenous contrast could pose an added difficulty in differentiating an enhancing lesion from tagged material and should be avoided in patients with oral stool and fluid tagging. A suggested CT colonography MDCT protocol is illustrated in Table 30-3.

TABLE <b>30-3</b>		ol for Computed nography Using 16-Slice nputed Tomography			
Techn	ical Parameters	16-Slice MDCT			
Scan a Scan c Respir Detect Pitch Feed t Gantry Kilovo Millian	position prea lirection atory phase tor configuration rable (mm/rotation) rotation time (s) lt peak (kVp) hpere (mA) struction	Supine and prone Entire abdomen and pelvis Craniocaudal Inspiration 16 × 0.625 mm 1.375 13.75 0.5 120 Smart mA (GE Medical Systems, Milwaukee, WI), with noise index of 50 or 35 to 75 mAs (effective) without automatic tube current modulation Standard/full			
Thickn Interva	000	1.25 mm 0.8 mm			
MDCT,	MDCT, Multidetector computed tomography.				



MDCT scanners generate volumetric data sets that can be used for traditional 2D axial images and multiplanar reformatted images as well as to produce 3D endoluminal views. A standard reconstruction kernel should be used for CT colonographic data reconstruction. State-of-the-art CT colonography also requires a sophisticated and specialized computer workstation with advanced graphic software that displays 2D and 3D views of the colon. The thin-section source images are sent to a workstation for advanced modeling and interpretation and to the picture archiving and communications system for storage.

## COMPUTED TOMOGRAPHY COLONOGRAPHY AND RADIATION DOSE

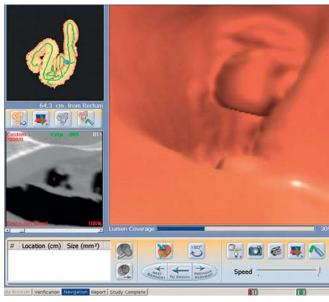
Because CT colonography is intended to be used as a screening test, optimization of scan parameters to minimize radiation exposure is necessary. The intrinsic high contrast between the intraluminal gas and the soft tissue of the colonic wall offers an opportunity to reduce the milliampere-second (mAs) to decrease the effective radiation dose. An automatic tube-current modulation system, which is routinely available with 16- and 64-slice CT scanners, can be set at a noise index of 50 to result in significant dose reduction. Macari and colleagues<sup>16</sup> demonstrated effective radiation doses for CT colonography to be 5.0 millisieverts (mSv) for men and 7.8 mSv for women. The radiation dose can be further reduced using ultra-low-dose CT colonography as demonstrated by Iannaccone and coworkers,<sup>1</sup> who employed an effective milliampere-second of 10 using a four-row MDCT to obtain an effective dose of 1.8 mSv in men and 2.4 mSv in women. Although there is a very small theoretical risk for cancer as a result of low-dose radiation exposure (0.14% for combined supine and prone virtual colonoscopy scans for a 50-year-old person),<sup>18</sup> the benefits of screening for colorectal cancer prevention clearly outweigh these risks.

## COMPUTED TOMOGRAPHIC COLONOGRAPHY VISUALIZATION

The CT colonography study can be interpreted using the conventional 2D multiplanar reconstruction or 3D visualization using specialized software. The debate as to the relative value of 2D versus 3D for primary interpretation of CT colonography does not preclude the basic tenet of thorough colonic preparation and adequate reader training in CT colonography examinations. In practice, it is important to be comfortable in using both 2D and 3D methods. Depending on reader preference and training, either of the two methods could be used for primary reads and the other view could be used as a problem-solving tool. However, in practice use of both the 2D and 3D views provides better results in cohorts with low polyp prevalence compared with using the 2D method alone.<sup>19</sup>

## Two-Dimensional Visualization

Different images can be viewed simultaneously with linked axial, coronal, sagittal, or oblique multiplanar reformatted images (see Figure 30-2). Various window-level settings with presets for lung, soft tissue, and bone can be employed. Advantages of 2D visualization include familiarity of radiologists in the use of multiplanar reformatted images, detection of annular lesions, polyps submerged in fluid, and segments with partial or total luminal collapse. It is also excellent for confirming the soft tissue nature of polyps and recognizing the heterogeneous



**Figure 30-3** Three-dimensional visualization provides an endoluminal surface- or volume-rendered view of the colon that can be generated via a near-accurate automated center line.

texture of stool. However, it can be a relatively ineffective and tedious method for detecting polyps in a cohort of low prevalence.

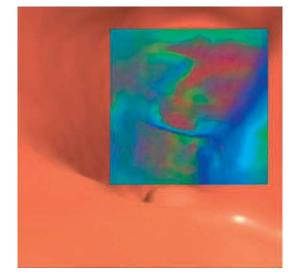
## **Three-Dimensional Visualization**

3D visualization provides an endoluminal surface- or volumerendered view of the colon that can be generated by a nearaccurate automated center line (Figure 30-3). The specialized software program eliminates gas-containing structures such as the stomach, small intestines, and lung bases and allows the user to bridge collapsed segments. The reader is able to fly through the colon at a set speed or manually with capabilities to control the viewing direction and the viewing angle. Most software programs have the ability to compare the 3D images to corresponding 2D images for immediate problem solving. To examine the entire colon, a fly-through should be performed in both antegrade and retrograde directions for both supine and prone positions, resulting in a total of four fly-throughs per CT colonographic study. Some of the disadvantages of 3D visualization include the possibility of solid stool appearing as a polyp and the ileocecal valve may appear polypoid. However, correlation with 2D images can minimize these potential errors. Longer interpretation times for 3D endoluminal evaluation can be potentially fatiguing.

## Newer Display Methods

To overcome problems posed by 2D and 3D methods, researchers have developed several interesting display methods. These include the following:

- *Virtual pathology/dissection:* The Virtual Dissection (VD) (GE Healthcare, Piscataway, NJ) program cuts the colon open and displays it either in segments or showing the entire colon in one screen.
- *Filet view:* It is similar to other cut-open views but additionally creates a movie loop of the cut-open colon displayed for a short segment at a time.



**Figure 30-4** Translucency rendering uses color mapping in which a polyp has a red center and shifts to blue over green at its borders.

- *Panoramic views:* This 3D view enlarges the regular endoluminal view at its margins and depicts the colon in both the antegrade and retrograde directions in the same window.
- *Translucency rendering*: Color mapping is used in which a polyp has a red center and shifts to blue over green at its borders, while tagged stool appears white if the density of the tagged stool is 200 Hounsfield units or greater (Figure 30-4).

## Computed Tomographic Colonography Interpretation

The Working Group on Virtual Colonoscopy<sup>20</sup> proposed a practical reporting scheme and categorization system for CT colonographic findings with follow-up recommendations. This report intends to facilitate uniformity and quality control in the performance of CT colonography. Although a detailed description is beyond the scope of this chapter, review and implementation of these recommendations are suggested. According to this report, for screening purposes the minimum size for reporting polyp lesions is 6 mm. Medium-sized lesions (6 to 9 mm) are rarely malignant, but these patients are offered same-day colonoscopy. Patients with lesions 1 cm or larger should be referred for colonoscopy.

## **Pros and Cons**

CT colonography could attract new patients who have previously refused colorectal screening, because it is relatively noninvasive and has a very low rate of complications. Thus, compliance with colon cancer screening overall could be increased.

Many radiologists are better trained in cross-sectional techniques than barium radiology, which is more labor intensive and relatively poorly reimbursed when compared with virtual colonoscopy. The concern about an insufficient number of gastroenterologists able to provide screening colonoscopy can be addressed with radiologists contributing to colorectal cancer screening with CT colonography.

CT colonography has potential disadvantages. The performance of an optimal CT colonographic study depends on

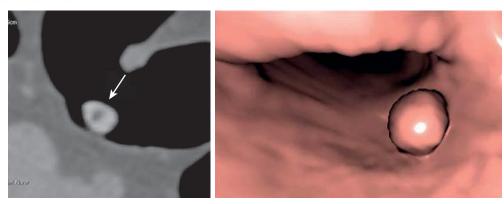


Figure 30-5 Fecal material can be falsely interpreted as a polyp. It may show the presence of a radiolucent area consistent with fat and may change its position on supine and prone images.

adequate bowel preparation, reader training, and expertise. Virtual colonoscopy would have to be 54% less expensive than conventional colonoscopy to be as cost effective in a 10-year interval screening program.<sup>21</sup> In addition, significant abnormal findings have to be followed by colonoscopy for treatment (implying higher costs and a separate bowel preparation). The ability to detect extracolonic findings can be an advantage and a disadvantage. It can be a valuable tool in identifying potentially life-threatening or significant extracolonic findings that have the potential for positive effects on patient care (e.g., lymphadenopathy, solid hepatic, renal or pancreatic masses, and aortic aneurysm).<sup>22</sup> However, this feature of virtual colonoscopy also may be a drawback (e.g., unnecessary workups for benign incidental findings could add increased costs).<sup>23</sup> Moreover, a screening CT colonography is a noncontrast examination, which makes the evaluation of extracolonic solid organs suboptimal.

## **Controversies**

Two large studies have been published in major journals regarding the efficacy of CT colonography. A large study by Pickhardt and coworkers<sup>11</sup> demonstrated outstanding results with virtual colonoscopy outperforming optical colonoscopy on a per-polyp basis at both the 8-mm level (94% vs. 92%) and the 10-mm level (94% vs. 88%). However, a subsequent study by Cotton and associates<sup>24</sup> found only a 52% sensitivity for 10-mm polyps and only 32% for polyps over 6 mm. This study was criticized by virtual colonoscopy researchers because of inadequate reader training, no documentation of examination quality, outdated scan techniques, and unorthodox reporting of results, which tended to bias the results in favor of optical colonoscopy.<sup>25</sup>

## Normal Anatomy

Knowledge of normal colonic anatomy and its variants, common pitfalls, and pseudolesions as demonstrated on CT colonography is essential to provide a confident and accurate report.<sup>26</sup> The common pitfalls of CT colonography are discussed in the following paragraphs.

Collapsed or underdistended segments are difficult to evaluate, and significant pathologic processes may be missed. Furthermore, collapsed segments of colon may be misinterpreted as annular carcinomas or strictures. Supine and prone imaging and use of  $CO_2$  for colonic distention may improve distention. Fecal material can be a major source of false-positive findings on CT colonography and is misinterpreted as polyps or neoplasms. Fecal material may show the presence of a radiolucent area consistent with fat (Figure 30-5). Use of both prone and supine imaging is helpful to differentiate mobile stool from a fixed lesion.

Intraluminal fluid may limit evaluation of the colonic mucosa and hide significant pathologic processes (Figure 30-6). The use of phospho-soda colon preparations results in a drier colonic mucosa in addition to prone and supine imaging.

Haustral folds are poorly distended, thickened folds that may meet in the midline (kissing folds) and could mimic masses. Conversely, infiltrating tumors may appear as isolated haustral fold thickening.

Diverticula may become impacted with stool or inverted and may simulate polyps even on axial images. Stool-containing diverticula usually can be seen to project beyond the colonic lumen and have pockets of air or retained barium. Inverted diverticula need careful inspection of axial images that reveal the pericolic fat within them.

"Difficult" polyps include pedunculated polyps that may move with a change in patient position, thus being misinterpreted as stool (Figure 30-7). Direct visualization of the stalk, homogeneous density of a polyp, and air trapped within the stool can aid in differentiation.

Flat or sessile polyps are only minimally raised from the colonic mucosa and can be missed (Figure 30-8). Lung and soft tissue window settings with axial images supplemented with endoluminal views could be helpful.

A prominent ileocecal valve may mimic a mass lesion. The characteristic location of the valve on the medial wall of the cecum, its relationship to the terminal ileum, and the presence of fat within the valve are some of its signature features (Figure 30-9). External compression or indentation of the air-distended colon by liver, loops of bowel, the psoas muscle, or aorta may simulate a mass on endoluminal images, especially in thin patients. Review of axial 2D images can overcome this misinterpretation.

Breathing and peristalsis may cause misregistration artifacts on reconstructed images. Rapid image acquisition using multislice CT scanners has almost eliminated motion artifacts. Metallic artifact or beam hardening artifact may degrade both axial and endoluminal images, particularly in the pelvis in patients with hip prostheses. Stair-step artifact is more prominent in the rectum and cecum on endoluminal images. They

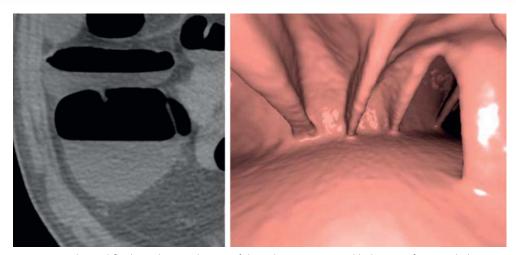


Figure 30-6 Intraluminal fluid may limit evaluation of the colonic mucosa and hide a significant pathologic process.

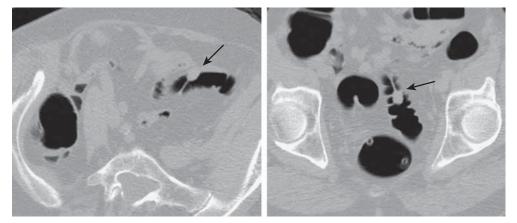


Figure 30-7 Pedunculated polyps (arrows) may move with a change in patient position because of the presence of a long stalk and thus be misinterpreted as stool.

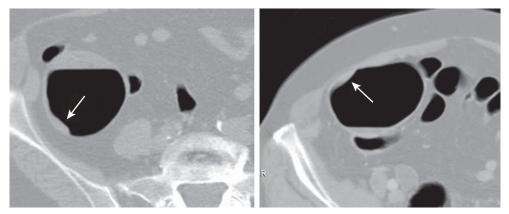


Figure 30-8 Flat or sessile polyps (arrows) that are only minimally raised from the colonic mucosa can be missed. The apparent change in position of the lesion is due to movement of the cecum itself.

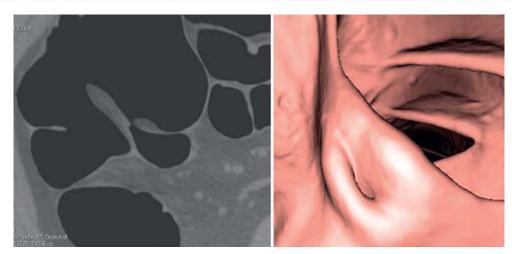


Figure 30-9 A prominent ileocecal valve may mimic a mass lesion; characteristic location and the presence of fat aid in identification.

appear as multiple low-attenuation rings spiraling around the lumen of the distended colon but rarely interfere with interpretation.

## **Future Trends and Developments**

Computer-aided detection can be defined as a diagnosis made by using the output of a computerized scheme for automated image analysis as a diagnostic aid. This second opinion has the potential to improve radiologists' detection performance and reduce variability of the diagnostic accuracy among radiologists; however, the radiologist must be familiar with common pitfalls leading to computer-aided detection false-positive results.<sup>27</sup>

## Pathophysiology

Advances in molecular genetics and new technologic approaches provide valuable insights into the evolution of colorectal cancer, enabling a more comprehensive understanding of the pathologic processes and genetic basis of the disease process.<sup>28</sup>

## ADENOMA

Adenoma is considered to be the immediate precursor of colorectal cancer. The colonocytes that make up this minute neoplasm show an adenomatous phenotype or dysplasia; they are the progeny of crypt stem cells and typically exhibit *APC* gene mutations.

## Adenoma Variants

The architectural pattern that the neoplastic glands of the adenoma assume as they grow can be described as tubular, villous, or tubulovillous, as follows:

- A tubular adenoma is composed of straight or branched J tubules (crypts) lined by adenomatous (dysplastic) epithelium.
- Villous growth (constituting >75% of the polyp) consists of adjacent crypts that are elongated to give an appearance of hairlike or leaflike extensions of adenomatous mucosa.

• Tubulovillous growth is composed of a villous component of 25% to 75% of the polyp, according to the standard nomenclature.

## Adenoma Progression

By definition, all adenomas show at least low-grade dysplasia. The adenomatous phenotype represents transformed colonocytes that have enlarged elongated nuclei, mucus depletion of the cytoplasm, and disordered growth patterns of associated crypts or glands.

High-grade dysplasia represents the interface between benign adenoma and invasive cancer. Increased nuclear atypia and extreme gland architectural abnormalities are seen, almost identical to the morphology of adenocarcinoma, but without invasion.

Advanced adenoma is usually an adenoma that has at least a 25% component of villous growth or is larger than 1 cm or shows high-grade dysplasia or invasive cancer on pathologic examination. It represents a biomarker for present and future colorectal cancer risk.

## Classification of Adenoma Shape and Cancer Risk

Adenomas are classified according to their shape as flat or polypoid (protruding), with the latter either sessile or pedunculated. The rate of invasive carcinoma in flat adenomas is slightly lower than but not remarkably different from those in protruded polyps. Depressed adenoma is an uncommon finding in a screening population but has a reported frequency of highgrade dysplasia or submucosal invasion up to 50%.

## Adenoma Size and Cancer Risk

The most practical measure of high-grade dysplasia and malignant transformation risk in adenomas may be size. There is, however, no standard method for measuring adenoma size in current clinical practice.

## Pathologic and Molecular Pathways from Adenoma to Carcinoma

Three distinctive pathways have been identified and are outlined in Table 30-4.

TABLE 30-4	Pathologic and Molecular Pathways from Adenoma to Carcinoma			
Pathw	ay	Incidence	Molecular Genetic Pattern	Location
	PC, LOH, or microsatellite le pathway	60%-80% of colorectal adenocarcinomas	APC mutation, LOH of suppressor genes, chromosomal instability, and aneuploidy	Distal and left side of colon
The m path	icrosatellite instability way	10%-15% of colorectal adenomas—frequently mucin-producing carcinomas	Mutation in both alleles of a mismatch repair gene such as <i>hMLH1</i> , inactivation of the gene as a result of hypermethylation of its promoter region	Right sided
The M	SI low pathway	5%-10% of colorectal cancers More aggressive	Distinctive molecular profile of LOH without APC mutation but associated with low levels of MSI	Distal and left side of colon

LOH, Loss of heterozygosity.

Key Points

- CT colonography can be suitably employed in the early identification of precursor adenomatous polyps for colorectal cancer.
- A robust colonic preparation is the most important step of the CT colonography study.
- CT colonography has proved to be as accurate as optical colonoscopy in the detection of significant polyps.
- Knowledge of normal colonic anatomy and its variants, common pitfalls, and pseudolesions as demonstrated on CT colonography is essential to provide a confident and accurate report.
- Future technologic advances such as computer-aided detection will further enhance the accuracy of CT colonography while decreasing interpretation time.

## **SUGGESTED READINGS**

- Dachman AH, Lefere P, Gryspeerdt S, et al: CT colonography: visualization methods, interpretation, and pitfalls. *Radiol Clin North Am* 45:347–359, 2007.
- Hawes RH: Does virtual colonoscopy have a major role in population-based screening? Gastrointest Endosc Clin N Am 12:85–91, 2002.
- Hofstad B: Colon polyps: prevalence rates, incidence rates, and growth rates. In Waye JD, Rex DK, Williams CB, editors: *Colonoscopy principles and practice*, London, 2003, Blackwell, pp 358–376.
- Kashida H, Kudo S: Magnifying colonoscopy, early colorectal cancer, and flat adenomas. In Waye JD, Rex DK, Williams CB, editors: *Colonoscopy principles and practice*, London, 2003, Blackwell, pp 478–508.
- Landeras LA, Aslam R, Yee J: Virtual colonoscopy: technique and accuracy. *Radiol Clin North Am* 45:333–345, 2007.
- Mcahon PM, Gazelle GS: Colorectal cancer screening issues: a role for CT colonography? *Abdom Imaging* 27:235–243, 2002.
- Mulhall BP, Veerappan GR, Jackson JL: Metaanalysis: computed tomographic colonography. *Ann Intern Med* 142:635–650, 2005.
- Robinson C, Halligan S, Taylor SA, et al: CT colonography: a systematic review of standard of reporting for studies of computer-aided detection. *Radiology* 246:426–433, 2008.

## REFERENCES

- 1. Jemal A, Thomas A, Murray T, et al: Cancer statistics, 2002. *CA Cancer J Clin* 52:23–47, 2002.
- Rex DK, Johnson DA, Lieberman DA, et al: Colorectal cancer prevention 2000: screening recommendations of the American College of Gastroenterology. Am J Gastroenterol 95:868– 877, 2000.
- Fletcher JG, Johnson CD, Welch TJ, et al: Optimization of CT colonography technique: prospective trial in 180 patients. *Radiology* 216: 704–711, 2000.
- 4. Gelfand DW, Chen MYM, Ott DJ: Preparing the colon for the barium enema examination. *Radiology* 178:609–613, 1991.
- Hookey LC, Depew WT, Vanner SJ: A prospective randomized trial comparing low-dose oral sodium phosphate plus stimulant laxatives with large volume polyethylene glycol solution for colon cleansing. *Am J Gastroenterol* 99:2217– 2222, 2004.
- Arezzo A: Prospective randomized trial comparing bowel cleaning preparations for colonoscopy. Surg Laparosc Endosc Percutan Tech 10: 215–217, 2000.

- Sharma VK, Chockalingham SK, Ugheoke EA, et al: Prospective, randomized, controlled comparison of the use of polyethylene glycol electrolyte lavage solution in four-liter versus two-liter volumes and pretreatment with either magnesium citrate or bisacodyl for colonoscopy preparation. *Gastrointest Endosc* 47:167–171, 1998.
- Wiberg JJ, Turner GG, Nuttall FQ: Effect of phosphate or magnesium cathartics on serum calcium: observations in normocalcemic patients. *Arch Intern Med* 138:1114–1116, 1978.
- Ehrenpreis ED, Nogueras JJ, Botoman VA, et al: Serum electrolyte abnormalities secondary to Fleet's Phospho-Soda colonoscopy prep. *Surg Endosc* 10:1022–1024, 1996.
- Zalis ME, Hahn PF: Digital subtraction bowel cleansing in CT colonography. *AJR Am J Roentgenol* 176:646–648, 2002.
- Pickhardt PJ, Choi JR, Hwang I, et al: Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *N Engl J Med* 349:2191–2200, 2003.

- 12. American College of Radiology: ACR-SAR-SCBT-MR practice parameter for the performance of computed tomography (CT) colonography in adults, Reston, VA, 2014, American College of Radiology.
- Shinners TJ, Pickhardt PJ, Taylor AJ, et al: Patient-controlled room air insufflation versus automated carbon dioxide delivery for CT colonography. AJR Am J Roentgenol 186:1491, 2006.
- Yee J, Kumar NN, Hung RK, et al: Comparison of supine and prone scanning separately and in combination at CT colonography. *Radiology* 226:653–661, 2003.
- Goei R, Nix M, Kessels AH, et al: Use of antispasmodic drugs in double contrast barium enema examination: glucagon or Buscopan? *Clin Radiol* 50:553–557, 1995.
- Macari M, Bini EJ, Xue X, et al: Colorectal neoplasms: prospective comparison of thin section low-dose multi-detector row CT colonography and conventional colonoscopy for detection. *Radiology* 224:383–392, 2002.
- 17. Iannaccone R, Laghi A, Catalano C, et al: Detection of colorectal lesions: lower-dose

multi-detector row helical CT colonography compared with conventional colonoscopy. *Radiology* 229:775–781, 2003.

- Brenner DJ, Georgsson MA: Mass screening with CT colonography: should the radiation exposure be of concern? *Gastroenterology* 129: 328–337, 2005.
- Macari M, Milano A, Lavelle M, et al: Comparison of time-efficient CT colonography with two- and three-dimensional colonic evaluation for detecting colorectal polyps. *AJR Am J Roentgenol* 174:1543–1549, 2000.
   Zalis ME, Barish MA, Choi JR, et al; Working
- Zalis ME, Barish MA, Choi JR, et al; Working Group on Virtual Colonoscopy: CT colonography reporting and data system: a consensus proposal. *Radiology* 236:3–9, 2005.
- 21. Sonnenberg A, Delco F, Inadomi JM: Costeffectiveness of colonoscopy in screening for

colorectal cancer. Ann Intern Med 133:573–584, 2000.

- Yee J, Kumar NN, Godara S, et al: Extracolonic abnormalities discovered incidentally at CT colonography in a male population. *Radiology* 236:519–526, 2005.
- Hara AK, Johnson CD, MacCarty RL, et al: Incidental extracolonic findings at CT colonography. *Radiology* 215:353–357, 2000.
- 24. Cotton PB, Durkalski VL, Pineau BC, et al: Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia. *JAMA* 291:1713–1719, 2004.
- Ferrucci JT: Colonoscopy: virtual and optical another look, another view. *Radiology* 235:13– 16, 2005.
- 26. Gryspeerdt S, Lefere P: How to avoid pitfalls in imaging: causes and solutions to overcome false negatives and false positives. In Lefere P, Gryspeerdt S, editors: *Medical radiology: diagnostic imaging—virtual colonoscopy: a practical guide*, Berlin, 2006, Springer, pp 87–116.
- Trilisky I, Dachman AH, Wroblewski K, et al: CT colonography with computer-aided detection: recognizing the causes of false-positive reader results. *Radiographics* 34:1885–1905, 2014.
- Jass JR, Whitehall VLJ, Young J, et al: Emerging concepts in colorectal neoplasia. *Gastroenterol*ogy 123:862–876, 2002.

## Inflammatory and Infectious Colonic Lesions

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## Etiology

Colonic inflammation may be caused by numerous processes and is typically thought of as colitis.<sup>1,2</sup> Some inflammatory conditions of the colon such as diverticulitis and epiploic appendagitis also represent inflammatory lesions of the colon and, on occasion, may be difficult to distinguish from each other and from neoplastic conditions.

Colitis may be due to infection, autoimmune processes (Crohn's and ulcerative colitis), ischemia (low flow, emboli, vasculitides), irradiation, direct toxic insults, chronic abuse of cathartic agents, and intrinsic pathologic inflammatory conditions such as diverticulitis and epiploic appendagitis.<sup>3-11</sup>

In the case of ulcerative colitis and Crohn's colitis, ongoing activation of the mucosal immune system is thought to represent the underlying cause.<sup>9,10</sup> There are numerous stimulants to the activation of this abnormal autoimmune process in patients with Crohn's and ulcerative colitis, but both genetic and environmental factors are important.9 Infectious colitis may be due to bacteria, parasites, or viruses. The patient's underlying immune status is important to know when considering the differential diagnosis of infectious colitis. In addition to typical infectious agents that may cause colitis, persons with altered immunity are at risk for opportunistic infections. A history of recent travel and food ingestion can be helpful when considering infectious causes. Although certain imaging findings are helpful in the differential diagnosis, they are often nonspecific in the case of infectious colitis, and culture of the stools is often necessary to determine the exact cause of infectious colitis.<sup>1-</sup> Additionally, direct toxin or pathologic abnormality may be the cause of the colonic inflammation. In this chapter the focus is on the imaging findings and differential diagnosis of nonischemic causes of colonic inflammation.

## **Prevalence and Epidemiology**

The prevalence of colonic inflammation is related to the cause of the process and the age of the patient.<sup>8-10</sup> Ulcerative colitis affects 10 to 12 in 100,000 individuals in the United States, with the peak incidence occurring between ages 15 and 25 years.<sup>10</sup> The prevalence of Crohn's disease is similar, affecting up to 20 to 40 to 100,000 individuals of Northern European descent.<sup>11</sup> Although most patients with these conditions are young, there is a bimodal age distribution with a second peak in older individuals.<sup>9,10</sup>

Diverticular disease affects up to 10% of the population older than the age of 50, and up to 20% of these patients will develop symptomatic diverticulitis.<sup>12</sup> Infectious colitis can

affect anyone, but is very common in immunocompromised individuals.<sup>13-15</sup> Other forms of colonic inflammation including stercoral colitis, epiploic appendagitis, cathartic colon, and glutaraldehyde colitis occur much less frequently.<sup>2,5,6,16</sup>

## **Clinical Presentation**

Most patients with colonic inflammation present with crampy abdominal pain, fever, leukocytosis, and some form of change in bowel habits.<sup>1,2,9,10,12</sup> The change in bowel habits is usually diarrhea. Diarrhea may be bloody or nonbloody and is related to the type of inflammation. Although the clinical presentation, nature and frequency of the diarrhea, age of the patient, and other epidemiologic factors may indicate a particular type of colonic inflammation, laboratory testing, cross-sectional imaging, endoscopy with biopsy, and culture of the stool are critical in establishing the correct diagnosis.

## Pathophysiology

When considering the imaging findings that help narrow the differential diagnosis of a pathologic colonic inflammatory condition, several factors are important. These include the length of involvement, location of involvement, degree of thickening, and extraintestinal manifestations of the disease. By carefully considering these anatomic considerations the differential diagnosis can be considerably narrowed.<sup>4</sup>

## Imaging

## **GENERAL CONSIDERATIONS**

Because the clinical manifestations of patients with colonic inflammation are broad and overlap with other colonic diseases, a patterned approach using several key observations can help narrow the differential diagnosis.

## Length of Involvement

The length of diseased colon is important in narrowing the differential diagnosis. Certain entities tend to be focal, segmental, or diffuse.

### Focal Disease (2 to 10 cm)

- Neoplasm
- Diverticulitis
- Epiploic appendagitis
- Infection (tuberculosis/amebiasis)

## Segmental Disease (10 to 40 cm)

- Usually colitis
  - Crohn's colitis
  - Glutaraldehyde colitis
  - Ischemia
  - Infection
  - Ulcerative colitis (typically begins in the rectum and spreads proximally)
- Rarely neoplasm (especially lymphoma)

## Diffuse Disease (Most of the Colon)

- Always benign
  - Infection
  - Ulcerative colitis
  - Vasculitis (almost always involves the small bowel as well)

## Location of Involvement

Whereas almost any pathologic condition can affect any area of the colon, some pathologic entities have a propensity to localize to certain areas of the colon.

## **Cecal Region**

- Amebiasis
- Typhlitis (neutropenic colitis)
- Tuberculosis

## Isolated Splenic Flexure and Proximal Descending Colon

• Watershed area for low-flow intestinal ischemia

#### Rectum

- Early stages of ulcerative colitis
- Stercoral colitis

## **Multiple Skip Regions**

Crohn's disease

## Degree of Thickening

There is significant overlap in the degree of colonic wall thickening among different colonic pathologic processes. Mild thickening may be seen in plaque-like tumors and mild colonic inflammation. Marked colonic thickening greater than 1.0 to 1.5 cm may be seen in pseudomembranous, tuberculous, and cytomegaloviral colitis, as well as colonic neoplasms and vasculitis.<sup>4</sup> Occasionally, the degree of thickening and the imaging appearance of colon cancer and diverticulitis may overlap (Figures 31-1 and 31-2).<sup>17-19</sup> In both cases the disease is usually



**Figure 31-2** Axial computed tomography scan shows focal thickening of the descending colon (*arrow*) with adjacent adenopathy (*arrowhead*). Resected specimen revealed adenocarcinoma. Lymphadenopathy adjacent to focal colon thickening favors the diagnosis of colon cancer over diverticulitis.

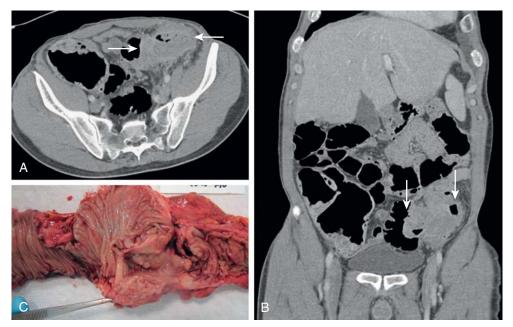


Figure 31-1 A, Axial contrast-enhanced computed tomography (CT) image shows marked thickening of the sigmoid colon (arrows). B, Coronal reformatted CT image from same examination better demonstrates segmental (approximately 10 cm) distribution of disease (arrows). C, Resected specimen reveals florid diverticulitis.

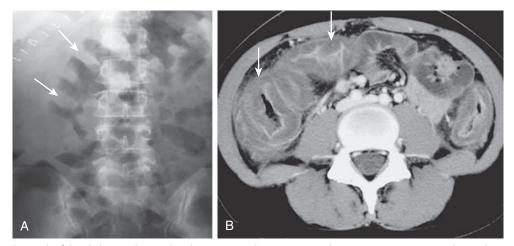


Figure 31-3 A, Radiograph of the abdomen shows "thumbprinting" in the transverse colon (arrows). B, Contrast-enhanced computed tomography in the same patient shows marked colonic wall thickening (arrows) with mural stratification. The patient underwent a cholecystectomy and had *Clostridium difficile* colitis.

focal or involves a short segment of colon and may be associated with marked thickening of the bowel wall. Inflammatory changes in the mesentery have been shown to favor the diagnosis of diverticulitis, and adjacent lymphadenopathy has been shown to favor colon cancer.<sup>17,19</sup> However, because there is considerable overlap in the degree of thickening of different colonic pathologic processes, overall the degree of thickening has limited value in itself for narrowing the differential diagnosis.

## Pattern of Enhancement

The pattern of enhancement can be important in discriminating different forms of intestinal pathology.<sup>4</sup>

## **Target and Double Halo**

### • Edema

- Infection, inflammation (ulcerative and Crohn's colitis), ischemia, vasculitis
- Submucosal fat
  - Chronic inflammation
- Normal variant
- Neoplasm
  - Rarely scirrhous carcinoma of rectum

#### Homogeneous

• Neoplasm, chronic inflammation

#### Heterogeneous

- Neoplasm
- Diminished
  - Ischemia

#### **Extraintestinal Manifestations**

When an abnormal segment of colon is evaluated, the adjacent mesentery, presence and attenuation of abdominal lymph nodes, and status of the vasculature must be assessed.<sup>4,8,14</sup> Abnormalities pertaining to these structures can be helpful in narrowing the differential diagnosis. Low-attenuated lymph nodes are often associated with tuberculosis. Mesenteric changes including fibrofatty proliferation, sinus formation, and hyperemia in the vessels subtending an abnormal segment suggest

Crohn's disease. Filling defects in the vessels suggest colonic ischemia.

#### RADIOGRAPHY

The hallmark of acute colonic inflammation on radiographs of the abdomen is the "thumbprinting" sign (Figure 31-3). This finding represents thickened haustral folds with intracolonic gas outlining the thickened haustral folds. This is a nonspecific finding and is related to edema in the colonic submucosa. This finding correlates with the "double halo" or "target" sign that is seen on computed tomography (CT).<sup>1,2,4</sup> Thumbprinting on radiographs and the double halo sign on CT may be seen in any form of acute colonic inflammation, including infection, ischemia, ulcerative colitis, Crohn's disease, and vasculitis.

Another finding that may be present on radiographs and may suggest a specific diagnosis is an ahaustral colon. On imaging, this manifests as a featureless tubular appearance of the colon. This is usually seen in the descending colon and represents chronic scarring that may be seen in ulcerative colitis and rarely in cathartic colon (Figure 31-4).

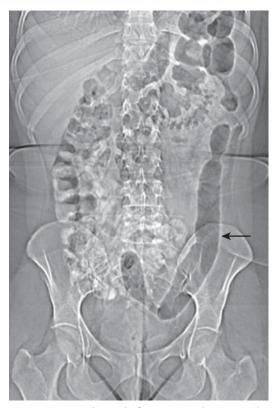
Finally, plain radiographs of the abdomen may show small filling defects in the colon (Figure 31-5). The differential diagnosis includes a polyposis syndrome such as familial adenomatous polyposis and postinflammatory pseudopolyps in the colon, which may be seen in ulcerative colitis and Crohn's disease. Other than these imaging findings, radiographs of the abdomen are of limited utility in the evaluation of colonic inflammation.

Barium studies of the colon used to be the primary noninvasive imaging technique to evaluate the colon in case of colonic inflammation. However, CT and endoscopy are now the primary imaging techniques to evaluate the patient with colonic inflammation.

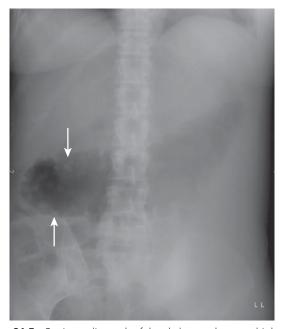
## COMPUTED TOMOGRAPHY

#### Normal Colon

CT is the primary imaging tool used to evaluate patients with abdominal pain and suspected colonic disease. There are three main findings on CT that correlate with colonic inflammation: colonic wall thickening, mural stratification ("target" sign)



**Figure 31-4** Scout radiograph for computed tomography shows ahaustral left colon (*arrow*). Differential diagnosis includes cathartic colon (melanosis coli) and chronic ulcerative colitis. The patient had chronic ulcerative colitis.



**Figure 31-5** Supine radiograph of the abdomen shows multiple small filling defects in the transverse colon (*arrows*). The differential diagnosis includes polyposis syndrome and postinflammatory polyps. There were postinflammatory polyps in this patient with ulcerative colitis.

after intravenous contrast administration, and pericolonic fat stranding.

The normal colonic wall is thin, measuring between 1 and 2 mm when the lumen is well distended. However, there is considerable variation in the thickness of the normal colonic wall depending on the degree of luminal distention. It is not unusual for the wall of the normal colon to measure up to 5 mm in the supine position and 1 mm in the prone position and vice versa. As a result, different criteria have been used to diagnose colonic wall thickening.<sup>1,2,4,20,21</sup>

Frequently, because of internal fecal contents, fluid, or colonic redundancy the true thickness is difficult to ascertain. This is most true for the sigmoid colon and is a location where bowel wall thickening is often "over-called" on CT. In these cases, carefully following the colonic wall to a region where the colon is well distended with gas will often demonstrate the true thickness of the wall (Figure 31-6). Observing the enhancement pattern and changes in the pericolonic fat are also helpful in determining whether the bowel is truly abnormal.

Typically, no specific colonic preparation is used when performing routine abdominal and pelvic CT. However, if there is a concern regarding the true thickness of the colonic wall, insufflation of the colon with room air via a small rectal catheter can be helpful in revealing the true thickness.

The normal colonic wall enhances after an adequate intravenous bolus of contrast agent has been administered. When abdominal CT is performed, a 20- to 22-gauge catheter should be inserted into an arm vein and 1.5 to 2.0 mL/kg of iodinated contrast agent (270-370 mgI/mL concentration) should be injected at a rate of at least 2.5 to 3.0 mL/s. Enhancement is usually greater on the mucosal aspect of the bowel wall. This enhancement should not be mistaken as a pathologic process. Recognizing that the wall is not thickened and that no perienteric inflammation is present will allow one to differentiate normal enhancement from a pathologic process. If an intravenous contrast agent is not administered, significant colonic pathologic processes may be overlooked (Figure 31-7).

Multiplanar images can be extremely helpful when evaluating the bowel because of the redundant nature of both the small bowel and colon.

## Specific Pathologic Causes of Colonic Inflammation

The hallmark of inflammation at CT is the "double halo" or "target" sign (Figure 31-8).<sup>1,2,4</sup> The target sign was first described as a specific sign for Crohn's disease, but it is now recognized that any non-neoplastic condition may lead to a target appearance in the small bowel or colon (Figures 31-9 to 31-12).<sup>21</sup> Rarely, infiltrating scirrhous carcinomas of the stomach or colon may display a target or double-halo appearance at CT. It may be difficult to distinguish rectosigmoid inflammation from an infiltrating neoplasm (Figure 31-13). Although infiltrating scirrhous type neoplasms frequently show marked thickening, adjacent adenopathy, and an abrupt transition, a high index of suspicion is necessary to consider this in the differential diagnosis.

As discussed earlier, the extraintestinal manifestations of colonic inflammation and the clinical history can be very useful in narrowing the differential diagnosis.

Focal colonic inflammation in the cecum may be caused by ischemia, infection, fecal impaction, Crohn's disease, and typhlitis.<sup>22,23</sup> The imaging appearance of these entities may be similar, but there are usually imaging findings that aid in distinguishing these processes.

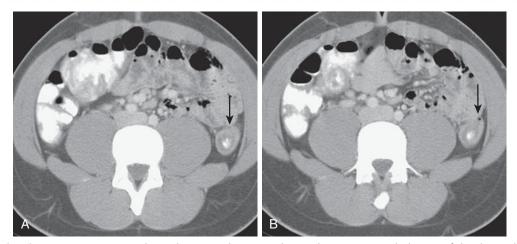


Figure 31-6 Oral and intravenous contrast-enhanced computed tomography (A) shows apparent thickening of the descending colon (arrow). Image obtained 1 cm caudal (B) shows small bubble of gas adjacent to nondependent wall (arrow). The true thickness of the colon wall is 1 to 2 mm. Note there is no pericolonic stranding to suggest a pathologic process.

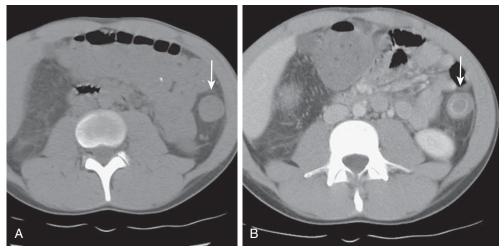
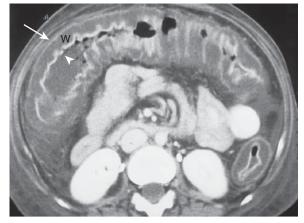
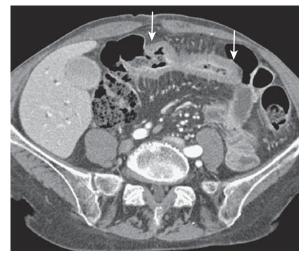


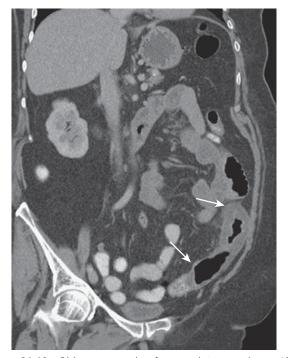
Figure 31-7 Axial unenhanced computed tomography image (A) shows no obvious abnormality in the descending colon (*arrow*). Two hours later the scan was repeated after intravenous contrast agent administration (B). Note target appearance (*arrow*) to the enhancement of the descending colon consistent with acute inflammation. Biopsy revealed Crohn's disease.



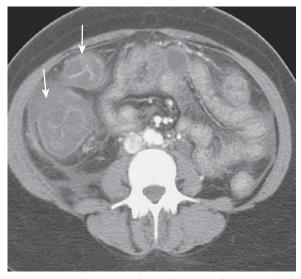
**Figure 31-8** Axial contrast-enhanced computed tomography image shows target appearance to the enhancement of the abnormal colon. Enhancement of serosa and muscularis (*arrow*), enhancement of the mucosa (*arrowhead*), and low attenuation of the submucosa (*W*) represent the target appearance.



**Figure 31-9** Axial contrast-enhanced computed tomography shows 15-cm segment of colonic wall thickening with target appearance and irregularity to the mucosa (*arrows*). There is prominence of the vasa recta adjacent to this segment and fibrofatty proliferation consistent with Crohn's colitis.



**Figure 31-10** Oblique coronal reformatted image shows 12-cm segment of thickening of the descending colon (*arrows*). The patient had a colonoscopy the previous day with random biopsies in the region. The findings are consistent with glutaraldehyde colitis.



**Figure 31-11** Axial contrast-enhanced computed tomography shows marked thickening of ascending colon and transverse colon with target appearance (*arrows*). The patient had lupus vasculitis, and this inflammation/ischemia in the colon improved after corticosteroid therapy.

Focal inflammation in the cecum with an associated liver abscess should raise the possibility of amebiasis (Figure 31-14).<sup>2,23</sup> Amebiasis is caused by the protozoa *Entamoeba his-tolytica*, which is endemic in various parts of the tropics. The disease manifests clinically as bloody diarrhea; and, although any area of the colon may be involved, it has a propensity for the right colon and particularly the cecum. The terminal ileum



**Figure 31-12** Axial contrast-enhanced computed tomography shows mild wall thickening in the descending colon (*arrow*). The finding is nonspecific. At colonoscopy, melanotic changes were present and biopsy revealed melanosis coli, indicative of chronic laxative abuse.



**Figure 31-13** Axial contrast-enhanced computed tomography (CT) shows mural stratification in the sigmoid colon extending from the rectum (*arrow*). Note lymphadenopathy (*arrowhead*). Biopsy revealed infiltrating scirrhous carcinoma. A "double halo" appearance is almost always indicative of inflammation or ischemia. Rarely, infiltrating adenocarcinomas of the rectum and stomach may show a double halo appearance on contrast-enhanced CT.

is usually spared, and with chronic disease the cecum may obtain a cone-like configuration. Amebic liver abscess is the most important complication and is present in approximately 94% of fatal cases.<sup>23</sup>

Intestinal tuberculosis is typically acquired by ingesting contaminated milk or swallowing tracheobronchial secretions in patients with pulmonary tuberculosis.<sup>2</sup> However, intestinal and peritoneal tuberculosis may be present with no pulmonary findings. Intestinal tuberculosis typically affects the ileocecal region (Figure 31-15). The imaging appearance of the tuberculosis in the colon resembles Crohn's disease.<sup>24,25</sup> There are typically focal or short segments of colonic wall thickening with associated mesenteric changes, including fistula and abscess. On barium examinations, linear ulcers that mimic Crohn's disease may be seen. A distinguishing feature often present with intestinal tuberculosis is the associated low-attenuated mesenteric lymphadenopathy (see Figure 31-15). This is likely due to the caseating necrosis seen with tuberculosis.

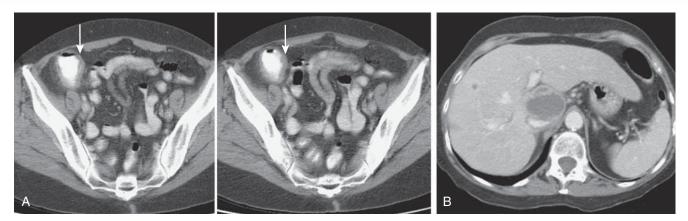


Figure 31-14 A, Axial contrast-enhanced computed tomography (CT) scans (left and right) several millimeters apart show focal thickening of the cecum (*arrows*) with irregularity to the mucosa and minimal stranding of the adjacent fat. The remainder of the bowel was normal. B, Axial contrast-enhanced CT image in the same patient shows a hepatic abscess in the caudate lobe. Amebiasis was confirmed at histologic evaluation.

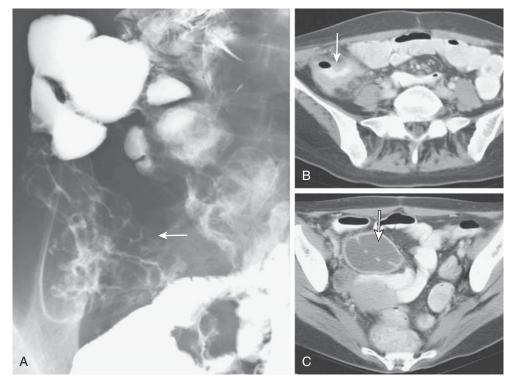


Figure 31-15 A, Spot radiograph of the cecum from a barium enema shows multiple linear ulcerations (arrow). The finding suggests Crohn's disease. B, Axial contrast-enhanced computed tomography (CT) image in same patient shows nonspecific thickening of ileocecal region (arrow). C, Axial contrast-enhanced CT several centimeters caudal shows large, low-attenuated lymph node (arrow). Tuberculosis was confirmed at biopsy and culture.

Typhlitis, also known as neutropenic colitis, primarily affects the cecal region, but any region of the small bowel or colon may be involved, including the appendix (Figure 31-16).<sup>22</sup> The condition is seen most frequently in patients being treated for acute leukemia. The colonic inflammation is usually multifactorial and often the result of a combination of fungal and bacterial infections as well as ischemia and hemorrhage. CT is the modality of choice in the evaluation of patients with suspected neutropenic colitis, and colonoscopic evaluation is often contraindicated because these patients are usually quite sick, the colon is very friable and at risk for perforation, and thrombocytopenia is often present increasing

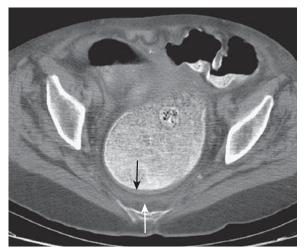
the risk for bleeding. Therapy is usually antimicrobial and supportive.

Stercoral colitis is an inflammatory colitis related to increased intraluminal pressure from impacted fecal material in the colon (Figures 31-17).<sup>5</sup> This rare condition, first reported in 1894, has been primarily described in the surgical and gastrointestinal literature. As a result of the fecal impaction, a focal pressure colitis may occur with ulceration resulting in colonic perforation. When stercoral colitis is associated with colonic perforation, a 35% mortality rate has been reported.<sup>5</sup>

Radiation-induced colitis is less frequent than radiationinduced enteritis but does occur.<sup>1,2</sup> It tends to be segmental and



**Figure 31-16** Coronal reformatted computed tomography image obtained after oral contrast administration shows only marked thickening of the cecum (*arrow*). The patient had acute myelogenous leukemia and was neutropenic. Note hepatosplenomegaly.



**Figure 31-17** Axial contrast-enhanced computed tomography image of the rectum shows fecal impaction with wall thickening (*black arrow*) and perirectal fat stranding (*white arrow*). Findings are indicative of stercoral colitis.

corresponds to the radiation port. Whenever a localized inflammatory process is noted in the small bowel or colon that does not seem to localize to any specific vascular territory, radiation injury should be suspected. In the acute stages, nonspecific bowel wall thickening may be present with a target appearance and perienteric fat stranding. In the chronic stages, fibrosis and stricture with obstruction may occur.

Glutaraldehyde colitis is a direct toxic response to the colon because of inadequate removal of the disinfectant glutaralde-



**Figure 31-18** Oblique coronal reformatted computed tomography image shows tethering and probable fistulization (*arrow*) of the right colon and small bowel in this patient with known Crohn's disease.

hyde from the colonoscope before an endoscopic procedure (see Figure 31-10).<sup>16</sup> The condition typically occurs 24 to 48 hours after colonoscopy. Patients will present with severe crampy abdominal pain, bloody diarrhea, and occasionally mild leukocytosis.<sup>16</sup> At CT the colon usually shows segmental, circumferential, mural stratification with moderate to marked wall thickening. Often the location is proximal to the rectum and is at the site of a mucosal biopsy. The proximal location is thought to be related to the disinfectant being trapped in the chamber of the biopsy forceps. As the biopsy device is used, the glutaraldehyde acts as a toxin to the colonic mucosa, causing intramural hemorrhage. The condition is self-limiting, and conservative management leads to improvement.

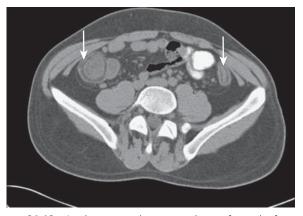
Although Crohn's disease may be focal, it is usually segmental, involving anywhere between 10 and 30 cm of intestine.<sup>8,26-28</sup> Crohn's disease is often associated with skip lesions. Extraintestinal manifestations include sinus formation, fistula, abscess, the "comb" sign, and fibrofatty proliferation. These imaging features help to distinguish Crohn's disease from other entities (Figure 31-18).<sup>26,27</sup>

Irregularity of the mucosa with ulceration may be seen on CT and suggests the diagnosis of Crohn's disease.<sup>28</sup> This may enable differentiation of Crohn's disease and other entities such as amebiasis and tuberculosis from other conditions such as vasculitis and low-flow ischemia, which typically show a submucosal pattern of bowel thickening (compare Figures 31-9 and 31-14 with 31-11).<sup>28,29</sup> Although the mucosal changes may be assessed at CT, they are usually better evaluated at endoscopy.

In cases of chronic colitis, whether it be Crohn's or ulcerative colitis, submucosal fat deposition may occur (Figure 31-19).<sup>8</sup> Recognition of the fat attenuation within the submucosa will allow differentiation from edema. However, a recent study demonstrated that submucosal fat deposition may be a normal

variant and not necessarily associated with chronic bowel inflammation.<sup>30</sup> In a study of 100 patients undergoing noncontrast CT to evaluate for kidney stones, 21 patients were shown to have submucosal adipose tissue in the bowel and in 4% it was in the terminal ileum. These patients had no history of chronic bowel inflammation. Therefore, if this finding is seen at CT, correlation with the clinical history is essential.

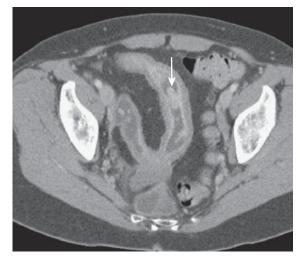
As discussed earlier, ulcerative colitis is an autoimmune condition associated with mucosal ulceration, mural edema, and occasionally extraintestinal manifestations such as bony ankylosis and primary sclerosing cholangitis (Figure 31-20).<sup>8</sup> Typically, the bowel wall thickening in ulcerative colitis shows mural stratification and the degree of thickening is mild; however,



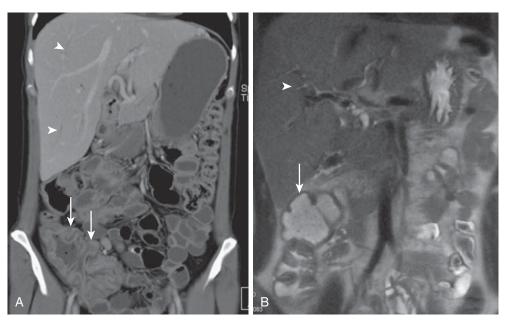
**Figure 31-19** Axial computed tomography performed after oral administration of a contrast agent shows only target appearance to the right and left colon (*arrows*). Region of interest cursor placed in the submucosa measured –50 Hounsfield units. Findings are consistent with chronic inflammation in this patient with a 2-year history of ulcerative colitis.

occasionally bowel wall thickening can exceed 1 cm in patients with severe ulcerative colitis.<sup>3</sup> Ulcerative colitis begins in the rectum; and as the inflammation progresses, the disease continues proximally without skip areas.<sup>8</sup>

In both Crohn's disease and ulcerative colitis, postinflammatory pseudopolyps may be seen on CT (Figures 31-21 and 31-22).<sup>8,31</sup> These lesions represent an abnormal proliferation of the inflamed colonic mucosa. They can get quite large and morphologically may be difficult to distinguish and make detection of carcinoma in the colon challenging. This is a



**Figure 31-21** Axial contrast-enhanced computed tomography of the ileum shows segmental wall thickening, a target appearance, and an enhancing intraluminal filling defect (*arrow*) consistent with a postin-flammatory pseudopolyp in this patient with long-standing Crohn's disease.



**Figure 31-20** A, Coronal reformatted computed tomography (CT) image in this patient with chronic ulcerative colitis shows mural stratification in the right colon (*arrows*). Note mild biliary dilatation (*arrowheads*) in this patient with known sclerosing cholangitis. **B**, Coronal magnetic resonance image in same patient shows mural stratification in the right colon (*arrow*). Note mild biliary dilatation (*arrowheads*). Magnetic resonance imaging often can show similar findings to those of CT without the need for ionizing radiation.

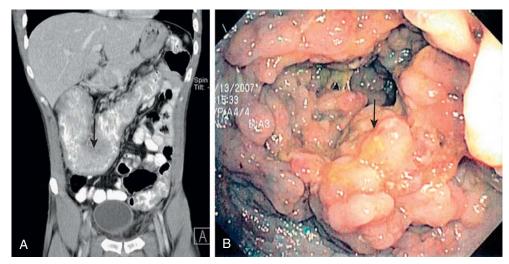


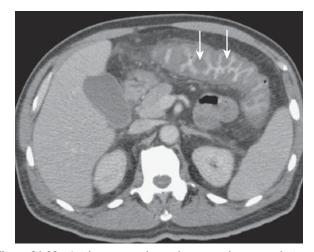
Figure 31-22 A, Coronal reformatted computed tomography image obtained after oral and intravenous administration of contrast agents in a patient with chronic ulcerative colitis shows irregular frondlike filling defects (*arrow*). B, Endoscopic image from same patient shows multiple irregular filling defects (*arrow*). Biopsy revealed postinflammatory pseudopolyps.

major problem because in both chronic ulcerative colitis and Crohn's colitis the risk for colon cancer is increased over the general population.

When colonic inflammation affects the entire colon a "pancolitis" is present. The differential diagnosis of pancolitis is infection and ulcerative colitis.<sup>4</sup> Rarely, vasculitis may affect the entire colon, but the small bowel usually also is associated.<sup>29</sup>

Pseudomembranous colitis, also known as antibiotic-related colitis, is due to Clostridium difficile overgrowth and is a major cause of hospital-acquired morbidity in the United States today. C. difficile is a gram-positive anaerobic bacillus that can cause a spectrum of enteric disease ranging from mild diarrhea to fulminant life-threatening colitis.<sup>3</sup> Almost all cases of pseudomembranous colitis are associated with recent antibiotic therapy.<sup>3</sup> Infrequently, a history of antibiotic use may not be elicited in documented cases of C. difficile colitis. Almost all antibiotics and some antineoplastic agents have been implicated as a factor leading to C. difficile colitis. By altering the normal colonic flora, antibiotic use allows C. difficile to proliferate, resulting in the clinical disease. Earlier recognition and treatment of C. difficile-related colitis with appropriate antibiotics decreases the incidence of fulminant colitis that may develop in these patients. Previously the most common cause of toxic megacolon was ulcerative colitis; however, pseudomembranous colitis is currently the most common cause of this life-threatening condition.<sup>32,33</sup>

Pseudomembranous colitis is clinically suggested in the setting of a recent history of antibiotic use, concurrent diarrhea, and positive stool assay for *C. difficile*. On CT, the colon may look normal or show marked wall thickening.<sup>3,34,35</sup> The "accordion" sign is defined as alternating edematous haustral folds separated by transverse mucosal ridges filled with oral contrast material, simulating the appearance of an accordion (Figure 31-23).<sup>34,35</sup> This CT finding was originally reported to be a specific sign of severe *C. difficile*–related colitis. The degree of colonic wall thickening caused by the pseudomembranes and edematous tissues has been suggested as the reason for the sign's specificity.<sup>34</sup> However, other conditions may cause the appear-



**Figure 31-23** Axial contrast-enhanced computed tomography image shows marked thickening of the wall of the colon (*arrows*) with barium trapped between the folds. The finding is consistent with the "accordion" sign in this patient with pseudomembranous colitis.

ance of an accordion at CT, including lupus, ischemia, portal hypertension–related edema, and infectious causes, including cytomegaloviral colitis in immunocompromised patients.<sup>3,36,37</sup>

In patients with cirrhosis the finding of bowel edema has been reported at both barium enema studies and on CT.<sup>37,38</sup> Intestinal wall thickening is common on contrast-enhanced images and is seen in up to 64% of patients. The bowel edema may be mild or marked when secondary to portal hypertension (Figure 31-24). When edema from portal hypertension is present in the colon, it can look like any other form of intestinal inflammation and may mimic infection or even ischemia. The edema typically occurs in the ascending colon. Observation that the patient has cirrhosis and correlation with clinical findings will usually suggest the correct diagnosis.

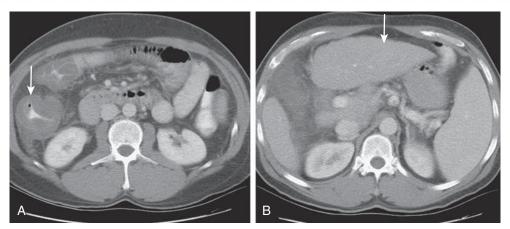


Figure 31-24 A, Axial contrast-enhanced computed tomography (CT) image shows marked thickening of the right colon (arrow). The patient had no intestinal symptoms. B, Axial contrast-enhanced CT image in the same patient shows cirrhosis (arrow). The findings in the colon are consistent with edema related to portal hypertension.

As demonstrated earlier, the differential diagnosis of colonic inflammation is broad. CT is the primary imaging modality used to evaluate the patient with colonic inflammation. Imaging is often supplemented with endoscopic evaluation. In addition to all of the previously listed causes of colonic inflammation, colonic ischemia should always be considered in the differential diagnosis of a thickened colon.<sup>39</sup> Careful inspection of the mesenteric vasculature should always be performed; and if suspected, correlation with serum lactic acid level should be recommended.

## MAGNETIC RESONANCE IMAGING

Due to the increased concern for radiation-induced carcinogenesis, there is more awareness of the potential effects of the increased number of CT examinations and mutiphasic examinations being performed.<sup>40,41</sup> MRI has gained a role in the evaluation of colonic inflammation.<sup>41,42</sup> Although CT remains the primary imaging modality used to evaluate colonic inflammation, MRI allows detection of the same findings as CT. In particular, MRI is useful in observing patients with Crohn's disease (see Figure 31-20). These patients are young and typically receive multiple CT examinations over their lifetime, and MRI is playing a greater role in their care.

#### **Classic Signs**

- Thumbprinting: Indicates colonic edema on plain films.
- Ahaustral colon: Indicates chronic colonic inflammation on plain radiograph or CT.
- Target sign: Indicates colonic edema; very rarely can be seen in scirrhous carcinomas of the colon.
- "Comb" sign: Prominent vasa recta subtending an inflamed segment of bowel seen commonly in Crohn's disease.
- Fibrofatty proliferation: Proliferation of adipose tissue around a segment of chronic Crohn's disease.
- Low-attenuated caseating adenopathy: Seen commonly in tuberculosis.

## **Differential Diagnosis**

The following conditions can cause focal, segmental, or diffuse colonic disease:

- Crohn's disease
- Ulcerative colitis
- Diverticulitis
- Infectious colitis
- Ischemic colitis
- Epiploic appendagitis
- Vasculitis
- Colon cancer

Imaging, especially with CT and endoscopy, can help narrow the differential diagnosis of the following conditions:

- Crohn's disease
- Ulcerative colitis
- Diverticulitis
- · Infectious colitis
- Ischemic colitis
- Epiploic appendagitis
- Vasculitis
- Colon cancer

## Treatment

Most cases of colonic inflammation are treated conservatively with antiinflammatory medications, antibiotics, and/or supportive care depending on the cause of the inflammation.

If medical management fails, the bowel perforates, or toxic megacolon develops, surgical intervention is warranted in cases of colonic inflammation.

## What the Referring Physician Needs to Know

- Although radiographs of the abdomen may suggest the diagnosis, plain radiographs have limited use in the evaluation of colonic inflammation.
- Barium studies (barium enema) used to be the primary noninvasive imaging technique to evaluate colonic inflammation.

### 31 Inflammatory and Infectious Colonic Lesions 283

• Many different inflammatory and infectious conditions

• The location in the colon, length of involvement, and

• Diverticular disease and colon cancer may have a similar

enhancement pattern are helpful in narrowing the

imaging appearance at multidetector CT.

endoscopic correlation is indicated.

When a confident diagnosis cannot be made,

#### What the Referring Physician Needs to Know-cont'd

- CT and endoscopy are now the primary imaging techniques to evaluate the patient with colonic inflammation.
- CT is the primary noninvasive imaging modality to evaluate colon inflammation.
- The differential diagnosis of colonic inflammation is broad, and by using a patterned approach on CT the differential diagnosis can usually be narrowed.
- MRI, because of its similar sensitivity to CT and lack of ionizing radiation, plays an increasingly important role in the evaluation of patients with colonic inflammation.

#### SUGGESTED READINGS

- Balthazar EJ: CT of the gastrointestinal tract: principles and interpretation. AJR Am J Roentgenol 156:23–32, 1991.
- Gore RM, Balthazar EJ, Ghahremani GG, et al: CT features of ulcerative colitis and Crohn's disease. *AJR Am J Roentgenol* 167:3–15, 1996.

### REFERENCES

- Horton KM, Corl FM, Fishman EK: CT evaluation of the colon: Inflammatory disease. *Radiographics* 20:399–418, 2000.
- Thoeni RF, Cello JP: CT imaging of colitis. Radiology 240:623–638, 2006.
- Macari M, Balthazar EJ, Megibow AJ: The accordion sign on CT: a nonspecific finding in patients with colonic edema. *Radiology* 211:734– 746, 1999.
- Macari M, Balthazar EJ: Computed tomography of bowel wall thickening: significance and pitfalls of interpretation [Review]. AJR Am J Roentgenol 176:1105–1116, 2001.
- Heffernan C, Pachter HL, Megibow AJ, et al: Stercoral colitis leading to fatal peritonitis: CT findings [Original report]. *AJR Am J Roentgenol* 184:189–193, 2005.
- Singh AK, Gervais DA, Hahn PF, et al: CT appearance of acute epiploic appendagitis. AJR Am J Roentgenol 183:1303–1307, 2004.
- Balthazar EJ: CT of the gastrointestinal tract: principles and interpretation. AJR Am J Roentgenol 156:23–32, 1991.
- Gore RM, Balthazar EJ, Ghahremani GG, et al: CT features of ulcerative colitis and Crohn's disease. AJR Am J Roentgenol 167:3–15, 1996.
- 9. Podolsky DK: Inflammatory bowel disease. N Engl J Med 347:417–429, 2002.
- Hanauer SB: Inflammatory bowel disease. N Engl J Med 334:841–848, 1996.
- Bernstein CN: The epidemiology of inflammatory bowel disease in Canada: a populationbased study. Am J Gastroenterol 101:1559–1568, 2006.
- Ferzoco LB, Raptopoulos V, Silen W: Acute diverticulitis. N Engl J Med 338:1521–1526, 1998.
- Radin R: HIV infection: analysis in 259 consecutive patients with abnormal abdominal CT findings. *Radiology* 197:712–717, 1995.
- Bini EJ, Cohen J: Diagnostic yield and costeffectiveness of endoscopy in chronic human immunodeficiency virus-related diarrhea. *Gastrointest Endosc* 48:354–361, 1998.
- Lew EA, Poles MA, Dietrich DT: Diarrheal diseases associated with HIV infection. *Gastroenterol Clin North Am* 26:259–290, 1997.

#### Horton KM, Corl FM, Fishman EK: CT evaluation of the colon: inflammatory disease. *Radiographics* 20:399–418, 2000.

**Key Points** 

can affect the colon.

differential diagnosis.

- Macari M, Balthazar EJ: Computed tomography of bowel wall thickening: significance and pitfalls of
- interpretation [Review]. AJR Am J Roentgenol 176:1105–1116, 2001.
- Thoeni RF, Cello JP: CT imaging of colitis. *Radiology* 240:623–638, 2006.
- Birnbaum BA, Gordon RB, Jacobs JE: Glutaraldehyde colitis: radiologic features. *Radiology* 195:131–134, 1995.
- Padidar AM, Jeffrey RB, Mindelzun RE, et al: Differentiating sigmoid diverticulitis from carcinoma on CT scans: mesenteric inflammation suggests diverticulitis. *AJR Am J Roentgenol* 163: 81–83, 1994.
- 18. Deleted in review.
- Chintapalli KN, Esola CC, Chopra S, et al: Pericolic mesenteric lymph nodes: an aid to distinguishing diverticulitis from cancer in the colon. *AJR Am J Roentgenol* 19:1253–1255, 1997.
- Karahan OI, Dodd GD, III, Chintapalli KN, et al: Gastrointestinal wall thickening in patients with cirrhosis: frequency and patterns at contrast-enhanced CT. *Radiology* 215:103–107, 2000.
- Frager DH, Goldman M, Beneventano TC: Computed tomography in Crohn disease. *J Comput Assist Tomogr* 7:819–824, 1983.
- 22. Kirkpatrick ID, Greenberg HM: Gastrointestinal complications in the neutropenic patient: characterization and differentiation with abdominal CT. *Radiology* 226:668–674, 2003.
- Elizondo G, Weissleder R, Stark DD, et al: Amebic liver abscess: diagnosis and treatment with MR imaging. *Radiology* 165:795–800, 1987.
- Baoudiaf M, Zidi SH, Soyer P, et al: Tuberculous colitis mimicking Crohn's disease: utility of computed tomography in the differentiation. *Eur Radiol* 8:1221–1223, 1998.
- Makanjuola D: Is it Crohn's disease or intestinal tuberculosis? CT analysis. *Eur J Radiol* 1:55–61, 1998.
- 26. Madureira AJ: The comb sign. *Radiology* 230: 783–784, 2004.
- 27. Herlinger H, Furth EE, Rubesin SE: Fibrofatty proliferation of the mesentery in Crohn disease. *Abdom Imaging* 23:446–448, 1998.
- Macari M, Megibow AJ, Balthazar EJ: A pattern approach to the abnormal small bowel: observations at MDCT and CT enterography. *AJR Am J Roentgenol* 188:1344–1355, 2007.
- 29. Lalani TA, Kanne JP, Hatfield GA, et al: Imaging findings in systemic lupus erythematosus. *Radiographics* 24:1069–1086, 2004.

- Harisinghani MG, Wittenberg J, Lee W, et al: Bowel wall fat halo sign in patients without intestinal disease. *AJR Am J Roentgenol* 181:781– 784, 2003.
- Zegel H, Laufer I: Filliform polyposis. *Radiology* 127:615–619, 1978.
- Bartlett JG, Perl TM: The new Clostridium difficile: what does it mean? N Engl J Med 355:2503– 2504, 2005.
- McDonald LC, Killgore GE, Thompson A, et al: An epidemic, toxin gene-variant strain of *Clostridium difficile*. N Engl J Med 355:2433–2441, 2005.
- O'Sullivan SG: The accordion sign. Radiology 206:177–178, 1998.
- Fishman EK, Kavuru M, Jones B, et al: Pseudomembranous colitis: CT evaluation of 26 cases. *Radiology* 180:57–60, 1991.
- Wall SD, Jones B: Gastrointestinal tract in the immunocompromised host: opportunistic infections and other complications. *Radiology* 18: 327–335, 1992.
- Karahan OI, Dodd GD, Chintapalli KN, et al: Gastrointestinal wall thickening in patients with cirrhosis: frequency and patterns at contrast enhanced CT. *Radiology* 215:103–107, 2000.
- Balthazar EJ, Gade MF: Gastrointestinal edema in cirrhotics. *Gastrointest Radiol* 1:215–223, 1976.
- Balthazar EJ, Yen BC, Gordon RB: Ischemic colitis: CT evaluation of 54 cases. *Radiology* 211: 381–388, 1999.
- Jaffe TA, Gaca AM, Delaney S, et al: Radiation doses from small-bowel follow-through and abdominopelvic MDCT in Crohn's disease. AJR Am J Roentgenol 189:1015–1022, 2007.
- Brenner DJ, Hall EJ: Computed tomography: an increasing source of radiation exposure. N Engl J Med 357:2277–2284, 2007.
- 42. Gourtsoyiannis N, Papanikolaou N, Grammatikakis J, et al: Assessment of Crohn's disease activity in the small bowel with MR and conventional enteroclysis: preliminary results. *Eur Radiol* 14:1017–1024, 2004.

# **Colonic Vascular Lesions**

NAVEEN M. KULKARNI | OZDEN NARIN | NICOLE D. HORST

## **Etiology**

Vascular lesions of the colon are an important medical problem and have now been recognized as a significant cause of gastrointestinal bleeding.<sup>1</sup> They can be solitary or multifocal, benign or malignant, or associated with a syndrome or systemic disorder. There are three main groups: vascular malformations, neoplastic lesions, and non-neoplastic lesions (Figure 32-1). Vascular malformations can be broadly classified into arterial, venous, and arteriovenous types. Neoplastic lesions include hemangiomas, hemangioendotheliomas, and angiosarcomas. Non-neoplastic lesions can be further divided into inflammatory lesions (e.g., vasculitis) and obstructive lesions (e.g., ischemic colitis). Few systemic conditions and syndromes manifest with vascular lesions, such as colonic varices in portal hypertension or vasculitis in systemic lupus erythematosus, polyarteritis nodosa, Ehlers-Danlos syndrome, Osler-Weber-Rendu disease, Marfan syndrome, and systemic sclerosis. This chapter focuses on vascular lesions that cause gastrointestinal bleeding and that are representative of the spectrum of vascular lesions of the gastrointestinal tract.

## **Prevalence and Epidemiology**

The prevalence is related to the cause and age of the patient. The prevalence of angiodysplasia is 0.8% in healthy patients older than 50 years who are undergoing screening colonoscopy.<sup>2</sup> These lesions characteristically appear in the right colon and cecum in older patients, although they may be found anywhere in the lower gastrointestinal tract, may be multiple, and can occur in younger patients.<sup>1,3</sup> Dieulafoy's lesion involving the colon is rare and more frequently affects the stomach. It is twice as common in men as in women and manifests at a mean age of 52 years.<sup>4</sup> Hemangiomas are benign vascular tumors that can be found throughout the gastrointestinal tract, often in the rectum or colon. The incidence of gastrointestinal hemangioma is reported as 0.3%, and these tumors account for 5% to 10% of all benign intestinal tumors.<sup>5</sup> In some populations these lesions are multiple and associated with skin lesions, such as the blue rubber bleb nevus syndrome with purple-blue cutaneous hemangiomas or the Klippel-Trenaunay syndrome with portwine-colored cutaneous hemangiomas, hemihypertrophy, and varicose veins.<sup>6-8</sup> Rare vascular malignant neoplasms of the gastrointestinal tract include angiosarcomas, hemangiopericytomas, and hemangioendotheliomas.<sup>6,9,10</sup> The incidence of these lesions is highly variable. Telangiectases are similar to angiodysplasias but occur in all the layers of the bowel wall, are usually congenital, and often occur in other organ systems.<sup>1</sup> Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu disease) is an autosomal dominant disorder with telangiectases involving the lips; mucous membranes, especially in the mouth and nose; gastrointestinal tract, especially the stomach and small bowel; liver; lung; retina; and central nervous system.<sup>11,1</sup>

## **Clinical Presentation**

Although many vascular lesions are asymptomatic, those that manifest with bleeding require expeditious localization and control. These lesions may be responsible for severe, acute, and overt bleeding or alternatively can cause chronic or occult bleeding.<sup>1,13</sup> Some of these lesions are difficult to localize on cross-sectional imaging and colonoscopy and necessitate use of more invasive modalities such as angiography. Although the clinical presentation, age of the patient, and other epidemiologic factors may indicate a particular type of colonic vascular lesion, endoscopy with biopsy and visceral angiography are critical in establishing the correct diagnosis.

## **Pathophysiology and Pathology**

Pathologic processes of vascular lesions involving the colon depends on the underlying cause, which can be vascular, neoplastic, or non-neoplastic in origin.

## ANGIODYSPLASIA

These lesions are acquired vascular ectasias, possibly caused by chronic, low-grade colonic obstruction. Histologic identification is difficult unless special techniques are used.<sup>14,15</sup> Microscopically, angiodysplasias are composed of clusters of dilated, tortuous, thin-walled veins, venules, and capillaries localized in the colonic mucosa and submucosa.

## DIEULAFOY'S LESION

Dieulafoy's lesion belongs to an arterial type of vascular abnormality with abnormally large (caliber-persistent) submucosal end-arteries; in some instances, there is a small, overlying mucosal defect.<sup>16-18</sup>

## CONGENITAL ARTERIOVENOUS MALFORMATIONS

Histologically, arteriovenous malformations are persistent congenital communication between arteries and veins located in the submucosa. Characteristically, arterialization of the veins is seen. The veins are tortuous and dilated, having thick walls with smooth muscle hypertrophy and intimal thickening.<sup>19,20</sup>

## **HEMANGIOMA**

Hemangioma is the second most common vascular lesion of colon and may be solitary or may be multiple in patients with multisystem involvement.<sup>6,9,21</sup> Histologically, hemangiomas can be divided into cavernous, capillary, and mixed. Cavernous hemangiomas are composed of large, dilated spaces filled with blood and are covered with a thin wall of abnormal vessels.

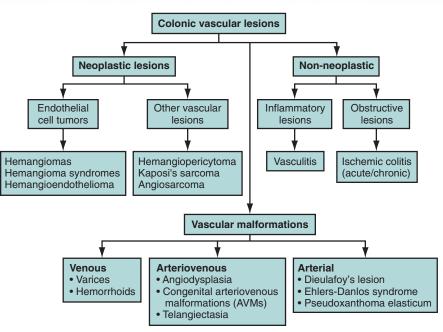


Figure 32-1 Algorithm for colonic vascular lesions.

#### BOX 32-1 CLINICAL FACTORS IN DIFFERENTIATING COLONIC VASCULAR LESIONS

- Age
  - Elderly
    - Angiodysplasia
    - Dieulafoy's lesion
      Ischemic colitis
  - Ischemic d
     Children
    - Hemangiomas
    - Hereditary hemorrhagic telangiectasia
- Location of Involvement
  - Angiodysplasia: Cecum and proximal ascending colon
- Hemangiomas: Predilection for rectosigmoid region
- Multifocal Involvement
  - Hemangioma

Capillary hemangiomas consist of conglomerates of small, thin-walled vessels.<sup>6,9</sup>

## Imaging

Because the clinical presentation and manifestations of patients with colonic vascular lesions in the form of lower gastrointestinal bleeding overlap with those of other colonic diseases, a precise identification of cause is possible only with a high degree of suspicion and by using different imaging modalities. A precise knowledge of clinical background with imaging findings can help narrow the differential diagnosis. Although there is no specific algorithm, the information presented in Box 32-1 and Table 32-1 should be kept in mind when there is a high index of suspicion of a vascular lesion.

## ANGIODYSPLASIA

Angiodysplasia or vascular ectasia is the most common vascular malformation of the gastrointestinal tract in the elderly and one

of the major causes of lower gastrointestinal bleeding. Accurate diagnosis may require a combination of diagnostic techniques, such as angiography, nuclear scanning, and colonoscopy.<sup>15,22-24</sup>

## **Barium Studies**

Because the lesions of angiodysplasia are small in diameter and do not distort the mucosa, double-contrast barium enema studies are of no value in the diagnosis of angiodysplasia. This technique is useful, however, to rule out other causes of gastro-intestinal bleeding, such as neoplastic lesions.<sup>22</sup>

## Computed Tomography

The role of CT is evolving, and at present there is limited literature on its role in evaluating angiodysplasia. There are some reports of being able to detect these lesions by multidetector CT (MDCT) scans and CT angiography (CTA) techniques. In a study of 30 patients with clinical suspicion of angiodysplasia, CTA had a sensitivity of 78% and a specificity of 100% when compared with colonoscopy, which had a sensitivity of 68% to 80% and a specificity of 90%. Accumulation of ectatic, dilated vessels in the colon wall, an early filling vein, and an enlarged ileocolic artery (Figure 32-2) can be observed in CTA images.<sup>25</sup>

## Magnetic Resonance Imaging

The role of magnetic resonance imaging (MRI) is still investigational and evolving.

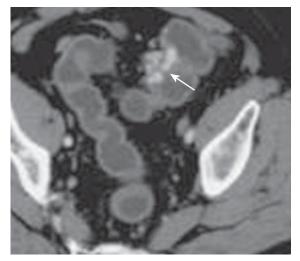
## Nuclear Medicine

Nuclear scintigraphy is a sensitive method of detecting gastrointestinal bleeding at a rate of 0.1 mL/min. It is more sensitive than angiography but less specific than a positive endoscopic or angiographic examination (Figure 32-3). A major disadvantage of nuclear imaging is that it localizes bleeding only to an area of the abdomen. Nuclear scintigraphy has proved more useful as an adjunct to angiography by localizing and confirming the presence of bleeding, minimizing the number of angiograms that do not yield meaningful diagnostic information, and

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TABLE 32-1	General Information and Diagnostic Modalities				
	Angiody	splasia	Hemangioma	Dieulafoy's Lesion	
Age	Older th	an 50 years	Younger age group	No specific age distribution	
Diagno moda		py, catheter angiography, angiography	CT and endoscopy	Endoscopy and angiography	
Radiog	raphs N/A		Phleboliths can be seen on radiographs.	N/A	
CT/CT/ Findi	ngs of cold	dilated vessels in the wall on, an early filling vein, n enlarged ileocolic artery	Enhancing lesion with phleboliths	N/A	
MRI fin	dings N/A		Thickened colon wall with high signal intensity on T2-weighted imaging	N/A	
Colono		are flat, 2-5 mm in ter, and red.	Elevated blue nodular lesions or dilated vessels	Caliber-persistent artery protruding from the mucosa	

CT, Computed tomography; CTA, CT angiography; MRI, magnetic resonance imaging; N/A, not applicable.



**Figure 32-2** Axial, contrast-enhanced CT at the level of the pelvis shows a tangle of vessels in the sigmoid colon (*arrow*) caused by angiodysplasia. (*Reprinted from Miller FH: Case 185. In Miller FH, Rubesin SE, editors:* The teaching files: gastrointestinal, *Philadelphia, 2009, Saunders; Courtesy Richard M. Gore, MD, Evanston, IL.*)

allowing rapid selection of the artery to be injected by angiography.  $^{15,26,27}$ 

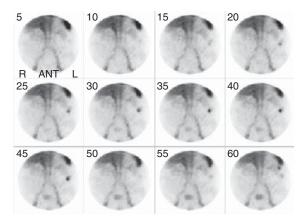
#### Colonoscopy

Three main ideas underlying colonoscopy are as follows:

- Determination of the location of lesion and type of bleeding
- Identification of patients with ongoing hemorrhage or at high risk for rebleeding
- Potential for endoscopic intervention

Angiodysplastic lesions are often described as discrete and small, with scalloped or frondlike edges and a visible draining vein (Figure 32-4). They can be flat or slightly raised and can be hidden within mucosal folds.<sup>22,24</sup> The endoscopist's ability to diagnose the specific nature of a vascular lesion is limited by the similar appearance of multiple lesions. The following lesions should be considered in the differential diagnosis:

- Hereditary hemorrhagic telangiectasia
- Angiomas



**Figure 32-3** Serial images from technetium-99m red blood cell scintigram show radionuclide tracer uptake in the descending colon caused by bleeding angiodysplasia. *ANT*, Anterior; *L*, left; *R*, right.



Figure 32-4 Angiodysplasia identified on cecal wall during colonoscopy.

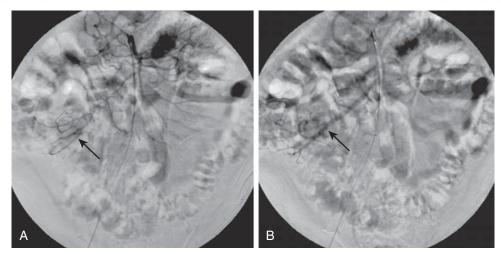


Figure 32-5 A, Early angiogram shows focal arterial enlargement (arrow). B, On a subsequent angiogram, an accompanying enlarged draining vein is seen (arrow) consistent with cecal angiodysplasia.

- Focal hypervascularity of radiation colitis
- Ulcerative colitis
- Crohn's disease
- Ischemic colitis

Because the appearance of vascular lesions is influenced by a patient's blood pressure, blood volume, and state of hydration, such lesions may not be evident in those with hypovolemia or shock; thus, accurate evaluation may not be possible until such deficits are corrected.<sup>27</sup>

## Angiography

Angiography is used to determine the site and nature of a lesion during active bleeding. Three reliable angiographic signs of angiodysplasia are a densely opacified, slowly emptying, dilated, tortuous vein; a vascular tuft; and an early-filling vein. The slowly emptying vein persists late into the venous phase, after the other mesenteric veins have emptied (Figure 32-5). When the lesion is bleeding, intraluminal extravasation of contrast material usually appears during the arterial phase of angiography and persists throughout the study.<sup>20,27</sup> Extravasation identifies the site of active bleeding and in the absence of other signs of angiodysplasia, suggests another cause for the bleeding.

### HEMANGIOMAS

Hemangiomas are the second most common vascular lesion of the colon and may occur as solitary or multiple lesions limited to the colon or as part of diffuse gastrointestinal or multisystem angiomatoses.<sup>5,8</sup> Hemangiomas may be classified as cavernous, capillary, or mixed types. The capillary hemangiomas are usually incidental findings at autopsy. Diffuse cavernous hemangioma of the rectosigmoid colon is the most common type (75% to 80%).<sup>8,28-30</sup> Most are small, ranging from a few millimeters to 2 cm, but larger lesions occur, especially in the rectum. Patients with blue rubber bleb nevus and Klippel-Trenaunay syndromes can have lesions anywhere in the gastrointestinal tract.<sup>6,9</sup> The diagnosis is best established by CT and endoscopy, including enteroscopy, because radiographic studies, including angiography, are frequently normal.

## Radiography

The diagnosis of cavernous hemangioma of the rectum often can be suggested on plain films of the abdomen by the presence of phleboliths and displacement or distortion of the rectal air column.<sup>3,31</sup> However, absence of phleboliths does not rule out the diagnosis.

#### **Barium Studies**

Like plain abdominal radiographs, barium studies are too nonspecific and insensitive in evaluating hemangiomas. Barium contrast examinations show only poorly specific signs such as large polypoid or obstructing lesion that may change configuration after compression or distention. The affected bowel lumen may show narrowing and rigidity, scalloping of the wall, and widening of the presacral space when the rectum is involved.<sup>3,8,28,31</sup> Furthermore, dense barium interferes with subsequent MDCT examinations, colonoscopy, and transcatheter interventions.

## Computed Tomography

On CT, hemangiomas manifest as an enhancing lesion or clusters of intraluminal polypoid lesions that may diffusely infiltrate the submucosa with extraserosal extension into the mesentery and adjacent organs.<sup>8,32</sup> Presence of phleboliths can confirm the diagnosis (Figure 32-6). CT helps in localization, assessment of the extent of the lesion, and pericolonic involvement to guide surgical management. When the extent of the lesion is limited, with no phleboliths, thickening of colon or rectosigmoid wall might not be sufficiently specific for CT to be diagnostic.<sup>6,9</sup> Moreover, CT may not be preferred when repeated examinations might be necessary for follow-up in young patients because it involves radiation exposure and requires intravenous iodinated contrast material.

## Magnetic Resonance Imaging

The colon wall will be markedly thickened with high signal intensity on T2-weighted images. This feature appears to be related to slow flow in vascular malformation. Sometimes serpiginous structures thought to represent small vessels supplying the diffuse cavernous hemangioma may be seen.<sup>7,33,34</sup> MRI allows correct evaluation of the extent of bowel wall involvement and visualization of extracolonic extension.<sup>28,35</sup> Depiction



**Figure 32-6** Axial contrast-enhanced computed tomography scan shows cecum wall thickening with avid enhancement and calcified phleboliths (arrows). (Reprinted from Rubesin SE, Furth EE: Other tumors of the colon. In Gore RM, Levine MS, editors: Textbook of gastrointestinal radiology, ed 3, Philadelphia, 2007, Saunders, p 1171.)

of phleboliths by MRI again can help in confirming the diagnosis.

#### Endoscopy

Endoscopically, one sees elevated plum-red nodules or vascular congestion; ulcers and proctitis also may be present. Hemangiomas also may manifest as sessile polypoid lesions, appearing bluish. The entire colon needs screening to look for multiple lesions, especially in patients with systemic disorders in which pancolonic involvement is common. Endoscopic biopsy should be avoided because of bleeding risk.<sup>6,36-39</sup>

## Angiography

Angiography can demonstrate these lesions but seldom is necessary to establish the diagnosis.

### Dieulafoy's Lesion

This vascular lesion is an unusual cause of massive gastrointestinal hemorrhage, usually from the stomach but sometimes from the small or large bowel. The vascular abnormality is the presence of persistently large-caliber arteries in the submucosa and, more rarely, the mucosa, typically with a small, overlying mucosal defect.<sup>4</sup> It may be difficult to find a Dieulafoy lesion in a patient with lower gastrointestinal bleeding because the overlying mucosal defect may be small and hidden between the mucosal folds and the caliber-persistent vessel may constrict and retract after the bleeding episode.<sup>18,40</sup>

## Nuclear Scintigraphy

The approach for Dieulafoy's lesion is similar to that mentioned in the discussion on angiodysplasia.

## Endoscopy

Endoscopy reveals a reddish-brown protruding spot with small erosion and no ulcer.<sup>26</sup> Because the lesion is so small, it can be easily missed, especially when the colon is full of blood. It can be noticed more easily when pulsating or oozing blood or a longitudinal clot with a small area of adhesion to the colon wall can be seen.<sup>16,17,41-43</sup>

#### Angiography

In difficult cases, angiography may be useful when endoscopy fails to identify the lesion, especially in nongastric sites. On angiography, abnormal blush with extravasation of contrast agent is appreciated.<sup>16,17,41-44</sup>

## CONGENITAL ARTERIOVENOUS MALFORMATIONS

Arteriovenous malformations (AVMs) are embryonic growth defects and are considered to be developmental anomalies. Although AVMs are found mainly in the extremities, they may occur anywhere in the vascular tree. In the colon, they may be small and resemble angiodysplasia or they may involve a long segment of bowel. The most extensive lesions typically are in the rectum and sigmoid.<sup>45</sup> AVMs of the bowel are characterized by thick-walled blood vessels that extend through the mucosa and submucosa into the muscle. Conversely, vascular ectasia (angiodysplasia) is characterized by thin or normal-sized blood vessels that proliferate in the submucosa.<sup>45,46</sup> True AVMs tend to occur in younger patients, whereas vascular ectasia is a disease of the elderly that predominates in the right colon. Unlike vascular ectasia, which may be subtle on pathologic examination, AVMs represent substantial lesions that may actually distort adjacent tissues.43,45,47 Although AVMs may be detected by endoscopy or exceptionally by barium studies, only the visible mucosal component of the AVMs is assessable by these means. Definitive diagnosis and determination of the site and extension of intestinal AVMs is still best achieved by selective mesenteric angiography. Involved vessels and flow pattern, as depicted by angiography, are used to classify AVMs into low- and high-flow AVMs.

## Computed Tomography

CT appears to be able to reveal AVMs of bowel and can be performed in patients who are hemodynamically stable and do not require emergency vascular or surgical intervention. Rapid scanning techniques and administration of contrast material at rates typically used in CT angiography are essential for an accurate diagnosis. Use of water as oral contrast media is also critical to distend the bowel and highlight enhancing vessels within the bowel wall. Use of oral contrast media can obscure identification of blood within the bowel lumen and interfere with diagnosis of an AVM.

On unenhanced CT, blood may be evident within the lumen or bowel wall. On enhanced CT, during the arterial phase, dilated vessels in the bowel wall enhance similar to the aorta. Active contrast agent extravasation also may be appreciated. These enhancing vessels tend to become less conspicuous in the venous phase.

TABLE 32-2	Treatment Options for Colonic Lesions			
		Angiodysplasia	Hemangioma	Dieulafoy's Lesion
Medica	al treatment	Systemic hormonal therapy with estrogen	N/A	N/A
Interve	entional therapy			
Colc	onoscopy	Endoscopic thermocoagulation, electrocoagulation, or photocoagulation	Endoscopic polypectomy if the lesion is pedunculated, polypoid, and ≤2.5 cm	Bipolar cautery, laser photocoagulation, and hemoclipping
Angi	iography	Superselective arterial embolization or direct vasopressin infusion	Not useful	Embolization with absorbable sponges
Surgica	al therapy	Reserved for severe bleeding	Surgical resection of hemangioma	Reserved for intractable bleeding

Effort should be made to screen other parts of the bowel because AVMs are known to be multiple.

## Endoscopy

Flat or elevated bright red lesions can be seen.

## Angiography

The constant angiographic sign of an arteriovenous malformation is the enlargement and increase in the number of arteries, small vessels, and veins. The feeding artery is dilated, and an early venous return is observed.<sup>20,48</sup> Patients with significant bleeding from large AVMs should undergo resection of the involved segment; transendoscopic therapy may be beneficial for smaller lesions.

## Treatment

## MEDICAL TREATMENT

Management of an incidentally detected vascular lesion is expectant, and in such cases no therapy is warranted. Hormonal therapy with estrogens in combination with progestins has been used to treat patients with a variety of vascular lesions of the gastrointestinal tract, in an attempt to reduce or terminate bleeding. It is likely that hormonal therapy affects various vascular lesions differently and that vascular lesions in the small intestine may respond differently than the same lesions in the colon. Bleeding also can be controlled endoscopically or angiographically in most patients, thereby avoiding the morbidity and mortality of emergency operation (Table 32-2). Argon and neodymium:yttrium-aluminum-garnet (Nd:YAG) laser, endoscopic sclerosis, monopolar and bipolar electrocoagulation, hemoclips in combination with cautery, and endoscopic band ligation have been used to ablate vascular lesions throughout the gastrointestinal tract and can be used to control active bleeding. Angiography with superselective microcoil embolization is largely used to control bleeding and has replaced intraarterial vasopressin infusion. Vasopressin is still recommended, however, when intestinal lesions are diffuse throughout the bowel or when superselective catheterization is not possible.

## SURGICAL TREATMENT

Surgical management either in the form of segmental or hemicolectomy depending on the site and multiplicity of lesion is indicated when a vascular lesion has been identified by either colonoscopy or angiography and when therapy by either or both of these two modalities is unsuccessful, cannot be performed, or is unavailable (see Table 32-2).

## What the Referring Physician Needs to Know

- Vascular lesions should be considered in both acute and chronic gastrointestinal bleeding, especially when initial endoscopic examination reveals no abnormalities.
- Multiplicity of vascular lesions always should be considered when initial endoscopic or vascular therapy is unsuccessful and bleeding seems to continue based on clinical evidence.
- Argon plasma coagulation is a preferred method of therapy in several vascular abnormalities.
- The roles of CT- and MRI-based diagnostic imaging techniques for vascular lesions of all types are evolving, and conventional angiography at present is more important for therapy than for diagnosis.

#### SUGGESTED READINGS

- Bounds BC, Kelsey PB: Lower gastrointestinal bleeding. Gastrointest Endoscopy Clin North Am 17: 273–288, 2007.
- Cappell MS: Gastrointestinal vascular malformations or neoplasms: arterial, venous, arteriovenous, and capillary. In Yamada T, Alpers DH, Kaplowitz N, et al, editors: *Textbook of Gastroenterology*, 4th ed, Philadelphia, 2003, Lippincott Williams & Wilkins, pp 2722–2741.
- Gore RM, Yaghmai V, Thakra KH, et al: Imaging in intestinal ischemic disorders. *Radiol Clin North Am* 46:845–875, 2008.
- Paterno F, Longo WE: The etiology and pathogenesis of vascular disorders of the intestine. *Radiol Clin North Am* 46:877–885, 2008.
- Regula J, Wronska E, Pachlewski J: Vascular lesions of gastrointestinal tract. Best Pract Res Clin Gastroenterol 22:313–328, 2008.
- Richardson JD: Vascular lesions of the intestines. *Am J Surg* 161:283–293, 1991.

#### REFERENCES

- 1. Farman J: Vascular lesions of the colon. Br J Radiol 39:575–582, 1966.
- Foutch PG, Rex DK, Lieberman DA: Prevalence and natural history of colonic angiodysplasia among healthy asymptomatic people. *Am J Gastroenterol* 90:564–567, 1995.
- Boley SJ, Brandt LJ, Mitsudo SM: Vascular lesions of the colon. *Adv Intern Med* 29:301–326, 1984.
- Fockens P, Tytgat GN: Dieulafoy's disease. Gastrointest Endosc Clin North Am 6:739–752, 1996.
- Yorozuya K, Watanabe M, Hasegawa H, et al: Diffuse cavernous hemangioma of the rectum: report of a case. *Surg Today* 33:309–311, 2003.
- Vilallonga R, Espin Basany E, Armengol M: Cavernous hemangioma: unusual benign tumor of the transverse colon. *Turk J Gastroenterol* 20:146–149, 2009.
- Kandpal H, Sharma R, Srivastava DN, et al: Diffuse cavernous haemangioma of colon: magnetic resonance imaging features: report of two cases. *Australas Radiol* 51(Spec No):B147–B151, 2007.
- 8. Wang AY, Ahmad NA: Diffuse cavernous hemangioma of the colon and rectum. *Clin Gastroenterol Hepatol* 5:A25, 2007.
- Sylla P, Deutsch G, Luo J, et al: Cavernous, arteriovenous, and mixed hemangiomalymphangioma of the rectosigmoid: rare causes of rectal bleeding—case series and review of the literature. *Int I Colorectal Dis* 23:653–658, 2008.
- Genter B, Mir R, Strauss R, et al: Hemangiopericytoma of the colon: report of a case and review of literature. *Dis Colon Rectum* 25:149–156, 1982.
- 11. Byrne ST, McDonald MJ, Poonnoose SI: Tenyear follow-up of a patient with Osler-Weber-Rendu syndrome and recurrent cerebral abscess secondary to pulmonary arteriovenous fistula. *J Clin Neurosci* 16:1095–1096, 2009.
- Giordano P, Nigro A, Lenato GM, et al: Screening for children from families with Rendu-Osler-Weber disease: from geneticist to clinician. *J Thromb Haemost* 4:1237–1245, 2006.
- Zuccaro G: Epidemiology of lower gastrointestinal bleeding. *Best Pract Res Clin Gastroenterol* 22:225–232, 2008.
- 14. Boley SJ, Sammartano R, Adams A, et al: On the nature and etiology of vascular ectasias of the colon: degenerative lesions of aging. *Gastroenterology* 72:650–660, 1977.
- Sharma R, Gorbien MJ: Angiodysplasia and lower gastrointestinal tract bleeding in elderly patients. Arch Intern Med 155:807–812, 1995.

- Jain R, Chetty R: Dieulafoy disease of the colon. Arch Pathol Lab Med 133:1865–1867, 2009.
- Njeru M, Seifi A, Salam Z, et al: Dieulafoy lesion: a rare cause of gastrointestinal bleeding. *South Med J* 102:336–337, 2009.
- Schmulewitz N, Baillie J: Dieulafoy lesions: a review of 6 years of experience at a tertiary referral center. Am J Gastroenterol 96:1688– 1694, 2001.
- Cooperman AM, Kelly KA, Bernatz PE, et al: Arteriovenous malformation of the intestine: an uncommon cause of gastrointestinal bleeding. *Arch Surg* 104:284–287, 1972.
- Moore JD, Thompson NW, Appelman HD, et al: Arteriovenous malformations of the gastrointestinal tract. Arch Surg 111:381–389, 1976.
- Ng EK, Cheung FK, Chiu PW: Blue rubber bleb nevus syndrome: treatment of multiple gastrointestinal hemangiomas with argon plasma coagulator. *Dig Endosc* 21:40–42, 2009.
- 22. Foutch PG: Angiodysplasia of the gastrointestinal tract. *Am J Gastroenterol* 88:807–818, 1993.
- 23. Dodda G, Trotman BW: Gastrointestinal angiodysplasia. J Assoc Acad Minor Phys 8:16–19, 1997.
- Accordino R, Paties C, Inzani E, et al: [Angiodysplasia of the right colon]. *Minerva Chir* 50:703–706, 1995.
- Junquera F, Quiroga S, Saperas E, et al: Accuracy of helical computed tomographic angiography for the diagnosis of colonic angiodysplasia. *Gastroenterology* 119:293–299, 2000.
- Regula J, Wronska E, Pachlewski J: Vascular lesions of the gastrointestinal tract. *Best Pract Res Clin Gastroenterol* 22:313–328, 2008.
- Wolff WI, Grossman MB, Shinya H: Angiodysplasia of the colon: diagnosis and treatment. *Gastroenterology* 72:329–333, 1977.
- 28. Holman CC: Haemangioma of the sigmoid colon: report of a case. *Br J Surg* 36:210, 1948.
- Olnick HM, Woodhall JP, Jr, Clay CB, Jr: Hemangioma of the colon. J Med Assoc Ga 46:383– 384, passim, 1957.
- Clark HH, McKay ER: Mixed cavernous and capillary hemangiomatosis involving the large bowel. J Int Coll Surg 27:218–225, 1957.
- Camilleri M, Chadwick VS, Hodgson HJ: Vascular anomalies of the gastrointestinal tract. *Hepatogastroenterology* 31:149–153, 1984.
- 32. Hervias D, Turrion JP, Herrera M, et al: Diffuse cavernous hemangioma of the rectum: an atypical cause of rectal bleeding. *Rev Esp Enferm Dig* 96:346–352, 2004.
- Eadie DG: Cavernous haemangioma of the descending colon. Br J Surg 46:223–224, 1958.

- 34. Ichikawa T, Koyama A, Fujimoto H, et al: Diffuse arteriovenous malformation involving jejunum and total colon with mesenteric varices: case report. *Clin Imaging* 18:221–223, 1994.
- Bailey JJ, Barrick CW, Jenkinson EL: Hemangioma of colon. JAMA 160:658–659, 1956.
   Czekajska-Chehab E, Borowiec D, Drop A, et al:
- Diffuse hemangioma of the rectum detected on multi-slice CT in an 18-year-old woman with Klippel-Trenaunay syndrome. Ann Univ Mariae Curie Sklodowska [Med] 59:356–360, 2004.
- Machicado GA, Jensen DM: Endoscopic diagnosis and treatment of severe lower gastrointestinal bleeding. *Indian J Gastroenterol* 25(Suppl 1): S43–S51, 2006.
- Matsuhashi N, Nakagama H, Moriya K, et al: Multiple diffuse hemangiomas of the large intestine. *Gastroenterol Jpn* 26:654–660, 1991.
- Scopinaro F, Signori C, Massa R, et al: Right colonic hemangioma diagnosed by scintigraphy with 99mTc sucralfate: a case report. *Ital J Surg Sci* 19:89–92, 1989.
- Katsinelos P, Pilpilidis I, Paroutoglou G, et al: Dieulafoy-like lesion of the colon presenting with massive lower gastrointestinal bleeding. *Surg Endosc* 18:346, 2004.
- Bou Jaoude J, Hobeika E, Yaghi C, et al: [Endoscopic treatment of Dieulafoy's lesion: a case report and review of the literature]. *J Med Liban* 51:55–58, 2003.
- Golubovic G, Kiurski M, Spica V, et al: [Vascular gastric anomalies as a cause of relapsing bleeding]. Vojnosanit Pregl 65:710–713, 2008.
- Yano T, Yamamoto H: [Vascular lesions of the small intestine]. *Nippon Rinsho* 66:1335–1341, 2008.
- Labenz J, Borsch G: [Vascular anomalies as the cause of recurrent intestinal hemorrhages]. Dtsch Med Wochenschr 115:575–579, 1990.
- Lesur G, Julie C, Romdhane N, et al: Vascular malformation of the colon and lower gastrointestinal tract. *Gastroenterol Clin Biol* 30:483– 484, 2006.
- Marescaux J, Petit B, Pavis d'Escurac X, et al: [Vascular malformations of the colon: a frequently undetected etiology of lower digestive hemorrhage]. *Presse Med* 15:2204–2207, 1986.
- de la Torre L, Carrasco D, Mora MA, et al: Vascular malformations of the colon in children. *J Pediatr Surg* 37:1754–1757, 2002.
- Pariente D, Cauquil P, Gallaire C, et al: Vascular malformations of the cecum: treatment by embolization: apropos of 2 cases. *Gastroenterol Clin Biol* 12:61–65, 1988.

33

# Colon Cancer and Screening Strategies

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### Etiology

The causes of the development of colorectal carcinoma and its precursor lesion, the colonic adenoma, are multifactorial and include both genetic predisposition and environmental insults. Risk factors for colorectal carcinoma include familial polyposis syndrome, ulcerative colitis, family history of colorectal cancer, age, male gender, smoking, alcohol intake, and obesity.<sup>1</sup>

### **Prevalence and Epidemiology**

Colon cancer is the third most commonly diagnosed cancer and third most common cause of cancer-related death in both men and women. It is responsible for 10% of new cancer cases and 9% of cancer-related deaths annually in the United States, representing an estimated 146,970 new cases and 24,680 deaths each year. The lifetime risk for developing colorectal carcinoma is 5.5% in men and 5.1% in women.<sup>2</sup> Winawer and associates<sup>3</sup> demonstrated a marked reduction in colorectal carcinoma incidence after colonoscopic polypectomy, indicating that screening techniques are essential in the prevention and early detection of colorectal carcinoma.

### **Clinical Presentation**

The clinical manifestation of colorectal cancer includes blood in the stool, change in bowel habits, bowel obstruction, bowel perforation, abdominal pain, diminished appetite, or systemic symptoms such as generalized fatigue and weight loss. However, colorectal carcinoma is often detected in asymptomatic patients at screening.

The late presentation of colon cancer includes symptoms related to metastatic disease. Colon cancer spreads hematogenously most commonly to the liver and lungs and via lymphatics to regional lymph nodes.

Laboratory findings can include microcytic anemia related to blood loss and elevation of the carcinoembryonic antigen tumor marker.

### **Pathophysiology and Pathology**

### HISTOLOGIC FINDINGS OF COLONIC POLYPS

Colonic polyps are growths into the bowel lumen and can develop as isolated polyps or in the setting of polyposis syndromes. Isolated colonic polyps of all sizes are seen in approximately 37.6% of the screening population,<sup>4</sup> whereas potentially clinically significant polyps 6 mm or greater have a prevalence

of 14%.<sup>5</sup> Polyps are histologically characterized as adenomatous, hyperplastic, and other. The "other" category includes juvenile/hamartomatous polyps, inflammatory polyps, lymphoid aggregates, mucosal tags, and submucosal lipomas.

Of all the types of polyps, only adenomatous polyps are of concern with respect to colon cancer. The adenoma is a precursor lesion that can potentially harbor dysplasia and develop into colon cancer; this prevailing view on the pathogenesis of colon cancer is called the *adenoma-carcinoma sequence* (see later discussion).

Adenomas are further characterized into three subtypes based on their histologic architecture: tubular, tubulovillous, and villous. Adenomas containing less than 25% villous features are classified as tubular adenomas; those with 25% to 75% villous features are tubulovillous adenomas; and those with more than 75% villous features are villous adenomas.

Adenomas also can be characterized based on the degree of cellular atypia seen on pathology (mild, moderate, or severe dysplasia), depending on the amount of nuclear changes and number of mitotic figures.<sup>6</sup>

With imaging studies and/or colonoscopy as screening tools, the radiologist and gastroenterologist cannot visually distinguish among the different types of polyps (with the exception of lipomas), nor can they determine the histologic factors or degree of cellular atypia of an adenoma. Thus, generally all encountered polyps seen on colonoscopy and those meeting a certain size threshold on noninvasive studies such as computed tomography (CT) colonography are removed.<sup>7</sup>

### LOCATION OF ADENOMAS

Adenomas can develop anywhere in the colon or rectum but are seen with the greatest frequency in the sigmoid colon. In a recent colonoscopy/CT colonography series, the distribution of adenomas and carcinomas was rectal, 13.4%; sigmoid colon, 25.1%; descending colon, 10.7%; transverse colon, 18.4%; ascending colon, 19.8%; and cecum, 12.6%.<sup>8</sup>

### ADENOMA-CARCINOMA SEQUENCE

The currently accepted evolution of colon cancer is via the adenoma-carcinoma sequence, a name first coined by Jackman and Mayo in 1951<sup>9</sup> and further developed and refined by pathologists, including Morson, Muto, and Bussey.<sup>6,10</sup>

The model for progression from normal epithelium to adenoma to carcinoma is a series of genetic mutations.<sup>11</sup> Colonic neoplasms are thought to arise as a result of mutational activation of oncogenes (*RAS* gene on chromosome 12p) coupled

with the mutational inactivation or loss of tumor suppression genes (familial adenomatous polyposis gene on chromosome 5q, *TP53* gene on chromosome 17p, and *DCC* gene on chromosome 18q). These mutations act at a number of steps in the progression from normal epithelium to hyperproliferative epithelium to early, intermediate, and late adenoma and, finally, to carcinoma.

The degree of dysplasia is highly correlated with the risk for malignancy because on a genetic and cellular level increasing atypia leads to a stepwise progression toward carcinoma. The presence of high-grade dysplasia is therefore the best predictor of which adenomas will progress to carcinomas.

There is a close relationship between the size of an adenoma and its propensity to harbor malignancy. In a colonoscopy series of a nonscreening population, the rate of carcinoma in adenomas greater than 2 cm was 19.4%, whereas that in adenomas less than 1 cm was 0.07%.<sup>12</sup> In an older surgical series, the rate of carcinoma in adenomas larger than 2 cm was 46% whereas that in adenomas smaller than 1 cm was 1.3%.<sup>10</sup>

Accordingly, adenoma size is correlated with the degree of cellular dysplasia. Some authors have also proposed a direct relationship between increasing the villous component seen on histologic examination and the degree of dysplasia.<sup>13</sup> As a result, the degree of dysplasia, adenoma size, and histologic characteristics are used as markers for malignancy risk in removed polyps.

### ADVANCED ADENOMA

Screening studies should be targeted toward the removal of adenomas that have the highest potential for developing into colorectal carcinoma. These "advanced adenomas" have traditionally been defined by any of the following three criteria: high-grade dysplasia, size 1 cm or greater, or a substantial (>25%) villous component (i.e., tubulovillous or villous adenomas). These lesions are at high risk for developing into colorectal carcinomas compared with their less-advanced counterparts. In an asymptomatic screening population, the overall prevalence of an advanced adenoma or carcinoma (collectively termed *advanced neoplasia*) is 3.3%.<sup>4</sup>

### MULTIPLE ADENOMAS

Patients who have an adenoma, advanced or otherwise, detected on a screening study are more likely to have additional adenomas detected on the same examination (synchronous) or on future examinations (metachronous). The presence of multiple adenomas (two or more) has been shown to confer an increased risk for developing an advanced adenoma on subsequent follow-up studies.<sup>14</sup> Therefore, the factors that inform our current screening guidelines include adenoma size, histologic features (i.e., presence of villous component), cellular features (i.e., degree of dysplasia), and total number.

### Screening

# THEORY OF SCREENING AND COST-BENEFIT ANALYSIS

The goal of any cancer screening, including colon cancer screening, is to achieve a reduction in mortality by identifying disease at earlier stages and thus reducing the incidence of advanced disease.

The 5-year survival is 90% for disease confined to the wall of the bowel; however, it falls to 68% for regional disease and plummets to 10% for metastatic disease.<sup>15</sup> It thus becomes clear that if cancer can be caught at earlier stages, mortality from the disease will be drastically reduced. In fact, prospective randomized trials and observational studies have demonstrated a reduction in mortality by detection of invasive disease and subsequent therapy.<sup>16-19</sup>

The American Cancer Society first issued formal guidelines for colorectal screening in 1980,<sup>20</sup> followed by guidelines from the U.S. Preventive Services Task Force,<sup>21,22</sup> the American College of Radiology,<sup>23</sup> and the U.S. Multi-Society Task Force on Colorectal Cancer.<sup>24,25</sup> Although there are differences among the guidelines, there is growing consensus, with the latest iteration being a collaborative effort by all of these groups.<sup>26</sup> The recommendations include continued support of the fecal occult blood test (FOBT) as well as the fecal immunohistochemical test (FIT) and stool DNA testing, assuming a patient is willing to undergo an invasive procedure in the instance of a positive test. The recommendations prefer tests that detect lesions earlier, including optical colonoscopy (OC) every 10 years or flexible sigmoidoscopy (FSIG), CT colonography (CTC), or double-contrast barium enema (DCBE) every 5 years.

The clinical effectiveness of screening is often assessed in terms of life-years gained. A measure of this is the incremental cost-effectiveness ratio (ICER), defined as the difference in cost among strategies divided by the difference in life expectancy among those strategies. Although controversial, an ICER threshold of \$50,000 per life-year gained is often used to differentiate a relatively efficient procedure from an inefficient procedure.<sup>27</sup> Pickhardt and colleagues<sup>28</sup> compared CTC and OC screening strategies for a population of 100,000 and found a nonscreening cumulative loss of 29,925 life-years from colorectal cancer. Fiveyear CTC demonstrated a gain of 6250 life-years as a result of colorectal cancer prevention and early treatment, and 10-year OC demonstrated a gain of 6032 life years. If CTC is reduced to a 10-year interval, the life-years gained is 5518. CTC also identified aortic aneurysms, saving an additional 1536 lifeyears, for a total of 7786 years of life saved. Compared with no screening, 10-year screening protocols cost just over \$1000 per year of life saved, yielding a remarkable cost-benefit ratio.<sup>21</sup>

### Screening Modalities

### Fecal Occult Blood Test and Other Stool-Based Examinations

*Theory.* The principle behind the FOBT and other stoolbased examinations is that invasive carcinoma will cause bleeding, which can detected using methods such as guaiac staining, immunohistochemistry, and DNA. Small polyps tend not to bleed, and larger lesions tend to bleed intermittently. As a result, these tests are subject to sampling error and are more likely to detect cancer rather than precancerous lesions.<sup>29,30</sup>

**Benefit.** FOBT is supported by randomized controlled studies, which demonstrate that its use leads to cancers being detected at an earlier and more curable stage compared with no screening, leading to reductions in colorectal cancer mortality of 15% to 33%.<sup>31-33</sup>

*Limitations.* The limitations of stool testing include the necessity for annual testing, low individual test sensitivity, and the need to follow any positive test with an invasive test.<sup>26</sup>

Furthermore, the sensitivity is highly variable and depends on hydration status of the feces, brand and style of the test, as well as chosen target lesion (i.e., adenoma versus carcinoma). As mentioned earlier, small polyps are unlikely to bleed; thus, sensitivity for these tests is very low, and FOBT is useful only for detecting advanced adenomas and cancers, with a sensitivity ranging from 37.1% to 79.4% when used correctly.<sup>29</sup> Many physicians use an in-office FOBT examination that has a sensitivity of only 4.9% for advanced adenoma and 9% for cancer.<sup>34</sup>

**Recommendation.** Given the limited availability of all screening modalities for the entire population, the Multi-Society Task Force continues to recommend properly performed stool testing as one alternative screening methodology.

### Flexible Sigmoidoscopy

**Theory.** FSIG is an optical endoscopic procedure that examines the most distal portion of the colon lumen. It is most often performed with a 60-cm endoscope but also can be performed with a variety of alternative scopes.

**Benefits.** FSIG was associated with a 60% to 80% reduction in colorectal cancer mortality for the area of colon within its reach. Overall decreased incidence compared with an unscreened group also has been demonstrated.<sup>35-38</sup> Its principal advantages over colonoscopy are that it requires a less extensive bowel preparation than a full colonic examination, and because it is less invasive than colonoscopy, sedation is not required. It also allows for concurrent sampling and/or removal of detected lesions.

*Limitations.* Like colonoscopy, FSIG can be complicated by patient discomfort and, more importantly, bowel perforation. Its greatest limitation, however, is its failure to evaluate the entire colon. Defenders of FSIG note that many people who have a proximal lesion will also have a distal lesion that would be detected on FSIG; thus, the incremental benefit of colonoscopy or colonography over FSIG is less pronounced. Finally, there is substantial variation in the depth of insertion of the scope given the lack of sedation, and insufficient insertion leads to inadequate examination.<sup>39,40</sup>

*Recommendation.* The Multi-Society Task Force continues to recommend FSIG every 5 years up to a distance of 40 cm within the colon.

### **Double-Contrast Barium Enema**

*Theory.* DCBE is a fluoroscopic examination executed by coating the mucosa with barium and distending the colon with air insufflated through a tube inserted in the rectum. Multiple images are obtained both fluoroscopically as well as by overhead method.

**Benefits.** DCBE evaluates the entire colon and detects most cancers and the majority of significant polyps. Sensitivity for cancer has been shown to vary from 85% to 97%.<sup>41</sup> In a meta-analysis, DCBE was 70% sensitive and 71% specific for polyps 10 mm or larger.<sup>42</sup> When performed properly, the examination can be completed with minimal discomfort.<sup>43</sup>

*Limitations.* Because it is an imaging examination, DCBE does not permit tissue biopsy. No randomized controlled studies have been performed to evaluate its efficacy, and the studies that have been done are predominately retrospective. The differential in results highlights the operator dependency of the examination. With the advent of CT colonography and increased use of colonoscopy, fewer DCBE examinations are performed annually and, consequently, radiologists currently in

training will have less experience with DCBE than their predecessors.

**Recommendation.** Although controversy remains, DCBE every 5 years continues to be recommended by some as an acceptable screening methodology in asymptomatic, averagerisk populations 50 years and older.<sup>26</sup>

### Colonoscopy

**Theory.** Colonoscopy is an optical procedure that evaluates the entire colon. It is one of the most commonly performed medical procedures.<sup>44</sup> Patients require an extensive colonic cleansing preparation, and the procedure is performed under sedation. Because it allows for direct optical visualization, biopsies are often performed.

**Benefits.** The greatest advantage to colonoscopy is that usually the entire colon can be screened and suspicious lesions sampled in a single visit. The seminal paper by Winawer and colleagues demonstrated a reduction in incidence of colon cancer of 76% to 90%.<sup>3</sup> Although no prospective randomized controlled trial has been performed to evaluate colonoscopy,<sup>26</sup> its health benefits are undisputed. A U.S. Department of Veterans\* Affairs study demonstrated a 50% reduction in mortality when colonoscopy was performed on a symptomatic population.<sup>45</sup> Numerous additional cohort studies have demonstrated reductions in colorectal carcinoma incidence and mortality.<sup>46</sup> Multiple additional studies by Winawer and colleagues<sup>14,24,25,47</sup> have reinforced these benefits.

*Limitations.* The limitations of colonoscopy include the need for colon cleansing and patient sedation. Because of sedation, a patient chaperone is needed. Controlled studies have shown the colonoscopy miss rate for adenomas 10 mm or larger to be 6% to 12%.<sup>48,49</sup> The additional risks of colonoscopy related to sedation and biopsy include cardiopulmonary events such as arrhythmia and hypotension as well as postpolypectomy bleeding and perforation.<sup>48,50</sup>

**Recommendation.** Colonoscopy every 10 years beginning at age 50 is recommended as a screening option for colorectal cancer.<sup>26</sup>

### **Computed Tomography Colonography**

**Theory.** CTC is a minimally invasive examination that uses CT to acquire images of the colon and two-dimensional and three-dimensional displays for interpretation. The mechanism and technique are explained in detail elsewhere in this book.

**Benefits.** CTC evaluates the entire colon, including those segments that are particularly redundant and difficult to evaluate with colonoscopy. Additionally, the examination can be performed without sedation. The examination also can detect extracolonic findings. In one study, 9% of the total patients had clinically important extracolonic findings.<sup>51</sup> Meta-analysis of 33 studies on nearly 6400 patients demonstrated an 85% to 93% sensitivity and 97% specificity for polyps 10 mm and larger. The 96% sensitivity of CTC for invasive cancer was comparable to that of optical colonoscopy.<sup>49,52-54</sup>

*Limitations.* One of the greatest limitations of CTC is its availability. Because funding is not widely available for screening CTC, the professional capacity is markedly limited.<sup>26</sup> CTC requires a cathartic bowel preparation, although studies are underway to eliminate this need. The most notable limitation is that CTC is an imaging study only, and patients must be referred to optical colonoscopy for biopsy and/or removal if a significant colonic lesion is encountered. However, Pickhardt

### TABLE Accuracy, Limitations, and Pitfalls of the Modalities Used in Screening for Colon Cancer

33-1			
Modality	Accuracy	Limitations	Pitfalls
FOBT	37%-79% cancer <sup>29</sup>	Positive result requires invasive test; does not detect small lesions	Single test is insufficient.
FSIG	60%-70% advanced adenoma and cancer <sup>26</sup>	Does not detect proximal disease	Less accurate in older patients because proximal disease is more common after age 65
DCBE	85%-97% cancer <sup>26</sup> 70% advanced adenoma <sup>60</sup>	Positive result requires invasive test.	Operator dependent
СТС	85%-93% sensitive; 97% specific for 10-mm polyp <sup>49,52-54</sup>	Positive result requires invasive test; limited availability	Training dependent
OC	88%-94% sensitive for 10-mm polyp <sup>48,49</sup>	Tortuous colon can lead to incomplete studies Invasive test with risks for bleeding, perforation	

CTC, Computed tomography colonoscopy; DCBE, double-contrast barium enema; FOBT, fecal occult blood test; FSIG, flexible sigmoidoscopy; OC, optical colonoscopy.

and colleagues<sup>55</sup> demonstrated a coordinated approach with gastroenterology that allows for same-day colonoscopy and biopsy in instances of positive CTC findings.

*Recommendation.* CTC every 5 years for patients older than 50 years of age is an acceptable screening option for colorectal cancer.<sup>26</sup>

### Recommendation

An overall recommendation given the multiple methodologies of screening is challenging. The U.S. Multi-Society Task Force leaned heavily toward screening tests that could prevent cancer rather than simply detect it at a later stage and thus implied a preference away from stool testing and toward direct mucosal evaluation. At this time there is insufficient capacity to screen the entire population using any one modality. Given this, and the fact that patients have shown varied preferences for the screening tests, the goal is to encourage screening using any modality with which a patient is willing to comply, with preference for those modalities that evaluate the entire colonic mucosa (Table 33-1).<sup>56-59</sup>

### Imaging

# EARLY-STAGE ADENOCARCINOMA AND THE ADENOMATOUS POLYP

The primary target of colon cancer screening is the early adenocarcinoma or the adenomatous polyp.<sup>26</sup> It has been estimated that 35% to 50% of the adult population older than 50 years of age will have at least one polyp; however, the majority of these will be diminutive lesions.<sup>55</sup> The prevalence using a 6-mm threshold is approximately 14%.<sup>55</sup> Using a 10-mm threshold, the prevalence falls to 5% to 6%.<sup>55</sup> It thus becomes a critical question as to the appropriate polyp size as the target for screening examinations and the actions to be taken on discovery of the target lesion.

### The Diminutive Lesion (<6 mm)

The American Gastroenterological Association Future Trends Report from 2004 claimed that such diminutive polyps are not a compelling reason for colonoscopy and polypectomy. Approximately a third of such polyps are adenomatous, with the majority manifesting as mucosal tags or hyperplasia.<sup>55</sup> Lieberman and associates<sup>60</sup> noted that despite the increased number of diminutive polyps compared with small polyps, the prevalence of advanced histology in diminutive polyps is lower.<sup>60</sup> Although some continue to argue for colonoscopy in diminutive lesions, there is near consensus that these lesions do not require intervention.

### The Small Lesion (6 to 9 mm)

Two thirds of small polyps are adenomatous, and approximately 4% will have advanced histologic findings.<sup>8,55,61</sup> With an 8% screening prevalence of small adenomas and 4% advanced histologic findings, the overall prevalence of the advanced, small adenoma is 0.3%. In Pickhardt and colleagues' screening experience of over 1000 small polyps, they did not find any invasive cancers.<sup>55</sup> Without any intervention, the 5-year colorectal cancer death rate in patients with 6- to 9-mm polyps is 0.08%, a sevenfold decrease from that of the a priori screening population.<sup>55</sup> Pickhardt and colleagues<sup>61</sup> recommend a 3-year CTC surveillance for 6- to 9-mm lesions discovered on CTC but agreed with the American Gastroenterological Association that there remains a need to define the natural history of such polyps with a large longitudinal study.

### The Large Polyp (≥10 mm)

Large polyps are the group is the least controversial, and there is near unanimity that these lesions merit tissue sampling. Studies have shown a 30.6% prevalence of advanced status on histologic examination in large polyps.<sup>60</sup> If these are detected on CTC, these patients should be referred for colonoscopy and biopsy.

### What the Referring Physician Needs to Know

- There is a 90% 5-year survival rate for cancer limited to the colon; it is 68% for regional disease and 10% for metastatic disease.
- Screening has a definite benefit in the prevention of colorectal carcinoma.
- Both CTC and OC are cost-effective in colorectal cancer screening.

• Less preferred but acceptable screening options:

goal is to screen as many people as possible.

DCBE every 5 years

• Stool-based examinations conducted as a full program

• Different patients have different preferences. The key

### **Key Points**

- CTC is comparable to optical colonoscopy in detection of clinically significant (≥10 mm) lesions.
- Acceptable screening options include:
  - CTC every 5 years
  - Optical colonoscopy every 10 years
  - FSIG every 5 years

### REFERENCES

- 1. American Cancer Society: Colorectal Cancer Facts & Figures 2008-2010; 1-32. <a href="http://www.cancer.org/downloads/STT/F861708\_finalforweb.pdf">http://www.cancer.org/downloads/STT/F861708\_finalforweb.pdf</a>>, (Accessed 23.12.15.)
- 2. Jemal A, Siegel R, Ward E, et al: Cancer statistics, 2009. *CA Cancer J Clin* 59:225–249, 2009.
- 3. Winawer SJ, Zauber AG, Ho MN, et al: Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *N Engl J Med* 329:1977–1981, 1993.
- Kim DH, Pickhardt PJ, Taylor AJ, et al: CT colonography versus colonoscopy for the detection of advanced neoplasia. *N Engl J Med* 357:1403– 1412, 2007.
- Pickhardt PJ, Kim DH: Colorectal cancer screening with CT colonography: key concepts regarding polyp prevalence, size, histology, morphology, and natural history. *AJR Am J Roent*genol 193:40–46, 2009.
- 6. Morson B: President's address: the polyp-cancer sequence in the large bowel. *Proc R Soc Med* 67:451–457, 1974.
- Zalis ME, Barish MA, Choi JR, et al: CT colonography reporting and data system: a consensus proposal. *Radiology* 236:3–9, 2005.
- Johnson CD, Chen MH, Toledano AY, et al: Accuracy of CT colonography for detection of large adenomas and cancers. N Engl J Med 359:1207–1217, 2008.
- 9. Jackman RJ, Mayo CW: The adenomacarcinoma sequence in cancer of the colon. *Surg Gynecol Obstet* 93:327–330, 1951.
- Muto T, Bussey HJ, Morson BC: The evolution of cancer of the colon and rectum. *Cancer* 36:2251–2270, 1975.
- 11. Fearon ER, Vogelstein B: A genetic model for colorectal tumorigenesis. *Cell* 61:759–767, 1990.
- Odom SR, Duffy SD, Barone JE, et al: The rate of adenocarcinoma in endoscopically removed colorectal polyps. *Am Surg* 71:1024–1026, 2005.
- O'Brien MJ, Winawer SJ, Zauber AG, et al: The National Polyp Study: patient and polyp characteristics associated with high-grade dysplasia in colorectal adenomas. *Gastroenterology* 98: 371–379, 1990.
- Winawer SJ, Zauber AG, O'Brian MJ, et al: Randomized comparison of surveillance intervals after colonoscopic removal of newly diagnosed adenomatous polyps. The National Polyp Study Workgroup. N Engl J Med 328:901–906, 1993.
- Ries L, Melbert D, Krapcho M, et al, editors: SEER Cancer Statistics Review 1975-2004, Bethesda, MD, 2007, National Cancer Institute.
- Smith RA, Cokkinides V, Eyre HJ: Cancer screening in the United States, 2007: a review of current guidelines, practices and prospects. CA Cancer J Clin 57:90–104, 2007.
- Selby JV, Friedman GD, Quesenberry CP, Jr, et al: A case control study of screening sigmoidoscopy and mortality from colorectal cancer. *N Engl J Med* 326:653–657, 1992.

- Kronborg O, Fenger C, Olsen J, et al: Randomised study of screening for colorectal cancer with faecal occult blood test. *Lancet* 348:1467– 1471, 1996.
- Mandel JS, Church TR, Bond JH, et al: The effect of fecal occult-blood screening on the incidence of colorectal cancer. N Engl J Med 343:1603–1607, 2000.
- 20. Eddy D: ACS report on the cancer-related health checkup. *CA Cancer J Clin* 30:193–240, 1980.
- U.S. Preventive Services Task Force: *Guide to Clinical Preventive Services*, ed 2, Baltimore, 1996, Williams & Wilkins.
- U.S. Preventive Services Task Force: Screening for colorectal cancer: recommendation and rationale. Ann Intern Med 137:129–131, 2002.
- Heiken JP, Bree RL, Foley WD, et al: Colorectal cancer screening: American College of Radiology (ACR) Appropriateness Criteria, Reston, VA, 2006, American College of Radiology.
   Winawer SJ, Fletcher RH, Miller L, et al:
- Winawer SJ, Fletcher RH, Miller L, et al: Colorectal cancer screening: clinical guidelines and rationale. *Gastroenterology* 112:594–642, 1997.
- Winawer SJ, Fletcher RH, Rex D, et al: Colorectal cancer screening: clinical guidelines and surveillance—clinical guidelines and rationale. Update based on new evidence. *Gastroenterology* 124:544–560, 2003.
- 26. Levin B, Lieberman DA, McFarland B, et al: Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *CA Cancer J Clin* 58:130– 160, 2008.
- Tengs TO, Wallace A: One thousand health related quality-of-life estimates. *Med Care* 38:583–637, 2000.
- Pickhardt PJ, Hassan C, Laghi A, et al: CT colonography to screen for colorectal cancer and aortic aneurysm in the Medicare population: cost-effectiveness analysis. *AJR Am J Roentgenol* 192:1332–1340, 2009.
- Allison JE, Tekawa IS, Ransom LJ, et al: A comparison of fecal occult blood tests for colorectal cancer screening. *N Engl J Med* 334:155–159, 1996.
- Simon JB: Occult blood screening for colorectal carcinoma: a critical review. *Gastroenterology* 88:820–837, 1985.
- Hardcastle JD, Chamberlain JO, Robinson MH, et al: Randomised controlled trial of faecaloccult-blood screening for colorectal cancer. *Lancet* 348:1472–1477, 1996.
- 32. Kronborg O, Fenger C, Olsen J, et al: Randomised study of screening for colorectal cancer with faecal-occult-blood test. *Lancet* 348:1467– 1471, 1996.
- 33. Young GP, St John DJ: Selecting an occult blood test for use as a screening tool for large bowel

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cancer. In Rozen P, Reich CB, Winawer SJ, editors: Frontiers of Gastrointestinal Research: Advances in Large Bowel Cancer—Policy, Prevention, Research and Treatment, Basel, 1991, Karger, pp 135–156.

- 34. Collins JF, Lieberman DA, Durbin TE, et al: Accuracy of screening for fecal occult blood on a single stool sample obtained by digital rectal examination: a comparison with recommended sampling practice. *Ann Intern Med* 142:81–85, 2005.
- Selby JV, Friedman GD, Quesenberry CP, Jr, et al: A case control study of screening sigmoidoscopy and mortality from colorectal cancer. *N Engl J Med* 326:653–657, 1992.
- Newcomb PA, Norfleet RG, Storer BE, et al: Screening sigmoidoscopy and colorectal cancer mortality. J Natl Cancer Inst 84:1572–1575, 1992.
- Thiis-Evensen E, Hoff GS, Sauar J, et al: Population-based surveillance by colonoscopy: effect on the incidence of colorectal cancer. Telemark Polyp Study I. *Scand J Gastroenterol* 34:414–420, 1999.
- Newcomb PA, Storer BE, Morimoto LM, et al: Long-term efficacy of sigmoidoscopy in the reduction of colorectal cancer incidence. J Natl Cancer Inst 95:622–625, 2003.
- Schoen RE, Pinsky PF, Weissfeld JL, et al: Results of repeat sigmoidoscopy 3 years after a negative examination. JAMA 290:41–48, 2003.
- Doria-Rose VP, Newcomb PA, Levin TR: Incomplete screening flexible sigmoidoscopy associated with female sex, age, and increased risk of colorectal cancer. *Gut* 54:1273–1278, 2005.
- Johnson CD, Carlson HC, Taylor WF, et al: Barium enemas of carcinoma of the colon: sensitivity of double- and single-contrast studies. *AJR Am J Roentgenol* 140:1143–1149, 1983.
- 42. Sosna J, Sella T, Sy O, et al: Critical analysis of the performance of double-contrast barium enema for detecting colorectal polyps > or = 6 mm in the era of CT colonography. AJR Am J Roentgenol 190:374–385, 2008.
- Scholz FJ: Tips for the comfortable doublecontrast barium enema: the open tube technique with active drainage. *Semin Roentgenol* 35:342–356, 2000.
- Seeff LC, Richards TB, Shapiro JA, et al: How many endoscopies are performed for colorectal cancer screening? Results from CDC's survey of endoscopic capacity. *Gastroenterology* 127:1670– 1677, 2004.
- Muller AD, Sonnenberg A: Prevention of colorectal cancer by flexible endoscopy and polypectomy: a case control study of 32,702 veterans. Ann Intern Med 123:904–910, 1995.
- Kahi CJ, Imperiali TE, Juliar BE, et al: Effects of screening colonoscopy on colorectal cancer incidence and mortality. *Clin Gastroenterol Hepatol* 7:770–775, 2009.

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- 47. Rex DK, Bond JH, Winawer S, et al: Quality in the technical performance of colonoscopy and the continuous quality improvement process for colonoscopy: recommendations of the U.S. Multisociety Task Force on Colorectal Cancer. *Am J Gastroenterol* 97:1296–1308, 2002.
- Rex DK, Cutler CS, Lemmel GT, et al: Colonoscopic miss rates of adenomas determined by back to back colonoscopies. *Gastroenterology* 112:24–28, 1997.
- Pickhardt PJ, Nugent PA, Mysliwiec PA, et al: Location of adenomas missed by optical colonoscopy. Ann Intern Med 141:352–359, 2004.
- Gatto NM, Frucht H, Sundararajan V, et al: Risk of perforation after colonoscopy: a populationbased study. J Natl Cancer Inst 95:230–236, 2003.
- Yee J, Kumar NN, Godara SS, et al: Extracolonic abnormalities discovered incidentally at CT colonography in a male population. *Radiology* 236:519–526, 2005.
- 52. Farrar WD, Sawhney MS, Nelson DB, et al: Colorectal cancers found after a complete colo-

noscopy. Clin Gastroenterol Hepatol 4:1259–1264, 2006.

- Halligan S, Altman DG, Taylor SA, et al: CT colonography in the detection of colorectal polyps and cancer: systematic review, metaanalysis, and proposed minimum data set for study level reporting. *Radiology* 237:893–904, 2005.
- Mulhall BP, Veerappan GR, Jackson JL: Metaanalysis: computed tomographic colonography. *Ann Intern Med* 142:635–650, 2005.
- Pickhardt PJ, Kim DH: Colorectal cancer screening with CT colonography: key concepts regarding polyp prevalence, size, histology, morphology and natural history. *AJR Am J Roentgenol* 193:40–46, 2009.
- Vernon SW: Participation in colorectal cancer screening; a review. J Natl Cancer Inst 89:1406– 1433, 1997.
- Schroy PC, 3rd, Heeren TC: Patient perceptions of stool based DNA testing for colorectal cancer screening. Am J Prev Med 28:208–214, 2005.

- Tangka FK, Molinari NA, Chattopadhyay SK, et al: Market for colorectal cancer screening by endoscopy in the United States. *Am J Prev Med* 29:54–60, 2005.
- Lafata JE, Divine G, Moon C, et al: Patientphysician colorectal cancer screening discussions and screening use. *Am J Prev Med* 31:202–209, 2006.
- Lieberman D, Morave M, Holub J, et al: Polyp size and advanced histology in patients undergoing colonoscopy screening: implications for CT colonography. *Gastroenterology* 135:1100– 1105, 2008.
- Pickhardt PJ, Choi JR, Hwang I, et al: Nonadenomatous polyps at CT colonography: prevalence, size distribution, and detection rates. *Radiology* 232:784–790, 2004.

# Imaging of the Postoperative Bowel

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Surgical procedures performed on the bowel are innumerable, and their detailed discussion is beyond the scope of this chapter. To understand the related imaging, it is important to be familiar with the postoperative anatomy. Our purpose in this chapter is to present tools to approach the postoperative bowel by discussing some commonly performed surgical procedures, their appearance on imaging, and common complications.

### **Procedures**

### ESOPHAGEAL RESECTION

All surgical techniques used for esophageal resection have a common characteristic—a segment of the esophagus is resected and reconstructed with anastomosis. The most frequently performed are the transthoracic esophagectomy (either right-sided or left-sided approach), transhiatal esophagectomy, and Ivor-Lewis technique.

# Indications, Contraindications, Purpose, and Underlying Mechanisms

Esophageal resection is the treatment of choice for several benign and neoplastic conditions. Benign causes include esophageal perforation, refractory peptic stricture, and large leiomyomas (>5 cm). The most common neoplastic causes include adenocarcinoma and squamous cell carcinoma of the esophagus.

Once the affected part of the esophagus is localized, the surgeon will determine the technique. For example, right-sided transthoracic esophagectomy (Figure 34-1) is preferred in cases involving the upper two thirds of the esophagus because the aorta does not limit access to the esophagus, whereas the left-sided approach is used in cases involving the distal esophagus. The Ivor-Lewis technique is an excellent procedure for patients with midesophageal carcinomas, Barrett's esophagus, and esophageal destruction (e.g., perforation, caustic injury, persistent esophageal ulcer).<sup>1</sup> This procedure combines a laparotomy with right thoracotomy and intrathoracic anastomosis.

Transhiatal esophagectomy was developed because of multiple complications involved with the thoracotomy approach. This technique involves mobilization of the esophagus through the esophageal hiatus; then the entire thoracic esophagus is transected, and the esophagus is reconstructed with the stomach by an anastomosis with the remaining cervical esophagus (Figure 34-2).

### Expected Appearance on Relevant Modalities

The operative report should be reviewed before fluoroscopic evaluation and the anastomotic location is known. In the preoperative or postoperative setting the imaging modality of choice is esophagography. Preoperatively it allows for evaluation of the lesion in question, the location in the esophagus (upper, middle, or lower third), and the preoperative functionality of the esophagus. Postoperatively, it allows evaluation of patency of the anastomosis, functionality of the reconstructed esophagus, and possible recurrent disease. In cases of potential perforation, water-soluble contrast should be used initially to exclude leak and prevent complications such as a chemical mediastinitis.

Considering most complications occur at the anastomosis, this area should be thoroughly evaluated. In cases of transhiatal esophagectomy and gastric pull-through, images on barium esophagography will demonstrate a narrowing within the cervical esophagus that represents the anastomosis and a reconstructed esophagus demonstrating gastric mucosal folds (Figure 34-3). If Ivor-Lewis esophagectomy or a left/right thoracotomy and esophagectomy technique were performed, the esophago-gram will show the anastomosis within the chest (Figures 34-4 and 34-5).

# POTENTIAL COMPLICATIONS AND RADIOLOGIC APPEARANCE

Possible postesophagectomy complications include pulmonary (atelectasis, pleural effusions), anastomotic stricture, the most feared complications of anastomosis failure and leak (Figure 34-6), and recurrent disease in patients with esophageal cancer.<sup>2</sup> At our institution, patients are evaluated in the first 24 hours with water-soluble contrast to exclude anastomotic leak. If extraluminal contrast is seen, additional images (e.g., right posterior oblique, anteroposterior, left posterior oblique, magnification) should be obtained for documentation and potential surgical planning. If an anastomotic leak is excluded, the examination can be continued with barium for improved detail.

### ANTIREFLUX SURGERY

Surgical intervention is an option in gastroesophageal reflux refractory to medical treatment or in suspected esophageal injury.

### Indications, Contraindications, Purpose, and Underlying Mechanisms

Antireflux surgery aims to construct a valve mechanism to reestablish gastroesophageal junction competence. The three most popular are the Nissen fundoplication, the Belsey Mark IV repair, and the Hill posterior gastropexy (Figure 34-7). These procedures can be performed through laparotomy (Nissen, Hill), thoracotomy (Belsey), or laparoscopy (Nissen, Hill).

The surgical technique of choice depends on the patient's preoperative esophageal length and motility (Table 34-1).<sup>3</sup>

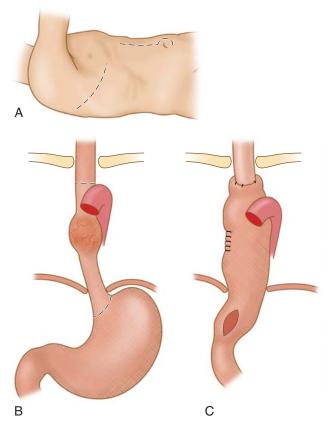


Figure 34-1 Overview of right thoracotomy (A) with esophageal resection, (B) gastric mobilization, and (C) intrathoracic anastomosis. (Redrawn from Townsend CM: Sabiston textbook of surgery, ed 17, Philadelphia, 2004, Saunders, p 1134.)

TABLE 34-1	Types of Antireflux Surgery and Indications	
Esophageal Length and		Recommended
Preoperative Motility		Antireflux Surgery

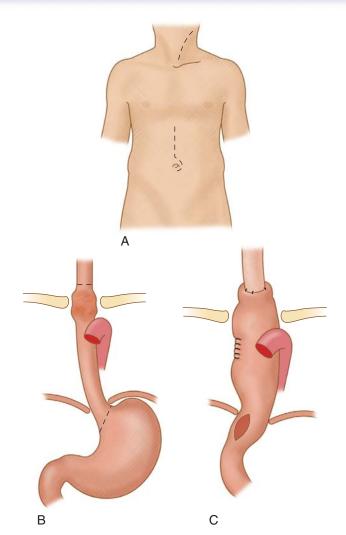
Normal length and m	otility	Nissen fundoplication
Normal length but abnormal motility		Hill or Belsey operation
Normal length and me but prior stomach s	otility urgery	Hill operation

### Expected Appearance on Relevant Modalities

Postoperative esophagography remains the optimal study for evaluation. In the preoperative setting it provides information regarding the following:

- Esophageal motility
- Presence of sliding or paraesophageal hernia (>5 cm)
- Significant esophageal stricture or Barrett's esophagus (segment >3 cm)

The typical appearance of a fundoplication on esophagography is a smooth circumferential narrowing of the distal esophagus that extends for 2 to 3 cm and is associated with a filling defect within the stomach fundus representing the portion used for the wraparound (Figure 34-8).<sup>4</sup>



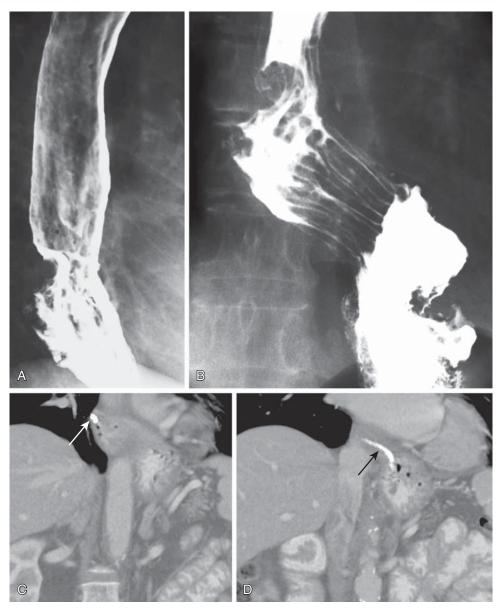
**Figure 34-2** Overview of transhiatal esophagectomy with gastric mobilization and gastric pull-up for cervicoesophagogastric anastomosis. (Modified from Ellis FH Jr: Esophagogastrectomy for carcinoma: technical considerations based on anatomic location of lesion. Surg Clin North Am 60:275, 1980.)

# Potential Complications and Radiologic Appearance

In the postoperative setting, patients presenting with symptoms of dysphagia, epigastric pain, or recurrent reflux warrant evaluation of the fundoplication. These symptoms may be secondary to (1) a tight fundoplication or a long fundoplication that prevents adequate passage of a food bolus, (2) partially or completely herniated fundoplication (Figure 34-9) and acquired paraesophageal hernia, or (3) partially or completely disrupted fundoplication.<sup>5</sup>

### GASTRIC BYPASS

Bariatric surgery is more commonly used in obese patients to improve long-term outcome. The resulting weight loss can improve the quality of life<sup>6</sup> and decrease the use of medications for cardiovascular disease or diabetes.<sup>7</sup>



**Figure 34-3** Spot right posterior oblique images of a barium esophagogram at the level of the distal esophagus (A) and proximal stomach (B) in a patient after partial distal esophagectomy and reanastomosis. Coronal computed tomography images (C and D) demonstrate a linear hyperdensity near the gastroesophageal junction (*arrows*) representing the new gastroesophageal anastomosis.

# Indications, Contraindications, Purpose, and Underlying Mechanisms

Bariatric surgery is indicated in patients with a body mass index (BMI) of more than 40 kg/m<sup>2</sup> or a BMI of 35 kg/m<sup>2</sup> associated with comorbidities, such as sleep apnea, diabetes, and obesity-related cardiomyopathy.

Bariatric procedures are divided into two main categories: restrictive and malabsorptive techniques (Box 34-1). Restrictive procedures reduce caloric intake by limiting gastric capacity. Malabsorptive procedures reduce the absorption of calories by reduction of the length of the small intestine. The Roux-en-Y

### BOX 34-1 TYPES OF GASTRIC BYPASS SURGERY

#### RESTRICTIVE

- Vertical banded gastroplasty
- Gastric banding

#### MALABSORPTIVE

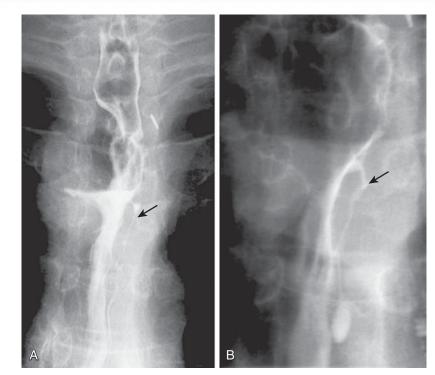
- Jejunoileal bypass
- Biliopancreatic diversion with duodenal switch

#### COMBINED

• Roux-en-Y gastric bypass



**Figure 34-4** Frontal image of a barium esophagogram of a patient who underwent an Ivor-Lewis procedure shows a narrowing within the cervical esophagus (*white arrow*) with the distal reconstructed esophagus demonstrating folds typical of stomach mucosa (*black arrow*).



**Figure 34-6** Spot anteroposterior (A) and right posterior oblique (B) images of a barium esophagogram after recent esophagectomy and gastric pull-through demonstrate a small linear area of extraluminal contrast medium (*arrows*) consistent with an anastomotic leak.

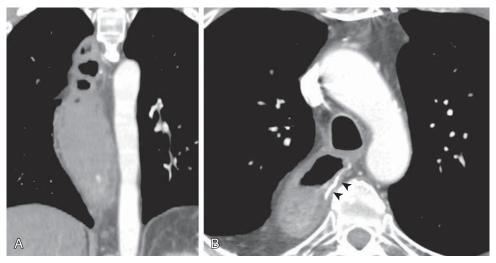
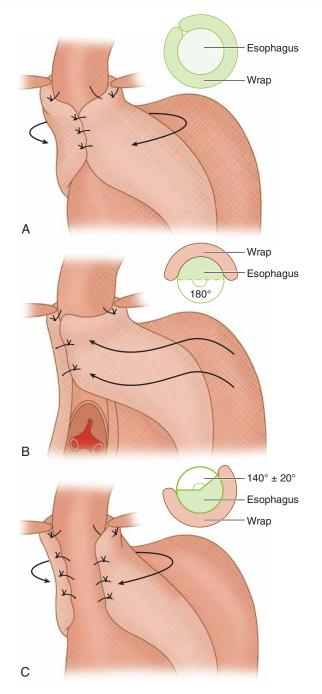


Figure 34-5 A, Coronal computed tomography (CT) image of the patient in Figure 34-4 demonstrates stomach replacing the distal esophagus. B, Axial CT image at the level of the upper thorax demonstrates a linear high-density material (*arrowheads*) adjacent to the reconstructed esophagus, representing the suture material used for the thoracic anastomosis.



**Figure 34-7** Overview of the most common fundoplications. **A**, Nissen fundoplication. **B**, The Belsey Mark IV repair is performed transthoracically, whereas the Hill procedure (**C**) is performed via the abdominal route. (*Redrawn from Townsend CM*: Sabiston textbook of surgery, ed 17, Philadelphia, 2004, Saunders, p 1160.)

gastric bypass is a combination of both. The gastric pouch serves as the restrictive component, and the gastrojejunal anastomosis represents the malabsorptive component (Figure 34-10). The laparoscopic Roux-en-Y gastric bypass has become the preferred method owing to decreased hospital stays and faster recovery.<sup>8,9</sup>

To perform these surgeries, the anatomy of the upper gastrointestinal system has to be intact. Underlying malignancy or

### BOX 34-2 POTENTIAL COMPLICATIONS IN GASTRIC BYPASS PATIENTS

#### **FIRST 24 HOURS**

- Anastomotic leak
- Anastomotic stricture
- Small bowel obstruction
- Stricture at mesocolic window

#### LATE COMPLICATIONS

- Gastrogastric fistula
- Internal hernia
- Ulcer at anastomosis

an inflammatory process affecting this system needs to be excluded before surgery.

#### Expected Appearance on Relevant Modalities

Imaging can be challenging because of patients' body habitus and must be optimized. The two main imaging modalities used are esophagography and CT. The esophagography allows evaluation of the anatomy, patency of the anastomosis in cases of Roux-en-Y gastric bypass, and functionality of the gastric bypass (Figure 34-11). CT allows for evaluation of postsurgical complications such as abdominal free fluid from anastomotic leak and abscess (Figure 34-12) or secondary complications related to the altered anatomy such as afferent loop syndrome. At the gastrojejunal anastomosis after Roux-en-Y gastric bypass, narrowing within the first 24 hours after surgery can be secondary to postoperative edema.

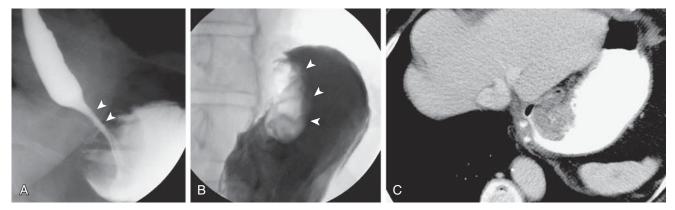
In patients with laparoscopic adjustable gastric banding, the band can be seen on plain radiographs. These are connected to the access port that adjusts the band (Figure 34-13). The most important part of each evaluation is to determine if the components of the laparoscopic adjustable gastric banding are intact.

# Potential Complications and Radiologic Appearance

Postoperative complications include bleeding, infection, anastomotic ulcer, stricture, and internal hernia, among others (Box 34-2). Fluoroscopy and CT are central in evaluating these complications and are complementary, with CT being central in evaluating unstable patients and those with life-threatening complications such as pneumoperitoneum and closed-loop bowel obstruction.

On the first day, the most feared complication in patients with malabsorptive technique or Roux-en-Y gastric bypass procedure is anastomotic leak, because this could be life-threatening and needs immediate attention (Figure 34-14). Narrowing of the anastomosis postoperatively may be secondary to postoperative edema. However, significant narrowing resulting in obstructive symptoms and preventing passage of contrast could be secondary to tight sutures. In cases of Roux-en-Y gastric bypass with a retrocolic approach, there could be stricture where the Roux limb traverses the mesocolon (Figure 34-15).

In patients after gastric pouch creation, degradation of the suture line or a gastrogastric fistula could manifest with a patient reporting decreased satiety or weight gain (Figure 34-16). Small bowel obstruction could be secondary to



**Figure 34-8** Spot radiographs from barium esophagography at the level of the distal esophagus (A) and proximal stomach (B) reveal a typical fundoplication defect (*arrowheads*). Note the circumferential narrowing of the distal esophagus and gastroesophageal junction, extending for 2 to 3 cm. Computed tomography image (C) after Nissen fundoplication demonstrates a curved apparent gastric wall thickening that represents the stomach fundus wrapped around the distal esophagus at the gastroesophageal junction.



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**Figure 34-9** Spot left posterior oblique image status post-Nissen fundoplication who complained of dysphagia shows the filling defect at the stomach fundus typical of a fundoplication. However, the stomach fundus and proximal body have herniated above the diaphragm.

postoperative edema. However, if it develops later, this could be secondary to an internal hernia, intussusception (Figure 34-17), or adhesions.<sup>10</sup> Identification of a transition point on CT can be helpful because these patients often need surgical exploration. Prompt diagnosis is important because perforation or anastomotic leak can occur secondary to tension caused by severe small bowel obstruction.

### GASTRECTOMY, BILLROTH I AND II PROCEDURES, AND ESOPHAGOJEJUNOSTOMY

The incidence of gastric cancer has decreased in the United States since 1930; however, approximately 21,260 new cases are

Figure 34-10 Roux-en-Y gastric. (*Redrawn from Cameron JL*: Current surgical therapy, ed 7, St Louis, 2005, Mosby, p 99.)

diagnosed yearly.<sup>11</sup> The choice of total or subtotal gastrectomy depends on the tumor location. If the tumor is in the upper third of the stomach, is infiltrative, or is a large midgastric mass, total gastrectomy is preferred. If the tumor is in the distal two thirds of the stomach, subtotal gastrectomy may be an option. Therefore, the precise location should be described for surgical planning. Gastrectomy is also used for the treatment of severe peptic ulcer disease and its complications (e.g., severe perforation and ulceration, stricture).

# Indications, Contraindications, Purpose, and Underlying Mechanisms

Billroth I or II reanastomosis is commonly used to restore the anatomy after partial gastrectomy. The Billroth I procedure involves an antrectomy and an end-to-end anastomosis between the remnant stomach and the duodenum. In the Billroth II operation, after the antrectomy is performed, the duodenal stump is closed and a gastrojejunal anastomosis or a side-to-side duodenojejunal anastomosis is created (Figure 34-18).<sup>12</sup>

In cases of total gastrectomy, a Roux-en-Y esophagojejunostomy with end-to-side anastomosis is created.



**Figure 34-11** Spot anteroposterior image from a patient after Rouxen-Y gastric bypass demonstrates a stomach pouch filled with contrast and passage into the gastrojejunal anastomosis without evidence of obstruction or extraluminal filling.

### Expected Appearance on Relevant Modalities

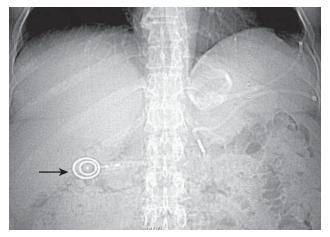
Radiology is crucial in the evaluation of symptomatic patients after gastrectomy and proximal small bowel surgeries.<sup>13</sup> Reviewing the surgical procedure should be the first step. Single- and double-contrast fluoroscopy is excellent to follow to the anastomosis, searching for anastomotic leaks and strictures, and to evaluate functionality after surgery (Figure 34-19).

CT has become the primary means for evaluation of acute symptoms or if recurrent disease is suspected. On CT, surgical staples or sutures indicate where an anastomosis has been created and serves as guideline for the postsurgical anatomy. Particular attention should be given to the anastomotic site.

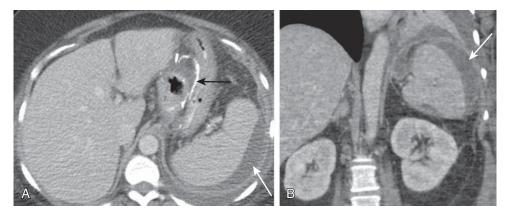
## Potential Complications and Radiologic Appearance

MDCT is useful in identifying postoperative anatomic changes, complications, and tumor recurrence.<sup>12</sup> Postsurgical complications after a partial or total gastrectomy include the following:

- Early or late dumping syndrome
- Postvagotomy diarrhea



**Figure 34-13** Scout image from computed tomography scan after laparoscopic adjustable gastric banding demonstrates intact band in the left upper quadrant. This is connected to the access port in the right side of the abdomen (*arrow*).



**Figure 34-12** Axial (A) and coronal (B) CT images from a patient after Roux-en-Y gastric bypass surgery who had an anastomotic leak and presents with left upper quadrant pain secondary to an abscess in the left subphrenic space (*white arrow*). Note the linear hyperdensity along the stomach that represents suture material from surgery (*black arrow*).



**Figure 34-14** Spot image of an esophagogram performed with watersoluble contrast agent from a patient after Roux-en-Y gastric bypass demonstrates contrast agent within the peritoneal cavity in the left upper quadrant (*arrow*).



**Figure 34-15** Barium esophagogram after Roux-en-Y gastric bypass demonstrates a long-segment narrowing at the jejunojejunostomy (distal anastomosis) that caused obstructive symptoms. During surgery, a narrowing at the mesocolon was found.

- Roux stasis syndrome
- Alkaline reflux gastritis
- Duodenal stump leakage
- Intraabdominal bleeding
- Afferent or efferent loop syndrome



**Figure 34-16** Anteroposterior image of a water-soluble esophagogram shows contrast agent within the excluded stomach segment (*arrow*) in this patient who had a Roux-en-Y gastric bypass.

Afferent loop syndrome, duodenal stump leakage (Figure 34-20), and postoperative hemorrhage are complications requiring prompt recognition because they can be life-threatening and management is surgical.

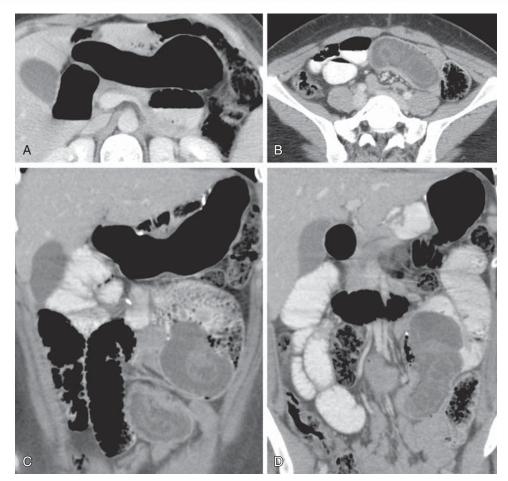
Among these, afferent loop syndrome is a life-threatening condition that is underdiagnosed. The acute syndrome manifests as complete obstruction of the afferent loop (Figure 34-21) and is a surgical emergency with a reported mortality up to 57%. Afferent loop syndrome can be caused by several conditions (Figure 34-22), including the following:

- Entrapment of the afferent loop by adhesions
- Internal hernia through mesocolic defect<sup>13</sup>
- Volvulus of the intestinal segment
- Recurrence of cancer at the anastomosis
- Scarring from marginal ulceration

When the afferent loop is obstructed, pooling of pancreas and bile secretions result in overdistention of the afferent limb, causing a blowout of the duodenal stump. Other potential complications of this entity include ascending cholangitis and pancreatitis.

# SURGERY OF SMALL BOWEL, COLON, AND RECTUM

The complexity of the small bowel, colon, and rectum prevents detailed description of each possible procedure. The purpose of this section is to provide some indications for surgery and their respective radiologic appearances.



**Figure 34-17** Computed tomography (CT) images from a patient with intussusception after Roux-en-Y gastric bypass. A, Axial CT image at the level of the stomach and duodenum; the excluded stomach and duodenum are markedly distended with gas. Axial (B) and coronal (C and D) CT images of the same patient demonstrate an intussusception at the level of the distal anastomosis causing obstructive symptoms.

# Indications, Contraindications, Purpose, and Underlying Mechanisms

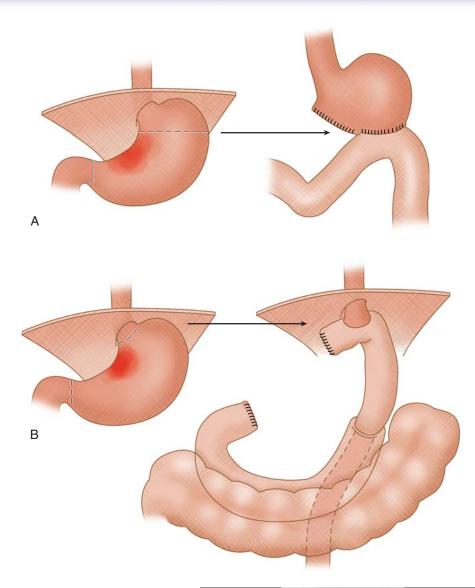
Small bowel surgery is used in cases of refractory inflammatory bowel disease with stricture, small bowel perforation, carcinoma, closed-loop obstruction, severe/strangulating small bowel obstruction, pneumatosis intestinalis, and small bowel fistula, among others. Most of these cases involve a partial resection of the affected segment with anastomosis of the remaining small bowel.

Partial or complete colonic resection (Figure 34-23) is used for conditions such as colon cancer and acute conditions, including perforated diverticulitis, toxic megacolon, severe colitis, severe colonic obstruction, or refractory lower gastrointestinal bleeding. When the entire colon needs to be removed, a total colectomy is performed. A total proctocolectomy removes the colon, rectum, and anus; and an ileal pouch/anal anastomosis or end ileostomy with permanent ileal stoma can be performed. A colostomy is performed when part of the colon needs to be bypassed. If the distal rectum and anal sphincter are preserved, the colostomy can be reversed (colostomy takedown). In cases in which rectum and anal sphincter have been removed, the colostomy is permanent. Surgery involving the rectum is primarily for treatment of rectal carcinoma. For rectal carcinoma, high-resolution MRI is applied as part of the initial evaluation because it can define tumor infiltration into the mesorectal fascia and perirectal lymph nodes.<sup>14,15</sup> These findings are important for presurgical planning because they will determine which of the three major surgical options for rectal cancer can be used: local excision, sphincter-preserving abdominal surgery (low anterior resection), or abdominoperineal resection.

### Expected Appearance on Relevant Modalities

Imaging of the postoperative small bowel is variable and depends on the small bowel involved. In routine postoperative evaluation, a small bowel series should be performed to delineate the postoperative anatomy and functionality of the anastomosis (Figure 34-24). If the surgery is recent and there is a concern of leak or anastomotic breakdown, water-soluble contrast should be used. When reviewing CT images after small bowel resection, the sutures will identify the anastomosis (Figure 34-25). The anastomosis requires special attention because most complications or recurrent disease occur at this site.

After a partial resection, a diverting colostomy may be a temporary or permanent solution. For those who have a



**Figure 34-18** A, Total gastrectomy with a Roux-en-Y anastomosis. B, Subtotal gastrectomy with a Billroth II anastomosis. (*Redrawn from Townsend CM:* Sabiston textbook of surgery, ed 17, Philadelphia, 2004, Saunders, p 1310.)

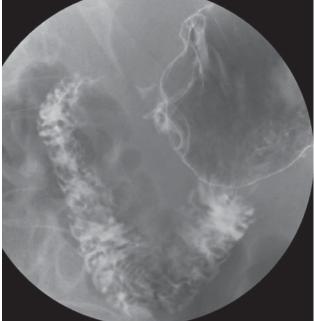
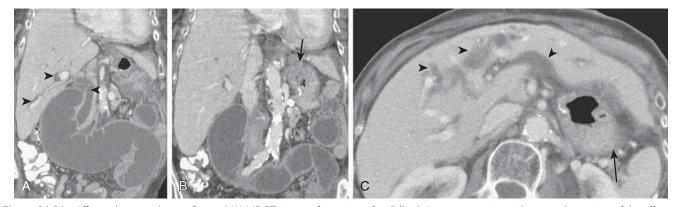


Figure 34-19 Spot image of double-contrast small bowel series from a patient after a Billroth II shows the changes related to antrectomy and end-to-end anastomosis between the remnant stomach and duodenum. Document téléchargé de ClinicalKey.fr par Faculte de Medecine de Tunis août 30, 2016. Pour un usage personnel seulement. Aucune autre utilisation n'est autorisée. Copyright ©2016. Elsevier Inc. Tous droits réservés.



Figure 34-20 Axial multidetector computed tomography images from a patient after Billroth II demonstrate (A) perforation at the duodenal stump (circle) with (B) extraluminal oral contrast filling, a small pocket of gas, and a fluid collection anterior to the liver (arrow).



**Figure 34-21** Afferent loop syndrome. Coronal (A) MDCT image of a patient after Billroth II now presenting with acute obstruction of the afferent limb. Note the dilated common bile duct and proximal intrahepatic biliary tree (*arrowheads*, A and C). Coronal (B) and axial (C) MDCT images on the same patient demonstrate the obstructed afferent limb and increased thickening, nodularity, and heterogeneous enhancement (*arrows*) of the stomach secondary to recurrent gastric carcinoma.

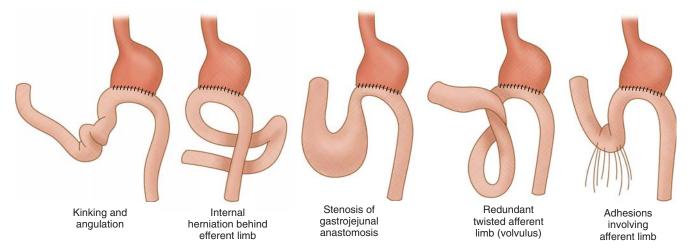
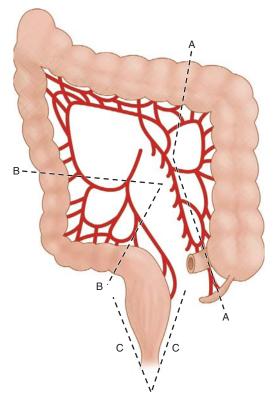


Figure 34-22 Causes of afferent loop syndrome. (*Redrawn from Townsend CM*: Sabiston textbook of surgery, ed 17, *Philadelphia*, 2004, *Saunders*, p 1297.)



**Figure 34-23** Operative procedures for right-sided colon cancer, sigmoid diverticulitis, and low-lying rectal cancer. Right hemicolectomy involves resection of the terminal ileum and colon up to the division of the middle colic vessels (A). Sigmoidectomy consists of removing colon between the partially retroperitoneal descending colon and the rectum (B). Abdominoperineal resection of the rectum is a combined approach through the abdomen and perineum with resection of the entire rectum (C). (Redrawn from Townsend CM: Sabiston textbook of surgery, ed 17, Philadelphia, 2004, Saunders, p 1459.)

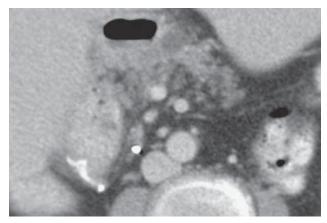
temporary colostomy, surgeons may require a preoperative fluoroscopic evaluation of the colon before reversal. A barium enema (Figure 34-26) is used to verify adequate colonic caliber and the absence of a leak before reanastomosis. For evaluation of the colostomy site, a small catheter (e.g., Foley catheter) may be introduced into the colostomy and contrast instilled (Figure 34-27).

Patients who undergo sphincter-sparing total colectomy may have a Hartmann closure or an ileal pouch/anal anastomosis (Figure 34-28) as options to avoid a permanent stoma, thus allowing patients to have bowel movements per rectum. The ileal pouch/anal anastomosis is a procedure in which a distal ileal loop reservoir and a diverting ileostomy are created initially. Several months later an anastomosis between the ileostomy and the ileal loop is created. Barium enema may be performed using a 14-French Foley catheter to evaluate the patency and anatomy of the pouch (Figure 34-29) and exclude a leak.<sup>16</sup> MDCT is used when acute symptoms related to surgery are suspected. The normal appearance of the ileal pouch/anal anastomosis on MDCT demonstrates two rows of sutures delineating the pouch (Figure 34-30).

Rectal surgery may be complicated because many cases involve rectal cancer or a fistula. In the postoperative setting, the anastomosis should be the focus of the examination. Although MDCT plays an important role for evaluation in the



**Figure 34-24** Spot image of a small bowel series shows surgical staples (*arrowheads*) in the right upper quadrant near the duodenal anastomosis in this patient who underwent partial resection of the duodenum.



**Figure 34-25** Axial multidetector computed tomography image from the patient in Figure 34-24. Note the linear high-density material in the duodenum representing the suture material used for anastomosis after partial resection of the duodenum.

postoperative setting, MRI and positron emission tomography (PET) or PET/CT have become key in patients with rectal cancer, owing to the increased sensitivity of these studies in discovering recurrent disease.

# Potential Complications and Radiologic Appearance

The most dreaded complication is anastomotic breakdown and leakage. If a patient presents with acute symptoms after recent surgery, one must be aware of severe complications such as a fluid collection or perforation. When a Hartmann pouch or an ileal pouch/anal anastomosis has been created, other possible complications include portal vein thrombosis,<sup>17</sup> small bowel obstruction, pouch fistula, pouchitis (Figure 34-31), anastomotic leakage, and pelvic abscess, among others.<sup>16</sup>

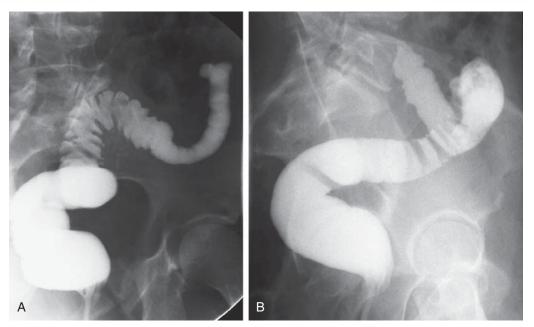
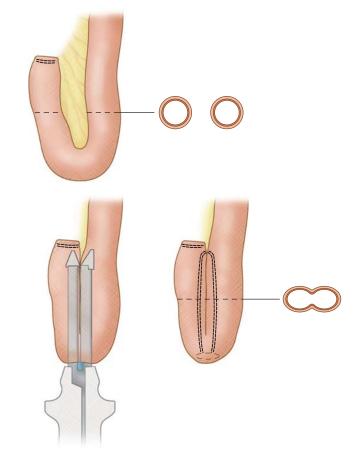


Figure 34-26 Anteroposterior (A) and lateral (B) spot images of a barium enema after partial colonic resection and colostomy show that the excluded colon appears intact with no extraluminal contrast agent or severe stricture.



**Figure 34-27** Oblique spot image after colostomy shows opacification of the colon without evidence of extraluminal contrast medium. Note the catheter (*arrow*) located within the colon that was used to instill the contrast agent into the ostomy.



**Figure 34-28** Creation of an ileal J-pouch with a linear stapler. (*Redrawn from Townsend CM:* Sabiston textbook of surgery, ed 17, *Philadelphia, 2004, Saunders, p 1433.*)



**Figure 34-29** Oblique spot fluoroscopy image demonstrates the typical appearance of an ileal pouch/anal anastomosis with an ileal loop reservoir and rectal anastomosis.



**Figure 34-30** Coronal multidetector computed tomography image from a patient after total colectomy and ileal pouch/anal anastomosis demonstrates two rows of sutures delineating the ileal pouch (*arrows*).

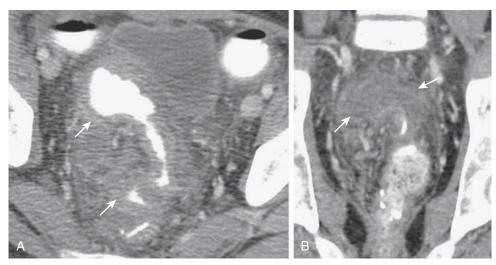


Figure 34-31 Axial (A) and coronal (B) multidetector images from a patient after total colectomy and creation of an ileal pouch demonstrate bowel wall thickening (arrows) at the pouch in this patient diagnosed with pouchitis.

### What the Referring Physician Needs to Know

### **Esophageal Resection**

- Preoperatively and postoperatively, esophagography remains the imaging of choice.
- For preoperative planning, report the exact location of the lesion preoperatively.
- The most common site of complications is the anastomosis.
- In esophageal neoplasms, recurrence commonly occurs at the anastomosis.

### Antireflux Surgery

- Antireflux surgery is an option for refractory cases.
- Preoperative functionality and esophageal length are key in choosing a surgical technique.
- Fundoplication patency and esophageal functionality should be evaluated postoperatively.
- If the fundoplication is longer than 3 cm, the patient may complain of dysphagia.

### **Gastric Bypass**

- Perform an evaluation with water-soluble contrast within the first 24 hours.
- An anastomotic leak is a life-threatening complication.

- Most patients are obese, and image quality could be suboptimal.
- Always evaluate the anastomosis.
- If closed-loop obstruction or an internal hernia is suspected, CT is more helpful.

### Gastrectomy, Billroth I and II Procedures, and Esophagojejunostomy

- Recognize the most common procedures.
- If available, review the performed surgical procedure before imaging.
- Multiplanar MDCT reconstructions are very useful for discerning the anatomy after surgery.
- Acute afferent loop syndrome, duodenal stump leak, and intraabdominal hemorrhage are emergencies.

#### Surgery of Small Bowel, Colon, and Rectum

- Fluoroscopy and MDCT are key in evaluating the postoperative small bowel.
- MRI has taken an important role in the preoperative planning of rectal cancer.
- Radiology plays a critical role in the routine postoperative evaluation of patients with ileal pouch/anal anastomosis.

### **Key Points**

### **Esophageal Resection**

- Barium esophagography is the study of choice.
- Carefully examine the anastomosis.
- If a leak is seen, obtain images at different angles to clearly document this finding.
- In the postoperative setting, CT can be an alternative for initial evaluation of patients with acute symptoms.

#### Antireflux Surgery

- Be aware of complications, some of them may require urgent surgery
- If symptoms of dysphagia or recurrent reflux occur, look carefully for a tight or disrupted fundoplication.

### **Gastric Bypass**

- Imaging may be challenging because of body habitus, and radiology equipment needs to be adjusted to acquire adequate images.
- CT and fluoroscopy are complementary evaluations for these patients.

- Review the type of bypass surgery that was performed before imaging.
- CT is the best study for unstable patients.
- Gastrectomy, Billroth I and II Procedures, and Esophagojejunostomy
- Gastrectomy is a treatment option for esophageal cancer and intractable ulcers.
- MDCT is essential in evaluating patients after gastrectomy who present with acute symptoms.
- Communicate urgent findings of postsurgical complications.

### Surgery of Small Bowel, Colon, and Rectum

- Fluoroscopy is useful for depicting anatomy and functionality of the postoperative bowel.
- Suture lines on MDCT are useful to identify the anastomosis and for its evaluation.
- MRI and PET/CT play a key role in the initial preoperative evaluation of rectal carcinoma and in follow-up studies for evaluation of recurrent disease.

### SUGGESTED READINGS

- Beets-Tan RGH, Geerard L, Beets GL: Rectal cancer: review with emphasis on MR imaging. Radiology 232:335-346, 2004.
- Canon CL, Morgan DE, Einstein DM, et al: Surgical approach to gastroesophageal reflux disease: what the radiologist needs to know. Radiographics 25:1485-1499, 2005.
- Kim KW, Choi BI, Han JK, et al: Postoperative anatomic and pathologic findings at CT following gastrectomy. Radiographics 22:323-336, 2002.
- Kim TJ, Lee HK, Kim KH, et al: Postoperative imaging of esophageal cancer: what chest radiologists need to know. Radiographics 27:409-429, 2007.
- Kim SY, Lee KS, Shim YM, et al: Esophageal resection: indications, techniques, and radiologic assessment. Radiographics 21:1119-1137, 2001.

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### REFERENCES

- Kim SY, Lee KS, Shim YM, et al: Esophageal resection: indications, techniques, and radiologic assessment. *Radiographics* 21:1119–1137, 2001.
- Kim TJ, Lee HK, Kim KH, et al: Postoperative imaging of esophageal cancer: what chest radiologists need to know. *Radiographics* 27:409– 429, 2007.
- Orlando RC: Reflux esophagitis. In Yamada T, editor: *Textbook of Gastroenterology*, Philadelphia, 1995, JP Lippincott, p 1214.
- Canon CL, Morgan DE, Einstein DM, et al: Surgical approach to gastroesophageal reflux disease: what the radiologist needs to know. *Radiographics* 25:1485–1499, 2005.
- Baker ME, Einstein DM, Herts BR, et al: Gastroesophageal reflux disease: integrating the barium esophagram before and after antireflux surgery. *Radiology* 243:329–339, 2007.
- Karlsson J, Sjöström L, Sullivan M: Swedish obese subjects (SOS): an intervention study of obesity: two-year follow-up of health-related quality of life (HRQL) and eating behavior after gastric surgery for severe obesity. *Int J Obes Relat Metab Disord* 22:113–126, 1998.

- 7. Narbro K, Nagren G, Jonsson E, et al: Pharmaceutical costs in obese individuals: comparison with a randomly selected population sample and long-term changes after conventional and surgical treatment: the SOS intervention study. *Arch Intern Med* 162:2061, 2002.
- Nguyen NT, Goldman C, Rosenquist CJ, et al: Laparoscopic versus open gastric bypass: a randomized study of outcomes, quality of life, and costs. *Ann Surg* 234:279–289, 2001.
- 9. Lujan JA, Frutos MD, Hernandez Q, et al: Laparoscopic versus open gastric bypass in the treatment of morbid obesity: a randomized prospective study. *Ann Surg* 239:433–437, 2004.
- Fleser PS, Villalba M: Afferent limb volvulus and perforation of the bypassed stomach as a complication of Roux-en-Y gastric bypass. Obes Surg 13:453–456, 2003.
- 11. Jemal A, Siegel R, Ward E, et al: Cancer statistics, 2007. CA Cancer J Clin 57:43–66, 2007.
- Kim KW, Choi BI, Han JK, et al: Postoperative anatomic and pathologic findings at CT following gastrectomy. *Radiographics* 22:323–336, 2002.

- Smith C, Dezie DJl, Kubicka RA: Evaluation of the postoperative stomach and duodenum. *Radiographics* 14:67–86, 1994.
- 14. Beets-Tan RGH, Beets GL: Rectal cancer: review with emphasis on MR imaging. *Radiology* 232:335–346, 2004.
- Vliegen RFA, Beets GL, Lammering G, et al: Mesorectal fascia invasion after neoadjuvant chemotherapy and radiation therapy for locally advanced rectal cancer: accuracy of MR imaging for prediction. *Radiology* 246:454–462, 2008.
- Alfisher MM, Scholz FJ, Roberts PL, et al: Radiology of ileal pouch-anal anastomosis: normal findings, examination pitfalls, and complications. *Radiographics* 17:81–98, 1997.
- Stocchi L, Nelson H, Sargent D, et al: Impact of surgical and pathologic variables in rectal cancer: a United States community and cooperative group report. J Clin Oncol 19:3895, 2001.

# 35 Imaging of the Liver

JOSEPH R. GRAJO

### Ultrasound

### TECHNICAL ASPECTS

Ultrasound is a widely accessible, noninvasive imaging method that has many advantages over other imaging methods. It is portable and relatively inexpensive with high spatial and temporal resolution. It does not involve ionizing radiation and can be repeated frequently. Despite increased use of other imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI), ultrasound remains, in many settings, the first-line imaging technique for the liver and bile ducts. Indications for liver sonography include screening for pathologic processes, diagnosis, and guidance for interventional procedures.<sup>1-3</sup>

### Technique

**Patient Preparation and Positioning.** Whenever possible, 4to 6-hour fasting is desirable, not only to allow the gallbladder to distend but also to reduce the artifacts from bowel gas that interfere in the visualization of the left hepatic lobe. However, in the acute setting or in patients with an unstable clinical status, preparation is not a prerequisite.

A curvilinear probe of 3 to 5 MHz is generally effective for optimal evaluation of the liver. However, in small adults or children when body penetration is not an issue, a linear probe of higher frequency such as 7.5 to 10 MHz is preferred.

Generally, a supine or right anterior supine position allows assessment of the entire liver. However, if excessive overlying bowel gas from the colon or stomach is present, changing the patient's position to the right anterior oblique or left anterior oblique might help to displace bowel gas.

**Scanning Approach and Anatomic Overview.** To adequately scan the parenchyma of the liver and adequately localize a lesion, it is necessary to acknowledge the hepatic segmental nomenclature and separating landmarks.

The majority of the liver parenchyma lies above the costal margin. A subcostal approach with superior angulation allows a good overview of the parenchyma. Intercostal scanning can be helpful to visualize the subphrenic space.

The approaches generally used are those in the longitudinal and transverse planes (Figures 35-1 and 35-2).

When the lower segments of the right lower lobe have not been adequately visualized on the previously mentioned scanning orientations, the patient can be placed slightly on the left, for a left anterior oblique approach. In this setting, the transverse colon and the duodenum are displaced to the midline of the abdomen, allowing better visualization of the right lobe. If the described scans still do not allow good visualization of the parenchyma and vascular structures, the patient can be placed in the left lateral decubitus position.

### NORMAL ANATOMY

### **Relevant Morphologic Features**

Each hepatic segment should be carefully evaluated in sagittal and transverse projections. The operator should assess for liver size, contours, echogenicity, and focal masses.

The normal liver size is difficult to determine on ultrasound. It has been estimated that a longitudinal diameter of 16 cm at the midclavicular line can indicate hepatomegaly. However, it is important to consider anatomic variants that can simulate hepatomegaly, such as Riedel's lobe.<sup>4</sup>

The normal echogenicity of the liver parenchyma is homogeneously mid-echogenic, slightly hypoechoic compared with the spleen, and hyperechoic to isoechoic with respect to the renal cortex. When diffuse abnormal parenchymal echogenicity is encountered, diffuse pathologic processes are suggested.

The border of the liver should be smooth. If nodular or irregular borders are present, cirrhosis or diffuse metastatic infiltration is suggested. It is important to look for small or focal outpouchings of the liver contour and to not dismiss the presence of any focal isoechoic subcapsular lesion, such as focal nodular hyperplasia (FNH), some metastases, and small hepatocellular carcinomas. Therefore, to detect poorly conspicuous lesions, it is important to look for secondary signs, such as deformation of the liver contour, compression of vascular structures, and displacement of the bile ducts and gallbladder.

The portal vein, as well as both of its branches, the hepatic veins, and the hepatic artery should be assessed for thrombosis with color Doppler imaging. Differentiating portal veins and hepatic veins can be difficult. The portal triad contains a branch of the portal vein, hepatic artery, and bile duct, contained within connective tissue, giving the portal veins a more echogenic wall, which hepatic veins do not have.<sup>4,5</sup>

### Normal Hemodynamics

The liver receives a dual blood supply from the portal vein and the hepatic artery. The portal vein supplies approximately 75% of the blood flow, carrying partially oxygenated venous blood from the bowel and spleen. Its intrahepatic portion can be identified within the porta hepatis adjacent to the hepatic artery and common hepatic duct. It is relatively unaffected by the systemic pressure changes from the cardiac cycle, and therefore

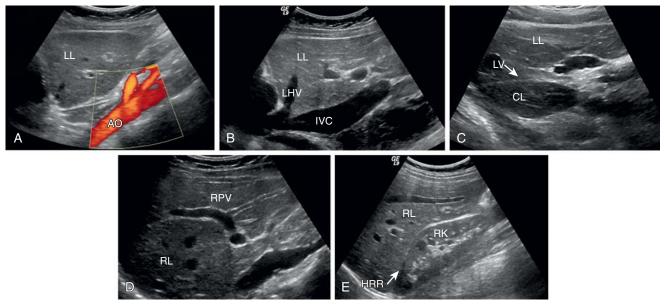


Figure 35-1 A to E, Longitudinal planes of scanning and anatomic landmarks.

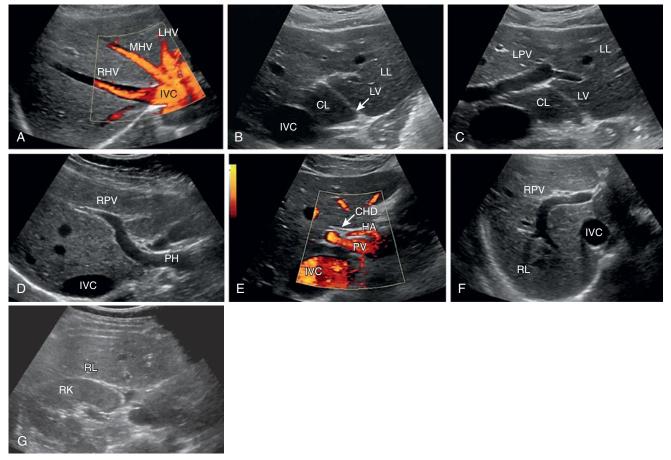
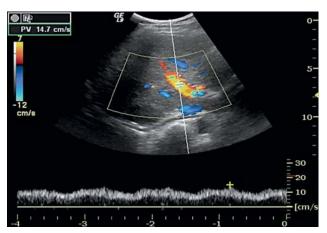
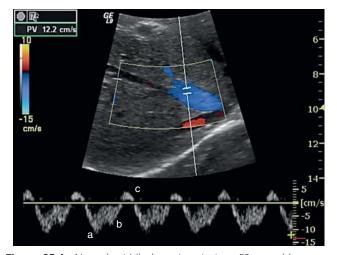


Figure 35-2 A to G, Transverse planes of scanning and anatomic landmarks.

Reversal of blood flow within the main portal vein or its branches, from the normal hepatopetal to hepatofugal direction away from the liver parenchyma, can be a sign of portal hypertension and is more often present in patients with advanced hepatic disease. The hepatic veins drain into the inferior vena cava near the right atrium, and the flow depends on the rightsided heart cycle. The flow pattern is triphasic, consisting of two anterograde waveforms corresponding to atrial diastole and ventricular systole as well as one retrograde pulse secondary to the right-sided heart contraction of atrial systole (Figure 35-4). The main hepatic artery runs anterior to the main portal vein within the porta hepatis. It provides only 20% to 30% of the liver parenchyma circulation, but it is the main supplier to the



**Figure 35-3** Normal portal vein in a healthy 27-year-old woman. Color and duplex Doppler image demonstrates normal hepatopetal portal flow with venous monophasic waveform and minimal respiratory cycling.



**Figure 35-4** Normal middle hepatic vein in a 29-year-old woman. Color and duplex Doppler image demonstrates normal triphasic flow. *a*, Atrial diastole; *b*, ventricular systole; *c*, atrial systole.

biliary tree. The normal hepatic flow pattern is a low-resistance arterial waveform with continuous well-maintained anterograde diastolic flow (Figure 35-5). The normal systolic velocity measures 30 to 40 cm/s with a diastolic velocity of 10 to 15 cm/s. The resistive index in the hepatic artery varies from 0.55 to 0.8<sup>-7.8</sup>

### Diffuse Liver Disease

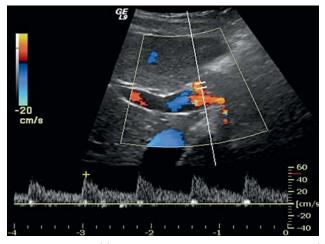
In many instances, imaging is used to determine the cause of diffuse liver disease, which can be caused by diverse pathologic processes. Ultrasound, although nonspecific, is generally the first-line modality for assessment of the liver parenchyma, with a reported sensitivity ranging from 56% to 89% in detecting abnormalities.<sup>9</sup>

Two patterns of diffuse liver abnormalities have been reported. The most common pattern, the "bright liver," has been reported in fatty infiltration, chronic hepatitis, and cirrhosis. In this setting, the liver exhibits increased echogenicity and reduced penetration of the sound beam with relatively decreased definitions of portal venules. In the second pattern, in which the parenchyma manifests decreased echogenicity, there is accentuation of the portal venues structures. This is often seen in the setting of acute hepatitis, leukemia, and a few other diseases. According to the findings, the severity of the disease can be categorized into mild, moderate, or severe.<sup>10</sup>

### **Computed Tomography**

### **TECHNICAL ASPECTS**

The advent of multidetector computed tomography (MDCT) scanners has led to alteration and improvement of various CT applications and protocols. Scanners are now capable of producing images as thin as 0.625 mm of isotropic voxel resolution, which improves the detection of liver lesion conspicuity and, more importantly, the detection and characterization of small malignant tumors, with better characterization of the benign pathologic processes and the details of vascular flow.<sup>11,12</sup> Because of reduction in the hepatic arterial phase acquisition time and thin collimation provided from MDCT, image postprocessing and CT angiography are much better, with a significant reduction in volume averaging artifacts.<sup>13,14</sup>



**Figure 35-5** Normal hepatic artery in an asymptomatic 30-year-old woman. Color and duplex Doppler image of the porta hepatis shows a normal low-resistance arterial spectral pattern.

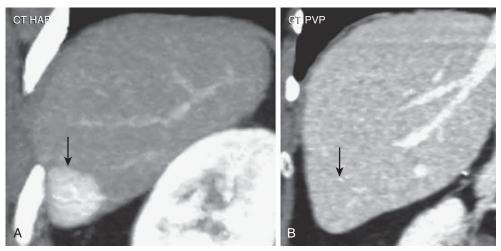
### Dual-Phase Imaging

Normally, 75% of liver blood supply comes from the portal venous system and the remaining 25% comes from the hepatic arterial system.<sup>15</sup> When iodinated contrast media is injected rapidly (3 to 5 mL/s), the hepatic arterial system is usually the first to opacify—that is, 20 to 30 seconds followed by the portal venous system (50 to 60 seconds); hepatic venous opacification occurs at 65 to 75 seconds. Depending on the scan delay used to acquire the hepatic arterial phase, the images can show mere opacification of hepatic arterial anatomy without parenchymal enhancement (arterial only phase) or with parenchymal enhancement (arterial dominant phase). This is a vital consideration in tailoring MDCT protocols because hypervascular lesions are best visualized in the arterial dominant phase. In other words, better hepatic parenchymal contrast in the hepatic

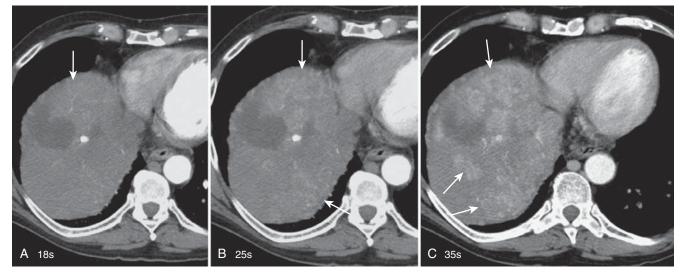
arterial phase is produced as a consequence of better enhancement of only the hypervascular lesions in relation to the rest of the hepatic parenchyma (Figure 35-6). On the other hand, hypovascular lesions are more evident on the portal venous phase and usually appear hypodense compared with the contrast enhancement of background liver parenchyma.<sup>16</sup> Hence, dual-phase CT of the liver is performed in the arterial dominant and portal venous phases (Figure 35-7). The use of triple-phase scanning (arterial only and dominant with portal venous phase acquisitions) has been discouraged because there is no significant benefit to obtaining arterial only scans. Moreover, there is the disadvantage of increased radiation dose to the patient.

### Contrast Volume

For optimal image quality, 120 to 150 mL of contrast media of 300 mgI or 100 to 120 mL of 370 mgI is recommended.  $^{17}$ 



**Figure 35-6** Hepatocellular carcinoma (HCC). Coronal reformatted computed tomography images of the liver showing intensely enhancing HCC (arrow) in the arterial phase (A). Note better contrast in the lesion to the parenchyma in this phase in comparison to portal venous phase image (B), in which the lesion is not appreciated (arrow). (From Sahani DV, Singh AH: Dual-phase liver MDCT. In Mannudeep K, Saini S, Rubin G, editors: MDCT from protocols to practice, Berlin, 2006, Springer-Verlag, pp 83–92. Reprinted with permission.)



**Figure 35-7** Improved detection of hepatocellular carcinoma in the late arterial phase. Serial images obtained at 18 seconds (A), 25 seconds (B), and 35 seconds (C) after initiation of contrast injection. Although arterially enhancing lesions are seen on images A and B, better enhancement and more lesions (*arrows*) are evident on the late arterial phase image (C). (*From Sahani DV, Singh AH: Dual-phase liver MDCT. In Mannudeep K, Saini S, Rubin G, editors: MDCT from protocols to practice, Berlin, 2006, Springer-Verlag, pp 83–92. Reprinted with permission.*)

Patients with cirrhosis require a higher volume of contrast agent to achieve optimal parenchymal enhancement owing to decreased liver perfusion, but authorities have discouraged the use of any iodinated contrast above 150 mL.

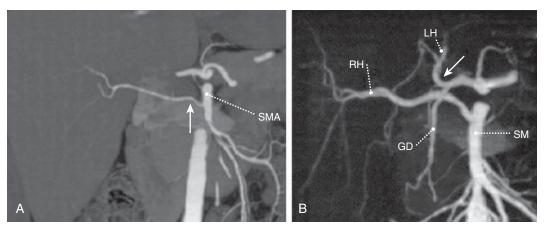
Injection rate is a crucial factor while considering the amount of contrast volume that needs to be injected. Although an injection rate of 3 to 4 mL/s may be used for injection of 300 mgI, it is advisable to increase the injection rate to 4 to 5 mL/s to ensure optimal opacification and contrast volume in desired structures. Increasing the injection rate of less volume of high concentration of iodinated contrast media, in other words, compensates for the volume compromise. Thus, with use of higher or lower iodine concentration contrast media, appropriate adjustments in injection rate and contrast volume are needed.

### Technical Aspects for Image Postprocessing

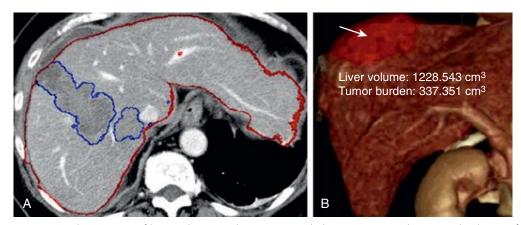
The advent and advances in MDCT technology have helped immensely in exploring dimensions of image postprocessing (Figure 35-8). The thinner the axial sections, the better is the image quality; a scan thickness of 2.5 mm is appropriate for ensuring optimal three-dimensional (3D) postprocessing, even for advanced applications such as liver and tumor volume estimations and performance of computer-assisted techniques (Figure 35-9). A reduction in scan length wherever possible should be employed, and appropriate calibration of kilovoltage peak and milliampere settings should be chosen to reduce radiation dose delivery to the patient while simultaneously ensuring absence of image noise.

### Postprocessing Techniques for Computed Tomography Angiography

Advances in MDCT scanners have propelled the benefits of image postprocessing and extended its applicability to the clinical scenario.<sup>18,19</sup> The most frequently employed postprocessing applications are common algorithms such as maximum intensity projection (MIP) and volume rendering (VR), which provide justification to the thin acquisitions if liver CT angiograms are performed for purposes of preoperative planning of tumor and donor surgeries and placement of intraarterial



**Figure 35-8** Multidetector computed tomography–maximum intensity projection images (MIPs) from a 43-year-old man showing hepatic arterial anatomy. A, Accessory origin of right hepatic artery (*arrow*) is seen from the superior mesenteric artery (*SMA*). **B**, A background-subtracted MIP highlighting the gastroduodenal (*GD*), the right hepatic (*RH*), the left hepatic (*LH*) origin from the proper hepatic artery (*arrow*) and the superior mesenteric artery (*SM*). (*A*, from Sahani DV, Singh AH: Dual-phase liver MDCT. In Mannudeep K, Saini S, Rubin G, editors: MDCT from protocols to practice, Berlin, 2006, Springer-Verlag, pp 83–92. Reprinted with permission.)



**Figure 35-9** Computer-assisted generation of liver and tumor volumes using multidetector computed tomography data set from a 42-year-old male patient with hepatocellular carcinoma. A, Segmentation of liver (*red*) and tumor (*blue*) by detection of their margins. B, Automated generation of liver and tumor volumes based on segmentation of structures. The area of tumor is displayed in *red (arrow)*.

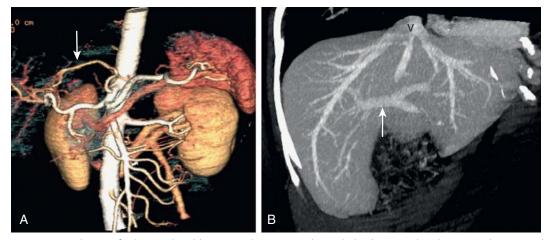
chemotherapy pumps. Certain advanced applications such as volumetry and computer-assisted detection have recently gained importance owing to technical advances in liver and tumor segmentation techniques, which complement a busy workflow.

Preoperative knowledge of arterial variants can help avoid complications such as inadvertent ligation or injury of various hepatic arteries, hepatic ischemia, hemorrhage, and biliary leak. Variations in celiac axis anatomy with respect to liver supply are common, and preoperative knowledge is especially important in obese patients who have large amounts of lymphatic and fatty tissue in the duodenal hepatic ligament and the porta hepatis.<sup>20</sup> The techniques usually used for CT angiography of the liver are MIP and VR.<sup>21</sup> Optimal delay time, contrast concentration, and opacification are important. MIP is the most frequently employed postprocessing algorithm for the liver vascular anatomy and its variants, which is crucial for preoperative planning (Figures 35-10 and 35-11). It is essential to visualize and report subtle vascular details in relation to the liver's

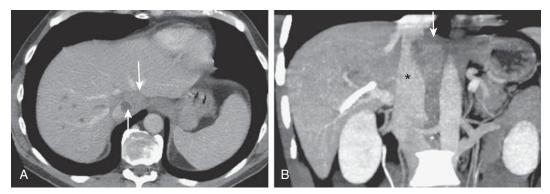
segmental anatomy, such as the arterial branch to segment 4. In addition, 3D vascular maps also help surgeons increase their preoperative confidence with localization of such smalldiameter vessels, which is essential for prevention of bleeding complications. VR has an additive effect to the MIP images, but at times visualization of very thin diameter vessels may pose a problem. However, as a routine practice, it is advisable for radiologists to view CT angiographic liver studies by reviewing axial data sets followed by MIPs acquired in axial and coronal planes and eventually the 3D vascular maps to confirm their findings. For referring physicians, 3D image maps of MIPs and VR are optimal for providing semblance to the intraoperative picture (Figure 35-12).<sup>22</sup>

### Advanced Postprocessing Applications

Most workstations are now equipped to provide advanced postprocessing application tools for segmentation, volume estimations, and virtual endoscopy. Segmentation of the liver on CT to estimate total liver volume, partial liver lobe volume, and tumor volumes is an advanced application, the automation of



**Figure 35-10** Preoperative planning for living related liver transplantation. Color-coded volume-rendered computed tomography angiography image (A) demonstrates an anomalous origin of the left hepatic artery from the left gastric artery (*arrow*). A venous phase, subvolume maximum intensity projection image in the coronal oblique plane (B) demonstrates normal portal and hepatic venous anatomy (*arrow*). (*From Sahari DV*, *Singh AH: Dual-phase liver MDCT. In Mannudeep K, Saini S, Rubin G, editor:* MDCT from protocols to practice, *Berlin, 2006, Springer-Verlag, pp 83–92. Reprinted with permission.*)



**Figure 35-11** Preoperative planning of cholangiocarcinoma. A, Contrast-enhanced axial image shows an infiltrative mass in the dome of the liver with suspicion of inferior vena cava invasion (*arrows*) seen as a filling defect. **B**, However, the corresponding coronal subvolume maximum intensity projection image confirmed only extrinsic compression and not invasion of the inferior vena cava (*asterisk*) by the tumor (*arrow*) and therefore surgery was feasible. (*From Sahani DV, Singh AH: Dual-phase liver MDCT. In Mannudeep K, Saini S, Rubin G, editors: MDCT from protocols to practice, Berlin, 2006, Springer-Verlag, pp 83–92. Reprinted with permission.)* 

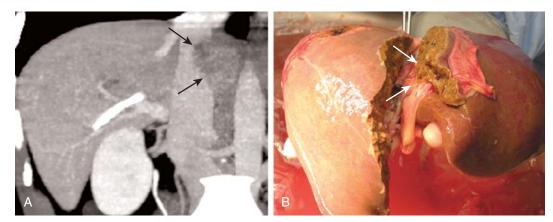
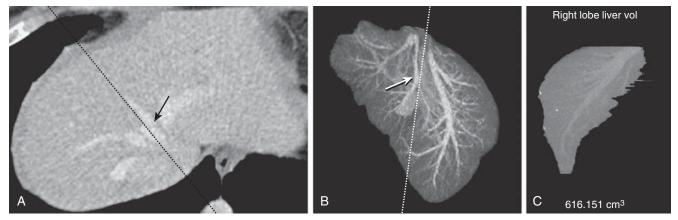


Figure 35-12 Images from a 49-year-old man with cholangiocarcinoma. A, Coronal multidetector computed tomography reformatted image shows invasion of the intrahepatic inferior vena cava by the tumor (arrows). B, An intraoperative picture of partially resected liver tumor confirming the same finding (arrows).



**Figure 35-13** Images from a 38-year-old female liver donor illustrating the technique for generation of partial liver volumes. Axial multidetector computed tomography (MDCT) image (A) and a coronal volume-rendered MDCT posterior reconstruction (B) show the manually computer-generated intervening plane that divides the liver into two parts and is parallel to the right side of the middle hepatic vein (*arrow*). This corresponds to the median fissure, which extends from the gallbladder fossa to the inferior vena cava (Cantlie's line). C, Subsequent generation of right lobe liver volume is shown.

which is being actively investigated (Figure 35-13).<sup>23</sup> Knowledge of total and partial liver volumes is important for planning liver transplants, and estimation of liver tumor volumes is a vital indicator for assessing response to chemotherapy and for planning irradiation.<sup>24</sup> Considering the volume of CT cases of such patients, recent work is more focused on automating these advanced postprocessing applications by computer-aided techniques. Virtual CT cholangioscopy refers to navigation through the common bile duct for assessment of calculi and stenosis, but feasibility of this application.<sup>25</sup>

### Dual-Energy Computed Tomography

Dual-energy CT (DECT) is an exciting advance in CT image acquisition and postprocessing, providing radiologists with the ability to improve liver lesion detection and characterization. It offers several potential applications in hepatic imaging previously unavailable with conventional single-energy CT. DECT images are obtained at two distinct energy levels, typically 80 kVp and 140 kVp. This allows for advanced postprocessing of two sets of raw data and the ability to separate materials based on their atomic number. Iodine, water, fat, and calcium can therefore be separated to generate material decomposition (or material density) images. Virtual monochromatic images also can be created to simulate a scan obtained from a monochromatic beam (between 40 and 140 keV), which can be customized to balance contrast and noise.

Increased lesion conspicuity is of particular interest in liver imaging, where detection and characterization can have a big impact on patient imaging, particularly in the oncologic setting. Early experience with DECT has shown that liver lesions are more conspicuous on iodine images obtained at lower energy levels (e.g., 80 kVp) compared to single-energy CT (e.g., 120 kVp).<sup>26-28</sup> In addition to more easily identifying liver lesions, DECT offers potential for improved lesion characterization. Lesions previously deemed "too small to characterize" on conventional CT can potentially be differentiated as benign cysts or enhancing lesions based on their attenuation on iodine images. Enhancing lesions can be further distinguished based on their pattern of dynamic enhancement, such as arterial



**Figure 35-14** Dual energy computed tomography scan of a 28-yearold woman with focal nodular hyperplasia (FNH). Color overlay iodine image in the arterial phase demonstrates iodine uptake within the segment 3 mass (*arrow*), compatible with arterial enhancement seen in FNH.

enhancement in benign lesions such as FNH (Figure 35-14). Lesion characterization can be further advanced by using water (or virtual unenhanced) images to identify hemorrhage or calcification within a lesion and fat images to evaluate for fat content.

Beyond assessment of liver lesions, DECT can aid in hepatic imaging by helping differentiate tumor thrombus from bland thrombus (i.e., in the setting of hepatocellular carcinoma). Enhancing thrombus can be more easily detected as uptake on iodine images. This has important implications on tumor staging, including determination of liver transplant candidacy. Additional areas of current research include quantification of liver fat content on fat material decomposition images and grading of fibrosis on iodine images based on pooling of iodine in chronic liver disease.

### **Magnetic Resonance Imaging**

### INDICATIONS

There are many indications for performing MRI of the liver. The American College of Radiology practice guideline highlights the most common recommended indications.<sup>29</sup> MRI of the liver is a clinically proved and valuable tool in the detection, evaluation, and monitoring of focal and diffuse liver disease.

### **TECHNICAL ASPECTS**

MRI of the liver can be performed using different hardware and software configurations that are available to the radiologist. Recommendations for performing an optimal examination include using magnets with field strengths of 1.5 T or higher, gradient rise times of at least 600 ms, torso phased-array coils, MR-compatible power injectors, oxygen availability for patients with breath-holding difficulty, and a dedicated 3D workstation to review the images and perform advanced postprocessing techniques. In the past few years, there has been tremendous progress in the development of hardware and sequence design, high-performance gradients, parallel imaging techniques, and advanced torso phased-array coils, enabling faster scanning and improved image quality.

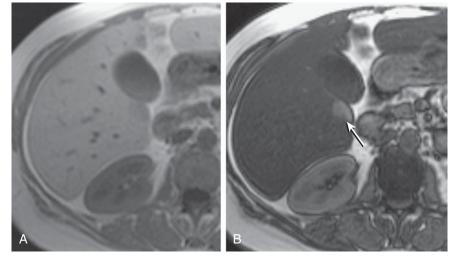
Faster scanning has many benefits. The primary benefit is the reduction of scan times to fit within a breath-hold (<25 seconds). By acquiring images during a breath-hold, respiratory motion artifact is greatly reduced. Technologists should practice breath-holding with the patient before the examination to familiarize him or her with the technique and improve compliance. Suspending respiration at end-expiration results in more reproducible levels of lung volume and permits accurate slab selection and ability to perform subtraction imaging with better registration of precontrast and postcontrast images.

### T1-Weighted Imaging

Short repetition time (TR) and short echo time (TE) are used to obtain T1 weighting. Normal hepatic parenchyma has a relatively short T1 relaxation time of approximately 575 ms at 1.5 T and demonstrates signal intensity that is isointense or hyperintense to muscle and hyperintense to spleen.<sup>30</sup> Most focal hepatic lesions, including cysts, hemangiomas, hepatocellular carcinomas, and metastases, possess longer T1 relaxation times and consequently appear hypointense relative to hepatic parenchyma on T1-weighted images. Other lesions, such as fatcontaining lesions (adenomas and some hepatocellular carcinomas), hemorrhagic lesions, melanin-containing lesions, and proteinaceous lesions possess shorter T1 relaxation times and appear hyperintense relative to hepatic parenchyma.

T1-weighted fast/turbo spin echo or spin echo imaging is almost never used for liver imaging owing to a longer acquisition time compared with gradient recalled echo (GRE) sequences. The T1-weighted in-phase and opposed-phase GRE sequence provides T1-weighted images. This sequence, also known as *chemical shift imaging*, is valuable in determining the T1-weighted signal properties of lesions and to detect the presence of microscopic or intravoxel fat within focal and diffuse liver diseases.<sup>31</sup> The difference in the local molecular environment between protons in fat and protons in water results in different precessional frequencies of these protons when they are placed in a uniform magnetic field. At 1.5 T, fat protons will precess approximately 220 Hz slower than water protons. At 3.0 T, fat protons will precess approximately 440 Hz slower than water protons.<sup>32</sup> Although this difference is small compared with the Larmor frequency of protons of approximately 64 MHz at 1.5 T, it is easily exploited to detect the presence of a mixture of fat and water protons within an imaging voxel. At 1.5 T, this difference in precessional frequencies results in fat and water protons being out of phase and in phase at approximately 2.2 and 4.4 ms, respectively. At 6.6 ms, the protons will be out of phase again. Consequently, obtaining dual echoes at these strategic times will enable discrimination of the proton population in an imaging voxel. And, by collecting dual echoes during one acquisition, the registration of images between out-of-phase and in-phase images is optimized.

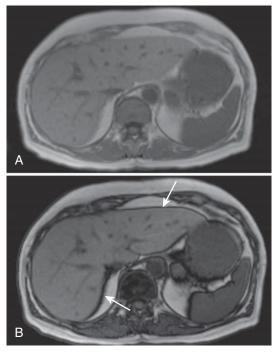
A voxel containing pure fat protons or pure water protons will not demonstrate loss of signal on the opposed-phase sequence because all the protons will precess at the same frequency. However, if there is a mixed population of fat and water protons, there will be loss of signal on the opposed-phase sequence because the number of fat protons will cancel an equal number of water protons (Figure 35-15). The resultant signal



**Figure 35-15** AxialT1-weighted in-phase (A) and out-of-phase (B) images of the liver demonstrate signal loss of the hepatic parenchyma on the out-of-phase image consistent with hepatic steatosis. There is an area of fat sparing adjacent to the gallbladder fossa (*arrow*).

will arise from the absolute value of the difference in number between fat protons and water protons. This means a voxel containing 70% fat protons and 30% water protons will demonstrate an equal amount of signal loss on the opposed-phase sequence as a voxel containing 30% fat protons and 70% water protons (fat/water ambiguity). Consequently, a small degree of signal loss may not necessarily translate into "mild" fatty infiltration; in these cases MR spectroscopy has a role in determining the dominant species.<sup>33</sup> For a voxel containing an equal number of fat and water protons, there will be cancellation of all the protons, resulting in no signal from that voxel. This phenomenon is also responsible for the India ink artifact that occurs at interfaces between water- and fat-containing structures, as commonly seen at the surfaces of abdominal organs (Figure 35-16). The Dixon method also can be applied to obtain fat-only and water-only images in addition to standard in-phase and opposed-phase sequences. These techniques allow for reliable and reproducible quantification of liver fat.<sup>34</sup>

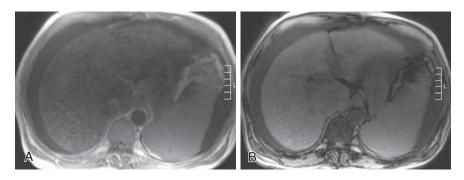
MRI is also effective in detecting iron deposition because of the paramagnetic properties of iron. In the dual-echo sequence, the presence of iron will result in T2\* effects that decrease the signal intensity as the TE is increased. This occurs because of increased dephasing in the region containing iron. Consequently, the second echo will yield lower signal intensity of iron-containing structures. This phenomenon is the reason why out-of-phase images are typically obtained before in-phase images. If the out-of-phase images are obtained after the in-phase images and there is signal loss on the out-of-phase images, it is unclear whether the signal loss occurred secondary to the cancellation of fat and water protons of fatty infiltration or whether there is signal loss from the T2\* effects of iron deposition on this longer TE sequence. By acquiring the out-ofphase images first, fatty infiltration will demonstrate lower signal on the out-of-phase, shorter TE images and iron deposition will demonstrate lower signal on the in-phase, longer TE images (Figure 35-17). Chemical shift imaging allows characterization of focal liver lesions. For example, intracellular lipid may be seen within hepatocellular carcinoma, regenerative nodules, hepatic adenoma, FNH, and focal fatty infiltration.<sup>35</sup>



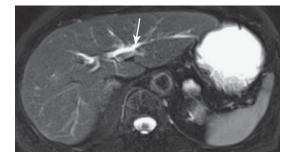
**Figure 35-16** Axial T1-weighted in-phase (A) and out-of-phase (B) images of normal liver demonstrate no signal loss of the hepatic parenchyma on the out-of-phase image. There is a *dark line* at the fat/ water interfaces (India ink artifact, *arrows*) on the out-of-phase image.

### T2-Weighted Imaging

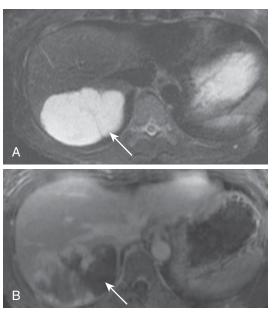
Long repetition time (TR) and long echo time (TE) are used to obtain T2 weighting. T2-weighted sequences are valuable for detecting lesions and pathologic processes. Most normal tissues possess short T1 and T2 values (Figure 35-18). Benign liver lesions such as cysts and hemangiomas (Figure 35-19), malignant lesions such as hepatocellular carcinoma and hepatic metastases (Figure 35-20), and fluid such as edema



**Figure 35-17** Axial T1-weighted in-phase (A) and out-of-phase (B) images of the liver in a patient with cirrhosis demonstrate signal loss of the hepatic parenchyma on the in-phase image consistent with diffuse iron deposition. There is associated perihepatic and perisplenic ascites.



**Figure 35-18** Axial fat-suppressed T2-weighted image through the normal liver and spleen. Note the relative low signal intensity of the liver parenchyma compared with that of the spleen (*arrow*). Most focal liver lesions have higher signal intensity than normal liver parenchyma, which increases their conspicuity on this sequence. There is minimal intrahepatic biliary distention in this patient after cholecystectomy.



**Figure 35-19** Hepatic hemangioma. Axial fat-suppressed T2-weighted image (A) demonstrates a large hyperintense lesion in the right hepatic lobe (arrow). Axial postcontrast fat-suppressed T1-weighted image (B) obtained during the portal venous phase demonstrates the characteristic nodular peripheral enhancement of the hepatic hemangioma (arrow).

and ascites possess long T1 and T2 values, which increase their conspicuity.

Echo-train imaging (fast spin echo [FSE] or turbo spin echo [TSE] sequences) provides T2-weighted images through the acquisition of multiple echoes to spatially encode an image after



**Figure 35-20** Axial T2-weighted image demonstrating multiple hyperintense hepatic metastases of both hepatic lobes *(arrows)*.

a single excitation pulse.<sup>30</sup> The echo train length (ETL), or number of echoes acquired, is a measure of the efficiency of the echo train pulse sequence compared with conventional spin echo sequences. The higher the echo train length, the shorter the acquisition time. The ETL can be adjusted so that acquisition times are decreased sufficiently to fit a breath-hold. Breath-hold imaging results in fewer motion-related artifacts. Frequency-selective fat suppression is performed to improve image contrast and conspicuity of lesions and pathologic processes. The drawback of this sequence compared with conventional spin-echo sequences is decreased image contrast owing to the combined T1- and T2-weighted imaging effects of using a range of echo times. Using longer ETLs will result in a longer effective TE and in greater T2 weighting. The half-Fourier acquisition single-shot turbo spin echo sequence (half-Fourier acquisition single-shot turbo spin echo [HASTE], Siemens) is a long echo train imaging technique that enables acquisition of T2-weighted images in less time than conventional spin echo imaging. HASTE is a single-shot technique that fills just over half of k space in one echo train.<sup>30</sup> The remainder of k space is mathematically filled based on the symmetric properties of k space. The acquisition times are generally less than 1 second, permitting essentially motion-free T2-weighted images. This technique is useful in uncooperative patients or patients who cannot adequately hold their breath. The main drawback, however, is the low signal-to-noise ratio. This decreases the sensitivity for liver lesion detection but allows for quick assessment of the biliary tree (Figure 35-21).

### Contrast-Enhanced Imaging

The 3D T1-weighted fat-suppressed GRE sequence, performed before and after contrast administration, is the workhorse of liver MR secondary to its high spatial and temporal resolution.<sup>36-38</sup> This volumetric acquisition allows accurate detection and characterization of focal and diffuse liver diseases and accurate depiction of the segmental, vascular, and biliary anatomy with high precision to guide further therapeutic management.<sup>37,39</sup> The advantages over 2D imaging include thinner sections, no gaps between slices (thereby minimizing partial volume effects), higher signal-to-noise ratios, and nearly isotropic voxels (enabling advanced 3D image postprocessing). Contrast-to-noise ratios may be improved by implementing fat-suppression techniques. The complete volume of the liver may be imaged within a single breath-hold to minimize respiratory and other motion artifacts and allow advanced 3D image postprocessing. The volumetric interpolated breath-hold examination (VIBE) was developed on the Siemens platform to serve this purpose.<sup>36</sup> Contrast-enhanced images are essential in detecting and characterizing focal and diffuse liver diseases. Image acquisition during the hepatic arterial, portal venous, and equilibrium phases (Figure 35-22), and a delayed phase for certain lesions, can demonstrate enhancement patterns that are characteristic of particular liver lesions, allowing for their accurate diagnosis or, at least, narrowing of the differential



**Figure 35-21** Coronal half-Fourier acquisition single-shot turbo spin echo sequence (HASTE) image demonstrates the normal common bile duct (*long arrow*) and distal pancreatic duct (*short arrow*).

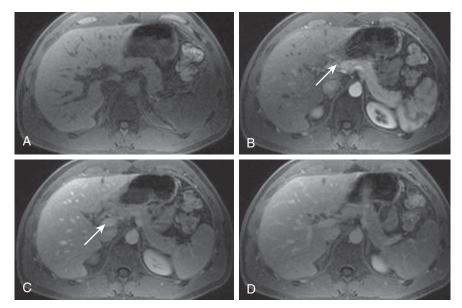
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diagnosis.<sup>38</sup> Hypervascular liver lesions include hepatocellular carcinoma, FNH, hepatic adenoma, hypervascular metastases, and hemangioma. In the case of hemangioma, the arterial phase images may demonstrate the characteristic discontinuous nodular peripheral enhancement to confirm the diagnosis (see Figure 35-19). Delayed-phase enhancing liver lesions include cholangiocarcinoma, the central scar of FNH, hepatic fibrosis, and peliosis hepatis. The enhancement pattern of different liver lesions is discussed in further detail elsewhere in this text.

### Gadolinium Contrast Agents

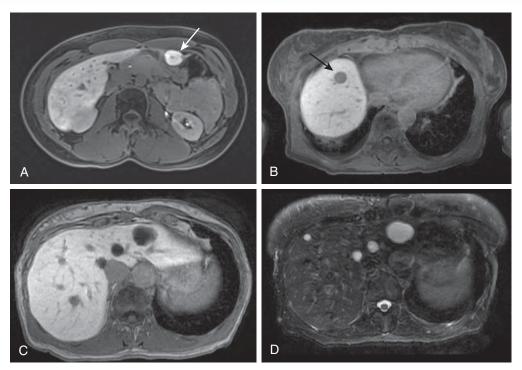
Until recently, contrast-enhanced liver MRI was performed almost exclusively with extracellular gadolinium-based contrast agents (i.e., Magnevist, Gadavist, etc.). Extracellular agents exhibit pharmacokinetics similar to iodinated CT contrast media and are excreted by the kidneys through glomerular filtration. They rapidly diffuse from the intravascular space into the interstitial space with a nonspecific distribution.<sup>40</sup> Within the past decade, hepatobiliary (or hepatocyte-specific) contrast agents (i.e., Eovist, MultiHance) were introduced into clinical practice. In addition to assessing tissue vascularity like extracellular agents, hepatobiliary agents allow assessment of hepatocellular uptake and biliary excretion in delayed phases (8 to 20 minutes). Eovist is actively transported from the sinusoidal space into hepatocytes via organic anion transporting polypeptides. This hepatocyte uptake results in intense hepatic parenchymal enhancement that peaks 20 minutes after injection (Figure 35-23). Eovist is then excreted from the hepatocyte into bile canaliculi via multidrug resistance-associated proteins. Approximately half of the hepatobiliary contrast agent is excreted in this fashion, and the other half is excreted by glomerular filtration (Figure 35-24). Limitations of hepatobiliary agents include a weaker arterial phase of enhancement because of a lower gadolinium dose (approximately one-quarter the concentration of gadolinium compared to that of extracellular agents), lack of the equilibrium phase (which can make evaluation of small hemangiomas challenging), and dependence on liver function (for appropriate hepatocyte uptake).41 Whether extracellular or hepatobiliary agents are considered, the use of

**Figure 35-22** Axial postcontrast threedimensional gradient echo fat-suppressed T1weighted images of the normal liver obtained before (A) and after intravenous contrast administration, during the arterial (B), portal venous (C), and equilibrium phases (D). Note the hepatic artery opacification (*long arrow*) during the arterial phase and the portal veno opacification (*short arrow*) during the portal venous phase.



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**Figure 35-23** Liver lesions on hepatobiliary imaging after Eovist administration. A, Hepatobiliary imaging at 20 minutes in a 28-year-old woman demonstrating uptake in a segment 3 focal nodular hyperplasia (*arrow*), which contains functional hepatocytes. B to D, A 67-year-old woman with breast cancer demonstrating both malignant and benign liver lesions. Twenty-minute hepatobiliary imaging shows lack of uptake in lesions without normal hepatocytes, such as a metastasis (*arrow* in B). Benign lesions such as cysts (left hepatic lesions in C) also show lack of Eovist uptake. Correlation with T2 signal is necessary for differentiating cysts (D) or hemangiomas from metastases.



**Figure 35-24** Coronal fat-saturated postcontrast T1 image at 20 minutes after Eovist administration demonstrating hepatobiliary excretion of contrast into the common bile duct (*short arrow*) and duodenum (*long arrow*).

gadolinium is not recommended in patients with a glomerular filtration rate less than 30 mL/min/1.73 m<sup>2</sup> because of the risk for nephrogenic systemic fibrosis.<sup>42</sup>

### Superparamagnetic Iron Oxide Particles (Ferumoxides)

Superparamagnetic iron oxide (SPIO) particles distribute to hepatic Kupffer cells. Their superparamagnetic properties produce magnetic susceptibility effects with darkening of the liver parenchyma and spleen. This increases lesion-to-liver contrast on T2-weighted images. SPIO-enhanced MRI has been shown to be superior to dual-phase CT in the depiction of colorectal metastases.<sup>43</sup> SPIO particles have been used sequentially with gadolinium chelates in one study session, with a benefit for screening for hepatocellular carcinoma<sup>44</sup> and diagnosis of hepatic fibrosis.<sup>45</sup>

# TECHNIQUE OPTIMIZATION AND NEW DEVELOPMENTS

### Diffusion Weighted Magnetic Resonance Imaging

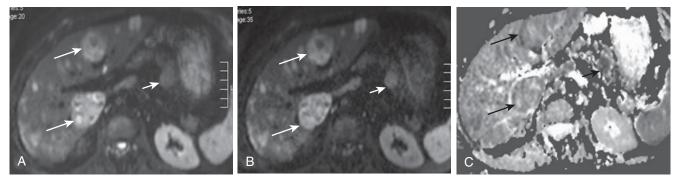
Diffusion weighted MRI (DWI) can be used for in vivo quantification of the combined effects of capillary perfusion and diffusion. DWI has the unique capability of tissue characterization without the need for intravenous contrast, which makes it a potential alternative or adjunct technique to gadoliniumenhanced sequences, owing to the risk for nephrogenic systemic fibrosis in patients with renal insufficiency.

A breath-hold or respiratory-triggered single-shot epiplanar sequence can be used to obtain diffusion weighted images on 1.5- or 3.0-T scanners with phased-array coils and parallel imaging. We typically use b-values of 100 and 600 s/mm<sup>2</sup>; 100 is used for detection and 600 for characterization. DWI has mostly been used for focal liver lesion detection and characterization.46-49 DWI images with low b-values are similar to T2-weighted black blood images, in which the background signal of vessels in the liver parenchyma is suppressed and better lesion conspicuity can be obtained,<sup>50</sup> whereas higher b-values give diffusion information that helps lesion characterization.<sup>48</sup> In addition, it has been shown that apparent diffusion coefficient (ADC) values are higher in benign lesions, compared with malignant lesions (Figure 35-25). A threshold ADC value of less than  $1.5 \times 103 \text{ mm}^2/\text{s}$  for diagnosis of malignant liver lesions has been shown to result in a sensitivity and specificity of 84% and 89%, respectively.48

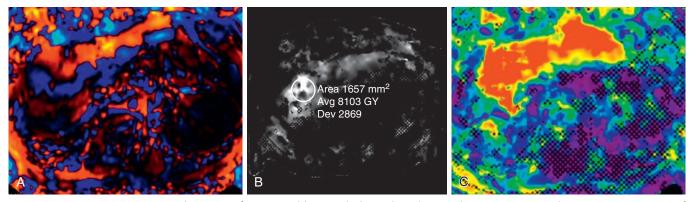
#### Elastography

MR elastography (MRE) is an emerging technique used to evaluate liver stiffness. MRE can help distinguish grades of fibrosis and detect underlying chronic liver disease earlier than conventional CT or MR in patients with hepatitis B, hepatitis C, and nonalcoholic fatty liver disease (NAFLD). NAFLD is a growing epidemic comprising a spectrum of disease involving simple steatosis, steatohepatitis (NASH), and steatohepatitis with cirrhosis.<sup>51</sup> Distinction among these entities is of paramount importance to the referring physician.

MRE image generation involves propagation of mechanical shear waves through the liver, most commonly via an external audio device (active driver) and a passive pneumatic drum (passive driver) overlying the patient's right hepatic lobe. Grayscale and color stiffness maps are created, from which regions of interest (ROI) can be placed to estimate liver stiffness. An ROI is placed in the right lobe to avoid motion artifact in the left lobe caused by cardiac pulsation (Figure 35-26).<sup>51</sup> Most normal livers and livers with simple steatosis have estimated Young's modulus values of less than 2.5 kPa. Chen and colleagues<sup>52</sup> demonstrated an ability to differentiate simple steatosis from NASH with an accuracy of 93% using a cutoff value of 2.74 kPa; Kim and colleagues<sup>53</sup> used a cutoff of 4.15 kPa to detect NASH with advanced cirrhosis with 95.4% accuracy. The value of measuring stiffness in focal lesions is an area of active research.



**Figure 35-25** Single-shot echoplanar imaging diffusion weighted images in a patient with metastatic neuroendocrine tumor of the pancreas. Diffusion images show the pancreatic body lesion (*short arrow*) and multiple liver metastases (*long arrows*), which are hyperintense at b = 0 (A) and remain hyperintense at  $b = 500 \text{ s/mm}^2$  (B) compared with the normal pancreatic/liver parenchyma, consistent with malignant lesions. ADC map (C) shows a low apparent diffusion coefficient of the pancreatic and liver lesions.



**Figure 35-26** Magnetic resonance elastogram of a 63-year-old man with chronic liver disease. The wave images (A) demonstrate propagation of the mechanical shear wave through the liver generated by the pneumatic drum. Gray-scale and color stiffness maps are displayed. A region of interest is placed in the right lobe on the gray-scale image (B), showing a stiffness value of 8.1 kPa, compatible with severe fibrosis. The color map (C) is diffusely red throughout the liver, indicating a stiffness value exceeding the 0 to 8-kPa scale allotted for this particular sequence.

## **Nuclear Medicine**

## **TECHNICAL ASPECTS**

#### Radiopharmaceuticals

Various technetium-99m (<sup>99m</sup>Tc)-labeled hepatobiliary radiopharmaceuticals have been used over the years. <sup>99m</sup>Tc-disofenin (DISIDA, 2,6-diisopropylacetanilidoiminodiacetic acid) or <sup>99m</sup>Tc-mebrofenin (BRIDA, bromo-2,4,6-trimethylacetanildoiminodiacetic acid) are administered intravenously in doses of 1.5 to 5.0 mCi (50 to 200 MBq) for adults, with 3 to 10 mCi (100 to 370 MBq) used for hyperbilirubinemia.

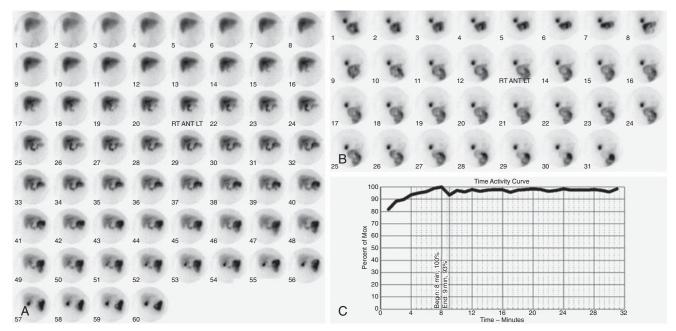
## CHOLESCINTIGRAPHY

A gamma camera with a large field of view and equipped with a low-energy, all-purpose, or high-resolution collimator is typically used. Whenever possible, continuous computer acquisition should be performed (1 minute per frame) (Figure 35-27). Imaging should begin at injection and continue serially for 60 minutes or until activity is seen in both the gallbladder (which confirms patency of the cystic duct) and the small bowel (which confirms patency of the common bile duct). Additional views (e.g., right lateral, left, or right anterior oblique) may be obtained as needed to clarify anatomy. When acute cholecystitis is suspected and the gallbladder is not seen within 60 minutes, 3- to 4-hour delayed images should be obtained or morphine augmentation may be used in lieu of delayed imaging. Delayed imaging at 18 to 24 hours may be necessary in some patients (e.g., severely ill patients or those with suggested common bile duct obstruction, suggested leak, or suggested biliary atresia).54Several studies have reported an overall sensitivity of 98% and specificity of 90%.<sup>57,58</sup> Although reports have suggested high accuracy for ultrasonography, cholescintigraphy has consistent, superior accuracy in direct comparison studies.<sup>59,60</sup> Failure of gallbladder filling in the presence of normal hepatic uptake and biliary excretion reliably indicates acute cholecystitis, whereas normal gallbladder visualization excludes the diagnosis (Figure 35-28).

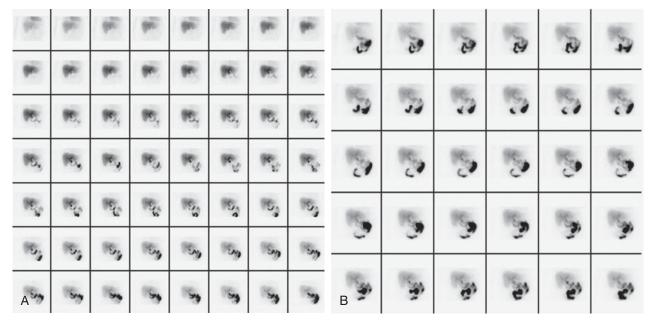
#### Patient Preparation

Fasting for 3 to 4 hours before cholescintigraphy has become standard protocol. Half of the normal subjects who eat within 1 hour of cholescintigraphy will have gallbladder nonvisualization.<sup>61</sup> Postprandially, the gallbladder is contracted owing to endogenous stimulation by cholecystokinin (CCK). Gallbladder nonvisualization also often occurs in patients fasting for more than 24 hours.<sup>62</sup>

**Cholecystokinin and Morphine Sulfate.** CCK has been used for many years in conjunction with cholescintigraphy to empty concentrated bile from the gallbladder, shorten the length of the procedure, and reduce the number of false-positive studies for acute cholecystitis.<sup>63</sup> Sincalide, a synthetic C-terminal octapeptide of CCK, is given intravenously in doses of 0.01 to 0.02 g/kg 30 to 60 minutes before hepatobiliary tracer injection to differentiate obstruction from functional causes and minimize the potential for a false-positive study result. To assess gallbladder contraction, the study involves a 30-minute intravenous infusion after the gallbladder is maximally filled with radiopharmaceutical (usually 60 minutes after the injection) and there is minimal activity in the liver. Dynamic acquisition then continues for 30 minutes (see Figure 35-27).



**Figure 35-27** A, Dynamic images at 1 minute per frame after injection of 5 mCi technium-99mTc-mebrofenin. There is appropriate tracer concentration by the liver with gallbladder filling and excretion into the small bowel during the initial 60 minutes, excluding cholecystitis. The patient was subsequently given 0.02 mcg/kg cholecystokinin (CCK) as a slow intravenous infusion over 30 minutes during imaging at 1 minute per frame (B), which demonstrates little gallbladder contraction during the CCK infusion. The time-activity curve (C) confirms an abnormal gallbladder ejection fraction.



**Figure 35-28** Acute cholecystitis. The initial 56 frames (A) at 1 minute per frame after intravenous injection of 5 mCi technium-99m–mebrofenin demonstrate appropriate tracer concentration by the liver and a patent common bile duct. The gallbladder was not visualized. Therefore, 0.04 mg/ kg of morphine sulfate was given intravenously and imaging continued at 1 minute per frame for 30 minutes (B), during which the gallbladder was persistently nonvisualized. Cholecystectomy confirmed acute cholecystitis.

## **INDICATIONS**

## Acute Cholecystitis

Evaluation for acute cholecystitis is easily the most common indication for cholescintigraphy. The hallmark of acute cholecystitis (acalculous and calculous) is persistent gallbladder nonvisualization after morphine administration or on 3- to 4-hour delayed images. A pericholecystic hepatic band of increased activity (the rim sign)<sup>64</sup> is often associated with severe phlegmonous/gangrenous acute cholecystitis.

#### **Bile Leaks**

Bile leaks after cholecystectomy are common. Small quantities of leakage after cholecystectomy do not usually lead to serious medical complications. The cause of bile leakage after cholecystectomy is often caused by surgical transection of small biliary radicles entering directly into the gallbladder bed (i.e., bile ducts of Luschka). Less frequently, biliary extravasation occurs from direct injury to the biliary tree at surgery.

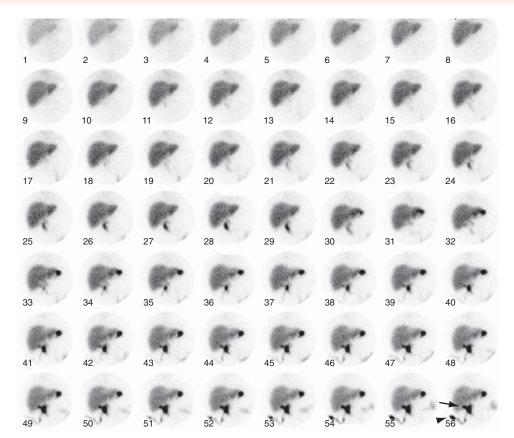
CT and ultrasound have high sensitivities for detection of perihepatic fluid collections and free peritoneal fluid. However, they often cannot determine the type of fluid present. Postoperative collections other than bile include seroma, hematoma, lymphocele, and abscess. Cholescintigraphy can confirm that a fluid collection is derived from the biliary system, identify active biliary leakage, and estimate the rate of leakage (Figure 35-29).

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#### **Key Points**

- Ultrasound is a sensitive imaging technique to evaluate the liver parenchyma and bile ducts.
- Doppler imaging is useful to establish the presence or absence of vascular pathology.
- Advanced MDCT scanners are capable of producing thin slices of isotropic voxel resolution, 3D vascular maps, and advanced applications such as volumetry and computerassisted diagnosis.
- Dual-energy CT can increase lesion conspicuity to aid in detection and characterization.
- MRI is useful for problem solving in both focal and diffuse liver disease. Hepatobiliary contrast agents have further increased its role in oncologic imaging.
- Nuclear imaging evaluation of the hepatobiliary system usually involves evaluation for acute cholecystitis or bile leak.



**Figure 35-29** Anterior images of the abdomen at 1 minute per frame after injection of 5 mCi technium-99mTc-mebrofenin in a patient with pain after cholecystectomy demonstrate concentration of tracer by the liver with excretion into the small bowel. However, a significant portion of the excreted tracer is seen leaking into the gallbladder fossa (arrow) and into a drain (arrowhead).

#### SUGGESTED READINGS

Kono Y, Mattrey R: Ultrasound of the liver. *Radiol Clin North Am* 43:815–826, 2005. Laghi A: Multidetector CT (64 slices) of the liver: examination techniques. *Eur Radiol* 17:675–683, 2007. Venkatesh SK, Ehman RL: Magnetic resonance elastography of liver. Magn Reson Imaging Clin N Am 22:433–446, 2014.

#### REFERENCES

- 1. Chong W, Shah M: Sonography of right upper quadrant pain. *Ultrasound Clin* 3:121–138, 2008.
- Chalasani N, Horlander J, Said A, et al: Screening for hepatocellular carcinoma in patients with advanced cirrhosis. *Am J Gastroenterol* 94:2988–2993, 1999.
- Douglas B, Charboneau W, Reading C: Ultrasound-guided intervention. *Radiol Clin North Am* 39:415–428, 2001.
- 4. Rumack CM, Wilson SR, Charboneau JW: Diagnostic ultrasound, ed 3, St. Louis, 2005, Mosby.
- 5. Schmidt G: *Differential diagnosis in ultrasound imaging: a teaching atlas*, Stuttgart, 2005, Georg Thieme.
- Swart J, Sheth S: Role of vascular ultrasound in the evaluation of liver disease. *Ultrasound Clin* 2:355–375, 2007.
- Ackermand S, Irshad A: The role of sonography in the liver transplantation. *Ultrasound Clin* 2:377–390, 2007.
- McNamara M, Lockhart M, Robbin M: Emergency Doppler evaluation of the liver and kidneys. *Radiol Clin North Am* 42:397–415, 2004.

- Needleman L, Kurtz A, Rifkin M, et al: Sonography of diffuse benign liver disease: accuracy of patterns recognition and grading. *AJR Am J Roentgenol* 146:1011–1015, 1985.
- Mergo P, Ros P, Buetow P, et al: Diffuse disease of the liver: radiologic-pathologic correlation. *Radiographics* 14:1291–1307, 1994.
- Tsurusaki M, Sugimoto K, Fujii M, et al: Multidetector row helical CT of the liver: quantitative assessment of iodine concentration of intravenous contrast material on multi phasic CT—a prospective randomized study. *Radiat Med* 22:239–245, 2004.
- Abdelmoumene A, Chevallier P, Chalaron M, et al: Detection of liver metastases under 2 cm: comparison of different acquisition protocols in four row multidetector-CT (MDCT). *Eur Radiol* 15:1881–1887, 2005.
- Weg N, Scheer MR, Gabor MP: Liver lesions: improved detection with dual-detector-array CT and routine 2.5-mm thin collimation. *Radiology* 209:417–426, 1998.

- Spielmann AL: Liver imaging with MDCT and high concentration contrast media. *Eur J Radiol* 45(Suppl 1):S50–S52, 2003.
- Bader TR, Prokesch RW, Grabenwoger F: Timing of the hepatic arterial phase during contrast-enhanced computed tomography of the liver: assessment of normal values in 25 volunteers. *Invest Radiol* 35:486–492, 2000.
- Hollett MD, Jeffrey RB, Jr, Nino-Murcia M, et al: Dual-phase helical CT of the liver: value of arterial phase scans in the detection of small (≤1.5 cm) malignant hepatic neoplasms. *AJR Am J Roentgenol* 164:879–884, 1995.
- Choi BI, Han JK, Cho JM, et al: Characterization of focal hepatic tumors: value of two-phase scanning with spiral computed tomography. *Cancer* 76:2434–2442, 1995.
- Singh AK, Sahani DV, Blake MA, et al: Assessment of pancreatic tumor resectability with multidetector computed tomography semiautomated console-generated images versus dedicated workstation-generated images. Acad Radiol 15:1058–1068, 2008.

- Singh AK, Sahani DV, Kagay CR, et al: Semiautomated MIP images created directly on 16-section multidetector CT console for evaluation of living renal donors. *Radiology* 244:583–590, 2007.
- Stemmler BJ, Paulson EK, Thornton FJ, et al: Dual-phase 3D MDCT angiography for evaluation of the liver before hepatic resection. *AJR Am J Roentgenol* 183:1551–1557, 2004.
- Johnson PT, Halpern EJ, Kuszyk BS, et al: Renal artery stenosis: CT angiography comparison of real-time volume rendering and maximum intensity projection algorithms. *Radiology* 211: 337–343, 1999.
- Lee WJ: [Applications of multidetector-row CT for the imaging diagnosis of liver disease.]. *Korean* J Gastroenterol 48:241–246, 2006. [Korean.]
- Carrascosa PM, Capuñay CM, Sisco P, et al: [Liver evaluation with multidetector CT: angiotomography, volume determination and virtual hepatectomy.]. Acta Gastroenterol Latinoam 36:131–138, 2006. [Spanish.]
- Duran C, Aydinli B, Tokat Y, et al: Stereological evaluation of liver volume in living donor liver transplantation using MDCT via the Cavalieri method. *Liver Transpl* 13:693–698, 2007.
- 25. Koito K, Namieno T, Hirokawa N, et al: Virtual CT cholangioscopy: comparison with fiberoptic cholangioscopy. *Endoscopy* 33:676–681, 2001.
- Agrawal MD, Pinho DF, Kulkarni NM, et al: Oncologic applications of dual-energy CT in the abdomen. *Radiographics* 34:589–612, 2014.
- Silva AC, Morse BG, Hara AK, et al: Dualenergy (spectral) CT: applications in abdominal imaging. *Radiographics* 31:1031–1046, 2011.
- 28. Coursey CA, Nelson RC, Boll DT, et al: Dualenergy multidetector CT: how does it work, what can it tell us, and when can we use it in abdominopelvic imaging? *Radiographics* 30: 1037–1055, 2010.
- American College of Radiology: Practice guideline for the performance of magnetic resonance imaging (MRI) of the liver. ACR Pract Guideline, 2005, pp 427–430.
- Lee VS, Cardiovascular MRI: *Physical principles* to practical protocols, Philadelphia, 2005, Lippincott Williams & Wilkins, p 402.
- 31. Merkle EM, Nelson RC: Dual gradient-echo in-phase and opposed-phase hepatic MR imaging: a useful tool for evaluating more than fatty infiltration or fatty sparing. *Radiographics* 26:1409–1418, 2006.
- Lee VS, Hecht EM, Taouli B, et al: Body and cardiovascular MR imaging at 3.0 T. *Radiology* 244:692–705, 2007.
- 33. Chang JS, Taouli B, Salibi N, et al: Opposedphase MRI for fat quantification in fat-water phantoms with 1H MR spectroscopy to resolve ambiguity of fat or water dominance. AJR Am J Roentgenol 187:103–106, 2006.
- Fischer MA, Raptis DA, Montani M, et al: Liver fat quantification by dual-echo MR imaging outperforms traditional histopathological analysis. Acad Radiol 19:1208–1214, 2012.

- Prasad SR, Wang H, Rosas H, et al: Fatcontaining lesions of the liver: radiologicpathologic correlation. *Radiographics* 25: 321–331, 2005.
- Rofsky NM, Lee VS, Laub G, et al: Abdominal MR imaging with a volumetric interpolated breath-hold examination. *Radiology* 212:876– 884, 1999.
- Lee VS, Lavelle MT, Krinsky GA, et al: Volumetric MR imaging of the liver and applications. *Magn Reson Imaging Clin North Am* 9:697–716, v-vi, 2001.
- Elsayes KM, Narra VR, Yin Y, et al: Focal hepatic lesions: diagnostic value of enhancement pattern approach with contrast-enhanced 3D gradient-echo MR imaging. *Radiographics* 25: 1299–1320, 2005.
- Lavelle MT, Lee VS, Rofsky NM, et al: Dynamic contrast-enhanced three-dimensional MR imaging of liver parenchyma: source images and angiographic reconstructions to define hepatic arterial anatomy. *Radiology* 218:389–394, 2001.
- Bellin MF, Van Der Molen AJ: Extracellular gadolinium-based contrast media: an overview. *Eur J Radiol* 66:160–167, 2008.
- 41. Campos JT, Sirlin CB, Choi JY: Focal hepatic lesions in Gd-EOB-DTPA enhanced MRI: the atlas. *Insights Imaging* 3:451–474, 2012.
- Sadowski EA, Bennett LK, Chan MR, et al: Nephrogenic systemic fibrosis: risk factors and incidence estimation. *Radiology* 243:148–157, 2007.
- 43. Ward J, Naik KS, Guthrie JA, et al: Hepatic lesion detection: comparison of MR imaging after the administration of superparamagnetic iron oxide with dual-phase CT by using alternative-free response receiver operating characteristic analysis. *Radiology* 210:459–466, 1999.
- 44. Imai Y, Murakami T, Yoshida S, et al: Superparamagnetic iron oxide-enhanced magnetic resonance images of hepatocellular carcinoma: correlation with histological grading. *Hepatology* 32:205–212, 2000.
- Aguirre DA, Behling CA, Alpert E, et al: Liver fibrosis: noninvasive diagnosis with double contrast material-enhanced MR imaging. *Radiology* 239:425–437, 2006.
- 46. Kim T, Murakami T, Takahashi S, et al: Diffusion-weighted single-shot echoplanar MR imaging for liver disease. *AJR Am J Roentgenol* 173:393–398, 1999.
- 47. Nasu K, Kuroki Y, Nawano S, et al: Hepatic metastases: diffusion-weighted sensitivityencoding versus SPIO-enhanced MR imaging. *Radiology* 239:122–130, 2006.
- Taouli B, Vilgrain V, Dumont E, et al: Evaluation of liver diffusion isotropy and characterization of focal hepatic lesions with two single-shot echo-planar MR imaging sequences: prospective study in 66 patients. *Radiology* 226:71–78, 2003.
- 49. Yoshikawa T, Kawamitsu H, Mitchell DG, et al: ADC measurement of abdominal organs and

lesions using parallel imaging technique. AJR Am J Roentgenol 187:1521–1530, 2006.

- 50. Hussain SM, De Becker J, Hop WC, et al: Can a single-shot black-blood T2-weighted spin-echo echo-planar imaging sequence with sensitivity encoding replace the respiratory-triggered turbo spin-echo sequence for the liver? An optimization and feasibility study. J Magn Reson Imaging 21:219–229, 2005.
- Venkatesh SK, Ehman RL: Magnetic resonance elastography of liver. Magn Reson Imaging Clin N Am 22:433–446, 2014.
- Chen J, Talwalkar JA, Yin M, et al: Early detection of nonalcoholic steatohepatitis in patients with nonalcoholic fatty liver disease by using MR elastography. *Radiology* 259:749–756, 2011.
- Kim D, Kim WR, Talwalkar JA, et al: Advanced fibrosis in nonalcoholic fatty liver disease: noninvasive assessment with MR elastography. *Radiology* 268:411–419, 2013.
- Eikman EA, Cameron JL, Colman M, et al: A test for patency of the cystic duct in acute cholecysitis. *Ann Intern Med* 82:318–322, 1975.
- Zeman RK, Burrell MI, Cahow CE, et al: Diagnostic utility of cholescintigraphy and ultrasonography in acute cholecystitis. *Am J Surg* 141: 446–451, 1981.
- Mauro MA, McCartney WH, Melmed JR: Hepatobiliary scanning with 99mTc-PIPIDA in acute cholecystitis. *Radiology* 142:193–197, 1982.
- Samuels BI, Freitas JE, Bree RL, et al: A comparison of radionuclide hepatobiliary imaging and real-time ultrasonography for detection of acute cholecystitis. *Radiology* 147:2017–2020, 1983.
- Ralls PW, Colletti PM, Halls JM, et al: Prospective evaluation of 99mTc-IDA cholescintigraphy and gray-scale ultrasound in the diagnosis of acute cholecystitis. *Radiology* 144:369–371, 1982.
- Worthen NJ, Usler JM, Funamura JL: Cholecystitis: prospective evaluation of sonography and 99mTc-HIDA cholescintigraphy. *AJR Am J Roentgenol* 137:973–978, 1981.
- 60. Chatziioannou SN, Moore WH, Ford PV, et al: Hepatobiliary scintigraphy is superior to abdominal ultrasonography in suspected acute cholecystitis. *Surgery* 127:609–613, 2000.
- Baker RJ, Marion MA: Biliary scanning with Tc-99, pyridoxylideneglutamate: the effect of food in normal subjects: concise communication. J Nucl Med 18:793–795, 1977.
- Larson MJ, Klingensmith WC, Kuni CC: Radionuclide hepatobiliary imaging: non-visualization of the gallbladder secondary to prolonged fasting. J Nucl Med 23:1003–1005, 1982.
- Nicholson RW, Hastings DL, Testa HF, et al: HIDA scanning in gallbladder disease. Br J Radiol 53:878–882, 1980.
- 64. Swayne LC, Ginsberg HN: Diagnosis of acute cholecystitis by cholescintigraphy: significance of pericholecystic hepatic uptake. *AJR Am Roentgenol* 152:1211–1213, 1989.

# **Benign Focal Lesions**

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# Etiology

36

Although benign hepatic tumors have been classified into several histiotypes according to their cell of origin (i.e., hepatocytes, biliary epithelium, or mesenchymal cells), our focus in this discussion is on those lesions most frequently encountered in clinical practice, including simple (nonparasitic) cyst, hemangioma, hepatocellular adenoma, focal nodular hyperplasia (FNH), large benign regenerative nodules, and hepatic abscess (Table 36-1).

## **Prevalence and Epidemiology**

With the widespread use of sensitive imaging studies, benign hepatic tumors are increasingly reported. Notably, even in patients with a known primary malignancy, approximately 50% of small hepatic lesions (<1.5 cm) are benign.<sup>1</sup>

## **Clinical Presentation**

Most benign hepatic tumors are an incidental finding in asymptomatic patients during imaging workup for an unrelated medical problem. Larger lesions may occasionally produce signs and symptoms related to mass effect, such as abdominal discomfort and pain.

Hepatocellular adenoma (HCA) can manifest as acute onset of abdominal pain after intratumoral hemorrhage, whereas hepatic abscess is often accompanied by fever and leukocytosis.

## Pathophysiology

Although benign tumors can occur in every portion of the liver, the right and left hepatic lobes are unequally affected by some histiotypes.

## Pathology

Pathologic findings vary greatly according to the specific tumor type, and their appearance will be described in the sections on specific lesions.

## Imaging

Although combining multiple imaging studies allows a confident diagnosis in the majority of cases, atypical lesions may still represent a diagnostic challenge.

## COMPUTED TOMOGRAPHY

With the advent of multidetector computed tomography (MDCT), remarkable improvements have been accomplished with scanning speed, scan volumes, and image quality. As a result, CT currently represents the most commonly used imaging modality for evaluating the liver.

Besides lesion detection, the main goal of CT is to firmly establish a diagnosis of benign hepatic tumors. Indeed, mistaking an incidental benign lesion for a malignant tumor may lead to unnecessary aggressive management or possibly preclude surgery when benign and malignant lesions coexist within the same liver. Although simple cysts can be confidently characterized based only on their appearance on precontrast and singlephase contrast-enhanced CT during the portal venous phase, reliable diagnosis of other benign hepatic tumors generally requires assessment of lesion enhancement pattern with multiphasic contrast-enhanced CT (i.e., hepatic arterial phase, portal venous phase, and delayed phase).

## MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) represents a powerful technique for the detection and characterization of either benign or malignant liver tumors. MRI protocol includes pulse sequences that assess different tissue characteristics such as T1 and T2 contrast of liver tumors, as well as assessment of tumor-specific enhancement patterns after intravenous administration of gadolinium-based contrast agents. Diffusion weighted imaging measures the microscopic movement of water molecules, which is related to tissue cellularity and organization. Hepatobiliary contrast materials (gadobenate dimeglumine [Gd-BOPTA] and gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid [Gd-EOB-DTPA]) distribute in the extracellular fluid compartment first and subsequently enter functioning hepatocytes.<sup>2</sup> This provides additional information, especially to differentiate lesions with functioning hepatocytes (i.e., lesions with organic anionic transport proteins) from hepatocellular lesions without organic anionic transport proteins and nonhepatocellular lesions.

#### **ULTRASONOGRAPHY**

Because of its high contrast resolution, low cost, and wide availability, ultrasonography frequently represents the primary modality for the study of the liver. However, operator dependency, substantial image degradation in obese patients, and a

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	Associated Signs and Predisposing Factors	tal	tal	tal	Vascular abnormality	Oral contraceptives assumption	Budd-Chiari syndrome and other vascular disorders		
		Congenital	Congenital	Congenital	Vascular	Oral contrace assumption	Budd-Chiari and othe disorders	Bacterial	
	Bleed	Rare	No	No	°Z	Yes	No	No	
	Scar	No	Rare (larger lesions)	No	Present in 50% Hyperintense on T2-weighted images and on delayed post-gadolinium T1-weighted images	No	Larger lesions	ON	
	Fat	No	No	No	Very rare	Often	No	No	
	Number Calcifications	Rare (peripheral)	Sometimes in large ones	No	1%	5%	No	No	
lasms	Number	One or few	One or few	One or few	One or few	One or few	Multiple	One or few	
Clinical and Radiologic Features of Benign Hepatic Neoplasms	Size	Variable	Variable (3-20 cm)	Usually smaller than 2 cm	3 cm (1-14 cm)	5.5 cm	0.5-4 cm	Variable	
s of Benig	Capsule	No	No	No	°Z	25%	No	Yes	
logic Feature	Age	5th-6th decade	2nd-5th decade	2nd-5th decade	3rd-4th decade	3rd-4th decade	3rd-4th decade	5th-7th decade	
nd Radio	Sex	∑ ∧ ⊥	₹ ×	₹ ×	∑ ∦ ⊥	≥ ⊗ ⊔	∑ ^ ⊥	M E E	
TABLE Clinical ar	Neoplasm	Hepatic cyst	Cavernous hemangioma	Capillary hemangioma	Focal nodular hyperplasia	Hepatocellular adenoma	Large benign regenerative nodules	Pyogenic abscess	<i>F</i> , Female; <i>M</i> , male.

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limited field of view, represent major limitations that explain the low appeal of ultrasonography among referring physicians and surgeons.

Some benign liver tumors, such as simple cysts or hemangiomas, typically demonstrate a classic, virtually diagnostic appearance on ultrasonography. Some other lesions (e.g., FNH) may, however, be difficult to distinguish from normal liver owing to their hepatocellular nature.

Microbubble contrast agents have substantially enhanced the available diagnostic information.<sup>3</sup> Besides the evaluation of tumor enhancement pattern during both arterial and portal venous phases, contrast-enhanced images also can be acquired during a late parenchymal phase with potential improvement of lesion detection.

## **Specific Lesions**

## SIMPLE (BILE DUCT) CYST

#### Etiology

Simple (nonparasitic) cysts likely result from a congenital defective development of the intrahepatic biliary ducts.

## Prevalence and Epidemiology

Simple hepatic cysts are among the most common liver lesions, with an estimated incidence of 2.5% in the general population.<sup>4</sup> Although cysts can occur in both sexes at all ages, middle-aged women are more frequently affected (male-to-female ratio, 1:5).

### **Clinical Presentation**

Typically, cysts are incidental imaging findings in asymptomatic patients. Occasionally, larger lesions may produce signs and symptoms related to mass effect, such as abdominal discomfort, chronic pain, nausea and vomiting, or early satiety because of compression of the stomach. Rarely, acute pain can develop after intralesional hemorrhage, spontaneous or traumatic rupture, or secondary infection.<sup>4</sup>

## Pathophysiology

Simple cysts originate twice as frequently within the right lobe of the liver than the left lobe.

## Pathology

Typically, simple cysts manifest as either solitary or multiple, well-defined lesions, varying in size from a few millimeters to several centimeters. Cysts do not communicate with the biliary tree and typically contain clear fluid. Occasionally, however, cystic content may be mucoid, purulent (if the cyst is infected), or hemorrhagic.<sup>4</sup>

On histologic examination the cyst lining consists of a single layer of columnar or cuboid epithelium, which is identical to bile duct epithelium. Epithelial cells rest on a basement membrane surrounded by a thin fibrous stroma.<sup>4</sup>

#### Liver Function

Liver function test results are generally unremarkable, although larger cysts may produce mild increase of alkaline phosphatase and bilirubin levels if there is mild mass effect on the intrahepatic biliary ducts.

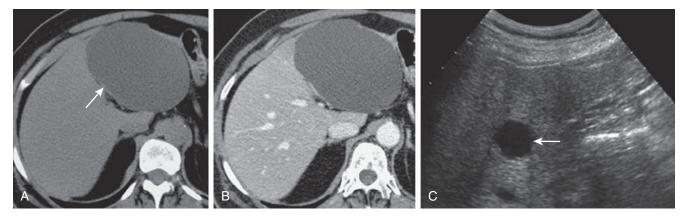
#### Imaging

Because of the high incidence in the general population, simple hepatic cysts are frequently discovered on ultrasonography, CT, or MRI of the liver.

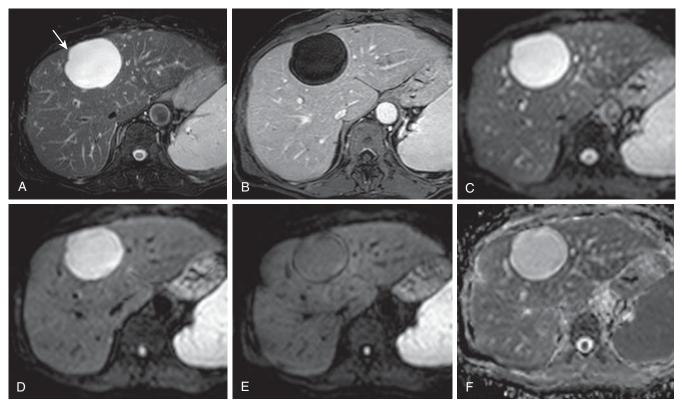
**Computed Tomography.** On precontrast CT, cysts manifest as rounded or oval, thin-walled, well-defined, water-attenuating (from –10 to +20 Hounsfield units) lesions.<sup>5</sup> Although most cysts are unilocular in appearance, multiple lesions that are clustered together may produce the appearance of a single, multiloculated lesion.

On contrast-enhanced CT, neither the cyst content nor the peripheral wall shows perceptible enhancement (Figure 36-1).<sup>5</sup> Rarely, complicated cysts may show atypical appearances, such as parietal calcifications, mural nodularity, or fluid levels that may resemble a cystic liver tumor or hepatic abscess.

**Magnetic Resonance Imaging.** Because cysts are composed almost entirely of fluid, their T1 and T2 values are extremely long, thus explaining the very low signal intensity on T1-weighted images and markedly high signal intensity on T2-weighted images (Figure 36-2). Characteristically, cysts further increase



**Figure 36-1** Typical presentation of hepatic (bile duct) simple cyst. **A**, Transverse precontrast computed tomography (CT) image shows a large, sharply defined lesion (*arrow*) in the left lobe of the liver that is hypoattenuating compared with the surrounding hepatic parenchyma and aorta. Hypoattenuation to the aorta on precontrast images is the single most important finding to diagnose cystic lesions on CT. **B**, Corresponding contrast-enhanced CT scan during portal venous phase demonstrates absence of lesion enhancement. **C**, Ultrasound image in a different patient shows a round, well-circumscribed mass (*arrow*) with imperceptible wall and increased through-transmission of sound waves.



**Figure 36-2** Typical presentation of hepatic (bile duct) simple cyst. A, Fat-suppressed T2-weighted fast spin echo magnetic resonance (MR) image shows markedly high intensity of the cyst (*arrow*). B, Gadolinium-enhanced T1-weighted gradient recalled echo MR image during portal venous phase demonstrates absence of lesion enhancement. C to E, On diffusion weighted images at b = 0 sec/mm<sup>2</sup> (C), b = 150 sec/mm<sup>2</sup> (D), and b = 800 sec/mm<sup>2</sup> (E) the cyst shows intensity decrease with increasing b-value. F, On corresponding apparent diffusion coefficient map the cyst shows strong hyperintensity.

their relative signal on T2-weighted images at longer echo times because of signal suppression from most abdominal parenchymal tissues. Hemorrhagic cysts can show variable signal intensity on T1- and T2-weighted images according to the age of hemorrhage and a fluid/fluid level as a result of mixed blood product.<sup>5</sup> On diffusion weighted images, cysts typically show signal intensity decrease with increasing b-values, and strong hyperintensity on apparent diffusion coefficient (ADC) map.<sup>6</sup>

As in the case of contrast-enhanced CT, simple cysts do not enhance on gadolinium-enhanced MRI. On hepatobiliary phase, cysts remain hypointense relative to the liver and biliary system. The lack of communication between cysts and the biliary tree can be demonstrated on T1-weighted magnetic resonance cholangiopancreatography (MRCP) after administration of hepatobiliary contrast agents, which demonstrate markedly increased signal intensity of the biliary tree and gallbladder but not of the noncommunicating liver cyst.

**Ultrasonography.** Typically, hepatic cysts manifest as well-defined, anechoic lesions with well-defined margins and posterior acoustic enhancement on gray-scale ultrasonography (see Figure 36-1). Complicated cysts may show atypical appearances, such as internal septations, debris, and a thickened wall with or without calcification.

**Imaging Algorithm.** An ideal algorithm is presented in Figure 36-15, at the end of this discussion.

#### **Classic Signs: Simple Cysts**

- Thin wall
  Anachaic systic content ar
- Anechoic cystic content and posterior echo enhancement
- No contrast enhancement after intravenous injection of a contrast agent
- Fluid filled
- Homogeneous

## **Differential Diagnosis**

Clinical findings usually do not contribute to the diagnosis of simple hepatic cysts. Strong hyperintensity on heavily T2-weighted MR images allows differentiation from most hepatic metastases, with the exception of those originating from neuroendocrine tumors. Unlike hepatic abscesses or cystic neoplasms, hepatic cysts manifest with a very thin, almost imperceptible nonenhancing wall, as well as lack of intralesional septa and mural nodules. Polycystic liver disease usually consists of numerous cystic lesions, with size varying from a few millimeters to several centimeters, and is associated with autosomal dominant polycystic kidney disease. Hydatid cyst usually contains several daughter cysts and is surrounded by calcified walls. Biliary hamartomas are usually numerous and smaller than 15-mm cystic lesions, whereas Caroli's disease will consist of multisegmental biliary dilatation, typically showing the "central

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dot sign," owing to a portal venous branch surrounded by a cystic lesion secondary to arrested development of the intrahepatic biliary tree (Figure 36-3 and Table 36-2).

#### Treatment

**Medical Treatment.** Because simple cysts are rarely complicated, they should be treated conservatively.

**Surgical Treatment.** Percutaneous catheter drainage with alcohol sclerosis can be an effective therapy for larger,

symptomatic cysts. Rarely, hepatic cysts are treated surgically, most commonly via laparoscopic fenestration.

## **HEPATIC HEMANGIOMA**

## Etiology

Hemangiomas are probably congenital in origin, and no definite predisposing factors have been identified. Because they increase with multiparity, female sex hormones have been suggested as a cause.



TABLE 36-2 Demographics and Pathologic and Clinical Features of Hydatid Cyst, Simple Cyst, Pyogenic Abscess, Biliary Cystadenoma, Polycystic Liver Disease, Biliary Hamartomas, and Caroli's Disease

Features	Hydatid Cyst	Simple Cyst	Pyogenic Abscess	Biliary Cystadenoma	Polycystic Liver Disease	Biliary Hamartomas	Caroli's Disease
Sex	F = M	F > M	F = M	F > M	F > M	M > F	F > M
Age	3rd-4th decade	5th-6th decade	5th-7th decade	2nd-5th decade	5th-6th decade	Any age	2nd-3rd decade
Frequency	Depend on geographic area	Very common	Common	Rare	Rare	Common	Very rare
Clinical Features	Asymptomatic	Asymptomatic	Fever, pain	Asymptomatic	Mass effect	Asymptomatic	Fever (cholangitis)
Location	Right lobe > left	All liver segments	Right lobe > left	Right lobe > left	All liver segments	All liver segments	All liver segments
Number	Multiple (60%)	Solitary > Multiple	Multiple	Solitary	Multiple	Multiple	Multiple
Size	3-30 cm	0.5-30 cm	0.5-10 cm	1-20 cm	1-10 cm	<15 mm	0.5-5 cm
Wall calcification	Yes	Rare, peripheral	No	Rare	Rare	No	No
Septations	Present	Absent	Present	Present	Absent	Absent	Absent
Gas	No	No	Present (20%)	No	No	No	No
Inflammatory changes	Absent	Absent	Present	Absent	No	No	No
Multiplicity	Possible	Absent	Present	No	No	No	Yes
Signs at imaging and associated conditions	Intralesional daughter cysts and wall calcifications	Increased through- transmission on ultrasonography, hypoattenuation to blood pool on unenhanced CT	Cluster sign		Adult recessive polycystic kidney disease	Multiplicity and small (<15 mm) size, congenital hepatic fibrosis, Caroli's disease	Dot sign, congenital hepatic fibrosis, biliary hamartomas

CT, Computed tomography; F, female; M, male.

# What the Referring Physician Needs to Know: Simple Cysts

- Simple cysts are among the most common liver lesions.
- Conservative management is warranted with the exception of larger, symptomatic cysts.
- Ultrasonography is usually sufficient to confirm or rule out the diagnosis.

## Prevalence and Epidemiology

Hemangioma is the most common benign hepatic tumor, with an estimated incidence of 5% to 20% in the general population.<sup>4</sup> Although hemangiomas can occur in both sexes at all ages, middle-aged women are more frequently affected, perhaps reflecting the causative effect of female sex hormones.<sup>4</sup>

#### **Clinical Presentation**

Typically, hemangiomas are incidental imaging findings in asymptomatic patients. Occasionally, larger lesions may produce signs and symptoms related to mass effect, such as upper abdominal mass, abdominal discomfort, and pain. Rarely, sudden onset with acute pain can develop after either spontaneous or traumatic rupture of larger lesions. Giant hemangiomas can manifest as thrombocytopenia and consumptive coagulopathy (Kasabach-Merritt syndrome).

## Pathophysiology

Hemangiomas can occur in all liver segments with equal frequency.

### Pathology

Characteristically, hemangiomas manifest as either solitary or multiple, well-defined masses, varying in size from a few millimeters to several centimeters.<sup>4</sup> Hemangiomas are infrequently detected or are generally smaller when occurring within a cirrhotic liver, probably owing to progressive tumor shrinkage by liver fibrosis.<sup>7</sup> On sectioning, hemangiomas show a typical redblue appearance with a spongy or honeycombing surface.<sup>8</sup> Organized thrombi, fibrosis, and calcification may be noted grossly, particularly in the central area of larger lesions. Occasionally, sclerosis may involve the entire lesion, which manifests as a firm, gray-white nodule of fibrous tissue (the so-called *sclerosed hemangioma*).

Association of hemangioma with other benign liver lesions, such as FNH and hepatocellular adenoma, has been described.<sup>8</sup>

On histologic examination, hemangioma consists of several communicating blood-filled spaces, lined by a single layer of flat endothelial cells, which are supported by a thin basement membrane.<sup>4</sup>

## Liver Function

Liver function test results are generally unremarkable, although patients with giant hemangiomas occasionally can have a mild increase in alkaline phosphatase level.

## Imaging

Because of the high incidence in the general population, hemangiomas are frequently discovered incidentally on ultrasonography, CT, or MRI of the liver.

**Computed Tomography.** On precontrast CT, most hemangiomas manifest as hypoattenuating lesions relative to the liver. However, because lesions may be hyperattenuating if occurring in the setting of diffuse fatty liver disease secondary to uniformly decreased attenuation of the hepatic parenchyma,<sup>9</sup> a more reliable criterion for the diagnosis of hemangioma is isoattenuation to the aorta and intrahepatic vessels. Central calcifications may occur in giant hemangiomas.

With contrast-enhanced CT, hemangiomas classically show early, discontinuous, peripheral, nodular enhancement, with centripetal progression. The enhancing areas of hemangiomas are isoattenuating to the aorta during the hepatic arterial phase and to blood pool during the portal venous phase and delayed phase (Figure 36-4).<sup>10,11</sup> When all typical criteria are observed,

lack of complete lesion enhancement on the delayed phase should not dissuade from the diagnosis of hemangioma. Giant hemangiomas usually lack complete enhancement on delayed phase imaging owing to thrombosis or sclerosis of the central portion of the tumor.

Small hemangiomas (<2 cm)—also known as *capillary hemangiomas* or *flash filling hemangiomas*—may enhance rapidly and homogeneously during the hepatic arterial phase (Figure 36-5), thus mimicking other benign or malignant hypervascular liver tumors (Tables 36-3 and 36-4). Transient peritumoral enhancement during the hepatic arterial phase is frequently observed owing to associated arteriovenous shunt.

A sclerosed hemangioma usually lacks any contrast enhancement on different vascular phases.

**Magnetic Resonance Imaging.** Because hemangiomas are composed almost entirely of blood, their T1 and T2 values are very long, thus explaining the very low signal intensity on T1-weighted images and markedly high signal intensity on T2-weighted images, even at longer echo times.<sup>12</sup> The complex internal architecture of giant hemangiomas can be better depicted on T2-weighted images as low-signal strands of fibrous stroma, which gives the lesion a characteristic appearance. On diffusion weighted images, hemangiomas typically show marked hyperintensity at b 0 s/mm<sup>2</sup>, with signal intensity decrease or

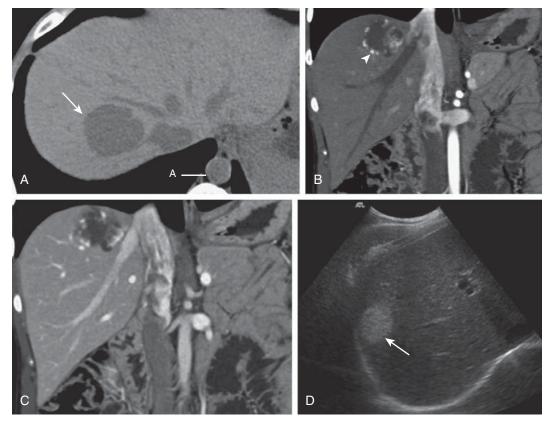
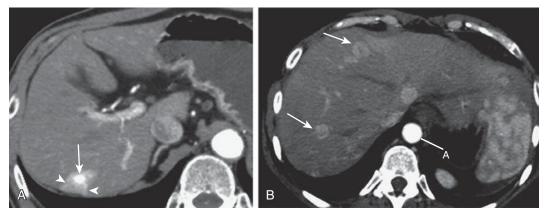


Figure 36-4 Typical cavernous hemangioma. A, Transverse precontrast computed tomographic image shows a 4-cm, hypoattenuating lesion (*arrow*) in the right lobe of the liver. Note the equal attenuation of the lesion with both aorta (A) and intrahepatic vessels. B and C, Coronally reformatted images of the same patient demonstrate nodular, peripheral, discontinuous enhancement (*arrowhead*, B) on both (B) hepatic arterial phase and (C) portal venous phase, which is comparable to vessels on all vascular phases. D, Ultrasound image in a different patient shows a homogeneous, well-defined, hyperechoic lesion (*arrow*) of the right hepatic lobe.



**Figure 36-5** Imaging findings and differential diagnosis between capillary hemangioma and hypervascular metastases from breast carcinoma on transverse contrast-enhanced computed tomography during hepatic arterial phase. A, Capillary hemangioma (*arrow*) manifests as an isoattenuating lesion compared with the aorta, surrounded by a wedge-shaped, homogeneous, moderately hyperattenuating area (*arrowheads*) secondary to arteriovenous shunt. B, Hypervascular metastases (*arrows*) are multiple and demonstrate more heterogeneous enhancement, which is not as strong as that of the aorta (*A*). Enhancement characteristics along with a history of primary tumor allow the correct diagnosis.

### TABLE Differential Features Among Capillary Hemangioma, Cavernous Hemangioma, Metastases, Focal Nodular 36-3 Hyperplasia, and Large Benign Regenerative Nodules

Features	Capillary Hemangioma	Cavernous Hemangioma	Metastases	Focal Nodular Hyperplasia	Large Benign Regenerative Nodules
Sex	F > M	F > M	M = F	$F \gg M$	F > M
Age	2nd-5th decade	2nd-5th decade	6th-7th decade	3rd-4th decade	3rd-4th decade
Ultrasound findings	Hypointense with hyperechoic border	Hyperechoic	Hypoechoic	Isoechoic	Variable
Sustained enhancement on portal venous and delayed phases	Yes	Yes	No	Yes	Yes
Isoattenuating to vessels on CT	Yes	Yes	No	No	No
Hyperintensity on T2	Strong	Strong	Mild*	Mild	No
Homogeneous enhancement on hepatic arterial phase	Yes	No	No	Yes	Yes
Enhancement	Homogeneous	Peripheral, discontinuous	Peripheral, ringlike	Homogeneous	Homogeneous
Calcifications	No	Central if present	No <sup>†</sup>	1%	No
Scar	No	Rare (larger lesions)	No	Yes	Larger lesions
Necrosis	No	No	Yes	No	No
Number	Single > multiple	Single > multiple	Multiple	Single (75%)	Multiple
History of malignancy	No	No	Yes	No	No

CT, Computed tomography; F, female; M, male.

\*Except for neuroendocrine tumors, mucinous colon cancer, and breast cancer that may be strongly hyperintense.

<sup>†</sup>Except for mucinous colon cancer metastases that may have scattered calcifications.

persistent hyperintensity (T2 shine-through effect) at high b-values, and moderate hyperintensity on ADC map.<sup>13</sup> The ADC values of hemangiomas are lower than those of simple cysts.<sup>14</sup> On dynamic phases, hemangiomas show an enhancement pattern, which is substantially comparable to that with CT (Figure 36-6). In the hepatobiliary phase, hemangiomas retain the contrast material, but they typically show hypointensity because of increased signal intensity of the surrounding liver.<sup>15</sup> With Gd-EOB-DTPA, however, hemangiomas can show isointensity or hypointensity on portal venous and 3-minute delayed phases (pseudo washout)<sup>16</sup> or they can show peripheral hypointensity in the hepatobiliary phase.<sup>17</sup>

**Ultrasonography.** Typically, hemangioma manifests as a homogeneous, hyperechoic mass with well-defined margins on gray-scale ultrasonography (see Figure 36-4). Occasionally, lesions appear isoechoic or hypoechoic relative to the liver, surrounded by a peripheral hyperechoic rim. With microbubble contrast agents, a contrast enhancement pattern closely resembles that found on CT and MRI (Figure 36-7).

TABLE **36-4** 

Differential Features Among Focal Nodular Hyperplasia, Large Benign Regenerative Nodules, Hepatocellular Adenoma, Hepatocellular Carcinoma, Hypervascular Metastases, and Cavernous Hemangioma

FNH	LBRN	HCA/ Adenomatosis	нсс	Hypervascular Metastases	Cavernous Hemangioma
$F \gg M$	F > M	$F \gg M$	M > F	M = F	F > M
3rd-4th decade	3rd-4th decade	3rd-4th decade	6th-7th decade	6th-7th decade	2nd-5th decade
No	No	No	Yes	No	No
No	No	Yes	No	No	No
Normal	Normal	Normal	Abnormal	Normal	Normal
Isoechoic	Variable	Variable	Hypoechoic	Hypoechoic	Hyperechoic
Strong	Strong	Mild to strong*	Mild	Mild	Nodular, peripheral
Yes	Yes	No	No	No	No
1%	No	Rare	Rare	No	Rare (larger lesions)
Rare	No	Yes	Rare	No	No
Hyperintense (mild)	Hypointense	Hyperintense (mild to strong*)	Hyperintense (mild)	Hyperintense (mild†)	Hyperintense (strong)
No	No	Yes	Yes	Yes	No
lsointensity or hyperintense	lsointensity or hyperintense	Hypointense	Hypointense	Hypointense	Hypointense
	F ≫ M 3rd-4th decade No No Normal Isoechoic Strong Yes 1% Rare Hyperintense (mild) No Isointensity or	F ≫ MF > M3rd-4th decade3rd-4th decadeNoNoNoNoNoNoNormalNormal VariableIsoechoicVariableStrongStrongYesYes1%NoRareNoHyperintense (mild)HypointenseNoNoIsointensity orIsointensity or	FNHLBRNAdenomatosis $F \gg M$ $F > M$ $F \gg M$ $3rd-4th$ $3rd-4th$ $3rd-4th$ decade $decade$ $decade$ $decade$ NoNoNoNoNoYesNormalNormalNormalIsoechoicVariableVariableStrongStrongMild to strong*YesYesNo1%NoRareRareNoYesHyperintense (mild)HypointenseHyperintense (mild to strong*)NoNoYes	FNHLBRNAdenomatosisHCC $F \gg M$ $F > M$ $F \gg M$ $M > F$ $3rd$ -4th $3rd$ -4th $3rd$ -4th decade $6th$ -7th $decade$ $decade$ $decade$ $decade$ NoNoNoYesNoNoYesNoNormalNormalNormalAbnormalIsoechoicVariableVariableHypoechoicStrongStrongMild to strong*MildYesYesNoRareRareRareNoYesRareRareHyperintense (mild)HypointenseHyperintense (mild to strong*)Hyperintense (mild)NoNoYesHyperintense (mild)HypointenseIsointensity orIsointensity orHypointenseHypointense	FNHLBRNAdenomatosisHCCMetastases $F \gg M$ $F > M$ $F \gg M$ $M > F$ $M = F$ $3rd$ -4th $3rd$ -4th $3rd$ -4th decade $6th$ -7th $6th$ -7th $decade$ $decade$ $decade$ $decade$ $decade$ NoNoNoYesNoNoNoYesNoNoNoYesNoNormalNormalNormalAbnormalIsoechoicVariableVariableHypoechoicStrongStrongMild to strong*MildYesYesNoNo1%NoRareRareNoYesRareNoHyperintense (mild)HypointenseHyperintense (mild to strong*)NoNoYesYesIsointensity orIsointensity orHypointenseIsointensity orIsointensity orHypointenseHypointenseHypointenseHypointenseHypointenseHypointenseHypointense

F, Female; FNH, focal nodular hyperplasia; HCA, hepatocellular adenoma; HCC, hepatocellular carcinoma; LBRN, Large benign regenerative nodules; M, male; MRI, magnetic resonance imaging.

\*Findings depending on HCA subtype.

<sup>†</sup>Except for neuroendocrine tumors, mucinous colon cancer, and breast cancer that may be strongly hyperintense.

**Imaging Algorithm.** An ideal algorithm is presented in Figure 36-15.

### **Classic Signs: Hemangiomas**

- Isoattenuation to blood pool on all phases.
- Discontinuous, peripheral, nodular enhancement.
- Marked hyperintensity on T2-weighted MR images.

## **Differential Diagnosis**

Clinical findings usually do not contribute to the diagnosis of hepatic hemangiomas. Unlike most primary or secondary hypervascular malignant liver tumors, hemangiomas invariably show sustained enhancement comparable to blood pool during the portal venous and delayed phases of CT (see Figure 36-5) or MRI. In addition, unlike most malignant liver tumors, marked hyperintensity of hemangiomas on T2-weighted MR images (see Figure 36-6) typically persists with longer echo times (see Table 36-3).

Metastases from neuroendocrine tumors, mucinous cancer of the colon, and breast cancer may show strong hyperintensity on T2-weighted images that may mimic that of hemangiomas (see Table 36-4). Biopsy may be necessary in doubtful cases.

#### Treatment

**Medical Treatment.** Because hemangiomas virtually never cause complications, they should be treated conservatively.

**Surgical Treatment.** Larger lesions can be treated with enucleation or resection when clinically symptomatic.

# What the Referring Physician Needs to Know: Hemangiomas

- Hemangiomas occur most often in middle-aged women.
- If the appearance is classic for hemangioma on ultrasonography, no further evaluation should be required in patients without a history of underlying malignancy.
- Conservative management is warranted, unless large symptomatic lesions are present.
- Lesions may occasionally enlarge.

## HEPATOCELLULAR ADENOMA

#### Etiology

HCAs are a group of benign hepatocellular tumors with risk for malignant transformation.<sup>18</sup> The cause is multifactorial.<sup>18</sup> Female sex and steroid medications (i.e., estrogen-containing or androgen-containing) represent major factors<sup>18</sup> Other, less common, risk factors include glycogen storage disease and congenital or acquired abnormalities of hepatic vasculature.

## Prevalence and Epidemiology

HCA most frequently occurs in women of reproductive age (male-to-female ratio, 1:10). The estimated incidence of HCA in patients undergoing steroid therapy is four cases in every 100,000 steroid users.

#### **Clinical Presentation**

Most HCAs are discovered incidentally. Larger HCAs may manifest with nonspecific symptoms such as palpable abdominal

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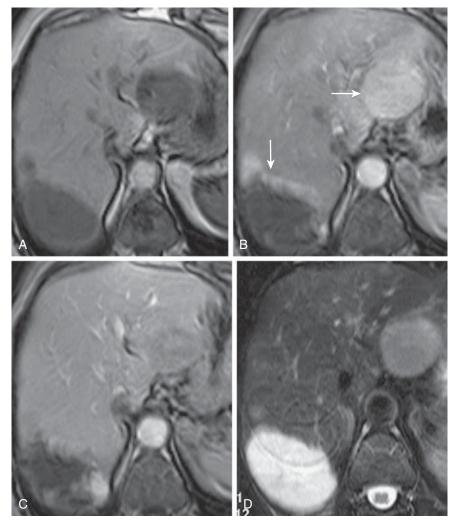


Figure 36-6 Imaging findings and differential diagnosis on magnetic resonance imaging (MRI) between cavernous hemangioma and hypervascular sarcoma metastasis coexisting in the same liver. A, Although both lesions are hypointense to surrounding liver parenchyma on T1-weighted gradient recalled echo MRI, metastasis (horizontal arrow, B) shows moderate hypervascularity and rapid washout on gadolinium-enhanced T1-weighted gradient recalled echo MR image during the hepatic arterial phase (B) and portal venous phase (C), respectively. B and C, In the same imaging phases, cavernous hemangioma (vertical arrow, B) typically shows nodular, peripheral, discontinuous enhancement, which progresses centripetally. D, Fat-suppressed T2weighted fast spin echo MR image shows strong hyperintensity of hemangioma with only moderate hyperintensity of metastasis.

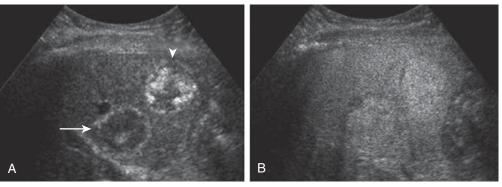


Figure 36-7 Typical ultrasound images of two hepatic hemangiomas. A, During the hepatic arterial phase, lesions show either minimal, peripheral enhancement (*arrow*) or prominent, peripheral, globular enhancement (*arrowhead*). B, During the portal venous phase, both lesions show centripetal progression of enhancement to complete fill.

mass, discomfort, and pain. Occasionally, severe hemorrhage may produce hemorrhagic shock, thus requiring emergency surgery.

## Pathophysiology

HCA most commonly originates within the right liver lobe (75% of cases), particularly underneath the hepatic capsule.

## Pathology

Typically, HCAs manifest as well-demarcated solitary masses originating in a normal liver.<sup>4</sup> Multiple lesions are most commonly present in patients with liver steatosis.<sup>19</sup> Liver adenomatosis is a distinct entity characterized by the presence of multiple (>10) HCAs in patients without associated predisposing factors.<sup>20</sup> Histologically, HCAs consist of normal-appearing hepatocytes arranged in sheets and cords without acinar architecture.<sup>16</sup> Based on genetic mutations, HCAs are classified into four subtypes with different malignant potential: (1) HNF 1 $\alpha$ -mutated HCAs, corresponding to steatotic HCAs; (2) inflammatory HCAs; (3) beta-catenin–mutated HCAs; and unclassified HCAs, which are unrelated to specific immunophenotypical alterations.<sup>18</sup> Beta-catenin mutation increases the risk for malignant transformation.

#### Liver Function

Liver function test results are generally unremarkable. Increased alpha-fetoprotein levels are suggestive of malignant transformation.

#### Imaging

Contrast-enhanced CT and MRI and, more recently, contrastenhanced ultrasonography represent the modalities of choice for preoperative assessment of HCA.

**Computed Tomography.** CT findings of HCA correspond to its appearance on gross inspection. On precontrast CT, most tumors manifest as large, heterogeneous masses because of hemorrhage, necrosis, and calcification,<sup>21</sup> although smaller lesions may be isoattenuating relative to liver.

Because of the increased arterial supply, HCA is usually hypervascular and appears as a hyperattenuating lesion compared with the surrounding liver on contrast-enhanced CT during the hepatic arterial phase, with the only exception of intratumoral areas of hemorrhage, fat, and necrosis. HCA generally shows variable washout during the portal venous and delayed phases.<sup>4</sup>

When occurring in the setting of diffuse fatty liver disease, HCA is hyperattenuating relative to the liver either before or after administration of a contrast agent.

**Magnetic Resonance Imaging.** MR imaging findings of HCA closely resemble those of either primary or secondary malignant liver lesions. The histologic subtype affects the signal intensity on T2- and T1-weighted images and the enhancement pattern.<sup>22</sup>

Hepatocyte nuclear factor (HNF)- $1\alpha$ -mutated HCAs (steatotic HCAs) show hyperintensity or isointensity on T1-weighted images, with diffuse signal decrease on out-of-phase images, isointensity to slightly hyperintensity on T2-weighted images, and mild arterial enhancement.<sup>22</sup>

I Telangiectatic and inflammatory HCAs show strong hyperintensity on T2-weighted images, isointensity or mildly hyperintensity on T1-weighted images, intense arterial enhancement, which persists in the portal venous and delayed phases (Figure 36-8).<sup>22</sup> Beta-catenin–mutated HCAs can show strong arterial enhancement, with washout on the portal venous and delayed phases, or they can display the same MRI appearance of inflammatory HCAs.<sup>24</sup> Unclassified HCAs show heterogeneous signal intensity because of hemorrhage and fat.<sup>21</sup>

Unlike FNHs, HCAs do not generally take up hepatobiliary contrast agents, and typically appear as hypointense masses on hepatobiliary phase, with the exception of inflammatory HCAs, which in approximately 30% of cases show isointensity to hyperintensity.<sup>23,24</sup> Atypical signal intensity could be related to severe hepatic steatosis and reduced blood flow secondary to large cavities and sinusoidal dilatation.<sup>23,24</sup> On diffusion weighted images, most HCAs show restricted diffusion as a result of increased cellularity.<sup>25</sup>

**Ultrasonography.** HCAs show a variable, nonspecific appearance on gray-scale ultrasonography. By providing insights into the vascular enhancement pattern of liver lesions, microbubble contrast agents have been shown to provide reliable differentiation between HCA and FNH. Unlike FNH, HCA is characterized by a centripetal or mixed filling in the arterial phase without the typical stellate vascularity.<sup>26</sup>

**Imaging Algorithm.** An ideal algorithm is presented in Figure 36-15.

## Classic Signs: Hepatocellular Adenoma

- Hypervascularity with washout
- Signal drop on out-of-phase images consistent with fat content
- Heterogeneous appearance resulting from hemorrhage and necrosis
- Rupture
- Degeneration
- Associated with other benign hepatic tumors

## DIFFERENTIAL DIAGNOSIS

Tumor interval growth with or without increased alphafetoprotein levels is highly suggestive of hepatocellular carcinoma (HCC) or, alternatively, malignant degeneration of HCA. Although larger HCA can be easily differentiated from FNH based on the heterogeneous appearance (see Figure 36-8), the differential diagnosis can be challenging on imaging and even on histopathologic examination when the lesions are small (see Table 36-4). Hepatobiliary contrast agents have been shown to be accurate in differentiating HCA from FNH, because the absence of biliary ductules precludes active contrast uptake on delayed imaging by tumor cells in HCA.<sup>20</sup>

Because HCA cannot be differentiated with confidence from both HCC and hypervascular liver metastases, hepatic biopsy is warranted for diagnosis (see Table 36-4).

## Treatment

**Medical Treatment.** Discontinuation of steroid medication is indicated in the conservative management of smaller lesions (<5 cm).

**Surgical Treatment.** Because of the increased risk for complications (i.e., rupture or malignant transformation), surgical resection is warranted for larger lesions (>5 cm). Emergency surgery is required in the event of lesion rupture.

### What the Referring Physician Needs to Know: Hepatocellular Adenoma

- Women of reproductive age with a long-term history of use of oral contraceptives are more commonly affected.
- Smaller lesions (<5 cm) can be treated conservatively with discontinuation of contraceptive medication and follow-up.
- Larger lesions (>5 cm) generally require surgery.

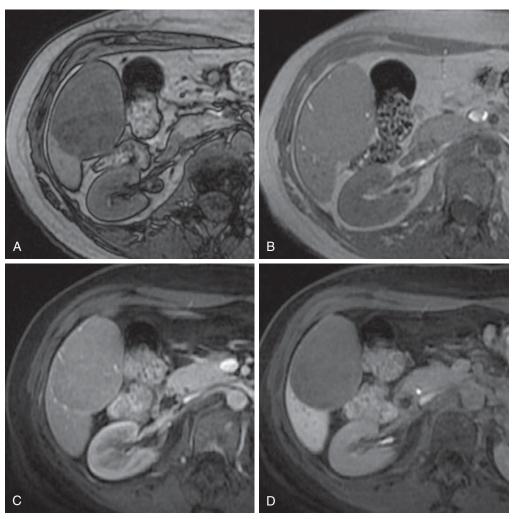
## FOCAL NODULAR HYPERPLASIA

#### Etiology

Rather than a neoplastic process, FNH is considered to be a hyperplastic response of the hepatic parenchyma to a congenital

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**Figure 36-8** Typical magnetic resonance imaging (MRI) findings of steatotic hepatocellular adenoma. A and B, Transverse T1-weighted gradient echo images show diffuse signal intensity decrease of the adenoma on an out-of-phase image (A) compared with that on the in-phase image (B). C and D, On gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced T1-weighted gradient recalled echo MR image the adenoma shows mild enhancement during the hepatic arterial phase (C) and hypointensity on hepatobiliary phase (D).

or acquired anomaly of the arterial blood supply leading to focal hyperperfusion.<sup>27</sup> Oral contraceptives do not play a role for the development of FNH, but their use may stimulate its growth.

## Prevalence and Epidemiology

FNH most frequently occurs in women of childbearing age (male-to-female ratio, 1:8). After hemangioma, FNH is the second most common benign tumor of the liver, with an estimated incidence of 3% to 8% in the general population.

#### **Clinical Presentation**

Typically, FNH is an incidental finding in asymptomatic patients. Rarely, larger lesions may manifest as an abdominal mass and/or abdominal discomfort, which is occasionally associated with pain.

## Pathophysiology

FNH can occur in all liver segments. In 25% of cases, FNH is multiple.

## Pathology

Characteristically, FNH manifests as a single, well-circumscribed, unencapsulated mass, varying in size from a few millimeters to several centimeters. On sectioning, lobulated margins are seen. A stellate fibrous scar (either central or eccentric) represents a hallmark for the diagnosis. Association of FNH with hepatic hemangioma<sup>8,28</sup> and HCA<sup>29</sup> has been described.

On histologic examination, FNH consists of multiple monoacinar nodules (~1 mm in diameter) composed of normalappearing hepatocytes arranged in cell plates 1 to 2 mm thick.<sup>23,27</sup> Nodules are clustered around a fibrous core with radiating septa that contain enlarged feeding arteries and numerous capillaries.<sup>4,30,31</sup> At the interface between hepatocytes and fibrous bands, a cholangiolar proliferation surrounded by an inflammatory infiltrate of variable amount is usually present. Occasionally, lesions show some degree of fatty infiltration.

#### Liver Function

Liver function test results are generally unremarkable.

## Imaging

With current advances in modern cross-sectional imaging, an increasing number of lesions of FNH are incidentally detected in asymptomatic patients.

**Computed Tomography.** On precontrast CT, FNH is typically isoattenuating to the adjacent liver and thus cannot be reliably detected. When occurring in the setting of diffuse fatty liver disease, FNH is typically hyperattenuating because of uniformly decreased attenuation of the hepatic parenchyma.

With the only exception of the central fibrous scar, FNH shows vivid enhancement on contrast-enhanced CT during the hepatic arterial phase<sup>29</sup> and manifests as homogeneous hyperattenuating lesions compared with the surrounding liver. Whereas lesions gradually fade during the portal venous and delayed phases, thus becoming isoattenuating relative to the liver, the central scar typically shows delayed enhancement.

Although most lesions can be confidently diagnosed based on this characteristic enhancement pattern, in a limited number of cases, FNH may show atypical imaging findings, such as washout during the portal venous and delayed phases, peripheral rim enhancement, absence of a central scar (particularly for lesions <3 cm), or lack of delayed enhancement of the central scar.<sup>30</sup> Atypical FNH may simulate either primary or secondary hypervascular malignant liver tumors and thus warrant further investigation with MRI or biopsy.

**Magnetic Resonance Imaging.** Because FNH is almost entirely composed of normal hepatocytes, lesions are nearly isointense compared with the adjacent liver on both T1- and T2-weighted MR images,<sup>31</sup> with the only exception of the central scar, which is typically hypointense on T1-weighted images and hyperintense on T2-weighted images owing to an abundance of myxomatous stroma. Most FNHs show restricted diffusion because of increased cellularity.<sup>25</sup>

On dynamic phases, the FNH enhancement pattern is substantially comparable to that on CT (Figure 36-9).<sup>23</sup> Unlike HCAs and most malignant liver tumors, FNHs take up hepatobiliary contrast agents and thus show isointensity or hyperintensity to background liver on hepatobiliary phase.<sup>23</sup>

**Ultrasonography.** According to recent reports, FNH can be reliably diagnosed on ultrasonography with microbubble contrast agents based on the distinctive enhancement characterized by centrifugal filling of the lesion during the hepatic arterial phase (the so-called *spokewheel appearance*). In addition, FNH shows sustained enhancement in the late parenchymal phase.<sup>26</sup>

**Imaging Algorithm.** An ideal algorithm is presented in Figure 36-15.

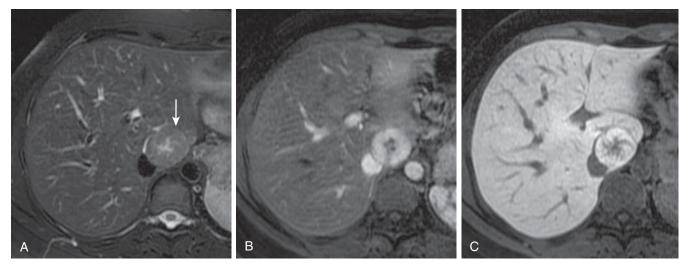
#### Classic Signs: Focal Nodular Hyperplasia

- Homogeneous, bright enhancement on hepatic arterial phase
- Same enhancement of background "nonfatty" liver on noncontrast images and portal venous and delayed phases
- Contrast retention of scar on delayed phase images
- Hyperintense scar on T2-weighted images

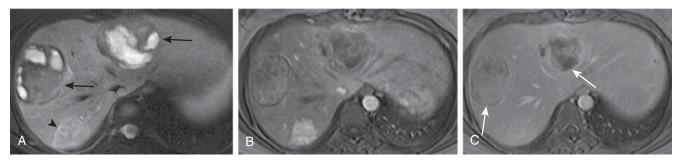
#### **Differential Diagnosis**

Clinical findings usually do not contribute to the diagnosis of FNH. Although FNH can be easily differentiated from HCA based on characteristic imaging findings (Figure 36-10), their appearance may overlap in smaller lesions. Hepatobiliary contrast agents<sup>23</sup> and dynamic evaluation of the lesion perfusion on contrast-enhanced ultrasonography<sup>26</sup> may provide additional clues for differential diagnosis on imaging.

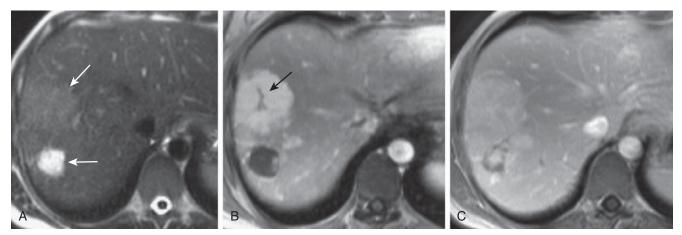
Hepatobiliary contrast agents also enable discrimination of FNH from either primary or secondary hypervascular malignant liver tumors (see Table 36-1). In comparison to large benign regenerative nodules, FNH usually manifests as solitary



**Figure 36-9** Typical magnetic resonance imaging (MRI) findings of focal nodular hyperplasia (FNH). **A**, Fat-suppressed T2-weighted turbo spin echo MR image shows a nearly isointense lesion (*arrow*) with a central, hyperintense scar. **B**, Gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced T1-weighted gradient recalled echo MR image during hepatic arterial phase shows strong and homogeneous enhancement of FNH, with the exception of a central hypointense scar. **C**, Corresponding hepatobiliary phase shows hyperintensity of FNH, with a hypointense central scar.



**Figure 36-10** Magnetic resonance imaging (MRI) findings and differential diagnosis between focal nodular hyperplasia (FNH) and bleeding Hepatocellular adenomas coexisting in the same liver. Axial T2-weighted (A), hepatic arterial phase T1-weighted (B), and delayed phase T1-weighted (C) MR images. Typical imaging findings of FNH include slight hyperintensity (*arrowhead*, A) in comparison with the surrounding liver on T2-weighted image and strong and homogeneous enhancement on T1-weighted gradient recalled echo MR image during the hepatic arterial phase, which fades to isointensity on the corresponding delayed phase image, with the exception of the enhancing central scar. On the other side, adenomas (*arrows*) demonstrate heterogeneous signal intensity on a T2-weighted image, which correspond to areas of intralesional bleeding. Lesions show minimal, heterogeneous enhancement in the hepatic arterial phase and washout on delayed phase images, with the exception of a peripherally enhancing capsule (*white arrows*).



**Figure 36-11** Magnetic resonance imaging (MRI) findings and differential diagnosis between focal nodular hyperplasia (FNH) and cavernous hemangioma coexisting in the same liver. **A**, Unlike FNH (*oblique arrow*), which is only mildly hyperintense compared with the liver, hemangioma (*horizontal arrow*) demonstrates marked hyperintensity on this transverse T2-weighted MR image, which is comparable to cerebrospinal fluid intensity ("light-bulb" sign). **B** and **C**, On gadolinium-enhanced T1-weighted gradient recalled echo MR images, hemangioma shows nodular peripheral enhancement with progressive, centripetal fill and FNH demonstrates strong, immediate enhancement apart from the central hypointense scar (*arrow*) on hepatic arterial phase (**B**). FNH is nearly isointense to surrounding liver during the delayed phase (**C**).

larger lesions originating within a normal liver (see Tables 36-3 and 36-4).

Because of rapid and homogeneous enhancement, small hemangiomas can mimic FNH during the hepatic arterial phase (the flash-filling hemangiomas). However, marked hyperintensity on T2-weighted images, as well as isointensity to blood vessels on contrast-enhanced images, and hypointensity on hepatobiliary phase, usually allows a confident diagnosis of hemangioma (see Table 36-3). Differential diagnosis between FNH and cavernous hemangioma is usually not a challenge, based on the characteristic enhancement pattern and intensity of both lesions (Figure 36-11) (see Tables 36-3 and 36-4).

#### Treatment

**Medical Treatment.** Withdrawal of oral contraceptives usually results in lesion size reduction or stability.

**Surgical Treatment.** Because of the lack of malignant potential and the extremely low complication rate, FNH warrants conservative management.

# What the Referring Physician Needs to Know: Focal Nodular Hyperplasia

- Young women are affected.
- Conservative management is warranted owing to lack of malignant potential and extremely low complication rate.
- Discontinuation of contraceptive medication is recommended owing to its stimulating effect on lesion growth.

## LARGE BENIGN REGENERATIVE NODULES

## Etiology

Large benign regenerative nodules represent a hyperplastic response of the liver in areas with preserved blood supply secondary to impaired perfusion of the remaining hepatic parenchyma. Although several liver disorders may lead to development of large benign regenerative nodules, most cases have been reported in patients with Budd-Chiari syndrome.

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## Prevalence and Epidemiology

Large benign regenerative nodules most frequently occur in young to middle-aged women, perhaps reflecting the gender prevalence of the underlying disorders. They are infrequently reported in childhood. Large benign regenerative nodules almost invariably coexist with diffuse nodular regenerative hyperplasia (NRH) of the liver, which is characterized by diffuse micronodular transformation of the hepatic parenchyma with minimal or no fibrosis.

## **Clinical Presentation**

Although NRH and large benign regenerative nodules may be completely asymptomatic, occasionally patients may develop symptoms, such as portal hypertension and hepatic failure.

## Pathophysiology

Large benign regenerative nodules may occur anywhere within the liver.

## Pathology

Characteristically, large benign regenerative nodules manifest as multiple, rounded, well-circumscribed, unencapsulated masses, varying in size from 0.5 to 4.0 cm.<sup>4</sup> Histologically, large benign regenerative nodules consist of multiacinar nodules that are composed of normal-appearing hepatocytes arranged in cell plates 1 to 2 mm thick and are supplied by enlarged feeding arteries.<sup>4</sup>

#### Liver Function

Liver test results are usually normal or mildly abnormal because of mild elevation of alkaline phosphatase and gamma-glutamyl transpeptidase. As a general rule, alpha-fetoprotein levels are unremarkable.

#### Imaging

Although large benign regenerative nodules have been considered a rare entity, their reported frequency is rising as a result of higher resolution contrast-enhanced CT and MRI performed with multiphasic acquisition protocols.

**Computed Tomography.** Like FNH, large benign regenerative nodules are isoattenuating compared with the adjacent liver on precontrast CT and show marked, homogeneous enhancement

on contrast-enhanced CT during the hepatic arterial phase.<sup>32,33</sup> During the portal venous and delayed phases, large benign regenerative nodules show sustained enhancement and persistent hyperattenuation relative to the hepatic parenchyma.<sup>32,33</sup>

**Magnetic Resonance Imaging.** Unlike FNH, which is almost invariably isointense relative to the liver on precontrast MRI, large benign regenerative nodules usually show hypointensity and hyperintensity on T2-weighted and T1-weighted images, respectively. These findings, which have been related to increased content of paramagnetic metal ions (e.g., copper) within lesion hepatocytes, differentiate large regenerative nodules from FNH on imaging.<sup>32,33</sup>

In dynamic phases, the tumor enhancement pattern is substantially comparable to that on CT (Figure 36-12).<sup>32,33</sup> Like FNH, large benign regenerative nodules show isointensity or hyperintensity in the hepatobiliary phase.<sup>34</sup>

**Ultrasonography.** Large benign regenerative nodules show a variable echoic pattern on ultrasonography, with most lesions (53% of cases) being hyperechoic compared with the surrounding liver.

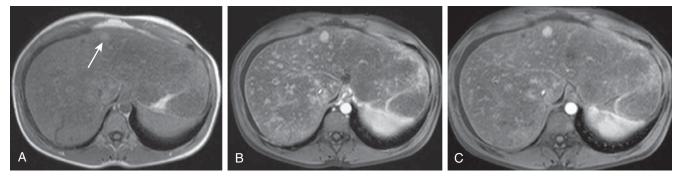
**Imaging Algorithm.** An ideal algorithm is presented in Figure 36-15.

## **Classic Signs: Large Benign Regenerative Nodules**

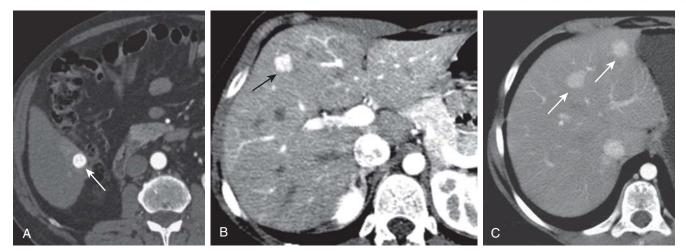
- Multiple
- Hypointense on T2-weighted images
- Hyperintense on T1-weighted images
- Hypervascular
- Sustained enhancement on portal venous and delayed phases

## **Differential Diagnosis**

Large benign regenerative nodules should be strongly suspected when multiple small hypervascular liver lesions are discovered in association with Budd-Chiari syndrome. Because the same initiating mechanism (i.e., focal hyperperfusion of the liver) seems to precede the development of large benign regenerative nodules and FNH, in a substantial number of cases both lesions may not be differentiated on either imaging evaluation or



**Figure 36-12** Typical imaging findings of large benign regenerative nodules in Budd-Chiari syndrome. A, Lesion (*arrow*) is hyperintense compared with the adjacent liver on precontrast T1-weighted image. B, On gadolinium-enhanced T1-weighted gradient recalled echo magnetic resonance image, lesion shows bright enhancement during hepatic arterial phase. C, There is sustained enhancement during portal venous phase. Note the small amount of ascites surrounding the enlarged liver.



**Figure 36-13** Imaging findings and differential diagnosis among small (<2 cm) hypervascular liver lesions, including capillary hemangioma, focal nodular hyperplasia (FNH), and large benign regenerative nodules. Although all lesions demonstrate strong, homogeneous enhancement during the hepatic arterial phase, some clues can be used for a differential diagnosis. A, Capillary hemangioma (*arrow*) demonstrates well-defined margins and characteristic enhancement comparable to aorta. Note the small, wedge-shaped, hyperattenuating area surrounding this lesion, which corresponds to an arteriovenous shunt (*arrow*). B, Unlike hemangioma, FNH (*arrow*) shows finely lobulated margins and a very thin central fibrous scar, which represents its diagnostic hallmark. C, Large benign regenerative nodules are typically multiple (*arrows*), as in this case, and almost invariably occur in the setting of impaired perfusion abnormalities of the liver (more commonly Budd-Chiari syndrome).

histopathologic analysis (Figure 36-13). Unlike FNH, large benign regenerative nodules are usually multiple, are almost invariably associated with vascular disorders of the liver (especially Budd-Chiari syndrome), and rarely show a central scar. In addition, owing to increased content of paramagnetic metal ions, large benign regenerative nodules are characteristically hypointense and hyperintense on T2- and T1-weighted MR images, respectively.

Although HCA can be confidently differentiated from large benign regenerative nodules in the majority of cases based on typical imaging findings (see Table 36-3), lesion uptake of hepatobiliary contrast agents can be the only imaging clue for differentiating large benign regenerative nodules from liver adenomatosis.

Increased uptake of hepatobiliary contrast agents as well as sustained enhancement during the portal venous and delayed phases usually enable confident discrimination of large benign regenerative nodules from primary and secondary hypervascular malignant liver tumors (see Table 36-3).

### Treatment

**Medical Treatment.** Because of low malignant potential,<sup>34</sup> large benign regenerative nodules warrant imaging follow-up. Therapeutic approaches are usually directed toward the management of portal hypertension and include beta-blocker medication and sclerotherapy for esophageal varices.

**Surgical Treatment.** In patients with refractory portal hypertension, transjugular intrahepatic portosystemic shunt is the treatment of choice. Liver transplantation represents the only potential curative therapy in patients with end-stage liver disease and progressive hepatic failure.

## **PYOGENIC HEPATIC ABSCESS**

## Etiology

The most common organisms include *Escherichia coli*, *Klebsiella*, and *Enterobacter*. More than half are polymicrobic.

# What the Referring Physician Needs to Know: Large Benign Regenerative Nodules

- Large benign regenerative nodules are almost invariably associated with an underlying liver disorder, most commonly Budd-Chiari syndrome.
- Because of low malignant potential, conservative management and follow-up are warranted.

Choledocholithiasis, obstructive malignancy, and postsurgical strictures cause extrahepatic biliary obstruction leading to ascending cholangitis and bacterial proliferation and are the most common causes of pyogenic liver abscess formation. Biliary-enteric anastomoses, pylephlebitis from appendicitis and diverticulitis, perforated gastric or duodenal ulcer, infection of infarcted hepatic parenchyma, blunt or penetrating injuries, and septicemia from bacterial endocarditis also have been associated with a high incidence of liver abscesses.

## Prevalence and Epidemiology

Pyogenic hepatic abscesses are defined as localized collection of pus in the liver secondary to an infectious process, with destruction of hepatic parenchyma and stroma. Patients are typically middle-aged.

### Clinical Presentation

Patients typically present with fever and right upper quadrant pain.

### Pathophysiology

Infections in organs draining into the portal system can cause a localized septic thrombophlebitis, which can lead to the development of liver abscesses. Septic emboli can result in formation of microabscesses that are initially multiple ("cluster" sign) but usually coalesce into a solitary lesion.<sup>35</sup>

## Pathology

On gross pathologic examination, sectioning through the pyogenic abscess cavity usually reveals multiple loculated foci, varying in size from a few millimeters to several centimeters. The cavities are usually filled with thick, purulent material and lined by pale fibrous tissue. The fibrous cuff around the abscess is often a centimeter or more thick and gradually merges into the liver parenchyma. Microscopic sections of the abscesses show necrotic fibrinopurulent debris. The edges of the cavities are lined by a chronic inflammatory infiltrate consisting of epithelioid macrophages, lymphocytes, eosinophils, and neutrophils. The fibrous tissue around the abscess cavity can contain a sparser infiltrate as well as small necrotizing and non-necrotizing granulomas.<sup>36</sup>

#### Liver Function

The white blood cell count is usually above normal, and the sedimentation rate is elevated in virtually all cases. Alkaline phosphatase is greater than the age-appropriate level in 50% of cases.

#### Imaging

Tender hepatomegaly, hypoalbuminemia, chills, anorexia, malaise, nausea, vomiting, weight loss, cough secondary to diaphragmatic irritation, atelectasis, and pleural effusion are commonly observed in patients harboring hepatic abscesses. Laboratory data reveal increased leukocytes and serum alkaline phosphatase level (67% to 90%).

**Computed Tomography.** On precontrast CT images, abscesses are hypoattenuating than the surrounding liver. On contrast enhanced images, abscesses typically show capsule and septal enhancement with central hypovascularity (Figure 36-14). Small abscesses aggregate to coalesce into a single, usually



**Figure 36-14** Computed tomography (CT) findings of pyogenic abscess. Transverse contrast-enhanced CT image shows a round, well-defined, hypoattenuating lesion (*arrow*) in the right hepatic lobe, with a thick, peripherally enhancing capsule. Note bulky lymph node (*asterisk*) at the hepatic hilum. In this case, the differential diagnosis between either pyogenic or amebic abscess is not possible based on imaging criteria alone.

septated, larger cavity. Air bubbles and fluid/debris levels might be seen. Intense arterial enhancement of liver parenchyma adjacent to the abscess, when present, is caused by venous compression and poor venous drainage.<sup>36</sup>

**Magnetic Resonance Imaging.** On T1-weighted MR images, pyogenic abscesses show hypointensity relative to the surrounding liver. On T2-weighted images, the wall of the abscess shows slight hyperintensity and the center shows moderate hyperintensity. The wall of the abscess shows hyperintensity on both high b-value diffusion weighted images and ADC map, indicating no restricted diffusion, whereas the center of the abscess shows variable signal intensity depending on the degree of abscess maturation (i.e., the higher the pus viscosity, the higher is the signal intensity on high b-value diffusion weighted images and the lower the signal intensity on ADC map).<sup>36</sup>

On gadolinium-enhanced MRI, abscess wall and septa show intense arterial enhancement, which typically persists on portal venous and delayed phases.<sup>36</sup> Periabscess liver parenchyma sometimes shows high signal intensity on T2-weighted images and intense arterial enhancement.

**Ultrasonography.** On ultrasonography, abscesses appear hypoechoic and heterogeneous in echotexture.

**Imaging Algorithm.** An ideal algorithm is presented in Figure 36-15.

#### **Classic Signs: Hepatic Abscess**

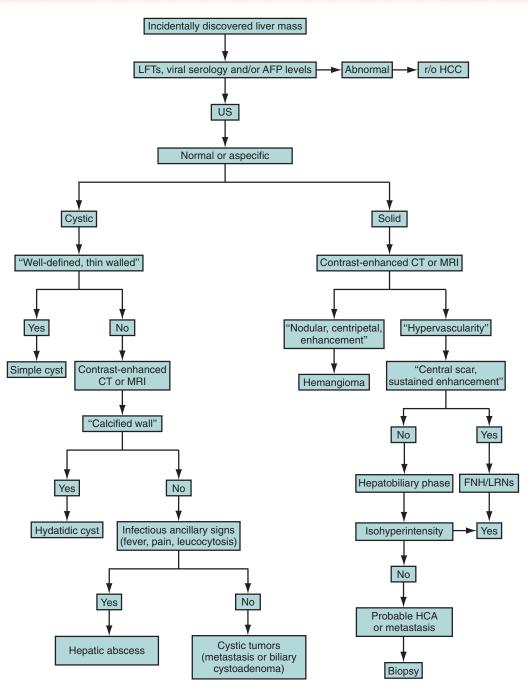
- Small abscesses coalesce into big cavity: "Cluster" sign
- Thick capsule
- Fluid content
- Presence of central gas or fluid level (see Table 36-2)

#### **Differential Diagnosis**

Pyogenic abscess can be difficult to differentiate from amebic abscess on imaging. Amebic abscess is usually sharply defined, hypoechoic or low attenuation, and most often solitary, and shows a thicker wall compared with pyogenic abscesses. Knowing the patient's history is important for the differential diagnosis. A history of diarrhea with mucus in the stool of recent immigrants and homosexuals is more suggestive of amebic rather than pyogenic abscess.

If hepatic abscess is associated with weight loss and anemia, malignancy often is the initial consideration. Metastases, however, are not associated with fever or leukocytosis. Metastases after ablative treatment or infarction in liver transplant can mimic the appearance of a pyogenic abscess on imaging.

A cluster of small cystic lesions or a single large cavity surrounded by a capsule is the classic presentation of pyogenic abscess. Simple hepatic cysts usually have a thin wall and homogeneous content. Liver malignancies are more commonly solid and more enhancing. However, nonliquefied abscess may simulate solid tumor. Metastases usually do not appear as a cluster or septated cystic mass. Treated necrotic metastases may be indistinguishable from abscess. Hepatic hydatid cyst consists of a large cystic liver mass with peripheral daughter cysts and curvilinear or ringlike pericyst calcification. They can cause dilated intrahepatic bile ducts owing to mass effect and/or rupture into bile ducts. Biliary cystadenocarcinoma is a rare,



**Figure 36-15** Flow chart of a practical diagnostic approach to management of benign hepatic lesions. *AFP*, Alpha-fetoprotein; *CAs*, contrast agents; *CT*, computed tomography; *FNH*, focal nodular hyperplasia; *HCA*, hepatocellular adenoma; *HCC*, hepatocellular carcinoma; *LFTs*, liver function tests; *LRNs*, large regenerative nodules; *MRI*, magnetic resonance imaging; *r/o*, rule out; *US*, ultrasound.

multiseptated, water-density cystic mass that can be difficult to differentiate from abscess based on imaging alone. Infarction in liver transplant secondary to hepatic artery thrombosis with hepatic and biliary necrosis can be indistinguishable from pyogenic abscess (see Table 36-2).

#### Treatment

**Medical Treatment.** Intravenous antibiotics and percutaneous drainage are the standard of care. Medical treatment consists of antibiotic or antifungal therapy.

**Surgical Treatment.** Aggressive surgical management with débridement or enucleation of the abscesses is favored if abscesses are not amenable to percutaneous drainage secondary to location, if there is coexistence of other intraabdominal disease requiring operative management, or if combined treatment with antibiotic therapy and percutaneous drainage has failed. Surgery is, however, contraindicated in the presence of multiple abscesses, associated malignancy or immunosuppressive disease, or coexistence of other multiple complicated medical conditions.

# What the Referring Physician Needs to Know: Pyogenic Hepatic Abscess

- Hepatic abscess is associated with elevated white blood cell count, fever, and right upper quadrant pain.
- Causes are an ascending infection in the biliary tract (ascending cholangitis), direct invasion from a nearby source, trauma, diverticulitis, or appendicitis.
- Life-threatening sepsis can develop.
- CT is the most useful imaging technique.
- A cluster of small pyogenic abscesses coalesces into a single large cavity.
- Hepatic abscesses must be differentiated from metastases, hepatic amebic abscess, biliary cyst, biliary cystadenocarcinoma, hydatid cyst, and infarction.

## **Summary**

Assessment of focal liver abnormalities typically relies on several cross-sectional imaging modalities, such as ultrasonography, CT, and MRI, which may be used independently or, even more commonly, in combination (Table 36-5). Although guidelines have been developed for the optimal diagnostic strategy in the diagnosis of most common malignant liver tumors, especially HCC, there is still no consensus on how to optimize the radiologic investigation of incidentally discovered benign liver lesions. Commonly, the diagnostic approach relies on the request of referring physicians, availability of equipment, and experience of the radiologists.

Because of low costs and wide availability, ultrasonography should be considered the first line in the evaluation of an incidentally discovered liver lesion. Despite its inherent limitations, ultrasonography can confidently diagnose two among the most common benign hepatic tumors-simple cysts and hemangioma. Although recently introduced microbubblebased ultrasound contrast agents can provide insights into hemodynamics of a liver lesion, most incidentally discovered solid liver lesions are still investigated with contrast-enhanced CT or MRI. Although both techniques provide reproducible image quality with excellent anatomic detail and have been demonstrated to be equally useful for lesion detection and characterization, CT still represents the modality of choice, owing to its broad availability and overall lower costs compared with MRI. Despite the fact that most benign liver lesions can be definitely characterized on contrast-enhanced CT, taking account of their enhancement pattern as well as the patient clinical history, in a limited number of cases imaging findings may overlap between benign and malignant liver tumors (see Tables 36-3 and 36-4). Owing to the introduction of liver-specific contrast agents and the inherent greater accuracy in exploring tissue characteristics, MRI can provide a more comprehensive workup of focal liver lesions. Because of improved diagnostic and decision-making processes, MRI has been recently proposed as a cost-effective, first-line imaging modality in the evaluation of liver disease. In addition, because of the lack of hazards of ionizing radiation, the use of MRI should be preferred in young patients. Finally, lesion biopsy should still be performed in a limited number of undetermined cases.

### What the Referring Physician Needs to Know: Benign Focal Liver Lesions

The role of imaging in the approach to benign focal liver lesions is to determine the following (see Table 36-5):

- Whether background liver is cirrhotic or noncirrhotic to narrow the differential diagnosis
- Whether lesion is solid or cystic

- Enhancement pattern
- Number, size, and location of liver lesions
- Whether a lesion can be confidently characterized as benign and therefore managed conservatively

TABLEAccuracy36-5	, Limitations, and Pitfalls of the Modalities Use	Limitations, and Pitfalls of the Modalities Used in Imaging of Benign Focal Hepatic Lesions							
Modality	Accuracy	Limitations	Pitfalls						
СТ	<ul> <li>Sensitivity 69%-71%</li> <li>Specificity 86%-91%</li> <li>76% hemangioma from fibrolamellar HCC and FNH</li> <li>76% FNH from fibrolamellar HCC and hemangioma</li> <li>47% sensitivity and 95% specificity in differentiating small hemangiomas from malignant tumors</li> </ul>	Radiation Limited use in patients with allergy or renal insufficiency Potential for anaphylactoid reaction	Lesion detection and characterization may be difficult in fatty liver						
MRI	80%	Motion artifact in uncooperative patients Claustrophobic patients Patients with cardiac pacemaker Risk for nephrogenic systemic fibrosis in patients with renal insufficiency High costs	Calcifications not well visualized						
Ultrasonography	35% B-mode 78% contrast-enhanced ultrasonography	Poor performance in the case of obesity or overlying bowel gas Operator dependent	Calcifications not well visualized						

CT, Computed tomography; FNH, focal nodular hyperplasia; HCC, hepatocellular carcinoma; MRI, magnetic resonance imaging.

### **Key Points**

## Simple Cysts

- Well defined
- Thin walled
- Anechoic with posterior acoustic enhancement on ultrasonography
- Water attenuating on precontrast CT
- Markedly high signal intensity on T2-weighted MR images
- No enhancement after intravenous injection of a contrast agent

## Hemangiomas

- Peripheral, nodular, centripetal enhancement
- Isoattenuation/intensity to vessels on all phases
- Capillary hemangioma: Homogeneous, rapid ("flash filling") enhancement

#### Hepatocellular Adenoma

- Heterogeneous
- Hypervascular
- Washout
- Intratumoral hemorrhage
- Signal drop on out-of-phase imaging
- Hypointensity on hepatobiliary phase in most cases

## SUGGESTED READINGS

- Borhani AA, Wiant A, Heller MT, et al: Cystic hepatic lesions: a review and an algorithmic approach. *AJR Am J Roentgenol* 203:1192–1204, 2014.
- Brancatelli G, Vilgrain V, Federle MP, et al: Benign regenerative nodules in Budd-Chiari syndrome and other vascular disorders of the liver: radiologic-pathologic and clinical correlation. *Radiographics* 22:847–862, 2002.

#### REFERENCES

- Jones EC, Chezmar JL, Nelson RC, et al: The frequency and significance of small (less than or equal to 15 mm) hepatic lesions detected by CT. *AJR Am J Roentgenol* 158:535–539, 1992.
- 2. Seale MK, Catalano OA, Saini S, et al: Hepatobiliary-specific MR contrast agents: role in imaging the liver and biliary tree. *Radiographics* 29:1725–1748, 2009.
- Dai Y, Chen MH, Yin SS, et al: Focal liver lesions: can SonoVue-enhanced ultrasound be used to differentiate malignant from benign lesions? *Invest Radiol* 42:596–603, 2007.
- 4. Ishak KJ, Goodman ZD, Stocker JT, editors: Benign cholangiocellular tumors. In *Tumours* of the liver and intrahepatic bile ducts, ed 3, Washington, DC, 2001, Armed Forces Institute of Pathology, pp 113–114.
- Mortelé KJ, Ro PR: Cystic focal liver lesions in the adult: differential CT and MR imaging features. *Radiographics* 21:895–910, 2001.
- 6. Parikh T, Drew SJ, Lee VS, et al: Focal liver lesion detection and characterization with diffusion-weighted MR imaging: comparison with standard breath-hold T2-weighted imaging. *Radiology* 246:812–822, 2008.
- 7. Brancatelli G, Federle MP, Blachar A, et al: Hemangioma in the cirrhotic liver: diagnosis and natural history. *Radiology* 219:69–74, 2001.
- Vilgrain V, Uzan F, Brancatelli G, et al: Prevalence of hepatic hemangioma in patients with focal nodular hyperplasia: MR imaging analysis. *Radiology* 229:75–79, 2003.

- Choi BY, Nguyen MH: The diagnosis and management of benign hepatic tumors. J Clin Gastroenterol 39:401–412, 2005.
- Horton KM, Bluemke DA, Hruban RH, et al: CT and MR imaging of benign hepatic and biliary tumors. *Radiographics* 19:431–451, 1999.
- Seale MK, Catalano OA, Saini S, et al: Hepatobiliaryspecific MR contrast agents: role in imaging the
- Marsh JI, Gibney RG, Li DK: Hepatic hemangioma in the presence of fatty infiltration: an atypical sonographic appearance. *Gastrointest Radiol* 14:262–264, 1989.
- Nelson RC, Chezmar JL: Diagnostic approach to hepatic hemangiomas. *Radiology* 76:11–13, 1990.
- Quinn SF, Benjamin GG: Hepatic cavernous hemangiomas: simple diagnostic sign with dynamic bolus CT. *Radiology* 182:545–548, 1992.
- McFarland EG, Mayo-Smith WW, Saini S, et al: Hepatic hemangiomas and malignant tumors: improved differentiation with heavily T2-weighted conventional spin-echo MR imaging. *Radiology* 193:43–47, 1994.
- 13. Duran R, Ronot M, Kerbaol A, et al: Hepatic hemangiomas: factors associated with T2 shine-through effect on diffusion-weighted MR sequences. *Eur J Radiol* 83:468–478, 2014.
- Bruegel M, Jochen GJ: Characterization of focal liver lesions by ADC measurements using a respiratory triggered diffusion-weighted singleshot echo-planar MR imaging technique. *Eur Radiol* 18:477–485, 2008.
- Tamada T, Ito K, Yamamoto A, et al: Hepatic hemangiomas: evaluation of enhancement patterns at dynamic MRI with gadoxetate disodium. *AJR Am J Roentgenol* 196:824–830, 2011.
- 16. Gupta RT, Marin D, Boll DT, et al: Hepatic hemangiomas: difference in enhancement pattern on 3T MR imaging with gadobenate

#### Focal Nodular Hyperplasia

- Intense, homogeneous enhancement during hepatic arterial phase (either contrast-enhanced CT, MRI, or ultrasonography)
- Difficult to recognize from surrounding liver during unenhanced, portal venous, and delayed phases
- Isointensity or hyperintensity on hepatobiliary phase in most cases.

#### Large Regenerative Nodules

- Usually found in patients with Budd-Chiari syndrome
- Intense, homogeneous enhancement during hepatic arterial phase
- Sustained enhancement during portal venous and delayed phases
- Hypointensity on T2-weighted and hyperintensity on T1-weighted MR images

#### Hepatic Abscess

- Single or multiple
- Fever and right upper quadrant pain
- CT is the most useful imaging technique

liver and biliary tree. *Radiographics* 29:1725–1748, 2009

Shanbhogue AK, Prasad SR, Takahashi N, et al: Recent advances in cytogenetics and molecular biology of adult hepatocellular tumors: implications for imaging and management. *Radiology* 258:673–693, 2011.

dimeglumine versus gadoxetate disodium. *Eur J Radiol* 81:2457–2462, 2012.

- 17. Tamada T, Ito K, Ueki A, et al: Peripheral low intensity sign in hepatic hemangioma: diagnostic pitfall in hepatobiliary phase of Gd-EOB-DTPA-enhanced MRI of the liver. *J Magn Reson Imaging* 35:852–858, 2012.
- Bioulac-Sage P, Laumonier H, Couchy G, et al: Hepatocellular adenoma management and phenotypic classification: the Bordeaux experience. *Hepatology* 50:481–489, 2009.
- Furlan A, van der Windt DJ, Nalesnik MA, et al: Multiple hepatic adenomas associated with liver steatosis at CT and MRI: a case-control study. *AJR Am J Roentgenol* 191:1430–1435, 2008.
- Fléjou JF, Barge J, Menu Y, et al: Liver adenomatosis: an entity distinct from liver adenoma? *Gastroenterology* 89:1132–1138, 1985.
- Ichikawa T, Federle MP, Grazioli L, et al: Hepatocellular adenoma: multiphasic CT and pathologic findings in 25 patients. *Radiology* 214:861–868, 2000.
- 22. Laumonier H, Bioulac-Sage P, Laurent C, et al: Hepatocellular adenomas: magnetic resonance imaging features as a function of molecular pathological classification. *Hepatology* 48:808– 818, 2008.
- Grazioli L, Bondioni MP, Haradome H, et al: Hepatocellular adenoma and focal nodular hyperplasia: value of gadoxetic acid-enhanced MR imaging in differential diagnosis. *Radiology* 262:520–529, 2012.

- 24. Agarwal S, Fuentes-Orrego JM, Amason T, et al: Inflammatory hepatocellular adenomas can mimic focal nodular hyperplasia on gadoxetic acid-enhanced MRI. *AJR Am J Roentgenol* 203:W408–W414, 2014.
- 25. Agnello F, Ronot M, Valla DC, et al: High-bvalue diffusion-weighted MR imaging of benign hepatocellular lesions: quantitative and qualitative analysis. *Radiology* 262:511–519, 2012.
- Kim TK, Jang HJ, Burns PN, et al: Focal nodular hyperplasia and hepatic adenoma: differentiation with low-mechanical-index contrast-enhanced sonography. *AJR Am J Roentgenol* 190:58–66, 2008.
- Wanless IR, Mawdsley C, Adams R: On the pathogenesis of focal nodular hyperplasia of the liver. *Hepatology* 5:1194–2000, 1985.
- 28. Nguyen BN, Fléjou JF, Terris B, et al: Focal nodular hyperplasia of the liver: a comprehensive

pathologic study of 305 lesions and recognition of new histologic forms. *Am J Surg Pathol* 23:1441–1454, 1999.

- 29. Brancatelli G, Federle MP, Grazioli L, et al: Focal nodular hyperplasia: CT findings with emphasis on multiphasic helical CT in 78 patients. *Radiology* 219:61–68, 2001.
- Choi CS, Freeny PC: Triphasic helical CT of hepatic focal nodular hyperplasia: incidence of atypical findings. *AJR Am J Roentgenol* 170:391– 395, 1998.
- Vilgrain V, Fléou JF, et al: Focal nodular hyperplasia of the liver: MR imaging and pathologic correlation in 37 patients. *Radiology* 184:699– 703, 1992.
- Vilgrain V, Lewin M, Vons C, et al: Hepatic nodules in Budd-Chiari syndrome: imaging features. *Radiology* 210:443–450, 1999.
- 33. Brancatelli G, Federle MP, Katyal S, et al: Large regenerative nodules in Budd-Chiari syndrome and other vascular disorders of the liver: CT and MR imaging findings with clinico-pathologic correlation. *AJR Am J Roentgenol* 178:877–883, 2002.
- Moucari R, Rautou PE, Cazals-Hatem D, et al: Hepatocellular carcinoma in Budd-Chiari syndrome: characteristics and risk factors. *Gut* 57:828–835, 2008.
- Jeffrey RB, Jr, Tolentino CS, Chang FC, et al: CT of small pyogenic hepatic abscesses: the cluster sign. AJR Am J Roentgenol 151:487–489, 1988.
- 36. Park HJ, Kim SH, Jang KM, et al: Differentiating hepatic abscess from malignant mimickers: value of diffusion-weighted imaging with an emphasis on the periphery of the lesion. J Magn Reson Imaging 38:1333–1341, 2013.

# **Malignant Focal Lesions**

DANIELE MARIN | FRANCESCO AGNELLO | GIUSEPPE BRANCATELLI

## **Etiology**

37

Malignant liver tumors can be classified either by cell of origin as hepatocellular, cholangiocellular, or mesenchymal or by site of origin as primary or secondary. This chapter will describe the most frequently encountered malignant hepatic tumors arising in the noncirrhotic liver, including hepatocellular carcinoma (HCC), fibrolamellar HCC, epithelioid hemangioendothelioma (EHE), angiosarcoma, and metastatic disease. Also discussed are other rare primary liver tumors, such as lymphoma and hepatoblastoma. HCC arising in cirrhosis and intrahepatic cholangiocarcinoma are discussed elsewhere in this text.

# **Prevalence and Epidemiology**

Metastases are the most common malignant neoplasm of the liver, with an incidence of 40% in cancer patients at the time of death. Although HCC—one of the most common causes of cancer death worldwide—usually occurs in the setting of cirrhosis, in approximately 10% of cases this tumor occurs without cirrhosis or other known risk factors. Other primary malignant mesenchymal (i.e., angiosarcoma and EHE), hepatocellular (i.e., hepatoblastoma), or lymphoid (i.e., primary or secondary lymphoma) tumors are much rarer, accounting for only 1% to 2% of all primary malignant liver neoplasms.

## **Clinical Presentation**

Clinical presentation is usually nonspecific and includes fever of unknown origin, abdominal pain, malaise, weight loss, a palpable abdominal mass, or cachexia.

## Pathophysiology

Malignant liver lesions may occur anywhere in the liver. The ability of computed tomography (CT) and magnetic resonance imaging (MRI) to show hepatic tumors is enhanced by the dual blood supply of the liver. Although liver tumors generally receive nearly all their blood supply from the hepatic artery, after bolus intravenous injection of a contrast agent some of them enhance more than the surrounding liver parenchyma (hypervascular tumors) in the hepatic arterial phase, whereas others will be best depicted as low-attenuation or low-intensity lesions (hypovascular) against the background of enhanced liver during the portal venous phase.

# Pathology

Pathologic findings vary greatly according to the specific tumor type and degree of differentiation.

## **Liver Function**

Tumor markers such as alpha-fetoprotein, protein induced from the absence of vitamin K (PIVKA), carcinoembryonic antigen (CEA), and cancer antigen 19-9 (CA 19-9) are commonly used for differentiating focal liver lesions, although their role for diagnosis is controversial. Laboratory examination is nonspecific and can reveal increased levels of alkaline phosphatase and transaminases or minor elevation of bilirubin levels.

## Imaging

## COMPUTED TOMOGRAPHY

The multiphasic imaging capability of multidetector CT (MDCT) allows different protocols to be set for both hypovascular and hypervascular lesions. The advantages of MDCT include high speed with less motion artifact (i.e., improved temporal resolution), submillimeter slice thickness with true isotropic imaging, ease of image interpretation, and the ability to cover large volumes and create multiplanar reformatted images. Sagittal, coronal, or curved multiplanar reformatted images can better delineate those small subcapsular lesions in the dome of the liver that might not be well depicted with transverse imaging alone. In patients who are candidates for hepatic resection, CT angiography yields an excellent depiction of the relationship of the lesion to intrahepatic vessels.

## MAGNETIC RESONANCE IMAGING

The major advantages of MRI over CT are higher contrast resolution; better ability to detect, characterize, and quantify both intrahepatic and intralesional fat and iron; and the use of both extracellular and hepatobiliary contrast agents. The most diagnostically important information is usually obtained from multiphase gadolinium-enhanced, fat-suppressed threedimensional T1-weighted gradient recalled echo MRI, including a properly timed hepatic arterial phase, followed by portal venous and delayed phases. T2-weighted imaging is not used for lesion detection but rather for lesion characterization. Precontrast T1-weighted in-phase and opposed-phase imaging allows assessment of lipid and iron content within the liver or lesion. With the widespread of hepatobiliary contrast media (gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid [Gd-EOB-DTPA] and gadobenate dimeglumine [Gd-BOPTA]) and diffusion weighted imaging, MRI currently represents the modality of choice for the detection of hepatic metastases, with reported diagnostic accuracy values exceeding those of either ultrasonography or MDCT.

### ULTRASONOGRAPHY

Although ultrasonography is frequently the first-line modality for imaging of the liver because of low costs and widespread availability, its role is currently limited in the evaluation of patients with malignant liver tumors and must be invariably supplemented with either MDCT or MRI. By providing insights on lesion vascularity, ultrasound contrast agents have recently shown the potential to improve both detection and characterization of a lesion.

# POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

Because most malignant tumors show abnormally high fluorodeoxyglucose (FDG) metabolism, positron emission tomography (PET) provides a differentiating clue between malignant and benign hepatic lesions. Potential sources of confusion may occur with a minority of liver abscesses, which may simulate malignant lesions secondary to increased FDG uptake (falsepositive finding). Conversely, false-negative results may occur with smaller or well-differentiated HCCs, which may demonstrate only subtle increase in FDG uptake. Besides its wellestablished role in lesion detection, PET also can provide important clues for tumor staging and early detection of tumor recurrence after therapy.

#### What the Referring Physician Needs to Know: Malignant Focal Liver Lesions

The role of imaging in the approach to malignant focal liver lesions is to determine the following (Table 37-1):

- Number, size, and location
- Differentiation of benign versus malignant
- Differentiation of primary versus secondary
- Whether the background liver shows normal or altered morphology (e.g., chronic liver disease)
- Whether the background liver shows fatty infiltration
- Indications for biopsy (especially in smaller lesions)
- Suitability of resection (relationship of the tumor to surrounding vessels)
- Tumor staging (rule out extrahepatic metastatic disease)
- Reliable follow-up after treatment

## **Specific Lesions**

## EPITHELIOID HEMANGIOENDOTHELIOMA

## Etiology

There are no known risk factors for hepatic EHE.

## Prevalence and Epidemiology

Hepatic EHE is a low to intermediate grade malignant vascular neoplasm with an intermediate clinical course between that of cavernous hemangioma and malignant angiosarcoma. EHE shows a slight female predominance (male-to-female ratio, 2:3), with a peak incidence of approximately 50 years of age.<sup>1</sup>

## **Clinical Presentation**

Clinical manifestations are nonspecific and vary from asymptomatic patients to patients with portal hypertension or hepatic

failure. The most common findings are weakness, anorexia, weight loss, right upper quadrant pain, and hepatomegaly. Unusual manifestations includes acute abdomen from rupture of the tumor hemoperitoneum, Budd-Chiari–like syndrome, portal hypertension, and liver failure as a result of extensive replacement of liver parenchyma by the tumor.<sup>1</sup>

## Pathophysiology

Characteristically, EHE demonstrates a peripheral, subcapsular location, although in advanced cases lesions may grow to almost replace the entire liver. Compensatory hypertrophy of unaffected hepatic parenchyma can be seen in patients with extensive liver involvement.<sup>2</sup>

#### Pathology

Typically, EHE manifests as multiple lesions, ranging from 1 to 3 cm in diameter. On sectioning, lesions are white to tan and firm, with a fibrous, relatively hypocellular center surrounded by a rim of hyperemic, actively proliferating viable tissue. An additional peripheral hypovascular halo may be observed at the interface between the tumor and the surrounding hepatic parenchyma and has been related to a narrow avascular zone secondary to tumor occlusion of hepatic sinusoids and small vessels.<sup>2</sup> Larger lesions are generally confluent, thus forming aggregate masses that may sometimes contain coarse calcifications. Demonstration of the vascular or endothelial origin of the tumor is critical for diagnosis and requires immunostaining for endothelial markers, including factor VIII–related antigen, CD31, and CD34.<sup>1</sup>

## Liver Function

Increased alkaline phosphatase activity may be present in approximately two thirds of patients. Tumor marker levels, such as alphafetoprotein and CA 19-9 levels, are generally unremarkable.<sup>1</sup>

#### Imaging

**Computed Tomography.** CT findings reflect the gross appearance of the tumor and typically demonstrate multiple, peripheral, and partially confluent liver masses. Capsular retraction can be seen when lesions abut the liver surface. On precontrast CT, EHE is generally hypoattenuating compared with the liver, with the only exception being occasional intralesional calcifications. On contrast-enhanced CT, EHE shows a very characteristic target-type enhancement pattern with a central hypoattenuating area, which corresponds to the central fibrous core, surrounded by a peripheral thick enhancing ring and an outer hypoattenuating halo, which corresponds to the peripheral viable tumor and the avascular zone of transition, respectively (Figure 37-1).<sup>1-3</sup>

**Magnetic Resonance Imaging.** On T1-weighted MRI, EHE shows hypointensity with a markedly hypointense central area. On T2-weighted MR images, EHE shows a characteristic target appearance with a markedly hyperintense central area and a mild hyperintense peripheral rim (see Figure 37-1). On diffusion weighted images, the central area shows restricted diffusion, while the peripheral rim shows intensity decrease at high b-value. On dynamic images, the tumor enhancement pattern is substantially comparable to that on CT.<sup>2,3</sup>

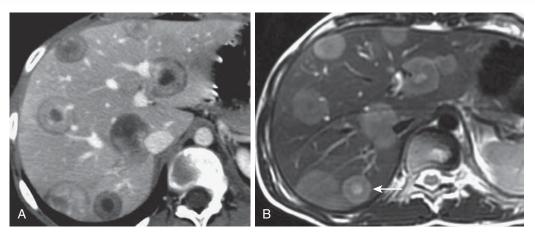
**Ultrasonography.** EHE appears as lobulated confluent hepatic lesions with variable echotexture on gray-scale ultrasonography and with most lesions being hypoechogenic.<sup>1</sup>

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TABLE Clinical and 37-1	Radiologi	c Features of	f Malignar	nt Focal	Clinical and Radiologic Features of Malignant Focal Liver Tumors						
Tumor	Sex	Age	Capsule	Size	Number	Calcification	Fat	Scar	Bleed	Bleed Necrosis	Associated Signs and Predisposing Factors
Epithelioid hemangioendothelioma	F > M ma	4th-5th decade	No	Variable	Multifocal	13%	No	No	No	No	Capsular retraction Subcapsular location
Angiosarcoma	M × E	M > F 6th-7th decade	о Z	Variable	Multiple nodules or large mass	Rare	No	No	Yes	Yes	Thorotrast
Fibrolamellar carcinoma		M = F 2d-3rd decade	35%	Large	Usually solitary	Central (68%)	No	Yes (80%) Hypo on T2-weighted	No	Yes	Lymphadenopathy
HCC in noncirrhotic liver	er M > F	: 5th-6th decade	51%	Large	One or few	Peripheral (28%)	10%		Rare	Yes	Hepatitis B and C
Hepatoblastoma	M × E	M > F Infants and children <3 yr	° Z	Large	Single or multinodular	30%	No	No	Yes	Yes	Genetic
Lymphoma	M V F	: 6th-7th decade	0 Z	Variable	Usually solitary Rare (10%)	Rare (10%)	No	No	No	No	Multiorgan involvement and lymphadenopathy
Hypervascular metastases Hypovascular metastases		M = F Variable M = F Variable	o N N N	Variable Variable	Multiple Multiple	Rare (neuroendocrine) No Rare (colon) No	N No	Rare (neuroendocrine) No No		Yes Yes	Primary malignancy Primary malignancy
F, Female; HCC, hepatocellular carcinoma; M, male.	sellular carc	inoma; <i>M</i> , mal∈	ci.								

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**Figure 37-1** Typical computed tomography (CT) and magnetic resonance imaging (MRI) findings of epithelioid hemangioendothelioma. **A**, Transverse contrast-enhanced CT image during portal venous phase shows multiple round masses with a typical target appearance resulting from a hypoattenuating center surrounded by a hyperattenuating inner rim and a thin hypoattenuating outer halo. **B**, On this T2-weighted turbo spin echo MR image, the central area appears markedly hyperintense compared with the adjacent liver and is surrounded by a mildly hyperintense rim (*arrow*) that corresponds to viable tumor.

# TABLE Differential Features Among Mesenchymal Liver Tumors (Hemangioma, Epithelioid Hemangioendothelioma, 37-2 and Angiosarcoma) and Angiosarcoma

Features	Hemangioma	EHE	Angiosarcoma
Sex	F > M	$F \ge M$	M > F
Age	2nd-5th decade	4th-5th decade	6th-7th decade
Location	Variable	Subcapsular	Diffuse liver involvement
Shape	Round/oval	Round	III-defined
Number	Single > multiple	Multiple	Multiple
Capsular retraction	No	Yes	No
Central scar	Rare (larger lesions)	No	No
Calcifications	Only large lesions	Uncommon	Uncommon
Enhancement	Centripetal	Low degree	Bizarre, centrifugal
Necrosis	No	No	Yes

E, Epithelioid hemangioendothelioma; F, female; M, male.

**Positron Emission Tomography With Computed Tomography.** <sup>18</sup>FDG-PET/CT has shown some utility for detection of EHE recurrence after resection.

**Imaging Algorithm.** An imaging algorithm is provided in Figure 37-14 at the end of this discussion.

#### Classic Signs: Epithelioid Hemangioendothelioma

- Multiple round lesions or large confluent masses
- Target appearance ("bull's eye")
- Subcapsular location with retraction of the overlying capsule

#### **Differential Diagnosis**

Absence of a known history of a primary tumor may be helpful in ruling-out metastatic disease. Because EHE may occasionally show delayed enhancement, lack of a history of cirrhosis helps in differentiating it from peripheral cholangiocarcinoma. Positive imaging findings, in addition to features such as occurrence in younger adults, relative indolent progression of the disease, and the presence of numerous intrahepatic tumors with a good clinical condition are suggestive of EHE.<sup>1</sup>

EHE can be confidently differentiated from hemangioma based on tumor enhancement as well as demonstration of retraction of the adjacent liver capsule (Table 37-2). In cases in which retraction of the liver capsule overlying a lesion is noted, absence of morphologic changes of cirrhosis and regenerative nodules is helpful to differentiate these lesions from confluent hepatic fibrosis and absence of biliary dilatation is key to differentiate them from peripheral cholangiocarcinoma (Table 37-3 and Figure 37-2). The definitive diagnosis requires core biopsy and histologic analysis, because the typical target sign observed in EHE can be mimicked by metastatic disease (Figure 37-3).<sup>1</sup>

#### Treatment

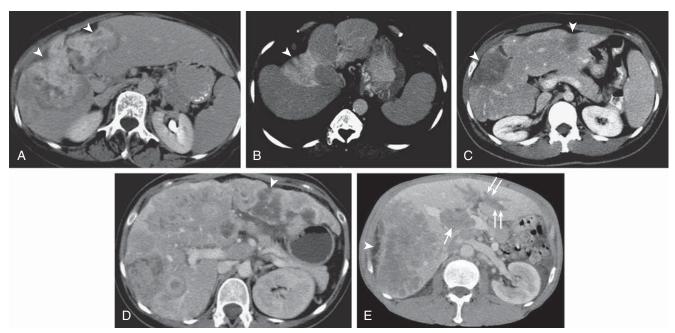
**Medical Treatment.** At present, the roles of radiation and chemotherapy are still undetermined.

#### TABLE **37-3**

Differential Features Associated With Retraction of the Liver Capsule (Peripheral Cholangiocarcinoma, Focal Confluent Fibrosis, Epithelioid Hemangioendothelioma, Metastases, and Hemangioma)

Features	Peripheral Cholangiocarcinoma	Focal Confluent Fibrosis	EHE	Metastases	Hemangioma
Sex	F = M	M > F	$F \geq M$	F = M	F > M
Age	6th-8th decade	6th-7th decade	4th-5th decade	Any age	2nd-5th decade
Predisposing factors	Primary sclerosing cholangitis	End-stage cirrhosis	None	Primary malignancy	None
Number	Single	Single	Multiple	Multiple	Single > multiple
Delayed enhancement	++	++	±	±	+++
Central calcifications	No	No	Uncommon	Uncommon (mucinous primary)	Uncommon (larger lesions)
Capsular retraction	++	++ (Advanced cirrhosis)	++	After chemotherapy	No
Necrosis	++	-	±	++	-
Enhancement on portal venous phase	+ (Ring)	Rare (trapped vessels)	-	±	++ (Nodular, peripheral, discontinuous)

EHE, Epithelioid hemangioendothelioma; F, female; M, male.



**Figure 37-2** Computed tomography imaging findings and differential diagnosis among liver lesions associated with capsular retraction, including peripheral cholangiocarcinoma, focal confluent fibrosis, epithelioid hemangioendothelioma, and treated metastases from breast and rectal adenocarcinoma. These conditions show capsular retraction (*arrowheads*) when abutting the liver surface. Peripheral cholangiocarcinoma (**A**) and focal confluent fibrosis (**B**) characteristically demonstrate enhancement during the delayed phase owing to an abundance of fibrotic tissue. **C**, Epithelioid hemangioendothelioma also can manifest as an infiltrative mass owing to the confluence of multiple lesions. **D**, Patients with metastatic breast carcinoma characteristically show a pseudocirrhotic appearance after chemotherapy. **E**, Note massive thrombosis into the main portal vein (*arrow*) and moderate left intrahepatic biliary duct dilatation (*double arrows*) secondary to neoplastic infiltration in this patient with metastatic rectal carcinoma.

**Surgical Treatment.** Surgical resection and liver transplantation are considered the treatments of choice. Liver transplantation is beneficial in patients with multiple lesions and extensive involvement of liver parenchyma.

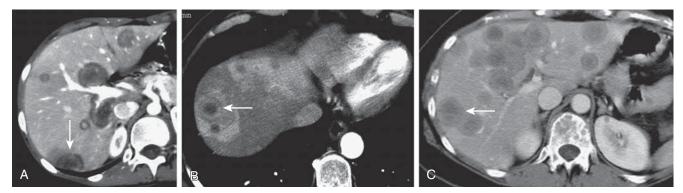
## ANGIOSARCOMA

## Etiology

Although several conditions, such as hemochromatosis, von Recklinghausen's disease, and environmental carcinogens

#### What the Referring Physician Needs to Know: Epithelioid Hemangioendothelioma

- EHE is a low-grade malignant primary tumor.
- CT and MRI are the best diagnostic tools but cannot provide a definitive diagnosis.
- Biopsy is required for definitive diagnosis.
- Liver resection and transplantation are the treatments of choice.



**Figure 37-3** Computed tomography imaging findings of epithelioid hemangioendothelioma (A), pancreatic (B), and breast (C) adenocarcinoma metastases. Lesions are multiple, are partially confluent, and have a "target" appearance (*arrows*) in all cases. The target sign is therefore not specific for epithelioid hemangioendothelioma.

(i.e., vinyl chloride, thorium dioxide, and arsenic), may favor the development of angiosarcoma, currently most cases occur in patients without known associated risk factors.<sup>4</sup>

### Prevalence and Epidemiology

Angiosarcoma is a high-grade malignant neoplasm of endothelial cells. This tumor represents the most common sarcoma of the liver. The peak age incidence is in the sixth and seventh decades, with a male-to-female ratio of 3:1.4

## **Clinical Presentation**

Angiosarcomas typically manifest at an advanced stage with hepatomegaly, ascites, abdominal pain, and weight loss. Sudden onset with acute symptoms may result from spontaneous tumor rupture and subsequent hemoperitoneum.<sup>4</sup>

#### Pathophysiology

Angiosarcoma manifests as a single or a multifocal lesion, and involves both liver lobes.<sup>4</sup>

#### Pathology

Typically, angiosarcoma is a well-circumscribed lesion with a variegated appearance resulting from areas of hemorrhage and necrosis. On histologic examination, tumor cells demonstrate a preferential growth along sinusoids, terminal hepatic venules, and portal vein branches that lead to progressive disruption of liver cell plates with the development of blood-filled cavitary spaces of varied size. Invasion of terminal hepatic venules and portal vein branches also leads to atrophy, infarction, and necrosis of hepatic parenchyma.<sup>4,5</sup>

#### Liver Function

The most reliable abnormalities include increased serum alkaline phosphatase activity, hyperbilirubinemia, and prolonged prothrombin time. $^5$ 

#### Imaging

Angiosarcomas show an aggressive behavior with metastases to spleen, lung, bone marrow, portohepatic nodes, and peritoneum. A rare complication is tumor rupture, which results in acute hemoperitoneum. Because of the tumor vascularity and associated coagulopathy and thrombocytopenia, liver biopsy is associated with significantly high morbidity and mortality rates.<sup>4</sup>



**Figure 37-4** Computed tomography (CT) imaging findings of angiosarcoma. Transverse contrast-enhanced CT image during portal venous phase shows multiple round, solid masses (*arrows*).

**Computed Tomography.** On precontrast CT, angiosarcoma is hypoattenuating or isoattenuating to surrounding liver. Focal hyperattenuating areas can be seen secondary to intralesional hemorrhage. On contrast-enhanced CT, lesions have a variable appearance. In some cases, angiosarcoma lacks obvious enhancement, whereas some other times it shows irregular arterially enhancing foci, which increase in size on portal venous and delayed phases<sup>4</sup> (Figure 37-4)

**Magnetic Resonance Imaging.** Because angiosarcomas are predominantly composed of blood-filled tumor cavities, they show heterogeneous and markedly high signal intensity on T2-weighted images and very low signal intensity on T1-weighted images. Intralesional hemorrhagic foci can be seen as focal areas of bright signal intensity on T1-weighted images. On low- and high b-value diffusion weighted images, angiosarcoma shows heterogeneous high intensity, with high intensity on apparent diffusion coefficient (ADC) map. On gadolinium-enhanced MRI, the tumor enhancement pattern is substantially comparable to that at CT.<sup>4,6</sup>

**Ultrasonography.** Angiosarcomas manifest as heterogeneously hyperechoic lesions.<sup>4,5</sup>

**Positron Emission Tomography With Computed Tomography.** Lesions show markedly increased accumulation of <sup>18</sup>FDG compared with the surrounding liver parenchyma. This technique is particularly sensitive for the detection of distant metastases.<sup>4</sup>

**Imaging Algorithm.** An imaging algorithm is provided in Figure 37-14.

### Classic Signs: Angiosarcoma

- Multifocal nodules
- Heterogeneous enhancement
- Progressive enhancement over time
- Distant metastases

#### Differential Diagnosis

Association with hemochromatosis or von Recklinghausen's disease or exposure to Thorotrast and arsenic can raise the suspicion of angiosarcoma.<sup>4,5</sup> BizaFrre shape of the enhancing foci, large size of dominant lesions, multifocal distribution, and intratumoral hemorrhage are useful differentiating features from those of cavernous hemangioma (see Table 37-2).<sup>4,5</sup>

#### Treatment

**Medical Treatment.** Chemotherapy or antiangiogenic therapy may be performed in patients with diffuse liver involvement that is not amenable to surgical treatment.

**Surgical Treatment.** Combined surgery and radiation therapy can offer the best chance of treatment, although the tumor is invariably associated with a poor outcome (5-year survival rate, 37%).

# What the Referring Physician Needs to Know: Angiosarcoma

- Angiosarcoma is the most common malignant mesenchymal tumor of the liver.
- It may be difficult to differentiate from other primary or secondary neoplasms.
- Multiphasic contrast-enhanced CT and MRI are the best diagnostic tools.
- Outcome is poor.
- The tumor can recur after surgery.

# HEPATOCELLULAR CARCINOMA IN THE NONCIRRHOTIC LIVER

#### Etiology

Although predisposing factors such as hepatitis, viral infection, or alcohol abuse have been reported in some cases, no underlying liver disease can be found in the majority of patients. Nonalcoholic fatty liver disease may represent the underlying causative factor in some instances.

Other causes include exposure to genotoxic substances (e.g., aflatoxin B1) and hereditary disorders (e.g., hemochromatosis and Wilson's disease).<sup>7</sup>

## Prevalence and Epidemiology

In a substantial number of cases, noncirrhotic HCC may arise de novo in an otherwise normal liver. Unlike cirrhotic HCC, noncirrhotic HCC shows a bimodal age distribution, peaking at the 2nd and 7th decades. Patients have a better prognosis as well as a longer survival rate than patients with HCC in the cirrhotic liver.<sup>7,8</sup>

## **Clinical Presentation**

Because the disease course is generally indolent and tumor surveillance is not performed, tumor size is typically large at diagnosis. At presentation, the most common signs and symptoms include abdominal pain, distention, weight loss, and anorexia. In a limited number of patients without referred symptoms, the tumor may be incidentally discovered at imaging studies for unrelated reasons.<sup>7,8</sup>

#### Pathophysiology

Noncirrhotic HCC occurs predominantly in the right hepatic lobe.<sup>7</sup>

#### Pathology

Noncirrhotic HCC typically manifests as a large, predominantly solitary or dominant mass with satellite lesions. Lesions may be well-defined and partially encapsulated, with areas of hemorrhage, macroscopic fat, and necrosis. Invasion of the portal vein or the biliary ducts and metastases to abdominal lymph nodes are occasionally observed. Despite the large size of lesions, most noncirrhotic HCCs are well to moderately differentiated at histologic analysis. This finding correlates well with the favorable prognosis of this tumor compared with that of noncirrhotic HCC.<sup>7</sup>

## Liver Function

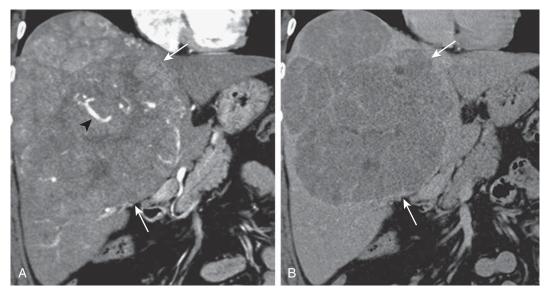
Although serologic levels of alpha-fetoprotein are abnormally increased in 65% of cases, in a consistent number of patients this tumor marker is within normal values (20 mcg/L or less).<sup>7</sup>

## Imaging

Noncirrhotic HCC comes to clinical attention because of a palpable abdominal mass, abdominal pain, distention, weight loss, anorexia, or cachexia.<sup>7</sup>

**Computed Tomography.** On precontrast CT, noncirrhotic HCC manifests as a large, dominant lesion that is hypoattenuating compared with the surrounding liver, with the exception of occasional peripheral calcification. With contrast-enhanced CT, noncirrhotic HCC shows heterogeneous, moderate enhancement during the hepatic arterial phase, followed by washout (i.e., the lesion is hypoattenuating relative to the liver) during the portal venous and delayed phases. Areas of necrosis or hemorrhage are frequently depicted as nonenhancing intralesional foci (Figure 37-5). Tumor invasion of the portal vein, hepatic veins, and biliary ducts is common.<sup>7,9</sup>

**Magnetic Resonance Imaging.** On precontrast MRI, noncirrhotic HCC shows nonspecific imaging findings with hypointensity and mild hyperintensity on T1- and T2-weighted MR images, respectively. Cystic-like or necrotic areas appear as markedly hypointense and hyperintense on T1- and T2-weighted images, respectively. On diffusion weighted images,



**Figure 37-5** Typical computed tomography (CT) imaging findings of hepatocellular carcinoma in a noncirrhotic liver. **A**, Coronal contrast-enhanced CT image during hepatic arterial phase demonstrates a large, heterogeneously enhancing mass (*arrows*) replacing almost the entire right liver lobe. Note prominent vascularity with large feeding arteries (*arrowhead*) entering the lesion. **B**, Corresponding CT image during portal venous phase shows washout of the tumor, which appears hypoattenuating compared with the adjacent liver. Note enhancement of peripheral fibrous capsule (*arrows*).

noncirrhotic HCC shows signal intensity increase with increasing b-values, indicating restricted diffusion. During dynamic phases, the tumor enhancement pattern is substantially comparable to that of CT. In the hepatobiliary phase, the tumor cannot take up hepatobiliary contrast agents and thus show hypointensity.<sup>7</sup>

**Ultrasonography.** HCC manifests as large, predominantly hypoechoic masses, with a complex appearance because of areas of necrosis and hemorrhage.

**Positron Emission Tomography With Computed Tomography.** <sup>18</sup>FDG-PET/CT is useful in the evaluation of HCC metastases, although its role in the diagnosis of primary HCC is more limited.

**Imaging Algorithm.** An imaging algorithm is provided in Figure 37-14.

# Classic Signs: Hepatocellular Carcinoma in the Noncirrhotic Liver

- Predominantly affects middle-aged men
- Solitary large lesion or dominant mass with smaller satellite nodules
- Capsule
- Heterogeneous hypervascularity
- Lymphadenopathy
- Vascular and, less commonly, biliary tract invasion
- Washout

## Differential Diagnosis

Absence of a primary tumor such as neuroendocrine, thyroid, or renal carcinoma may contribute to exclude hypervascular metastases.

	Differential Features Between Fibrolamellar
ABLE	Hepatocellular Carcinoma and Hepatocellular
57	Carcinoma in the Noncirrhotic Liver

Features	Fibrolamellar HCC	НСС
Features	Fibrolamellar HCC	псс
Sex	M = F	M > F
Average age	2nd-3rd decade	5th-6th decade
Calcifications	68% (central)	28% (peripheral)
Surface	Lobulated	Lobulated
Capsule	35%	51%
Average size	13 cm	12.4 cm
Lymphadenopathy	65%	21%
Intralesional fat	~0%	10%
Scar	Yes	No
Necrosis	Yes	Yes
Enhancement on hepatic arterial phase	Strong	Mild
Homogeneity on hepatic arterial phase	No	No

F, Female; HCC, hepatocellular carcinoma; M, male.

Larger lesion size as well as a noncirrhotic appearance of the background liver (i.e., regular liver margins and well-preserved liver morphology) represent useful imaging clues to rule out classic HCC. Lack of a "true" central scar with calcification can help in the differential diagnosis with fibrolamellar HCC (Table 37-4). Absence of delayed enhancement and of capsular retraction can reduce the likelihood of cholangiocarcinoma and mixed hepatocholangiocarcinoma.

#### Treatment

**Medical Treatment.** No medical treatment is effective in HCC occurring in a noncirrhotic liver.

**Surgical Treatment.** Extensive, aggressive surgery is the treatment of choice for HCC in the noncirrhotic liver. Because local tumor recurrence within the liver is a frequent occurrence, long-term follow-up is mandatory, because surgery for recurrent disease prolongs survival.<sup>8</sup>

What the Referring Physician Needs to Know: Hepatocellular Carcinoma in the Noncirrhotic Liver

- HCC can rarely occur in a noncirrhotic liver, usually in middle-aged men.
- HCC in the noncirrhotic liver occurs at a younger age than HCC in the cirrhotic liver.
- Hepatic resection is the optimal treatment strategy.
- CT and MRI are useful for planning hepatic resection, staging, and follow-up.

# FIBROLAMELLAR HEPATOCELLULAR CARCINOMA

#### Etiology

Fibrolamellar HCC is a distinct type of HCC. It is not associated with chronic liver disease. Etiologic factors for fibrolamellar HCC have not been identified.<sup>10</sup>

## Prevalence and Epidemiology

Fibrolamellar HCC is a rare primary hepatic malignancy with an epidemiology and clinical course different from that of cirrhotic HCC. Fibrolamellar HCC occurs in younger patients, with most cases diagnosed before the age of 40. Fibrolamellar HCC shows no sex predilection. Patients with fibrolamellar HCC show a better resectability rate as well as improved survival rate than those with cirrhotic HCC.<sup>10</sup>

#### **Clinical Presentation**

At clinical presentation, most lesions are symptomatic because of their large size. Signs and symptoms include abdominal pain, hepatomegaly, palpable right upper quadrant abdominal mass, and cachexia. Jaundice is an uncommon finding (5% of cases) and results from biliary compression by either the dominant tumor mass or mass effect of metastatic lymphadenopathy. The tumor also may manifest as symptoms related to metastatic dissemination to distant organs.<sup>10</sup>

## Pathophysiology

Fibrolamellar HCC occurs predominantly in the left hepatic lobe.<sup>11</sup>

## Pathology

Fibrolamellar HCC generally manifests as a large, single, welldefined but nonencapsulated mass. On sectioning, lesions show a lobulated appearance, firm to hard consistency, and a characteristic central fibrous scar with radiating septa. Areas of hemorrhage and necrosis can be seen within the tumor in fewer than half of cases. The background liver is almost invariably normal. On histologic examination, the distinctive features of fibrolamellar HCC are the coexistence of both fibrous stroma and tumor cells, typically arranged in a uniform sheetlike pattern.<sup>11</sup>

#### Liver Function

Liver function tests may be normal or mildly elevated. Fibrolamellar HCC is infrequently accompanied by increased circulating levels of alpha-fetoprotein.<sup>10</sup>

### Imaging

Fibrolamellar HCC comes to clinical attention because of either mass effect–related symptoms or nonspecific symptoms of malignancy.<sup>11</sup>

**Computed Tomography.** On precontrast CT, fibrolamellar HCC manifests as a large, solitary, well-demarcated and lobulated mass that is hypoattenuating compared with the surrounding liver. Intratumoral areas of hemorrhage, necrosis, and calcification are present in approximately two thirds of cases. On contrast-enhanced CT, fibrolamellar HCC shows vivid and heterogeneous enhancement with the exception of the central fibrous scar. During the portal venous and delayed phase, lesions show washout and become hypoattenuating compared with the liver. Notably, unlike other benign liver tumors with a central scar (e.g., focal nodular hyperplasia [FNH]), there is no delayed enhancement of the central fibrous scar. Multiple, bulky metastatic nodes can frequently be seen at the hepatic hilum and anterior cardiophrenic angles (Figure 37-6).<sup>11-13</sup>

**Magnetic Resonance Imaging.** On MRI, fibrolamellar HCC is hypointense and mildly hyperintense on T1- and T2-weighted images, respectively. Because of dense fibrous stroma and calcification, the central fibrous scar is characteristically hypointense on both T1- and T2-weighted images. On diffusion weighted images, fibrolamellar HCC shows restricted diffusion. On dynamic phases, the tumor enhancement pattern is substantially comparable to that of CT (see Figure 37-6). During the hepatobiliary phase, the tumor is typically hypointense.<sup>12-13</sup>

**Ultrasonography.** Fibrolamellar HCC shows variable appearance on gray-scale ultrasonography, with most lesions being predominantly hypoechoic. A central echogenic area with tiny hyperechoic foci may be frequently seen and corresponds to the central fibrous scar and calcifications at pathologic analysis.<sup>13</sup>

**Positron Emission Tomography With Computed Tomogra-phy.** The usefulness of PET/CT in the evaluation of fibrolamellar HCC has not been fully investigated.<sup>13</sup>

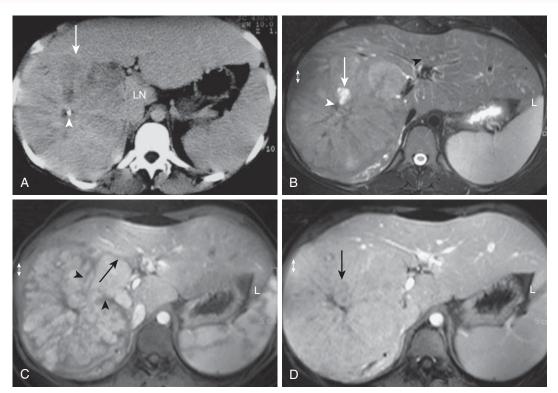
**Imaging Algorithm.** An imaging algorithm is provided in Figure 37-14.

#### Classic Signs: Fibrolamellar Hepatocellular Carcinoma

- Large lesion
- Heterogeneous, strong enhancement
- Washout
- Lobulated margins
- Central scar with calcifications
- Hypointensity of the scar on T2-weighted imaging
- Metastatic lymphadenopathy (cardiophrenic angle)

#### **Differential Diagnosis**

Younger age and lack of history of chronic liver disease allow the differential diagnosis with HCC. Because of some similarities in demographic and imaging appearances, the differential diagnosis of fibrolamellar HCC from FNH may be challenging (Figure 37-7 and Table 37-5). Besides common signs of malignancy, such as biliary or vascular invasion and metastatic

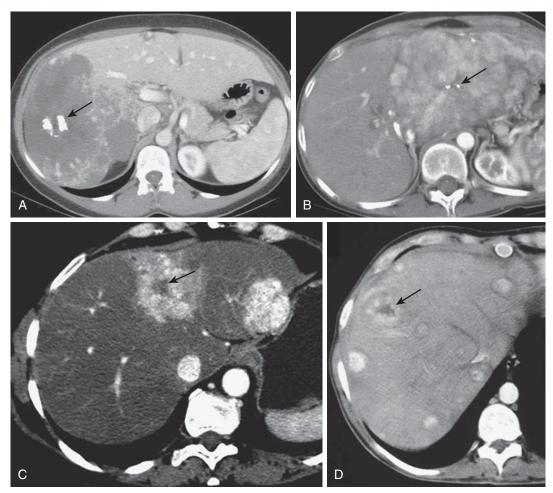


**Figure 37-6** Typical computed tomography (CT) and magnetic resonance imaging (MRI) findings of fibrolamellar hepatocellular carcinoma. A, Transverse contrast-enhanced CT image shows a large right liver lobe mass (*arrow*) with central calcification (*arrowhead*). Bulky lymphadenopathy (*LN*) is seen at hepatic hilum. **B**, On fat-suppressed T2-weighted turbo spin echo MR image, the mass demonstrates mild hyperintensity compared with the adjacent liver. The central scar (*arrowhead*) is hypointense. A hyperintense area (*arrow*), which corresponds to tumor necrosis, is also seen. **C**, On fat-suppressed T1-weighted gradient recalled echo MR image during the hepatic arterial phase, this lesion shows marked, heterogeneous enhancement and is hyperintense relative to the liver, with the only exception of the central fibrous scar, radiating septa (*arrowheads*), and capsule (*arrow*). **D**, On corresponding image during the portal venous phase, the tumor becomes isointense compared with the surrounding liver. A central portion of the tumor that was of high signal intensity on T2-weighted imaging is noted as low signal intensity (*arrow*) on this sequence. The central fibrous scar remains hypointense. (*From Brancatelli G, Federle MP*, et *al: Hepatocellular and fibrolamellar carcinoma. In Lencioni R, Cioni D, Bartolozzi C, editors:* Focal liver lesions: detection, characterization, ablation, *Berlin, 2005, Springer, pp 209–217. With kind permission of Springer Science+Business Media.*)

# TABLE Differential Features Among Lesions With Central Scar (Focal Nodular Hyperplasia, Fibrolamellar 37-5 Hepatocellular Carcinoma, Giant Hemangioma, Large Regenerative Nodules)

Features	Focal Nodular Hyperplasia	Fibrolamellar HCC	Giant Hemangioma	Large Regenerative Nodules
Sex	F > M	F = M	F > M	F > M
Age	3rd-4th decade	2nd-3rd decade	2nd-5th decade	3rd-4th decade
Central scar	Yes	Yes	Yes	Larger lesions
Enhancement degree on hepatic arterial phase	Very strong	Strong	Isoattenuating to aorta	Strong
Homogeneous enhancement on hepatic arterial phase	Yes	No	No	Yes
Central calcifications	No	68%	Yes	No
Capsule	No	35%	No	No
Lobulated shape	Yes	Yes	Yes	No
Lymph nodes	No	65%	No	No
Delayed enhancement of lesion	No	No	Yes	No
Delayed enhancement of scar	Yes	No	No	No
Washout on portal venous and delayed phases	No	Yes	No	No
Signal intensity on hepatobiliary phase	lsointense or hyperintense	Hypointense	Hypointense	lsointense or hyperintense
Scar hyperintensity on T2 weighting	Yes	No	Yes	Yes
Necrosis	No	Yes	No	No

HCC, Hepatocellular carcinoma.



**Figure 37-7** Computed tomography imaging findings and differential diagnosis among liver lesions showing a central fibrous scar, including giant hemangioma, fibrolamellar hepatocellular carcinoma (HCC), focal nodular hyperplasia (FNH), and large regenerative nodules. Although these lesions have a central fibrous scar, the differential diagnosis relies on imaging findings of both the lesion and the scar. A, Regardless its size, hemangioma invariably shows peripheral nodular enhancement that is isoattenuating to vessels and with centripetal progression. Larger lesions may manifest as a central, calcified scar, as in this case (*arrow*). **B**, Fibrolamellar HCC typically manifests as a large lesion originating in the left liver lobe that demonstrates strong, heterogeneous enhancement during the hepatic arterial phase and washout during the portal venous phase. Note coarse calcifications of the central scar (*arrow*) that represent a hallmark for this tumor. **C** and **D**, Unlike fibrolamellar HCC, FNH and large regenerative nodules both demonstrate strong enhancement during the hepatic arterial phase and no washout during the portal venous phase. Both lesions may show a central fibrous scar (*arrow*) that, as a general rule, does not calcify. Although multiplicity is a characteristic of large regenerative nodules, this finding also can be observed in patients with FNH, as in this case. (*B from Brancatelli G, Federle MP, et al: Hepatocellular and fibrolamellar carcinoma. In Lencioni R, Cioni D, Bartolozzi C, editors: Focal liver lesions: detection, characterization, ablation, <i>Berlin, 2005, Springer, pp 209–217. With kind permission of Springer Science+Business.*)

dissemination to lymph nodes or distant organs, additional clues for the diagnosis of fibrolamellar HCC include hypointensity on hepatobiliary phase, larger size, heterogeneous enhancement, and low signal intensity on T2-weighted images as well as lack of delayed enhancement of the central fibrous scar.<sup>11</sup> In some cases, giant hemangiomas also can show a central fibrous scar that is usually larger than fibrolamellar HCC. However, hemangiomas can be readily diagnosed based on their typical enhancement pattern (see Table 37-5).

## Treatment

**Medical Treatment.** Several chemotherapeutic regimens have been used, with partial responses.

**Surgical Treatment.** Partial resection or liver transplantation represents the optimal treatment in patients with fibrolamellar HCC. All series have reported long survival periods after

excision, with the longest postresection survival time of 21 years. The most significant determinant of survival is tumor stage.  $^{14}$ 

What the Referring Physician Needs to Know: Fibrolamellar Hepatocellular Carcinoma

- Fibrolamellar HCC typically occurs in patients younger than 40 years of age.
- It frequently demonstrates aggressive local invasion, with both nodal and distant metastases.
- The indolent growth rate is relative.
- Pretherapy imaging is important for staging.
- Aggressive surgical resection may prolong survival.
- Imaging after resection is important for surveillance.
- Prognosis is better than that of HCC when the tumor is resected.

#### **HEPATOBLASTOMA**

#### Etiology

Hepatoblastoma has been associated with prematurity and low birth weight. The coincidence of hepatoblastoma with familial adenomatous polyposis and Beckwith-Wiedemann syndrome suggests a role in the pathogenesis of hepatoblastoma for chromosomes 5 and 11, respectively.<sup>15</sup>

#### Prevalence and Epidemiology

Hepatoblastoma is the most frequent liver tumor in children, accounting for half of those that are malignant. Males are twice as commonly affected as females in early childhood, but tumor frequency is nearly equal in older children.<sup>15</sup>

#### **Clinical Presentation**

Common signs and symptoms include rapidly enlarging abdomen, weight loss or anorexia, nausea, vomiting, abdominal pain, and jaundice. Occasionally, paraneoplastic phenomena, such as precocious puberty with genital enlargement, appearance of pubic hair, and a deepening voice may appear, owing to tumor overproduction of human chorionic gonadotropin.<sup>15</sup>

#### Pathophysiology

He patoblastoma occurs more frequently in the right lobe of the liver.  $^{\rm 16}$ 

#### Pathology

On gross inspection, hepatoblastoma generally manifests as a large mass. On sectioning, it is well demarcated, with prominent vascularity and a variegated appearance as a result of areas of hemorrhage, necrosis, and calcification. Two types of hepatoblastoma have been described on histopathologic analysis: the epithelial type and the mixed epithelial type.<sup>16</sup>

#### Liver Function

Laboratory findings almost invariably show elevated alphafetoprotein levels, which is regarded as a reliable predictor of tumor response to chemotherapeutic treatment and patient outcome.<sup>15</sup>

#### Imaging

Hepatoblastoma usually manifests as an asymptomatic, firm, irregular mass noted on physical examination in the right abdomen. Because lesions are generally large, they may extend across the midline or down to the pelvic brim. Weight loss, anorexia, emesis, and abdominal pain indicate advanced disease.<sup>15</sup>

**Computed Tomography.** On precontrast CT, hepatoblastoma typically manifests as a large, solitary, predominantly hypoattenuating mass with heterogeneous internal texture as a result of intralesional hemorrhage, calcifications, and necrosis. On contrast-enhanced CT, the tumor shows slight and heterogeneous enhancement pattern, but remains hypoattenuating to the surrounding liver. Strong arterial enhancement of the septa and periphery sometimes can be observed (Figure 37-8). Vascular invasion and a peripheral rim of enhancement also can be seen.<sup>17</sup>

**Magnetic Resonance Imaging.** Because hepatoblastoma invariably occurs in children or younger patients, MRI is the modality of choice in the preoperative evaluation of the tumor owing to the lack of hazards of ionizing radiation. On precontrast MRI, hepatoblastoma shows nonspecific imaging findings with slight hypointensity and mild hyperintensity on T1- and T2-weighted images, respectively. Areas of hemorrhage can be seen as intratumoral hyperintense foci on T1-weighted images, whereas calcification is depicted as signal void on T2-weighted images. On dynamic phases, the tumor enhancement pattern is substantially comparable to that of CT.<sup>17</sup>

**Ultrasonography.** Hepatoblastomas generally manifest as welldefined, solid, echogenic lesions on gray-scale ultrasonography. Occasionally, tumors may show a spoked-wheel appearance owing to prominent fibrous bands. Calcification and mesenchymal elements can be seen as increased echogenic areas.<sup>17</sup>

**Positron Emission Tomography With Computed Tomography.** PET/CT may enable optimal evaluation of liver parenchyma

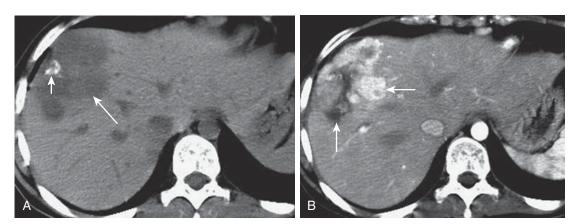


Figure 37-8 Computed tomography (CT) of a hepatoblastoma. A, Transverse precontrast CT image demonstrates a large, hypoattenuating mass (*arrow*) with a peripheral coarse calcification (*short arrow*) in the right lobe. B, On contrast-enhanced CT image during hepatic arterial phase, the mass shows marked, heterogeneous enhancement resulting from coexistence of both viable tumor (*horizontal arrow*) and necrosis (*vertical arrow*).

in patients with either primary or recurrent hepatoblastoma and also may detect metastatic sites not identified by other imaging techniques, thus allowing more precise tumor staging.

**Imaging Algorithm.** An imaging algorithm is provided in Figure 37-14.

- Classic signs: Hepatoblastoma
- Young age (<3 years)
- Right lobe of liver
- Large lesion
- Coarse calcifications
- Internal septa
- Peripheral rim enhancement

#### Differential Diagnosis

Patient age is the major clinical discriminator between hepatoblastoma and HCC. Elevated alpha-fetoprotein level, but normal serum vanillylmandelic acid level, may provide a clue for differentiating hepatoblastoma from neuroblastoma. Although diagnosis of hepatoblastoma can be rarely based on imaging findings, a pattern of coarse and dense calcifications is suggestive of this neoplasm and allows differentiation with the fine granular calcifications of infantile hemangioendothelioma.<sup>17</sup>

#### Treatment

**Medical Treatment.** Despite the fact that 40% to 60% of hepatoblastomas are considered to be unresectable at the time of diagnosis, nearly 85% of cases may become resectable after neoadjuvant chemotherapy.<sup>18</sup>

**Surgical Treatment.** Surgery remains the mainstay in the treatment of hepatoblastoma, with prognosis directly related to tumor stage. Lesions localized to a single lobe can be adequately treated by lobectomy. Liver transplantation has demonstrated promising results and is currently performed in patients with larger lesions, including those requiring preoperative chemotherapy.<sup>18</sup>

# What the Referring Physician Needs to Know: Hepatoblastoma

- Hepatoblastoma typically affects infants and children younger than 3 years of age.
- Some imaging features are helpful in differentiating hepatoblastoma from other pediatric tumors.
- Cure of hepatoblastoma can be achieved by surgical resection.
- Orthotopic liver transplantation is a suitable approach in patients with unresectable hepatoblastoma.
- MRI is the preferred modality to define tumor margins, determine tumor resectability, and detect residual or recurrent tumor after surgery.

# LYMPHOMA

#### Etiology

Although secondary involvement of the liver by advanced Hodgkin's or non-Hodgkin's lymphoma is relatively common, primary hepatic lymphoma is an exceedingly rare neoplasm. Its frequent association with hepatitis B and C virus infection suggests that this virus plays some role in the pathogenesis of the neoplasm.<sup>19</sup>

#### Prevalence and Epidemiology

Unlike secondary involvement of the liver in patients with multiorgan lymphoma, primary hepatic lymphoma is a malignant neoplasm that arises in, and is initially confined to, the liver. In the majority of cases, splenic involvement is also present at the time of detection. This tumor shows a slight predominance in males (male-to-female ratio, 2.5:1) with a peak incidence from the sixth to the seventh decade.<sup>19</sup>

#### **Clinical Presentation**

Symptoms are generally nonspecific and include abdominal pain, hepatomegaly, weight loss, and fever. Occasionally, hepatic lymphoma may be incidentally discovered in asymptomatic patients.<sup>19</sup>

#### Pathophysiology

Patients usually have an enlarged liver containing solitary or multiple masses.

#### Pathology

Primary and secondary hepatic lymphomas may manifest as either solitary or multifocal disease. Tumor size varies from a few millimeters to several centimeters and is generally larger for solitary lesions. Occasionally, tumors may manifest as a diffuse, infiltrative growth pattern.

On histologic examination, all hepatic lymphomas are classified as non-Hodgkin's with coexistence of both B- and T-cell lineage. Misdiagnosis—as metastatic carcinoma, chronic hepatitis, or inflammatory pseudotumor—is common.<sup>20</sup>

#### Liver Function

Serum liver enzymes, lactate dehydrogenase, and beta-2 microglobulin levels are usually elevated, whereas alpha-fetoprotein and CEA levels are within normal range.<sup>20</sup>

#### Imaging

Presenting complaints consist of abdominal pain, weakness, fatigue, and constitutional symptoms. Hepatomegaly is frequent.

**Computed Tomography.** On precontrast CT, hepatic lymphomas are generally isoattenuating to hypoattenuating compared with the surrounding liver. On contrast-enhanced CT, lymphomas manifest as either solitary or multifocal, well-defined hypoattenuating lesions (Figure 37-9). In cases of diffuse, infiltrative liver involvement, lymphoma manifests as diffuse areas of decreased attenuation with geographic configuration, thus mimicking focal fatty infiltration or hepatic metastases (Figure 37-10).<sup>20</sup>

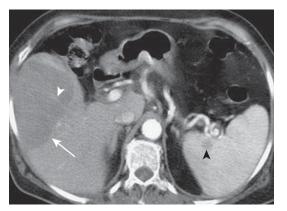
**Magnetic Resonance Imaging.** Hepatic lymphomas show a wide spectrum of imaging appearances on MRI. Although lesions are generally isointense to hypointense relative to the liver on T1-weighted images, their appearance can vary from low to moderate hyperintensity on T2-weighted images and may reflect differences in tumor vascularity, size of extracellular space, and presence of necrosis and fibrosis.

As a result of high cellularity, lymphomas typically show marked restricted diffusion. During dynamic phases, the tumor

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enhancement pattern is substantially comparable to that with CT.<sup>21</sup> In the hepatobiliary phase, lymphomas are typically hypointense.

**Ultrasonography.** On gray-scale ultrasonography, primary hepatic lymphomas generally appear as well-defined, either



**Figure 37-9** Typical computed tomography (CT) imaging findings of lymphoma. Transverse contrast-enhanced CT image during the portal venous phase shows a large, solitary mass (*arrow*) in the right liver lobe that is hypoattenuating compared with the adjacent hepatic parenchyma. A portal venous branch (*white arrowhead*) extending through the lesion is barely visible. A small splenic lesion (*black arrowhead*) is also seen.

anechoic or hypoechoic lesions that mimic simple hepatic cysts, except for the absence of increased through-transmission.<sup>20</sup>

**Positron Emission Tomography With Computed Tomography.** At present, PET/CT is commonly used to stage both Hodgkin's disease and non-Hodgkin's lymphoma. Besides its high sensitivity for detecting nodal disease regardless of the lesion site and size, PET/CT also can accurately demonstrate extranodal involvement, such as liver and splenic lesions. In addition, PET/CT is the modality of choice for evaluating recurrent lymphomas as well as tumor response to therapy.

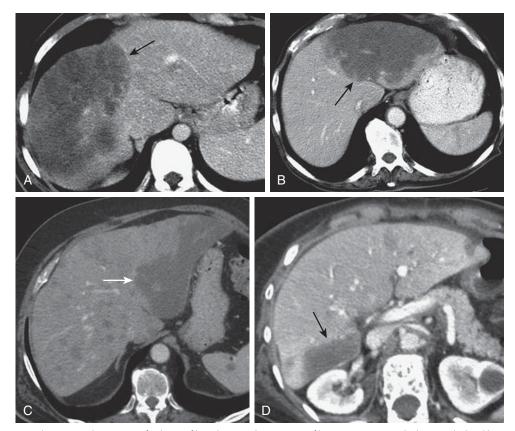
**Imaging Algorithm.** An imaging algorithm is provided in Figure 37-14.

#### Classic Signs: Lymphoma

- Rare
- Unknown cause
- Solitary
- Large
- Infiltrative pattern
- Decreased attenuation

# **Differential Diagnosis**

Clinical data do not provide any clue for the diagnosis of primary hepatic lymphoma. The absence of increased throughtransmission on ultrasonography is helpful for differentiation



**Figure 37-10** Computed tomography imaging findings of liver lesions showing an infiltrative pattern, including epithelioid hemangioendothelioma (A), lymphoma (B), fatty infiltration (C), and breast metastases (D). Although an infiltrative appearance (*arrows*) is generally regarded as a worrisome sign, differential diagnosis among both malignant and benign liver lesions is frequently challenging solely based on imaging findings.

TABLE 37-6

Differential Features among Lesions With Infiltrative Pattern (Epithelioid Hemangioendothelioma, Lymphoma, Fatty Infiltration, and Metastases)

Features	EHE	Lymphoma	Fatty Infiltration	Metastases
Sex	$F \ge M$	M > F	F = M	F = M
Age	4th-5th decade	6th-7th decade	5th decade	Any age
Associated conditions	None	Multiorgan involvement	Obesity, diabetes	Primary malignancy
Normal vessels through lesion	No	Yes	Yes	No
Lymph nodes	No	Yes	No	Yes
Capsular retraction	Yes	±	No	Yes if previous chemotherapy
Straight margins	No	No	Yes	No
Hypertrophy of unaffected liver	Yes	No	No	No
Signal drop on out-of-phase MRI	No	No	Yes	No

EHE, Epithelioid hemangioendothelioma; F, female; M, male; MRI, magnetic resonance imaging.

from a simple hepatic cyst.<sup>20</sup> On contrast-enhanced CT and MRI, lymphomas do not show the perilesional, continuous rim enhancement followed by centripetal filling that characterize metastases.

Differential diagnosis with other infiltrative liver lesions, such as EHE, infiltrative primary or secondary neoplasms, and focal steatosis, can be challenging (see Figure 37-10 and Table 37-6). Unlike in the setting of fatty liver disease, lymphomas do not show signal drop on opposed-phase MR images.

#### Treatment

**Medical Treatment.** Primary lymphoma shows an excellent response rate associated with the use of combination chemotherapy alone.<sup>19</sup>

**Surgical Treatment.** Surgery alone has been advocated for those patients with small solitary hepatic lesions, although its efficacy is frequently limited by early extrahepatic recurrence.<sup>19</sup>

# What the Referring Physician Needs to Know: Lymphoma

- Primary hepatic non-Hodgkin's lymphoma is rare and difficult to diagnose.
- Patients are typically male and middle-aged.
- This is a lymphoproliferative disorder of unknown cause.
- Typical presenting complaints are right upper quadrant pain, nausea, and emesis with significant weight loss.
- Prognosis in affected patients is dismal, with early disease recurrence at extrahepatic sites and short survival.
- Anthracycline-based chemotherapy is the most appropriate treatment.

#### **HEPATIC METASTASES**

#### Etiology

The liver provides a prime location for metastases from malignant tumors because of its location, blood supply, anatomy, as well as other poorly understood factors.

#### Prevalence and Epidemiology

Metastases are by far the most common malignant neoplasm of the liver. In the United States, it has been estimated that up to 40% of patients with cancer have metastatic dissemination to the liver at the time of death. After regional lymph nodes, the liver is the predominant site of metastasis. Although liver metastases are fed primarily by arterial blood supply, they have been arbitrarily classified as either hypervascular or hypovascular according to their enhancement pattern compared with that of the surrounding hepatic parenchyma at either contrastenhanced CT or MRI.

The most common primary sites for liver metastases include the gastrointestinal tract, pancreas, gallbladder, breast, lung, eye, and carcinoids.<sup>22,23</sup>

#### **Clinical Presentation**

Metastases are often detected during radiologic workup of patients with newly discovered primary tumors. In advanced stages, signs and symptoms are referred to liver involvement and include hepatomegaly, anorexia, weight loss, and right upper quadrant abdominal pain (30% to 40%). Less than 10% of patients may present with a palpable mass.<sup>22-24</sup>

#### Pathophysiology

Metastases may be found anywhere in the liver but usually occur more in the right lobe than the left. The reason for this distribution is unclear, although possible reasons may be the greater total mass of the right lobe compared with the left lobe and underlying differences in laminar portal vein flow patterns, which may guide the distribution of metastatic cells.

#### Pathology

Liver metastases typically manifest as multiple irregular nodules, with a variable size ranging from a few millimeters to several centimeters. Central areas of avascular necrosis can be frequently seen at the center of the lesions. After chemotherapy, metastases may demonstrate an umbilicated appearance owing to scarring and retraction. On histologic examination, metastases closely resemble the appearance of primary tumor. By taking advantage of histochemical and immunohistochemical stains, experienced pathologists often can suggest the primary site when unknown.<sup>22-24</sup>

#### Liver Function

Liver-associated enzymes, such as alkaline phosphatase and gamma-glutamyl transpeptidase, are frequently abnormal in patients with liver metastases. Elevated blood levels of CEA are commonly discovered in patients with liver metastases from colorectal and pancreatic adenocarcinomas.

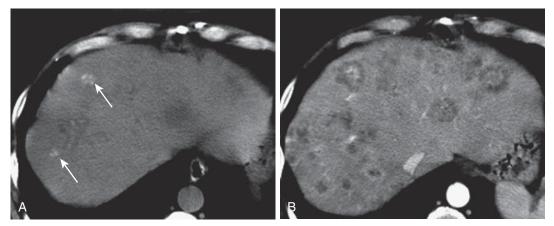
#### Imaging

Clinical signs and symptoms referable to the liver are generally associated with far advanced tumor stages as well as extensive liver involvement.

**Computed Tomography.** Although metastases can be mildly hypoattenuating relative to the liver, lesion conspicuity is relatively poor on precontrast CT. Occasionally, intratumoral calcifications can be seen in mucinous adenocarcinoma metastases (e.g., colon and ovary metastases) (Figure 37-11) or after local or systemic chemotherapy.<sup>25</sup> Hypervascular metastases, such as those from neuroendocrine tumors, thyroid, renal cell carcinoma, pheochromocytoma, and, occasionally, breast, melanoma, and gastrointestinal stromal tumors, are best depicted during the hepatic arterial phase when they manifest as hyperattenuating foci compared with the surrounding liver (Figure 37-12).<sup>26-27</sup> Hypovascular metastases, which encompass the vast

majority of cases (e.g., colon tumor metastases), manifest as hypoattenuating lesions during the portal venous phase when the maximum enhancement of hepatic parenchyma occurs (see Figure 37-11).<sup>28</sup> Early peripheral rim enhancement also can be seen in hypovascular liver metastases and reflects highly vascularized viable tumor at the periphery of the lesion.<sup>29</sup>

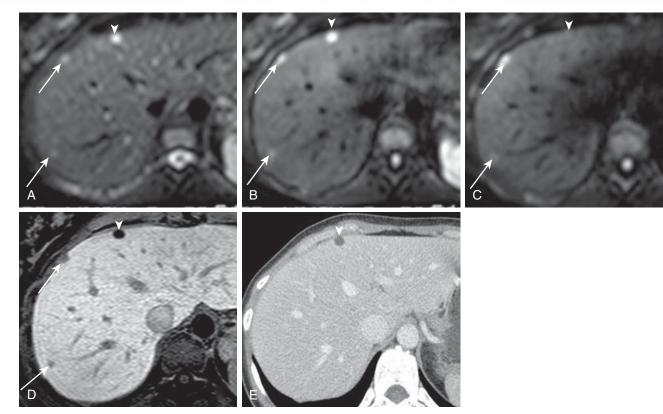
**Magnetic Resonance Imaging.** On MRI, metastases show nonspecific imaging findings with hypointensity and mild hyperintensity on T1- and T2-weighted MR images, respectively. In the setting of diffuse fatty liver disease, metastases may appear hyperintense on opposed-phase T1-weighted images owing to substantial signal drop of the surrounding hepatic parenchyma. On diffusion weighted images, metastases show restricted diffusion with uniform, variegated, or peripheral hyperintensity at high b-values.<sup>30</sup> During dynamic phases, the tumor enhancement pattern is substantially comparable to that at CT31. On hepatobiliary phase, metastases appear as hypointense masses or show a target appearance with a peripheral hypointense ring and a central hyperintense



**Figure 37-11** Typical computed tomography (CT) imaging findings of hypovascular liver metastases with calcifications from metastatic mucinous adenocarcinoma of the colon. **A**, Transverse precontrast CT image demonstrates two hepatic lesions with amorphous calcifications (*arrows*). **B**, On contrast-enhanced CT image during the portal venous phase, multiple hypoattenuating lesions with peripheral rim enhancement are identified throughout the liver.



**Figure 37-12** Typical computed tomography imaging findings of a hypervascular liver metastasis from gastrointestinal stromal tumor. Based on the strong, homogeneous hypervascularity (*arrow*, **B**) during the hepatic arterial phase and on the central area of hypoattenuation simulating a central scar (*long thin arrow*, **B**), the lesion enters in differential diagnosis with focal nodular hyperplasia. However, strong hypoattenuation (*arrow*-*head*) on noncontrast image (**A**), washout during the portal venous phase (**C**), and the history of a known primary neoplasm all favor metastatic disease.



**Figure 37-13** Added value of hepatobiliary phase and diffusion weighted images in the detection of small hepatic metastases. Transverse diffusion weighted images demonstrate two small metastases (*arrow*), which show hyperintensity at b 0 sec/mm<sup>2</sup>, and remain hyperintense at b 150 sec/mm<sup>2</sup> (**B**) and b 600 sec/mm<sup>2</sup> (**C**), indicating restricted diffusion. **D**, On corresponding hepatobiliary phase gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance imaging, the metastases show hypointensity. Also note a small cyst (*arrowhead*) with signal intensity decrease at b 600 sec/mm<sup>2</sup> compared with that at b 0, and marked hypointensity on hepatobiliary phase. **E**, On contrast-enhanced CT obtained during the portal-venous phase the metastasis are not identifiable, while the cyst is hypoattenuating.

area.<sup>32</sup> The combination of hepatobiliary phase and diffusion weighted images improve the detection of metastases, especially those with a diameter of 1 cm or less, compared with dynamic phase MR images and contrast-enhanced CT images (Figure 37-13).<sup>33-34</sup>

**Ultrasonography.** Hepatic metastases show a variable appearance on gray-scale ultrasonography. Although ultrasonography is generally associated with a poor diagnostic performance, microbubble contrast agents have shown the potential to increase the accuracy of ultrasonography for the detection of liver metastases.

Intraoperative ultrasonography is a crucial adjunct during surgery to accurately define the anatomic relationship between tumors and major vascular and biliary structures and for detection of previously unsuspected liver lesions.

#### Positron Emission Tomography With Computed Tomogra-

**phy.** Besides its leading role in the assessment of primary tumor as well as regional lymph node involvement, functional metabolic imaging with PET/CT also plays a key role in the detection of distant metastases. Because of their increased metabolic rate, hepatic metastases typically demonstrate increased <sup>18</sup>FDG uptake compared with the normal liver.<sup>31</sup>

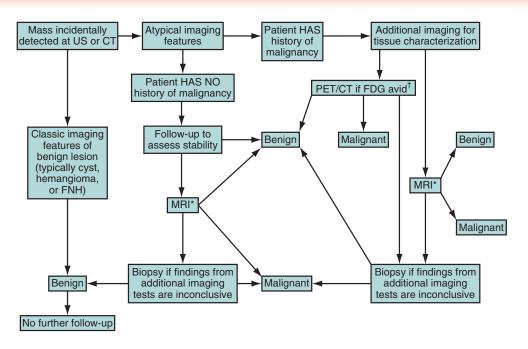
**Imaging Algorithm.** An imaging algorithm is provided in Figure 37-14.

#### **Classic Signs: Hepatic Metastases**

- Multiple lesions
- Heterogeneous enhancement
- Rim enhancement
- Slow, centripetal enhancement
- Central necrosis
- Calcifications on unenhanced CT (metastases from primary mucinous adenocarcinoma)
- Either hypervascular or hypovascular

#### Differential Diagnosis

A known history of malignancy raises the pretest probability of a diagnosis of hepatic metastases. Although the peripheral rim enhancement of hypovascular metastases with centripetal progression can be mistaken for cavernous hemangiomas, lesion washout on delayed images, mild hyperintensity on T2-weighted images, and, lower apparent diffusion coefficient values on diffusion weighted images are all indicative findings of liver metastases. Unlike focal nodular hyperplasia (FNH), hypervascular metastases are heterogeneous because of areas of necrosis and demonstrate washout during the portal venous (see Figure 37-12) and delayed phases and hypointensity on hepatobiliary phase. In the setting of diffuse metastatic liver involvement from breast cancer, a macronodular appearance of hepatic margins can be seen after systemic



\* Presence of focal fat can be ascertained with MRI using in-phase and out-of-phase scanning

<sup>†</sup> Metastatic disease from melanoma, colon and esophageal cancer, breast cancer, sarcoma

Figure 37-14 Flow chart of a practical approach to the diagnosis of malignant hepatic lesions. *CT*, Computed tomography; *FDG*, fluorodeoxy-glucose; *FNH*, focal nodular hyperplasia; *MRI*, magnetic resonance imaging; *PET*, positron emission tomography; *US*, ultrasound.

chemotherapy (see Figure 37-2) and should not be mistaken for cirrhosis (see Tables 37-3 and 37-6).<sup>22</sup> Liver adenomatosis may closely mimic metastatic disease, although adenomas should be suspected when lesions demonstrate a fatty component. Metastases occasionally can manifest a cystic appearance due to extensive necrosis. Cystic metastases show marked hyperintensity on T2-weighted MR images, lack of metabolic activity on <sup>18</sup>FDG-PET, and high ADC values on diffusion weighted MRI. These findings may not be differentiated from those of a simple cyst or hemangioma and require further investigation with liver biopsy.<sup>35</sup>

#### Treatment

**Medical Treatment.** Chemotherapy represents the treatment of choice in patients with liver metastases in whom surgical resection cannot be performed. Furthermore, adjuvant chemotherapy is often combined with liver surgery in patients with metastatic disease. Several therapeutic regimens have been developed according to the primary tumor. Targeted delivery of chemotherapy to liver metastases via a surgically placed hepatic artery infusion pump represents an effective treatment in patients with unresectable hepatic colorectal metastases.

**Surgical Treatment.** Hepatic metastases are surgically resectable if they are confined within a single lobe and if no extrahepatic disease is present. Less invasive alternatives to surgical resection include hepatic artery chemoembolization and percutaneous tumor ablation by using methods such as radiofrequency, cryosurgery, microwaves, ethanol, or interstitial laser thermotherapy.

#### What the Referring Physician Needs to Know: Hepatic Metastases

- CT is the primary imaging modality for the detection of hepatic metastases.
- Liver dual blood supply contributes to the metastases.
- Metastases are treated with chemotherapy, resection, or ablation techniques.
- CT and MRI are the preferred modalities for diagnosis of liver metastases and assessment of response to treatment.
- PET is the most sensitive noninvasive imaging method for detection of hepatic metastases from colorectal, gastric, or esophageal cancers.

# Summary

The discovery of a focal liver lesion, either incidentally or in a patient at higher risk for a liver tumor, commonly triggers multiple diagnostic tests, including general and liver function tests, circulating tumor markers, virology tests, and several imaging examinations (Table 37-7). Although primary detection may rely on transabdominal ultrasonography, this technique is hampered by poor sensitivity and specificity in the assessment of focal malignant liver tumors, with the only notable exception of intraoperative ultrasound evaluation.

Multiphasic contrast-enhanced CT and MRI currently play a key role in the evaluation of patients with liver tumors. Besides remarkable capabilities for lesion detection, both techniques also can provide excellent depiction of the anatomic

TABLE			
37-7 Accuracy	, Limitations, and Pitfalls of	the Modalities Used in Imaging of Malignant	Focal Liver Lesions
Modality	Accuracy	Limitations	Pitfalls
СТ	Sensitivity 69%-71% Specificity 86%-91% 76% fibrolamellar HCC from hemangioma and FNH	Radiation Limited use in patients with allergy or renal insufficiency Potential for anaphylactoid reaction	Lesion detection and characterization may be difficult in fatty liver
MRI	80%	Motion artifact in uncooperative patients and in patients with ascites Risk for nephrogenic systemic fibrosis in patients with renal insufficiency Claustrophobic patients Patients with cardiac pacemaker High cost	Calcifications not well visualized
Ultrasonography	91% before contrast enhanced ultrasonography)	Poor performances in the case of obesity or overlying bowel gas Operator dependent	Calcifications not well visualized
PET/CT	85%	Radiation High cost	Mismatches between the fused images, for example, resulting from respiratory movement

CT, Computed tomography; FNH, focal nodular hyperplasia; HCC, hepatocellular carcinoma; MRI, magnetic resonance imaging; PET, positron emission tomography.

relationship of the tumor with major intrahepatic biliary and vascular structures, which is of paramount importance for treatment planning. Although CT is commonly used as the first-line modality owing to its broad availability and relatively limited costs, with the recent introduction of liver-specific MR contrast agents as well as remarkable improvements in image quality, MRI is emerging as the modality of choice, particularly in the evaluation of patients with liver metastases.

Recently, PET/CT is gaining greater popularity because of its capability to couple standard anatomic information with functional assessment of tumor metabolic activity (at the molecular level).

#### **Key Points**

#### Epithelioid Hemangioendothelioma

- Rare
- Vascular origin
- Younger adults
- Good clinical condition
- Slow course of the disease
- Numerous intrahepatic lesions
- Nodules tend to merge into each other
- Peripheral location
- Capsular retraction
- Hypertrophy of the unaffected liver segments

#### Angiosarcoma

- Heterogeneous enhancement pattern
- Progressive enhancement
- Multifocal
- Hemorrhage and necrosis
- Rapid metastatic dissemination
- Aggressive behavior
- Tend to recur after treatment

# Poor prognosis

#### Hepatocellular Carcinoma in the Noncirrhotic Liver

- Middle-aged men
- Large at diagnosis
- Solitary lesion or dominant mass with smaller satellite lesions
- Heterogeneous
- Lobulated
- Mosaic pattern
- Tumor thrombus
- Biliary invasion

#### Fibrolamellar Hepatocellular Carcinoma

- Noncirrhotic liver in young adults
- Large
- Often solitary
- Central scar in approximately 50% •
- Central calcifications in 68% •
- Strong arterial enhancement
- Washout
- Heterogeneous
- Biliary invasion
- Nodal and distant metastases

#### Hepatoblastoma

- Most commonly occurs in the first 3 years of life
- Large diameter at diagnosis
- Resection or transplantation can be curative

#### Lymphoma

- Rare

- Most common malignant hepatic lesion
- Usually multiple
- Hypovascular or hypervascular based on enhancement characteristics
- Heterogeneous enhancement

- Usually solitary
  - Infiltrative pattern
    - Large at presentation
      - Imaging findings are nonspecific

#### Hepatic Metastases

#### SUGGESTED READINGS

- Chung EM, Lattin GE, Jr, Cube R, et al: From the archives of the AFIP: pediatric liver masses: radiologic-pathologic correlation. II. Malignant tumors. *Radiographics* 31:483–507, 2011.
- Danet IM, Semelka RC, Leonardou P, et al: Spectrum of MRI appearances of untreated metastases of the liver. *AJR Am J Roentgenol* 181:809–817, 2003.
- Elsayes KM, Narra VR, Yin Y, et al: Focal hepatic lesions: diagnostic value of enhancement pattern

#### REFERENCES

- 1. Mehrabi A, Kashfi A, Fonouni H, et al: Primary malignant hepatic epithelioid hemangioendothelioma: a comprehensive review of the literature with emphasis on the surgical therapy. *Cancer* 107:2108–2121, 2006.
- 2. Miller WJ, Dodd DT, 1st, Federle MP, et al: Epithelioid hemangioendothelioma of the liver: imaging findings with pathologic correlation. *AJR Am J Roentgenol* 159:53–57, 1992.
- 3. Bruegel M, Muenzel D, Waldt S, et al: Hepatic epithelioid hemangioendothelioma: findings at CT and MRI including preliminary observations at diffusion-weighted echo-planar imaging. *Abdom Imaging* 36:415–424, 2011.
- Pickhardt PJ, Kitchin D, Lubner MG, et al: Primary hepatic angiosarcoma: multi-institutional comprehensive cancer centre review of multiphasic CT and MR imaging in 35 patients. *Eur Radiol* 25: 315–322, 2015.
- Buetow PC, Buck JL, Ros PR, et al: Malignant vascular tumors of the liver: radiologic-pathologic correlation. *Radiographics* 14:153–166, 1994.
- Bruegel M, Muenzel D, Waldt S, et al: Hepatic angiosarcoma: cross-sectional imaging findings in seven patients with emphasis on dynamic contrast-enhanced and diffusion-weighted MRI. *Abdom Imaging* 38:745–754, 2013.
- Gaddikeri S, McNeeley MF, Wang CL, et al: Hepatocellular carcinoma in the noncirrhotic liver. AJR Am J Roentgenol 203:W34–W47, 2014.
- Trevisani F, Frigerio M, Santi V, et al: Hepatocellular carcinoma in non-cirrhotic liver: a reappraisal. *Dig Liver Dis* 42:341–347, 2010.
- 9. Brancatelli G, Federle MP, Grazioli L, et al: Hepatocellular carcinoma in noncirrhotic liver: CT, clinical, and pathologic findings in 39 U.S. residents. *Radiology* 222:89–94, 2002.
- Torbenson M: Review of the clinicopathologic features of fibrolamellar carcinoma. Adv Anat Pathol 14:217–223, 2007.
- Ichikawa T, Federle MP, Grazioli L, et al: Fibrolamellar hepatocellular carcinoma: imaging and pathologic findings in 31 recent cases. *Radiology* 213:352–361, 1999.
- 12. Blachar A, Federle MP, Ferris JV, et al: Radiologists' performance in the diagnosis of liver

approach with contrast-enhanced 3D gradient-echo MR imaging. *Radiographics* 25:1299–1320, 2005.

- Gaddikeri S, McNeeley MF, Wang CL, et al: Hepatocellular carcinoma in the noncirrhotic liver. *AJR Am J Roentgenol* 203:W34–W47, 2014.
- Ganeshan D, Szklaruk J, Kundra V, et al: Imaging features of fibrolamellar hepatocellular carcinoma. *AJR Am J Roentgenol* 202:544–552, 2014.
- Levy AD: Malignant liver tumors. *Clin Liver Dis* 6:147–164, 2002.

tumors with central scars by using specific CT criteria. *Radiology* 223:532–539, 2002.

- Ganeshan D, Szklaruk J, Kundra V, et al: Imaging features of fibrolamellar hepatocellular carcinoma. AJR Am J Roentgenol 202:544–552, 2014.
- Ichikawa T, Federle MP, Grazioli L, et al: Fibrolamellar hepatocellular carcinoma: pre- and posttherapy evaluation with CT and MR imaging. *Radiology* 217:145–151, 2000.
- Schnater JM, Köhler SE, Lamers WH, et al: Where do we stand with hepatoblastoma? A review. *Cancer* 15(98):668–678, 2003.
- 16. Stocker JT: Hepatoblastoma. Semin Diagn Pathol 11:136–143, 1994.
- Dachman AH, Pakter RS, Ros PR, et al: Hepatoblastoma: radiologic-pathologic correlation in 50 cases. *Radiology* 164:15–19, 1987.
- Meyers RL: Tumors of the liver in children. Surg Oncol 16:195–203, 2007.
- 19. Page RD, Romaguera JE, Osborne B, et al: Primary hepatic lymphoma: favorable outcome after combination chemotherapy. *Cancer* 92: 2023–2029, 2001.
- Sanders LM, Botet JF, Straus DJ, et al: CT of primary lymphoma of the liver. AJR Am J Roentgenol 152:973–976, 1989.
- Kelekis NL, Semelka RC, Worawattanakul S, et al: Focal hepatic lymphoma: magnetic resonance demonstration using current techniques including gadolinium enhancement. *Magn Reson Imaging* 15:625–636, 1997.
- Paulson EK: Evaluation of the liver for metastatic disease. Semin Liver Dis 21:225–236, 2001.
- Namasivayam S, Martin DR, Saini S: Imaging of liver metastases: MRI. *Cancer Imaging* 7:2–9, 2007.
- 24. Kanematsu M, Kondo H, Goshima S, et al: Imaging liver metastases: review and update. *Eur J Radiol* 58:217–228, 2006.
- Valls C, Andia E, Sánchez A, et al: Hepatic metastases from colorectal cancer: preoperative detection and assessment of resectability with helical CT. *Radiology* 218:55–60, 2001.
- Paulson EK, McDermott VG, Keogan MT, et al: Carcinoid metastases to the liver: role of triplephase helical CT. *Radiology* 206:143–150, 1998.

- Pedro MS, Semelka RC, Braga L: MR imaging of hepatic metastases. *Magn Reson Imaging Clin N* Am 10:15–29, 2002.
- Sica GT, Ji H, Ros PR, et al: CT and MR imaging of hepatic metastases. *AJR Am J Roentgenol* 174:691– 698, 2000.
- Tomasian A, Sandrasegaran K, Elsayes KM, et al: Hematologic malignancies of the liver: spectrum of disease. *Radiographics* 35:71–86, 2015.
- Braga L, Semelka RC, Pietrobon R, et al: Does hypervascularity of liver metastases as detected on MRI predict disease progression in breast cancer patients? *AJR Am J Roentgenol* 182:1207– 1213, 2004.
- Soyer P, Poccard M, Boudiaf M, et al: Detection of hypovascular hepatic metastases at triplephase helical CT: sensitivity of phases and comparison with surgical and histopathologic findings. *Radiology* 231:413–420, 2004.
- Yu JS, Rofsky NM: Hepatic metastases: perilesional enhancement on dynamic MRI. AJR Am J Roentgenol 186:1051–1058, 2006.
- Scurr ED, Collins DJ, Temple L, et al: Appearances of colorectal hepatic metastases at diffusion-weighted MRI compared with histopathology: initial observations. *Br J Radiol* 85:225–230, 2012.
- Bipat S, van Leeuwen MS, Comans FE, et al: Colorectal liver metastases: CT, MR imaging, and PET for diagnosis—meta-analysis. *Radiol*ogy 237:123–131, 2005.
- 32. Kim A, Lee CH, Kim BH, et al: Gadoxetic acidenhanced 3.0T MRI for the evaluation of hepatic metastasis from colorectal cancer: metastasis is not always seen as a "defect" on the hepatobiliary phase. *Eur J Radiol* 81:3998–4004, 2012.
- 33. Macera A, Lario C, Petracchini M, et al: Staging of colorectal liver metastases after preoperative chemotherapy: diffusion-weighted imaging in combination with Gd-EOB-DTPA MRI sequences increases sensitivity and diagnostic accuracy. Eur Radiol 23:739–747, 2013.
- 34. Hammerstingl R, Huppertz A, Breuer J, et al: Diagnostic efficacy of gadoxetic acid (Primovist)-enhanced MRI and spiral CT for a therapeutic strategy: comparison with intraoperative and histopathologic findings in focal liver lesions. *Eur Radiol* 18:457–467, 2008.
- 35. Kim T, Federle MP, Baron RL, et al: Discrimination of small hepatic hemangiomas from hypervascular malignant tumors smaller than 3 cm with three-phase helical CT. *Radiology* 219:699– 706, 2001.

# 38

# **Fatty Liver Disease**

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# Etiology

*Fatty liver* is a generic term that refers to the accumulation of lipids within hepatocytes. This chapter focuses on nonalcoholic fatty liver disease (NAFLD), the most common form of fatty liver. Histologically, it resembles alcoholic liver injury but occurs in patients who deny significant alcohol consumption. NAFLD encompasses a spectrum of conditions, ranging from benign hepatocellular steatosis to inflammatory nonalcoholic steatohepatitis (NASH), fibrosis, and cirrhosis.<sup>1</sup> NAFLD is associated with obesity and insulin resistance and is considered the hepatic manifestation of the metabolic syndrome, a combination of medical conditions including type 2 diabetes mellitus, hypertension, hyperlipidemia, and visceral adiposity.<sup>2</sup>

Other conditions associated with fatty liver include alcoholic liver disease, viral hepatitis, effects of certain medications (e.g., corticosteroids, tamoxifen, amiodarone, methotrexate, valproic acid, and select chemotherapy agents), human immunodeficiency virus (HIV) infection with lipodystrophy, total parenteral nutrition, pregnancy, and intestinal bypass surgery for weight loss.<sup>3</sup>

The pathogenesis of NAFLD and its progression to NASH is complex and remains incompletely understood. The most widely accepted paradigm is the so-called *two-hit hypothesis.*<sup>4</sup> In this model, the initial abnormality (first hit) is the accumulation of lipids within hepatocytes (steatosis), which is mediated by insulin resistance.<sup>5-8</sup> The majority of hepatocellular lipids are stored as triglycerides, but other lipid metabolites, such as free fatty acids, cholesterol, and phospholipids, also may be present and play a role in disease progression.<sup>9</sup>

The accumulated hepatocellular lipids promote oxidative stress, which is the subsequent insult ("second hit") responsible for the progression from simple steatosis to steatohepatitis (NASH). Inflammatory and hormonal mediators secreted by adipocytes may contribute to the development of hepatic inflammation, apoptosis, and fibrosis.<sup>7</sup>

# **Prevalence and Epidemiology**

NAFLD is the most common form of chronic liver disease among adults and children in the United States and has been reported in many other parts of the world.<sup>1,10</sup> It is thought to be the leading cause of asymptomatic elevations of serum aminotransferase values and likely accounts for the majority of cases of cryptogenic cirrhosis. Determining the prevalence of NAFLD, however, is challenging. This is because it is generally a silent condition, and liver biopsy, which is the gold standard for the diagnosis of NAFLD, is not a tenable tool for establishing disease prevalence in the general population. Consequently, serum levels of aminotransferases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) and imaging studies (ultrasound and magnetic resonance [MR] spectroscopy) have been used as surrogate markers to estimate population prevalence in most series.

Depending on the cutoff values used to define the upper limit of normal for aminotransferase levels, the estimated prevalence of NAFLD in the general United States population ranges from 5.4% to 24%, but these values may be underestimations because aminotransferase levels have limited sensitivity for steatosis.<sup>11,12</sup> Histologic estimates of NAFLD prevalence via preoperative or intraoperative liver biopsy, mainly obtained from individuals evaluated as donors for living-donor liver transplantation, are 33% to 88%.<sup>13-15</sup> In children, NAFLD prevalence has been estimated to be 9.6%; of great concern, 2% to 8% of children with NAFLD progress to cirrhosis.<sup>16,17</sup>

Obesity is the most important risk factor for NAFLD; the prevalence of NAFLD is 4.6 times greater in the obese, and up to 74% of obese individuals have fatty livers.<sup>18</sup> Among morbidly obese patients undergoing bariatric surgery for weight loss, 84% to 96% have NAFLD, 25% to 55% have NASH, and 2% to 12% have severe fibrosis or cirrhosis.<sup>19-22</sup> NAFLD is also strongly associated with hepatic and adipose tissue insulin resistance and metabolic syndrome.<sup>23</sup> Although NAFLD is clearly linked to obesity and metabolic syndrome, it may occur in up to 29% of lean patients lacking associative risk factors.<sup>24</sup>

Other factors that influence the development of NAFLD include age, sex, race, and ethnicity.<sup>25-29</sup> The prevalence of NAFLD increases with age in both adults and children.<sup>26</sup> NAFLD is more common among men than women younger than the age of 50; however, higher prevalence rates are seen in women older than the age of 50, perhaps related to hormonal changes occurring after menopause.<sup>12</sup> The highest rates of NAFLD are seen among Mexican-Americans, followed by non-Hispanic whites.<sup>27,28</sup> Non-Hispanic blacks display the lowest rates of NAFLD, despite the high prevalence of obesity and type 2 diabetes in this population.<sup>13</sup>

Metabolic syndrome and its associated conditions are commonly affiliated with NAFLD. The prevalence of NAFLD is estimated to be at least twice as common among individuals who meet criteria for metabolic syndrome.<sup>29</sup> Among individuals with NAFLD, it is estimated that over 90% have some features of metabolic syndrome.<sup>2</sup> Diabetes is reported in 33% to 50% of patients with NAFLD, whereas insulin resistance may occur in as many as 75%.<sup>2,30</sup>

# **Clinical Presentation**

The natural history of NAFLD is poorly understood but seems to be related to the severity of histologic disease. In simple steatosis, less than 5% of patients progress to cirrhosis over a 5- to 17-year period; alternatively, 25% of patients with NASH advance to cirrhosis within 10 years.<sup>31</sup> The rate of development of hepatocellular carcinoma is not well characterized but is thought to be lower than in viral liver disease.

Most patients with NAFLD are asymptomatic. When symptomatic, patients may experience malaise and nonspecific right upper quadrant discomfort. On physical examination, hepatomegaly may be detected.<sup>3</sup> Patients characteristically have abdominal or visceral obesity. Those who progress to cirrhosis may exhibit stigmata of chronic liver disease and complications of portal hypertension.<sup>3</sup>

Typically, NAFLD is discovered incidentally when routine laboratory studies reveal a mild to modest elevation in ALT (less than five times the upper limit of normal), although AST is also often elevated to a milder degree. Serum aminotransferase levels may fluctuate, however, and some patients with NAFLD have normal levels. A careful history should exclude significant alcohol use. Laboratory testing must exclude viral hepatitis and iron overload syndromes. Imaging can be used to noninvasively suggest fatty deposition. Although unnecessary to secure the diagnosis, a liver biopsy may provide staging and prognostic information.

# Pathology

On gross inspection, the fatty liver is enlarged and soft, with a yellowish tinge and greasy consistency. Microscopically, the spectrum of fatty liver disease is assessed on the basis of steatosis, steatohepatitis, cell injury, and fibrosis. These histologic changes are often shared by alcoholic liver disease and NAFLD; at times, only a detailed alcohol history will distinguish the two diagnoses.

Steatosis is predominantly in the form of large-droplet (macrovesicular) fat, although small-droplet (microvesicular) fat and mixed patterns may be seen. Fat-laden hepatocytes are found primarily in centrilobular areas, with progression to a panlobular distribution in severe cases. Steatosis is assessed by visually estimating the proportion of fat-laden hepatocytes and reported in broad brackets of severity: normal (<5% of hepatocytes), moderate (30% to 60% of hepatocytes), and severe (>60% of hepatocytes).

When present, steatohepatitis is usually mild and characterized by a mixed inflammatory infiltrate of neutrophils and mononuclear cells (lymphocytes, macrophages, and Kupffer cells). In adults, the distribution is multifocal and may affect all zones of the liver lobule, which contrasts to the prominent portal inflammation seen in pediatric NASH.<sup>32</sup>

The hallmark feature of cellular injury in fatty liver disease is hepatocellular ballooning, thought by some to be the most important defining criterion in distinguishing NASH from simple steatosis. Ballooning refers to swollen, enlarged hepatocytes with partially cleared cytoplasm, found mainly in centrilobular regions near areas of steatosis.<sup>32</sup> Mallory's hyaline (ropey clumps of dense perinuclear cytoplasmic deposits composed of intermediate filaments) and acidophil bodies (apoptotic or necrotic hepatocytes with eosinophilic cytoplasmic globules) can be seen in NAFLD, although they are more frequently observed in alcoholic liver disease.

In adults, fibrosis is mainly centrilobular, radiating outward from terminal hepatic veins in a perisinusoidal or pericellular pattern. This "chicken wire" appearance of fibrosis progresses in advanced disease, causing a bridging of fibrous bands and, ultimately, cirrhosis. In advanced disease ("burnt-out NASH"), there is a paucity of fatty deposition because the parenchyma has been replaced by fibrotic tissue. Pediatric fatty liver disease has distinct histologic features, such as predominance of periportal fibrosis, which is rarely seen in adults.<sup>33</sup>

Several scoring systems have been proposed for histologic grading and staging of fatty liver disease. Recently, the Pathology Committee of the NASH Clinical Research Network proposed a NAFLD activity score (NAS) based on steatosis (0 to 3), lobular inflammation (0 to 2), and hepatocellular ballooning (0 to 2). In this system, NASH is probable if the NAS is greater than 4, unlikely if less than 3, and of intermediate probability if 3 or 4.<sup>34</sup> Staging is based on the extent of fibrosis (0 to 4).

Differing patterns of steatosis arise in patients with hepatitis C infection or as a result of medication effects. In hepatitis C, macrovesicular fat droplets have a periportal, rather than centrilobular, distribution. The amount of steatosis increases with disease severity and is most commonly associated with genotype 3 hepatitis C virus. A number of medications lead to steatosis, including cytotoxic and cytostatic drugs, antibiotics, nucleoside analogs, and corticosteroids. The pattern of injury in drug-induced steatosis is nonspecific, typically consisting of macrovesicular fat deposits. Notable exceptions are Reye's syndrome, associated with aspirin use in children, and tetracycline, both of which may lead to microvesicular steatosis.

# Imaging

The radiologic features of fatty liver disease stem from the increased fat content of the liver parenchyma. The spatial pattern may be diffuse and homogeneous or heterogeneous, with focal fat deposition in an otherwise normal liver or areas of focal fat sparing in a diffusely fatty liver (Table 38-1). The homogeneous form is the most common; the heterogeneous and focal forms may simulate perfusion abnormalities, diffusely infiltrative disease, nodular lesions, or masses.<sup>35,36</sup> Such findings may be especially problematic in the setting of known malignancy. Therefore, it is important not only to recognize fatty liver on imaging but also to discriminate it from other pathologic processes.

TABLE 38-1	Spatial Pattern of Steatosis			
Spatia	l Pattern	Remarks		
Diffuse and homogeneous		Most common form		
Diffuse and heterogeneous		Ill-defined, geographic, segmental or lobar areas of fatty deposition		
	deposition paring	Typically adjacent to falciform ligament, porta hepatis, gallbladder fossa, and subcapsular regions; speculated to be due to anomalous venous drainage and/or locally variable insulin effects		
Multifocal deposition		Multiple round or oval nodular fat depositions in atypical locations		
Perivas	scular	Halos of fat surrounding hepatic veins, portal veins, or both		
Subcap	osular	Seen in patients receiving peritoneal dialysis with insulin-containing dialysate		

TABLE     Classic Imaging Signs of Fatty Liver Disease				
Modality	Diffuse Fat Deposition	Focal Fat Deposition	Focal Fat Sparing	
Ultrasound	Hyperechoic relative to adjacent kidney or spleen	Hyperechoic area in an otherwise normal liver	Hypoechoic area within a hyperechoic liver	
	Attenuation of the ultrasound beam Decreased visualization of hepatic and portal veins Loss of definition of the diaphragm Hepatomegaly	gallbladder fossa, a Geographic margins	ations: adjacent to falciform ligament, nd porta hepatis with nondistortion of traversing vessels	
Unenhanced CT	Hypodense liver measuring <40 HU Liver-spleen difference ≥10 HU Liver/spleen ratio <0.9	Hypodense area in an otherwise normal liver	Hyperdense area within a diffusely low attenuated liver	
Enhanced CT	Absolute liver attenuation <40 HU	Hypodense area in an otherwise normally enhancing liver	Isodense/hyperdense area compared with the liver parenchyma	
		Enhancement si	milar to background liver	
MR spectroscopy	Spectral peak at resonance frequency of fat (e.g., methylene protons -CH2- at 3.2 ppm)	Not useful for focal f unless a multivoxe	at deposition and/or focal fat sparing I approach is used	
MRI	Relative signal loss on the fat-saturated image on frequency-selective imaging (fat saturated versus non-fat saturated) Relative signal loss on out-of-phase images compared with in-phase images on phase-interference imaging	Focal area of signal loss on fat-saturated or out-of-phase image	Focal sparing of signal loss on fat- saturated or out-of-phase image	

CT, Computed tomography; MR, magnetic resonance.

The most important modalities used in the assessment of hepatic steatosis are ultrasound, CT, and MRI and MR spectroscopy (Table 38-2). These modalities vary in their accuracy to diagnose and grade steatosis, as discussed later. To date, no noninvasive method reliably differentiates NASH from simple steatosis. Several MR techniques (diffusion weighted and perfusion weighted MRI, MR elastography, and double-contrast enhanced MRI) show promise for detecting and staging the severity of liver fibrosis, but these techniques have not been validated in large clinical trials and are considered experimental. Ultrasound elastography, particularly shear wave elastography, is also being studied for its ability to noninvasively detect early liver fibrosis. Elastography techniques are discussed in more detail elsewhere in this book.

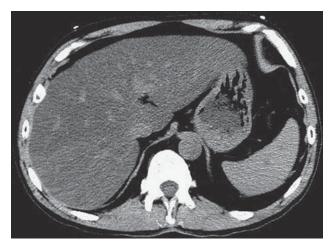
#### RADIOGRAPHY

Plain radiography does not have a significant role in the assessment of fatty liver disease. Hepatomegaly and ascites may be appreciated in patients with early and advanced disease, respectively.

# COMPUTED TOMOGRAPHY

CT has been widely used in the evaluation of fatty liver disease in adults. The use of ionizing radiation precludes its use as a research tool in children, although fatty liver may be observed in children on scans done for clinical purposes.<sup>37</sup>

Fat deposition in the liver is characterized by a reduction in the attenuation of the hepatic parenchyma. On unenhanced CT, normal liver parenchyma has slightly greater attenuation than the spleen or blood. However, with increasing hepatic steatosis, liver attenuation decreases and the liver may become less dense



**Figure 38-1** Diffuse liver steatosis. Axial unenhanced computed tomography scan reveals diffuse low attenuation of the liver compared with that of the spleen and the intrahepatic vessels. The appearance mimics that of a contrast-enhanced scan.

than the intrahepatic vessels, simulating the appearance of that on a contrast-enhanced scan (Figure 38-1).<sup>38</sup>

A subjective 5-point qualitative grading has been proposed for the degree of hepatic steatosis based on hepatic attenuation and visualization of hepatic vessels (hepatic and portal veins):

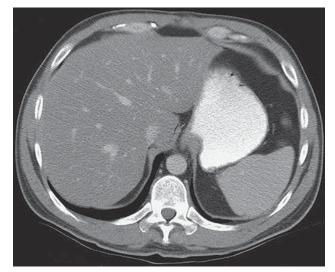
- *Grade 1:* Hepatic vessels show lower attenuation than the hepatic parenchyma out to the peripheral third of liver.
- *Grade 2:* Hepatic vessels show lower attenuation than the hepatic parenchyma out to the middle third of liver.
- *Grade 3:* Hepatic vessels show lower attenuation than hepatic parenchyma in the central third of liver.

- *Grade 4:* Hepatic vessels show the same attenuation as that of the hepatic parenchyma.
- *Grade 5:* Hepatic vessels show higher attenuation than the hepatic parenchyma.

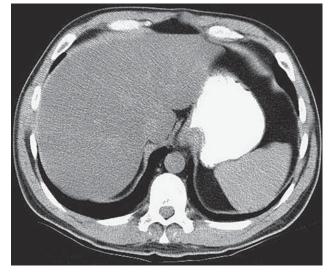
Several criteria for the diagnosis of hepatic steatosis on unenhanced CT have been proposed. The first such criterion is an absolute liver attenuation of less than 40 Hounsfield units (HU). However, because the normal hepatic parenchyma attenuation ranges from 60 to 70 HU, the 40-HU cutoff value has high specificity but low sensitivity. Moreover, absolute attenuation values on unenhanced CT are subject to technical variations, such as scanner type. The second and third criteria attempt to overcome this limitation by expressing hepatic steatosis in relation to other organs known to be free of fat, such as the spleen. In these criteria (Hepatic Attenuation Index Criteria), an attenuation difference between liver and spleen of less than -10 HU and liver-to-spleen attenuation ratio of 0.9 indicate steatosis (Figure 38-2).<sup>39,40</sup> Liver attenuation may be affected by a variety of factors other than liver fat, such as iron, copper, glycogen, fibrosis, edema, or amiodarone use. Assessment of liver fat by CT attenuation may be unreliable, and CT methods are insensitive to mild steatosis. The reported sensitivity and specificity of unenhanced CT for detection of moderate or severe steatosis (>30% on histologic examination) ranges from 73% to 100% and 95% to 100%, respectively.<sup>3</sup>

On enhanced CT, the presence of iodine contrast interferes with attenuation, adding a confounding factor. Perfusion alterations, timing of acquisitions, and contrast type, dosage, and injection rate may influence hepatic and splenic attenuation. Nevertheless, criteria have been proposed to detect hepatic steatosis at enhanced CT, including a liver-spleen attenuation difference of at least 20 HU between 80 to 100 seconds or at least 18.5 HU between 100 to 120 seconds after intravenous contrast injection (Figure 38-3). Sensitivity and specificity of these attenuation differences range from 54% to 93% and 87% to 93%, respectively.<sup>37</sup> Ultimately, however, the quantitative criteria for diagnosing fatty liver at enhanced CT are protocol specific and have significant overlap of liver-spleen attenuation values between normal and fatty liver, thereby limiting its clinical role.

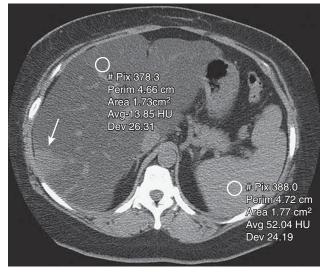
On CT, focal hepatic steatosis appears as a hypodense area in an otherwise normal liver, whereas focal fat sparing appears as a hyperdense region within a liver of diffuse low attenuation (Figures 38-4 and 38-5). Focal fatty changes (either infiltration or sparing) typically occur at classic locations, namely, adjacent to the falciform ligament (typically in segment IV), within the gallbladder fossa, in the subcapsular liver, and in the region of



**Figure 38-3** Diffuse liver steatosis (patient in Figure 38-2). On axial enhanced computed tomography scan during the portal venous phase, the difference between hepatic (57 HU) and splenic (101 HU) attenuation is 45 HU, which exceeds the 20 HU threshold proposed by some investigators as diagnostic of fatty liver.



**Figure 38-2** Diffuse liver steatosis. Axial unenhanced computed tomography scan reveals diffuse low attenuation of the liver. The absolute hepatic attenuation value is 26 HU, considered diagnostic of fatty liver. When comparing liver with spleen (55 HU), the difference between hepatic and splenic attenuations is -29 HU and the liver-to-spleen attenuation ratio is approximately 0.5. Both parameters indicate steatosis greater than 30% on histology.



**Figure 38-4** Focal fat sparing. Axial unenhanced computed tomography scan reveals a geographically shaped area of high attenuation (*arrow*) in the subcapsular region of the right lobe of a fatty liver, consistent with focal fatty sparing. *Avg*, Average; *Perim*, perimeter.



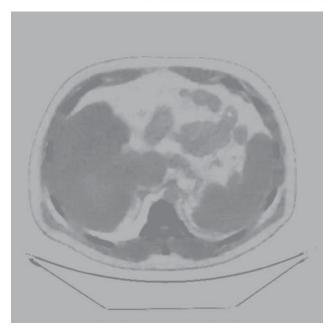
**Figure 38-5** Focal fat sparing. Axial unenhanced computed tomography scan reveals a focal small high-attenuation area (*arrow*) in a diffuse low-attenuation liver, consistent with an area of focal sparing in a fatty liver.

the porta hepatis. Although areas of focal fat deposition and focal fat sparing are usually geographic in shape and occur at these specific locations, they can be nodular or occur in an atypical region, raising concern for a true hepatic mass.<sup>35</sup> Other characteristic features include geographic margins, absence of mass effect, and nondistortion of the portal and hepatic venous branches traversing through regions of fat deposition or sparing.

Dual-energy CT (DECT) also has been shown to have a role in the detection and characterization of hepatic steatosis. In DECT, the liver is imaged at two different energy levels (80 kVp and 140 kVp). This allows for processing of material decomposition images or multimaterial decomposition images, based on the attenuation differences of tissues at varying energy levels. Material separation allows for the generation of iodine, water, and fat images because of differences in chemical composition. In addition, virtual monochromatic images can be processed to optimize the contrast-to-noise ratio. Because fat attenuates high-energy photons more than low-energy photons compared to water, fatty content within the liver can be differentiated from water content at DECT (Figure 38-6). Moreover, DECT has the potential to quantitate fat content within the liver independent of a region of interest placement.<sup>41</sup> This offers potential in the evaluation of both focal and diffuse fatty infiltration of the liver.

#### MAGNETIC RESONANCE IMAGING

MRI is generally considered the most definitive radiologic modality for the qualitative and quantitative assessment of fatty liver disease. Visual recognition of fatty liver disease usually is straightforward, because it is most often characterized by diffuse and homogeneous liver involvement. However, atypical fat distribution, like that seen in focal and multifocal fatty disease, may simulate other lesions and presents a diagnostic challenge. Key distinguishing imaging features of fatty liver disease, other than the fat content, include lack of increased gadolinium enhancement (isoenhancing to hypoenhancing compared with normal liver tissue), geographic distribution, ill-defined margins, characteristic locations of focal fat deposition or sparing, and absence of mass effect on surrounding structures.



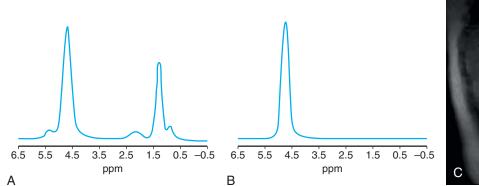
**Figure 38-6** Fatty liver on dual-energy computed tomography (CT). Fat-only multimaterial decomposition image from a dual-energy CT scan demonstrating a liver with 20% fat.

In fatty liver, both fat and water protons contribute to the observed MR signal. Because of the chemical shift, the fat and water protons resonate and precess at different frequencies. MR spectroscopy, frequency-selective MRI, and phase-interference MRI are three techniques that exploit the fat-water chemical shift to assess fatty liver disease.

Spatially selective proton MR spectroscopy allows direct measurement of the chemical (proton) composition within a specified volume of the liver.<sup>36</sup> The MR spectrum describes the intensity of MR signal as a function of precession frequency. At field strengths of 1.5 Tesla (T) or greater, the water peak at 4.7 parts per million (ppm) and the dominant fat peak at 1.2 ppm of -(CH2)n- can be resolved and identified as distinct spectral peaks. In fatty liver disease, both water and fat spectral peaks are present (Figure 38-7). In normal (nonfatty) liver, only the water peak is seen.

Frequency-selective imaging applies a saturation (or excitation) radiofrequency pulse to the fat or water frequency range to selectively suppress (or excite) fat or water signals. In particular, fat saturation is a common option for many clinical imaging sequences, including most spin echo and gradient echo-based sequences at 1.5 T and higher. With fat saturation, the images coincide with the water signal alone; without fat saturation, they represent the sum of fat and water signals. Therefore, hepatic fat may be assessed by comparing these two sets of images. In fatty liver disease, the fat-saturated images show relative signal loss compared with unsaturated images (Figure 38-8). In normal liver, fat saturation has no effect and the two sets of images have similar signal intensities.

Phase-interference imaging takes advantage of the echo time-dependent phase-interference effect between fat and water gradient echo signals. Because fat and water signals precess at different frequencies, they undergo phase interference at predictable periodicity. Consequently, the fat and water signals cancel at out-of-phase and add at in-phase echo times.



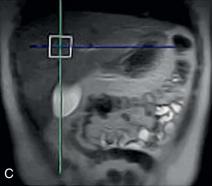


Figure 38-7 Liver proton magnetic resonance (MR) spectroscopy. A, Findings in a 49-year-old man with severe fatty liver show a large fat signal peak at 1.2 ppm as well as hepatic water at 4.7 ppm; fat fraction = 33%. B, Findings in a healthy 14-year-old boy with only hepatic water peak; fat fraction <1%. C, An example of MR spectroscopic voxel placement.

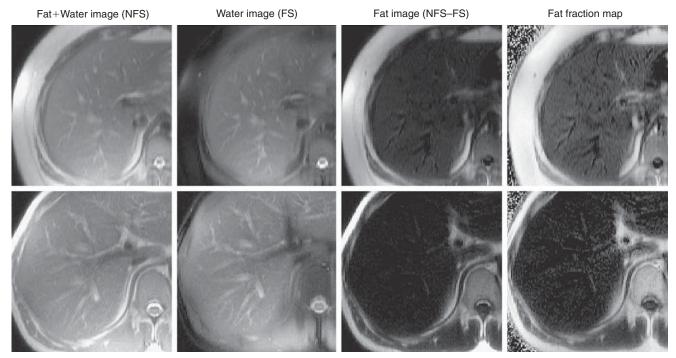


Figure 38-8 Frequency-selective magnetic resonance imaging. *Top*, Findings in a 48-year-old man with 23% fat fraction by spectroscopy. *Bottom*, Findings in a 34-year-old healthy man with 1% fat fraction. *FS*, Fat saturated; *NFS*, non–fat saturated. (Images were acquired at 1.5 T.)

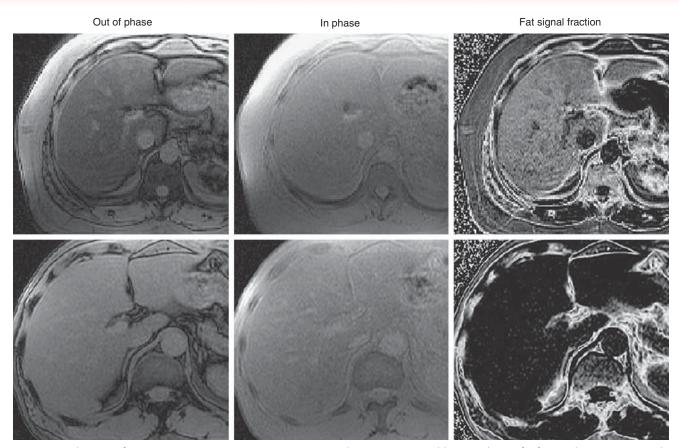
Hepatic fat may be assessed by comparing sequential out-ofphase and in-phase images. In fatty liver disease, the out-ofphase images show relative signal loss resulting from signal cancellation (Figure 38-9). In normal liver, the out-of-phase and in-phase images have similar intensities. When possible, the out-of-phase pulse sequence should be obtained before the in-phase sequence to ensure that perceived signal loss is due to fat deposition and not T2\* decay.

The distinct advantage of the various MRI techniques over CT and ultrasound is the capability to noninvasively quantify steatosis as a "fat fraction." Using a non–T1-weighted sequence (long relaxation time and/or low flip angle) and multiple echo time acquisition, it is possible to estimate individual fat and water proton densities from the spectroscopic or imaging data. The fat fraction can then be calculated as a ratio of fat proton density to total (fat and water) proton density.<sup>36,42</sup> From the proton density of fat and water and prior knowledge of the fatty acids' chemical compositions, the molecular triglyceride concentration can be determined. In spectroscopy, the proton density fat fraction has been validated using biochemical assay of tissue samples.<sup>36,43</sup> Although no direct comparison with biochemical assay has been performed for imaging, a recent study shows close agreement between the proton density fat fraction determined by spectroscopy and by phase-interference imaging.<sup>44</sup>

#### ULTRASOUND

Transabdominal ultrasound is the most common imaging modality used to initially evaluate and diagnose hepatic

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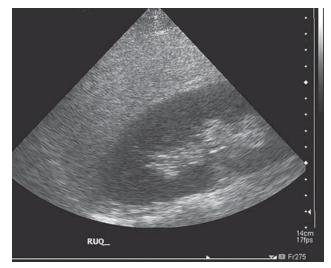
**Figure 38-9** Phase-interference magnetic resonance imaging. *Top*, Findings in a 45-year-old man with 26% fat fraction by spectroscopy show marked signal loss on the out-of-phase image compared with the in-phase image. Fat fraction map demonstrates diffuse fat deposition throughout the liver. *Bottom*, Findings in a 61-year-old healthy man with 1% fat fraction by spectroscopy show no significant signal difference between out-of-phase and in-phase images; fat fraction map demonstrates no fat in the liver. (Images were acquired at 1.5 T.)

steatosis because of its low cost, noninvasiveness, and widespread availability.<sup>38</sup> The echogenicity of the normal liver is similar or minimally exceeds that of the renal cortex or spleen. At ultrasonography, diffuse fatty liver is characterized by hyperechogenicity of the liver parenchyma relative to the adjacent right kidney or spleen (the so-called *bright liver*) (Figure 38-10). Focal fat deposition appears as a hyperechoic area in an otherwise normal liver, whereas focal fat sparing is represented by a hypoechoic area within diffusely hyperechoic liver parenchyma.<sup>36</sup> Other frequently described ultrasound features of fatty liver include attenuation of the ultrasound beam (poor or difficult beam penetration), decreased visualization of vascular margins, loss of definition of the diaphragm, and hepatomegaly (Figure 38-11).<sup>45</sup>

The degree of fat accumulation in the liver can be classified subjectively by ultrasound as mild, moderate, or severe. The qualitative grading for hepatic steatosis is as follows:

- *Mild*: Mild increase in liver echogenicity with visualization of hepatic and portal vein walls
- *Moderate:* Increased liver echogenicity obscuring visualization of hepatic and portal vein walls
- *Severe:* Increased liver echogenicity with significant posterior attenuation that impairs evaluation of deep liver parenchyma and diaphragm

Ultrasound has several limitations in the detection of both diffuse and focal hepatic steatosis. It is highly operator



**Figure 38-10** Diffuse liver steatosis. Ultrasound image of the liver shows a hyperechoic liver. The adjacent renal cortex appears hypoechoic by comparison. The intrahepatic vessels are not well depicted, and the diaphragm is poorly delineated.

dependent, nonreproducible, and limited by abdominal gas and patient body habitus. The last inadequacy is highlighted in this patient population because the majority of cases of fatty liver disease occur in overweight or obese individuals. Similar to CT, however, ultrasound is not a quantitative method and may be unable to distinguish simple steatosis from advanced fibrosis or early cirrhosis. Ultrasound has low sensitivity and specificity for detecting small amounts of fat in the liver. For detecting moderate and severe fat accumulation (>30% by histologic



**Figure 38-11** Diffuse liver steatosis. Sagittal ultrasound image of the liver shows a hyperechoic liver, decreased visualization of intrahepatic vessels and vessel walls, posterior darkness, and loss of definition of the diaphragm (posterior beam attenuation).

examination), ultrasound sensitivity and specificity range from 60% to 95% and 84% to 100%, respectively.<sup>37</sup>

#### NUCLEAR MEDICINE

Scintigraphy with xenon-133 (<sup>133</sup>Xe) was used to detect hepatic steatosis in the 1980s and 1990s but is now no longer incorporated in diagnostic algorithms. <sup>133</sup>Xe is a highly fat-soluble gas that, after being inhaled or injected, remains in the fatty tissue after blood pool clearing. The <sup>133</sup>Xe hepatic retention ratio is increased in patients with fatty liver, with reported sensitivity and specificity of 95% and 94%, respectively.<sup>46</sup>

#### IMAGING ALGORITHM

Ultrasound is the most inexpensive modality for diagnosis of fatty liver disease but is limited by its low sensitivity and operator, observer, and body habitus dependence (Table 38-3). Although CT is objective, is more reproducible, and may be more sensitive, it involves ionizing radiation and is not suitable for routine examinations, especially in the pediatric population. MRI is the most definitive radiologic modality for hepatic fat assessment but is relatively costly. However, a focused fatty liver protocol can be performed in less than 10 minutes and may be a reasonable option for routine fatty liver screening and follow-up. Such a protocol would include localizing, followed by noncontrast fat detection and quantification sequences. These are detailed as discussed in the following section.

#### Hepatic Fat Detection

High T1-weighting (high flip angle or short relaxation time) makes the fat signal more conspicuous for detection and preferentially amplifies the fat signal because of its shorter T1 relative to lean liver. This accentuates the relative signal loss on

Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Fatty Liver Disease				
Modality	Accuracy	Limitations	Pitfalls	
Unenhanced CT	<ul> <li>73%-100% sensitivity for diagnosis of moderate/severe steatosis (histologic steatosis &gt;30%)<sup>38</sup></li> <li>95%-100% specificity for diagnosis of moderate/severe steatosis<sup>38</sup></li> </ul>	Radiation exposure No role in pediatric populations for sole purpose of fat assessment	Confounded by multiple variables (see text) Confusion with other hypoattenuating lesions if atypical in distribution (see text)	
Enhanced CT	54%-93% sensitivity for diagnosis of moderate/severe steatosis <sup>38</sup> 87%-93% specificity for diagnosis of moderate/severe steatosis <sup>38</sup>	Radiation exposure Because of risks for intravenous contrast agents, no role in any population for sole purpose of fat assessment		
MRI	<ul> <li>81% sensitivity and 100% specificity for diagnosis of moderate/severe steatosis<sup>49</sup></li> <li>84%-98% sensitivity and 88%- 100% specificity for diagnosis of mild steatosis (histologic steatosis of 5%-10%)<sup>50</sup></li> </ul>	Patient cooperation required High costs Not widely available Dedicated pulse-sequence needed for accurate diagnosis and fat grading	Out-of-phase/in-phase imaging has low sensitivity in presence of iron unless T2* correction is performed. Frequency-selective imaging unreliable in inhomogeneity (e.g., metal artifact, high susceptibility)	
Ultrasonography	60%-95% sensitivity in detection of moderate/severe steatosis <sup>38</sup> 84%-100% specificity in detection of moderate/severe steatosis <sup>38</sup>	Operator dependent Nonreproducible Limited by overlying bowel gas and patient body habitus Subjective	Confusion with other hyperechoic lesions if atypical in distribution (see text) Liver with severe fibrosis or early cirrhosis may mimic the sonographic appearance of mild steatosis, potentially causing gross underestimation of disease severity.	
Nuclear medicine (xenon-133)	95% sensitivity and 94% specificity <sup>47</sup>	Poor spatial resolution		

Document téléchargé de ClinicalKey.fr par Faculte de Medecine de Tunis août 30, 2016. Pour un usage personnel seulement. Aucune autre utilisation n'est autorisée. Copyright ©2016. Elsevier Inc. Tous droits réservés. fat-saturated or out-of-phase images and aids visual detection of the fat signal.

#### Hepatic Fat Quantification

Low T1-weighting is essential to suppress arbitrary T1-dependent fat signal amplification. A long relaxation time (>4 × T1 liver) or low flip angle (5 to 20 degrees) should be used to minimize T1-weighting. Regardless of the imaging sequence used, multiple echo time acquisition should be considered to correct for T2\* signal decay that may confound fat fraction estimation.<sup>47</sup> Such dedicated fat-quantification sequences are becoming commercially available.

# **Differential Diagnosis**

The clinical differential diagnosis of NAFLD mirrors that of hepatic steatosis. Among patients with elevated serum aminotransferase values, the cause is usually established through a careful evaluation of their history (medication use, risk factors for viral hepatitis, history of alcohol and drug use, and review of comorbidities), a series of screening blood tests for causes of chronic liver disease (viral serologic studies, iron studies, autoimmune markers, ceruloplasmin, and alpha-1 antitrypsin), supportive imaging studies (initial evaluation is usually with ultrasound), and, sometimes, liver biopsy. If other causes of chronic liver disease have been excluded, risk factors for NAFLD have been identified, and the presence of fatty liver is confirmed by imaging studies, the clinician is challenged with establishing the cause of hepatic steatosis.<sup>48,49</sup>

Alcoholic liver disease encompasses a spectrum of conditions provoked by alcohol ingestion, including fatty liver disease, alcoholic hepatitis, and cirrhosis. It has been estimated that almost all patients with heavy alcohol consumption develop fatty liver, although only 10% to 35% develop alcoholic hepatitis and 8% to 20% progress to alcoholic cirrhosis.<sup>50</sup> In individuals who admit to moderate alcohol intake, the differentiation between NAFLD and alcoholic fatty liver disease is difficult because laboratory, imaging, and histologic findings are similar. Unfortunately, strong data are lacking to determine accurate thresholds for alcohol consumption required to cause fatty liver. Historically, daily alcohol intake of 20 g in women and 30 g in men has been used to distinguish alcoholic fatty liver disease from NAFLD, although the validity of these thresholds is unknown.<sup>51</sup> If liver biopsy specimens are obtained, individuals with alcoholic liver disease tend to have more Mallory's hyaline and acidophil bodies and less glycogenated nuclei than those with NAFLD, although these findings are not reliable.

Hepatic steatosis also may occur in chronic hepatitis C virus infection, where it is related to host factors such as metabolic syndrome and viral factors in those infected with genotype 3 hepatitis C virus. Steatosis in hepatitis C is significant because it contributes to disease progression and decreases response rates to treatment with interferon-based therapy.<sup>52</sup>

Certain drugs may produce de novo steatohepatitis (e.g., amiodarone, perhexiline maleate, diethylaminoethoxyhexestrol) and others may exacerbate NASH (tamoxifen, corticosteroids, diethylstilbestrol, estrogens).<sup>53</sup> Oxaliplatin and irinotecan administered as preoperative chemotherapy before surgical resection of hepatic metastases have been associated with steatohepatitis, with irinotecan-associated steatohepatitis associated with poorer outcomes after hepatic resection.<sup>54,55</sup> Other conditions capable of eliciting fatty liver include intestinal bypass surgery for weight loss (classically seen with jejunoileal bypass surgery), HIV infection with lipodystrophy, and parenteral nutrition.<sup>3</sup> If these secondary causes of fatty liver are excluded (alcohol, viral hepatitis, drug-induced, jejunoileal bypass surgery, HIV infection, and parenteral nutrition support), a diagnosis of NAFLD can be made.

Because the radiologic findings of hepatic steatosis are common from a variety of causes, the differential diagnosis is largely discriminated on clinical and laboratory grounds.<sup>43</sup> Special attention needs to be given to the possible imaging overlap between simple steatosis and advanced fibrosis or early cirrhosis; these disparate conditions are often, but not always, easily distinguished clinically.

A major challenge in the differential diagnosis of hepatic steatosis occurs when the radiologic findings of focal fat deposition or focal fat sparing simulate hepatic nodular lesions such as abscess, benign neoplasm, or primary or metastatic malignancy. The diagnosis of focal fat deposition or sparing is supported by their occurrence in typical locations, a wedge shape, the lack of mass effect, and the absence of vascular displacement or distortion inside the lesion. If doubt exists, MRI may be performed.

# Treatment

#### MEDICAL TREATMENT

The standard of care in managing patients with NAFLD consists of lifestyle modification through diet and exercise, with the goal of gradual weight loss in patients who are overweight or obese. Weight loss and exercise decrease adipose stores and improve insulin sensitivity, thereby targeting the underlying causative factor of insulin resistance. Evidence for the efficacy of this strategy comes from trials that have demonstrated histologic regression of steatosis with weight loss.<sup>56,57</sup> In patients with associated metabolic syndrome, optimal control of diabetes, hyperlipidemia, and hypertension are routinely recommended, although the effects of such treatment on histology are poorly characterized and are unlikely to produce complete resolution of NAFLD in most cases.<sup>3</sup>

To date, no pharmacologic therapy has been approved for the treatment of NAFLD. Based on current understanding of the pathogenesis of NASH, pharmacologic therapy has been attempted with weight loss–promoting medications (orlistat), antioxidants (vitamin E and betaine), cytoprotective agents (ursodeoxycholic acid), and insulin sensitizers (metformin and thiazolidinediones).<sup>58-64</sup> Although some of these agents have promoted decreases in aminotransferase levels and histologic improvement, their trials have often been poorly powered or nonrandomized. Therefore, treatment with these various medications is controversial and not typically pursued in clinical practice. All patients with NAFLD should be treated with lifestyle modification and considered for referral to centers involved in clinical research until definitive pharmacotherapy is approved.

#### SURGICAL TREATMENT

Bariatric surgery is the primary surgical intervention for NAFLD in patients with a body mass index of more than 40 kg/m<sup>2</sup> or of 35 kg/m<sup>2</sup> with comorbidities.<sup>65</sup> Current bariatric surgical techniques include vertical banded gastroplasty, adjustable gastric banding, Roux-en-Y gastric bypass, biliopancreatic bypass, and biliopancreatic diversion with duodenal switch.

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Based on a recent meta-analysis, bariatric surgery is associated with significant histologic improvements in steatosis, steato-hepatitis, and fibrosis, with more than 50% of patients experiencing complete resolution of their fatty liver disease after surgery.<sup>66</sup> Although these results are compelling, the observational studies showed no relationship between histologic improvement and the amount of weight loss.

#### What the Referring Physician Needs to Know

- The distinction between simple steatosis and steatohepatitis (NASH) is important in determining prognosis in NAFLD, and, at the present time, this can be accomplished only with liver biopsy.
- Weight loss through diet and exercise is likely to provide some benefit in all patients with NAFLD.
- Obese patients with NASH who are not successful in lifestyle modification and meet criteria for bariatric surgery (body mass index >40 kg/m<sup>2</sup> or >35 kg/m<sup>2</sup>

**Key Points** 

- Patterns of fat accumulation include diffuse and homogeneous (most common), focal fat deposition, focal fat sparing, multinodular, subcapsular, and perivascular.
- In some circumstances, MRI may need to be performed to differentiate focal fat deposition or focal fat sparing from a true liver lesion, particularly in the evaluation of oncology patients.

#### Computed Tomography

- A noncontrast study is best for the evaluation of hepatic steatosis.
- Ionizing radiation is a concern, especially in children.
- The diagnosis is potentially confounded by multiple variables.
- Enhanced CT may be unreliable for the diagnosis of steatosis.
- CT has moderate sensitivity and is more reliable than ultrasound.

As with other causes of cirrhosis, liver transplantation is a viable option for patients with end-stage liver disease secondary to fatty liver disease, although a significant amount of preoperative weight loss in obese patients is necessary to make liver transplantation technically feasible. Posttransplant survival rates are similar to those in patients with transplants performed for other reasons.<sup>67</sup>

with comorbidities) may benefit from weight loss surgery.

- Among patients with NASH in whom there is risk for progression to cirrhosis, consideration should be given to refer patients for participation in clinical trials.
- Patients with cirrhosis secondary to NASH are at risk for hepatocellular carcinoma and should undergo regular screening examinations, although specific guidelines are lacking.

#### Ultrasound

- Findings are dependent on equipment, operator, and observer.
- It is not useful for longitudinal assessment of the severity of steatosis.
- Its use is limited in patients with a large body habitus.
- Of all the modalities, it is of lowest sensitivity and thus not recommended for screening of early disease.

#### Magnetic Resonance Imaging

- MR spectroscopy is theoretically most accurate but may not be available depending on the center.
- MRI (frequency-selective, phase-interference) is rapid and highly specific for the presence of fat.
- Dedicated fat quantification imaging or spectroscopy sequences are necessary for accurate diagnosis and grading of fatty liver disease and are being developed.

#### **SUGGESTED READINGS**

- Angulo P: Nonalcoholic fatty liver disease. N Engl J Med 346:1221–1231, 2002.
- Angulo P, Lindor KD: Non-alcoholic fatty liver disease. J Gastroenterol Hepatol 17(Suppl):S186– S190, 2002.
- Clark JM, Brancati FL, Diehl AM: Nonalcoholic fatty liver disease. *Gastroenterology* 122:1649–1657, 2002.

#### REFERENCES

- Kleiner DE, Brunt EM, Van Natta M, et al: Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology* 41:1313–1321, 2005.
- Marchesini G, Bugianesi E, Forlani G, et al: Nonalcoholic fatty liver, steatohepatitis, and the metabolic syndrome. *Hepatology* 37:917–923, 2003.
- 3. Angulo P: Nonalcoholic fatty liver disease. N Engl J Med 346:1221–1231, 2002.

- Hamer OW, Aguirre DA, Casola G, et al: Fatty liver: imaging patterns and pitfalls. *Radiographics* 26:1637–1653, 2006.
- Karcaaltinacaba M, Akhan O: Imaging of hepatic steatosis and fatty sparing. *Eur J Radiol* 61:33–43, 2007.
- Lall CG, Aisen AM, Bansal N, et al: Nonalcoholic fatty liver disease. *AJR Am J Roentgenol* 190:993–1002, 2008.
- Marchesini G, Bugianesi E, Forlani G, et al: Nonalcoholic fatty liver, steatohepatitis, and the metabolic syndrome. *Hepatology* 37:917–923, 2003.

Rofsky NM, Fleishaker H: CT and MRI of diffuse liver disease. Semin Ultrasound CT MR 16:16–33, 1995.

- Valls C, Iannacconne R, Alba E, et al: Fat in the liver: diagnosis and characterization. *Eur Radiol* 16: 2229–2308, 2006.
- Day CP, James OF: Steatohepatitis: a tale of two "hits"? Gastroenterology 114:842–845, 1998.
- Parekh S, Anania FA: Abnormal lipid and glucose metabolism in obesity: implications for nonalcoholic fatty liver disease. *Gastroenterology* 132:2191–2207, 2007.
- Goldberg IJ, Ginsberg HN: Ins and outs modulating hepatic triglyceride and development of nonalcoholic fatty liver disease. *Gastroenterology* 130:1343–1346, 2006.
- Edmison J, McCullough AJ: Pathogenesis of non-alcoholic steatohepatitis: human data. *Clin Liver Dis* 11:75–104, ix, 2007.
- Rajala MW, Scherer PE: Minireview: the adipocyte—at the crossroads of energy homeostasis, inflammation, and atherosclerosis. *Endocrinology* 144:3765–3773, 2003.
- Browning JD, Horton JD: Molecular mediators of hepatic steatosis and liver injury. J Clin Invest 114:147–152, 2004.

- Patton HM, Sirlin C, Behling C, et al: Pediatric nonalcoholic fatty liver disease: a critical appraisal of current data and implications for future research. J Pediatr Gastroenterol Nutr 43:413–427, 2006.
- Clark JM: The epidemiology of nonalcoholic fatty liver disease in adults. J Clin Gastroenterol 40:S5–S10, 2006.
- Clark JM, Brancati FL, Diehl AM: Nonalcoholic fatty liver disease. *Gastroenterology* 122:1649– 1657, 2002.
- Browning JD, Szczepaniak LS, Dobbins R, et al: Prevalence of hepatic steatosis in an urban population in the United States: impact of ethnicity. *Hepatology* 40:1387–1395, 2004.
- Ryan CK, Johnson LA, Germin BI, et al: One hundred consecutive hepatic biopsies in the workup of living donors for right lobe liver transplantation. *Liver Transpl* 8:1114–1122, 2002.
- Soejima Y, Shimada M, Suehiro T, et al: Use of steatotic graft in living-donor liver transplantation. *Transplantation* 76:344–348, 2003.
- Schwimmer JB, Deutsch R, Kahen T, et al: Prevalence of fatty liver in children and adolescents. *Pediatrics* 118:1388–1393, 2006.
- Dunn W, Schwimmer JB: The obesity epidemic and nonalcoholic fatty liver disease in children. *Curr Gastroenterol Rep* 10:67–72, 2008.
- Angulo P, Lindor KD: Non-alcoholic fatty liver disease. J Gastroenterol Hepatol 17(Suppl):S186– S190, 2002.
- Crespo J, Fernandez-Gil P, Hernandez-Guerra M, et al: Are there predictive factors of severe liver fibrosis in morbidly obese patients with non-alcoholic steatohepatitis? *Obes Surg* 11: 254–257, 2001.
- Dixon JB, Bhathal PS, O'Brien PE: Nonalcoholic fatty liver disease: predictors of nonalcoholic steatohepatitis and liver fibrosis in the severely obese. *Gastroenterology* 121:91–100, 2001.
- Beymer C, Kowdley KV, Larson A, et al: Prevalence and predictors of asymptomatic liver disease in patients undergoing gastric bypass surgery. *Arch Surg* 138:1240–1244, 2003.
- 22. Gholam PM, Kotler DP, Flancbaum LJ: Liver pathology in morbidly obese patients undergoing Roux-en-Y gastric bypass surgery. *Obes Surg* 12:49–51, 2002.
- Bugianesi E, Gastaldelli A, Vanni E, et al: Insulin resistance in non-diabetic patients with nonalcoholic fatty liver disease: sites and mechanisms. *Diabetologia* 48:634–642, 2005.
- Angulo P, Keach JC, Batts KP, et al: Independent predictors of liver fibrosis in patients with nonalcoholic steatohepatitis. *Hepatology* 30:1356– 1362, 1999.
- Schwimmer JB: Definitive diagnosis and assessment of risk for nonalcoholic fatty liver disease in children and adolescents. *Semin Liver Dis* 27:312–318, 2007.
- Fan JG, Zhu J, Li XJ, et al: Prevalence of and risk factors for fatty liver in a general population of Shanghai, China. J Hepatol 43:508–514, 2005.
- 27. Ruhl CE, Everhart JE: Relation of elevated serum alanine aminotransferase activity with iron and antioxidant levels in the United States. *Gastroenterology* 124:1821–1829, 2003.
- Clark JM, Brancati FL, Diehl AM: The prevalence and etiology of elevated aminotransferase levels in the United States. *Am J Gastroenterol* 98:960–967, 2003.
- 29. Liangpunsakul S, Chalasani N: Unexplained elevations in alanine aminotransferase in individuals with the metabolic syndrome: results from the third National Health and Nutrition

Survey (NHANES III). Am J Med Sci 329:111-116, 2005.

- Matteoni CA, Younossi ZM, Gramlich T, et al: Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. *Gastroenterol*ogy 116:1413–1419, 1999.
- Day CP: Natural history of NAFLD: remarkably benign in absence of cirrhosis. *Gastroenterology* 129:375–378, 2005.
- Hubscher SG: Histological assessment of nonalcoholic fatty liver disease. *Histopathology* 49:450–465, 2006.
- Schwimmer JB, Behling C, Newbury R, et al: Histopathology of pediatric nonalcoholic fatty liver disease. *Hepatology* 42:641–649, 2005.
- Kleiner DE, Brunt EM, Van Natta M, et al: Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology* 41:1313–1321, 2005.
- Karcaaltincaba M, Akhan O: Imaging of hepatic steatosis and fatty sparing. *Eur J Radiol* 61:33– 43, 2007.
- Hamer OW, Aguirre DA, Casola G, et al: Fatty liver: imaging patterns and pitfalls. *Radiographics* 26:1637–1653, 2006.
- Rofsky NM, Fleishaker H: CT and MRI of diffuse liver disease. Semin Ultrasound CT MR 16:16–33, 1995.
- Charatcharoenwitthaya P, Lindor KD: Role of radiologic modalities in the management of non-alcoholic steatohepatitis. *Clin Liver Dis* 11:37–45, 2007.
- Valls C, Iannacconne R, Alba E, et al: Fat in the liver: diagnosis and characterization. *Eur Radiol* 16:2229–2308, 2006.
- Park SH, Kim PN, Kim KW, et al: Macrovesicular hepatic steatosis in living liver donors: use of CT for quantitative and qualitative assessment. *Radiology* 239:105–112, 2006.
- Zheng X, Ren Y, Phillips WT, et al: Assessment of hepatic fatty infiltration using spectral computed tomography imaging: a pilot study. *J Comput Assist Tomogr* 37:134–141, 2013.
- Kodama Y, Ng CS, Wu TT, et al: Comparison of CT methods for determining the fat content of the liver. AJR Am J Roentgenol 188:1307–1312, 2007.
- 43. Kawamori Y, Matsui O, Takahashi S, et al: Focal hepatic fatty infiltration in the posterior edge of the medial segment associated with aberrant gastric venous drainage: CT, US, and MR findings. J Comput Assist Tomogr 20:356–359, 1996.
- 44. Matsui O, Kadoya M, Takahashi S, et al: Focal sparing of segment IV in fatty livers shown by sonography and CT: correlation with aberrant gastric venous drainage. *AJR Am J Roentgenol* 164:1137–1140, 1995.
- 45. Yokoo T, Bydder M, Hamilton G, et al: Hepatic fat quantification by low flip-angle multi-echo gradient-echo MR imaging: a clinical study with validation with MR spectroscopy. Presented before the annual meeting of the International Society for Magnetic Resonance in Medicine. Toronto, Canada, 2008, p 706.
- Lall CG, Aisen AM, Bansal N, et al: Nonalcoholic fatty liver disease. *AJR Am J Roentgenol* 190:993–1002, 2008.
- Yeh SH, Wu LC, Wang SJ, et al: Xenon-133 hepatic retention ratio: a useful index for fatty liver quantification. J Nucl Med 30:1708–1712, 1989.
- Itai Y, Saida Y: Pitfalls in liver imaging. Eur Radiol 12:1162–1174, 2002.
- Rinella ME, McCarthy R, Thakrar K, et al: Dualecho, chemical shift gradient-echo magnetic resonance imaging to quantify hepatic steatosis: implications for living liver donation. *Liver Transpl* 9:851–856, 2003.

- Pilleul F, Chave G, Dumortier J, et al: Fatty infiltration of the liver: detection and grading using dual T1 gradient echo sequences on clinical MR system. *Gastroenterol Clin Biol* 29:1143–1147, 2005.
- Lelbach WK: Epidemiology of alcoholic liver disease. In Popper H, Schaffner F, editors: *Progress in liver disease* (vol 5). New York, 1976, Grune & Stratton, pp 494–515.
- Neuschwander-Tetri BA, Caldwell SH: Nonalcoholic steatohepatitis: summary of an AASLD Single Topic Conference. *Hepatology* 37:1202– 1219, 2003.
- Patton HM, Patel K, Behling C, et al: The impact of steatosis on disease progression and early and sustained treatment response in chronic hepatitis C patients. *J Hepatol* 40:484–490, 2004.
- 54. Hasegawa T, Yoneda M, Nakamura K, et al: Plasma transforming growth factor-betal level and efficacy of alpha-tocopherol in patients with non-alcoholic steatohepatitis: a pilot study. *Aliment Pharmacol Ther* 15:1667–1672, 2001.
- 55. Fernandez FG, Ritter J, Goodwin JW, et al: Effect of steatohepatitis associated with irinotecan or oxaliplatin pretreatment on resectability of hepatic colorectal metastases. J Am Coll Surg 200:845–853, 2005.
- Zorzi D, Laurent A, Pawlik TM, et al: Chemotherapy-associated hepatotoxicity and surgery for colorectal liver metastases. *Br J Surg* 94:274–286, 2007.
- Huang MA, Greenson JK, Chao C, et al: Oneyear intense nutritional counseling results in histological improvement in patients with nonalcoholic steatohepatitis: a pilot study. *Am J Gastroenterol* 100:1072–1081, 2005.
- Andersen T, Gluud C, Franzmann MB, et al: Hepatic effects of dietary weight loss in morbidly obese subjects. J Hepatol 12:224–229, 1991.
- Harrison SA, Fincke C, Helinski D, et al: A pilot study of orlistat treatment in obese, nonalcoholic steatohepatitis patients. *Aliment Pharmacol Ther* 20:623–628, 2004.
- Lavine JE: Vitamin E treatment of nonalcoholic steatohepatitis in children: a pilot study. *J Pediatr* 136:734–738, 2000.
- Sanyal AJ, Mofrad PS, Contos MJ, et al: A pilot study of vitamin E versus vitamin E and pioglitazone for the treatment of nonalcoholic steatohepatitis. *Clin Gastroenterol Hepatol* 2:1107–1115, 2004.
- 62. Abdelmalek MF, Angulo P, Jorgensen RA, et al: Betaine, a promising new agent for patients with nonalcoholic steatohepatitis: results of a pilot study. *Am J Gastroenterol* 96:2711–2717, 2001.
- Lindor KD, Kowdley KV, Heathcote EJ, et al: Ursodeoxycholic acid for treatment of nonalcoholic steatohepatitis: results of a randomized trial. *Hepatology* 39:770–778, 2004.
- 64. Bugianesi E, Gentilcore E, Manini R, et al: A randomized controlled trial of metformin versus vitamin E or prescriptive diet in nonalcoholic fatty liver disease. Am J Gastroenterol 100:1082–1090, 2005.
- Belfort R, Harrison SA, Brown K, et al: A placebo-controlled trial of pioglitazone in subjects with nonalcoholic steatohepatitis. N Engl J Med 355:2297–2307, 2006.
- National Institutes of Health conference. Gastrointestinal surgery for severe obesity. Consensus Development Conference Panel. Ann Intern Med 115:956–961, 1991.
- 67. Mummadi RR, Kasturi KS, Chennareddygari S, et al: Effect of bariatric surgery on nonalcoholic fatty liver disease (NAFLD): a meta-analysis. *Hepatology* 46:A130, 2007.

# **Hepatic Iron Overload**

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# Etiology

Hepatic iron overload is a generic term that refers to the nonphysiologic accumulation of iron within the hepatic parenchyma. The most clinically significant cause of hepatic iron overload is hereditary hemochromatosis. Hereditary hemochromatosis is associated with several mutations in genes regulating iron metabolism, the most common of which are in the *HFE* gene. The *HFE* mutations result in dysregulated iron absorption, which may lead to total-body iron overload and accumulation of excess iron in tissue (hemosiderosis), including the liver, heart, and various endocrine organs. The iron accumulation causes tissue damage and, if untreated, may lead to cirrhosis and hepatocellular carcinoma, along with assorted cardiac and endocrine disturbances.

Secondary (acquired) causes of hepatic iron overload include the iron-loading anemias (thalassemia major, sideroblastic anemia, chronic hemolytic anemia, and spur cell anemia), long-term hemodialysis, and dietary iron overload. These usually do not lead to significant liver dysfunction, although they may cause dysfunction in other organs such as the heart. Chronic liver diseases (hepatitis B and C virus infection, alcohol-induced liver disease, nonalcoholic fatty liver disease, and porphyria cutanea tarda) also may be associated with hepatic iron overload, but the clinical picture is dominated by the primary hepatic abnormality and the excess liver iron is of secondary importance.

The average adult stores 1 to 3 g of iron, mainly within the liver and in red blood cells as hemoglobin. In normal persons, approximately 10% of dietary iron (1 mg/day) is absorbed daily.<sup>1</sup> A similar amount of iron is lost via sloughing of cells from the skin and mucosal surfaces.<sup>2,3</sup> In premenopausal women, menstruation increases the amount of iron loss to approximately 2 mg/day.<sup>2</sup> Ultimately, however, the body lacks a proficient iron excretion mechanism and pathologic excesses in iron overload are therefore unchecked and progressive. Systemic iron levels are kept within a narrow homeostatic range because of a complex regulatory mechanism monitoring the absorption of iron via the gastrointestinal tract and its accumulation in the body.<sup>3</sup>

Iron overload in hereditary hemochromatosis occurs when iron absorption via the digestive tract exceeds iron usage and excretion. The most common cause of hereditary hemochromatosis is a mutation in the *HFE* gene located on chromosome 6 that regulates iron homeostasis.<sup>4-7</sup> It also can result from genetic anomalies corresponding to other genes involved in iron metabolism.<sup>8,9</sup>

Regardless of the underlying genetic abnormality, when iron absorption exceeds the transport capacity of transferrin,

excess iron is deposited within parenchymal cells of various tissues, including the liver, heart, and endocrine organs. Hemosiderosis is to this excess parenchymal iron and may cause tissue damage by catalyzing the production of radical oxygen species from hydrogen peroxide. These radical oxygen species attack cell membranes, cellular proteins, and DNA.<sup>10</sup> The pathophysiologic sequelae depend on the organs and tissues involved.

Hepatic dysfunction from secondary hemosiderosis with these entities is rare, although clinically significant iron deposition in other organs (e.g., the heart) may occur. Chronic liver diseases (hepatitis B and C virus infection, alcohol-induced liver disease, nonalcoholic fatty liver disease, and porphyria cutanea tarda) are sometimes associated with hepatic iron overload; this has been attributed to diminished functional hepatocyte mass and reduced hepcidin production.<sup>11-13</sup> In these diseases, the primary liver condition is the paramount abnormality and the secondary iron overload is of relatively minor clinical relevance.

# Prevalence and Epidemiology

Hereditary hemochromatosis is the most common genetic disease in populations of Northern European ancestry. Homozygosity of the *C282Y* mutation has a prevalence of 1 per 200 persons (0.5%), 10 times higher than that of cystic fibrosis.<sup>6,7,14,15</sup> In the United States, approximately 1 million people carry the diagnosis of hereditary hemochromatosis. It is estimated that an additional 1.5 million have undiagnosed hereditary hemochromatosis and approximately 5% of individuals with hereditary hemochromatosis have cirrhosis.<sup>16-19</sup>

The development of hereditary hemochromatosis is impacted by ethnicity, race, sex, and age. Hereditary hemochromatosis is typically a disease of Northern European ancestry, with persons of Irish descent at greatest risk. In the United States, *C282Y* heterozygosity was demonstrated in 9.5% of non-Hispanic whites, 2.3% of blacks, and 2.8% of Hispanics.<sup>15</sup> Because of the countereffects of menstruation on iron accumulation, females are three times less likely to develop hereditary hemochromatosis than males and are two to three times less likely to progress to serious complications (e.g., cirrhosis, diabetes, heart failure). Hereditary hemochromatosis typically manifests in patients older than 40 years of age, and it appears later in women than men.

# **Clinical Presentation**

The clinical manifestations of hereditary hemochromatosis range from isolated biochemical abnormalities to multisystem

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disease involving the liver, heart, endocrine organs (e.g., pancreas and pituitary gland), joints, and skin. Most patients are asymptomatic at the time of diagnosis, which is discovered as a result of screening serum iron studies in individuals with elevated liver function tests or testing of family members of an affected proband.<sup>20</sup> In early disease, symptoms are nonspecific and include weakness, lethargy, and fatigue. Symptoms related to iron deposition within specific organs occur later. Involvement of the liver may be associated with hepatomegaly and right upper quadrant abdominal pain. If the disease progresses to cirrhosis, patients may develop portal hypertension or hepatocellular carcinoma. Other manifestations of hereditary hemochromatosis include arthropathy secondary to iron deposition in the joints (classically involving the second and third metacarpophalangeal joints and proximal interphalangeal joints); diabetes mellitus resulting from pancreatic iron deposition; loss of libido, impotence, and amenorrhea as a result of pituitary involvement; and dilated cardiomyopathy, congestive heart failure, conduction abnormalities, and arrhythmias because of iron deposition in the heart.<sup>4,21</sup> The characteristic darkening of the skin, termed bronze diabetes, is caused by increased levels of melanin and is an infrequent manifestation in late disease.<sup>2</sup>

Patients with hepatic involvement demonstrate mild, nonspecific elevations in serum levels of aminotransferases (<200 mg/dL) and bilirubin (<4 mg/dL). When hereditary hemochromatosis is suspected, however, serum iron studies hone the diagnosis. In mild disease, the excess iron is mainly in the plasma compartment and is shown by elevated serum iron levels and transferrin saturation and diminished transferrin. In advanced disease, iron is stored within parenchymal cells, shown by an elevated serum ferritin level. If serum ferritin and aspartate aminotransferase (AST) levels both are elevated and platelet counts are low, patients are at high risk for having or developing cirrhosis.<sup>22,23</sup> The diagnosis of hereditary hemochromatosis is confirmed by genetic testing for the C282Y and H63D mutations. Imaging does not play a diagnostic role in hereditary hemochromatosis, although certain imaging findings may support the diagnosis.

Liver biopsy, for the purpose of determining hepatic iron content and fibrosis staging, is reserved for patients who are homozygous for *C282Y* mutations, are older than 40 years of age, and have high ferritin levels (>1000 mg/L) and elevated serum AST levels. In individuals with results of serum iron studies that are of concern and who are not homozygous for the *C282Y* mutation, consideration should be given to other causes of liver disease. A liver biopsy in these patients may uncover other causes and determine hepatic iron content, which could guide the decision as to whether to pursue therapeutic phlebotomy.

The natural history of hereditary hemochromatosis varies according to type, and disease progression is accelerated with excess alcohol consumption, obesity, and viral hepatitis.<sup>24-28</sup> Primary liver cancer is an important complication of advanced hereditary hemochromatosis and is almost exclusively observed in patients with underlying cirrhosis. Importantly, the risk for malignancy persists after therapeutic phlebotomy, so appropriate screening should continue after this intervention. Large population-based studies analyzing the risk for malignancy are lacking, but it is clear that hepatocellular carcinoma is the most common primary liver malignancy in patients with hereditary hemochromatosis, followed by combined hepato-

cellular carcinoma and cholangiocarcinoma and cholangiocarcinoma alone.  $^{\rm 29}$ 

# Pathology

Iron deposition within the liver varies in distribution according to the cause. Generally, the iron distribution in hereditary hemochromatosis is predominantly within hepatocytes, whereas in most cases of secondary iron overload the iron is situated mainly within the reticuloendothelial system (e.g., Kupffer cells). However, in advanced stages of either of these groups of diseases, stainable iron may be found in both cell types. In microscopic sections, iron is demonstrated via a Perls stain (using acid ferrocyanide), which produces a Prussian blue reaction with ferritin and hemosiderin.

In hereditary hemochromatosis, stainable iron first appears as golden-yellow hemosiderin granules in the cytoplasm of periportal hepatocytes. With disease advancement, the iron deposition progresses in a portal to centrilobular fashion, eventually involving the entire lobule diffusely. When welldeveloped, there is a distinctive pericanalicular "chicken wire" distribution to the stainable iron, a result of accumulation of iron within subapical hepatocyte lysosomes.<sup>30</sup> Although the majority of iron is found within hepatocytes, Kupffer cells and biliary epithelium may contain iron later in the disease course.

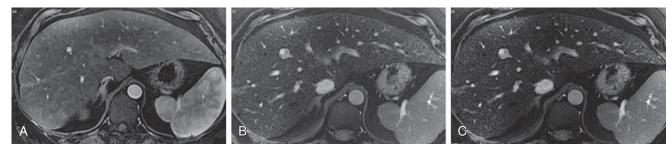
Because iron is a direct hepatotoxin, inflammation is characteristically absent; therefore, the identification of significant inflammation should prompt consideration of coexistent causes of chronic liver disease. As iron accumulates, fibrosis slowly develops in a periportal distribution. Eventually, portal-portal bridging fibrosis and cirrhosis ensue, resulting in a diffuse micronodular pattern. With phlebotomy, there is steady disappearance of stainable iron in a pattern that is the reverse of its accumulation, from centrilobular areas to portal tracts. Although iron deposition is typically diffuse in cirrhosis secondary to hereditary hemochromatosis, small regions spared by iron deposition have been theorized to represent preneoplastic lesions.<sup>31</sup>

# Imaging

As stated earlier, imaging does not play a role in the diagnosis of hereditary hemochromatosis. Nevertheless, imaging modalities may be used to monitor patients with established hereditary hemochromatosis, and patients with the disorder may undergo imaging studies for unrelated reasons. Patients with advanced disease may progress to cirrhosis (Figure 39-1), portal hypertension, and hepatocellular carcinoma; findings relevant to these complications are discussed in other chapters. In recent years, interest has grown in developing noninvasive methods to quantify hepatic iron, and a brief description is given of some of the proposed techniques.

#### RADIOGRAPHY

Radiographs play no role in the routine assessment of the liver in hereditary hemochromatosis but may be used to identify the characteristic arthropathy associated with the disorder. Findings in the hands of patients with hereditary hemochromatosis may include squared-off bone ends and hooklike osteophytes, joint space narrowing, sclerosis, and cyst formation.<sup>32</sup>



**Figure 39-1** Cirrhosis secondary to hemochromatosis. **A**, Axial three-dimensional (3D) T1-weighted gradient echo magnetic resonance (MR) image (TE = 1.6 ms) acquired during the late hepatic arterial phase after intravenous gadolinium administration shows heterogeneous parenchyma with scattered regenerative nodules and a focal scar indenting the right lateral surface of the liver. **B** and **C**, Axial 2D intermediate-weighted gradient echo MR images with echo times of 4 (**B**) and 8 ms (**C**) acquired several minutes after gadolinium administration show considerable signal loss with an increase in echo time. The signal loss is due to T2\* shortening from endogenous iron accumulation. In standard doses, gadolinium administration does not meaningfully shorten the T2\* of the liver. Note that, consistent with mild cirrhosis, there are fibrotic reticulations throughout the liver; these are most pronounced in the left lateral segment.

# COMPUTED TOMOGRAPHY

#### Unenhanced Computed Tomography

The normal liver parenchyma has an attenuation of 45 to 65 Hounsfield units (HU) on unenhanced, standard (singleenergy) computed tomography (CT). In hepatic hemosiderosis, secondary to hereditary hemochromatosis or other causes, unenhanced CT reveals elevated hepatic attenuation because of the greater electron density associated with iron atoms compared with normal liver. The characteristic CT finding is a "white liver" with a diffuse increase in liver density above 70 HU. In general, unenhanced CT accurately detects hepatic iron in advanced disease but is unable to do so for early or mild hepatic iron overload. Unenhanced CT has almost 100% sensitivity in detecting hepatic iron overload more than 5-fold above the upper limit of normal but only 60% sensitivity for detection of hepatic iron concentration 2.5-fold above the upper limit of normal. Increased hepatic attenuation is not specific for iron accumulation and also may be seen in storage disorders, sarcoidosis, Wilson's disease, and drug-induced (amiodarone, methotrexate, and gold) hepatotoxicity.

#### Contrast-Enhanced Computed Tomography

Contrast-enhanced CT is not relevant for the detection and monitoring of hepatic iron overload but may be performed for surveillance of hepatocellular carcinoma in patients who have progressed to cirrhosis.

**Extrahepatic Findings.** Patients with hereditary hemochromatosis may develop iron overload in the pancreas and myocardium. However, these tissues typically have normal attenuation at unenhanced CT. CT has limited sensitivity for detection of extrahepatic manifestations of hereditary hemochromatosis.

**Computed Tomography Quantification of Hepatic Iron Overload.** Although iron overload is associated with increased hepatic attenuation, the correlation between CT attenuation and hepatic iron concentration is poor. Conventional singleenergy CT does not permit reliable gradation of hepatic iron overload or accurate quantification of hepatic iron content.<sup>33</sup> However, dual-energy CT may offer the potential to quantitate liver iron content by using an iron-specific three-material decomposition algorithm, which negates the confounding effects of healthy liver attenuation variability and concomitant steatosis.<sup>34</sup> Larger multicenter trials are needed to reproduce and further explore this possibility.

# MAGNETIC RESONANCE IMAGING

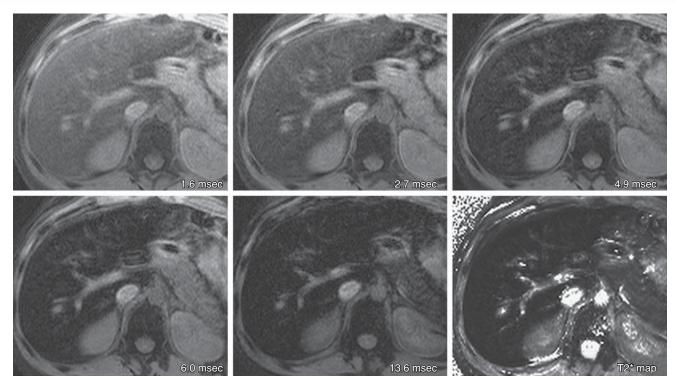
#### Unenhanced Magnetic Resonance Imaging

Because of susceptibility effects, iron accumulation in tissue leads to T2 and T2\* shortening, causing signal loss on T2-weighted and T2\*-weighted images. Gradient echoes are more sensitive to susceptibility effects than spin echoes, and the signal loss is more pronounced on gradient echo images. Thus, the affected liver appears relatively hypointense on T2\*-weighted images and, to a lesser extent, T2-weighted images (Figures 39-2 and 39-3). Mild cases of iron overload may be apparent only on gradient echo imaging. If iron overload is severe, the degree of signal loss may be marked on both types of images. Although iron primarily shortens the T2 and T2\* of the liver, it also shortens the T1, and the liver may have increased signal intensity on T1-weighted sequences acquired with very short echo times.

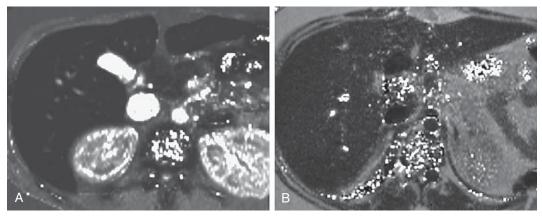
In-phase and out-of-phase gradient echo imaging typically is used to assess fat accumulation in tissue, but the images also can be used to detect iron (Figure 39-4); loss of signal on the second echo (later echo time) compared with the first echo (earlier echo time) indicates short T2\* relaxation and suggests the presence of parenchymal iron. Concomitant liver steatosis may confound the interpretation, however, because fat-water phase interference will alter the relative signal intensities of the in-phase and out-of-phase images.<sup>35</sup> To avoid this pitfall, dual-echo images can be acquired at in-phase echo times or after application of chemical fat saturation. Alternatively, multiple gradient echoes can be obtained and the effects of fat-water phase interference and T2\* relaxation modeled simultaneously.

#### Contrast-Enhanced Magnetic Resonance Imaging

The administration of gadolinium does not provide additional information regarding hepatic iron accumulation per se but may be necessary to evaluate focal lesions in the liver with iron overload. In general, the infusion of superparamagnetic iron oxides (SPIOs) should be avoided in patients with known hepatic iron overload, mainly because the particles further reduce  $T2^*$  and may diminish liver signal-to-noise ratio to a



**Figure 39-2** A T2\* map was generated by acquiring 12 co-localized fat-saturated spoiled gradient recalled echo magnetic resonance images. Echo times ranged from 1.6 to 13.6 ms. Of the series of 12 images, 5 are presented for illustrative purposes with echo times as shown. The T2\* value was calculated assuming monoexponential signal decay from the 12 echoes. The estimated T2\* relaxation value, 9 ms, suggests moderate iron overload.



**Figure 39-3** T2\* versus T2 maps in severe transfusional hemosiderosis. T2\* map (A) (generated using same technique as in Figure 39-2 and T2 map (B) (generated in analogous fashion to T2\* map but with nine spin echo images from 10 to 90 ms) in a patient with severe transfusional hemosiderosis. The estimated T2\* value in A is 4.5 ms, markedly less than a normal 25- to 30-ms T2\* value typically obtained with this particular imaging sequence and MR scanner. The estimated T2 value, 45 ms, is only slightly lower than the normal 50- to 60-ms T2 measured on this scanner. As shown in this example, a given amount of iron deposition causes greater T2\* shortening than T2 shortening.

subdiagnostic range. In principle, giving SPIOs also may exacerbate the hepatic iron overload.<sup>36</sup>

**Magnetic Resonance Features of Extrahepatic Iron Over-load.** T2-weighted and T2\*-weighted images may show hypointensity in the pancreas and, if acquired with cardiac gating, the myocardium.

**Magnetic Resonance Quantification of Hepatic Iron Overload.** Two magnetic resonance imaging (MRI) techniques are commonly used for grading the degree of hepatic iron deposition: (1) calculation of T2 or T2\* relaxation time constants using multiple echo times and (2) calculation of the signal intensity ratio between the liver and an internal reference tissue known to be unaffected by iron accumulation (e.g., paraspinal

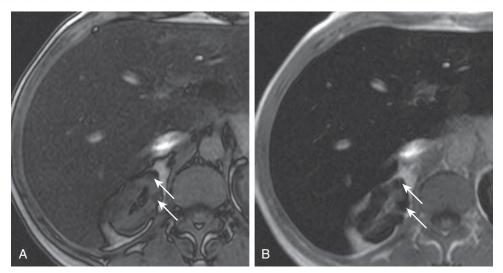
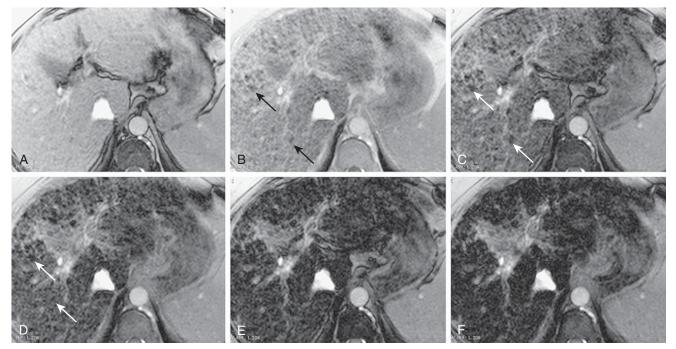


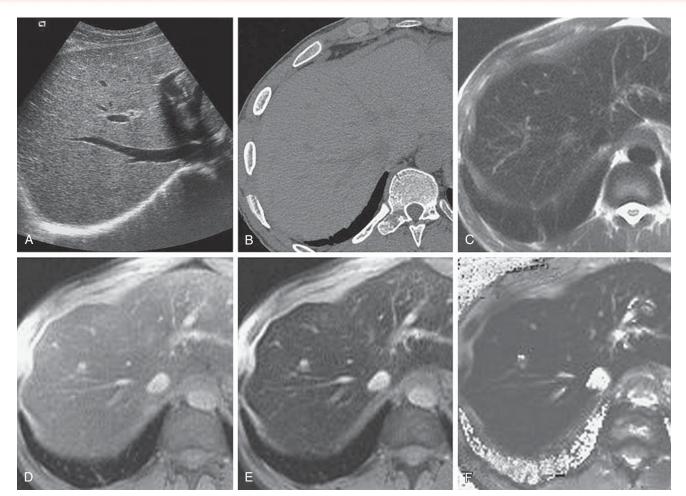
Figure 39-4 Use of out-of-phase and in-phase imaging for detecting iron overload. Axial spoiled gradient recalled echo magnetic resonance images through the liver at echo times of 2.3 ms (out-of-phase) (A) and 4.6 ms (in-phase) (B) show marked signal loss of the liver on the later echo, suggesting iron overload. The hepatic findings are consistent with hemochromatosis or secondary hemosiderosis. However, marked signal loss between echoes in the renal cortex (arrows) indicates renal parenchymal iron deposition. The involvement of the kidney favors secondary hemosiderosis.



**Figure 39-5** Acquired hemosiderosis as a result of cirrhosis in patient with chronic viral hepatitis. Co-localized spoiled gradient recalled echo magnetic resonance images acquired at echo times of 2.3 (A), 4.6 (B), 6.9 (C), 9.2 (D), 11.5 (E), and 13.5 (F) ms. The liver parenchyma progressively loses signal as echo time increases, consistent with short T2\* relaxation. Note several siderotic nodules on intermediate echoes, at 4.6 to 9.2 ms, which are visibly more hypointense (arrows) than the rest of the liver parenchyma. These siderotic nodules have higher concentrations of iron than the rest of the liver. Despite the reduced T2\* of the liver, the spleen (*right corner of images*) has normal T2\* and does not lose signal, indicating that the spleen is not iron overloaded.

muscles).<sup>33</sup> In patients with high levels of secondary iron overload, relaxation time constants have correlated closely with hepatic iron concentration determined by liver biopsy (Figure 39-5). If gradient echoes are used for T2\* measurements, it is important to reduce possible phase-interference effects from concomitant fat accumulation by acquiring echoes only at in-phase echo times or obtaining images with frequencyselective fat saturation (or water excitation).

A reduced signal intensity ratio of liver to paraspinal muscle has been shown to have high sensitivity and specificity for



**Figure 39-6** Varying sensitivity of imaging techniques in patient with moderate to severe transfusional iron overload. **A**, Ultrasound image is normal. **B**, Unenhanced computed tomography (CT) is borderline abnormal with CT attenuation of 75 Hounsfield units (HU). **C**, On axial single-shot fast spin echo magnetic resonance (MR) image, the liver is slightly more hypointense than normal liver parenchyma. On axial gradient recalled echo MR images with echo times of (**D**) 1.6 ms and (**E**) 5.9 ms, the liver loses signal with increased echo times in keeping with iron deposition. As calculated in Figure 67-3, the T2\* map (**F**) value measures 6 ms. This suggests moderate-to-severe iron overload. As shown in this example, ultrasound cannot detect iron deposition. CT has low sensitivity for moderate overload, and MRI has high sensitivity, particularly with gradient-echo imaging.

moderate degrees of iron accumulation. The exact ratio used for diagnostic classification depends on the imaging parameters of the sequence.<sup>33</sup>

#### ULTRASOUND

Iron particles are too small to scatter ultrasound waves, and, therefore, ultrasound does not detect iron overload in tissue (Figure 39-6). However, although ultrasound cannot monitor hepatic iron deposition in the liver, it may be the initial imaging modality used in the evaluation for cirrhosis and portal hypertension.

#### NUCLEAR MEDICINE

Liver scintigraphy is of limited clinical use. Uptake of sulfur colloid by the siderotic liver may be reduced secondary to Kupffer cell damage incurred from iron overload. The colloid scan may be abnormal, but the alteration tends to be mild and may be difficult to appreciate. Iron quantification is not possible.

#### **IMAGING ALGORITHM**

Imaging may be used to monitor parenchymal iron in patients with established hereditary hemochromatosis. For this purpose, we rely on T2\* relaxometry using MRI, although other centers may prefer T2 relaxometry (Table 39-1). If relaxometry is unavailable, liver-to-muscle signal intensity ratio measurements may suffice. Unenhanced CT is inaccurate for grading iron deposition, exposes the patient to ionizing radiation, and is not recommended. Ultrasound cannot detect parenchymal iron and plays no routine role.

#### **Classic Signs**

- The classic imaging features of hepatic iron overload are a diffuse increase in parenchymal attenuation on unenhanced CT images and hypointensity on unenhanced T2-weighted and T2\*-weighted MR images.
- T2-weighted images are more sensitive to mild to moderate iron overload than T2-weighted images.

TABLE A	Accuracy,	uracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Hepatic Iron Overload			
Modality		Accuracy	Pitfalls	Limitations	
Computed tomogra (CT)		Unenhanced CT has high sensitivity for detecting moderate to severe iron overload but low sensitivity for mild iron overload. Using standard CT techniques, it does not accurately grade the degree of overload.	Contrast-enhanced CT increases the liver parenchyma attenuation and makes iron difficult to detect.	Exposes patient to ionizing radiation Insensitive to mild iron overload	
Magnetic resonan imaging	nce	<ul> <li>T2*-weighted imaging and in-phase and out-of-phase imaging are useful for detecting the presence of iron.</li> <li>Multiple echo T2 and T2* relaxometry and liver-to-muscle signal intensity ratios also can be used to grade the degree of iron overload.</li> </ul>	If only in-phase and out-of-phase imaging are performed, the concomitant presence of fat may be a confounder for the detection of iron.	More costly than CT Accurate calculation of iron load using MRI requires standardized protocols. T2 and T2* values obtained using one protocol may not be reproducible using other protocols.	

# **Differential Diagnosis**

The clinical differential diagnosis of hereditary hemochromatosis attempts to distinguish between primary (genetic) and secondary (acquired) causes of iron overload. *C282Y/C282Y* homozygosity and *C282Y/H63D* compound heterozygosity, the most common *HFE* mutations, are easily diagnosed via genetic testing. Although genetic testing is not readily available for the non–*HFE*-related mutations, these conditions have characteristic clinical findings. Juvenile hemochromatosis resulting from mutations in either *HAMP* or *HFE2*, manifests at a younger age (typically in the teen years) than other non-*HFE* mutations and primarily exhibits cardiac and endocrine abnormalities.<sup>3,7</sup> Abnormalities in ferroportin resulting from mutations in *SLC40A1* can be diagnosed by pedigree analysis, because this iron overload disorder is uniquely inherited in an autosomal dominant fashion.

Secondary causes of hepatic iron overload are ruled out if genetic testing suggests a primary cause. History and review of laboratory tests identify those with transfusional iron overload and iron-loading anemias. In addition, most secondary causes of hepatic iron overload are characterized histologically by iron deposition within Kupffer cells rather than hepatocytes. Histologic examination also may provide evidence for a particular underlying disease (e.g., viral hepatitis and alcoholic and nonalcoholic fatty liver disease).

In patients with hyperattenuation of the liver on CT, the main radiologic differential diagnosis includes hereditary hemochromatosis, secondary hemosiderosis, glycogen storage diseases, and amiodarone therapy. In hereditary hemochromatosis, iron overload is restricted to the liver early in the course of disease, with subsequent involvement of the pancreas and myocardium. The reticuloendothelial organs (spleen, marrow, and lymph nodes) are relatively spared. By comparison, secondary hemosiderosis leads to uniform iron deposition in the reticuloendothelial system and also may involve the renal cortex. Patients with hepatic hyperattenuation as a result of glycogen storage disease may present with massive hepatomegaly as well as multiple hepatic adenomas. In liver disease caused by amiodarone therapy, the hyperattenuation of the liver is diffuse and homogeneous on unenhanced CT.

In patients with T2 or T2\* shortening of the liver on MRI, the differential diagnosis is limited to hereditary hemochromatosis and secondary hemosiderosis, because neither glycogen storage disease nor amiodarone therapy leads to T2 or T2\* shortening. Differentiation of hereditary hemochromatosis from secondary hemosiderosis on MRI is based on the distribution and severity of extrahepatic organ involvement as described for CT.

# Treatment

# MEDICAL TREATMENT

The primary treatment for patients with hereditary hemochromatosis is life-long therapeutic phlebotomy, which aims to remove excess iron and prevent tissue damage related to iron accumulation. Regression of liver fibrosis after therapy has been described.<sup>37</sup> Phlebotomy is initially performed weekly, with longer intervals between sessions once hemoglobin levels decrease or an acceptable serum ferritin and transferrin saturation is achieved.

Iron chelation agents, such as deferoxamine, are used with modest success in patients with secondary hemosiderosis. If successful, reduction in hepatic iron concentrations with chelation therapy significantly reduces the risk for clinical disease caused by iron overload in these patients.

#### SURGICAL TREATMENT

Surgical therapy for iron overload consists of liver transplantation for decompensated cirrhosis or resection of hepatocellular carcinoma. Posttransplantation survival is equivalent in patients who have undergone transplantation for hemochromatosis versus other causes of liver disease.

#### What the Referring Physician Needs To Know

- Genetic mutations causing hereditary hemochromatosis are prevalent, especially among persons of northern European descent, but phenotypic expression of the disease tends to be low.
- The majority of hereditary hemochromatosis cases are caused by the C282Y and H63D mutations in the HFE gene, with the large majority of cases seen in C282Y homozygotes.
- Iron overload is caused by excessive iron absorption by duodenal enterocytes.
- Iron overload is initially reflected by an increased transferrin saturation level and later by an increased ferritin level.
- Ferritin levels greater than 1000 mg/L indicate a greater risk for hepatic iron overload.
- Hepatic iron overload may progress to cirrhosis and increases the risk for hepatocellular carcinoma.
- The primary mode of therapy for iron overload is with phlebotomy to deplete iron stores, which may result in regression of hepatic fibrosis.

#### SUGGESTED READINGS

- Adams PC: The modern diagnosis and management of haemochromatosis [Review]. *Aliment Pharmacol Ther* 23:1681–1691, 2006.
- Andrews NC: Disorders of iron metabolism. N Engl J Med 341:1986–1995, 1999.
- Bacon BR: Hemochromatosis: diagnosis and management. *Gastroenterology* 120:718–725, 2001.

#### Key Points

- On unenhanced CT, normal liver attenuation ranges from 45 to 65 HU.
- Iron overload can result in a homogeneously hyperattenuating liver (75 to 135 HU) because of the high electron density associated with iron atoms.
- Iron overload causes T2 and T2\* shortening of the liver, which manifests as relative hypointensity on T2-weighted and T2\*-weighted images.
- Gradient echo sequences (T2\* relaxation) are more sensitive to mild iron overload than spin echo sequences (T2 relaxation).
- Steatosis may confound the interpretation of iron overload if only in-phase and out-of-phase imaging is performed.
- Ultrasound waves are not scattered by iron particles. Therefore, ultrasound cannot detect parenchymal iron.
- Jensen PD: Evaluation of iron overload. Br J Haematol 124:697-711, 2004.
- O'Neil J, Powell L: Clinical aspects of hemochromatosis. *Semin Liver Dis* 25:381–391, 2005.
- Pietrangelo A: Hereditary hemochromatosis: a new look at an old disease. *N Engl J Med* 350:2383–2397, 2004.
- Pietrangelo A: Hereditary hemochromatosis. Biochim Biophys Acta 1763:700–710, 2006.
- Yen AW, Fancher TL, Bowlus CL: Revisiting hereditary hemochromatosis: current concepts and progress. *Am J Med* 119:391–399, 2006.

#### REFERENCES

- 1. Cook JD, Skikne BS, Lynch SR, et al: Estimates of iron insufficiency in the US population. *Blood* 68:726–731, 1986.
- Bothwell TH, Charlton RW: A general approach to the problems of iron deficiency and iron overload in the population at large. *Semin Hematol* 19:54–67, 1982.
- Pietrangelo A: Hereditary hemochromatosis: a new look at an old disease. N Engl J Med 350:2383–2397, 2004.
- Bacon BR: Hemochromatosis: diagnosis and management. *Gastroenterology* 120:718–725, 2001.
- Adams PC: The modern diagnosis and management of haemochromatosis [Review]. Aliment Pharmacol Ther 23:1681–1691, 2006.
- Rochette J, Pointon JJ, Fisher CA, et al: Multicentric origin of hemochromatosis gene (*HFE*) mutations. *Am J Hum Genet* 64:1056–1062, 1999.
- 7. Pietrangelo A: Hereditary hemochromatosis. Biochim Biophys Acta 1763:700–710, 2006.
- Papanikolaou G, Samuels ME, Ludwig EH, et al: Mutations in *HFE2* cause iron overload in chromosome 1q-linked juvenile hemochromatosis. *Nat Genet* 36:77–82, 2004.
- Babitt JL, Huang FW, Wrighting DM, et al: Bone morphogenetic protein signaling by hemojuvelin regulates hepcidin expression. *Nat Genet* 38:531–539, 2006.
- Andrews NC: Disorders of iron metabolism. N Engl J Med 341:1986–1995, 1999.
- 11. Bridle K, Cheung TK, Murphy T, et al: Hepcidin is down-regulated in alcoholic liver injury:

implications for the pathogenesis of alcoholic liver disease. *Alcohol Clin Exp Res* 30:106–112, 2006.

- Harrison-Findik DD, Schafer D, Klein E, et al: Alcohol metabolism-mediated oxidative stress down-regulates hepcidin transcription and leads to increased duodenal iron transporter expression. J Biol Chem 281:22974–22982, 2006.
- Ludwig J, Hashimoto E, Porayko MK, et al: Hemosiderosis in cirrhosis: a study of 447 native livers. *Gastroenterology* 112:882–888, 1997.
- Merryweather-Clarke AT, Pointon JJ, Shearman JD, et al: Global prevalence of putative haemochromatosis mutations. J Med Genet 34:275– 278, 1997.
- 15. Steinberg KK, Cogswell ME, Chang JC, et al: Prevalence of *C282Y* and *H63D* mutations in the hemochromatosis (*HFE*) gene in the United States. *JAMA* 285:2216–2222, 2001.
- Asberg A, Hveem K, Thorstensen K, et al: Screening for hemochromatosis: high prevalence and low morbidity in an unselected population of 65,238 persons. *Scand J Gastroenterol* 36:1108–1115, 2001.
- Adams PC, Passmore L, Chakrabarti S, et al: Liver diseases in the hemochromatosis and iron overload screening study. *Clin Gastroenterol Hepatol* 4:918–923, quiz 807, 2006.
- Olynyk JK, Cullen DJ, Aquilia S, et al: A population-based study of the clinical expression of the hemochromatosis gene. *N Engl J Med* 341:718–724, 1999.
- 19. Powell LW, Dixon JL, Ramm GA, et al: Screening for hemochromatosis in asymptomatic

subjects with or without a family history. Arch Intern Med 166:294–301, 2006.

- Bacon BR, Sadiq SA: Hereditary hemochromatosis: presentation and diagnosis in the 1990s. *Am J Gastroenterol* 92:784–789, 1997.
- Yen AW, Fancher TL, Bowlus CL: Revisiting hereditary hemochromatosis: current concepts and progress. Am J Med 119:391–399, 2006.
- Guyader D, Jacquelinet C, Moirand R, et al: Noninvasive prediction of fibrosis in C282Y homozygous hemochromatosis. Gastroenterology 115:929–936, 1998.
- Beaton M, Guyader D, Deugnier Y, et al: Noninvasive prediction of cirrhosis in C282Y-linked hemochromatosis. *Hepatology* 36:673–678, 2002.
- 24. Pietrangelo A: Juvenile hemochromatosis. *J Hepatol* 45:892–894, 2006.
- Walsh A, Dixon JL, Ramm GA, et al: The clinical relevance of compound heterozygosity for the *C282Y* and *H63D* substitutions in hemochromatosis. *Clin Gastroenterol Hepatol* 4:1403– 1410, 2006.
- Gochee PA, Powell LW, Cullen DJ, et al: A population-based study of the biochemical and clinical expression of the *H63D* hemochromatosis mutation. *Gastroenterology* 122:646–651, 2002.
- Fletcher LM, Dixon JL, Purdie DM, et al: Excess alcohol greatly increases the prevalence of cirrhosis in hereditary hemochromatosis. *Gastroenterology* 122:281–289, 2002.
- Powell EE, Ali A, Clouston AD, et al: Steatosis is a cofactor in liver injury in hemochromatosis. *Gastroenterology* 129:1937–1943, 2005.

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- Morcos M, Dubois S, Bralet MP, et al: Primary liver carcinoma in genetic hemochromatosis reveals a broad histologic spectrum. *Am J Clin Pathol* 116:738–743, 2001.
- 30. Knisely AS, Crawford JM: Inherited and developmental disorders of the liver. In Odze RD, Golblum JR, Crawford JM, editors: Surgical pathology of the GI tract, liver, biliary tract, and pancreas, Philadelphia, 2004, WB Saunders, pp 986–987.
- 31. Deugnier YM, Guyader D, Crantock L, et al: Primary liver cancer in genetic hemochroma-

tosis: a clinical, pathological, and pathogenetic study of 54 cases. *Gastroenterology* 104:228–234, 1993.

- Jordan JM: Arthritis in hemochromatosis or iron storage disease. *Curr Opin Rheumatol* 16: 62–66, 2004.
- Jensen PD: Evaluation of iron overload. Br J Haematol 124:697–711, 2004.
- Fischer MA, Reiner CS, Raptis D, et al: Quantification of liver iron content with CT-added value of dual-energy. *Eur Radiol* 21:1727–1732, 2011.
- Westphalen AC, Qayyum A, Yeh BM, et al: Liver fat: effect of hepatic iron deposition on evaluation with opposed-phase MR imaging. *Radiol*ogy 242:450–455, 2007.
- Hanna RF, Aguirre DA, Kased N, et al: Cirrhosisassociated hepatocellular nodules: correlation of histopathologic and MR imaging features. *Radiographics* 28:747–769, 2008.
- O'Neil J, Powell L: Clinical aspects of hemochromatosis. Semin Liver Dis 25:381–391, 2005.

# **Hepatic Storage Disorders**

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The hepatic storage disorders are genetic conditions characterized by the accumulation of toxic substances within either hepatocytes or the hepatic extracellular matrix. This deposition causes secondary tissue damage, which may eventually progress to cirrhosis, portal hypertension, and hepatocellular carcinoma (HCC). As genetic conditions, their manifestations are wideranging and systemic, with hepatic involvement only one component of the larger illness. The most common of these disorders, hereditary hemochromatosis, is discussed in detail in its own chapter on hepatic iron overload. In this chapter, the focus is on the other relatively common storage disorders with hepatic manifestations: Wilson's disease, alpha-1 antitrypsin (A1AT) deficiency, and the glycogen storage diseases (GSDs). Other storage disorders, such as the porphyrias, amyloidosis, and lysosomal storage diseases (Gaucher's and Niemann-Pick diseases), are either very rare or primarily affect extrahepatic tissues. Nonalcoholic fatty liver disease shares some features of the storage disorders but is not inherited in mendelian fashion and so is not included in this disease category.

# Etiology

Wilson's disease, A1AT deficiency, and the GSDs are familial conditions inherited in autosomal recessive fashion caused by mutations in putative genes.

Wilson's disease, also called hepatolenticular degeneration, is a disorder of copper metabolism. It is characterized by progressive neurologic deterioration and chronic liver disease leading to cirrhosis.<sup>1</sup> The gene responsible for this disease is ATP7B, located on chromosome 13. Highly expressed in the liver, kidney, and placenta, it encodes a metal-transporting, copperdependent P-type adenosine triphosphatase that functions in the incorporation of copper into ceruloplasmin (plasma protein that binds copper) and excretion of excess copper into bile.<sup>2-4</sup>

A1AT deficiency is associated with the development of pulmonary emphysema, chronic liver disease, and HCC. It is caused by mutations in the SERPINA1 (formerly known as PI) gene located on chromosome 14, which encodes the A1AT serine protease.

The GSDs are a heterogeneous group of inborn errors of metabolism characterized by excessive glycogen content of the liver and muscles (among other tissues, including the kidneys and spleen) as a result of enzyme defects in glycogen synthesis or degradation. Enzymatic deficiencies in nearly every step of glycogen processing have been identified, accounting for at least 10 discrete diseases that are grouped into the GSDs (types 0, I, II, III, IV, V, VI, VII, IX, and XI). This chapter focuses on type I GSD (von Gierke's disease), by far the most common GSD associated with hepatic involvement. The other three GSDs

associated with liver disease, types 0, III (Cori's or Fanconi's disease), and IV (Andersen's disease), are rare.

Type I GSD is caused by mutations in the G6PC gene. Located on chromosome 13, G6PC encodes glucose-6-phosphatase, a vital enzyme of glycogenolysis. Individuals heterozygous for the G6PC mutation have no phenotypic expression.

# **Pathogenesis**

The pathogeneses of Wilson's disease, A1AT deficiency, and the GSDs are explained by the metabolic defects caused by their underlying genetic abnormalities.

### WILSON'S DISEASE

The liver is the main organ responsible for copper homeostasis.<sup>3</sup> Normal copper metabolism begins with the absorption of dietary copper by duodenal enterocytes and its transportation to hepatocytes via the portal circulation. Hepatocytes then excrete the copper into bile, leading to biliary copper excretion, which eventually results in fecal copper loss.<sup>4</sup>

Genetic defects in the ATP7B protein are associated with diminished incorporation of copper into ceruloplasmin and reduced excretion of copper into the bile. Unincorporated copper accumulates within hepatocytes, where it causes secondary oxidative tissue damage. Some of the excess copper enters the systemic circulation and is deposited in extrahepatic sites such as the brain (especially the basal ganglia and limbic system), cornea, and kidneys. Copper not deposited in tissues is excreted in the urine. Ceruloplasmin not incorporated with copper is released into the bloodstream and rapidly degraded.

#### ALPHA-1 ANTITRYPSIN DEFICIENCY

A1AT is normally synthesized in the liver and released into the blood. An acute-phase reactant, it is elevated during inflammation, infection, and cancer. Its most important physiologic role is to inactivate proteolytic enzymes in the lung (especially neutrophil elastase), which degrade lung matrix tissue after being released as a by-product of cellular immune responses to airborne pathogens. A1AT counterbalances this proteolytic activity, preventing the net degradation of the lung matrix and alveoli.

In A1AT deficiency, hepatic production of A1AT is compromised and pulmonary proteolytic activity is unopposed, resulting in chronic obstructive pulmonary disease (COPD) and emphysema. Liver disease is uncommon except in some forms of A1AT deficiency, which leads to a cascade of cellular events, including autophagy, mitochondrial injury, caspase inactivation, and hepatocellular damage. Eventually, fibrosis and cirrhosis may ensue. $^{6,7}$ 

#### **GLYCOGEN STORAGE DISEASES**

Glycogen is a highly-branched glucose polysaccharide. It is found in greatest concentration in the liver, and it functions as the body's primary form of short-term energy storage during fasting periods. In the GSDs, enzyme defects in glycogen metabolism lead to accumulation of glycogen or glycogen metabolites, resulting in hepatocyte swelling, marked hepatomegaly, and hypoglycemia.

In type I GSD, a deficiency in glucose-6-phosphatase (G6P) results in glycogen accumulation within hepatocytes and causes hepatocellular damage via oxidative reactions. The damaged hepatocytes form neoplasms (hepatic adenomas and HCCs) with relatively high frequency. Despite the hepatocellular damage and steatosis associated with type I GSD, liver fibrosis and cirrhosis do not occur.

The other GSDs associated with liver disease (types 0, III, and IV) are caused by enzymatic defects at other steps in glycogen metabolism; these disorders are associated with progressive liver disease, leading to cirrhosis and portal hypertension.

# **Prevalence and Epidemiology**

Wilson's disease is present across almost all races and ethnicities, with a roughly even male-to-female distribution. The prevalence is 1 per 30,000 persons, and the carrier frequency is 1 in 90.<sup>8-10</sup> Clinical presentation is usually in the second or third decade of life, although it has been described in patients younger than 5 years of age<sup>11</sup> and rarely older than age 45.

The incidence of A1AT deficiency is approximately 1 in 2000 live births.<sup>12-14</sup> Men and women are affected equally. In children, A1AT is the most common genetic cause of liver disease. The mean life span is 65 years in nonsmokers and is reduced to 50 years in smokers.

As a class, the GSDs occur in approximately 1 in 25,000 births; type I GSD has a prevalence of approximately 1 in 100,000 to 200,000 births.<sup>15</sup> Nearly all cases have been identified in individuals from North America, Europe, or the Middle East. There is no predilection for ethnicity, race, or gender. Seventy percent of patients are diagnosed before the age of 2 years, with the development of hepatic adenomas in the second decade of life.

# **Clinical Presentation**

#### WILSON'S DISEASE

Wilson's disease manifests over a wide spectrum and may involve hepatic or neuropsychiatric sequelae, either together or alone. The presentation may be either acute or chronic; acute disease typically manifests as fulminant hepatic failure, whereas chronic disease consists of chronic hepatitis, cirrhosis, and neuropsychiatric illness.<sup>16</sup> Patients who present with neuropsychiatric symptomstypically have asymptomatic hepatic involvement and are generally older than those who present with hepatic disease. Those presenting with hepatic disease typically will develop neuropsychiatric symptoms within 2 to 5 years.<sup>17</sup>

Hepatic involvement occurs as either fulminant hepatic failure or a progressive, indolent chronic hepatitis that may ultimately result in cirrhosis.<sup>18</sup> In the fulminant form, patients undergo rapid hepatic deterioration, with coagulopathy, encephalopathy, and renal failure. The chronic form develops over a period of decades, ultimately leading to the typical findings of cirrhosis and complications of portal hypertension. HCC is a rare complication, with fewer than 20 documented cases, but would predictably occur in those with long-standing Wilson's disease. Neuropsychiatric symptoms are the initial manifestation in 40% to 50% of patients.<sup>19</sup>

No single test determines the diagnosis of Wilson's disease, although an amalgamation of clinical and biochemical findings, as well as pedigree analysis, is suggestive in the correct clinical scenario. Serum aminotransferase levels are typically mildly elevated (<200 international units/L), with a proportional increase in total bilirubin (<4.0 mg/dL). Interestingly, the serum alkaline phosphatase concentration is reduced in fulminant disease; thus, a ratio of alkaline phosphatase to total bilirubin of less than 2 is highly suggestive of Wilson's disease in patients with fulminant hepatic failure.<sup>20</sup> Copper-specific findings include elevated serum copper and 24-hour urinary copper levels, as well as decreased serum ceruloplasmin levels. In some cases, liver biopsy is indicated with attention placed on the hepatic copper content.

# ALPHA-1 ANTITRYPSIN DEFICIENCY

Pulmonary disease is usually more severe than hepatic disease and may occur in isolation; hepatic disease in the absence of pulmonary disease is rare. Pulmonary disease is accelerated by noxious stimuli, such as tobacco and air pollutants. Generally manifesting in early adulthood, it eventually progresses to severe panacinar emphysema (predominantly in the lower lobes) and COPD, characterized by bronchial hyperreactivity. Recurrent pulmonary infections are common.

Hepatic manifestations may occur in neonates as isolated disease (e.g., without concurrent pulmonary disease) or in adults with pulmonary disease.<sup>21</sup> The neonatal manifestation is that of hepatitis with cholestasis, resulting in hepatomegaly and jaundice 4 to 8 weeks after birth, which spontaneously resolves after a few weeks. The presence of neonatal disease does not predict hepatic disease in adulthood.<sup>21</sup> In adults, hepatic disease manifests as hepatitis, eventually progressing to fibrosis and cirrhosis. Cirrhosis develops slowly, typically requiring 20 to 30 years for portal hypertension to occur, and is the most common stage of presentation. Patients may exhibit complications of portal hypertension, including variceal bleeding, hypersplenism, ascites, and hepatic encephalopathy. The incidence of HCC is thought to be higher in patients with A1AT deficiency, although its transformation rate has not been well characterized.<sup>22</sup> The diagnosis of A1AT deficiency should be considered in (1) any young patient with obstructive lung disease or in any person with concurrent lung and liver abnormalities; (2) a patient presenting with hepatomegaly, elevated transaminase or bilirubin levels, signs of portal hypertension, or cholestasis; (3) an individual with chronic hepatitis or cirrhosis of unknown cause.

#### **GLYCOGEN STORAGE DISEASES**

Type I GSD clinically manifests in the neonate, usually becoming evident within the first week of life.<sup>23</sup> The chief systemic metabolic abnormality is hypoglycemia, typically in the range of 25 to 50 mg/dL. G6P accumulation in the kidneys causes nephromegaly and may result in proteinuria, systemic hypertension, or Fanconi's syndrome. G6P accumulation in the liver causes hepatomegaly. By the second decade of life, hepatic adenomas develop in up to 75% of patients with type I GSD; these adenomas are considered premalignant and may transform into HCC in both pediatric and adult patients.<sup>24,25</sup>

# Pathology

# WILSON'S DISEASE

The hepatic manifestations of excess copper accumulation are variable and often progressive. In early disease, patients demonstrate nonspecific signs of injury. In fulminant disease, massive hepatic necrosis is seen. In some patients, chronic inflammation may be present with increased numbers of lymphocytes in portal tracts, which can mimic chronic viral hepatitis. In advanced disease, progressive fibrosis leads to portal-portal bridging with eventual macronodular cirrhosis. Histochemical staining with rhodanine may be used to detect cytoplasmic copper; however, staining may be focal and missed on needle biopsy. Electron microscopy reveals characteristic mitochondrial abnormalities, including swollen cristae and crystalline inclusions.

# ALPHA-1 ANTITRYPSIN DEFICIENCY

Accumulated hepatocellular A1AT can be detected by histochemical staining with diastase-positive periodic acid–Schiff (PAS-D) or by immunohistochemical staining for A1AT. PAS-D staining reveals characteristic inclusions consisting of roundto-oval, purple-red globules within the cytoplasm of periportal hepatocytes. They may display hepatitis with features of canalicular cholestasis, giant cell transformation, swollen ("ballooning") hepatocytes, and diminished bile ducts. Other histologic findings in the liver are nonspecific and include fatty change and, rarely, Mallory hyaline.

#### **GLYCOGEN STORAGE DISEASES**

In type I GSD, accumulation of glycogen metabolites within hepatocytes leads to hepatic enlargement. These metabolites may be seen on light microscopy as intracellular cytoplasmic vacuoles. The hepatocytes take on a pale appearance with prominent cell membranes.

# Imaging

The diagnosis of Wilson's disease is generally based on clinical and laboratory findings; complicated cases are confirmed by increased hepatic copper concentration in biopsy samples of liver tissue. In patients with cirrhosis secondary to Wilson's disease, abdominal imaging may play a role in surveillance for HCC and detecting complications of portal hypertension.<sup>3</sup>

A1AT deficiency primarily affects the lungs. Pulmonary manifestations include panlobular emphysema, predominantly involving the lung bases. Liver abnormalities are less frequent and usually less severe. There are no characteristic liver imaging findings.<sup>22</sup> As with Wilson's disease, abdominal imaging is used in advanced disease for the assessment of stigmata of cirrhosis and portal hypertension, as well as surveillance for HCC.



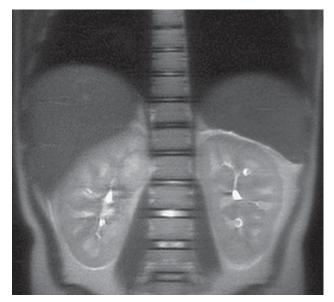
**Figure 40-1** A 19-year-old man with history of type I glycogen storage disease. Coronal reformatted postcontrast computed tomography image during the portal venous phase reveals massive enlargement of the liver, almost completely filling the abdomen, with the tip of the right lobe of the liver projecting into the pelvis. Note the stomach (arrow) displaced inferiorly.

Accumulation of glycogen metabolites within the liver, kidneys, and spleen may result in enlarged organs, manifesting as hepatomegaly (Figure 40-1), bilateral nephromegaly (Figure 40-2), and splenomegaly, respectively.<sup>26</sup> The liver is the most frequently involved organ, and hepatomegaly may be massive, fully occupying the abdomen and extending into the pelvis. A variable degree of fat accumulation within the liver parenchyma may also be evident.<sup>27</sup> Because of the high incidence of adenomas and the potential risk for malignant transformation, patients with type I GSD usually undergo periodic imaging studies to assess for and monitor hepatic tumors.<sup>28</sup>

# COMPUTED TOMOGRAPHY, MAGNETIC RESONANCE IMAGING, AND ULTRASOUND

#### Wilson's Disease

In the early stages of Wilson's disease, the liver usually has a normal imaging appearance, although nonspecific findings such as hepatomegaly may be observed. On unenhanced CT images, the liver may have increased attenuation as a result of deposited copper. However, there is no correlation between the degree of CT attenuation and hepatic copper concentration and the CT findings do not permit quantitative assessment of copper deposition. Copper has no ferromagnetic effect on MRI, and the signal intensity of the involved liver is usually normal.<sup>29</sup> Similarly, copper does not scatter the ultrasound beam and the affected liver has normal echogenicity.<sup>29</sup>



**Figure 40-2** A 19-year-old man with history of type I glycogen storage disease. Coronal single-shot turbo spin echo image reveals diffuse enlargement of the kidneys bilaterally. The right kidney measures 15.8 cm, and the left kidney measures 15.2 cm.

In fulminant presentations, necrotic portions of the liver may fail to enhance after intravenous administration of contrast agents.<sup>30</sup> In advanced chronic cases, a macronodular contour of cirrhosis is apparent. This is indistinguishable from that of other causes of end-stage liver disease, although Wilson's disease can be accompanied by normal to decreased caudate lobe size, and high hepatic attenuation on unenhanced CT due resulting from deposition (Figure 40-3).<sup>29</sup>

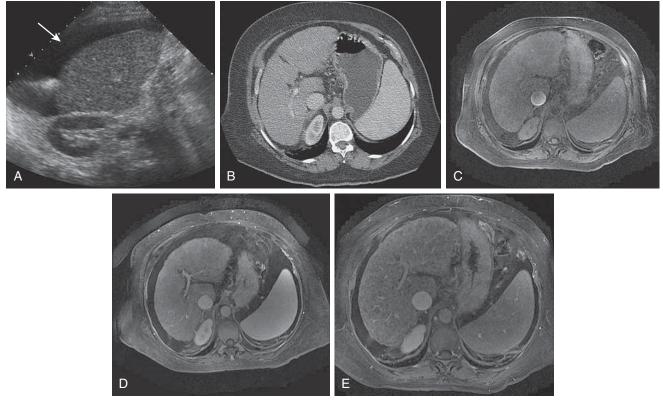
On brain MRI, high-intensity signal abnormalities on T1-weighted and T2-weighted images are usually seen in the basal ganglia. The putamen is involved most frequently, with other sites of involvement including the globus pallidus, caudate, and thalami.<sup>31</sup>

#### Alpha-1 Antitrypsin Deficiency

The CT, MRI, and ultrasound findings of patients with A1AT deficiency depend on the severity of liver involvement.<sup>5</sup> In the precirrhotic phase, the liver usually has a normal imaging appearance, although hepatomegaly, heterogeneity of hepatic parenchyma, and heterogeneous enhancement may be apparent.<sup>22</sup> The cirrhotic phase is characterized by findings common to the other causes of end-stage liver disease (Figure 40-4).

#### Glycogen Storage Diseases

CT, MRI, and ultrasound may depict hepatomegaly, splenomegaly, and nephromegaly. Hepatic steatosis manifests as



**Figure 40-3** Wilson's disease in a 56-year-old man. **A**, On the longitudinal sonogram, the liver is small and has a heterogeneous echotexture. There is moderate ascites (*arrow*). **B**, Axial contrast-enhanced computed tomography (CT) image demonstrates the nodular surface of the liver. The right lobe is relatively diminutive. **C**, Precontrast magnetic resonance (MR) image shows fibrous septa, in addition to the morphologic alterations of cirrhosis (also shown in **A** and **B**). **D**, Appearance of fibrous septa during portal venous phase after intravenous administration of gadolinium administration. **E**, Double-contrast–enhanced MR image shows hyperintense fibrotic reticulations delineating small hypointense regenerative nodules. Note that the discrete regenerative nodules and fibrotic scars are not visible on the ultrasound or CT images.

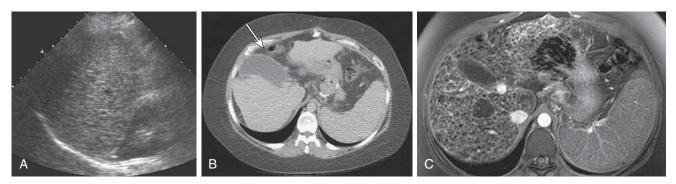
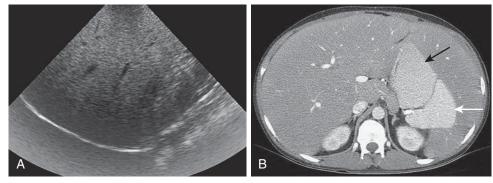


Figure 40-4 Alpha-1 antitrypsin deficiency in a 47-year-old woman with cirrhosis. A, Longitudinal ultrasound image shows the diffuse heterogeneous echotexture of the liver parenchyma. B, Axial postcontrast computed tomography image during the portal venous phase shows nodularity of the liver surface and an enlarged pericholecystic space (arrow) filled with adipose tissue (expanded gallbladder fossa sign). C, Axial combined contrast-enhanced magnetic resonance image shows, in addition to the morphologic alterations depicted in A and B, hyperintense reticulations throughout the liver parenchyma associated with various hypointense regenerative nodules. Also note mild enlargement of the spleen.



**Figure 40-5** A 19-year-old man with history of type I glycogen storage disease. A, Longitudinal ultrasound image of the liver shows parenchymal hyperechogenicity and posterior beam attenuation. Intrahepatic vessels are poorly visualized. B, Axial contrast-enhanced computed tomography image reveals massive hepatomegaly. Note that the left lobe of the liver surrounds and medially displaces the stomach (*black arrow*) and spleen (*white arrow*). The spleen is of normal size.

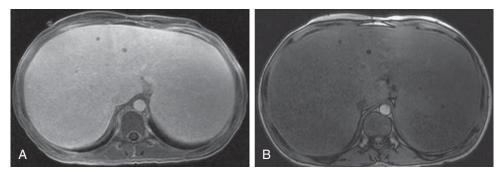
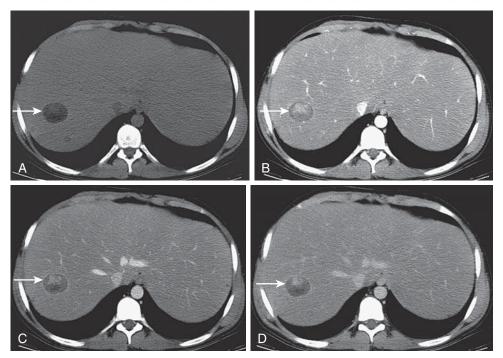


Figure 40-6 A 19-year-old man with history of type I glycogen storage disease. In-phase (A) and out-of-phase (B) T1-weighted gradient recalled echo axial magnetic resonance images show loss of signal on the out-of-phase images, indicating fat accumulation within the liver parenchyma.

hyperechogenicity on ultrasonography, low attenuation on unenhanced CT, and signal loss on out-of-phase MR images (Figures 40-5 and 40-6). Excess glycogen manifests as hyperechogenicity on ultrasound and hyperattenuation on CT; opposed-phase MRI can be used to assess for steatosis with greater specificity.<sup>27</sup>

Hepatocellular adenomas have variable degrees of fat, hemorrhage, and necrosis and may be heterogeneous in imaging appearance on both CT (Figure 40-7) and MRI (Figures 40-8 and 40-9).<sup>18</sup> On MRI, adenomas are typically hyperintense on T2-weighted imaging and with extracellular gadolinium contrast agents will demonstrate enhancement in the arterial phase, with isointense to hypointense signal in the delayed phase on T1-weighted imaging. Important differential considerations include focal nodular hyperplasia (FNH) and HCC. The use of hepatocyte-specific contrast agents such as gadoxetic acid (Gd-EOB-DPTA) can aid in the differentiation from FNH and are typically isointense to liver at delayed hepatobiliary phase imaging, whereas most adenomas are hypointense.<sup>32</sup> For suspected hepatic adenomas, longitudinal follow-up may



**Figure 40-7** A 19-year-old man with history of type I glycogen storage disease. A, Axial unenhanced computed tomography image reveals massive hepatomegaly with diffuse hypoattenuation of the liver parenchyma, suggestive of steatosis. Note the hypoattenuating well-defined hepatic lesion (*arrow*) located in segment 7 of the liver, measuring 3.2 cm. The lesion attenuation on the pre-contrast image is –18 HU, suggesting the presence of intralesional fat. The lesion (*arrows*) enhances heterogeneously during the arterial phase (**B**) and fades during the portal venous (**C**) and delayed phases (**D**). It was resected and proved to be an adenoma.

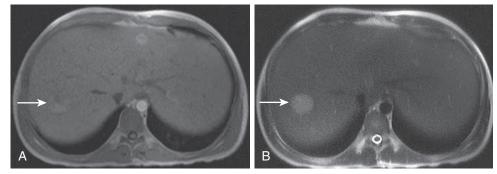


Figure 40-8 A 19-year-old man with history of type I glycogen storage disease. Axial T1-weighted (A) and T2-weighted (B) magnetic resonance images of the liver. The well-defined nodular lesion (*arrows*) located in segment 7 of the liver has high signal intensity.



**Figure 40-9** A 19-year-old man with history of type I glycogen storage disease. A 3.2-cm adenoma (*black arrow*) shows loss of signal on the outof-phase (**B**) compared with the in-phase (**A**) image, indicating the presence of fat within the lesion. The fat signal fraction map (**C**) shows pixel by pixel the percentage of the total magnetic resonance signal that comes from fat protons. Tissues that contain fat appear hyperintense, and tissues that do not contain fat appear hypointense. The blood vessels and the capsule of the 3.2-cm adenoma are devoid of fat and thus appear hypointense, whereas the liver parenchyma and the adenoma itself (*black arrow*) contain fat and thus appears hyperintense. The adenoma has greater fat content than the liver. Note several other smaller fat-containing adenomas (*white arrows*) that lose signal on the out-of-phase image and appear hyperintense on the fat signal fraction map.

be undertaken to monitor for transformation to HCC; findings that suggest malignant transformation include rapid interval growth and/or change in imaging features.<sup>17</sup>

#### **IMAGING ALGORITHM**

#### Wilson's Disease and Alpha-1 Antitrypsin Deficiency

Patients with a clinical history suggestive of Wilson's disease or A1AT deficiency may be imaged for signs of cirrhosis and portal hypertension and screened for HCC, as described in other chapters. Ultrasound and CT are usually the imaging studies performed initially, with MRI reserved for problem solving or if CT is contraindicated (Tables 40-1 and 40-2). The American Association for the Study of Liver Diseases does not offer specific guidelines for screening for HCC in patients with Wilson's disease or A1AT deficiency because the HCC transformation rate is poorly understood. Regardless, many institutions advocate semi-annual screening (via ultrasound or CT). In patients with fulminant presentations of Wilson's disease, CT may be performed to assess the extent of necrosis.<sup>3</sup> Imaging does not play a role in assessing the degree of copper deposition.

Imaging techniques to grade the severity of liver fibrosis in precirrhotic stages of chronic liver disease, including Wilson's disease and A1AT deficiency, are under development. An advantage of CT over ultrasound and MRI for the assessment of patients with A1AT deficiency is that CT can simultaneously evaluate the lung parenchyma and the liver.

#### Glycogen Storage Diseases

Patients with type I GSD should undergo surveillance imaging to detect and monitor hepatic tumors. MRI is probably the superior modality for this indication, because as it does not employ ionizing radiation and has high sensitivity for focal lesion detection. Ultrasound is insensitive for identification of small solid liver tumors, especially in the setting of hepatic steatosis. CT exposes the patient to ionizing radiation and should be avoided if possible in pediatric patients and young adults who may need lifelong monitoring.

#### **Classic Signs**

#### Wilson's Disease

- The liver parenchyma may be hyperattenuating at unenhanced CT secondary to deposited copper.
- In cirrhosis resulting from Wilson's disease, the caudate lobe is characteristically normal in size.

#### Alpha-1 Antitrypsin Deficiency

- The classic signs of liver cirrhosis secondary to A1AT deficiency are indistinguishable from the imaging findings of cirrhosis from other causes.
- Cirrhosis in conjunction with panlobular emphysema is suggestive.

#### Glycogen Storage Diseases

- There may be marked hepatomegaly with variable nephromegaly and infrequent splenomegaly.
- CT attenuation may be low, normal, or high depending on the balance of fat and glycogen accumulation.
- Hepatic adenomas are frequent and may contain fat and/or blood.
- Rapid interval growth or change in imaging features of adenomas suggests malignant transformation. Stigmata of cirrhosis and portal hypertension are absent even in advanced stages of disease.

TABLE 40-1	Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Wilson's Disease			
Modal	ity	Limitations	Pitfalls	Accuracy
Compu- tome	uted ography (CT)	lonizing radiation	CT attenuation does not correlate with copper concentration.	Data on the imaging accuracy for the diagnosis of Wilson's disease are not available. CT may depict increased hepatic attenuation because of copper deposition and probably has higher sensitivity than MRI or ultrasound.
	etic resonance ging (MRI)	Copper does not alter liver signal intensity.		
Ultrasc	ound	Copper does not alter liver echogenicity.		

TABLE <b>40-2</b>	Accuracy, I	imitations, and Pitfalls of the	Modalities Used in Imagi	ng for Alpha-1 Antitrypsin Deficiency
Moda	lity	Limitations	Pitfalls	Accuracy
Comp tom	uted ography (CT)	Ionizing radiation Risk for intravenous contrast reactions	Cirrhosis may coexist with emphysema of other causes.	No data on the accuracy of CT, MRI, or ultrasound for the diagnosis of alpha-1 antitrypsin deficiency. In principle, CT may have higher sensitivity and specificity than the other modalities because it can depict the pulmonary manifestations of panlobular emphysema.
MRI		Cannot assess the pulmonary manifestations (panlobular emphysema) directly		
Ultraso	bund	Cannot assess the pulmonary manifestations (panlobular emphysema) directly		

# **Differential Diagnosis**

#### WILSON'S DISEASE

The clinical differential diagnosis for Wilson's disease differs depending on whether the presentation is predominantly hepatic or neuropsychiatric. If the presentation is hepatic, Wilson's disease must be considered in the differential diagnosis of any chronic liver disease of unexplained origin, particularly if the patient is younger than 40 years of age. Wilson's disease is easily differentiated from other causes of chronic liver disease (e.g., viral hepatitis, autoimmune hepatitis, alcoholic or nonalcoholic fatty liver disease) by history and characteristic blood tests (e.g., low ceruloplasmin and high urinary copper levels, lack of serologic findings of viral hepatitis, or autoimmune markers). Kayser-Fleischer rings and high levels of hepatic copper on liver biopsy are sensitive and specific for Wilson's disease and confirm the diagnosis.

Assessment of the liver usually permits clinical differentiation. Unlike Wilson's disease, which has quiescent hepatic involvement (via elevated aminotransferase levels and hepatic copper deposition on liver biopsy) even in strict neuropsychiatric presentations, these other conditions are not associated with liver disease.

Radiologically, hepatomegaly related to Wilson's disease must be differentiated from hepatomegaly resulting from other causes, such as acute hepatitis, toxic-metabolic disorders, vascular disorders, and lymphoproliferative diseases. Hepatic hyperattenuation on unenhanced CT, if present, may suggest the correct diagnosis.

The imaging features of patients with cirrhosis secondary to advanced Wilson's disease overlap with the imaging findings of other causes of end-stage liver disease. The presence of cirrhosis associated with hepatic hyperattenuation on CT suggests Wilson's disease, hereditary hemochromatosis, or cirrhosis with secondary hemosiderosis.

#### ALPHA-1 ANTITRYPSIN DEFICIENCY

The clinical differential diagnosis is limited to A1AT deficiency when both significant pulmonary and hepatic disease are present, because this combination of organ involvement is unique. When there is primarily pulmonary involvement, consideration must be given to other causes of chronic airway obstruction, including COPD, smoking-related emphysema and bronchitis, bronchiectasis, and chronic asthma. These diagnoses are differentiated from A1AT deficiency by normal serum A1AT levels and no suggestive factors in a family history.

In adults, the differential diagnosis of predominant hepatic disease as a result of A1AT deficiency includes all causes of chronic liver disease and/or cirrhosis. If other causes are excluded based on history, serologic findings of viral hepatitis, autoimmune markers, and iron studies, then serum A1AT levels should be checked.

Neonatal A1AT deficiency should be distinguished from other causes of neonatal liver disease, including infection (e.g., Epstein-Barr virus, cytomegalovirus, hepatitis B virus) and biliary atresia.

The imaging findings of end-stage liver disease secondary to A1AT deficiency are nonspecific. However, the presence of cirrhosis in conjunction with panlobular emphysema suggests A1AT deficiency.

# **GLYCOGEN STORAGE DISEASES**

The clinical differential diagnosis of type I GSD is narrow owing to its unique manifestation of hypoglycemia, lactic acidosis, hyperuricemia, hyperlipidemia, and hepatomegaly in the neonatal period, along with growth retardation and developmental delay in subsequent years. Depending on the clinical manifestations, consideration may be given to other inborn errors of metabolism (e.g., the remaining GSDs, particularly types III and IV), fructose-1,6-bisphosphatase deficiency, and various disorders associated with growth retardation (e.g., Crohn's disease and growth hormone deficiency). Hepatoblastoma, a rare malignant hepatic tumor of infancy, causes marked hepatomegaly, which may mimic that of type I GSD.

Massive hepatomegaly, in which the liver comprises the entire abdomen and extends into the pelvis, has a narrower differential diagnosis than mild hepatomegaly. In particular, massive hepatomegaly may be caused by lymphoproliferative diseases such as lymphoma, infectious diseases such as viral hepatitis, and other metabolic disorders such as lysosomal storage diseases. Polycystic liver disease also may cause severe hepatomegaly but is easily distinguished from GSD by the presence of cysts. Hepatomegaly and nephromegaly in association with hepatic adenomas suggest the diagnosis of type I GSD because this combination of findings is rarely seen in other conditions.<sup>33</sup>

# Treatment

#### MEDICAL TREATMENT

#### Wilson's Disease

Treatment of Wilson's disease has been shown to slow the progression of both hepatic and neuropsychiatric disease and limit symptom recurrence. Medical therapy is reserved for those with chronic hepatic and neurologic disease and is of no benefit in patients with a fulminant presentation. The mainstay of treatment is lifelong therapy with a chelating agent, either D-pencillamine or trientine, which absorbs free copper in the bloodstream and enhances its removal in the urine.<sup>34</sup>

#### Alpha-1 Antitrypsin Deficiency

The treatment of A1AT deficiency focuses on management of pulmonary disease. Smoking cessation is stressed to prevent pulmonary disease progression. Active disease is treated with a variety of inhalers (bronchodilators and corticosteroids), systemic corticosteroids, and antibiotics. Substitution therapy with intravenously administered A1AT has been advocated in patients with pulmonary disease, although rigorous outcome analyses are lacking.<sup>5</sup>

Medical management does not alter the course of hepatic disease. Hepatic disease is supportively managed, with attention to prevention of complications of portal hypertension and screening for HCC.

#### Glycogen Storage Diseases

In type I GSD, the primary treatment goals are to correct systemic metabolic abnormalities, counteract hypoglycemia, and reduce the severity of malnourishment and growth retardation. Nutritional supplementation with nocturnal high-starch feeds through a nasogastric or gastrostomy tube and small, frequent daytime feedings are usually required.<sup>35</sup> Severe cases of acidosis may require infusion of sodium bicarbonate. Allopurinol is used to prevent the joint and renal complications of hyperuricemia.

### SURGICAL TREATMENT

#### Wilson's Disease

Liver transplantation is indicated for patients with decompensated liver disease unresponsive to medical therapy and those presenting with fulminant hepatic failure.

#### Alpha-1 Antitrypsin Deficiency

Surgical therapy for A1AT deficiency may be pursued for endstage pulmonary or hepatic disease. Lung transplantation is a viable option for those with the most advanced pulmonary disease. Progressive liver dysfunction is an indication for liver transplantation, which has demonstrated survival rates greater than 92% at 5 years after transplantation.<sup>36</sup>

#### Glycogen Storage Diseases

Liver transplantation has been performed in a handful of patients with GSDs, most commonly in patients with cirrhosis resulting from type IV GSD.<sup>37</sup> Liver transplantation for type I GSD is rarely performed and only in those patients with bulky hepatic adenomas or HCC.

#### What the Referring Physician Needs to Know

#### Wilson's Disease

- Also called hepatolenticular degeneration, Wilson's disease is a disorder of copper metabolism characterized by progressive neurologic deterioration and chronic liver disease leading to cirrhosis.
- Caused by mutations in the ATP7B gene, Wilson's disease is a state of copper excess in which copper accumulates in the liver, lentiform nucleus, and other sites.
- The clinical presentation includes hepatic and neuropsychiatric sequelae, either together or alone.
- The hepatic manifestation may be either as fulminant hepatic failure or progressive, indolent chronic hepatitis, ultimately resulting in cirrhosis.
- Hepatic copper concentration of sampled liver tissue is a useful diagnostic tool in some circumstances.
- HCC is a rare complication of long-standing Wilson's disease.
- Treatment consists of oral chelators, zinc, and, in advanced cases, liver transplantation.

### Alpha-1 Antitrypsin Deficiency

- A1AT deficiency manifests as a combination of pulmonary emphysema and chronic liver disease; neonates may present with solitary hepatitis.
- Caused by mutations in the SERPINA1 gene, the A1AT protein accumulates within the liver and is thus unable to counteract the destructive effects of pulmonary proteases on the lung matrix.
- Cirrhosis develops over a period of decades.

- The incidence of HCC is thought to be higher than in other causes of end-stage liver disease, although the transformation rate is not well characterized.
- Characteristic histologic inclusions can confirm the diagnosis if gel electrophoresis is unrevealing.
- Although there are a few alternatives for the medical therapy of pulmonary disease, no such options exist to prevent the progression of hepatic disease.
- Lung and liver transplantation are viable options in patients with end-stage disease.

#### Glycogen Storage Diseases

- The GSDs are a heterogeneous group of inborn errors of metabolism characterized by excessive glycogen content of the liver and muscles resulting from enzyme defects in glycogen synthesis or degradation.
- Type I GSD is the most common GSD associated with hepatic involvement.
- As a result of mutations in the G6PC gene, glucose-6phosphatase activity is diminished, resulting in the hepatic accumulation of G6P, its upstream metabolite, and glycogen itself.
- Other features include hepatic steatosis and the formation of hepatic adenomas; hepatic adenomas may transform into HCCs.
- Hepatic fibrosis and cirrhosis do not occur.
- Clinical manifestations include massive hepatomegaly, recalcitrant hypoglycemia, lactic acidosis, growth retardation, and developmental delay.

#### **Key Points**

#### Wilson's Disease

- High density of the liver parenchyma at unenhanced CT may be seen as a result of deposited copper.
- In cirrhosis, the caudate typically is normal in size, but this finding is not specific for Wilson's disease.
- Cirrhosis associated with hepatic hyperattenuation on CT raises the possibility of Wilson's disease but is not specific for it. The differential diagnosis includes hereditary hemochromatosis and cirrhosis of any cause with secondary hemosiderosis.
- Fulminant hepatic failure may be the first manifestation.

• Copper does not affect liver signal intensity at MRI or echogenicity at ultrasonography.

# Alpha-1 Antitrypsin Deficiency

- Liver involvement is less frequent than lung involvement.
- Liver severity is variable and unrelated to lung severity.Liver manifestations are nonspecific in the precirrhotic
- phase.
- In the cirrhotic phase, imaging findings overlap with other causes of end-stage liver disease.
- Cirrhosis in conjunction with panlobular emphysema suggests A1AT deficiency.

#### Key Points—cont'd

#### **Glycogen Storage Diseases**

- Liver attenuation on unenhanced CT depends on the balance of glycogen (increases attenuation) and steatosis (reduces attenuation).
- Bilateral nephromegaly with increased frequency of calculi is common.

#### SUGGESTED READINGS

- Fink S, Schilsky ML: Inherited metabolic disease of the liver. Curr Opin Gastroenterol 23:237–243, 2007.
- Kohnlein T, Welte T: Alpha-1 antitrypsin deficiency: pathogenesis, clinical presentation, diagnosis, and treatment. *Am J Med* 121:3–9, 2008.

Medici V, Rossaro L, Sturniolo GC: Wilson disease: a practical approach to diagnosis, treatment and follow-up. *Dig Liver Dis* 39:397–408, 2007.

#### REFERENCES

- 1. Wilson S: Progressive lenticular degeneration: a familial nervous disease associated with cirrhosis of the liver. *Brain* 34:295–507, 1912.
- Bull PC, Thomas GR, Rommens JM, et al: The Wilson disease gene is a putative copper transporting P-type ATPase similar to the Menkes gene. *Nat Genet* 5:327–337, 1993.
- Ala A, Walker AP, Ashkan K, et al: Wilson's disease. *Lancet* 369:397–408, 2007.
- Ala A, Schilsky ML: Wilson disease: pathophysiology, diagnosis, treatment, and screening. *Clin Liver Dis* 8:787–805, 2004.
- Kohnlein T, Welte T: Alpha-1 antitrypsin deficiency: pathogenesis, clinical presentation, diagnosis, and treatment. *Am J Med* 121:3–9, 2008.
- 6. Teckman JH: Alpha1-antitrypsin deficiency in childhood. *Semin Liver Dis* 27:274–281, 2007.
- Ogushi F, Fells GA, Hubbard RC, et al: Z-type alpha 1-antitrypsin is less competent than M1-type alpha 1-antitrypsin as an inhibitor of neutrophil elastase. J Clin Invest 80:1366–1374, 1987.
- 8. Frydman M: Genetic aspects of Wilson's disease. *J Gastroenterol Hepatol* 5:483–490, 1990.
- Lovicu M, Dessi V, Zappu A, et al: Efficient strategy for molecular diagnosis of Wilson disease in the Sardinia population. *Clin Chem* 49:496–498, 2003.
- Kusuda Y, Hamaguchi K, Mori T, et al: Novel mutations of the *ATP7B* gene in Japanese patients with Wilson disease. *J Hum Genet* 45: 86–91, 2000.
- Wilson DC, Phillips MJ, Cox DW, et al: Severe hepatic Wilson's disease in preschool-aged children. J Pediatr 137:719–722, 2000.
- Blanco I, de Serres FJ, Fernandez-Bustillo E, et al: Estimated numbers and prevalence of PI\*S and PI\*Z alleles of alpha 1-antitrypsin deficiency in European countries. *Eur Respir J* 27:77–84, 2006.
- Lieberman J, Winter B, Sastre A: Alpha 1-antitrypsin Pi-types in 965 COPD patients. *Chest* 89:370–373, 1986.
- 14. de Serres FJ, Blanco I, Fernandez-Bustillo E: Genetic epidemiology of alpha-1 antitrypsin

Ozen H: Glycogen storage diseases: new perspectives. *World J Gastroenterol* 13:2541–2553, 2007. Perlmutter DH: Alpha-1-antitrypsin deficiency:

- diagnosis and treatment. *Clin Liver Dis* 8:839–859, 2004. Roberts EA, Schilsky ML: American association for
- study of liver diseases: Diagnosis and treatment of Wilson disease: an update. *Hepatology* 47:2089– 2111, 2008.

deficiency in North America and Australia/New Zealand: Australia, Canada, New Zealand and the United States of America. *Clin Genet* 64:382–397, 2003.

- Talente GM, Coleman RA, Alter C, et al: Glycogen storage disease in adults. *Ann Intern Med* 120:218–226, 1994.
- Roberts EA, Schilsky ML: A practice guideline on Wilson disease. *Hepatology* 37:1475–1492, 2003.
- Medici V, Mirante VG, Fassati LR, et al; Monotematica AISF 2000 OLT Study Group: Liver transplantation for Wilson's disease: the burden of neurological and psychiatric disorders. *Liver Transpl* 11:1056–1063, 2005.
- Ostapowicz G, Fontana RJ, Schiodt FV, et al; U.S. Acute Liver Failure Study Group: Results of a prospective study of acute liver failure at 17 tertiary care centers in the United States. *Ann Intern Med* 137:947–954, 2002.
- 19. Walshe JM: Wilson's disease: the presenting symptoms. *Arch Dis Child* 37:253–256, 1962.
- Sallie R, Katsiyiannakis L, Baldwin D, et al: Failure of simple biochemical indexes to reliably differentiate fulminant Wilson's disease from other causes of fulminant liver failure. *Hepatol*ogy 16:1206–1211, 1992.
- Perlmutter DH: Alpha-1-antitrypsin deficiency: diagnosis and treatment. *Clin Liver Dis* 8:839– 859, 2004.
- 22. Propst T, Propst A, Dietze O, et al: Alpha-1-antitrypsin deficiency and liver disease. *Dig Dis* 12:139–149, 1994.
- 23. Sadeghi-Nejad A, Presente E, Binkiewicz A, et al: Studies in type I glycogenosis of the liver: the genesis and disposition of lactate. *J Pediatr* 85:49–54, 1974.
- 24. Howell RR, Stevenson RE, Ben-Menachem Y, et al: Hepatic adenomata with type 1 glycogen storage disease. *JAMA* 236:1481–1484, 1976.
- Limmer J, Fleig WE, Leupold D, et al: Hepatocellular carcinoma in type I glycogen storage disease. *Hepatology* 8:531–537, 1988.
- 26. Lin CC, Tsai JD, Lin SP, et al: Renal sonographic findings of type I glycogen storage disease in

Talente GM, Coleman RA, Alter C, et al: Glycogen

• The spleen is less frequently involved, although

• With age, hepatic adenomas tend to increase in both size

splenomegaly may be observed.

and number.

- storage disease in adults. Ann Intern Med 120:218– 226, 1994.
- Teckman JH: Alpha-1-antitrypsin deficiency in childhood. *Semin Liver Dis* 27:274–281, 2007.

infancy and early childhood. *Pediatr Radiol* 35:786–791, 2005.

- Pozzato C, Dall'asta C, Radaelli G, et al: Usefulness of chemical-shift MRI in discriminating increased liver echogenicity in glycogenosis. *Dig Liver Dis* 39:1018–1023, 2007.
- Lee PJ: Glycogen storage disease type I: pathophysiology of liver adenomas. *Eur J Pediatr* 161(Suppl 1):S46–S49, 2002.
- Akhan O, Akpinar E, Karcaaltincaba M, et al: Imaging findings of liver involvement of Wilson's disease. *Eur J Radiol* 69:145–155, 2009.
- Williams R: Acute liver failure: practical management. Acta Gastroenterol Belg 70:210–213, 2007.
- King AD, Walshe JM, Kendall BE, et al: Cranial MR imaging in Wilson's disease. AJR Am J Roentgenol 167:1579–1584, 1996.
- Denecke T, Steffen IG, Agarwal S, et al: Appearance of hepatocellular adenomas on gadoxetic acid-enhanced MRI. *Eur Radiol* 22:1769–1775, 2012.
- Moraru E, Cuvinciuc O, Antonesei L, et al: Glycogen storage disease type I: between chronic ambulatory follow-up and pediatric emergency. *J Gastrointest Liver Dis* 16:47–51, 2007.
- Roberts EA, Schilsky ML: American association for study of liver diseases: Diagnosis and treatment of Wilson disease: an update. *Hepatology* 47:2089–2111, 2008.
- Leonard JV, Dunger DB: Hypoglycaemia complicating feeding regimens for glycogen-storage disease. *Lancet* 2:1203–1204, 1978.
- Kayler LK, Merion RM, Lee S, et al: Long-term survival after liver transplantation in children with metabolic disorders. *Pediatr Transplant* 6:295–300, 2002.
- Starzl TE, Demetris AJ, Trucco M, et al: Chimerism after liver transplantation for type IV glycogen storage disease and type 1 Gaucher's disease. N Engl J Med 328:745–749, 1993.

# **Cirrhosis and Hepatitis**

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# Cirrhosis

# **ETIOLOGY**

Virtually any chronic insult to the liver, if sufficiently severe and long-standing, may result in cirrhosis. In the United States, the most common causes are hepatitis C virus (HCV) infection and alcohol ingestion, whereas in Asia and sub-Saharan Africa, chronic hepatitis B virus (HBV) infection is the most frequent culprit. Nonalcoholic fatty liver disease (NAFLD) is increasing in prevalence and is now the third most common cause of cirrhosis in North America and in parts of Europe and South America. Other common causes in adults include nonviral infections (mainly, parasitic [e.g., schistosomiasis]), autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, genetic disorders (hemochromatosis, Wilson's disease, alpha-1 antitrypsin deficiency, and glycogen storage diseases), medications (e.g., amiodarone and methotrexate), and veno-occlusive disease (especially Budd-Chiari syndrome; sinusoidal obstruction syndrome generally does not cause cirrhosis). Cryptogenic cirrhosis describes cirrhosis of unknown cause; once a frequent diagnosis, the term has become less common in the past 2 decades with the discovery of HCV and the recognition of NAFLD.

The fundamental pathogenic mechanism of cirrhosis is that of injury and repair. Hepatocytes may be injured by a variety of etiologic factors, initiating an inflammatory response. Atypical, dysfunctional hepatocytes aggressively multiply to counteract the effects of hepatocyte injury, forming regenerative nodules. Isolated insults cause self-limited inflammation, and the liver's wound-healing mechanisms successfully repair the damage. Repetitive or chronic injuries, however, overwhelm these restorative processes, leading to the dysregulated production of cytokines (e.g., transforming growth factor beta) and activation of profibrogenic perisinusoidal stellate cells. The end result is the unchecked deposition of excess macromolecules and collagen in the extracellular matrix (fibrosis).<sup>2</sup>

Fibrosis initially occurs in the space of Disse, where it obliterates normal endothelial fenestrations. Further scar deposition in the perisinusoidal and sinusoidal spaces obstructs sinusoidal blood flow and causes portal hypertension. Because of the elevated intrahepatic resistance, portal venous blood is shunted to systemic veins with lower pressures and returned to the heart without passing through the liver. The microvascular architecture of the liver remodels in response. Abnormal connections develop between the portal vein and terminal hepatic vein, which contribute to the shunting of blood from the hepatic parenchyma. As a result of portal hypertension and microvascular hepatic alterations, varices form, ascites develops, and hypersplenism occurs. Toxins normally metabolized and eliminated by the liver accumulate in the blood and contribute to the development of hepatic encephalopathy.

Loss of hepatocytes affect hepatic synthetic function, resulting in reduced levels of essential proteins (e.g., blood clotting factors and albumin) and causing coagulation abnormalities as well as reduced intravascular oncotic pressure. Atypical hepatocytes have impaired ability to secrete bile into canaliculi, which not only causes intestinal fat and vitamin malabsorption and steatorrhea but also results in cholestasis (accumulation of bile within hepatocytes), which may perpetuate hepatocellular damage. Because the liver is required for the normal metabolism and supply of glucose and lipids to the rest of the body, hepatocellular dysfunction leads to muscle breakdown, inefficient mobilization of energy stores, and redistribution of adipose tissue. Clearance of estrogens may be reduced, leading to gynecomastia in males.

Systemically, patients with cirrhosis exhibit a hyperdynamic circulation as a result of decreased systemic vascular resistance and peripheral vasodilation, mediated by nitric oxide among other factors.<sup>3</sup> End consequences include increased cardiac output, splanchnic vasodilation, renal vasoconstriction and hypoperfusion, and salt and water retention. Additionally, the intestinal mucosa becomes hyperpermeable, perhaps related to reduced oncotic pressure; this may account for bacterial translocation from the gut to the peritoneal space, resulting in spontaneous bacterial peritonitis.4

#### PREVALENCE AND EPIDEMIOLOGY

The prevalence of cirrhosis is difficult to ascertain and is probably underestimated because large numbers of patients with compensated cirrhosis go undetected. This is especially the case in patients with cirrhosis resulting from NAFLD or HCV infection, conditions with asymptomatic phases of long duration. In the United States, the prevalence of cirrhosis is estimated to be 0.27%, which would represent 633,323 American adults based on 2010 U.S. Census data.<sup>5</sup> However, cirrhosis is undoubtedly more frequent in Africa and Asia, where vertically transmitted HBV infection is common, although precise estimates are unavailable.

Age, sex, and ethnicity all influence the risk for cirrhosis. Cirrhosis rarely afflicts children (<18 years) or the elderly (>75 years), occurring 80% of the time in patients between the ages of 25 to 64. Sixty-five percent of cases occur in males. Although there is little variation in the prevalence of cirrhosis among different ethnicities, there are differences with regard to cirrhosis-related death. In 2001, chronic liver disease with cirrhosis was the 12th leading cause of death in the United States; however, it was the 6th and 7th most frequent cause of death in Native Americans and Hispanics, respectively.6

#### **CLINICAL PRESENTATION**

Cirrhosis is often indolent and unsuspected until its complications arise. Some asymptomatic patients present for the evaluation of unrelated problems and are incidentally found to have cirrhosis based on physical examination, laboratory findings, or imaging. Owing to the large number of abnormalities in liver function caused by cirrhosis and the central role the liver plays in whole-body physiology, symptomatic patients may present with a broad spectrum of clinical manifestations.

Common manifesting symptoms of compensated cirrhosis include fatigue, weakness, anorexia, jaundice, itching, and easy bruising. On physical examination, patients may exhibit muscular and temporal wasting, ecchymoses, and jaundice. Dermatologic stigmata of chronic liver disease, such as spider angiomas and palmar erythema, are present in 33% of cases.<sup>8</sup> Gynecomastia occurs in the majority of male patients. Hypogonadism, secondary to either primary gonadal injury or disruption of the hypothalamic-pituitary axis, results in testicular atrophy, impotence, infertility, and feminization. The liver itself may be enlarged (characteristically observed in alcoholic and nonalcoholic fatty liver disease, storage diseases, and Budd-Chiari syndrome) or shrunken with firm edges (characteristically observed in viral causes). Portal hypertension frequently causes splenomegaly and caput medusae.<sup>9</sup>

With hepatic decompensation, more advanced signs and symptoms may manifest. Ascites, the most common complication of cirrhosis, occurs as a result of portal hypertension and salt and water retention. Over 60% of patients with cirrhosis develop ascites within 10 years of diagnosis; and once ascites occurs, 2-year survival is only approximately 50%.<sup>10</sup> Spontaneous bacterial peritonitis is a life-threatening complication of ascites and is one of the reasons for the high ascites-related fatality.

Portosystemic collaterals, or varices, develop as a result of portal hypertension. The most clinically significant varices are located in the distal esophagus and upper stomach. These esophagogastric varices occur in approximately 60% of patients with cirrhosis, with 30% of them experiencing bleeding complications.

Hepatic encephalopathy refers to a spectrum of neuropsychiatric abnormalities caused by the retention of ammonia and other toxic substances normally metabolized and cleared by the liver. Precipitating factors include dehydration, electrolyte and metabolic derangements, gastrointestinal bleeding, infections, and sedating medications. Transjugular intrahepatic portosystemic shunt (TIPS) and surgical shunt procedures hasten the development of hepatic encephalopathy in approximately 40% of patients.<sup>11</sup>

Hepatorenal syndrome refers to acute renal failure in patients with cirrhosis without underlying renal abnormalities. It is thought to occur because of splanchnic vasodilatation, which results in unremitting, hormone-mediated renovascular vaso-constriction and reduced renal perfusion. Occurring in approximately 40% of patients with cirrhosis and ascites by 5 years, hepatorenal syndrome is a terminal complication of cirrhosis and has a poor prognosis.<sup>12,13</sup>

In the majority of patients, the diagnosis of cirrhosis is based on history, physical examination, basic laboratory studies, and imaging studies. In general, serum aminotransferase levels are mildly elevated (generally, <100 units/L), the total bilirubin level is proportionally elevated, and the albumin value is reduced. Because the liver synthesizes many of the blood clotting factors, the prothrombin time may be prolonged. Hyponatremia, secondary to impaired free water secretion, and renal insufficiency are seen in advanced cirrhosis and are poor prognostic signs.<sup>14</sup> Serum alpha-fetoprotein levels are sometimes elevated in patients presenting with cirrhosis complicated by hepatocellular carcinoma (HCC).

Once cirrhosis has been diagnosed, the severity historically has been graded by the Child-Turcotte-Pugh classification (e.g., Child class A, B, or C), with higher point totals coinciding with greater short-term and perioperative fatality. More recently, the Model for End-Stage Liver Disease (MELD) score has gained preference.<sup>15</sup> This score is calculated from a logarithmic formula using the patient's total bilirubin, international normalized ratio, and creatinine concentration.

The natural history of cirrhosis is that of an inexorably progressive condition. Within 10 years, 58% of patients with cirrhosis develop various forms of hepatic decompensation.<sup>10-17</sup> The annual incidence of HCC in patients with cirrhosis is approximately 5%<sup>18</sup> but ranges from less than 1% up to 10%, depending on the cause of cirrhosis and presence of comorbidities, such as human immunodeficiency virus infection or diabetes, which may increase the hepatocarcinogenesis risk.

#### PATHOLOGY

Cirrhosis is a diffuse process affecting the architecture of the entire liver; localized scarring does not constitute cirrhosis. In advanced cirrhosis, it is not possible to determine the cause with certainty. However, in early-stage cirrhosis, different hepatic insults may cause varied patterns of cirrhosis.

Gross examination of the cirrhotic liver typically reveals a shrunken and firm organ, although the liver may be enlarged depending on the cause. Cirrhosis is defined histologically by the presence of fibrous septa that divide the liver parenchyma into nodules. The septa range from delicate fibrous bands to large fibrous tracts that obliterate multiple lobules.<sup>19</sup> The fibrous septa may connect portal tracts and centrilobular hepatic terminal veins in portal-portal, portal-central, or central-central patterns. The nodules are variably sized and arbitrarily defined as micronodules (<3 mm) or macronodules (>3 mm).<sup>19</sup>

By far, the most common nodules are regenerative (RNs). These tend to be relatively uniform in size and appearance. Occasionally, nodules may arise that are conspicuous in terms of size, color, texture, or degree of bulging from the cut surface of the liver. These may represent low- or high-grade dysplastic nodules (DNs) or HCC. Low-grade DNs have been alternatively referred to as large RNs and macroregenerative nodules. The hepatocytes in low-grade DNs are essentially indistinguishable from background hepatocytes, although subtle variations in cell size may be seen. High-grade DNs are distinguished microscopically from low-grade DNs via recognition of cytologic alterations (increased nuclear to cytoplasmic ratio) and architectural changes (thickening of hepatocyte cell plates and pseudo-gland formation). Grossly, high-grade DNs frequently show a "nodule-in-nodule" appearance, reflecting patchy proliferative activity. Low-grade DNs are considered benign, whereas high-grade DNs are thought to be precursors of HCC.

Recently, focal nodular hyperplasia (FNH)-like lesions have been described in cirrhosis.<sup>21</sup> Both macroscopically and microscopically, these lesions appear identical to FNH in the noncirrhotic liver. Unlike true FNH, which is thought to arise in



**Figure 41-1** Hepatocellular carcinoma with invasion into the right portal vein. **A**, Axial computed tomography image during hepatic arterial phase after injection of intravenous contrast agent demonstrates a large, encapsulated mass in the right lobe of the liver (*black arrow*). Note the irregular arteries coursing through the lesion center (*white arrows*), a finding suggestive of hepatocellular carcinoma. **B**, On a more inferior slice, the right portal vein is expanded and contains linear areas of arterial hypervascularity (*arrow*). These represent tumor vessels within a malignant thrombus.

response to congenital arteriovenous malformations, FNH-like lesions are thought to arise from acquired vascular flow perturbations associated with cirrhosis.<sup>21</sup>

#### IMAGING

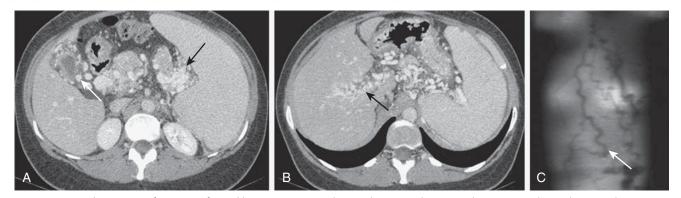
Imaging studies, including ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI), are used to assess liver size, the biliary tree, patency of hepatic vasculature, and sequelae of portal hypertension (e.g., ascites, varices, and splenomegaly) and to screen for HCC. Although the portosystemic pressure gradient may be directly measured via transjugular cannulation of the hepatic veins, this is invasive and often unnecessary because portal hypertension can be inferred by endoscopic findings of varices and sequelae of portal hypertension seen on imaging.

On cross-sectional imaging, the cirrhotic liver may demonstrate a nodular surface, widened fissures between lobes, and an increase in size of the hypertrophied caudate lobe relative to the atrophied right lobe. The ratio of caudate lobe hypertrophy to right lobe atrophy has most recently been defined by the modified ratio of caudate to right lobe, in which the lobes are divided anatomically by the bifurcation of the right portal vein. A ratio greater than 0.65 predicts cirrhosis with high specificity and positive predictive value.<sup>22</sup> Depending on the modality and imaging technique, fibrotic reticulations, fatty changes, and the presence of various hepatocellular nodules (RNs, DNs, HCC, FNH-like lesions) may be visible. The critical diagnostic distinction is between malignant nodules (e.g., HCC) and nonmalignant nodules (e.g., RNs, DNs, and FNH-like lesions).<sup>23</sup> Although DNs have higher rates of malignant transformation than RNs, the transformation rate is not sufficiently high to warrant ablation or other intervention, nor to increase imaging surveillance frequency or alter surveillance strategies.<sup>24</sup> The natural history of FNH-like lesions in cirrhosis is unknown, but these lesions are considered benign.<sup>21</sup> Simple hepatic cysts and hemangiomas are observed less frequently in the cirrhotic liver than in the noncirrhotic liver. These lesions are described elsewhere in this text. Peribiliary cysts are serous cysts that are hypothesized to represent obstructed periductal glands in patients who have severe liver disease. Recognition of these cysts on imaging helps radiologists to avoid the incorrect diagnosis of dilated bile ducts, abscesses, or cystic neoplasms.<sup>2</sup>

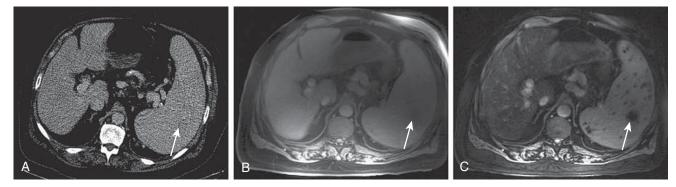
Classic vascular manifestations of cirrhosis include hepatic artery dilatation, tortuosity of hepatic arteries within the liver ("corkscrew" arteries, which may be observed with high-resolution CT and MRI), portal vein dilation in early portal hypertension, portal vein occlusion in late portal hypertension as a result of sluggish portal flow, and formation of shunts. Intrahepatic shunts (arterioportal and arteriovenous) may manifest on dynamic imaging studies as small (<2 cm) hyper-vascular pseudo-lesions and may be mistaken for nodules.<sup>26</sup> Portosystemic shunts manifest as varices (e.g., esophagogastric and paraumbilical); these are usually located outside the liver, although intrahepatic varices may also occur. In addition to varices, other sequelae of portal hypertension (e.g., ascites, splenomegaly, peribiliary cysts, and Gamna-Gandy bodies) may be noted (Figures 41-1 to 41-3).<sup>27</sup>

#### Computed Tomography

Technical Considerations. The primary indications for performing multiphasic CT in patients with cirrhosis are the evaluation of disease progression, surveillance for HCC, and follow-up of known lesions. Contrast enhancement of vessels, liver, and other solid organs may be impaired in patients with cirrhosis owing to third spacing of fluid and leakage of contrast material into the pulmonary interstitium during passage through the right-sided circulation. For this reason, patients with cirrhosis may require higher rates and concentrations of contrast material than patients without cirrhosis. The critical phases for image acquisition are the late arterial (typically at 35 to 40 seconds), portal venous (at 60 to 80 seconds), and equilibrium (at 3 to 5 minutes).28 Unenhanced images usually are recommended as cirrhotic nodules that may be intrinsically hyperdense because of copper or iron deposition or high glycogen content. These nodules may thus appear hyperdense at hepatic arterial phase and be mistakenly characterized as hypervascular if unenhanced images are not acquired first. Some authors also advocate early arterial phase images (typically at 20 to 25 seconds) to detect very early enhancement of malignant lesions and permit more precise characterization of lesion enhancement features, but this strategy has not been proved to be superior for lesion diagnosis in large clinical trials and increases the radiation dose. CT hepatic artery angiography, CT portography, and CT after transarterial administration of iodized oil may be performed in select cases but are not used



**Figure 41-2** Extrahepatic manifestations of portal hypertension. A and B, Axial computed tomography contrast-enhanced images show extensive intra-abdominal varices in a patient with long-standing portal venous thrombosis. Note pericholecystic (A, *white arrow*), peripancreatic, perisplenic (A, *black arrows*), and left gastric varices as well as cavernous transformation of the right portal vein (B, *arrow*). C, Coronal single-shot fast spin echo T2-weighted image in a different patient reveals varices along the anterior abdominal wall (*arrow*).



**Figure 41-3** Gamna-Gandy bodies (GGBs). A, On axial portal venous phase computed tomography (CT) image, GGBs are difficult to visualize (arrow). B, On axial unenhanced gradient recalled echo magnetic resonance (MR) image with ultrashort echo time (0.08 ms), a 1-cm GGB (arrow) and several subcentimeter GGBs are barely perceptible. C, On axial unenhanced co-localized gradient recalled echo MR image with echo time of 9 ms generated by the same radiofrequency excitation as in B, the 1-cm GGB (arrow) and several other GGBs are easily visible as focal hypointense lesions with associated blooming artifacts. Signal loss and blooming in GGBs are due to susceptibility from hemosiderin. As illustrated in this case, GGBs are more visible on MR images than on CT images, especially on T2\*-weighted gradient recalled echo acquisitions.

routinely in the assessment of cirrhotic patients; their discussion is beyond the scope of this chapter.

Fibrosis. On unenhanced images, the attenuation of normal liver is typically approximately 10 Hounsfield units greater than that of the spleen. However, the density of the cirrhotic liver or of focal lesions may be reduced (e.g., by steatosis, fibrosis, or edema) or increased (e.g., by iron or copper deposition). Fibrosis typically is not visible on unenhanced CT; if sufficiently severe, fibrosis may manifest as a diffuse lacework of hypoattenuating bands or as mottled areas of decreased density. Regions of confluent fibrosis are characterized as hypoattenuating wedge-shaped or geographically shaped regions radiating from the portal hilus and causing retraction of the overlying hepatic capsule (Figure 41-4). Involvement of the medial segment of the left lobe or anterior segment of the right lobe is characteristic, but other segments may be involved as well. Confluent fibrosis is observed more commonly in alcoholic liver disease and primary sclerosing cholangitis than in viral and other liver diseases. On contrast-enhanced CT, fibrosis, especially if confluent, may show progressive enhancement and appear hyperattenuating on delayed images. Confluent fibrosis occasionally may be masslike and cause diagnostic confusion. Differentiation from HCC is usually possible based on the

characteristic capsular retraction, volume loss, and progressive enhancement pattern associated with confluent fibrosis. In difficult cases, follow-up imaging may be necessary; progressive volume loss, if observed, clinches the diagnosis of confluent fibrosis.<sup>29</sup>

**Nodules.** FNH-like lesions are small, ranging up to approximately 1 cm in diameter.<sup>30</sup> Isodense on unenhanced imaging, these lesions hyperenhance on the arterial phase and then fade to isoattenuation on more delayed images. On both unenhanced and contrast-enhanced CT, RNs usually are isodense relative to the surrounding hepatic parenchyma and are difficult to visualize (Figures 41-5 and 41-6), although siderotic RNs may be hyperdense. On unenhanced CT, large DNs are hyperattenuating relative to surrounding parenchyma because of the presence of increased iron and glycogen, whereas small DNs remain isodense. Conversely, DNs enhance simultaneously with normal parenchyma on contrast-enhanced CT, appearing isodense. With increased dedifferentiation, however, these DNs may appear hyperattenuating because of increased vascularity and consequent increased contrast uptake.<sup>26</sup>

HCCs may have a varied appearance at CT depending on tumor size, vascularity, steatosis, cholestasis, hemorrhage, and necrosis. On unenhanced CT, HCCs generally appear as

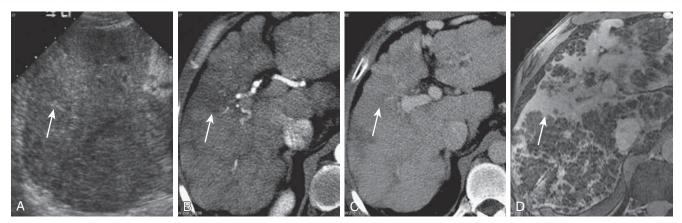
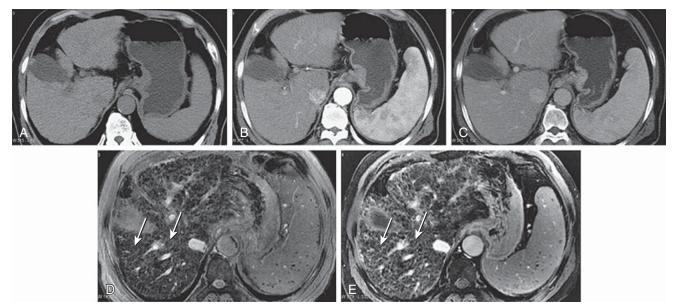


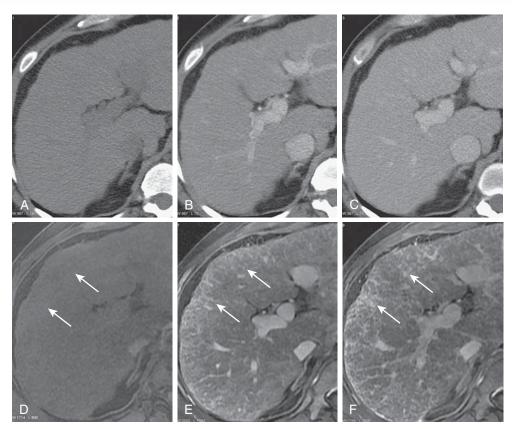
Figure 41-4 Confluent fibrosis. Coronal ultrasound (A), hepatic arterial phase contrast-enhanced computed tomography (CT) (B), portal venous phase contrast-enhanced CT (C), and double-contrast-enhanced axial two-dimensional spoiled gradient echo (D) images obtained at 3.0 T with an echo time of 5.8 ms. A, On ultrasonography, individual regenerative nodules and reticulations of fibrotic tissue are difficult to delineate but the liver displays patchy areas of increased echogenicity (*white arrow*) suggesting increased fibrotic tissue in the liver. B and C, Unenhanced and contrast-enhanced CT images show confluent fibrosis as a hypoattenuating geographically shaped region radiating from the portal hilus and causing minimal intensity in the same geographically shaped formation that is seen on the CT images, while the surrounding regenerative tissue appears dark because of superparamagnetic iron oxide uptake.



**Figure 41-5** Regenerative nodules (RNs). Axial unenhanced (A) and contrast-enhanced (B) arterial and portal venous phase (C) CT images. A to C, The liver parenchyma shows minimal heterogeneity, and discrete RNs are not confidently characterized. D, At the same level as the CT images, on axial two-dimensional spoiled gradient echo magnetic resonance (MR) image obtained at 3.0 T with echo time of 5.8 ms after superparamagnetic iron oxide (SPIO) administration, the RNs are visible as sharply demarcated hypointense nodules (*arrows*) owing to phagocytic uptake of SPIO, which causes T2\* shortening. **E**, On double-contrast–enhanced MR image after gadolinium administration, fibrotic reticulations display an increase in signal intensity owing to the extracellular accumulation of the low molecular weight contrast agent. Enhancement of fibrotic tissue further increases visibility of RNs (*arrows*). Note that this image shows innumerable RNs carpeting the liver. The two representative RNs as labeled for illustrative purposes are examples of SPIO-enhanced and double-contrast–enhanced MRI.

hypoattenuating or heterogeneously attenuating lesions. Intralesional fat or blood products may be difficult to identify on CT; these features are more readily observed on MRI. After administration of contrast agents, HCCs become hyperattenuating or heterogeneously enhancing during the arterial phase, then wash out to hypoattenuation on venous and delayed phases. If a tumor capsule is present, it often enhances progressively and retains contrast material on delayed images. Vascular invasion, if present, is more easily appreciated on contrastenhanced images.

Perfusional pseudo-lesions secondary to arteriovenous or arterioportal shunts enhance during the arterial phase and then fade to isoattenuation on images acquired during the portal venous and equilibrium phases. As opposed to true nodules, pseudo-lesions tend to have ill-defined or straight borders and may have blood vessels running through their center. In



**Figure 41-6** Dynamic enhancement of fibrotic tissue in the cirrhotic liver. Dynamic contrast-enhanced (A), unenhanced portal venous phase (B) and delayed phase (C) computed tomography (CT) images show the nodular liver surface diagnostic of cirrhosis. The liver parenchyma is homogeneous, with neither fibrotic reticulations nor RNs clearly identified. Dynamic gadolinium-enhanced axial gradient recalled unenhanced (D), portal venous (E), and delayed (F) phase magnetic resonance (MR) images obtained at the same level as the CT images show progressive enhancement of the fibrotic reticulations as a result of accumulation of the low molecular weight gadolinium. Dynamic MR images depict the enhancement of the fibrotic septa (*arrows*) with higher clarity than CT.

diagnostically challenging cases, longitudinal imaging is necessary. At follow-up, pseudo-lesions regress or are stable but rarely grow.

#### Magnetic Resonance Imaging

Technical Considerations. MRI provides the best performance characteristics for the diagnosis of cirrhosis but requires longer scan times than CT and is more costly. Controversy exists regarding which MR technique and contrast agent is optimal for evaluation of cirrhotic patients. For T1-weighted imaging, dual-phase in-phase and out-of-phase gradient echo images are commonly acquired because these permit assessment of parenchymal and lesional fat content in addition to characterizing T1 relaxation properties. T2-weighted fast spin echo imaging is useful for evaluating bile ducts, cysts, and fluid collections; single-shot fast spin echo sequences are particularly useful for this purpose. T2-weighted imaging also helps characterize RNs and DNs but has low sensitivity for detecting HCC. On diffusion weighted imaging, HCCs may have restricted diffusion and appear bright on diffusion weighted images and dark on corresponding apparent diffusion coefficient maps.

The most common dynamic technique to evaluate the liver is MRI after a rapid bolus injection of gadolinium-based contrast. Volumetric three-dimensional T1-weighted, fat-saturated spoiled gradient echo acquisitions are usually used for dynamic imaging. The key phases for extracellular contrast agents are the hepatic arterial-dominant phase (in which the acquisition of the center of k space coincides with peak arterial perfusion of hepatic nodules), portal venous phase (acquired 60 to 80 seconds after gadolinium injection [see Figure 41-6]), and equilibrium phase (acquired 3 to 5 minutes after injection).<sup>31-33</sup> For purposes of HCC screening and evaluating response to locoregional therapy (i.e., tumor ablation, transcatheter arterial chemoembolization), extracellular agents such as Magnevist are typically preferred because of their high gadolinium concentration and mechanism of action, which includes an equilibrium phase to detect tumor washout. Hepatobiliary agents such as Eovist can be helpful in distinguishing true masses from perfusional pseudo-lesions, because the latter will not appear as a hypointense filling defect on 20-minute delayed imaging.

Superparamagnetic iron oxides (SPIOs) may be given to evaluate phagocytic function of hepatic Kupffer cells. The agent is administered as a slow infusion, typically over 30 minutes. Uptake of SPIOs results in T2 and T2\* shortening.<sup>34</sup> Lesions with Kupffer cells (most RNs and DNs) lose signal intensity on SPIO-enhanced T2-weighted and T2\*-weighted images, whereas lesions deficient in Kupffer cells (most HCCs and cirrhotic scars) do not lose signal intensity and appear relatively hyperintense. There is controversy regarding whether spin echo or gradient echo techniques are most well suited for evaluating SPIO uptake.<sup>35</sup> In select centers, double-contrast–enhanced imaging, in which SPIO followed by gadolinium are administered sequentially in the same examination, is performed. The sequential administration of two agents theoretically improves the characterization of cirrhotic nodules by permitting the assessment of two complementary biological features (phagocytic activity of Kupffer cells and vascularity).<sup>36</sup>

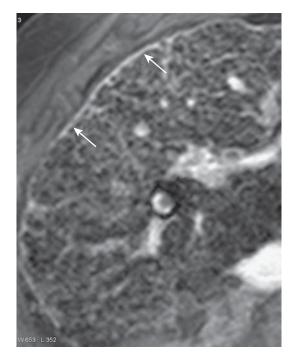
Fibrosis. Fibrosis in the cirrhotic liver has low signal intensity on unenhanced T1-weighted images and high signal on T2-weighted images. Similar to its appearance on CT, confluent fibrosis tends to have straight borders and is associated with progressive volume loss over time at follow-up imaging. When gadolinium is administered, fibrotic tissue slowly enhances in the arterial phase and retains contrast on portal venous and delayed images. As a result, fibrosis has relatively high signal on delayed gadolinium-enhanced images (see Figures 41-4 and 41-5). Fibrosis, which lacks Kupffer cells, also has relatively high signal intensity on T2-weighted and T2\*-weighted images after SPIO administration. Double-contrast-enhanced gradient echo images show the reticulations and bands of liver fibrosis to greatest advantage; the fibrotic tissue appears hyperintense as a result of gadolinium accumulation, while the background liver parenchyma appears hypointense because of SPIO accumulation. Such images also show other features of cirrhosis, including capsular thickening (Figure 41-7) and nonuniform distribution of fibrosis (Figure 41-8).

**Nodules.** FNH-like lesions are typically isointense on T1-weighted and isointense to hypointense on T2-weighted imaging. Similar to their appearance on contrast-enhanced CT, these lesions enhance during the hepatic arterial phase after injection of gadolinium-based agents and then fade to isointensity on more delayed phases. Like FNH, they also take up Eovist and appear isointense to parenchyma on the hepatocyte phase.<sup>37</sup>

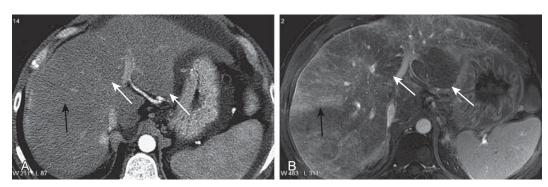
RNs have a variable appearance at unenhanced T1-weighted imaging and may be hypointense, isointense, or hyperintense. Some RNs are steatotic and lose signal intensity on out-of-phase compared with in-phase imaging (Figure 41-9). Most RNs are isointense and not detectable at T2-weighted imaging, whereas some RNs, particularly those with high iron concentration, are hypointense at T2-weighted and T2\*-weighted imaging.<sup>38,39</sup>

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High signal intensity on T2-weighted images is distinctly unusual for RNs; marked T2 hyperintensity suggests a simple cyst, whereas mild to moderate T2 hyperintensity raises suspicion for HCC. On administration of gadolinium, RNs enhance to a degree similar to that of surrounding parenchyma and usually appear isointense. However, both RNs and DNs can demonstrate arterial enhancement but then fade to isointensity on delayed imaging (rather than washing out). RNs and DNs typically take up hepatobiliary contrast agents and appear isointense at 20 minutes.<sup>37</sup> When SPIOs are administered, RNs take up the iron



**Figure 41-7** Hepatic capsular thickening. On this axial doublecontrast-enhanced magnetic resonance image, the hepatic capsule can be seen retaining gadolinium and has high signal intensity similar to the fibrotic reticulations distributed throughout the liver. As illustrated in this case, the fibrotic thickening of the liver capsule (*arrows*) is a frequent manifestation of cirrhosis but it is not always observed on imaging.



**Figure 41-8** Nonuniform distribution of fibrosis. **A**, On this axial arterial-phase contrast-enhanced computed tomography image, the liver has an unusual contour and there is relative hypertrophy of the posterior portion of the lateral segment of the left lobe (*black arrow*). The liver parenchyma is relatively heterogeneous with areas of hyperattenuation and hypoattenuation (*white arrows*). **B**, The axial double-contrast–enhanced magnetic resonance image shows to better advantage the nonuniform distribution of fibrosis within this cirrhotic liver. Note that areas of atrophy and volume loss are associated with a higher density of fibrotic tissue (*black arrow*) than areas of hypertrophy (*white arrows*).

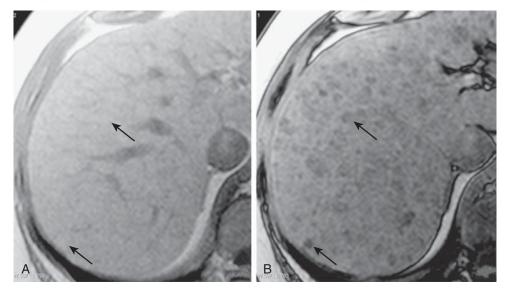


Figure 41-9 Fatty regenerative nodules (RNs). On axial unenhanced magnetic resonance in-phase (A) and out-of-phase (B) images, RNs can be appreciated (*arrows*). The RNs lose signal, as evidenced by the decrease in signal intensity on out-of-phase images, indicating the presence of intralesional fat. Innumerable nodules are present in the images.

particles and, as a result of superparamagnetic effects, appear hypointense on T2-weighted and T2\*-weighted images (see Figure 41-5). DNs, like RNs, have variable signal intensity on unenhanced T1-weighted images and appear isointense or hypointense on T2-weighted images. On gadolinium and SPIOenhanced imaging, low-grade DNs typically are difficult to distinguish from RNs, whereas high-grade dysplastic nodules may resemble well-differentiated HCCs.

HCCs display variable signal intensity on unenhanced T1-weighted imaging. They characteristically appear hyperintense at T2-weighted imaging, but T2-weighted imaging has limited sensitivity for HCCs and may render them invisible or mildly hypointense. After administration of gadolinium, hypervascular HCCs enhance rapidly to high signal intensity on arterial phase images and then become hypointense on portal venous and delayed images. When Eovist is administered, HCCs almost always appear hypointense on the hepatocyte phase. Rarely, well-differentiated HCCs can take up and excrete hepatobiliary agents.<sup>37</sup> Compared with RNs and DNs, HCCs tend to have a reduced concentration of Kupffer cells and diminished phagocytic capacity. Hence, when SPIOs are administered, HCCs do not take up the particles and have high signal intensity relative to the adjacent non-neoplastic parenchyma. Focal areas of fibrosis also have high signal on such images and may be mistaken for HCCs on low-resolution SPIO-enhanced images. High-resolution SPIO-enhanced imaging usually permits differentiation of fibrosis (reticulated morphology) from HCC (nodular morphology). In challenging cases, gadolinium administration or follow-up imaging is necessary.

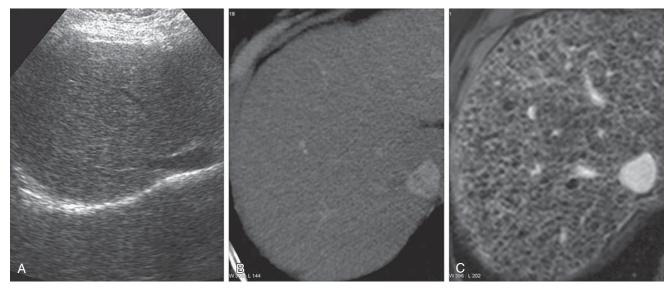
Perfusional pseudo-lesions may be indistinguishable from FNH-like lesions. Similar to FNH-like lesions, the pseudolesions hyperenhance during the arterial phase and then fade to isointensity. Both will typically appear isointense at delayed hepatobiliary imaging. Differentiation is not clinically important, however, because both FNH-like lesions and perfusional pseudo-lesions are benign. If these entities are suspected, follow-up imaging rather than intervention is recommended.

#### Ultrasound

Technical Considerations. Because of its low cost and lack of radiation, ultrasonography is typically the initial imaging modality performed in patients with cirrhosis. It provides information about liver size and shape and, if high-frequency transducers are used, may detect subtle nodularity along the liver surface to establish the diagnosis of cirrhosis in clinically equivocal cases. In patients with established cirrhosis, ultrasound plays an important role in assessing sequelae of portal hypertension (e.g., splenomegaly and ascites). On gray-scale images, features suggestive of portal hypertension include dilation of the portal vein to greater than 13 mm, splenic vein to greater than 11 mm, and superior mesenteric vein to greater than 12 mm. Color Doppler tracings can be used to further characterize portal vein patency and direction of flow. Portal hypertension is associated with increased pulsatility of the portal vein Doppler tracing and loss of the normal triphasic hepatic vein Doppler tracing. When portal flow is hepatofugal, the liver has progressed to end-stage disease and shunt placement or liver transplantation may be required. Color Doppler tracings can also be used to monitor shunt patency as well as patency of vascular anastomoses after transplantation.

In Europe, Asia, and select centers in North America, microbubble-based contrast agents may be administered intravenously to assess lesion vascularity using ultrasonography. Similar to CT and MRI, multiple phases are acquired: arterial phase (15 to 30 seconds after injection), portal phase (30 to 60 seconds after injection), and sinusoidal (or blood pool) phase (60 to 240 seconds after injection).<sup>26</sup>

**Nodules.** Ultrasound has limited sensitivity for cirrhosisassociated nodules. Discrete RNs are rarely identified even if they are obvious on other imaging modalities. Coarsening and heterogeneity of the liver echotexture may suggest the presence of RNs, but this finding is neither sensitive nor specific, and the liver parenchyma may appear normal even if cirrhosis is



**Figure 41-10** Ultrasound (A), computed tomography (CT) (B), and magnetic resonance (MR) (C) images of the liver of a male patient with cirrhosis. On the ultrasound image the liver has increased echogenicity and heterogeneity, although specific reticulations are difficult to identify. On the axial CT image, reticulations are again difficult to appreciate. However, on the double-contrast–enhanced MR image the fibrotic tissue forms honeycomblike reticulations of high signal intensity surrounding the low-signal regenerative nodules. Of the three modalities, the extent and degree of fibrosis are more easily appreciated with MR imaging.

advanced (see Figures 41-4 and 41-10). Another indirect clue to the presence of RNs includes nodularity of the liver surface, most reliably appreciated if high-resolution transducers are used. In this setting, the RNs themselves are usually not visible and their presence is inferred by the bulging of the liver capsule.

Nodules sufficiently large or anomalous to be visible in the cirrhotic liver on ultrasound evaluation are likely to be HCCs. If visible on ultrasound, HCCs tend to be hypoechoic or have mixed echogenicity. Unenhanced ultrasonography has limited sensitivity for HCC, however, and most HCCs are not visible unless large or associated with vascular invasion. If microbubbles are administered, HCCs typically hyperenhance and become vividly hyperechoic on the arterial phase and then wash out to become hypoechoic on the portal and sinusoidal phases.

**Fibrosis.** Similar to cirrhotic nodules, ultrasonography has low sensitivity for fibrosis. Advanced fibrosis associated with cirrhosis may manifest as diffuse increase in echogenicity, with poor visualization of coursing liver vessels. Findings overlap with those of simple steatosis. It is common for cirrhosis to be misdiagnosed as fatty liver on the basis of ultrasound findings.

# Liver Imaging Reporting and Data System and Organ Procurement and Transplantation Network

Two reporting systems have gained popularity in attempts to standardize interpretation of focal findings on CT and MRI in patients with chronic liver disease. Analogous to the Breast Imaging Reporting and Data System (BI-RADS) for breast imaging, the Liver Imaging Reporting and Data System (LI-RADS) algorithm was created by a workgroup of the American College of Radiology to facilitate all radiologists in characterizing focal liver lesions on CT and MRI for patients at risk for the development of HCC. Another reporting system employed by the Organ Procurement and Transplantation Network (OPTN) was designed for radiologists at liver transplant centers to standardize reporting of focal liver lesions on CT and MRI in patients at risk for HCC who are being considered for liver transplantation.

The goals of LI-RADS include limiting variability in liver lesion interpretation, standardizing reporting of findings, and improving communication with referring physicians to help guide patient management.<sup>40</sup> There are five basic categories available to classify lesions on CT and MRI in patients at risk for HCC. These include LR-1 (definitely benign), LR-2 (probably benign), LR-3 (indeterminate probability of being HCC), LR-4 (probably HCC), and LR-5 (definitely HCC). Two additional categories are available for special circumstances, namely LR-5V for tumor thrombus within the portal vein (or less likely a hepatic vein) and LR-M for a lesion that is probably malignant but is nonspecific for HCC (i.e., cholangiocarcinoma). Assignment of a lesion to one of the LI-RADS categories relies on assessment of lesion diameter and the presence of four specific major features: arterial phase hyperenhancement, washout on portal venous or equilibrium phases, presence of a capsule/ pseudocapsule, and threshold growth compared to prior imaging.<sup>41</sup> Of note, enhancement characteristics describe patterns seen with extracellular agents (i.e., Magnevist for MRI). The threshold growth is defined as 50% or greater increase in diameter in a period of 6 months or less, at which point the lesion is designated LR-5g. Assignment of a lesion to a LI-RADS category of LR-2, LR-3, or LR-4 should include recommendations for additional imaging or discussion, such as routine surveillance, accelerated follow-up, alternative imaging, or multidisciplinary discussion. Recommendations for biopsy or treatment should not accompany a LI-RADS designation.<sup>4</sup>

Whereas LI-RADS was designed for characterizing focal lesions in patients at risk for HCC, the OPTN classification system focuses on HCC assessment in regard to candidacy for liver transplantation. The classification system does not intend

to maximize sensitivity for HCC detection but rather to increase specificity for the purposes of driving MELD exception points in patients with unequivocal imaging findings of HCC who are viable candidates for transplant.<sup>42</sup> For focal lesions in cirrhotic livers, the OPTN class number designates whether an examination is nondiagnostic (OPTN class 0) or contains at least one treated or untreated HCC (OPTN class 5). OPTN class 5 lesions meet imaging criteria for HCC and are subdivided into 5A, 5A-g, 5B, 5B-g, 5T, and 5X. Class 5A lesions measure between 1 and 2 cm and demonstrate arterial enhancement with washout and peripheral rim enhancement (capsule/pseudocapsule). Class 5A-g lesions are arterially enhancing lesions measuring 1 to 2 cm that demonstrate growth of 50% or more in a period of 6 months or less (like LR-5g lesions in the LI-RADS classification scheme). Class 5B lesions measure between 2 to 5 cm, showing arterial enhancement and washout or capsule/pseudocapsule. Lesions of this size that demonstrate growth of 50% or more in 6 months or less can also be classified as class 5B-g. A class 5T designation denotes an HCC treated by locoregional therapy (i.e., ablation, transcatheter arterial chemoembolization). Finally, a class 5X lesion shows arterial enhancement and washout or peripheral rim enhancement but is greater than 5 cm in size and, therefore, beyond acceptable limits for transplantation per the Milan criteria. As with LI-RADS, imaging characteristics for OPTN classification are based on administration of extracellular contrast agents. Ancillary features such as intralesional fat, T2 hyperintensity, and restricted diffusion can be considered by the experienced radiologist, but should be used with caution.42

#### Imaging Algorithm

The most appropriate method for assessing cirrhosis and screening for HCC through imaging is complicated and controversial. The American Association for the Study of Liver Diseases recommends sonographic screening every 6 to 12 months, but ultrasound has low sensitivity and may fail to detect HCC until advanced stages when it is no longer curable.<sup>43</sup> Therefore, many centers use CT for initial screening, with contrast-enhanced MRI reserved for further characterization of known lesions. Although MRI offers higher sensitivity to contrast agents, higher tissue contrast, and a larger variety of contrast agents with different biologic properties, MR costs and time preclude it from being used as a screening modality in most centers. Even so, some academic centers primarily use MRI for screening purposes because of its perceived benefits.

#### DIFFERENTIAL DIAGNOSIS

Because cirrhosis systemically affects physiology and has effects on diverse organs, its diagnosis is rarely disputed. Its characteristic physical examination, laboratory findings, and imaging findings infrequently overlap with other conditions; thus, there usually is no clinical differential diagnosis for cirrhosis. The main diagnostic challenge for the clinician is to determine the cause of cirrhosis through careful history and laboratory testing. Elucidating the underlying cause is important because it may have implications for management and prognosis. For example, cirrhosis caused by HBV or HCV is more likely to be complicated by HCC than cirrhosis resulting from NAFLD and, therefore, may warrant more aggressive cancer screening and treatment. Additionally, knowledge of the cause directs preventive measures, including the screening for high-risk behaviors in family members of patients with cirrhosis resulting from alcohol use or HCV infection and genetic testing in relatives of those diagnosed with an inherited storage disease.<sup>44</sup>

The radiologic differential diagnosis of cirrhosis is limited and includes diseases that mimic the fibrotic and nodular pattern of cirrhosis. Treated metastases may shrink and fibrose, simulating a nodular liver contour. Sarcoid lesions appear as hypoattenuating nodules (usually <2 cm) at CT and are hypointense on T2-weighted MR images, resembling RNs and DNs.

The most common focal lesions in cirrhosis (RNs, DNs, HCCs, FNH-like lesions, perfusional pseudo-lesions, and confluent fibrosis) are differentiated by CT and MRI.

#### TREATMENT

#### Medical Treatment

Because cirrhosis is thought to be irreversible, its management focuses on the prevention and treatment of its complications, with the goal of liver transplantation in select patients. Recent advances, however, suggest that the halting of cirrhosis, or perhaps even its regression, is possible in some cases.<sup>44</sup> Some patients with well-compensated cirrhosis secondary to HBV or HCV infection are candidates for antiviral therapy, which may slow the progression of cirrhosis and decrease the risk for development of HCC.<sup>45</sup>

Patients who present with variceal hemorrhage require immediate stabilization with volume resuscitation via intravenous fluids, blood transfusion, reversal of coagulopathy, and intensive care unit monitoring. Administration of somatostatin analogs to lower splanchnic pressure and antibiotics to prevent spontaneous bacterial peritonitis are also mainstays of therapy.<sup>46</sup> Endoscopic management, via band ligation or sclerotherapy, is definitive treatment. Prophylaxis of variceal hemorrhage is attained by periodic surveillance with upper endoscopy and the use of nonselective beta blockers, which decrease portal pressure and variceal size.<sup>47</sup>

### Surgical Treatment

Shunt placement is used as a bridge to liver transplantation in patients with adequate hepatic reserve and complications of portal hypertension that are refractory to medical or endoscopic therapy, most notably, varices and ascites. The most common shunts are TIPS, although patients with surgical mesocaval or portocaval shunts are still encountered. TIPS decreases the portosystemic gradient by providing ancillary venous outflow that bypasses the increasing intrahepatic sinusoidal pressure; it is preferred to surgical shunting at most centers because it avoids laparotomy, does not require general anesthesia, has fewer serious complications, and rarely results in procedure-related death. It decompresses the portal circulation in 90% of cases, has a greater than 70% success rate in producing hemostasis in active or recurrent variceal hemorrhage, and resolves ascites 75% of the time.48,49 Drawbacks include limited long-term TIPS patency and the need for frequent endovascular reintervention.49

Cadaveric or living-donor liver transplantation is the only "cure" for cirrhosis and its complications. Approximately 6000 liver transplants are performed annually in the United States. Adult recipients are prioritized according to the MELD scoring system and are committed to lifelong immunosuppression.

#### What the Referring Physician Needs to Know

- Cirrhosis is the final common clinical and histologic pathway of various chronic conditions affecting the liver, characterized by the replacement of normal hepatic architecture with fibrosis and RNs and manifested as portal hypertension and liver failure.
- In the United States, the most common causes of cirrhosis are HCV infection and alcoholic liver disease, although nonalcoholic liver disease is a burgeoning epidemic. HBV predominates in Asia and sub-Saharan Africa.
- The main clinical manifestations of cirrhosis are the complications of portal hypertension, including ascites (with or without spontaneous bacterial peritonitis), esophageal varices (with or without hemorrhage), hepatic encephalopathy, and hepatorenal syndrome.
- Cirrhosis is thought to be irreversible; management focuses on treating its various complications, screening for HCC, and evaluating appropriate patients for liver transplantation.

#### **Key Points**

- Classic vascular manifestations of cirrhosis include hepatic artery dilatation, intrahepatic artery tortuosity ("corkscrew" vessels), portal vein dilation in early portal hypertension, portal vein occlusion in late portal hypertension resulting from sluggish portal flow, and formation of shunts.
- Because of third spacing of fluid and leakage of contrast material, patients with cirrhosis sometimes require higher rates and concentrations of contrast material than patients without cirrhosis.
- Confluent fibrosis occasionally may be masslike and confused for HCC on CT or MRI, but differentiation is usually possible based on its characteristic morphology, associated capsular retraction and volume loss, and progressive enhancement pattern.
- The American Association for the Study of Liver Diseases recommends sonographic screening every 6 to 12 months, but ultrasound has low sensitivity and may fail to detect HCC until advanced stages, when it is no longer curable. Therefore, many centers use CT for initial screening, with contrast-enhanced MRI reserved for further characterization of known lesions.

# Hepatitis

# ETIOLOGY

Hepatitis is broadly defined as diffuse inflammation of the liver. More than two thirds of cases of hepatitis are caused by viruses.<sup>50</sup> Hepatotropic viruses, such as hepatitis A (HAV), B (HBV), C (HCV), D (HDV), and E (HEV), are the most commonly implicated, but examples of other possible causes include autoimmune disorders, metabolic conditions (e.g., Wilson's disease), toxic injury, and drug reaction. The focus here is on hepatotropic viral hepatitis, with special attention provided to the most prevalent of these, HBV and HCV.

#### PREVALENCE AND EPIDEMIOLOGY

HBV is the principal member of the DNA family of viruses known as Hepadnaviridae.<sup>51</sup> The prevalence of HBV varies from 0.1% to 2% in the United States and Western Europe to up to 20% in endemic areas such as China, Southeast Asia, and sub-Saharan Africa. The main modes of transmission are via unprotected sexual intercourse and needle sharing during intravenous drug use.

HCV is a small, enveloped, single-stranded RNA virus of the Flaviviridae family.<sup>52</sup> In the United States, HCV is the most common cause of virally transmitted chronic liver disease. Approximately 4.1 million Americans are infected, and approximately 10,000 Americans die annually of complications related to HCV infection. The two main risk factors for HCV transmission are the sharing of needles during intravenous drug use and receiving a blood transfusion before 1990. Other risk factors include multiple sex partners, tattoos, and needlestick exposure.<sup>52</sup>

#### **CLINICAL PRESENTATION**

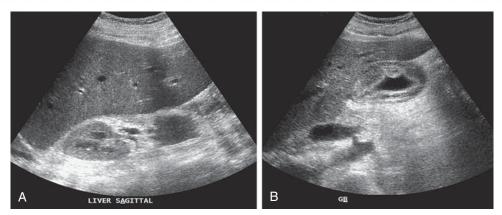
Clinically, hepatitis can be divided into acute and chronic forms, based on the duration of the disease as assessed via biochemical (e.g., elevations of transaminases) and histologic means. Severity of acute viral hepatitis ranges from subclinical infection to symptomatic disease and, rarely, fulminant hepatic failure.<sup>53</sup> In acute viral hepatitis, full clinical and biochemical resolution occurs within 6 months. However, a proportion of patients may proceed to chronic hepatitis, characterized by evidence of hepatocyte damage and inflammation beyond 6 months. The chronic form may manifest decades later as cirrhosis and portal hypertension.<sup>51</sup>

Approximately 5% of immunocompetent adults infected with HBV are unable to clear the virus and thus advance to chronic HBV infection. Approximately 20% of patients with chronic HBV infection progress to cirrhosis decades after initial infection. Chronic HBV infection is an independent risk factor for the development of HCC, with chronic carriers being 100 times more likely to develop HCC than noncarriers. In contrast to other viral hepatitides, patients with long-standing chronic HBV infection have an elevated risk for HCC development even in the absence of underlying cirrhosis.<sup>51</sup>

As opposed to HBV infection, most patients infected with HCV advance to chronic HCV infection. The natural course of HCV infection is indolent; 20% to 30% of patients with chronic HCV infection develop cirrhosis in 20 to 30 years. The risk for developing HCC in patients with HCV cirrhosis has been estimated to be approximately 2% per year. In the absence of cirrhosis, the risk for HCC is considered small.<sup>54</sup>

#### PATHOLOGY

Hepatitis is defined pathologically by hepatocyte necrosis and hepatic inflammation.<sup>55</sup> In nonfulminant acute hepatitis, the liver is typically enlarged and erythematous with a tense capsule. Microscopically, there is hepatocyte swelling (hepatocellular enlargement and cytoplasmic rarefaction), spotty hepatocellular necrosis and apoptosis, lobular disarray (disruption of the normal architecture of the liver), and mononuclear inflammatory infiltrates. In fulminant acute hepatitis, the liver is shrunken and soft, with a wrinkled capsule and a mottled cut surface.



**Figure 41-11** Acute hepatitis in a 28-year-old woman resulting from acetaminophen overdose. A, Sagittal ultrasound image shows an enlarged liver that measures 21 cm in length. B, Oblique ultrasound image through the left lobe of the liver demonstrates a markedly thickened gallbladder (*GB*).

Microscopically, there is extensive hepatocyte loss, proliferation of bile ductules, and a mixed inflammatory infiltrate.<sup>56</sup>

Chronic hepatitis is characterized microscopically by a combination of portal inflammation, parenchymal or lobular inflammation, interface hepatitis, spotty hepatocyte necrosis, and progressive fibrosis. Interface hepatitis, also known as *piece-meal necrosis*, refers to mononuclear inflammation extending from the limiting plate of the portal tract to envelop adjacent hepatocytes. Ongoing interface hepatitis causes hepatocyte loss and fibrosis. The end stage of this process is cirrhosis, in which dense fibrous bands divide the liver into parenchymal nodules.

Currently, liver biopsy is the gold standard for diagnosis, staging, and follow-up of chronic liver disease. However, liver biopsy has limitations, such as high costs, a false-negative rate of up to 24%, a sampling error rate ranging from 25% to 40%, and morbidity and fatality rates of 3% and 0.3%, respectively.<sup>57</sup>

#### IMAGING

#### Acute Hepatitis

Because acute hepatitis is diagnosed by clinical examination and liver function tests, imaging studies play a limited role in evaluating patients with this condition. The imaging findings are nonspecific and may include hepatomegaly and gallbladder wall thickening (Figure 41-11). If steatohepatitis is present, diffuse fat deposition dominates the imaging findings. Other features may include parenchymal heterogeneity, accentuation of the portal triads, and heterogeneous perfusion (Figure 41-12).<sup>58</sup>

In patients with an atypical clinical presentation, imaging may be performed to assess for biliary obstruction, cholangitis, or vascular occlusion. In cases with fulminant manifestations, imaging may assess the extent of necrosis and exclude complications of acute hepatitis, such as ascites and spontaneous hepatic rupture. Because of its portability, low cost, and widespread availability, transabdominal ultrasonography is the most common imaging modality used initially in these clinical settings, although CT may be performed as well (Figure 41-13).

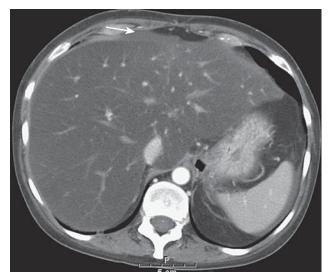
**Computed Tomography.** The CT findings in acute hepatitis are also nonspecific, including hepatomegaly, gallbladder wall thickening, and periportal edema, which manifests as low



**Figure 41-12** Acute hepatitis in a 19-year-old man with a clinical history of acute hepatitis. Transverse ultrasound image of the liver shows mild prominence of portal triads.

attenuation regions along the portal triads. Additionally, after the intravenous injection of contrast material, the liver parenchyma may enhance heterogeneously. Patchy areas of arterial phase hyperenhancement may be visible and superficially resemble the appearance of an infiltrative malignancy. A key distinguishing feature is that perfusional hyperenhancement resulting from acute inflammation fades to isoattenuation during the venous phases; by comparison, infiltrative malignancies tend to appear heterogeneous and washout during the venous phases.<sup>59</sup>

**Magnetic Resonance Imaging.** MRI is not commonly used in the assessment of patients with acute hepatitis. However, some MRI findings, such as heterogeneous hepatic signal intensity most apparent on T2-weighted images, periportal edema presenting as low signal on T1-weighted and high signal on T2-weighted images, and irregular patchy areas of abnormal increased heterogeneous enhancement seen on the arterial phase immediately after intravenous contrast agent administration, have been described in patients with acute hepatitis. These MRI findings are analogous to the ones reported with contrastenhanced CT.<sup>60</sup> **Imaging Algorithm.** Patients presenting with a clinical history of malaise, nausea, anorexia, fever, and right upper quadrant abdominal pain associated with jaundice and pruritus should



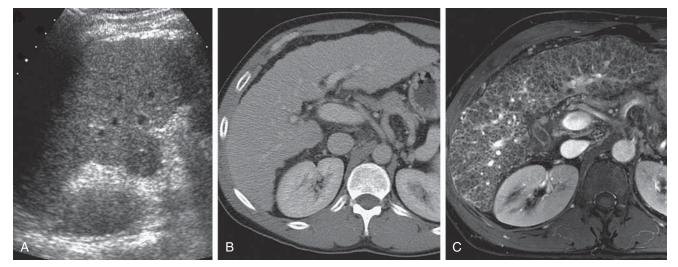
**Figure 41-13** Acute hepatitis in a 35-year-old woman who presented to the emergency department with acute severe hepatitis. Computed tomography shows an enlarged liver with severe fat accumulation. Note that the attenuation of the liver is lower than that of ascites (*arrow*). She died 6 days later of fulminant liver failure.

be investigated promptly with liver function tests and an abdominal ultrasound evaluation. When the clinical presentation is atypical or there is a finding of concern evident on ultrasound, CT is recommended for optimal assessment of the liver and biliary system. CT is helpful to rule out the presence of biliary obstruction, cholangitis, or vascular occlusion. Meanwhile, in patients with fulminant presentations, CT is also performed to assess the extent of necrosis and to exclude complications such as ascites and spontaneous hepatic rupture. Conversely, MRI is infrequently used in the assessment of patients with acute hepatitis and usually is reserved for patients with contraindications to the use of intravenous iodine contrast and for further imaging characterization.

#### Chronic Hepatitis

Until recently, the role of imaging studies in patients with chronic hepatitis was limited to the identification of individuals with cirrhosis or its complications and the early detection of HCC. Using standard ultrasound, CT, and MRI techniques, the liver usually has a normal imaging appearance in patients with chronic viral hepatitis until cirrhosis has developed. Other possible findings include nonspecific parenchymal heterogeneity, heterogeneous enhancement after intravenous contrast agent administration, and lymphadenopathy. Lymphadenopathy, in particular, is an important consideration because it is present in up to 65% of cases and may be the only indication of chronic active hepatitis in up to 35% of cases.<sup>59</sup> The lymph nodes of the porta hepatis, hepatoduodenal ligament, and retroperitoneum are most commonly involved.

Once cirrhosis becomes evident, the imaging features of end-stage liver disease secondary to chronic hepatitis are similar to those of other causes of cirrhosis (Figure 41-14). In recent years, the rising prevalence of chronic hepatitis in Western nations has spurred the development of noninvasive, imagingbased techniques to assess parenchymal inflammation, hepatocellular injury, and liver fibrosis.



**Figure 41-14** Ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) findings in a 59-year-old man with cirrhosis secondary to chronic hepatitis C infection. **A**, Transverse ultrasound image shows nodular contours of the liver and a diffusely heterogeneous parenchymal echotexture. **B**, Axial postcontrast CT image during the portal venous phase shows nodularity of the liver surface, atrophy of the right lobe, and widening of the porta hepatis. **C**, Axial combined contrast-enhanced MR image additionally shows hyperintense reticulations throughout the liver parenchyma. Note the innumerable hypointense regenerative nodules carpeting the liver diffusely. Discrete regenerative nodules and fibrotic scars are not visible on ultrasound or CT images.

Computed Tomography. CT is frequently used in the assessment and monitoring of patients with chronic liver disease because it accurately demonstrates the intrahepatic and extrahepatic manifestations of cirrhosis and portal hypertension. However, CT is insensitive in assessing pre-cirrhotic liver disease and early stages of fibrosis. Recently, the use of an imaging processing method based on textural analysis for assessing liver fibrosis using unenhanced CT scans ("fibro-CT") was reported.<sup>60</sup> The fibrosis stage estimated by fibro-CT was closely correlated with the histologic fibrosis stage ascertained by biopsy, suggesting a possible role for fibro-CT in the longitudinal monitoring of patients with chronic hepatitis. Dual-energy CT (DECT) is also being studied for its ability to detect and quantify liver fibrosis based on a combination of the multimaterial decomposition algorithm and hemodynamic properties of fibrotic livers. A small study by Lamb and colleagues<sup>61</sup> proposed a DECT method generating quantitative maps to display spatial distribution and severity of liver fibrosis in a fashion similar to both liver biopsy and current imaging methods such as magnetic resonance elastography. Both fibro-CT and DECT methods for liver fibrosis quantification require further research and refinement.

**Magnetic Resonance Imaging.** Because of its intrinsic contrast resolution, MRI is more sensitive than CT in the assessment of patients with chronic liver disease. Conventional MR sequences can easily depict the morphologic changes associated with cirrhosis and the signs suggestive of portal hypertension. During the pre-cirrhotic stages of liver disease, heterogeneity of hepatic parenchyma may be seen after intravenous contrast agent administration; however, this finding is nonspecific and has not been shown to permit noninvasive staging of liver fibrosis.

Recently, diverse experimental MR techniques have been used for assessment of liver fibrosis in chronic hepatitis, including combined double-contrast–enhanced MRI, diffusion weighted imaging, MR elastography, MR spectroscopy, and MR perfusion.<sup>62</sup> These evolving techniques are described elsewhere in this text (see Chapter 35).

**Ultrasound.** Like CT and MRI, new ultrasound techniques have been recently introduced to evaluate for fibrosis in patients with chronic hepatitis, particularly in earlier stages before the liver develops gross morphologic changes. In particular, transient and shear wave ultrasound elastography have shown potential to identify liver fibrosis as early as the F2 stage, when treatment can be implemented before irreversible cirrhosis incurs (see Chapter 5).

**Imaging Algorithm.** It is recommended that patients with cirrhosis secondary to chronic hepatitis undergo imaging to assess for sequelae of portal hypertension and screen for HCC. Ultrasound and CT are usually the imaging studies performed initially in patients who have advanced to cirrhosis. Ultrasound depicts a liver usually decreased in size with heterogeneous echotexture and is useful for assessing portal venous flow direction and waveforms. CT better demonstrates the hepatic morphologic changes of advanced fibrosis and extrahepatic sequelae of portal hypertension. MRI can subsequently be used if the CT is equivocal or to better characterize nodules. Some centers routinely use CT or MRI in their HCC screening and surveillance protocols despite the fact that the American Association for the Study of Liver Diseases (AASLD) advocates the use of ultrasound.

#### DIFFERENTIAL DIAGNOSIS

The clinical differential diagnosis of acute hepatitis includes all hepatic insults resulting in the signs, symptoms, and laboratory abnormalities described in earlier sections. These causes include exposure to various toxins or toxin ingestion, metabolic disease, and autoimmune hepatitis. They are generally easily distinguishable by obtaining a complete history and evaluating copper studies, autoimmune markers, and viral hepatitis serologic studies.

The clinical differential diagnosis of chronic hepatitis is similar to that of the various causes of cirrhosis. As with acute hepatitis, a careful history and evaluation of laboratory studies provides direction. Liver biopsy also may be helpful in distinguishing some processes.

#### TREATMENT

#### **Medical Treatment**

The treatment of acute hepatitis is largely supportive, because the symptomatic phases of most cases resolve spontaneously after a few weeks. An exception to this is patients with acute HBV infection, who are often started on antiviral therapy.

Treatment options for chronic hepatitis are reserved for patients with HBV or HCV infection. There are a variety of antiviral agents available for the treatment of chronic HBV infection, including lamivudine, adefovir, entecavir, and others. HCV infection, on the other hand, has a single effective regimen, consisting of interferon and ribavirin.

#### Surgical Treatment

Liver transplantation is the only accepted surgical treatment for acute hepatitis that has progressed to fulminant hepatic failure or chronic hepatitis that has advanced to cirrhosis, HCC, or both. Cirrhosis secondary to HCV is the most common indication of liver transplantation in the United States, accounting for approximately 2000 transplants annually.

#### **Key Points**

#### Acute Hepatitis

- Imaging studies have a limited role in the diagnosis of acute hepatitis.
- When imaging studies are performed, imaging findings of acute hepatitis are nonspecific.
- The most common findings, regardless of modality, are hepatomegaly and gallbladder wall thickening, with other nonspecific findings including heterogeneous parenchyma, accentuation of the portal triads, and periportal edema.

#### **Chronic Hepatitis**

- Conventional ultrasound, CT, and MRI techniques do not permit assessment of pre-cirrhotic stages of chronic hepatitis.
- MRI is the most accurate noninvasive diagnostic modality for the diagnosis of cirrhosis and, in patients who have advanced to cirrhosis, for depiction of fibrosis and regenerative nodules.
- Experimental techniques to assess liver fibrosis noninvasively are under development and may eventually replace liver biopsy.

#### SUGGESTED READINGS

- Danrad R, Martin DR: MR imaging of diffuse liver diseases. Magn Reson Imaging Clin North Am 13:277–293, vi, 2005.
- Hanna RF, Aguirre DA, Kased N, et al: Cirrhosisassociated hepatocellular nodules: correlation of histopathologic and MR imaging features. *Radiographics* 28:747–769, 2008.

#### REFERENCES

- Clark JM, Diehl AM: Nonalcoholic fatty liver disease: an underrecognized cause of cryptogenic cirrhosis. JAMA 289:3000–3004, 2003.
- Morreira RK: Hepatic stellate cells and liver fibrosis. Arch Pathol Lab Med 131:1728–1734, 2007.
- Blei AT, Mazhar S, Davidson CJ, et al: Hemodynamic evaluation before liver transplantation: insights into the portal hypertensive syndrome. *J Clin Gastroenterol* 41(10 Suppl 3):S323–S329, 2007.
- 4. Such J, Runyon BA: Spontaneous bacterial peritonitis. *Clin Infect Dis* 27:669–674, 1998.
- 5. Scaglione S, Kliethermes S, Cao G, et al: The epidemiology of cirrhosis in the United States: a population-based study. *J Clin Gastroenterol* 49:690–696, 2015.
- 6. U.S. Department of Health and Human Services: *National center for health statistics*, Series 13, Hyattsville, MD, 2005, Centers for Disease Control and Prevention.
- Anderson RN, Smith BL: Deaths: leading causes for 2001. Natl Vital Stat Rep 52:1–85, 2003.
- Li CP, Lee FY, Hwang SJ, et al: Spider angiomas in patients with liver cirrhosis: role of alcoholism and impaired liver function. *Scand J Gastroenterol* 34:520–523, 1999.
- Reynolds TB, Redeker AG, Geller HM: Wedged hepatic vein pressure: a clinical evaluation. *Am J Med* 22:341–350, 1957.
- Gines P, Quintero E, Arroyo V, et al: Compensated cirrhosis: natural history and prognostic factors. *Hepatology* 7:122–128, 1987.
- Riggio O, Masini A, Efrate C, et al: Pharmacological prophylaxis of hepatic encephalopathy after transjugular intrahepatic portosystemic shunt: a randomized controlled study. J Hepatol 42:674–679, 2005.
- Gines A, Escorsell A, Gines P, et al: Incidence, predictive factors, and prognosis of the hepatorenal syndrome in cirrhosis with ascites. *Gastroenterology* 105:229–236, 1993.
- Turban S, Thuluvath PJ, Atta MG: Hepatorenal syndrome. World J Gastroenterol 13:4046–4055, 2007.
- Marti-Llahi M, Guevera M, Gines P: Hyponatremia in cirrhosis: clinical features and management. *Gastroenterol Clin Biol* 30:1144–1151, 2006.
- Kamath PS, Wiesner RH, Malinchoc M, et al: A model to predict survival in patients with end-stage liver disease. *Hepatology* 33:464–470, 2001.
- Gines P, Quintero E, Arroyo V, et al: Compensated cirrhosis: natural history and prognostic factors. *Hepatology* 7:122–128, 1987.
- Sorensen HT, Thulstrup AM, Mellemkjar L, et al: Long-term survival and cause-specific mortality in patients with cirrhosis of the liver: a nationwide cohort study in Denmark. *J Clin Epidemiol* 56:88–93, 2003.
- Montalto G, Cervello M, Giannitrapani L, et al: Epidemiology, risk factors, and natural history

- Ito K, Mitchell DG: Imaging diagnosis of cirrhosis and chronic hepatitis. *Intervirology* 47:134–143, 2004.
- Rockey DC: Noninvasive assessment of liver fibrosis and portal hypertension with transient elastography. *Gastroenterology* 134:8–14, 2008.

Yin M, Talwalkar JA, Glaser KJ, et al: Assessment of hepatic fibrosis with magnetic resonance elastography. *Clin Gastroenterol Hepatol* 5:1207–1213, 2007.

of hepatocellular carcinoma. *Ann NY Acad Sci* 963:13–20, 2002.

- Crawford JM: Basic mechanisms in hepatopathology. In Burt AD, Portmann BC, Ferrell LD, editors: *MacSween's pathology of the liver*, ed 5, New York, 2006, Churchill Livingstone, p 108.
- Goodman ZD, Terraciano LM: Tumours and tumour-like lesions in the liver. In Burt AD, Portmann BC, Ferrell LD, editors: *MacSween's pathology of the liver*, ed 5, New York, 2006, Churchill Livingstone, p 767.
- Lee YH, Kim SH, Cho MY, et al: Focal nodular hyperplasia–like nodules in alcoholic liver cirrhosis: radiologic-pathologic correlation. *AJR Am J Roentgenol* 188:W459–W463, 2007.
- 22. Awaya H, Mitchell DG, Kamishima T, et al: Cirrhosis: modified caudate-right lobe ratio. *Radiology* 224:769–774, 2002.
- International Working Party: Terminology of nodular hepatocellular lesions. *Hepatology* 22: 983–993, 1995.
- 24. United Network for Organ Sharing: *Policy 3.6: organ distribution: allocation of livers*. Revised December 14, 2006. <<u>http://www.optn.org/</u> <u>policiesAndBylaws/policies.asp></u>, (Accessed 18.09.07.).
- Baron RL, Campbell WL, Dodd GD, 3rd: Peribiliary cysts associated with severe liver disease: imaging-pathologic correlation. AJR Am J Roentgenol 162:631–636, 1994.
- Federle M: Liver anatomy and imaging issues. In Federle M, Jeffrey RB, Anne VS, editors: *Diagnostic imaging: abdomen*, Salt Lake City, 2004, Amirsys, pp 2–43.
- Seguchi T, Akiyama Y, Itoh H, et al: Multiple hepatic peribiliary cysts with cirrhosis. J Gastroenterol 39:384–390, 2004.
- Gore RM: Radionuclide imaging of the liver and spleen. In Spies WG, editor: *Textbook of gastrointestinal radiology*, ed 2, Philadelphia, 2000, WB Saunders, pp 1442–1464.
- Ohtomo K, Baron RL, Dodd GD, 3rd, et al: Confluent hepatic fibrosis in advanced cirrhosis: appearance at CT. *Radiology* 188:31–35, 1993.
- Libbrecht L, Cassiman D, Verslype C, et al: Clinicopathological features of focal nodular hyperplasia-like nodules in 130 cirrhotic explant livers. Am J Gastroenterol 101:2341–2346, 2006.
- Gandhi SN, Brown MA, Wong JG, et al: MR contrast agents for liver imaging: what, when, how. *Radiographics* 26:1621–1636, 2006.
- 32. Lutz AM, Willmann JK, Goepfert K, et al: Hepatocellular carcinoma in cirrhosis: enhancement patterns at dynamic gadolinium- and superparamagnetic iron oxide–enhanced T1-weighted MR imaging. *Radiology* 237:520–528, 2005.
- Vogl TJ, Stupavsky A, Pegios W, et al: Hepatocellular carcinoma: evaluation with dynamic and static gadobenate dimeglumine-enhanced MR imaging and histopathologic correlation. *Radiology* 205:721–728, 1997.
- 34. Qayyum A, Thoeni RF, Coakley FV, et al: Detection of hepatocellular carcinoma by

ferumoxides-enhanced MR imaging in cirrhosis: incremental value of dynamic gadoliniumenhancement. J Magn Reson Imaging 23:17–22, 2006.

- Hanna RF, Aguirre DA, Kased N, et al: Cirrhosisassociated hepatocellular nodules: correlation of histopathologic and MR imaging features. *Radiographics* 28:747–769, 2008.
- Hanna RF, Kased N, Kwan SW, et al: Doublecontrast MRI for accurate staging of hepatocellular carcinoma in patients with cirrhosis. AJR Am J Roentgenol 190:47–57, 2008.
- Campos JT, Sirlin CB, Choi JY: Focal hepatic lesions in Gd-EOB-DTPA enhanced MRI: the atlas. *Insights Imaging* 3:451–474, 2012.
- Hussain SM, Zondervan PE, Ijzermans JN, et al: Benign versus malignant hepatic nodules: MR imaging findings with pathologic correlation. *Radiographics* 22:1023–1036, discussion 37-39, 2002.
- Zhang J, Krinsky GA: Iron-containing nodules of cirrhosis. NMR Biomed 17:459–464, 2004.
- Purysko AS, Remer EM, Coppa CP, et al: LI-RADS: a case-based review of the new categorization of liver findings in patients with endstage liver disease. *Radiographics* 32:1977–1995, 2012.
- 41. Mitchell DG, Bruix J, Sherman M: LI-RADS (Liver Imaging Reporting and Data System): summary, discussion, and consensus of the LI-RADS management working group and future directions. *Hepatology* 2014 Jul 12 [Epub ahead of print].
- Wald C, Russo MW, Heimbach JK, et al: New OPTN/UNOS policy for liver transplant allocation: standardization of liver imaging, diagnosis, classification, and reporting of hepatocellular carcinoma. *Radiology* 266:376–382, 2013.
- Bruix J, Sherman M: Management of hepatocellular carcinoma. *Hepatology* 42:1208–1236, 2005.
- Schuppan D, Afdhal NH: Liver cirrhosis. Lancet 371:838–851, 2008.
- 45. Yoshida H, Shiratori Y, Moriyama M, et al: Interferon therapy reduces the risk for hepatocellular carcinoma: national surveillance program of cirrhotic and noncirrhotic patients with chronic hepatitis C in Japan. *Ann Intern Med* 131:174–181, 1999.
- Sharara AI, Rockey DC: Gastroesophageal variceal hemorrhage. N Engl J Med 345:669–681, 2001.
- Garcia-Tsao G: Preventing the development of varices in cirrhosis. J Clin Gastroenterol 41(10 Suppl 3):S300–S304, 2007.
- Ochs A, Rossle M, Haag K, et al: The transjugular intrahepatic portosystemic stent-shunt procedure for refractory ascites. N Engl J Med 332:1192–1197, 1995.
- Colombato L: The role of transjugular intrahepatic portosystemic shunt (TIPS) in the management of portal hypertension. J Clin Gastroenterol 41:S344–S351, 2007.

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- Wasley A, Miller JR, Finelli L: Surveillance for acute viral hepatitis: United States, 2005. MMWR Surveill Summ 56:1–24, 2007.
- Ganem D, Prince AM: Hepatitis B viral infection: natural history and clinical consequences. *N Engl J Med* 350:1118–1129, 2004.
- 52. Lauer GM, Walker BD: Hepatitis C virus infection. *N Engl J Med* 345:41–52, 2001.
- Taylor RM, Davern T, Munoz S, et al: Fulminant hepatitis A virus infection in the United States: incidence, prognosis, and outcomes. *Hepatology* 44:1589–1597, 2006.
- 54. Hu KQ, Tong MJ: The long-term outcomes of patients with compensated hepatitis C virusrelated cirrhosis and history of parenteral exposure in the United States. *Hepatology* 29: 1311–1316, 1999.
- Lamps LW, Washington K: Acute and chronic hepatitis. In Odze RD, Goldblum JR, Crawford JM, editors: Surgical pathology of the GI tract, liver, biliary tract, and pancreas, Philadelphia, 2004, Elsevier, p 783.
- 56. Theise ND, Bodenheimer HC, Ferrell LD: Acute and chronic viral hepatitis. In Burt AD, Portmann BC, Ferrell LD, editors: *MacSween's pathology of the liver*, ed 5, Philadelphia, 2007, Elsevier, p 405.
- Thampanitchawong P, Piratvisuth T: Liver biopsy: complications and risk factors. World J Gastroenterol 5:301–304, 1999.
- Tchelepi H, Ralls PW, Radin R, et al: Sonography of diffuse liver disease. J Ultrasound Med 21:1023–1032, 2002.
- Gore RM, Vogelzang RL, Nemcek AA, Jr: Lymphadenopathy in chronic active hepatitis: CT observations. *AJR Am J Roentgenol* 151:75– 78, 1988.
- Romero-Gómez M, Gómez-González E, Madrazo A, et al: Optical analysis of computed tomography images of the liver predicts fibrosis stage and distribution in chronic hepatitis C. *Hepatology* 47:810–816, 2008.
- Lamb P, Sahani D, Fuentes-Orrego J, et al: Stratification of patients with liver fibrosis using dual-energy CT. *IEEE Trans Med Imaging* 34: 807–815, 2015.
- 62. Martin DR: Magnetic resonance imaging of diffuse liver diseases. *Top Magn Reson Imaging* 13:151–163, 2002.

# Hepatic Veno-occlusive Diseases

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The hepatic veno-occlusive diseases are a heterogeneous group of circulatory disorders characterized by obstruction of hepatic venous outflow at the sinusoidal or postsinusoidal levels. These disorders uniquely manifest portal hypertension before overt hepatic parenchymal disease and dysfunction, in contrast to other causes of hepatic disease in which hepatic dysfunction precedes portal hypertension.<sup>1</sup> The focus in this chapter is on the most common types of sinusoidal (sinusoidal obstruction syndrome) and postsinusoidal (Budd-Chiari syndrome) venoocclusive disease.

# **Etiology**

#### SINUSOIDAL OBSTRUCTION SYNDROME

Sinusoidal obstruction syndrome (SOS) (formerly known as hepatic veno-occlusive disease [VOD]) is a toxin-induced, usually iatrogenic, vascular hepatic disorder. Previously thought to require the involvement of the hepatic venules, it is now recognized that SOS primarily afflicts the sinusoids and may spare the hepatic venules.<sup>2</sup>

SOS was first linked to the ingestion of pyrrolizidine alkaloids in teas from Senecio, Heliotropium, and Crotalaria, sometimes resulting in epidemics of SOS in developing areas.<sup>3</sup> In the West, SOS occurs almost exclusively in patients with cancer as a complication of chemotherapy and abdominal irradiation. Several chemotherapeutic and immunosuppressive agents have been implicated,<sup>4</sup> but the most serious cases of SOS develop after hematopoietic stem cell transplantation with myeloablative conditioning.<sup>5</sup> In patients undergoing stem cell transplant, the risk for developing SOS includes a history of prior stem cell transplantation, hepatitis C infection with elevated levels of aminotransaminases, underlying hepatic fibrosis or cirrhosis, advanced age, and infection at the time of transplant.<sup>3</sup> Although controversial, there is no convincing evidence to support causation by thrombosis secondary to clotting and hypercoagulable states.

#### **BUDD-CHIARI SYNDROME**

Budd-Chiari syndrome (BCS) refers to postsinusoidal obstruction at any level, from the small hepatic veins to the junction of the inferior vena cava (IVC) with the right atrium.<sup>5</sup> Mechanical obstruction can be either primary or secondary. In primary BCS, the obstruction arises from the venous wall (fibrosis or phlebitis) or lumen (thrombosis). In secondary BCS, the obstruction originates from outside the vein and may be caused by extrinsic compression (abscess, cyst, or solid tumor) or tumor invasion.<sup>7</sup>

Intravascular thrombosis is the most common mechanism of hepatic venous obstruction in primary BCS; at least one acquired or inherited procoagulative disorder is identified in up to 75% of patients.<sup>8</sup> Acquired myeloproliferative disorders, such as polycythemia vera and, less commonly, essential thrombocythemia and myelofibrosis, account for 50% of cases of BCS.<sup>9</sup> In the majority of cases, BCS is the initial manifestation of the underlying myeloproliferative disorder. Other acquired procoagulative states include paroxysmal nocturnal hemoglobinuria, malignancy, anti–phospholipid antibody syndrome, Behçet's disease, pregnancy, and oral contraceptive use. The most common inherited procoagulative disorder is factor V Leiden deficiency, occurring in up to 30% of cases of BCS.<sup>10</sup> Other inherited states result in elevations of prothrombin, factors VII and VIII, and homocysteine and in deficiencies of antithrombin, protein C, and protein S.

Secondary BCS is sometimes seen when a malignant tumor grows within the lumen of its associated venous outflow tract (hepatocellular carcinoma [HCC], renal cell carcinoma, Wilms' tumor, and hepatic angiosarcoma). It also can result from extrinsic compression by malignant and benign solid tumors of the liver or adjacent organs, intrahepatic hematomas, hepatic abscesses, hydatid cysts, and hepatic cysts in polycystic kidney disease. No precipitating cause is identified in 10% of cases of BCS.<sup>8</sup>

# **Pathogenesis**

#### SINUSOIDAL OBSTRUCTION SYNDROME

The inciting event in SOS is toxin-mediated sinusoidal endothelial injury. The injured endothelial cells undergo a morphologic transformation from their normal spindle shape to a rounder configuration, which narrows the sinusoidal lumen and introduces gaps between the cells. Blood flows through the gaps into the space of Disse, detaching endothelial as well as other perisinusoidal cells. The detached cells embolize downstream, causing further sinusoidal and possibly venular obstruction. Eventually, sinusoidal and centrilobular fibrosis ensues, causing hepatic congestion and manifesting clinically as portal hypertension. Later, the resulting low-flow state causes redistribution of the hepatic microcirculation and focal hepatic ischemia, culminating in centrilobular hepatocyte necrosis.<sup>11</sup>

#### **BUDD-CHIARI SYNDROME**

Postsinusoidal obstruction causes sinusoidal (and portal) pressure to increase. Increased sinusoidal pressure promotes centrilobular sinusoidal dilatation and congestion. The congested liver enlarges. Sinusoidal perfusion diminishes, and centrilobular ischemia and necrosis may occur. Stagnant blood flow and an underlying procoagulant state may precipitate concomitant thrombosis of the extrahepatic (10%) and intrahepatic (50%) portal veins. Areas in which there is simultaneous obstruction of the hepatic and portal veins undergo infarction.<sup>12</sup> Perivenular fibrosis develops within weeks of the obstruction.

# **Prevalence and Epidemiology**

SOS occurs after hematopoietic stem cell transplantation. Large-scale epidemiologic studies to assess prevalence, incidence, and demographic factors have not been conducted. The annual incidence of BCS is 1 in 100,000. Women in their third or fourth decades of life are afflicted most commonly.<sup>13</sup>

Veno-occlusive disease is a class of hepatic vascular disorders in which obstruction of sinusoidal or postsinusoidal hepatic venous outflow results in portal hypertension. Historically, this term was used to describe SOS only. More recently, the term has been broadened to include BCS as well as SOS.

BCS may be acute (presentation within 4 weeks of obstruction) or chronic (obstruction present for at least 6 months).

# **Clinical Presentation**

#### SINUSOIDAL OBSTRUCTION SYNDROME

SOS usually manifests 1 to 2 weeks after stem cell transplantation. The first symptom is abdominal pain, followed by ascites, tender hepatomegaly, jaundice, and weight gain (from fluid retention). Laboratory abnormalities include direct hyperbilirubinemia initially with subsequent elevations in alkaline phosphatase and aminotransferases. Renal dysfunction (with up to 50% of patients requiring dialysis), diuretic-resistant fluid retention, recalcitrant thrombocytopenia resulting from splenic sequestration, and encephalopathy occur later. SOS is an acute or subacute illness that either fully resolves, usually in 2 to 3 weeks, or ends in death. All-cause fatality from SOS varies according to disease severity, with fatality rates in one series reported as 9%, 23%, and 98%, in mild, moderate, and severe disease, respectively.<sup>14</sup> Patients who recover do not develop cirrhosis.

SOS is a clinical diagnosis that uses noninvasive criteria devised by groups from Seattle and Baltimore. Both sets of criteria use variable combinations of hyperbilirubinemia, weight gain, ascites, and hepatomegaly within 3 weeks of stem cell transplantation.<sup>15</sup> The diagnosis can be confirmed by liver biopsy. If percutaneous biopsy is contraindicated because of thrombocytopenia, a transjugular approach may be employed, at which time the hepatic venous pressure gradient may also be measured. When elevated above 10 mm Hg, this gradient has a specificity of 90% in the appropriate clinical scenario.<sup>16</sup>

#### **BUDD-CHIARI SYNDROME**

The clinical manifestations and severity of BCS depend on the location and acuity of the venous obstruction. Asymptomatic disease occurs in patients with obstruction of only one hepatic vein or more than one hepatic vein with the development of collateral vessels. Slow obstruction of two hepatic veins results in chronic disease, whereas sudden obstruction of all three hepatic veins or the extrahepatic IVC may produce fulminant hepatic failure.

Patients classically present with ascites, hepatosplenomegaly, and right upper quadrant abdominal pain. Lower extremity edema and venous collaterals on the abdominal wall may be evident. The presentation is acute in 20% of patients. Serum values of aminotransferases, alkaline phosphatase, and bilirubin are moderately elevated, whereas those of plasma coagulation factors are diminished. Twenty-five percent of patients with acute BCS progress to fulminant hepatic failure. The presentation is chronic in 80% of patients; 20% of these patients progress to cirrhosis.<sup>17</sup> Laboratory abnormalities are milder than in the acute form. The prognosis of chronic BCS has improved owing to advances in supportive care, with a current 1-year transplant-free survival of 80% and a 10-year transplant-free survival of 60%.<sup>18</sup>

BCS is an imaging diagnosis. Liver biopsy may suggest the diagnosis but is not specific.

# Pathology

SOS and BCS have similar pathologic features. In both conditions, acute venous obstruction is characterized by dilated centrilobular sinusoids filled with erythrocytes. Associated findings include parenchymal compression as well as atrophy and loss of hepatocytes. Erythrocytes may extravasate into the space of Disse and replace the disappearing hepatocytes. In severe cases, blood-filled lakes may form in the centrilobular zone, with little recognizable hepatic parenchyma. Cholestatic changes may develop at the periphery of the injured areas. Hemosiderinladen macrophages may be present, but inflammation is absent to minimal.

In chronic BCS, fibrosis of the centrilobular zones may develop and may progress to bridging fibrosis between central veins. This form of fibrosis spares the portal tracts, resulting in a pattern termed *reserve lobulation* or *venocentric cirrhosis*, although end-stage cases may be indistinguishable from cirrhosis from other causes.<sup>19</sup>

A key pathologic difference between SOS and BCS is that thrombus within central veins is characteristic of BCS but not of SOS. The central veins in SOS may contain fibrin deposits, as demonstrated via electron microscopy and immunohistochemistry, but thrombus is rare. Grossly, involvement of the liver tends to be uniform in SOS. Involvement may be uneven in BCS, depending on the sites of venous obstructions; areas of the liver drained by nonoccluded hepatic veins may undergo compensatory hypertrophy. BCS may progress to cirrhosis, but SOS does not.

# Imaging

Whereas SOS has a characteristic clinical manifestation and is a unique complication of chemoradiation or hematopoietic stem cell transplantation, hepatic venous obstruction secondary to BCS can be due to many causes, including HCC, venous invasion from an extrahepatic malignancy, or occlusion of the intrahepatic or suprahepatic IVC. Thus, the imaging evaluation should not only seek to secure the diagnosis of hepatic venous obstruction but also attempt to identify the cause of the obstruction.

#### RADIOGRAPHY

Plain radiography has no routine role in the assessment of SOS or BCS because hepatomegaly is the only reliable finding.<sup>20,21</sup>

The venographic findings in SOS are not well characterized. In BCS, venography is considered the diagnostic gold standard.

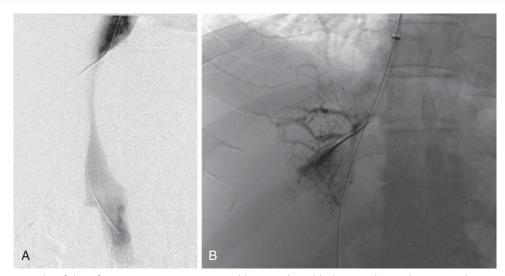
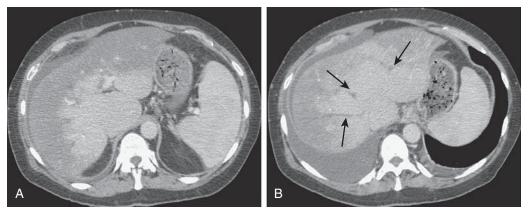


Figure 42-1 A, Venography of the inferior vena cava in a 61-year-old man with Budd-Chiari syndrome shows smooth extrinsic narrowing of the intrahepatic inferior vena cava. B, Injection of the right hepatic vein demonstrates occlusion of the vessel with numerous small collateral vessels in a characteristic spiderweb appearance.



**Figure 42-2** A, Computed tomography image of the abdomen in the patient in Figure 42-1 during the portal venous phase demonstrates the hyperenhancement of the central portions of the liver with hypoenhancement of the periphery. B, Equilibrium-phase image at the level of the hepatic veins continues to show this pattern of enhancement and demonstrates lack of enhancement of the vessels, consistent with occlusion (*arrows*). Also note the presence of ascites.

In acute BCS, liver edema may cause smooth extrinsic narrowing of the IVC and hepatic veins. In chronic BCS, collaterals may form between the hepatic and systemic veins.<sup>22</sup> These small collateral vessels have a characteristic "spiderweb" appearance during venography (Figure 42-1).

# COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING

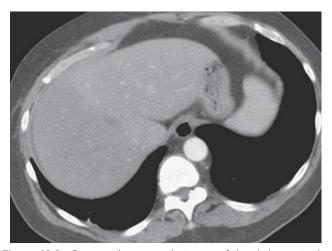
#### Sinusoidal Obstruction Syndrome

Compared to the unaffected liver parenchyma, the affected portion of the liver may be hypoattenuating on computed tomography (CT) and have heterogeneous signal intensity on magnetic resonance imaging (MRI) on unenhanced images. Low attenuation and heterogeneous signal intensity persist after the administration of contrast material.<sup>23</sup> Periportal edema is present and manifests as periportal low attenuation on CT24 and high signal on T2-weighted MRI.<sup>25</sup> Intrahepatic collateral vessels, which can appear as round foci of enhancement on the portal venous and delayed phases of contrast administration, may be observed.<sup>26</sup> Hepatic veins are narrow but patent. In the setting of liver irradiation, the affected region may have a geographic or polygonal morphology that does not conform to an anatomic segment. Other findings include hepatomegaly, gallbladder wall thickening, and ascites.

#### Budd-Chiari Syndrome

In the acute phase of BCS, the liver is enlarged. The periphery of the liver is hypoattenuating on unenhanced CT and of high signal intensity on T2-weighted MRI (Figure 42-2).<sup>27</sup> The liver enhances heterogeneously. Relative hypoenhancement of the periphery of the liver is characteristic.<sup>21</sup> Areas of the liver with independent venous drainage, such as the caudate lobe, hyperenhance on the arterial phase. The resulting fan-shaped enhancement pattern<sup>28</sup> (Figures 42-3 and 42-4) may reverse on delayed-phase imaging, with the caudate lobe and central portion of the liver demonstrating lower attenuation or signal intensity than the periphery. If only one or two hepatic veins are occluded, the characteristic enhancement pattern may be confined to the affected portions of the liver (Figure 42-5). The occluded hepatic veins may be nonvisualized or may show lack of intraluminal enhancement. Coronal imaging may be helpful to assess the IVC for compression or thrombus.<sup>27</sup>

In the chronic phase of BCS, liver fibrosis may be visible as reticulations of low attenuation on unenhanced CT or high signal on T2-weighted MRI. The liver atrophies, particularly in



**Figure 42-3** Computed tomography image of the abdomen in the patient in Figure 42-2 performed during the portal venous phase 2 months before the previous images demonstrates relative hypoattenuation of the right hepatic lobe as a result of occlusion of the right and middle hepatic veins. Note that the remainder of the liver demonstrates a normal enhancement pattern, because venous drainage of the left hepatic lobe is not obstructed.

the periphery. If the IVC is not obstructed, there may be compensatory hypertrophy of the caudate lobe as a result of direct venous drainage into the IVC. Ultimately, the hypertrophied caudate lobe may compress the intrahepatic IVC, exacerbating the outflow obstruction. Large intrahepatic and extrahepatic collateral vessels, as well as ascites and splenomegaly may be present (Figure 42-6).<sup>29,30</sup> The chronically thrombosed hepatic veins may be difficult to identify. The enhancement differences between the caudate lobe and the periphery of the liver become less noticeable and may no longer be appreciated.

Regenerative nodules (RNs), particularly in portal regions, may develop with long-standing hepatic venous obstruction. These nodules range from 0.5 to 4.0 cm and are sometimes hyperattenuating on unenhanced CT, hyperintense on T1-weighted, and hypointense on T2-weighted MR images, possibly owing to intralesional copper deposition (Figure 42-7).<sup>29</sup> The nodules may enhance avidly during the arterial phase and fade to isoattenuation or isointensity during the portal venous and equilibrium phases (Figure 42-8).<sup>29</sup> Distinguishing these RNs from HCC can be difficult, but HCCs tend to wash out to hypoattenuation or hypointensity during portal venous and delayed phases. In addition, multiplicity (>10) and smaller size (<4 cm) favor a diagnosis of RNs.<sup>30</sup>

#### ULTRASOUND

#### Sinusoidal Obstruction Syndrome

Ultrasound is frequently performed in suspected SOS, mainly to exclude other causes of hepatic dysfunction.<sup>20</sup> It is usually nonspecific, but some findings suggest the correct diagnosis in

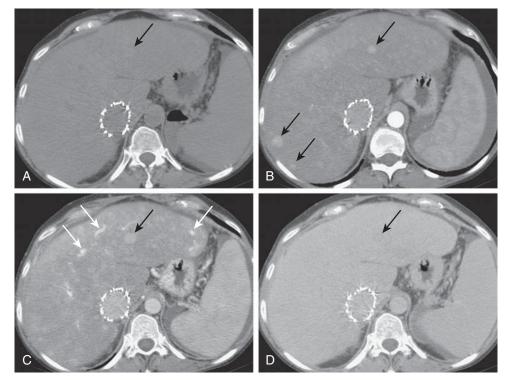
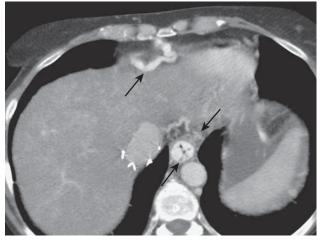


Figure 42-4 A, Unenhanced computed tomography image of the abdomen performed in a 56-year-old woman with chronic hepatic venous obstruction demonstrates a lobular liver with multiple regenerative nodules (*black arrow*). The nodules are slightly hyperattenuating. After the administration of an iodinated contrast agent, the nodules enhance avidly during the arterial (B) and portal venous (C) phases of the study, becoming slightly hypoattenuating on the equilibrium phase image (D). Note the intrahepatic collateral vessels (*white arrows*, C), ascites, and stent within the intrahepatic inferior vena cava.

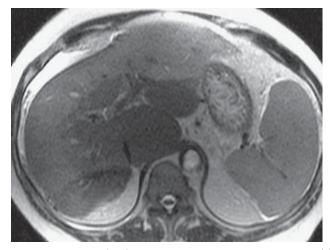


**Figure 42-5** Portal venous phase computed tomography image from the patient in Figure 42-4 demonstrates extrahepatic collateral vessels (*arrows*), as well as paraesophageal and submucosal esophageal varices.

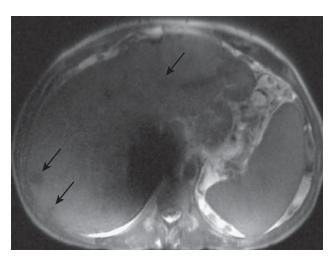
the appropriate clinical setting.<sup>31,32</sup> Elevation of the hepatic artery resistive index above 0.75 is characteristic of SOS and helps differentiate it from graft-versus-host disease (GVHD).<sup>33,34</sup> Abnormalities in the portal vein, including pulsatile, bidirectional, and reversed flow, also have been reported.<sup>35</sup> Gallbladder wall thickening, ascites, hepatomegaly, and narrowing of the hepatic veins are also evident.

#### Budd-Chiari Syndrome

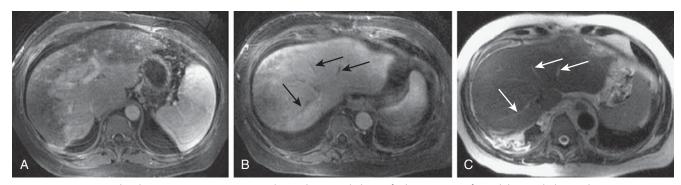
Doppler ultrasound imaging is highly sensitive and specific for the diagnosis of BCS. Abnormalities of flow within the hepatic veins are present in nearly all cases, often manifesting as an absent, flattened, or reversed waveform (Figure 42-9).<sup>36,37</sup> Acutely, thrombus may be detectable in the hepatic veins. Flow in the portal vein may be antegrade (hepatopetal), bidirectional, or retrograde (hepatofugal). In addition, the distribution of the abnormality may vary with the extent of hepatic venous occlusion, with abnormal portal flow present only in the affected segments. Ultrasonography may detect abnormalities of the IVC accounting for venous obstruction, such as thrombus or membranes. Heterogeneity of the liver parenchyma,



**Figure 42-6** T2-weighted magnetic resonance image in a 61-year-old man with Budd-Chiari syndrome (see also Figures 42-2 and 42-3) demonstrates increased T2 signal in the periphery of the liver.



**Figure 42-8** Proton-density imaging in the 56-year-old woman shown in Figure 42-4 demonstrates numerous regenerative nodules (*arrows*).



**Figure 42-7** A, T1-weighted magnetic resonance image during the arterial phase of administration of a gadolinium chelate in the patient in Figures 42-2, 42-3, and 42-6 demonstrates hyperenhancement of the central portion of the liver. B, In addition, occlusion of the hepatic veins (*arrows*, B and C) is demonstrated both by lack of enhancement during the delayed phase of imaging and by the absence of flow voids on the T2-weighted pre-gadolinium image (C).

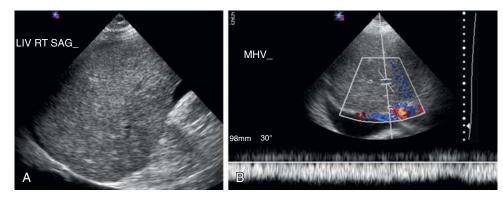


Figure 42-9 A, Ultrasound image of a 61-year-old man with Budd-Chiari syndrome (see also Figures 42-2, 42-3, 42-6, and 42-7) demonstrates a heterogeneous liver. B, Duplex Doppler ultrasound image in the region of the middle hepatic vein shows a flattened waveform with absence of the normal respiratory or cardiac variation.

hepatomegaly, ascites, collateral vessels, and splenomegaly also can be detected.

#### NUCLEAR MEDICINE

#### Sinusoidal Obstruction Syndrome

Nuclear medicine is not routinely used in the evaluation of SOS, although heterogeneous liver uptake and increased lung uptake of technetium-99m (<sup>99m</sup>Tc) sulfur colloid have been reported.<sup>38,39</sup>

#### Budd-Chiari Syndrome

Nuclear medicine has a limited role in the diagnosis of hepatic venous occlusion. Hepatobiliary iminodiacetic acid or <sup>99m</sup>Tc sulfur colloid scans may demonstrate an appearance very similar to that seen on contrast-enhanced MRI or CT, with poor uptake in the periphery of the liver and normal to increased uptake within the central liver and caudate lobe (Figure 42-10).<sup>40</sup>

#### IMAGING ALGORITHMS

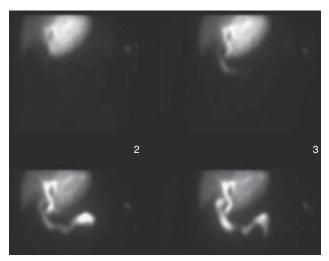
#### Sinusoidal Obstruction Syndrome

Imaging findings are not diagnostic of SOS but may be used to support clinical and laboratory data. A Doppler ultrasound or CT evaluation may initially be obtained to exclude other causes of post–stem cell transplant cholestasis. MRI may be performed if CT is contraindicated but adds little additional information.

#### Suspicion of Budd Chiari Syndrome

In acute BCS, Doppler ultrasound is initially performed to detect abnormal flow suggestive of venous obstruction and, in some instances, the thrombus itself. If the ultrasound evaluation is abnormal, further evaluation with CT or MRI is warranted to verify the obstruction and distinguish between intrahepatic and extrahepatic causes. If treatment is desired, venography may provide useful information to guide shunting or stenting.

In chronic BCS, CT or MRI is employed to detect parenchymal abnormalities suggestive of cirrhosis and sequelae of portal hypertension. If cirrhosis is present, patients are at increased risk for developing HCC and, in our opinion, should be considered for surveillance for this tumor. The incidence of HCC in patients with cirrhosis secondary to BCS is unknown, however, and the American Association for the Study of Liver Diseases (AASLD) does not provide specific guidelines for HCC surveillance in these patients.



**Figure 42-10** Hepatobiliary iminodiacetic acid scan performed at the time of occlusion of the right and middle hepatic veins in a 61-year-old-man (see also Figures 42-2, 42-3, 42-6, 42-7, and 42-9) demonstrates decreased uptake of radiotracer within the right hepatic lobe in a pattern similar to that seen on the computed tomography image in Figure 42-3.

# **Differential Diagnosis**

#### SINUSOIDAL OBSTRUCTION SYNDROME

Conditions in the clinical differential diagnosis of SOS are those that may result in post–stem cell transplant cholestasis. The most challenging distinction is from acute hepatic GVHD. Although the physical examination and laboratory findings are similar, hepatic GVHD typically occurs as part of a syndrome that includes a rash and diarrhea. Other causes of posttransplant cholestasis are easily differentiated from SOS on clinical and laboratory findings and include sepsis, viral and fungal hepatic infections, medication toxicity, hemolysis, and total parenteral nutrition.

Imaging findings may help differentiate SOS from GVHD in post–stem cell transplant patients. Periportal edema, narrowing of the hepatic veins, and elevation of the hepatic arterial resistive index suggest SOS, whereas small bowel wall thickening is more often seen in GVHD. As opposed to BCS, the central portions of the liver and caudate lobe do not demonstrate a different enhancement pattern from the rest of the liver.<sup>24</sup>

#### **Classic Signs**

#### Sinusoidal Obstruction Syndrome

- Patent but narrowed hepatic veins
- Elevated hepatic arterial resistive index
- Periportal edema and ascites
- Diffuse involvement of the liver or involvement of the region of the liver that has been irradiated (may not be in an anatomic distribution)

#### Acute Budd-Chiari Syndrome

- Hepatic venous collateral vessels in a spiderweb pattern
- Hyperenhancement of the central liver and caudate lobe on arterial phase imaging, which may reverse on delayed-phase imaging
- Intrahepatic collateral vessels
- Occluded hepatic veins
- Abnormal or absent hepatic venous waveform on Doppler ultrasonography

Chronic Budd-Chiari Syndrome

- Hypertrophy of the central liver and caudate with atrophy of the periphery
- RNs, which may show arterial phase hypervascularity

#### **BUDD-CHIARI SYNDROME**

Acute BCS shares clinical features with other causes of fulminant hepatic failure, such as acetaminophen toxicity, viral hepatitis, or ischemic hepatitis. Typically, however, the other causes of fulminant disease do not demonstrate prominent ascites and have serum aminotransferase values that are two to six times more elevated than seen in BCS.

Chronic BCS may resemble cirrhosis and portal hypertension as seen with any cause of chronic liver disease, and a comprehensive workup is required to systematically rule out other possibilities. Patients with right-sided heart failure may develop congestive hepatopathy similar to that observed in BCS but have distinguishing features of right-sided heart failure, such as jugular venous distention, and also may have signs of left-sided heart failure, such as pulmonary edema and diminished cardiac ejection fraction.

Acute BCS is associated with outflow obstruction and typically is easily differentiated with imaging from other causes of fulminant hepatic failure.

Distinguishing cirrhosis secondary to parenchymal disease such as hepatitis infection and changes resulting from chronic BCS can be challenging. In chronic BCS, the hepatic veins may be undetectable on CT or MRI. The RNs seen in most causes of cirrhosis do not typically demonstrate arterial enhancement and are often smaller than those seen in chronic BCS.

# **Treatment**

#### SINUSOIDAL OBSTRUCTION SYNDROME

Because effective therapies are lacking, focus has shifted to preventive strategies. Ultimately, the most successful prevention involves judicious selection of pretransplant conditioning regimens in patients at highest risk for developing SOS.

Targeted therapy is implemented in those with severe SOS, because most patients with mild or moderate SOS survive with supportive care alone. In severe SOS, dialysis and ventilatory support are often necessary; experimental anticoagulants show promise for salvage therapy.<sup>41</sup>

Transjugular intrahepatic portosystemic shunting (TIPS) may be necessary to control portal hypertension in patients with severe SOS.<sup>42</sup> Liver transplantation may be performed as an option of last resort in patients who received stem cell transplantation for benign conditions.

#### **BUDD-CHIARI SYNDROME**

Medical therapy for mild BCS uses diuretics to control ascites, anticoagulants to prevent thrombus extension, and thrombolytics to dissolve the clot.

The object of surgical therapy of BCS is to decompress the liver by restoring hepatic outflow, thereby reducing sinusoidal pressure. Minimally invasive techniques, such as angioplasty and stenting, are used in conjunction with either systemic or in situ thrombolytic therapy. Angioplasty maintains 2-year patency in 50% of patients. The addition of stents improves long-term patency to 90%, but stents generally are not removable and may potentially complicate liver transplantation if placed above the IVC.

Failure of angioplasty and stenting may require the placement of a TIPS or surgical shunt, particularly in the setting of acute hepatic decompensation or as a bridge to transplantation. TIPS alleviates sinusoidal pressure by providing ancillary venous outflow that bypasses the obstruction. It is preferred to surgical shunting at most centers because it avoids laparotomy and has fewer serious complications. Long-term TIPS patency approximates 50%. Portocaval and mesocaval shunts are the two most common surgical shunts. These shunts decompress the liver by inducing hepatofugal blood flow through the portal vein and are most effective when the IVC is patent. Shunt dysfunction occurs in 30% of patients secondary to thrombosis, stenosis, or compression of the IVC by the growing caudate lobe.<sup>43</sup>

Liver transplantation is an option in patients in whom TIPS or surgical shunting has failed or who present with fulminant hepatic failure or decompensated cirrhosis. Ten-year survival approaches 85% in some series.<sup>44</sup> When anticoagulation is administered, the risk for recurrent BCS following transplant is approximately 10%.<sup>45</sup>

#### What the Referring Physician Needs to Know

- As a class, the hepatic veno-occlusive diseases are circulatory disorders that cause portal hypertension by obstructing venous outflow at the sinusoidal or postsinusoidal level.
- SOS is a toxin-mediated disorder of hepatic sinusoids that occurs as a complication of chemoradiation or myeloablative hematopoietic stem cell transplantation.
- SOS manifests with varying severity and needs to be differentiated from other causes of posttransplant cholestasis.
- Treatment strategies for SOS are lacking, and thus attention is placed on prevention.

- BCS represents a postsinusoidal obstruction that may occur from the small hepatic veins to the suprahepatic IVC.
- Common causes of BCS include intravascular thrombosis, tumor invasion, or extrinsic compression.
- Treatment of BCS includes medical therapy with anticoagulation and thrombolytics, procedural interventions such as TIPS and surgical shunts, and, in the most severe cases, liver transplantation.
- Whereas imaging plays an accessory role to clinical presentation in the diagnosis of SOS, it is the primary diagnostic tool in BCS.

#### **Key Points**

- Although the diagnosis of SOS in high-risk patients is primarily based on clinical and laboratory findings, imaging findings supporting the diagnosis include periportal edema, narrowing of the hepatic veins, abnormal attenuation or signal intensity on unenhanced CT or MRI, respectively, and elevation of the hepatic arterial resistive index on Doppler ultrasound.
- Although venography remains the gold standard for the diagnosis of BCS, its current role is predominantly for procedural planning, such as before TIPS placement.
- Hyperenhancement of the central liver and caudate lobe during the arterial and portal venous phases of

contrast-enhanced CT or MRI is characteristic of acute occlusion of the hepatic veins.

- Chronic occlusion of the hepatic veins results in atrophy of the liver, with relative sparing or hypertrophy of the caudate lobe and formation of regenerative nodules and intrahepatic collateral vessels.
- Abnormalities of flow within the hepatic veins on Doppler ultrasound are present in nearly all cases of hepatic venous occlusion, manifesting as flattening of the waveform or reversal or absence of blood flow.

#### SUGGESTED READINGS

- Aydinli M, Bayraktar Y: Budd-Chiari syndrome: etiology, pathogenesis and diagnosis. World J Gastroenterol 13:2693–2696, 2007.
- Bayraktar UD, Seren S, Bayraktar Y: Hepatic venous outflow obstruction: three similar syndromes. *World J Gastroenterol* 13:1912–1927, 2007.
- Brancatelli G, Vilgrain V, Federle MP, et al: Budd-Chiari syndrome: spectrum of imaging findings. *AJR Am J Roentgenol* 188:W168–W176, 2007.
- Buckley O, O'Brien J, Snow A, et al: Imaging of Budd-Chiari syndrome. *Eur Radiol* 17:2071–2078, 2007.
- DeLeve LD: Vascular liver diseases. Curr Gastroenterol Rep 5:63-70, 2003.
- Helmy A: Updates in the pathogenesis and therapy of hepatic sinusoidal obstruction syndrome [Review]. *Aliment Pharmacol Ther* 23:11–25, 2006.
- Kumar S, DeLeve L, Kamath PS, et al: Hepatic veno-occlusive disease (sinusoidal obstruction syndrome) after hematopoietic stem cell transplantation. *Mayo Clin Proc* 78:589–598, 2003.

McDonald GB, Sharma P, Matthews DE, et al: Venoocclusive disease of the liver after bone marrow transplantation: diagnosis, incidence, and predisposing factors. *Hepatology* 4:116–122, 1984.

Senzolo M, Germani G, Cholongitas E, et al: Venoocclusive disease: update on clinical management. World J Gastroenterol 13:3918–3924, 2007.

#### REFERENCES

- 1. DeLeve LD: Vascular liver diseases. *Curr Gastroenterol Rep* 5:63–70, 2003.
- Shulman HM, Fisher LB, Schoch HG, et al: Veno-occlusive disease of the liver after marrow transplantation: histological correlates of clinical signs and symptoms. *Hepatology* 19:1171– 1180, 1994.
- Kumar S, DeLeve L, Kamath PS, et al: Hepatic veno-occlusive disease (sinusoidal obstruction syndrome) after hematopoietic stem cell transplantation. *Mayo Clin Proc* 78:589–598, 2003.
- Dawson LA, Ten Haken RK, Lawrence TS: Partial irradiation of the liver. Semin Radiat Oncol 11:240–246, 2001.
- McDonald GB, Sharma P, Matthews DE, et al: Veno-occlusive disease of the liver after bone marrow transplantation: diagnosis, incidence, and predisposing factors. *Hepatology* 4:116–122, 1984.

- 6. Helmy A: Updates in the pathogenesis and therapy of hepatic sinusoidal obstruction syndrome [Review]. *Aliment Pharmacol Ther* 23: 11–25, 2006.
- Aydinli M, Bayraktar Y: Budd-Chiari syndrome: etiology, pathogenesis and diagnosis. World J Gastroenterol 13:2693–2696, 2007.
- Denninger MH, Chait Y, Casadevall N, et al: Cause of portal or hepatic venous thrombosis in adults: the role of multiple concurrent factors. *Hepatology* 31:587–591, 2000.
- 9. Hirshberg B, Shouval D, Fibach E, et al: Flow cytometric analysis of autonomous growth of erythroid precursors in liquid culture detects occult polycythemia vera in the Budd-Chiari syndrome. *J Hepatol* 32:574–578, 2000.
- Deltenre P, Denninger MH, Hillaire S, et al: Factor V Leiden related Budd-Chiari syndrome. *Gut* 48:264–268, 2001.

- DeLeve LD, McCuskey RS, Wang X, et al: Characterization of a reproducible rat model of hepatic veno-occlusive disease. *Hepatology* 29: 1779–1791, 1999.
- Tanaka M, Wanless IR: Pathology of the liver in Budd-Chiari syndrome: portal vein thrombosis and the histogenesis of veno-centric cirrhosis, veno-portal cirrhosis, and large regenerative nodules. *Hepatology* 27:488–496, 1998.
- Mahmoud AF, Mendoza A, Meshikhes AN, et al: Clinical spectrum, investigations and treatment of Budd-Chiari syndrome. *Q J Med* 89:37–43, 1996.
- McDonald GB, Hinds MS, Fisher LD, et al: Veno-occlusive disease of the liver and multiorgan failure after bone marrow transplantation: a cohort study of 355 patients. *Ann Intern Med* 118:255–267, 1993.

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- Carreras E, Granena A, Navasa M, et al: On the reliability of clinical criteria for the diagnosis of hepatic veno-occlusive disease. *Ann Hematol* 66:77–80, 1993.
- Shulman HM, Gooley T, Dudley MD, et al: Utility of transvenous liver biopsies and wedged hepatic venous pressure measurements in sixty marrow transplant recipients. *Transplantation* 59:1015–1022, 1995.
- 17. De BK, Sen S, Biswas PK, et al: Occurrence of hepatopulmonary syndrome in Budd-Chiari syndrome and the role of venous decompression. *Gastroenterology* 122:897–903, 2002.
- Murad SD, Valla DC, de Groen PC, et al: Determinants of survival and the effect of portosystemic shunting in patients with Budd-Chiari syndrome. *Hepatology* 39:500–508, 2004.
- Wanless IR: Vascular disorders. In Burt AD, Portmann BC, Ferrell LD, editors: MacSween's pathology of the liver, ed 5, New York, 2006, Churchill Livingstone, p 621.
- Senzolo M, Germani G, Cholongitas E, et al: Veno-occlusive disease: update on clinical management. World J Gastroenterol 13:3918–3924, 2007.
- Buckley O, O'Brien J, Snow A, et al: Imaging of Budd-Chiari syndrome. *Eur Radiol* 17:2071– 2078, 2007.
- Cho OK, Koo JH, Kim YS, et al: Collateral pathways in Budd-Chiari syndrome: CT and venographic correlation. *AJR Am J Roentgenol* 167: 1163–1167, 1996.
- Chiou SY, Lee RC, Chi KH, et al: The triplephase CT image appearance of post-irradiated livers. *Acta Radiol* 42:526–531, 2001.
- 24. Erturk SM, Mortele KJ, Binkert CA, et al: CT features of hepatic veno-occlusive disease and hepatic graft-versus-host disease in patients after hematopoietic stem cell transplantation. *AJR Am J Roentgenol* 186:1497–1501, 2006.
- van den Bosch MA, van Hoe L: MR imaging findings in two patients with hepatic venoocclusive disease following bone marrow transplantation. *Eur Radiol* 10:1290–1293, 2000.

- 26. Mortele KJ, Van Vlierberghe H, Wiesner W, et al: Hepatic veno-occlusive disease: MRI findings. *Abdom Imaging* 27:523–526, 2002.
- Noone TC, Semelka RC, Siegelman ES, et al: Budd-Chiari syndrome: spectrum of appearances of acute, subacute, and chronic disease with magnetic resonance imaging. *J Magn Reson Imaging* 11:44–50, 2000.
- Camera L, Mainenti PP, Di Giacomo A, et al: Triphasic helical CT in Budd-Chiari syndrome: patterns of enhancement in acute, subacute and chronic disease. *Clin Radiol* 61:331–337, 2006.
- 29. Brancatelli G, Federle MP, Grazioli L, et al: Benign regenerative nodules in Budd-Chiari syndrome and other vascular disorders of the liver: radiologic-pathologic and clinical correlation. *Radiographics* 22:847–862, 2002.
- Brancatelli G, Vilgrain V, Federle MP, et al: Budd-Chiari syndrome: spectrum of imaging findings. *AJR Am J Roentgenol* 188:W168–W176, 2007.
- Teefey SA, Brink JA, Borson RA, et al: Diagnosis of veno-occlusive disease of the liver after bone marrow transplantation: value of duplex sonography. *AJR Am J Roentgenol* 164:1397–1401, 1995.
- 32. Hommeyer SC, Teefey SA, Jacobson AF, et al: Veno-occlusive disease of the liver: prospective study of US evaluation. *Radiology* 184:683–686, 1992.
- 33. Lassau N, Leclere J, Auperin A, et al: Hepatic veno-occlusive disease after myeloablative treatment and bone marrow transplantation: value of gray-scale and Doppler US in 100 patients. *Radiology* 204:545–552, 1997.
- Herbetko J, Grigg AP, Buckley AR, et al: Venoocclusive liver disease after bone marrow transplantation: findings at duplex sonography. *AJR Am J Roentgenol* 158:1001–1005, 1992.
- 35. Brown BP, Abu-Yousef M, Farner R, et al: Doppler sonography: a noninvasive method for evaluation of hepatic venocclusive disease. AJR Am J Roentgenol 154:721–724, 1990.

- Makuuchi M, Hasegawa H, Yamazaki S, et al: Primary Budd-Chiari syndrome: ultrasonic demonstration. *Radiology* 152:775–779, 1984.
- Millener P, Grant EG, Rose S, et al: Color Doppler imaging findings in patients with Budd-Chiari syndrome: correlation with venographic findings. *AJR Am J Roentgenol* 161:307– 312, 1993.
- Jacobson AF, Marks MA, Kaplan WD: Increased lung uptake on technetium-99m-sulfur colloid liver-spleen scans in patients with hepatic venoocclusive disease following bone marrow transplantation. J Nucl Med 31:372–374, 1990.
- Joshi MJ, Ford PV, Vogel JM, et al: Grossly abnormal liver-spleen scan in a patient with veno-occlusive disease of the liver that normalized completely on follow-up. *Clin Nucl Med* 18:590–593, 1993.
- 40. Meindok H, Langer B: Liver scan in Budd-Chiari syndrome. J Nucl Med 17:365–368, 1976.
- 41. Richardson PG, Murakami C, Jin Z, et al: Multiinstitutional use of defibrotide in 88 patients after stem cell transplantation with severe venoocclusive disease and multisystem organ failure: response without significant toxicity in a highrisk population and factors predictive of outcome. *Blood* 100:4337–4343, 2002.
- Zenz T, Rossle M, Bertz H, et al: Severe venoocclusive disease after allogeneic bone marrow or peripheral stem cell transplantation: role of transjugular intrahepatic portosystemic shunt (TIPS). *Liver* 21:31–36, 2001.
- Panis Y, Belghiti J, Valla D, et al: Portosystemic shunt in Budd-Chiari syndrome: long-term survival and factors affecting shunt patency in 25 patients in Western countries. *Surgery* 115:276– 281, 1994.
- 44. Ulrich F, Pratschke J, Neumann U, et al: Eighteen years of liver transplantation experience in patients with advanced Budd-Chiari syndrome. *Liver Transpl* 14:133–135, 2008.
- Srinivasan P, Rela M, Prachalias A, et al: Liver transplantation for Budd-Chiari syndrome. *Transplantation* 7:973–977, 2002.

# **Cholestatic Hepatic Disorders**

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Primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC) are the two most common and well-characterized primary cholestatic disorders. In contrast to pathologic processes derived primarily from hepatocellular dysfunction, such as viral hepatitis and autoimmune hepatitis, the primary insult in cholestatic diseases centers on the bile duct epithelium. As with other diffuse liver diseases, PBC and PSC may progress to liver fibrosis, portal hypertension, cirrhosis, and/or malignancy.

# **Etiology and Pathogenesis**

#### PRIMARY BILIARY CIRRHOSIS

PBC is a chronic, progressive cholestatic disease of autoimmune origin affecting the small to medium intrahepatic bile ducts. Pathogenically, this is manifested as immune-mediated destruction of bile ducts ("ductopenia"), as well as portal inflammation. As a result, biliary secretion is impaired, toxins accumulate within the liver, and inflammation is exacerbated. Ultimately, the process progresses to fibrosis and cirrhosis.<sup>1</sup>

The cause of PBC is multifactorial. Geographic variations in disease prevalence suggest that environmental factors play a role in the pathogenesis. It is thought that an environmental trigger, such as an infection or toxin, either directly causes bile duct injury or initiates the process of autoimmunity.<sup>2</sup> Infectious organisms, including *Helicobacter pylori, Escherichia coli, Chlamydia pneumoniae,* and retroviruses, as well as toxins containing halogenated hydrocarbons (found in pesticides and cosmetics), have been implicated.

Pathogenically, cellular and humoral immune mechanisms are involved. CD4+ and CD8+ T lymphocytes aggregate in regions of periportal inflammation and trigger cytokinemediated cytotoxic reactions. The antimitochondrial antibody (AMA), present in 90% to 95% of patients, is an autoantibody targeted to the E2 subunit of the pyruvate dehydrogenase complex (PDC-E2), which is associated with an immunologic cascade resulting in bile duct cell apoptosis.

#### PRIMARY SCLEROSING CHOLANGITIS

PSC is a chronic, cholestatic disorder associated with inflammatory bowel disease (IBD) and involves the medium to large intrahepatic and extrahepatic bile ducts. Pathogenically, the disease manifests as progressive biliary necroinflammation, fibrosis, multifocal stricturing, and obstruction. Prolonged retention of bile and associated toxins, along with inflammation resulting from recurrent or chronic cholangitis, may ultimately lead to hepatic fibrosis and cirrhosis. The cause of PSC is thought to be multifactorial. Proposed mechanisms include humoral and cell-mediated immunologic insults to the bile duct epithelium, ischemic ductal injury, and ductal damage induced by chronic cholangitis and recurrent portal phlebitis in IBD patients with increased bacterial permeability across the inflamed colonic wall.<sup>3</sup> As evidenced by familial pedigree studies, genetic factors may make certain patients particularly susceptible to PSC pathogenesis.<sup>4</sup>

The immunologic underpinnings of PSC are supported by the presence of various autoantibodies and immunoglobulins. Autoantibodies, such as antinuclear antibody (ANA), anti-smooth muscle antibody (ASMA), and peripheral antineutrophil cytoplasmic antibody (P-ANCA), suggest a loss of self-tolerance to autoantigens, whereas hypergammaglobulinemia and increased levels of serum immunoglobulin M (IgM) imply a heightened immunologic response. Later stages of the immunologic response are mediated by CD4+ and CD8+ T lymphocytes, which are heavily represented in the periportal inflammatory infiltration of PSC.

# **Prevalence and Epidemiology**

### PRIMARY BILIARY CIRRHOSIS

The prevalence of PBC varies geographically but is generally thought to be greatest among northern Europeans.<sup>1</sup> Published PBC prevalence rates range from 1.91 to 40.2 per 100,000 persons; incidence rates range from 0.33 to 5.8 per 100,000 persons/year.<sup>5</sup> Women account for 90% of cases. Disease onset is in adulthood, with a median age at diagnosis of 50 years. In familial pedigree studies, 6% of affected individuals have at least one family member with PBC. The concordance frequency of PBC in monozygotic twins is 63%.<sup>6,7</sup> Risk factors for PBC pathogenesis include smoking, prior abdominal surgeries, and other comorbid autoimmune diseases.<sup>8</sup>

#### PRIMARY SCLEROSING CHOLANGITIS

Worldwide, published prevalence rates of PSC range from 0 to 16.2 per 100,000 persons; incidence rates range from 0 to 1.3 per 100,000 persons per year.<sup>5</sup> As with PBC, rates vary geographically. Approximately 75% of patients with PSC are males, and the average age at diagnosis is 40 years. Family history appears to play an important role; the risk for PSC in first-degree relatives of afflicted patients is roughly 100-fold greater than in the general population.<sup>9</sup>

The most important risk factor for PSC is IBD. Approximately 75% of patients with PSC have IBD, with ulcerative colitis (UC) accounting for 90% of the IBD cases. Conversely,

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in patients with UC, the risk for developing PSC approaches 4%, with the highest risk in male patients with pancolitis.<sup>10</sup>

# **Clinical Presentation**

#### PRIMARY BILIARY CIRRHOSIS

PBC is a progressive disease. Approximately 40% of patients are symptomatic at diagnosis, and an additional 25% develop symptoms within a few years, with rapid progression to cirrhosis over a decade.<sup>11</sup>

The most common symptoms are fatigue and pruritus, occurring in 60% and 50% of patients, respectively.<sup>1</sup> Malabsorption secondary to bile salt deficiency may occur in advanced disease and manifest as steatorrhea and fat-soluble vitamin deficiencies. Bone pain and fractures resulting from osteopenia and osteoporosis related to vitamin D deficiency are common. The clinical manifestations of cirrhosis and portal hypertension in PBC are similar to other causes of chronic liver disease, except that variceal hemorrhage may occur earlier in the disease course, before the development of true cirrhosis.<sup>12</sup> In patients who have progressed to cirrhosis, hepatocellular carcinoma (HCC) occurs with an average yearly incidence of approximately 7%, which is slightly higher than the published incidence for most other causes of cirrhosis.<sup>13</sup>

The serologic hallmark of PBC is AMA positivity. These antibodies have a sensitivity and specificity for PBC of 90% and 95%, respectively.<sup>14</sup> Characteristically, these patients have striking elevations in the serum alkaline phosphatase level (three to four times the upper limit of normal), as well as elevations in gamma-glutamyltransferase (GGT) and abnormalities in immunoglobulins, particularly IgM. Imaging is obtained to exclude biliary obstruction. A liver biopsy is almost always performed for staging and prognostication and as a baseline for evaluating the response to treatment. A definitive diagnosis of PBC requires the presence of AMAs, elevated alkaline phosphatase for 6 months, and characteristic histologic findings; a probable diagnosis requires two of these three criteria.<sup>1</sup>

#### PRIMARY SCLEROSING CHOLANGITIS

Like PBC, PSC is a progressive disease. The most important prognostic factor for predicting the rate of progression is the presence or absence of symptoms at the time of diagnosis. Most patients with PSC are asymptomatic at the time of diagnosis; transplant-free survival in these patients is on average 10 to 12 years, whereas survival is halved in those symptomatic at diagnosis.

Characteristic symptoms of PSC are fatigue and pruritus, which typically do not occur until the disease progresses to more advanced stages. Frequent but nonspecific symptoms include right upper quadrant abdominal pain, nausea, anorexia, weight loss, and jaundice. Malabsorption secondary to bile salt deficiency, in the form of steatorrhea and fat-soluble vitamin deficiencies, and osteoporosis-related bone disease manifest in the latest stages of disease.

Twenty percent of patients develop a dominant stricture, manifesting as mechanical obstruction and acute cholangitis. A dominant stricture has been defined as a stenosis with a diameter of 1.5 mm in the common bile duct or 1 mm in the hepatic duct. Although stenotic lesions are far more often benign than malignant, this finding should always raise the suspicion of the presence of a cholangiocarcinoma. Patients with PSC are at risk for developing cholangiocarcinoma (10-year cumulative incidence of 7% to 9%), typically as patients reach their 40s, roughly 20 years before onset in patients without PSC.<sup>15</sup> The prognosis is grim, with median survival of 6 months after diagnosis. In patients in whom cirrhosis develops, HCC occurs at similar rates as in other causes of chronic liver disease.

As stated earlier, there is a strong association between PSC and UC. Although the symptoms of UC may predate or follow the diagnosis of PSC, the majority of patients (~75%) have established UC at the time of their PSC diagnosis. Proctocolectomy for UC has no impact on the course of PSC, and PSC may be detected years after proctocolectomy.<sup>16</sup> UC patients with PSC have a five times greater risk for developing colorectal cancer than UC patients without PSC.<sup>17</sup>

Serologic immunologic markers are abundant in patients with PSC: 30% have hypergammaglobulinemia, 50% demonstrate elevated serum IgM titers, and approximately 65% exhibit P-ANCAs.<sup>18</sup> In contrast to PBC, PSC patients lack AMA positivity. In addition to these immunologic measures, PSC is particularly suspected in patients with IBD with markedly elevated serum alkaline phosphatase levels and GGT. The serum aminotransferases are typically elevated to a lesser degree. The serum bilirubin value is normal early in the disease course but rises in advanced cases. Imaging plays a vital role in the diagnosis of PSC by elucidating ductal abnormalities, and for the detection of cholangiocarcinoma and HCC. Liver biopsy is obtained for prognostication and staging but may not help with diagnosis because the usual findings of ductopenia and portal inflammation and fibrosis are nonspecific and may be missed, owing to their patchy distribution and sampling error inherent to biopsy.

# Pathology

#### PRIMARY BILIARY CIRRHOSIS

In the early stages of PBC, the liver is slightly enlarged and is variably bile stained. In later stages, the liver is cirrhotic and has a green hue, reflecting the extensive cholestasis. The microscopic hallmark of PBC is destructive, nonsuppurative cholangitis affecting the interlobular and septal bile ducts, resulting in duct loss and subsequent biliary cirrhosis.<sup>19</sup>

With disease progression, there is patchy necrosis of the periportal hepatocytes and delicate periportal fibrosis, often with ductular proliferation. Florid duct lesions become less common as the disease advances into the later stages. Fibrous septa appear and extend in a portal-portal distribution, later evolving into biliary cirrhosis. This type of cirrhosis results in regenerative nodules (RNs) with serpentine or garland-like borders, as opposed to the roughly spherical RNs seen in the usual forms of cirrhosis. The RNs in biliary cirrhosis have some resemblance to the pieces of a jigsaw puzzle.

#### PRIMARY SCLEROSING CHOLANGITIS

Similar to the gross findings of PBC, the liver in early PSC is slightly enlarged and variably bile stained, progressing to biliary cirrhosis in the later stages. One characteristic gross finding in PSC is the presence in the hilum of cholangiectases, cystic collections of bilious, dark green material measuring up to several centimeters in size and representing cystically dilated intrahepatic ducts.<sup>20</sup>

TABLE         Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Cholestatic Hepatic Disorders			
Modality	Accuracy	Limitations	Pitfalls
PRIMARY BILIARY CIRRHOSIS			
СТ	No data on the accuracy of CT in the diagnosis of PBC		
MRI	In one retrospective study, periportal halo sign had 43% sensitivity and 100% specificity for diagnosis of PBC in patients with known cirrhosis	Low sensitivity	
MRCP	No data on the accuracy of MRCP in the diagnosis of PBC		
Ultrasound	No data on the accuracy of ultrasound in the diagnosis of PBC		
PRIMARY SCLEROSING CHOLANGITIS			
СТ	No data on the accuracy of CT in the diagnosis of PSC		
MRCP	Sensitivity of 85% to 88% Specificity of 92% to 97% Positive predictive value of 85% to 94% Negative predicted value of 93% to 94% Overall diagnostic accuracy is 90%.	May be negative in the early stages of PSC Lower spatial resolution than ERCP Does not permit tissue sampling or treatment of stenoses	Secondary causes of chronic cholangitis may be indistinguishable from PSC. Biliary neoplasia and PSC may be difficult to differentiate. Performed in the physiologic nondistended state, lending more difficulty to visualizing small ducts
ERCP	Considered the gold standard for the diagnosis Overall diagnostic accuracy is 97%	Invasive; may cause complications such as sepsis, hemorrhage, pancreatitis, bowel perforation, and cholangitis	Visualization of the peripheral ducts limited because of central obstruction from stones, strictures, and thick bile
Ultrasound	No data on the accuracy of ultrasound in the diagnosis of PSC		

CT, Computed tomography; ERCP, endoscopic retrograde cholangiopancreatography, MRCP, magnetic resonance cholangiopancreatography; MRI, magnetic resonance imaging; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis.

The pathognomonic microscopic finding of PSC is the concentric fibrous replacement of bile ducts in an "onionskin" pattern. This fibrous cholangitis is characterized by a mixed inflammatory infiltrate that, over time, results in loss of the bile duct in a process called fibrous obliterative cholangitis. As the disease progresses, fibrous septa form between portal tracts and ductopenia becomes more common; inflammation in this stage typically subsides.<sup>21</sup> End-stage PSC is indistinguishable from other causes of biliary cirrhosis, with large irregularly shaped, bile-stained RNs characteristically arranged in a jigsaw puzzle pattern.

# Imaging

Radiologic imaging is obtained in the initial evaluation of patients with PBC to assess the differential diagnosis of cholestasis and, importantly, rule out biliary obstruction. Imaging also plays an important role in the surveillance of this chronic condition, particularly with regard to the evolution of portal hypertension and detection of HCC.

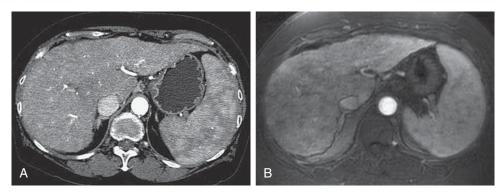
Rather than playing an ancillary role as it does in PBC, imaging has a central diagnostic responsibility in PSC and fundamentally affects treatment options. Similar to PBC, however, imaging is useful in excluding secondary causes of biliary obstruction and surveillance of complications of portal hypertension, cholangiocarcinoma, and HCC. The two principal techniques used to highlight the structure of the intrahepatic and extrahepatic ducts are cholangiography and magnetic resonance cholangiopancreatography (MRCP). Cholangiography, in particular, is most commonly accomplished via endoscopic retrograde cholangiopancreatography (ERCP); transhepatic cholangiography is generally pursued only if ERCP is unsuccessful. In all techniques, the characteristic finding of PSC is a "beaded" appearance of the biliary tree consisting of shortsegment, multifocal stricturing with intervening areas of normal or dilated intervening intrahepatic and extrahepatic ducts (Table 43-1).

#### COMPUTED TOMOGRAPHY, MAGNETIC RESONANCE IMAGING, ULTRASOUND, AND CHOLANGIOGRAPHY

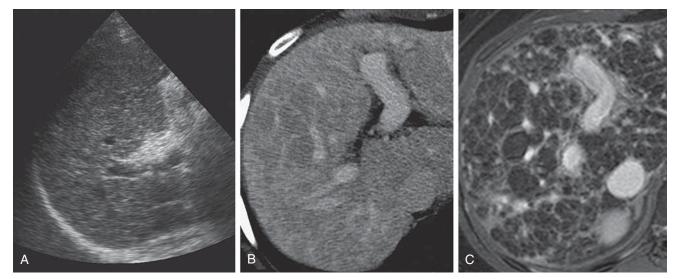
#### Primary Biliary Cirrhosis

Patients with PBC have a spectrum of disease severity ranging from asymptomatic to cirrhosis. In the initial presentation, the liver may be normal or slightly enlarged. Splenomegaly, sometimes severe, is a common finding in early stages. Early disease is also associated with periportal hyperintensity on T2-weighted magnetic resonance (MR) images, a finding that is less common in late PBC.<sup>22</sup>

With disease progression, the liver demonstrates heterogeneous enhancement that may be associated with small, punctuated arterial-portal shunts in the early phase of dynamic contrast injection (Figure 43-1). Hepatic fibrosis presenting as reticular, confluent, or both patterns also may be observed. In some cases, RNs of various sizes can be seen intercalated by coarse fibrous



**Figure 43-1** A 58-year-old woman with primary biliary cirrhosis. Axial contrast-enhanced computed tomography image (A) and three-dimensional dynamic gradient echo magnetic resonance axial image (B) obtained during the arterial phase after intravenous administration of iodine and a gadolinium-based contrast agent, respectively, demonstrate diffuse heterogeneous enhancement of the liver parenchyma.



**Figure 43-2** A 62-year-old woman with primary biliary cirrhosis. **A**, Transverse ultrasound image of the liver shows mild nonspecific diffuse heterogeneity of the hepatic parenchyma. **B**, Axial postcontrast computed tomography image acquired during the portal venous phase shows heterogeneity of the liver parenchyma. Note the diffuse reticular pattern, mainly in the periphery of the liver. **C**, Axial double-contrast–enhanced three-dimensional gradient echo magnetic resonance image of the liver obtained after intravenous administration of iron oxides and a gadolinium-based contrast agent shows regenerative nodules of various sizes intercalated by coarse fibrous reticulations.

reticulations (Figure 43-2). Additionally, upper abdominal and retroperitoneal lymphadenopathy is a frequent finding, seen in 60% to 80% of patients.<sup>23</sup>

The imaging features of advanced PBC usually resemble those seen in other causes of cirrhosis and portal hypertension. However, one imaging finding that may potentially differentiate cirrhosis secondary to PBC versus other causes is the periportal halo sign. This finding was described in 43% of patients with advanced PBC compared with none in cirrhotic patients without PBC, suggesting that this is a specific imaging finding for the diagnosis of PBC.<sup>24</sup> On MRI, the periportal halo sign is seen as a low signal intensity abnormality without mass effect on T1- and T2-weighted images, measuring 5 to 10 mm (Figure 43-3). This abnormality is centered on portal venous branches and is more conspicuous on the portal venous and equilibrium phases.<sup>24</sup> Additionally, in contrast to other chronic liver diseases, portal hypertension may occur even before cirrhosis has developed; therefore, some patients with severe portal hypertension secondary to PBC may have an enlarged liver, an unusual finding among other causes of chronic liver disease.<sup>24</sup>

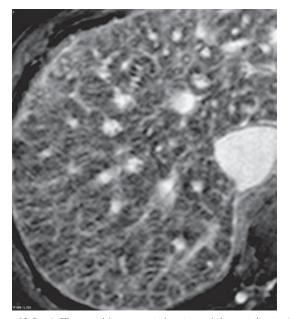
In PBC, cholangiography studies such as ERCP and MRCP are usually normal but in some cases demonstrate diffuse attenuation of the bile ducts.<sup>25</sup>

#### Primary Sclerosing Cholangitis

In the early stages of PSC, CT, MRI, and ultrasonography demonstrate hepatic parenchymal heterogeneity associated with a normal-appearing biliary tree. Nonetheless, in some cases, fine ulcerations of the common bile duct may be seen on ERCP.<sup>3</sup>

As PSC progresses, intrahepatic bile duct dilatation becomes more evident and is a characteristic finding observed in approximately 80% of patients. Additional findings of PSC include intrahepatic and extrahepatic bile duct stenosis in 64% and 50% of cases, respectively, and extrahepatic bile duct wall enhancement and thickening in 67% and 50%, respectively.<sup>26</sup> CT shows scattered dilated intrahepatic ducts, some of which may have no apparent connection to more central bile ducts. Biliary calculi may develop in obstructed ducts as a consequence of biliary stasis and secondary infection.<sup>26</sup> In a small subgroup of patients, the cystic duct or gallbladder may be involved. Ultrasound depicts intrahepatic and extrahepatic bile duct dilatation.

On MRI, heterogeneity of the liver parenchyma, with peripheral wedge-shaped areas and fine reticulations of increased signal intensity on T2-weighted images associated with bile

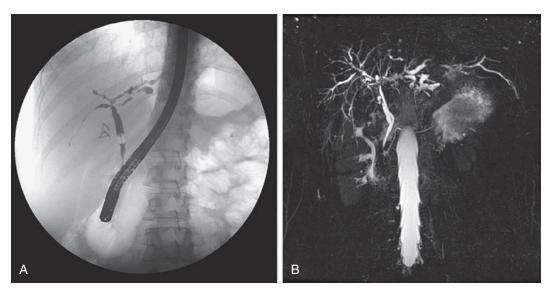


**Figure 43-3** A 57-year-old woman with primary biliary cirrhosis. Axial double-contrast–enhanced three-dimensional gradient echo magnetic resonance image of the liver obtained after intravenous administration of iron oxides and a gadolinium-based contrast agent shows innumerable small regenerative nodules intercalated by coarse fibrous reticulations. Note the areas of low signal intensity centered around portal triads in the middle of some of the nodules, characterizing the periportal halo sign.

duct dilatation, is suggestive of PSC.<sup>27</sup> Additional MRI findings include increased enhancement of the liver parenchyma on dynamic arterial-phase images, more evident in peripheral areas, in 56% of cases.<sup>26</sup>

A more precise diagnosis of PSC can be obtained with cholangiography, by ERCP or MRCP. ERCP can demonstrate multifocal areas of strictures and irregularities involving the intrahepatic and/or extrahepatic bile ducts intercalated with segments of normal or dilated ducts, producing the characteristic beaded appearance of PSC. The strictures can vary in size, ranging from 1 to 2 mm to several centimeters. In some cases, the lack of visualization of the peripheral ducts because of obliteration of the more central ducts causes a "pruned tree" appearance of the biliary tree (Figure 43-4). Although ERCP is currently the gold standard for diagnosing PSC, it is an invasive procedure that may cause complications such as sepsis, hemorrhage, pancreatitis, bowel perforation, and cholangitis. Transhepatic cholangiography may be performed if ERCP is unsuccessful.<sup>28</sup>

As with ERCP, the key MRCP feature of PSC is the characteristic beaded appearance of the biliary ducts. MRCP is also useful in demonstrating the extent of the strictured segment and displaying the dilated peripheral bile ducts that are not connected to central stenosed ducts (a finding that can be demonstrated only via MRCP) (see Figure 43-4). Less frequent findings include webs, stones, and diverticula. MRCP has a reported sensitivity of 85% to 88%, a specificity of 92% to 97%, a positive predictive value of 85% to 94%, and a negative predictive value of 93% to 94% in detecting PSC. Unfortunately, these performance characteristics are valid only in advanced disease, because MRCP may be normal in the early stages of PSC. The overall diagnostic accuracy of MRCP in patients with PSC is 90%, compared with 97% for ERCP.28 MRCP has the advantage of being a noninvasive method with less risk for complications when compared with ERCP. Furthermore, MRCP can depict

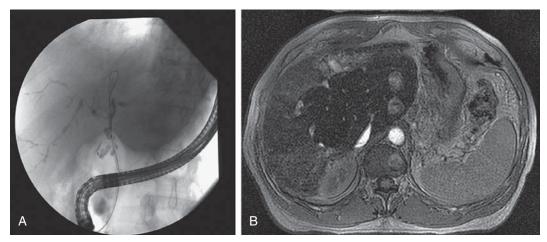


**Figure 43-4** A 48-year-old-man with primary sclerosing cholangitis. **A**, endoscopic retrograde cholangiopancreatography (ERCP) image demonstrates irregularity and narrowing of the intrahepatic and extrahepatic bile ducts intercalated with segments of normal or dilated ducts, producing a "beaded" appearance. Note the nonopacification of the peripheral ducts because of obstructions in the more central ducts, causing a "pruned tree" appearance of the biliary tree. **B**, Oblique coronal collapsed image from a respiratory-triggered three-dimensional magnetic resonance cholangiopancreatography (MRCP) sequence reveals diffuse beading of the intrahepatic ducts. Note that the peripheral ducts, which were unopacified at ERCP, are visible at MRCP. (*Case courtesy Scott Reeder, MD, PhD, University of Wisconsin.*)

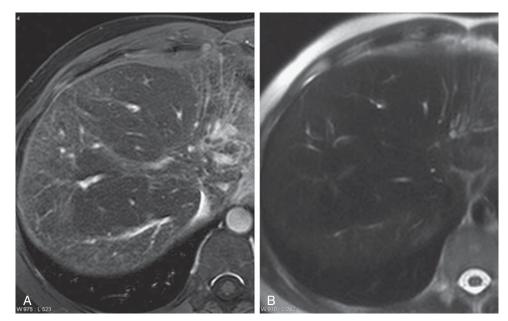
more strictures, especially of the peripheral intrahepatic ducts, and is better at visualizing bile ducts proximal to obstructed areas and unconnected to the central ducts; direct cholangiog-raphy cannot depict these regions because of nonfilling.<sup>29</sup>

In patients with cirrhosis secondary to PSC there is marked lobulation of the hepatic contours. Parenchymal atrophy occurs proximal to the obstructed bile ducts and is more frequently seen in the right lobe of the liver, whereas marked hypertrophy occurs in spared segments. Hypertrophy of the caudate lobe is seen in up to 98% of cases. The hypertrophied caudate lobe, surrounded by the atrophic right hepatic lobe, produces a masslike or pseudotumor appearance, which is a prominent feature of cirrhosis caused by PSC (Figure 43-5).<sup>30</sup> Although published reports emphasize hypertrophy of the caudate lobe, hypertrophic pseudotumors also may occur in other portions of the liver. Long broad scars of fibrosis may surround the hypertrophied segments that, in some cases, may show paucity of bile ducts (Figure 43-6).

Many PSC cases are complicated by cholangitis. Heterogeneous enhancement of the liver associated with biliary ductal



**Figure 43-5** A 50-year-old man with cirrhosis secondary to primary sclerosing cholangitis (PSC). **A**, Endoscopic retrograde cholangiopancreatography image demonstrates multifocal strictures of the intrahepatic and extrahepatic bile ducts intercalated with segments of normal-caliber ducts, producing the characteristic beaded appearance of PSC. **B**, Axial iron oxides–enhanced two-dimensional T2\*-weighted gradient echo magnetic resonance image of the liver shows a "pseudotumor" appearance of the markedly hypertrophic caudate lobe. Note the incidental ghost artifacts from the aorta over the left lobe of the liver.



**Figure 43-6** A 56-year-old-man with cirrhosis secondary to primary sclerosing cholangitis. **A**, Axial double-contrast–enhanced three-dimensional gradient echo magnetic resonance (MR) image of the liver obtained after intravenous administration of iron oxides and a gadolinium-based contrast agent shows hypertrophy of the central portions of segments 8 and 4a. The peripheral portion of segment 8 is atrophic, as are segments 7 and 2. The atrophic parenchyma has coarse reticulations consistent with fibrosis. **B**, Axial T2-weighted single-shot turbo spin echo MR image reveals a paucity of bile ducts within the hypertrophic segments.

dilatation and mural contrast enhancement of the bile duct are seen in patients with acute cholangitis and may predispose to hepatic abscess formation.<sup>2</sup>

Cholangiocarcinoma may occur in up to 20% of patients with PSC. The tumor is usually multifocal. Cholangiographic findings that suggest the presence of a superimposed cholangiocarcinoma include rapid progression of strictures, asymmetrically thickened bile duct walls, irregular luminal narrowing causing marked dilatation of ducts proximal to strictures, and development of intraluminal masses or polyps evident after delayed contrast enhancement.<sup>31</sup>

#### **IMAGING ALGORITHMS**

#### Primary Biliary Cirrhosis

Ultrasound is the initial modality used to evaluate patients with cholestatic serologic markers. If biliary obstruction is suggested, further characterization is achieved by CT or MRI. Imaging also plays a role in the long-term management of patients with PBC, which is associated with a significantly elevated risk for HCC compared with the general population (risk ratio 18.80 in a systematic meta-analysis).<sup>32</sup> The American Association for the Study of Liver Diseases (AASLD) recommends regular screening for HCC with cross-sectional imaging, with or without alpha-fetoprotein screening, at 6-month to 12-month intervals.<sup>33</sup> At some institutions, this is performed with ultrasound; at others, CT or MRI screening is performed every 6 months.

#### Primary Sclerosing Cholangitis

As with PBC, ultrasound is the initial modality used to evaluate cholestasis. Confirmation and further characterization of biliary obstruction is achieved by CT or MRI. The gold standard for PSC diagnosis is ERCP. If ERCP is contraindicated (particularly in elderly patients with comorbid conditions), MRCP is a valid alternative. However, it should be noted that MRCP is not therapeutic; if a dominant stricture is present, ERCP should be performed because of its capabilities in sampling the stricture for malignancy and dilating the narrowed region.

For the elevated risk for gallbladder carcinoma and cellular dysplasia, AASLD guidelines call for annual screening for gallbladder mass lesions with abdominal ultrasound and for referral for cholecystectomy on detection of a gallbladder mass or polyp of any size.<sup>18</sup>

Patients with PSC are at risk for the development of cholangiocarcinoma. However, regular screening with imaging is not advocated because no studies have demonstrated a benefit in patient outcomes using this strategy. As with other causes of chronic liver disease, patients with PSC are at risk for HCC. Because the rate of transformation to HCC is poorly characterized, the AASLD does not provide strict screening guidelines. However, some institutions pursue CT or MRI screening every 6 months.

# **Differential Diagnosis**

#### PRIMARY BILIARY CIRRHOSIS

The diagnosis of PBC is strongly suggested in a middle-aged woman presenting with fatigue and/or pruritus in the setting of cholestatic laboratory findings. The primary alternative diagnosis to be excluded is extrahepatic biliary obstruction in the form of a neoplasm, stricture, or choledocholithiasis. Neo-

#### **Classic Signs**

#### Primary Biliary Cirrhosis

- In its initial presentation, the liver of a patient with PBC may appear normal or slightly enlarged, with concomitant splenomegaly.
- On MRI, there is periportal hyperintensity on T2-weighted images. As the disease progresses, heterogeneous enhancement of the liver and lymphadenopathy may be seen. The biliary system is usually normal. Portal hypertension may develop early in the disease course, before the onset of cirrhosis.
- Findings in end-stage liver disease secondary to PBC are nonspecific; the periportal halo sign, if observed, may suggest a diagnosis of PBC.
- Primary Sclerosing Cholangitis
- Many imaging findings in cirrhosis secondary to advanced PSC are similar to those seen in other causes of end-stage liver disease.
- Findings more specific for PSC include biliary duct dilatation in the setting of the characteristic "beaded" appearance of the biliary tree, and marked hypertrophy of spared liver segments (notably, caudate lobe "pseudotumor").

plasms may involve either the common bile duct or ampulla of Vater, resulting in secondary biliary obstruction. Choledocholithiasis is common in certain groups, especially obese females older than the age of 40. These mechanical biliary obstructions generally are easily identifiable with noninvasive imaging (CT, MRI, MRCP). If liver biopsy is performed, mechanical obstructions are characterized histologically by the presence of ductal proliferation (rather than duct dropout) and neutrophilic (rather than lymphocytic) infiltration.

PBC also needs to be distinguished from PSC. The presence of AMA confirms the diagnosis of PBC, whereas the presence of IBD favors PSC. Histologic differences between these two conditions are slight and do not usually permit reliable differentiation.

Although granulomas are a histologic hallmark of PBC, other hepatic conditions, such as hepatic sarcoidosis and some cases of hepatitis C infection, also may be associated with granuloma formation and cholestatic liver function tests. The presence of AMA excludes these conditions.

Another diagnostic consideration is drug hepatotoxicity. Various ingestions or exposures (e.g., phenytoin, anabolic steroids, estrogens) may result in both hepatocellular and cholestatic biochemical profiles. Affected patients have a suggestive ingestion or exposure history and absent AMA and other autoimmune markers.

At the time of diagnosis, patients with PBC usually have a normal or enlarged liver with splenomegaly. When presenting with hepatomegaly, PBC needs to be differentiated from other causes of hepatomegaly, including hepatitis, lymphoproliferative diseases, toxic and drug-related diseases, metastatic diseases, metabolic disorders, and vascular disorders. In cirrhotic patients secondary to PBC, the imaging findings overlap with other causes of end-stage liver disease. However, portal hypertension may occur even before cirrhosis, and some patients with portal hypertension may have an enlarged liver, a useful finding

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in the differential diagnosis of PBC. Additionally, the periportal halo sign, if present, suggests the diagnosis of PBC.

#### PRIMARY SCLEROSING CHOLANGITIS

PSC is highly suggested in a patient with UC, cholestatic serologic tests, and characteristic cholangiographic findings. However, UC may be associated with hepatic abnormalities other than PSC. Such abnormalities may occur in the setting of normal bile ducts and include hepatic steatosis, as well as varying degrees of portal inflammation and fibrosis. These latter findings are differentiated on liver biopsy.

Distinguishing PSC from secondary biliary cirrhosis is sometimes arduous. Causes of secondary biliary cirrhosis that may be confused with PSC include choledocholithiasis, ischemic bile duct injury, prior biliary surgery, and congenital biliary abnormalities. Choledocholithiasis is frequent in certain groups, especially obese females older than the age of 40. Ischemic bile duct injury is most common after liver transplantation, although it has also been identified after transcatheter arterial chemoembolization therapy for HCC.<sup>31</sup> Biliary surgery may be complicated by mechanical stricturing. Congenital biliary abnormalities typically manifest as cholestasis in early life. Differentiating among these various concerns requires careful history-taking and radiologic investigation.

PSC may be difficult to differentiate from cholangiocarcinoma, particularly if there is a single or dominant stricture. Endoscopic ultrasound, with cytologic examination or biopsy via ERCP can be diagnostic for cholangiocarcinoma in some instances, although underlying PSC may be present. PSC is suggested if concomitant IBD is present, along with a history of cholestatic serologic liver tests.

Other differential considerations include acquired immunodeficiency syndrome (AIDS) cholangiopathy, IgG4-related sclerosing cholangitis, and drug reactions. AIDS cholangiopathy occurs in human immunodeficiency virus (HIV)-infected patients with CD4 counts below 100/mm<sup>3</sup> and within the context of concomitant infection; the most common infection is by intestinal *Cryptosporidium*, which yields nonbloody diarrhea (an infrequent symptom of PSC). The diagnostic workup of PSC should include serum IgG4 titers, because IgG4-related sclerosing cholangitis can have a similar clinical presentation and imaging appearance of biliary stricturing. Drug hepatotoxicity may produce cholestatic liver tests and requires a careful exposure/ingestion history.

Most imaging findings in cirrhosis secondary to advanced PSC are similar to those in other causes of end-stage liver disease. However, PSC is suggested by a "beaded" biliary tree and marked hypertrophy of spared segments.

Conditions that may mimic the cholangiographic findings of PSC include ascending cholangitis, AIDS cholangiopathy, recurrent pyogenic cholangitis, IgG4-related sclerosing cholangitis, and biliary ischemia as a result of intraarterial chemotherapy or liver transplantation surgery.<sup>34</sup> Ascending cholangitis, secondary to bacterial contamination of an obstructed duct, is a clinical diagnosis in which patients generally present with abdominal pain, fever, and jaundice, in the setting of a leukocytosis and positive blood cultures. AIDS cholangiopathy is best discriminated from PSC by its unique combination of intrahepatic ductal strictures and papillary stenosis. In chemotherapyinduced cholangitis, the most common cholangiographic findings are strictures of the bifurcation of the common hepatic duct with sparing of the distal common bile duct; this contrasts with PSC, which demonstrates diffuse involvement of the intrahepatic and extrahepatic bile ducts.<sup>28</sup>

### Treatment

#### MEDICAL TREATMENT

#### Primary Biliary Cirrhosis

Promoting the delivery of bile acids into the bile canaliculi, ursodeoxycholic acid (ursodiol [UDCA]) is the only treatment approved by the U.S. Food and Drug Administration (FDA) for PBC. It slows the progression of disease, delaying advancement to cirrhosis and the need for liver transplantation. Systematic review of published literature has found UDCA therapy to be associated with improvement in biochemical markers of cholestasis and histologic findings, but has not found a significant benefit of UDCA with respect to all-cause mortality.<sup>35</sup>

Liver transplantation is a viable option in patients with PBCinduced liver failure. Five-year survival of transplanted patients is 85%, although PBC recurs in 30% of patients at 10 years.<sup>36</sup> Retransplantation is required in 10% of cases. Indications for liver transplantation include hepatic decompensation, development of appropriate-stage HCC, and debilitating fatigue or pruritus.

#### Primary Sclerosing Cholangitis

No therapy has been shown to increase transplant-free survival or reverse the severity of histologic disease. Management focuses on treating the complications related to chronic cholestasis (e.g., pruritus, malabsorption), controlling associated conditions (e.g., IBD), and, once cirrhosis develops, monitoring for complications of portal hypertension and HCC. Various bile acids and antiinflammatory and immunosuppressive agents have been investigated, including corticosteroids, methotrexate, cyclosporine, etanercept, and tacrolimus.

Surgical management of PSC covers four areas: treatment of biliary strictures, proctocolectomy for concomitant UC, management of cholangiocarcinoma, and liver transplantation.

Endoscopic treatment via ERCP is the treatment of choice in these patients with symptomatic dominant strictures. Endoscopic management with balloon dilatation and stenting is most successful in the case of common bile duct strictures; these strategies are less effective if the stricture is in an intrahepatic duct. Stent placement is associated with recurrent stent occlusion and cholangitis. Stents may need to be exchanged at regular intervals. Endoscopic therapy may yield prolonged biochemical and symptomatic improvement for several years and is a reasonable "bridge" to liver transplantation. Cytologic brushings and/or endoscopic biopsies can be performed if there is a concern for cholangiocarcinoma. When endoscopic therapy for a dominant stricture is unavailable or unsuccessful, surgical intervention is an option. Biliary tract reconstructive procedures, such as bilioenteric bypass, are sometimes performed. Because of infectious complications, external biliary drains are not viable long-term options although they may be used in acute cholangitis when rapid biliary decompression is required.

Patients with concomitant UC are at high risk for colorectal cancer, and proctocolectomy is frequently performed prophylactically. As discussed earlier, proctocolectomy has no impact on the course of PSC. Liver transplantation has replaced biliary-enteric reconstruction as the surgical treatment of choice in patients with PSC. Five-year survival of transplanted patients is approximately 85%.<sup>37</sup> Recurrence of PSC after transplant occurs in approximately 20% of patients, usually manifesting within the first year.<sup>38</sup> The impact of liver transplantation on the course of concurrent IBD is variable; some patients experience regression of colitis and long-term remission, whereas others progress rapidly to require colectomy.

# What the Referring Physician Needs to Know

# Primary Biliary Cirrhosis

- Autoimmune-mediated destruction of small and mediumsized intrahepatic bile ducts occurs.
- This chronic, cholestatic condition is marked by fatigue, pruritus, jaundice, bone disease, and progressive liver disease.
- Pathogenesis is multifactorial, with genetic, environmental, and infectious underpinnings.
- AMA is the serologic hallmark.
- The diagnosis is strongly suggested in a middle-aged woman presenting with fatigue or jaundice who has cholestatic laboratory findings and AMA positivity.
- Annual incidence of HCC in patients with cirrhosis related to PBC is approximately 7%.
- UDCA is the only FDA-approved medical treatment, with liver transplantation reserved for those patients with progressive, decompensated liver failure, HCC, and/or intractable symptoms.

## **Primary Sclerosing Cholangitis**

 This chronic, cholestatic disorder associated with IBD involves the medium and large intrahepatic and extrahepatic bile ducts.

- It is characterized by pruritus, jaundice, recurrent episodes of cholangitis, cholangiocarcinoma, and progressive liver disease.
- There is a strong association with IBD: 75% of PSC patients have IBD, 90% of whom have UC.
- There is no serologic hallmark, although a variety of autoantibody and immunoglobulin levels may be elevated.
- The diagnosis is strongly suggested in a patient with UC, cholestatic serologic tests, and characteristic cholangiographic findings.
- Patients with cirrhosis as a result of PSC are at increased risk for HCC.
- Cholangiocarcinoma develops in up to 20% of patients.
- No medical treatment has proved reliably effective; endoscopic and surgical approaches, including liver transplantation, are commonly used in the setting of a dominant biliary stricture, decompensated liver failure, HCC, and/or cholangiocarcinoma.

# Key Points

# **Primary Biliary Cirrhosis**

- Periportal hyperintensity is seen on T2-weighted MR images at earlier stages.
- The periportal halo sign is seen in 43% of advanced cases.
- Upper abdominal lymphadenopathy occurs in 60% to 80% of cases.
- Cholangiographic studies are usually normal, although diffuse attenuation of the bile ducts may be observed.
- Portal hypertension may precede cirrhosis.
- For the elevated risk for HCC, screening with crosssectional imaging is advised at 6- to 12-month intervals.

#### Primary Sclerosing Cholangitis

- A characteristic finding is multiple areas of biliary duct strictures intercalated with segments of normal or dilated ducts, producing the characteristic beaded appearance.
- "Pruned tree" appearance of the biliary tree at ERCP is due to nonopacification of the peripheral ducts.
- For the elevated risk for gallbladder carcinoma, annual screening with ultrasound is recommended. The role of screening with cross-sectional imaging for cholangiocarcinoma or HCC is less well defined.

# **SUGGESTED READINGS**

- Chapman R, Fevery J, Practice Guideline Committee, American Association for the Study of Liver Diseases: Diagnosis and management of primary sclerosing cholangitis. *Hepatology* 51:660–678, 2010.
- Ernst O, Asselah T, Sergent G, et al: MR cholangiography in primary sclerosing cholangitis. *AJR Am J Roentgenol* 171:1027–1030, 1998.
- Ito K, Mitchell DG, Outwater EK, et al: Primary sclerosing cholangitis: MR imaging features. AJR Am J Roentgenol 172:1527–1533, 1999.
- Kaplan MM, Gershwin ME: Primary biliary cirrhosis. N Engl J Med 353:1261–1273, 2005.
- Lee YM, Kaplan MM: Primary sclerosing cholangitis. N Engl J Med 332:924–933, 1995.
- Lindor KD, Gershwin ME, Practice Guideline Committee, American Association for the Study of Liver Diseases: Primary biliary cirrhosis. *Hepatology* 50:291–308, 2009.
- Wenzel JS, Donohoe A, Ford KL, 3rd, et al: Primary biliary cirrhosis: MR imaging findings and description of MR imaging periportal halo sign. *AJR Am J Roentgenol* 176:885–889, 2001.

## REFERENCES

- Kaplan MM, Gershwin ME: Primary biliary cirrhosis. N Engl J Med 353:1261–1273, 2005.
- Bogdanos DP, Baum H, Grasso A, et al: Microbial mimics are major targets of crossreactivity with human pyruvate dehydrogenase in primary biliary cirrhosis. J Hepatol 40:31–39, 2004.
- Lee YM, Kaplan MM: Primary sclerosing cholangitis. N Engl J Med 332:924–933, 1995.
- Bergquist A, Lindberg G, Saarinen S, et al: Increased prevalence of primary sclerosing cholangitis among first-degree relatives. J Hepatol 42:252–256, 2005.
- Boonstra K, Beuers U, Ponsioen CY: Epidemiology of primary sclerosing cholangitis and primary biliary cirrhosis: a systematic review. *J Hepatol* 56:1181–1188, 2012.
- Bittencourt PL, Farias AQ, Abrantes-Lemos CP, et al: Prevalence of immune disturbances and chronic liver disease in family members of patients with primary biliary cirrhosis. J Gastroenterol Hepatol 19:873–878, 2004.
- Selmi C, Mayo MJ, Bach N, et al: Primary biliary cirrhosis in monozygotic and dizygotic twins: genetics, epigenetics, and environment. *Gastroenterology* 127:485–492, 2004.
- Parikh-Patel A, Gold EB, Worman H, et al: Risk factors for primary biliary cirrhosis in a cohort of patients from the United States. *Hepatology* 33:16–21, 2001.
- 9. Bergquist A, Lindberg G, Saarinen S, et al: Increased prevalence of primary sclerosing cholangitis among first-degree relatives. *J Hepatol* 42:252–256, 2005.
- Olsson R, Danielsson A, Jarnerot G, et al: Prevalence of primary sclerosing cholangitis in patients with ulcerative colitis. *Gastroenterology* 100:1319–1323, 1991.
- 11. Prince MI, Chetwynd A, Craig WL, et al: Asymptomatic primary biliary cirrhosis: clinical features, prognosis, and symptom progression in a large population-based cohort. *Gut* 53:865– 870, 2004.
- Thornton JR, Triger DR, Losowsky MS: Variceal bleeding is associated with reduced risk of severe cholestasis in primary biliary cirrhosis. Q J Med 71:467–471, 1989.
- Nijhawan PK, Therneau TM, Dickson ER, et al: Incidence of cancer in primary biliary cirrhosis: the Mayo experience. *Hepatology* 29:1396–1398, 1999.

- Van de Water J, Cooper A, Surh CD, et al: Detection of autoantibodies to recombinant mitochondrial proteins in patients with primary biliary cirrhosis. N Engl J Med 320:1377–1380, 1989.
- Chapman R, Fevery J, Practice Guideline Committee, American Association for the Study of Liver Diseases: Diagnosis and management of primary sclerosing cholangitis. *Hepatology* 51:660–678, 2010.
- Cangemi JR, Wiesner RH, Beaver SJ, et al: Effect of proctocolectomy for chronic ulcerative colitis on the natural history of primary sclerosing cholangitis. *Gastroenterology* 96:790–794, 1989.
- Soetikno RM, Lin OS, Heidenreich PA, et al: Increased risk of colorectal neoplasia in patients with primary sclerosing cholangitis and ulcerative colitis: a meta-analysis. *Gastrointest Endosc* 56:48–54, 2002.
- Duerr RH, Targan SR, Landers CJ, et al: Neutrophil cytoplasmic antibodies: a link between primary sclerosing cholangitis and ulcerative colitis. *Gastroenterology* 100:1385–1391, 1991.
- Portmann BC, Nakanuma Y: Diseases of the bile ducts. In Burt AD, Portmann BC, Ferrell LD, editors: *MacSween's pathology of the liver*, ed 5, New York, 2006, Churchill Livingstone, p 539.
- Batts KP: Autoimmune and cholestatic disorders of the liver. In Odze RD, Goldblum JR, Crawford JM, editors: Surgical pathology of the GI tract, liver, biliary tract, and pancreas, Philadelphia, 2006, WB Saunders, p 826.
- Portmann BC, Nakanuma Y: Diseases of the bile ducts. In Burt AD, Portmann BC, Ferrell LD, editors: *MacSween's pathology of the liver*, ed 5, New York, 2006, Churchill Livingstone, p 554.
- Kobayashi S, Matsui O, Gabata T, et al: MRI findings of primary biliary cirrhosis: correlation with Scheuer histologic staging. *Abdom Imaging* 30:71–76, 2005.
- Blachar A, Federle MP, Brancatelli G: Primary biliary cirrhosis: clinical, pathologic, and helical CT findings in 53 patients. *Radiology* 220:329– 336, 2001.
- 24. Wenzel JS, Donohoe A, Ford KL, 3rd, et al: Primary biliary cirrhosis: MR imaging findings and description of MR imaging periportal halo sign. *AJR Am J Roentgenol* 176:885–889, 2001.
- 25. Kumagi T, Heathcote EJ: Primary biliary cirrhosis. Orphanet J Rare Dis 3:1, 2008.

- Ito K, Mitchell DG, Outwater EK, et al: Primary sclerosing cholangitis: MR imaging features. *AJR Am J Roentgenol* 172:1527–1533, 1999.
- Revelon G, Rashid A, Kawamoto S, et al: Primary sclerosing cholangitis: MR imaging findings with pathologic correlation. *AJR Am J Roentgenol* 173:1037–1042, 1999.
- Vitellas KM, El-Dieb A, Vaswani KK, et al: MR cholangiopancreatography in patients with primary sclerosing cholangitis: interobserver variability and comparison with endoscopic retrograde cholangiopancreatography. *AJR Am J Roentgenol* 179:399–407, 2002.
- Ernst O, Asselah T, Sergent G, et al: MR cholangiography in primary sclerosing cholangitis. AJR Am J Roentgenol 171:1027–1030, 1998.
- Dodd GD, 3rd, Baron RL, Oliver JH, 3rd, et al: End-stage primary sclerosing cholangitis: CT findings of hepatic morphology in 36 patients. *Radiology* 211:357–362, 1999.
- Yu JS, Kim KW, Jeong MG, et al: Predisposing factors of bile duct injury after transcatheter arterial chemoembolization for hepatic malignancy. *Cardiovasc Intervent Radiol* 25:270–274, 2002.
- Liang Y, Yang Z, Zhong R: Primary biliary cirrhosis and cancer risk: a systematic review and meta-analysis. *Hepatology* 56:1409–1417, 2012.
- Lindor KD, Gershwin ME, Practice Guideline Committee, American Association for the Study of Liver Diseases: Primary biliary cirrhosis. *Hepatology* 50:291–308, 2009.
- Katabathina VS, Dasyam AK, Dasyam N, et al: Adult bile duct strictures: role of MR imaging and MR cholangiopancreatography in characterization. *Radiographics* 34:565–586, 2014.
- Rudic JS, Poropat G, Krstic MN, et al: Ursodeoxycholic acid for primary biliary cirrhosis. *Cochrane Database Syst Rev* (12):CD000551, 2012.
- Neuberger J: Liver transplantation for primary biliary cirrhosis: indications and risk of recurrence. J Hepatol 39:142–148, 2003.
- Graziadei IW, Wiesner RH, Marotta PJ, et al: Long-term results of patients undergoing liver transplantation for primary sclerosing cholangitis. *Hepatology* 30:1121–1127, 1999.
- Graziadei IW, Wiesner RH, Batts KP, et al: Recurrence of primary sclerosing cholangitis following liver transplantation. *Hepatology* 29: 1050–1056, 1999.

# **Hepatic Variants**

ONOFRIO CATALANO | LESLIE K. LEE | JOSEPH R. GRAJO | DUSHYANT V. SAHANI

# **Technical Aspects**

Diagnostic imaging of the hepatobiliary system, with multidetector computed tomography (MDCT) and magnetic resonance imaging (MRI), plays a major role in hepatobiliary surgery, helping to choose the best therapeutic approach, reduce complications, and identify the anatomy requiring special attention at surgery.

Anatomic variants of the biliary and hepatic vascular anatomy are common; they dictate the surgical technique and also may predict the risk for postsurgical complications, in both the case of complex surgeries, such as liver transplantation, and of more common procedures, such as laparoscopic cholecystectomy.

MDCT and MRI, especially when hepatobiliary contrast agents are used (e.g., gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid [Gd-EOB-DTPA], gadobenate dimeglumine [Gd-BOPTA], mangafodipir trisodium), clearly visualize both biliary and arterial anatomic variants, with a high degree of correlation with intraoperative cholangiography and digital subtraction angiography.<sup>1</sup>

# **Pros and Cons**

Contrast-enhanced MDCT and MRI are noninvasive techniques that permit angiographic and parenchymal evaluation of the liver.

MDCT and MR angiography have shown excellent correlation with catheter angiography but are devoid of its invasiveness and many of its complications. Moreover, the radiation burden is reduced in MDCT when compared with catheter angiography and absent in the case of MRI.

Because of the availability of biliary excreted contrast agents, cholangiography now can be performed in a noninvasive way by both MDCT and MRI. Currently, MDCT cholangiography, owing to the higher spatial resolution, allows better visualization of second-order bile ducts than MR cholangiography.

MDCT, MR angiography, and MR cholangiopancreatography (MRCP) protocols, used at our institution, are summarized in Tables 44-1 to 44-3. Raw data, obtained from MDCT and MRI are postprocessed to maximize the information they can provide; and multiplanar reformatted, three-dimensional reconstruction, maximum intensity projection (MIP), and volume rendering images are obtained.1

# Controversies

Whether MDCT or MRI is the better modality by which to assess hepatic variants remains unclear. Both methods have undergone rapid improvement, and each bears inherent advantages and disadvantages. Currently, the choice of a specific modality over the other is largely dictated by institutional preferences.

# Normal Anatomy

Anatomic variants of the biliary, hepatic arterial, hepatic venous, and portal venous anatomy are common. Classic biliary and hepatic arterial anatomy is found in only 58% and 55% of the population, respectively. To understand anatomic variants, a brief description of normal anatomy is provided.<sup>2,4-6</sup>

#### LIVER

The liver (Figure 44-1) is a large, wedge-shaped parenchymal organ that occupies most of the right hypochondrium and epigastrium and extends to the left epigastrium with its narrow end. The falciform ligament, the ligamentum teres, and the ligamentum venosum divide the liver into a large right lobe and a smaller left lobe. This anatomic description does not correlate with functional hepatic anatomy and is therefore inadequate for interventional radiology and surgery. Rather, functional anatomy of the liver is based on the vascular and biliary territories (Figure 44-2). Cantlie's line, running on a coronal oblique plane oriented 75 degrees toward the left, from the middle of the gallbladder to the left side of the inferior vena cava (IVC), divides the liver into right and left. Grossly, this yields the right liver and the left liver, which are two separate functional units, with independent vascular inflows and outflows and autonomous biliary drainage. The middle hepatic vein (MHV) lies along the cranial continuation of Cantlie's line. The right hepatic vein (RHV), MHV, and left hepatic vein (LHV) divide the liver into four sectors, each one supplied by an independent portal pedicle. They are the posterolateral and anteromedial sectors in the right liver and the posterior and anterior sectors in the left liver. The posterior sector is undivided and constitutes segment II. The anterior sector is divided by the umbilical fissure into a medial segment (IV) and a lateral segment (III). A transverse plane at the level of the main portal bifurcation divides the posterolateral sector into a posterior (VII) and an anterior segment (VI), the anteromedial sector into an anterior (V), and a posterior segment (VIII) and subdivides segment IV into a posterior (IVa) and an anterior segment (IVb). The caudate lobe constitutes segment I, or the Spigel lobe, which, owing to its autonomous vascularization, is considered separate from the others.

An ultrasound image of normal liver presents a homogeneous pattern of low-level echoes. Vessels and biliary ducts are anechoic (Figure 44-3).

On unenhanced MDCT, the liver exhibits homogeneous intermediate attenuation (50 to 75 Hounsfield units), similar to

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#### TABLE **Multidetector Computed Tomography** 44-1 Angiography Scanning Protocol **Hepatic Arterial** Phase Protocol Venous Phase Entire liver Entire liver Range 20-25 sec after start 60-65 sec Scan delay of bolus injection Empirical bolus Automatically triggered at tracking 125 HU in aorta at the celiac artery level Pitch 1-1.5 1-1.5 Slice thickness 1-2 mm 2-5 mm 120-140 120-140 Kilovoltage peak Milliamperes 200-280 200-280 Image reconstruction 1-2 mm and 50% 2-5 mm and 50% thickness overlap overlap

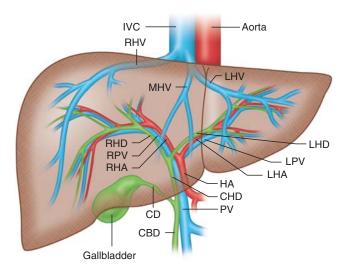
HU, Hounsfield units.

TABLE 44-2	Magnetic Resonance Angiography Protocol			
Protoc	col	Hepatic Arterial Phase	Venous Phase	Delayed Venous Phase
Scan delay		15-18 sec	60 sec	180 sec
TR/TE		Minimum/ 15 ms	Minimum/ 15 ms	Minimum/ 15 ms
Flip ar	ngle	100 degrees	100 degrees	100 degrees
Field c	of view	400 mm	400 mm	400 mm
Effecti	ve section	2-4 mm	2-4 mm	2-4 mm
Matrix		160 × 256	$160 \times 256$	$160 \times 256$

TR/TE, Repetition time/echo time.

TABLE 44-3	Magnetic Resonance Cholangiopancreatography Protocol		
Proto	col	T2-Weighted MRCP	3D SPGR
Scan c	delay	None	Gd-BOPTA: 60 min Gd-EOB-DTPA: 20 min
TR/TE		2800-3300/ 900-1100 ms	6.5/2.1 ms
Flip angle		0 degrees	15 degrees
Field of view		400 mm	400 mm
Effective section		60 mm	2.4 mm
Orient	ation	Coronal oblique	Axial and coronal
Matrix		160 × 256	160 × 256

Gd-BOPTA, Gadobenate dimeglumine; Gd-EOB-DTPA, gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid; MRCP, magnetic resonance cholangiopancreatography; 3D SPGR, three-dimensional spoiled gradient recalled echo; TR/TE, repetition time/echo time.

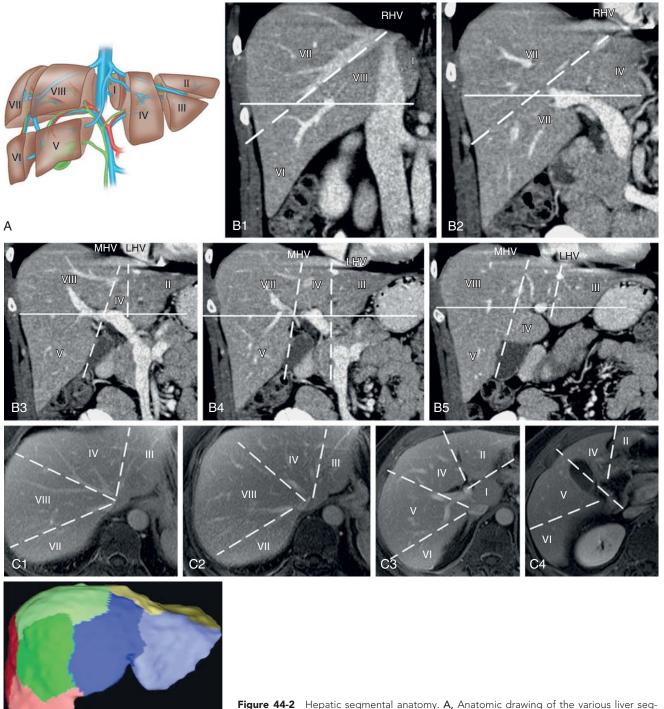


**Figure 44-1** Drawing of normal anatomy of the liver. *CBD*, Common bile duct; *CD*, cystic duct; *CHD*, common hepatic duct; *HA*, hepatic artery; *IVC*, inferior vena cava; *LHA*, left hepatic artery; *LHD*, left hepatic duct; *LHV*, left hepatic vein; *LPV*, left portal vein; *MHV*, middle hepatic vein; *PV*, portal vein; *RHA*, right hepatic artery; *RHD*, right hepatic duct; *RHV*, right hepatic vein.

that of the spleen (Figure 44-4). Vessels and biliary ducts are hypodense. During contrast-enhanced imaging, liver attenuation values progressively increase, with peak enhancement occurring during the portal and hepatic venous phases of enhancement. Maximal arterial enhancement occurs during hepatic arterial phase, usually around 30 seconds after the start of contrast injection; the portal and hepatic veins maximally enhance at approximately 70 seconds after contrast injection. Biliary ducts are unopacified, unless contrast media with biliary excretion are administered.

At MRI, the signal intensity of the normal liver varies by sequence. It presents hyperintense to the spleen on T1-weighted images, hypointense on T2-weighted images, and is always homogeneous (Figure 44-5).

Normal liver enhances homogeneously and transiently after administration of nonspecific gadolinium (Gd)-based contrast media, such as gadopentetate dimeglumine (Gd-DTPA). In contrast, hepatic-specific contrast agents are taken up by liver cells. Reticuloendothelial system-specific contrast agents, composed of iron microparticles, are taken up by Kupffer cells, with resultant reduction of the signal intensity of the liver on T2\*weighted images. Hepatocyte-specific contrast agents include gadoxetic acid (Gd-EOB-DTPA) and gadobenate dimeglumine (Gd-BOPTA), which are selectively taken up by hepatocytes without being metabolized, with resultant progressive increased signal intensity on delayed T1-weighted images and subsequent excretion into, and enhancement of, the biliary system. Biliary excretion accounts for approximately 50% of the administered Gd-EOB-DTPA dose, compared to 5% for Gd-BOPTA. It should be noted that Gd-EOB-DTPA is administered at onequarter the recommended clinical dose (0.025 mmol/kg vs. 0.1 mmol/kg) compared to nonspecific gadolinium contrast agents because of its relatively high relaxivity; this low clinical dose of Gd-EOB-DTPA may lead to less conspicuous vascular enhancement during arterial and venous phases, as well as to



**Figure 44-2** Hepatic segmental anatomy. **A**, Anatomic drawing of the various liver segments. Segmental anatomy of the liver in the coronal (**B1** to **B5**) and axial (**C1** to **C4**) planes from multidetector computed tomography and magnetic resonance imaging, respectively. **D**, Corresponding color-coded three-dimensional liver segmental reconstruction from a liver donor computed tomography examination.

bolus injection/acquisition timing errors because of the small injection volume.

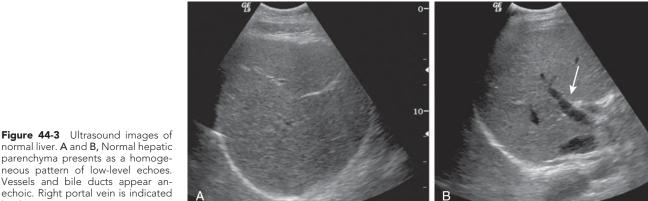
# HEPATIC ARTERIAL ANATOMY

The classic hepatic arterial anatomy, characterized by the proper hepatic artery dividing into right and left hepatic arteries, is observed in approximately 55% of the population (Figure 44-6). The Michel classification of hepatic arterial variant anatomy is illustrated in Table 44-4.

# HEPATIC VENOUS ANATOMY

Classic hepatic venous anatomy is characterized by three main hepatic veins—LHV, MHV, and RHV—draining into the IVC. The LHV drains segments II and III; the MHV drains segments

10



normal liver. A and B, Normal hepatic parenchyma presents as a homogeneous pattern of low-level echoes. Vessels and bile ducts appear anechoic. Right portal vein is indicated by the arrow.

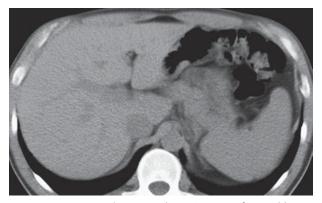


Figure 44-4 Computed tomography (CT) image of normal liver. On unenhanced multidetector CT, the liver exhibits homogeneous intermediate attenuation and appears similar to the spleen.

IV, V, and VIII; and the RHV drains segments V, VI, and VII. The MHV and LHV join to form a common trunk in approximately 60% of the population (Figure 44-7).

# PORTAL VENOUS ANATOMY

The normal portal venous anatomy is represented by the main portal vein branching, at the porta hepatis, into the right (RPV) and left (LPV) portal veins. The RPV subsequently divides into anterior and posterior branches (Figure 44-8).

#### HEPATIC BILIARY ANATOMY

The classic biliary anatomy, found in approximately 58% of the population, consists of the right hepatic duct (RHD) and the left hepatic duct (LHD) draining the right and left liver, respectively (Figure 44-9). The RHD divides into the right posterior hepatic duct (RPHD) and the right anterior hepatic duct (RAHD). The RPHD, draining posterior segments VI and VII, has a horizontal course and runs posterior to the RAHD, draining anterior segments V and VIII, which is more vertically oriented. The RPHD fuses with the RAHD from a medial approach to form a short RHD. Segmental tributaries draining left lobe segments II to IV form the LHD. The RHD and LHD fuse to constitute the common hepatic duct (CHD). The caudate lobe biliary radicals drain into the origin of the LHD or RHD. The

TABLE <b>44-4</b>	Hepatic Arterial Variants According to Michel's Classification		
Туре	Frequency (%)	Description	
I	55	RHA, MHA, LHA arise from CHA	
П	10	RHA, MHA, and LHA from CHA; replaced LHA from LGA	
Ш	11	RHA and MHA from CHA, replaced RHA from SMA	
IV	1	Replaced RHA and LHA	
V	8	RHA, MHA, LHA arise from CHA; accessory LHA from LGA	
VI	7	RHA, MHA, LHA arise from CHA; accessory RHA	
VII	1	Accessory RHA and LHA	
VIII	4	Replaced RHA and accessory LHA or replaced LHA and accessory RHA	
IX	4.5	Entire hepatic trunk from SMA	
Х	0.5	Entire hepatic trunk from LGA	

CHA, Common hepatic artery; LGA, left gastric artery; LHA, left hepatic artery; MHA, middle hepatic artery; RHA, right hepatic artery; SMA, superior mesenteric artery.

cystic duct usually fuses with the CHD from its lateral aspect, at the middle third.<sup>2,5,8-13</sup>

# Pathophysiology

Hepatic variants can be divided into parenchymal variants and hepatic vascular and biliary variants.

# PARENCHYMAL VARIANTS

Hepatic parenchymal variants are devoid of clinical implications unless they are confused with a mass lesion or hepatic volume is reduced, rendering the subject unsuitable to donate part of his or her liver for living-donor liver transplantation (LDLT).

The liver can undergo defective development, with resultant absence (agenesis) or small size (hypoplasia) of segments or even of an entire lobe (Figure 44-10), or excessive development, with resultant formation of accessory lobes, parenchymal bridges, or hyperplastic papillary lobes. Agenesis of the right or

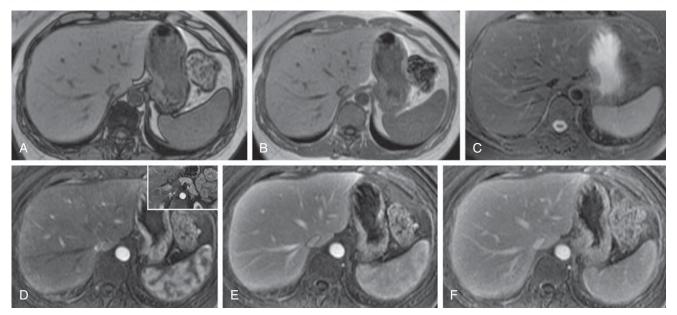
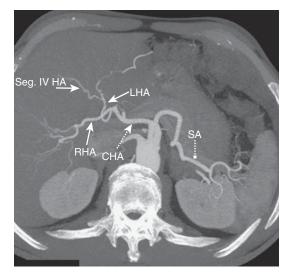


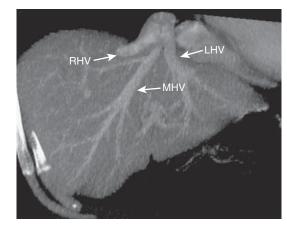
Figure 44-5 Magnetic resonance imaging (MRI) images of normal liver. On MRI, normal hepatic tissue presents hyperintense to the spleen on out-of-phase (A) and in-phase (B) T1-weighted images, is hypointense on T2-weighted images (C), and enhances homogeneously after administration of nonspecific gadolinium-based contrast media. In the arterial dominant phase of contrast enhancement, hepatic veins are unopacified (D), whereas contrast medium is detectable in the liver parenchyma and portal vein *(inset)*. During the portal (E) and late (F) phases of contrast enhancement, both hepatic veins and parenchyma are enhanced.



**Figure 44-6** Normal hepatic arterial anatomy. Axial maximum intensity projection image shows the normal anatomy of the hepatic artery. *CHA*, Common hepatic artery; *LHA*, left hepatic artery; *RHA*, right hepatic artery; *SA*, splenic artery; *Seg. IV HA*, segment IV hepatic artery.

left hepatic lobe is characterized by (1) absence of the involved lobe and corresponding branches of the hepatic artery, portal vein, and biliary system; (2) hypertrophy of the residual hepatic lobe and caudate; and (3) possible malposition of the gallbladder, colon, and spleen. Accessory lobes may be connected to the main liver or may be ectopic, in which case they are thought to arise from the extrahepatic biliary tract. Parenchymal bridges may circumscribe the gallbladder or envelop the IVC.

Papillary hyperplasia mainly occurs from the caudate lobe and the anteroinferior margin of the liver. In the latter case, the tongue-like parenchymal projection is Riedel's lobe.



**Figure 44-7** Hepatic vein confluence on multidetector maximum intensity projection coronal image. *LHV*, Left hepatic vein; *MHV*, middle hepatic vein; *RHV*, right hepatic vein.

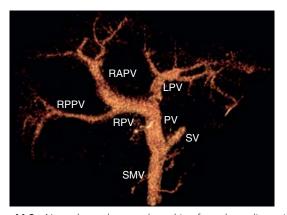
Diaphragmatic indentations are pseudolesions commonly confused with focal liver lesions. They appear as peripheral wedge-shaped hypodense areas, indenting the liver surface, devoid of contrast enhancement, and closely following the ribs. Coronal images may be useful in uncertain cases (Figure 44-11).

# VASCULAR AND BILIARY VARIANTS

Hepatic vascular and biliary variants usually are not responsible for any clinical symptomatology but, in the case of hepatobiliary surgery, may strongly influence patient management and prognosis. Their surgical relevance varies greatly depending on the surgical procedure that needs to be performed (e.g., liver transplantation or laparoscopic cholecystectomy). Therefore, hepatic vascular and biliary variants are subsequently described according to their implications on specific surgeries. They are anomalies in the number, origin, and course of the involved structure.

# Cholecystectomy

Although bile duct injuries can occur during either open or laparoscopic cholecystectomy, they are more common with the latter technique. An aberrant RHD (3.2% to 18.0% of the population), draining part of the right lobe of the liver into the



**Figure 44-8** Normal portal venous branching from three-dimensional computed tomography portography. *LPV*, Left portal vein; *PV*, portal vein; *RAPV*, right anterior portal vein; *RPPV*, right posterior portal vein; *RPV*, right portal vein; *SMV*, superior mesenteric vein; *SV*, splenic vein.

FIGURE 44-9 Normal biliary anatomy from contrast-enhanced threedimensional T1-weighted magnetic resonance cholangiography (A) and multidetector computed tomography cholangiography (B) in two different cases. *CBD*, Common bile duct; *CD*, cystic duct; *CHD*, common hepatic duct; *LHD*, left hepatic duct; *RHD*, right hepatic duct; *RHD*, right posterior hepatic duct; *Seg. IV BD*, segment IV draining biliary duct. extrahepatic biliary tree, is associated with such injuries. Being close to the cystohepatic angle, it may be inadvertently transected or ligated during cholecystectomy, with resultant biliary fistula, biloma, sepsis, pain, cholangitis, and even biliary atrophy with jaundice.

Variations of cystic duct insertion exist, including low and high insertion on the common duct, insertion on the RHD, and the presence of an accessory duct or cholecystohepatic duct. In approximately 10% of the population the cystic duct runs for a long distance before inserting low on the CHD, in a common fibrous sheath. In this situation, the CHD may be misinterpreted as the cystic duct, with resultant inadvertent transection or ligation of the CHD. The extrahepatic bile duct also may stricture if the long parallel cystic duct is ligated too close to the CHD.

Another potential complication is related to an excessively long cystic duct remnant left after surgery, which can predispose to calculus formation and postcholecystectomy syndrome.<sup>13,14</sup>

#### Living-Donor Liver Transplantation

For LDLT, adequate metabolic vitality to the hepatic lobe remnant in the donor and to the one transplanted into the recipient must be ensured. The hemihepatectomy is performed along a relatively avascular plane, close to Cantlie's line, that separates the left and right liver. It runs 1 cm to the right of the MHV and connects the gallbladder fossa and the IVC (Figure 44-12). Typically, a right lobe graft is harvested for adult-toadult LDLT; a left liver graft is usually employed for pediatric

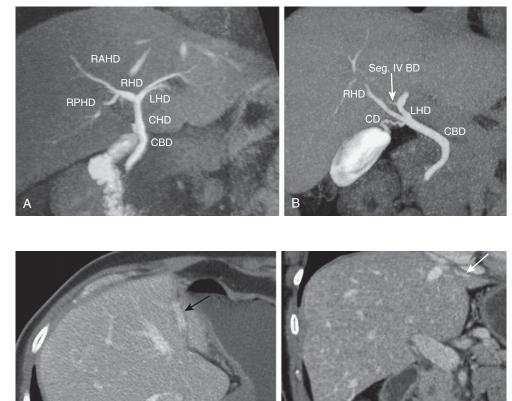
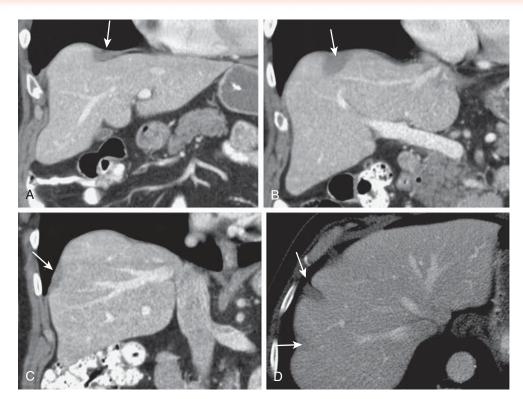
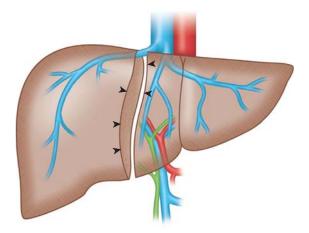


Figure 44-10 Left lobe hypoplasia. Axial (A) and coronal (B) multidetector computed tomography. Left lobe hypoplasia is characterized by a reduced volume of the left lobe of the liver. Corresponding biliary ducts and hepatic arterial, venous, and portal vessels are present but reduced in caliber. *Arrows* indicate left hepatic vein.



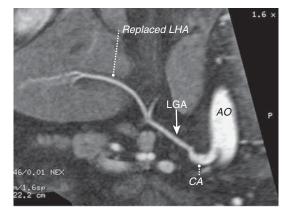
**Figure 44-11** Diaphragmatic indentations. Coronal (A to C) and axial (D) multidetector computed tomography. Diaphragmatic indentations (arrows) are caused by close apposition of the diaphragm to the liver. They manifest as wedge-shaped hypodense areas around the periphery of the liver, devoid of contrast enhancement. In uncertain cases their nature is more easily appreciated on coronal images.



**Figure 44-12** Anatomic drawing to demonstrate hemihepatectomy plane (*arrowheads*), which runs 1 cm to the right of the middle hepatic vein and connects the gallbladder fossa and the inferior vena cava.

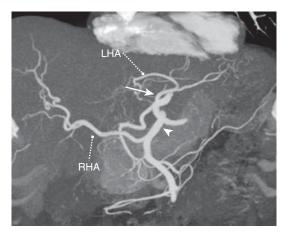
recipients or recipients of small size. For preoperative selection and planning, there are important vascular, biliary, and volumetric considerations.

The balance between the blood supply and venous drainage of the graft as well as adequate biliary drainage are prerequisites for successful liver transplantation. Inadvertent arterial or venous transection or ligation, with resultant hepatic arterial infarction or venous congestion, can seriously damage the graft, causing its failure; therefore, vessels running along the dissection plane need to be preoperatively identified to ascertain if the surgery is feasible and, if so, to guide decision making for the appropriate surgical approach.

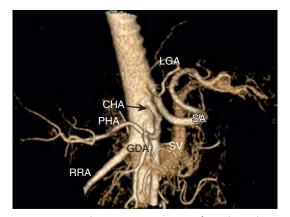


**Figure 44-13** Replaced left hepatic artery (*LHA*) from left gastric artery (*LGA*) from curved maximum intensity projection multidetector computed tomography. Replaced LHA arises from LGA. *AO*, Aorta; *CA*, celiac artery.

The level of importance of anatomic variants depends on whether they are found in the donor or in the recipient. For example, a replaced or accessory left hepatic artery from the left gastric artery is relevant in a recipient, owing to the extra steps required to ligate it at the origin during native liver removal, but it is not important in a donor (Figures 44-13 and 44-14). On the other hand, a variant origin of the artery to segment IV is extremely relevant in the donor because the hepatectomy plane would cut its arterial supply, but it is not important in the recipient. Other variants may require extra surgical steps in both the donor and the recipient (Figure 44-15). Arterial variants relevant in donors and in recipients are summarized in Table 44-5.



**Figure 44-14** Replaced right hepatic artery (*RHA*) and left hepatic artery (*LHA*) from coronal multidetector maximum intensity projection (MIP). Coronal MIP shows replaced *LHA* from gastric artery (*arrow*) and replaced *RHA* from superior mesenteric artery (*arrowhead*).



**Figure 44-15** Variant hepatic artery anatomy from three-dimensional volume rendering multidetector computed tomography. Common hepatic artery (*CHA*), splenic artery (*SA*), and left gastric artery (*LGA*) arise separately from the aorta. *GDA*, Gastroduodenal artery; *PHA*, proper hepatic artery; *RRA*, right interlobar renal artery; *SV*, splenic vein.

Among hepatic venous anomalies, variations in MHV and the presence of accessory hepatic veins have profound impact on transplantation surgery. The branching pattern of the MHV influences the location of the hepatectomy plane. Hepatic venous branches draining segments VIII and V may empty into the MHV. Drainage of the right superior anterior segment (segment VIII) into the MHV requires extra surgical steps to avoid venous congestion of the same segment (medial sector venous congestion), necrosis, and atrophy (Figure 44-16).

An accessory inferior RHV draining directly into the IVC is found in 47% of cases and is relevant in donors. When its distance along the IVC from the main hepatic venous drainage is more than 40 mm, it may be difficult to implant both veins into the recipient. Hepatic venous variants relevant in donors and in recipients are summarized in Table 44-6.

Of the many portal variants, trifurcation (Figure 44-17), found in 10% to 16% of patients, although not a surgical contraindication, requires extra surgical steps. Moreover, the distance between the bifurcation of the LPV and that of the RPV must be evaluated preoperatively because of its implications on

TABLE 44-5	Hepatic Arterial Vari Liver Transplantation				
Varia	Variant Implications for Surgery				
ARTE	RIAL VARIANTS RELEVAN	T IN DONORS			
MHA	from RHA	Hepatic plane would cut this artery, compromising arterial supply to left lobe of the liver			
	trifurcation into RHA, A, and GDA	Clamping or ligation of CHA can cause gastric or duodenal hypoperfusion.			
RHA or LHA from CHA before the origin of GDA		Clamping or ligation of CHA can cause gastric or duodenal hypoperfusion.			
ARTE	RIAL VARIANTS RELEVAN	T IN RECIPIENTS			
Short	RHA	Increases surgical complexity and can lead to difficult anastomosis			
Celiad	artery stenosis	Increases risks of graft failure and biliary complications			
(Mie hep	ced or accessory LHA chel II, V), replaced patic trunk arising from A (Michel IX)	Increases complexity of the surgery			

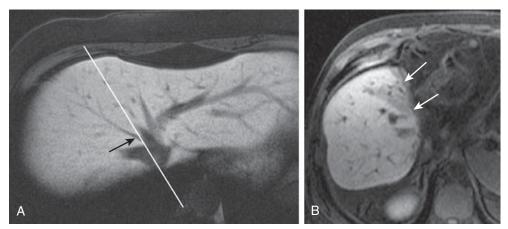
CHA, Common hepatic artery; GDA, gastroduodenal artery; LHA, left hepatic artery; MHA, middle hepatic artery; RHA, right hepatic artery; SMA, superior mesenteric artery.

surgical technique. Portal venous variants relevant in liver transplantation are summarized in Table 44-7.

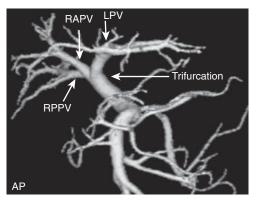
Biliary complications, which include bile leakage and bile duct stricture, occurring in 7% to 10% of donors, represent the most common cause of morbidity in living-donor liver transplantation. Preoperative imaging of biliary anatomic variants is useful to prevent this type of complication (Figure 44-18).

RPHD drainage into the LHD, one of the most common bile duct variants (15.6% of cases), can lead to inadvertent biliary tract injury in the donor. Other surgically relevant anatomic variants of the biliary tract include a posteroinferior branch of the RHD draining into the LHD and biliary trifurcation (Figure 44-19). Presurgical imaging evaluation of biliary anatomy variants (Figure 44-20), using MDCT cholangiography or MRCP can help prevent biliary tract injuries. Biliary variants relevant in donors and in recipients are summarized in Table 44-8.

Volumetric postprocessing of cross-sectional liver imaging is helpful for preoperative selection and surgical planning as well. Donor and recipient considerations factor into the decision of whether a right-sided or left-sided graft is transplanted. For the donor, the magnitude of the hepatectomy correlates with morbidity and mortality rates, an important consideration in an elective procedure. For the recipient, the donated graft must accommodate the increased portal flow and pressure that accompanies cirrhotic physiology. If the graft is insufficient, small for size syndrome can ensue, whereby excessive portal circulation damages the sinusoidal microvasculature and overwhelms graft function, resulting in hepatocyte ischemia and complications of hepatic insufficiency, cholestasis, and coagulopathy. Volumetric assessment of right, left, and caudate lobes allow for preoperative patient and graft selection and planning for additional vascular ligation, grafting, and reconstruction as necessary.15-2



**Figure 44-16** Segment VIII venous tributary into the middle hepatic vein (MHV). **A**, Axial T1-weighted magnetic resonance image (MRI) in the donor shows segment VIII tributary vein (*arrow*) emptying into the MHV. The hemihepatectomy plane (*white line*) intersects the accessory segment VIII hepatic vein before its confluence into the inferior vena cava. **B**, Postoperative axial T1-weighted MRI image in the recipient shows atrophy of the corresponding liver segment (*arrows*).



**Figure 44-17** Portal vein trifurcation from three-dimensional volumerendering multidetector computed tomography. Computed tomography angiography demonstrates trifurcation of the portal vein (*arrow*) into the left portal vein (*LPV*), right anterior portal vein (*RAPV*), and right posterior portal vein (*RPPV*).

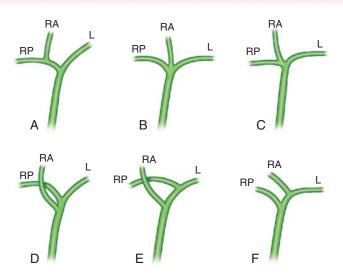
TABLE <b>44-6</b>	Hepatic Venous Varian Liver Transplantation	ts and			
Varian	Variant Implications for Surgery				
HEPATIC VENOUS VARIANTS RELEVANT IN DONORS           Accessory inferior RHV larger than 3 mm         Increases surgical complexity and surgical technique must be modified					
HEPATIC VENOUS VARIANTS RELEVANT IN RECIPIENTS           Accessory inferior RHV draining into IVC more than 3 cm from the main hepatic venous confluence with the IVC         Increases surgical complexity and surgical technique must be modified					
Early b vein	pranching of segment VIII	Increases surgical complexity and surgical technique must be modified			
	alous drainage of segments ad VII into the MHV	Risk for medial sector congestion and atrophy			
Early o	confluence of hepatic veins	Increases surgical complexity and surgical technique must be modified			
IVC, Inferior vena cava; MHV, middle hepatic vein; RHV, right hepatic					

IVC, Interior vena cava; MHV, middle hepatic vein; RHV, right hepatic vein.

TABLE Portal Venous Variants and 44-7 Liver Transplantation			
Variar	t	Implications for Surgery	
PORT	AL VENOUS VARIANT	S RELEVANT IN DONORS	
Trifurc vein	ation of the portal	Surgical planning must be modified because of the lack of a portal segment to clamp during surgery and to prevent bleeding in the donor and a difficult anastomosis in the recipient.	
	venules to nent V	Surgical planning must be modified to avoid bleeding and ischemia.	
PORTAL VENOUS VARIANTS RELEVANT IN RECIPIENTS			
VII s post	branch of segment upplying terosuperior area of t lobe	Surgical planning must be modified to prevent ischemia in the recipient.	
Trifurc vein	ation of the portal	Surgical planning must be modified because of the lack of a portal segment to clamp during surgery and to prevent bleeding in the donor and a difficult anastomosis in the recipient.	
	angle of portal vein aching	The liver during regeneration may engulf the veins and reduce blood supply, causing ischemia in the graft.	
Short	ength of portal vein	May cause allograft failure	

# Hepatic Tumor Resection

Hepatic tumor resection is mainly performed to treat hepatic metastatic disease. Accurate preoperative patient selection and surgical planning are invaluable for hepatic tumor resection in an otherwise healthy liver, and it is more important in the case of small residual liver volume or in patients with compromised hepatic function, in whom even minor complications such as bile leakage or partial hepatic necrosis may be fatal. Diagnostic imaging is therefore required to define hepatobiliary anatomy, the number, size, location, and surgical margins of metastases (see Figure 44-8) and thereby identify patients who can safely



**Figure 44-18** Drawing representing biliary variants. A, Normal bile duct anatomy. B, Trifurcation pattern. C, Short right hepatic duct. D, Right anterior hepatic duct (RAHD) continuation into the common hepatic duct. E, Right posterior hepatic duct drainage into the left hepatic duct (LHD). F, Right anterior hepatic duct drainage into LHD. L, Left; RA, right anterior; RP, right posterior.

undergo a procedure aimed to resect the lesions to a suitable end point. For this purpose, the anticipated remaining liver needs to be evaluated for sufficient remnant liver volume (including two contiguous hepatic segments), adequate vascular inflow and outflow, biliary drainage, and the presence or absence of steatosis.

Areas at risk for devascularization or venous congestion need to be preoperatively identified so that surgical feasibility can be ascertained and appropriate techniques can be adopted. The spatial relationship of the arterial and/or venous variant to the tumor dictates the level of importance and influence on surgical technique. A summary of the most important vascular variants relevant to hepatic tumor surgery is provided in Tables 44-9 to 44-11.

Biliary complications constitute an important cause of major morbidity in hepatic tumor resection (3.6% to 8.1%) and are important risk factors for liver failure (35.7%) and operative mortality (39.3%). One of the most serious complications is bile leakage. The complexity of bile duct confluence and the variability of the left intrahepatic bile ducts account for the higher incidence of biliary complications after left-sided hepatectomy. A summary of relevant bile duct variants in partial hepatic resection for tumor treatment is shown in Table 44-12.<sup>21-26</sup>

**Figure 44-19** Biliary trifurcation from conventional and mangafodipir trisodium–enhanced magnetic resonance (MR) cholangiography. Intraoperative cholangiography. Intraoperative cholangiography. Intraangiography maximum intensity projection image (B) shows biliary trifurcation. *LHD*, Left hepatic duct; *RAHD*, right anterior hepatic duct; *RPHD*, right posterior hepatic duct.

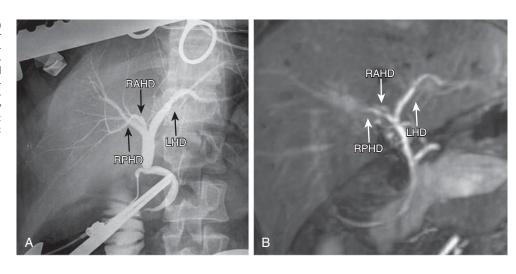
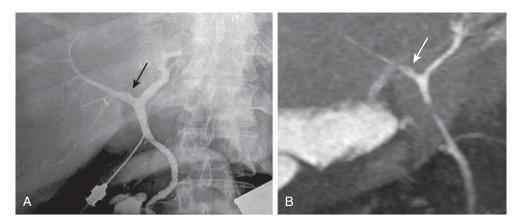


Figure 44-20 Early branching right hepatic duct (RHD) from conventional and mangafodipir trisodiumenhanced magnetic resonance (MR) cholangiography. Intraoperative cholangiogram (A) and mangafodipirenhanced MR cholangiography maximum intensity projection image (B) demonstrate early branching RHD (arrows).



# TABLEBiliary Duct Variants and44-8Liver Transplantation

#### **BILIARY DUCT VARIANTS RELEVANT IN DONORS**

Ducts	Percentage (%)		
RPHD draining directly into LHD	13-19		
Trifurcation: Simultaneous emptying of RAHD, RPHD, LHD into CHD	11		
RPHD draining directly into CHD	5		
Accessory hepatic ducts	2		
BILIARY DUCT VARIANTS RELEVANT IN RECIPIENTS			
LHD draining into RAHD	4%		
Trifurcation: Simultaneous emptying of RAHD, RPHD, LHD into CHD	11%		
Cystic duct draining into RHD	Very unusual		
Accessory hepatic ducts	2%		

CHD, Common hepatic duct; LHD, left hepatic duct; RAHD, right anterior hepatic duct; RPHD, right posterior hepatic duct.

TABLE	Arterial Variants and Influence on		
44-9	Tumor Resection		
		Right Lobe	Left Lobe Tumor

Arterial Variants	Resection	Resection
Replaced LHA from LGA (Michel II)	-	+
Replaced RHA from SMA (Michel III)	+	-
Replaced RHA and LHA (Michel IV)	-	+
Accessory LHA from LGA (Michel V)	-	+
Accessory RHA (Michel VI)	+	-
Accessory RHA and LHA (Michel VII)	+	+
Replaced RHA and accessory LHA or replaced LHA and accessory RHA (Michel VIII)	+	+
Entire hepatic trunk from SMA (Michel IX)	+	+
Entire hepatic trunk from LGA (Michel X)	+	+

LGA, Left gastric artery; LHA, left hepatic artery; RHA, right hepatic artery; SMA, superior mesenteric artery.

TABLE 44-10	Hepatic Venous Variants and Tumor Resection Surgery		
Venou	s Variants	Right Lobe Tumor Resection	Left Lobe Tumor Resection
Segment VIII drainage into MHV		_	+
Segment V and VI accessory inferior hepatic veins draining directly into IVC		+	-
Access into	ory MHV draining directly IVC	-	+

IVC, Inferior vena cava; MHV, middle hepatic vein.

# TABLEPortal Venous Variants and Tumor44-11Resection Surgery

Venous Variants	Right Lobe Tumor Resection	Left Lobe Tumor Resection
Trifurcation of portal vein Right and left portal branches supplying segment VIII	- +	+ -

# **44-12** Biliary Variants and Tumor Resection Surgery

Variants	Right Lobe Tumor Resection	Left Lobe Tumor Resection
RPHD draining directly into LHD	-	+
LHD draining directly into RHD	+	-
Trifurcation: simultaneous emptying of RAHD, RPHD, LHD into CHD	+	+

CHD, Common hepatic duct; LHD, left hepatic duct; RAHD, right anterior hepatic duct; RPHD, right portal hepatic duct.

# Intraarterial Therapy

For patients with advanced malignant disease involving the liver, whether derived from metastatic or primary hepatic malignancy, surgical resection or liver transplantation may not be a viable treatment option. In these cases, intraarterial transcatheter chemoembolization and radioembolization may be indicated.

Hepatic metastases derive most of their blood supply from the hepatic artery, whereas normal liver is mainly nourished by the portal vein. Therefore, transcatheter hepatic arterial embolization aims to deliver therapeutic agents to malignancies while minimizing dosages and toxicity to normal liver and other organs (nontarget embolization).

A thorough understanding of the patient's vascular anatomy and supply of target lesions is essential to treatment planning. This is partly achieved by preprocedure imaging and also by initial angiography directed to the celiac and superior mesenteric arteries. Imaging through the portal venous phase is necessary, because this population is at increased risk for portal vein thrombosis. Attention should be directed to identifying variant anatomy, as well as extrahepatic vascular supply parasitized by tumor. The latter case is of particular importance to large tumors (63% of tumors >6 cm), serosal location (17%), and prior embolization therapy. Collateral vessels may include phrenic, adrenal, right internal mammary, omental, renal, left gastric, and cystic arteries. In certain instances, prophylactic coil embolization of collateral vessels is needed to prevent nontarget embolization.

Finally, vascular considerations are also important in patients with colorectal metastases who undergo placement of a hepatic arterial infusion pump for liver-directed chemotherapy as an adjunct to systemic chemotherapy. Pump catheter positioning must ensure delivery of chemotherapy to the liver without perfusion of extrahepatic tissues, while minimizing in-situ turbulence that may result in arterial thrombosis. In patients with

TABLE 44-13 Accuracy,						
Modality	Accuracy	Limitations	Pitfalls			
Radiography	Conventional angiography 95.8%	Radiation exposure Invasiveness Possible procedural complications				
СТ	93.2%	Radiation exposure	Analysis of raw data and of postprocessed images to avoid diagnostic errors			
MRI	93%	Patient cooperation High cost	Analysis of raw data and of postprocessed images to avoid diagnostic errors			
Ultrasonography	N/A	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	Incomplete evaluation of vascular anatomy			
Nuclear medicine	N/A	Radiation exposure Currently no role	Unable to evaluate vascular anatomy			
PET/CT	N/A	Radiation exposure High cost	Unable to evaluate vascular anatomy			

MRI, Magnetic resonance imaging; N/A, not applicable; PET/CT, positron emission tomography/computed tomography.

normal arterial anatomy, the hepatic arterial infusion pump is inserted in the proper hepatic artery distal to the origin of the gastroduodenal artery. In patients with variant arterial anatomy, the pump should be placed within the dominant hepatic artery, as proximal as possible but distal to the origin of the gastroduodenal artery. In patients with arterial variants, such as the replaced RHA and LHA (Michel types II, III, and IV), modification of the technique may be required.<sup>27,28</sup>

# Imaging

# RADIOGRAPHY

Conventional radiology is unable to assess parenchymal and vascular variants of the liver. Catheter angiography represents the gold standard for vascular evaluation, but owing to its invasiveness, radiation burden, and the improved accuracy of MDCT and MR angiography, its use is mainly restricted to interventional procedures.

# Computed Tomography

MDCT allows accurate evaluation of parenchymal variants in the liver, including the presence of accessory lobes. MDCT angiography provides detailed images of the hepatic vascular anatomy, whereas MDCT cholangiography permits noninvasive detection of biliary variants.<sup>1-7,14,15</sup>

## Magnetic Resonance Imaging

MRI has the same potential as MDCT in evaluation of parenchymal, vascular, and biliary variants. Moreover, owing to the availability of hepatic-specific contrast agents, such as Gd-BOPTA and Gd-EOB-DTPA, it potentially can be used in the evaluation of suspected ectopic accessory hepatic lobes.\*

# ULTRASOUND

In many clinical scenarios, ultrasonography is the first diagnostic imaging tool used to evaluate the liver for parenchymal variants. However, it is limited in evaluation and characterization of vascular anatomy.

#### **IMAGING ALGORITHM**

MDCT and MR angiography and cholangiography are accurate imaging tools in hepatic anatomy assessment (Table 44-13). Careful evaluation of raw data and postprocessed images allows recognition of normal anatomy and identification of variant anatomy.

# What the Referring Physician Needs to Know

- Hepatic vascular and biliary anatomic variants are common.
- Anatomic variants are not responsible for clinical symptoms.
- Variants may strongly affect patient management, particularly in the case of surgery.

#### **Key Points**

- The role of hepatic vascular and biliary anatomic variants is dictated by the surgical procedure that needs to be performed.
- Preoperative imaging evaluation is mandatory for patient selection, surgical planning, and avoidance of complications.
- MDCT and MR angiography and cholangiography are as accurate as catheter angiography and intraoperative cholangiography.
- Postprocessed imaging is mandatory.

<sup>\*</sup>References 1, 2, 5, 7, 11, 22, 25.

#### SUGGESTED READINGS

Catalano OA, Singh AH, Uppot RN, et al: Vascular and biliary variants in the liver: implications for liver surgery. *Radiographics* 28:359–378, 2008.

Hyodo T, Kumano S, Kushihata F, et al: CT and MR cholangiography: advantages and pitfalls in perioperative evaluation of biliary tree. *Br J Radiol* 85:887–896, 2012.

## REFERENCES

- Sahani D, D'souza R, Kadavigere R, et al: Evaluation of living liver transplant donors: method for precise anatomic definition by using a dedicated contrast-enhanced MR imaging protocol. *Radiographics* 24:957–967, 2004.
- Sahani D, Mehta A, Blake B, et al: Preoperative hepatic vascular evaluation with CT and MR angiography: implications for surgery. *Radiographics* 24:1367–1380, 2004.
- Sahani D, Saini S, Pena C, et al: Using multidetector CT for preoperative vascular evaluation of liver neoplasms: technique and results. *AJR Am J Roentgenol* 179:53–59, 2002.
- 4. Limanond P, Raman S, Ghobrial M, et al: Preoperative imaging in adult-to-adult living related liver transplant donors: what surgeons want to know. *J Comput Assist Tomogr* 28:149– 157, 2004.
- Catalano OA, Singh AH, Uppot RN, et al: Vascular and biliary variants in the liver: implications for liver surgery. *Radiographics* 28:359–378, 2008.
- Pannu HK, Maley WR, Fishman EK: Liver transplantation: preoperative CT evaluation. *Radiographics* 21:S133–S146, 2001.
- 7. Yeh BM, Breiman RS, Taouli B, et al: Biliary tract depiction in living potential liver donors: comparison of conventional MR, mangafodipir trisodium-enhanced excretory MR, and multidetector row CT cholangiography—initial experience. *Radiology* 230:645–651, 2004.
- Cheng YF, Huang TL, Chen CL, et al: Variation of the intrahepatic portal vein; angiographic demonstration and application in living-related hepatic transplantation. *Transplant Proc* 28: 1667–1668, 1996.
- 9. Lerut JP, Laterre PF, Goffette P, et al: Adult liver transplantation and abnormalities of splanchnic veins: experience in 53 patients. *Transpl Int* 10:125–132, 1997.
- 10. Sugarbaker PH, Nelson RC, Muray DR, et al: A segmental approach to computerized tomo-

- Sahani D, Mehta A, Blake B, et al: Preoperative hepatic vascular evaluation with CT and MR angiography: implications for surgery. *Radiographics* 24:1367–1380, 2004.
- Singh AK, Cronin CG, Verma HA, et al: Imaging of preoperative liver transplantation in adults: what

graphic portography for hepatic resection. *Surg Gynecol Obstet* 171:189–195, 1990.

- Mortelé KJ, Ros PR: Anatomic variants of the biliary tree: MR cholangiographic findings and clinical applications. *AJR Am J Roentgenol* 177: 389–394, 2001.
- Gray H: Gray's anatomy: the anatomical basis of medicine and surgery, ed 38, Edinburgh, 1995, Churchill Livingstone, pp 1795–1802.
- Hyodo T, Kumano S, Kushihata F, et al: CT and MR cholangiography: advantages and pitfalls in perioperative evaluation of biliary tree. Br J Radiol 85:887–896, 2012.
- Turner MA, Fulcher AS: The cystic duct: normal anatomy and disease processes. *Radiographics* 2:3–22, 2001.
- Singh AK, Cronin CG, Verma HA, et al: Imaging of preoperative liver transplantation in adults: what radiologists should know. *Radiographics* 31:1017–1030, 2011.
- Coskun M, Kayahan E, Ozbek O, et al: Imaging of hepatic arterial anatomy for depicting vascular variations in living related liver transplant donor candidates with multidetector computed tomography: comparison with conventional angiography. *Transplant Proc* 37:1070–1073, 2005.
- Goldman J, Florman S, Varotti G, et al: Noninvasive preoperative evaluation of biliary anatomy in right-lobe living donors with mangafodipir trisodium-enhanced MR cholangiography. *Transplant Proc* 35:1421–1422, 2003.
- Quintini C, Aucejo F, Hashimoto K, et al: State of the art and future developments for surgical planning in LDLT. *Curr Transpl Rep* 1:35–42, 2014.
- Kamel IR, Lawler LP, Fishman EK: Variations in anatomy of the middle hepatic vein and their impact on formal right hepatectomy. *Abdom Imaging* 28:668–674, 2003.
- 20. Kapoor V, Peterson MS, Baron RL, et al: Intrahepatic biliary anatomy of living adult liver

donors: correlation of mangafodipir trisodiumenhanced MR cholangiography and intraoperative cholangiography. *AJR Am J Roentgenol* 

radiologists should know. Radiographics 31:1017-

1030, 2011.

- 179:1281–1286, 2002.
   Adams RB, Haller DG, Roh MS, et al: Improving resectability of hepatic colorectal metastases: expert consensus statement by Abdalla. Ann Surg Oncol 13:1281–1283, 2006.
- Allen PJ, Nissan A, Picon AI, et al: Technical complications and durability of hepatic artery infusion pumps for unresectable colorectal liver metastases: an institutional experience of 544 consecutive cases. J Am Coll Surg 201:57–65, 2005.
- Bipat S, van Leeuwen MS, Comans EF, et al: Colorectal liver metastases: CT, MR imaging, and PET for diagnosis—meta-analysis. *Radiol*ogy 237:123–131, 2005.
- Capussotti L, Ferrero A, Vigano L, et al: Bile leakage and liver resection: where is the risk? Arch Surg 141:690–694, discussion 695, 2006.
- Charnsangavej C, Clary B, Fong Y, et al: Selection of patients for resection of hepatic colorectal metastases: expert consensus statement. *Ann Surg Oncol* 13:1261–1268, 2006.
- Lo CM, Fan ST, Liu CL, et al: Biliary complications after hepatic resection: risk factors, management, and outcome. *Arch Surg* 133:156–161, 1998.
- Lee AJ, Gomes AS, Liu DM, et al: The road less traveled: importance of the lesser branches of the celiac axis in liver embolotherapy. *Radiographics* 32:1121–1132, 2012.
- Allen PJ, Stojadinovic A, Ben-Porat L, et al: The management of variant arterial anatomy during hepatic arterial infusion pump placement. *Ann* Surg Oncol 9:875–880, 2002.



# **Imaging of the Pancreas**

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# **Multidetector Computed Tomography**

Multidetector computed tomography (MDCT) has become a fundamental technique of pancreatic imaging. Today, higher image quality can be obtained in abdominal imaging, and this is even more significant in pancreatic imaging, in which the reduction of acquisition time, the possibility of multiple phases of enhancement imaging, and higher resolution images in all three spatial planes, with the possibility of excellent multiplanar image reconstructions, permit MDCT to provide excellent images of the anatomic layout of the pancreas and its vasculature. This technique is now used to diagnose a variety of congenital, neoplastic, inflammatory, and traumatic pancreatic disease processes.

# **PRE-EXAMINATION CONSIDERATIONS**

MDCT imaging of the pancreas is largely based on the study of the enhancement pattern of the lesions and the anatomic variants of the normal pancreas.

The first step of an MDCT study of the pancreas should be the administration of negative oral contrast medium to the patient, to distend the stomach and duodenum. Negative oral contrast medium should be preferred because it permits an easier evaluation of gastric and duodenal wall lesions and does not mask radiopaque stones in the common bile duct or pancreatic calcifications.<sup>1</sup>

Contrast-enhanced imaging of the pancreas is based on different contrast medium parameters, such as iodine concentration, volume administration, and injection rate.

The use of intravenous iodinated contrast media is routine with MDCT, and the dose and rate of contrast injection must be adapted to the higher scanning speeds of MDCT.

The maximum amount of iodine should not exceed 35 to 45 g, independently from the concentration of the contrast medium used.<sup>2</sup>

Achieving high concentrations of contrast enhancement to study the pancreas is possible either with increasing the increment of the injection rate or the iodine concentration of the contrast medium used (total iodine dose being kept constant); the latter is more important because it does not depend on the intravenous access and vessel diameter as the first is.

The contrast enhancement of the extracellular/extravascular space depends on the concentration gradient between intravascular and extracellular/extravascular spaces, the volume of the extracellular/extravascular space, the permeability of organ microvasculature and cellular interfaces, and surface area and time.<sup>3</sup> A high concentration gradient between intravascular and

extracellular/extravascular spaces allows a high influx of contrast material into the extracellular/extravascular space and contributes to high organ enhancement.

Keeping the rate of contrast injection and the total dose of iodine constant, the use of contrast medium with higher concentration improves significantly the arterial and portal venous phase enhancement compared with contrast medium with lower concentration.4

As a result, the use of high concentrations of contrast medium improve conspicuity of hypovascular and hypervascular lesions in the pancreas.<sup>5</sup>

# SCANNING TECHNIQUE

A plain computed tomography (CT) scan of the upper abdomen is performed using 10-mm slice collimation to cover the pancreas (Figure 45-1). Depending on the scanner type, a pancreatic phase is performed using 1- to 2-mm slice collimation. Acquisition of the pancreatic phase is usually at a delay of 35 to 40 seconds after a bolus of 125 to 150 mL of iodinated contrast medium injected at a rate of 4 to 5 mL/s. The scanned area extends from the diaphragm to below the transverse duodenum in a single breath-hold.<sup>6</sup> A weight-based approach to intravenous contrast medium administration is now considered more appropriate to optimize the iodine dose for a study. An iodine dose of 550 mg/kg can be used for both pancreatic and vascular enhancement, which translates into 1.8 to 2 mL/kg.

For the next phase, the patient is instructed to breathe deeply after the pancreatic phase acquisition, and a second spiral acquisition is performed at a 70- to 80-second scan delay (see Figure 45-1). This is the portal venous phase, which covers the entire upper abdomen using 2.5- to 5-mm slice collimation, depending on the patient's body habitus. This phase is critical for the detection of small hypodense liver metastases and the diagnosis of venous encasement by a tumor. Early arterial phase scans can be performed if a CT angiogram is desired.

# DYNAMIC IMAGING

Contrast-enhanced imaging of the pancreas is usually performed in three phases.<sup>7</sup> The first phase is the early arterial phase, which is obtained approximately 20 seconds after contrast administration (see Figure 45-1). In this phase, contrast medium is preferentially concentrated within the arterial tree with almost no enhancement of the pancreatic parenchyma. The delayed arterial phase, also called the pancreatic phase, is acquired nearly 35 to 40 seconds after contrast agent administration. In this phase, the pancreatic parenchyma enhances

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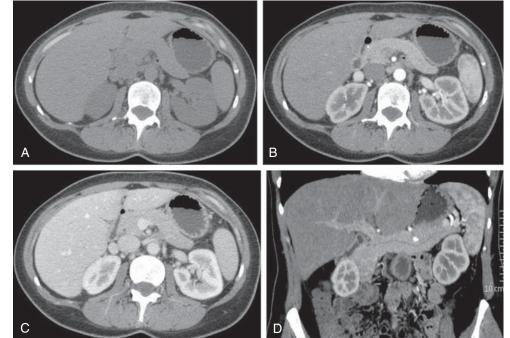


Figure 45-1 Computed tomography (CT) anatomy of the pancreas. Precontrast axial CT image of the pancreas (A) shows normal glandular thickness. On the pancreatic phase of the dynamic study (B), pancreatic parenchyma shows intense, homogeneous enhancement similar to the renal cortex, with washout during the portal venous phase (C). On coronal curved reformatted image (D), the whole main pancreatic duct can be depicted.

optimally.<sup>7</sup> On the third phase, the portal venous phase, usually acquired at 65 to 70 seconds after contrast agent administration, we have the highest contrast uptake by the portal venous vessels, as well as the liver parenchyma (see Figure 45-1).

The bolus tracking techniques, performed by placing a region of interest marker in the aorta just above the level of the pancreas and starting to acquire images when arterial enhancement peaks reach a predetermined Hounsfield unit (HU) trigger value (usually 120 to 130 HU), helps determine the exact timing of scan delay for a precise individual study for each patient.

Scanning for the pancreatic phase starts 15 seconds after threshold is reached.

# IMAGE POSTPROCESSING

A large variety of image processing options are available, such as curved reformatted images, minimum intensity projections, volume-rendered images, standard coronal and sagittal plane reformatted images, and coronal oblique reformatted images (see Figure 45-1). Among these, curved reformatted images give important information about vascular involvement and ductal abnormalities<sup>8</sup>; minimum intensity projections can be used to visualize low-attenuation structures, such as pancreatic and common bile ducts,<sup>9</sup> whereas maximum intensity projections can evaluate high-attenuation structures, such as peripancreatic vasculature. Volume-rendered images are of great aid in visualization of the peripancreatic vessels and tumor encasement.

Such additional two-dimensional (2D) and 3D reformatted images provide fundamental information about tumor extent, peripancreatic vascular involvement, or ductal abnormalities, which may be difficult to evaluate on axial images and are also useful to display the lesion characteristics to surgeons and gastroenterologists.<sup>8</sup>

# Magnetic Resonance Imaging

Recent technologic innovations to both hardware and software have made magnetic resonance imaging (MRI) a reliable technique for studying the pancreas. MRI is potentially the only diagnostic tool that makes it possible to simultaneously image the pancreatic parenchyma and focal (neoplasms, autoimmune pancreatitis) or diffuse (acute or chronic pancreatitis) pathologic processes, reveal dilatation of pancreatic and bile ducts, and identify gallstones, peripancreatic or hemorrhagic fluid accumulations, lymphadenopathies, hepatic metastases, and vascular anomalies.

In many centers, MRI is currently considered the third method for studying the pancreas, after ultrasonography and CT, not so much because of the technical problems but because of the high costs and, above all, the limited "machine time" useable by departments dealing with pancreatic disease.

# **TECHNICAL ASPECTS**

To achieve the best possible abdominal evaluation with MRI, it is important to use a high-intensity magnetic field (>1.0 tesla) that guarantees high signal-to-noise ratio (SNR), phased-array surface coils, automatic injectors, powerful gradients, and rapid sequences that can provide images without artifacts resulting from movement or breathing.<sup>10</sup>

The phased-array surface coils integrate the signal arriving from several coils, reconstructing the final image with a high SNR that ensures greater spatial resolution for the images acquired.<sup>11</sup> The recent development of high-power gradients has made it possible to obtain rapid sequences that ensure better images of the abdomen during breath-holding, thus eliminating the artifacts resulting from breathing that decrease image quality.<sup>12</sup> The fat saturation obtained with high field units improves the latitude for nonadipose tissues and reduces the artifacts along the phase-encoding direction resulting from movement of subcutaneous adipose tissues during scanning.<sup>13</sup>

The improvement in gradient performance and the development of new pulse sequences (e.g., the T1-weighted volumetric sequences with fat suppression or the half-Fourier rapid acquisition with relaxation enhancement [RARE] sequences) augment the possibility of obtaining better anatomic coverage with more homogeneous saturation of the signal emitted by the adipose tissue.<sup>14</sup>

The development of rapid sequences, associated with fat saturation, enables dynamic imaging of the upper abdomen during the administration of gadolinium chelates to study pancreatic parenchyma vascularization, to identify and characterize focal lesions, to evaluate any infiltration or involvement of the peripancreatic vessels, and to identify and characterize focal lesions in the liver.<sup>14</sup>

# PROTOCOL

The present protocol calls for use of the following techniques: T1-weighted, gradient recalled echo (GRE) sequence axial imaging with "in-phase" and "out-of-phase" echo time (TE); T2-weighted RARE axial imaging; T2-weighted half-Fourier RARE axial and coronal thin slice (5 to 6 mm) imaging; axial and coronal MR cholangiopancreatography (MRCP); and T1-weighted GRE precontrast axial imaging with fat suppression on the axial plane, possibly with 3D technique, before and during intravenous administration of gadolinium chelates.<sup>15</sup>

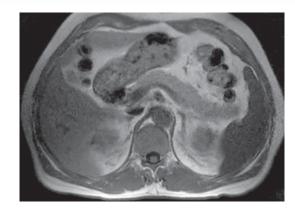
MRCP, an MRI technique that permits noninvasive study of the bile and pancreatic ducts without the use of a contrast medium, has replaced direct cholangiography in most diagnostic indications.<sup>16</sup> The underlying principle behind MRCP is the use of T2-weighted sequences with very long TE (>800 ms) so that when the echo is detected, only the present stationary fluids (bile and pancreatic juices) are able to provide a signal; the parenchymatous organs, on the other hand, are completely relaxed and thus do not emit any signal.<sup>17</sup> This results in good contrast resolution between the bile and pancreatic ducts and the parenchymatous organs. During intravenous administration of secretin, dynamic MRI improves visualization of the principal pancreatic and secondary ducts, thus permitting functional imaging of the pancreas.

# **IMAGING APPEARANCE**

# **T1-Weighted Images**

The pancreas is intrinsically hyperintense on T1-weighted images, with values higher than are seen in other hypochondriac organs (Figure 45-2). The reason for this is not fully known. The hypotheses advanced are the high quantity of pancreatic juice proteins within the pancreas glands; the presence of large quantities of endoplasmic reticula in the acinar cells; or the presence of paramagnetic ions such as manganese.<sup>13</sup> In the elderly, the high signal intensity of the pancreas can be lower than that of the liver, most likely as a result of age-related fibrosis.

T1-weighted GRE images can be used with a fat suppression pulse (Figure 45-3). Eliminating the signal emitted by the adipose tissues, which has a short T1 relaxation time, redistributes the gray scale over a narrower range, thus making the sequence more sensitive to minor variations in signal intensity.



**Figure 45-2** Normal magnetic resonance imaging anatomy of the pancreas: T1-weighted image. Axial T1-weighted gradient-echo image (repetition time/echo time [TR/TE]: 145/4.2 ms) shows pancreatic parenchyma of normal thickness. The intensity of pancreatic parenchyma is higher compared with that of the liver and spleen.



**Figure 45-3** Normal magnetic resonance imaging anatomy of the pancreas: fat-saturated T1-weighted image. The application of a fat-saturating pulse eliminates the high signal intensity fat on T1-weighted images, improving in this manner the dynamic range of the image.

The T1-weighted GRE images are used for dynamic imaging of the pancreas after intravenous administration of gadolinium chelates (Figure 45-4). The dynamic imaging is performed by acquiring 25- to 30-second images (arterial-capillary phase), 45-second images (pancreatic phase), and 80- to 90-second images (portal vein phase) (see Figure 45-4). T1-weighted fat-suppressed coronal images are obtained 5 to 10 minutes after gadolinium administration.<sup>15</sup>

Because of its glandular nature, the pancreas is a highly vascularized organ. For this reason it produces 76% to 115% higher signal intensity during the first minute after gadolinium administration.<sup>13</sup> On the delayed images, the pancreas shows signal intensity similar to that of the liver.

The T1-weighted GRE images with fat saturation and the arterial phase after contrast administration are the most sensitive sequences for identifying focal pancreatic lesions. The portal vein phase is the most useful in evaluating portal vein pathologic processes and identifying lymphadenopathies. The delayed images, obtained 10 minutes after administration of the contrast medium, are instead more useful in identifying cholangiocarcinoma, ascending cholangitis, peritoneal abscesses, and metastases.

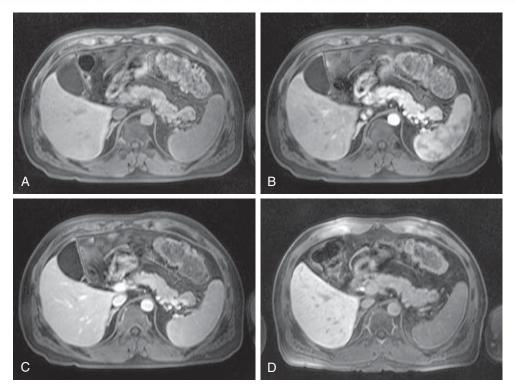
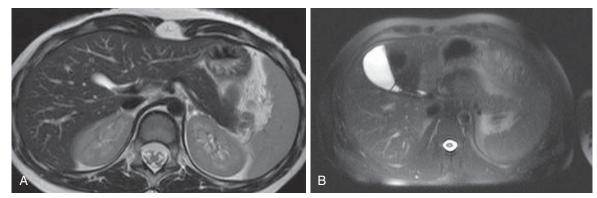


Figure 45-4 Normal magnetic resonance imaging anatomy of the pancreas: dynamic imaging during intravenous administration of gadolinium chelates. A, Axial T1-weighted gradient echo image before the administration of gadolinium chelates. B, Axial T1-weighted gradient echo images during the arterial (B), portal venous (C), and delayed phase (D) of the dynamic study. Of note is the marked signal intensity enhancement of the pancreatic parenchyma during the arterial/pancreatic phase, reflecting its glandular architecture.



**Figure 45-5** Normal magnetic resonance imaging of the pancreas: T2-weighted imaging. **A**, Axial T2-weighted rapid acquisition with relaxation enhancement (RARE) image (repetition time/echo time [TR/TE]: 3500/80 ms) of the pancreas shows the signal intensity of the pancreatic gland is lower compared with that of the liver and the spleen. **B**, The signal intensity changes are better appreciated on the fat-saturated half-Fourier single-shot turbo spin echo (HASTE) T2-weighted image (TR/TE: ∞/90 ms).

The T1-weighted images in GRE sequences, obtained with "in-phase" and "out-of-phase" echo times, are useful in identifying hepatic steatosis, lymphadenopathy, infiltration of the peripancreatic adipose tissue in acute pancreatitis, accumulation of fluids with high methemoglobin or protein concentrations, and adrenal adenoma.

# T2-Weighted Images

In T2-weighted images, the parenchymal signal is generally hypointense versus the hepatic parenchyma (Figure 45-5). Under physiologic conditions, the T2-weighted images provide excellent visualization of the bile and pancreatic duct anatomy and

pathologic processes as well as of any peripancreatic fluid accumulations, neuroendocrine tumors, and hepatic metastases.

Other uses of T2-weighted images include the identification of signal hypointensity of fibrosis and iron deposited during hemochromatosis, responsible for the marked hypointensity of the pancreatic gland signal.

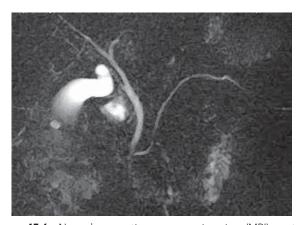
# Magnetic Resonance Cholangiopancreatography Images

MRCP is an imaging technique that is able to noninvasively assess bile and pancreatic ducts, in a multiplanar fashion, without injection of contrast material (Figure 45-6). MRCP takes advantage of the inherent contrast properties of stationary fluid in the biliary and pancreatic ducts.

The interest in MRCP in the past 5 years is due to its accuracy, safety, and availability with nearly all modern scanners, so that MRCP has replaced diagnostic endoscopic retrograde cholangiopancreatography in most indications.

The basic principle underlying MRCP is that body fluids such as bile and pancreatic secretions have high signal intensity on T2-weighted MR images whereas background signal generates no or little signal. The images of the pancreaticobiliary tree produced by MRCP are similar in appearance to those obtained by direct cholangiographies (i.e., endoscopic retrograde cholangiopancreatography [ERCP] or percutaneous transhepatic cholangiography [PTC]).

MRCP has been initially applied in investigating the biliary ducts; the first reports have focused on the accuracy of MRCP in detection of biliary duct dilatation and choledocholithiasis. The application of MRCP to the assessment of the pancreatic duct is less common because pancreatic disease is less frequent compared with biliary disease and the size of the main pancreatic duct is smaller compared with the common bile duct,



**Figure 45-6** Normal magnetic resonance imaging (MRI) anatomy of the pancreas: MR cholangiopancreatography (MRCP). Coronal T2-weighted half-Fourier single-shot turbo spin echo (HASTE) MRCP image (repetition time/repetition echo [TR/TE]:  $\infty$ /1100 ms) shows a normal-sized common bile duct and main pancreatic duct that reaches the duodenum at the major papilla, indicating a Wirsung duct.

resulting in SNRs that are less advantageous. Therefore, the visualization of the pancreatic ducts is more challenging compared with that of the biliary ducts.

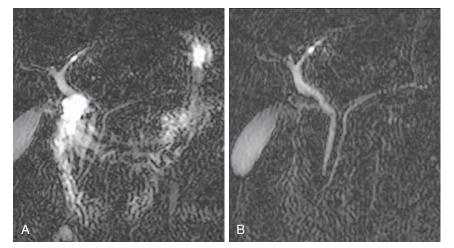
Despite these challenges, with the use of a surface coil, MRCP clearly showed the main pancreatic duct in the head, body, and tail of the gland, respectively, in 79%, 64%, and 53% of cases. Furthermore, in patients with chronic pancreatitis, MRCP showed moderate to high agreement with ERCP in assessing ductal abnormalities. In this group of patients, a high number of false-negative results have been reported because of the small size of the main pancreatic duct, especially in the tail of the pancreas and of the side branches.

MRCP images are able to demonstrate biliary and pancreatic duct lithiasis, stenoses, pancreatic cysts, and accumulations of peripancreatic fluids. As opposed to direct cholangiography, the T2-weighted MRCP images also can be used to study the ducts above a tight stenosis.

The exogenous administration of secretin also improves visualization of pancreatic ducts on MRCP (S-MRCP).<sup>18,19</sup> To obtain better results, MRCP images should employ a slice thickness that encompasses the pancreatic ducts, their emergence in the duodenum, and the common bile ducts. A negative contrast agent consisting of 200 mL of superparamagnetic iron oxide particles can be administered to eliminate overlapping fluid-containing organs (Figure 45-7).

Therefore, secretin can be employed as a contrast agent because it improves visualization of the pancreatic ducts (Figure 45-8).<sup>20</sup> However, at the same time, because it physiologically stimulates the exocrine pancreas, when its use is combined with high temporal resolution imaging, functional studies can be performed assessing the dynamics of pancreatic secretion and the pancreatic exocrine reserve.<sup>21,22</sup> Thus, S-MRCP enables morphologic and functional evaluation of the pancreas.

**Evaluation of the Response to Secretin.** Secretin improves visualization of the main pancreatic duct (see Figure 45-8), particularly in patients with normal or minimally dilated pancreatic ducts. In this group of patients, there was a significant improvement in main pancreatic duct visualization: 65% (164 of 252) of the segments before and 97% (245 of 252) after secretin. A nonsignificant improvement in main pancreatic duct visualization was also observed in patients with severe chronic pancreatitis, from 91% (85 of 93 segments) to 100%



**Figure 45-7** Coronal magnetic resonance cholangiopancreatography (MRCP) before (A) and after (B) oral administration of superparamagnetic contrast media. A, On coronal MRCP single-shot rapid acquisition with relaxation enhancement (RARE) image (repetition time/repetition echo [TR/TE]:  $\infty/800$  ms), the visualization of the main pancreatic duct is impaired by the presence of fluid inside the stomach and duodenum. B, The oral administration of superparamagnetic contrast medium improves main pancreatic duct visualization and enables assessment of duodenal filling.

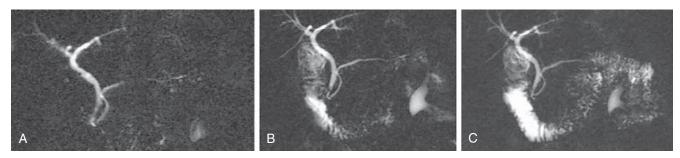
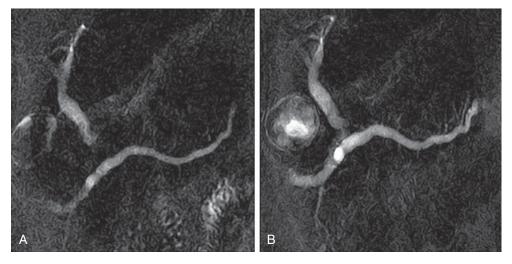


Figure 45-8 Normal magnetic resonance imaging anatomy of the pancreas: dynamic magnetic resonance cholangiopancreatography (MRCP) before and 3 and 10 minutes after secretin administration. A, On pre-secretin coronal T2-weighted half-Fourier acquisition single-shot turbo spin echo(HASTE) MRCP image (repetition time/repetition echo [TR/TE]: ∞/1100 ms), the main pancreatic duct is not completely visualized. B, At 3 minutes after secretin administration the main pancreatic duct can be visualized in its whole length. C, At 10 minutes after secretin administration the main pancreatic duct caliber decreases and there is duodenal filling.



**Figure 45-9** Dilated side branches. A, On coronal magnetic resonance cholangiopancreatography single-shot rapid acquisition with relaxation enhancement (RARE) image (repetition time/repetition echo TR/TE:  $\approx$ / 800 ms) before the administration of secretin, a slight dilation of the main pancreatic duct is observed. **B**, After secretin, dilated side branches in the body and tail of the pancreas are visualized.

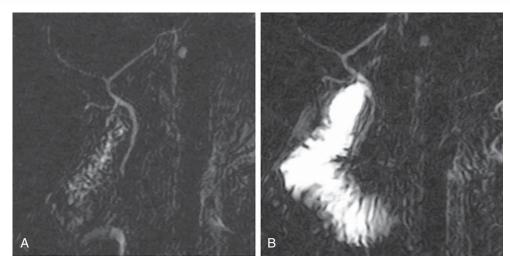
(93 of 93 segments). This was probably related to the enlargement of the main pancreatic duct, which represents the most frequent sign of severe chronic pancreatitis.<sup>22</sup>

The hallmark of ERCP diagnosis of early chronic pancreatitis is represented by the dilatation of side branches. Because of the small size of these branches, MRCP is not able to routinely recognize dilated side branches, therefore leading to a high false-negative rate. Secretin administration improves the visualization of the side branches (from 4% to 63% of the patients), thus aiding in diagnosing chronic pancreatitis in its early stage (Figure 45-9). This improved visualization of dilated side branches makes S-MRCP a promising alternative to diagnostic ERCP, with the endoscopic approach indicated only for therapeutic purposes.

Secretin administration also improves visualization of endoluminal filling defects. This improvement, however, is not significant in patients with severe chronic pancreatitis, because the main pancreatic duct is enlarged, containing a larger amount of fluid that encompasses the low-intensity protein plugs along most or all of their circumference. This improvement is therefore particularly important in mild or moderate chronic pancreatitis with a minimally dilated main pancreatic duct where there might be insufficient pancreatic secretion to delineate the whole circumference of the protein plugs. The detection of endoluminal filling defects is important in planning adequate treatment, such as interventional ERCP and/or lithotripsy. Pancreas divisum, a congenital abnormality that results from the failure of fusion of the dorsal and ventral ducts during organogenesis, has a prevalence of 12% at MRCP. There are other additional anatomic variants that share the feature of egression of the major fraction of pancreatic secretions via the dorsal duct orifice. These variants, characterized by a dominant dorsal duct, are found in nearly 10% of the population, double the prevalence of pancreas divisum. Dynamic MRCP after secretin stimulation improved detection of pancreas divisum in 23% of the patients.<sup>20,21</sup>

Secretin also improves the accuracy of MRCP in assessing ductal abnormalities. When comparing MRCP and S-MRCP findings with those from ERCP in patients with recurrent episodes of acute pancreatitis, MRCP showed an overall sensitivity, specificity, and diagnostic accuracy of 53%, 100%, and 93%, respectively, whereas S-MRCP showed an overall sensitivity, specificity, and diagnostic accuracy of 94%, 97%, and 97%, respectively. The slight reduction in specificity of S-MRCP compared with MRCP is due to three false-positive findings.

**Functional Evaluation.** The dynamic assessment obtainable with rapid imaging after secretin administration gives information on the main pancreatic duct flow dynamics and on the hydrodynamic changes induced by the increased fluid secretion and subsequent elimination into the duodenum (Figures 45-10 to 45-12).



**Figure 45-10** Duodenal filling after dynamic magnetic resonance cholangiopancreatography (MRCP), after secretin stimulation: preserved pancreatic exocrine reserve. Coronal T2-weighted half-Fourier acquisition single-shot turbo spin echo (HASTE) MRCP images (repetition time/repetition echo [TR/TE]:  $\infty$ /1100 ms) before (A) and 10 minutes after (B) secretin administration show duodenal filling beyond the genu inferius.

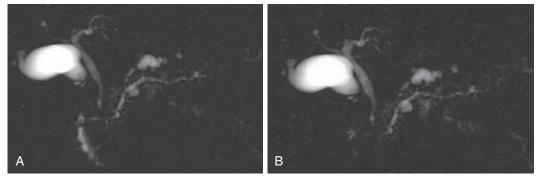


Figure 45-11 Duodenal filling after dynamic magnetic resonance cholangiopancreatography (MRCP), after secretin stimulation: impaired pancreatic exocrine reserve. Coronal T2-weighted half-Fourier acquisition single-shot turbo spin echo (HASTE) MRCP images (repetition time/repetition echo [TR/TE]: ∞/1100 ms) before (A) and 10 minutes after (B) secretin administration show duodenal filling up to the genu inferius.

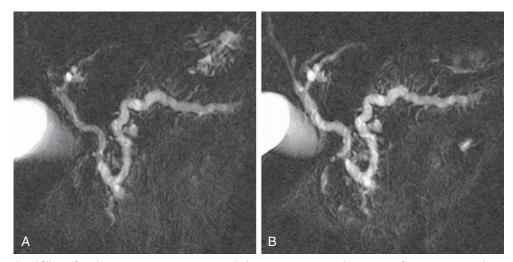
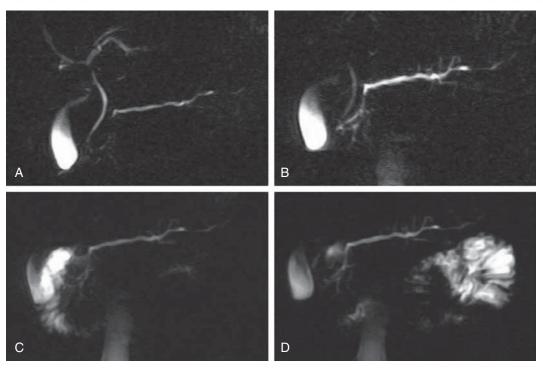


Figure 45-12 Duodenal filling after dynamic magnetic resonance cholangiopancreatography (MRCP), after secretin stimulation: markedly reduced pancreatic exocrine reserve. Coronal T2-weighted half-Fourier acquisition single-shot turbo spin echo (HASTE) MRCP images (repetition time/ repetition echo [TR/TE]: ∞/1100 ms) before (A) and 10 minutes after (B) secretin administration show absent duodenal filling.



**Figure 45-13** Dynamic magnetic resonance cholangiopancreatography (MRCP) after secretin stimulation in papillary stenosis. A, Coronal MRCP single-shot rapid acquisition with relaxation enhancement (RARE) image (repetition time/repetition echo [TR/TE]:  $\infty/800$  ms) before the administration of secretin shows a normal main pancreatic duct. B, At 3 minutes after the administration of secretin the main pancreatic duct enlarges and side branches are visualized. There is very limited duodenal filling. C, At 5 minutes after the administration of secretin the duodenal filling starts. D, At 10 minutes after the administration of the main pancreatic duct.

Papillary strictures can be detected by means of S-MRCP. Papillary stenosis is responsible for persistent dilation of the main pancreatic duct on delayed MRCP images after secretin administration. Ten minutes after secretin administration, the mean maximal diameter of the main pancreatic duct in patients with papillary stenosis was significantly larger than that in the control subjects without papillary stenosis; furthermore, there was no overlap between observed individual values for the patients with papillary stenosis and for the control subjects (Figure 45-13).

Another treatable cause of impeded pancreatic secretion outflow is santorinicele, which occurs in patients with pancreas divisum. Santorinicele is a cystic dilatation of the distal dorsal duct, just proximal to the minor papilla. It is termed santorin*icele* in analogy with ureteroceles and choledochoceles, and it is believed to result from a combination of relative obstruction and weakness of the distal duct wall, either acquired or congenital. Santorinicele has been suggested as a possible cause of relative stenosis of the accessory papilla,<sup>23</sup> which in association with unfused dorsal and ventral ducts results in high intraductal pressure. The increased intraductal pressure may be responsible for individual attacks of recurrent acute pancreatitis, which may be caused by temporary obstruction of the minor papilla during passage of protein aggregates. The hypothesis of reduced pancreatic outflow is further sustained by the remarkable reduction in size of the main pancreatic duct and of the santorinicele in patients who underwent sphincterotomy of the minor papilla on follow-up S-MRCP. Furthermore, patients who underwent endoscopic sphincterotomy also had clinical improvement with remission of symptoms.

Papillary stenosis, either idiopathic or the result of santorinicele, is responsible for a delay in duodenal filling after the administration of secretin. This duodenal filling after secretin stimulation can be used to semi-quantitatively evaluate the pancreatic secretion, which represents an indirect index of the pancreatic exocrine reserve (see Figure 45-10). The evaluation of the pancreatic exocrine reserve may be important because it can be used to help establish the clinical diagnosis and monitor the disease and its treatment. Currently, the most valuable pancreatic function tests are the duodenal and intraductal secretin tests with sampling of the duodenal juice or pure pancreatic juice. With invasive techniques, such as those just mentioned, the evaluation of the pancreatic exocrine function is performed by measuring bicarbonate output and concentration in the pure pancreatic juice collected after secretin stimulation.

Duodenal filling assessed by dynamic MRCP after secretin administration is a noninvasive means to assess pancreatic exocrine reserve. Patients with severe chronic pancreatitis showed a duodenal filling that was significantly inferior to that of patients with suspected chronic pancreatitis (P < .001), probably reflecting a reduced pancreatic exocrine reserve in the advanced phase of the disease.

Therefore, the combination of MRCP and secretin administration enhances pancreatic duct visualization and reduces the high false-negative ratio of MRCP. The improved side-branch visualization in S-MRCP can allow prompt diagnosis of early chronic pancreatitis, making S-MRCP a valid, noninvasive alternative to diagnostic ERCP in this group of patients. Furthermore, the dynamic assessment of the pancreatic duct



**Figure 45-14** Anatomy of the pancreas: ultrasonography. The pancreas is identified in front of the splenic vein and the splenomesenteric junction. The pancreatic parenchyma shows moderate hyperechoic structure.

enables detection of causes of impeded pancreatic secretion outflow, such as papillary stenosis or santorinicele.

# Ultrasonography

Conventional ultrasonography is a noninvasive imaging modality that can be considered the technique of choice in the initial evaluation of the pancreas (Figure 45-14). The pancreas can be visualized by ultrasonography in a high percentage of patients.<sup>23</sup> Nevertheless, it is sometimes difficult to visualize the pancreatic area owing to poor contrast between fat and pancreas and bowel meteorism.

Contrast-enhanced ultrasonography is a promising new technique in evaluating the pancreas. The parenchymography of the pancreas on contrast-enhanced ultrasonography is well correlated to the semiology of the gland. Contrast-enhanced ultrasonography can be used to better identify pancreatic lesions with respect to conventional ultrasonography as well as to characterize pancreatic lesions already visible on ultrasonography.<sup>24</sup>

# **TECHNICAL ASPECTS**

The use of multifrequency transducers enhances imaging of the pancreas at any depth. Furthermore, new technologies have improved pancreatic ultrasonographic imaging. Conventional imaging based not only on the amplitude information but also on the phase information of the return echo for the formation of images results in images with more information and greater resolution of detail.

The image quality also can be improved by using compound technology, which reduces speckle in the B-mode image, thus improving contrast resolution and border detection. Speckle is acoustic noise caused by the nature of ultrasound imaging and can be reduced by generating several images or frames of data with independent information and then averaging these several frames of independent or partially independent information.

B-mode technology also optimizes the image by differentiating vascular anatomy from acoustic artifacts and surrounding tissue.

Harmonic microbubble-specific imaging with a low acoustic ultrasound pressure is required for a dynamic contrastenhanced ultrasound examination using a second-generation contrast medium. While the background tissue signals are filtered by a specific algorithm of ultrasound image reconstruction, vascular enhancement signals in the regions of interest are related to the presence and the harmonic responses of the microbubbles. The enhancement at low-mechanical index harmonic imaging is immediately visible using second-generation ultrasonographic contrast media. Dynamic observation of the contrast-enhanced phases (early arterial, arterial, pancreatic, portal venous, and late sinusoidal phases) begins immediately after the injection of a second-generation contrast medium. Real-time evaluation of the enhancement is possible maintaining the same scanning frame rate as in the previous conventional B-mode examination.<sup>24</sup> Moreover, contrast-enhanced ultrasonography is the only imaging method that allows monitoring of the enhancement during the dynamic phases.

# **EXAMINATION PROTOCOLS**

In the study of the pancreas, ultrasound scan planes include transverse, longitudinal, and angled oblique scans. Bowel gas may be displaced by moving the transducer and applying compression when necessary. To obtain complete visualization of all the portions of the pancreatic gland it is helpful to employ different scanning techniques, such as filling the stomach with water, examining the patient with suspended inspiration or expiration, and changing the patient position to erect, supine, and left and right decubitus.<sup>23</sup>

Ultrasound examination of the pancreas is performed after a minimum fast of 6 hours. The purposes of the fast are to improve visualization of the pancreas, limit bowel gas, and ensure an empty stomach. Successful visualization of the pancreas is directly linked to the skill and persistence of the examiner. It is necessary to identify all portions of the pancreas—head, with the uncinate process, neck, body, and tail—in both the longitudinal and transverse planes. The pancreatic examination begins with the patient in the supine position. If the pancreas is poorly visualized, the water technique can be added.<sup>25</sup> The patient is asked to drink 100 to 300 mL of water through a straw while in the erect or the left lateral decubitus position.

The texture, size, and contour of the pancreas always should be evaluated. The echo pattern of the normal pancreas is isoechoic or hyperechoic compared with that of the normal liver.

During ultrasound examination of the pancreatic gland it is very important to identify the main pancreatic duct but also the intrapancreatic terminal tract of the common bile duct. The splenic, superior mesenteric, and portal veins together with the celiac and superior mesenteric arteries must be identified.

Considering that the blood supply of the pancreas is entirely arterial, the enhancement of the gland begins almost together with the aortic enhancement. On contrast-enhanced ultrasonography the enhancement reaches its peak between 15 and 20 seconds after contrast medium injection. Contrast-enhanced ultrasonography of the pancreas shows a marked parenchymal enhancement in the early contrast-enhanced phases<sup>26</sup>; afterward, there is a progressive washout of contrast medium with loss of gland echogenicity. The technique of contrast-enhanced ultrasonography of the pancreas should vary according to the clinical indications. To detect or study a small pancreatic lesion, to cover all the glandular sectors in the earliest contrastenhanced phases, two boluses, each of 2.4 mL of contrast medium, and the enhancement cancellation technique by means of high-acoustic pressure flash can be employed.<sup>26</sup> To study and stage a pancreatic lesion, a complete evaluation of the liver during the late sinusoidal phase must be performed to exclude the presence of liver metastases.<sup>27-29</sup>

Endoscopic ultrasonography is a novel technique in which the ultrasound probe is placed in close proximity to the pancreas by attaching it to the end of a standard gastrointestinal endoscope and passing the scope in the mouth, down to the duodenum. Lesions as small as 1 cm can be identified with this technique, and ultrasound-guided fine-needle aspiration can be performed.

# **Pros and Cons**

Pros and cons of the individual modalities used to image the pancreas are listed in Table 45-1.

# **Clinical Applications**

# INFLAMMATORY PATHOLOGIC PROCESSES

Multidetector Computed Tomography

# **Role of Computed Tomography in Acute Pancreatitis**

Establishes the diagnosis of acute pancreatitis
Helps in determining the underlying cause of acute pancreatitis (identifies choledocholithiasis and biliary ductal dilatation associated with biliary pancreatitis)

	TABLE 45-1	Pros and Cons of Modalities Used in Imaging the Pancreas					
	Modali	ity	Pros	Cons			
MDCT			High accuracy for diagnosis, characterization, and identification of complications Local and general staging High accuracy in detection of calcifications Parenchymal and vascular visualization Imaging postprocessing	Radiation dose			
	MRI and MRCP		Higher contrast resolution Parenchymal, vascular, and ductal visualization (MRCP) Functional study (secretin) Higher sensibility for early inflammatory modifications	Less sensitive for calcification characterization Needs high patient cooperation Absolute contraindications			
	and enha	nography contrast- nced sonography	Low cost Dynamic microcirculation study (contrast- enhanced)	Operator dependent			

# *MDCT*, Multidetector computed tomography; *MRCP*, magnetic resonance cholangiopancreatography; *MRI*, magnetic resonance imaging.

- Grades the severity of the disease and detects complications such as pancreatic necrosis, abscess, or pseudocysts
- Serves as an imaging modality for performing percutaneous interventions

# Magnetic Resonance Imaging

MRI also can be more sensitive than CT in identifying acute pancreatitis, particularly when mild, thanks to its greater contrast resolution.<sup>27,28</sup> Currently, however, the role of MRI in the evaluation of severe acute pancreatitis is not clear because the greatest drawback in this group of patients is the fact that they are generally too ill to cooperate.

# Role of Magnetic Resonance Imaging in Acute Pancreatitis

- Identifies the underlying causes of the pancreatitis such as choledocholithiasis, pancreas divisum, or pancreatic carcinoma
- Detects early peripancreatic inflammatory infiltration and the accumulation of peripancreatic fluids
- Identifies early stages of pancreatic necrosis, which gives an inhomogeneous appearance to the pancreas on contrast studies
- Detects acute hemorrhagic pancreatitis
- Helps identify complications of acute pancreatitis such as rupture of the main pancreatic duct, formation of pseudocysts or abscesses, fistulas, portal and splenic vein thromboses, and pseudoaneurysms of the splenic artery

# Role of Magnetic Resonance Imaging in Chronic Pancreati-

**tis.** Chronic pancreatitis is a chronic inflammation of the pancreas that results in exocrine and endocrine gland dysfunction.

- MRI is, nevertheless, more sensitive in identifying the initial phase of pancreatitis and/or cases that do not manifest calcifications (50%)<sup>30,31</sup>; under basic conditions and during the administration of secretin, MRCP sequences can be used to identify the initial alterations in the second-ary ducts.<sup>20,22</sup>
- MRI is able to detect the following duct alterations associated with chronic pancreatitis: dilatation, stenosis, parietal irregularities, twisting, secondary pancreatic duct ectasia, pseudocysts, and intraductal calculi. In addition, association with the thin section images makes it possible to detect the related morphologic modifications, such as parenchymal atrophy or focal enlargement of the pancreatic parenchyma.
- Intraductal pancreatic calculi are better identified with T2-weighted images, in which they appear as endoluminal filling defects, surrounded by the high-intensity signal of the pancreatic juice. The normal diameter of the main pancreatic duct is approximately 2 mm, whereas the normal secondary pancreatic ducts cannot be viewed by MRCP. The secondary pancreatic ducts are visible only after administration of secretin.<sup>20,22</sup> When visualized, they make it possible to diagnose mild chronic pancreatitis. In severe chronic pancreatitis, the marked dilatation of the main pancreatic duct and the secondary ducts makes the ductal system look like rosary beads.

# Ultrasonography

Abdominal CT is the technique of choice in the evaluation of patients who present with clinical features suggestive of

pancreatitis. However, ultrasonography is widely used. Biliary stones, peripancreatic collections, and pseudocysts can be detected.<sup>32-35</sup> Normal ultrasound findings can be seen in patients with mild acute pancreatitis. Although the pancreas can appear normal in acute pancreatitis, the most frequent findings are enlargement of the gland and a diffuse decrease in normal echogenicity.<sup>26</sup> Acute pancreatitis can be focal or diffuse, depending on the distribution. Focal pancreatitis generally occurs in the pancreatic head and manifests as a hypoechoic mass that is sometimes difficult to differentiate from a tumor, especially when focal acute pancreatitis occurs over chronic pancreatitis and the clinical findings are not clear or evident.<sup>26,32,36,37</sup>

The inflamed pancreatic segment shows increased contrast enhancement on contrast-enhanced ultrasonography.<sup>26,32,36,37</sup>

In severe acute pancreatitis, contrast-enhanced ultrasonography may improve the identification and delimitation of areas of parenchymal necrosis, which appear as nonvascular areas.<sup>26,33</sup>

Contrast-enhanced ultrasonography improves the ultrasonographic diagnosis of pseudocyst: the differential diagnosis between pseudocysts and cystic tumors of the pancreas is more reliable thanks to the evaluation of intralesional inclusion vascularization.<sup>37-39</sup>

Abscesses consist of encapsulated collections of purulent material within or near the pancreas. On ultrasonography they are seen as an anechoic or heterogeneous mass containing bright echoes from pus, debris, or gas bubbles. A pancreatic abscess should be suspected on the clinical evidence and when changes in the echogenicity of the content of pseudocysts are documented at ultrasound examination. Vascular complications including pseudoaneurysms and venous thrombosis may be seen in both acute and chronic pancreatitis. Hemorrhage may occur as a consequence of vascular injury.<sup>33</sup>

Chronic pancreatitis is an inflammatory disease characterized by the replacement of the glandular elements of the pancreas by fibrous tissue. The most significant ultrasound findings of chronic pancreatitis are pancreatic duct dilatation, intraductal calcifications, and pseudocysts.

# SOLID LESIONS

# Multidetector Computed Tomography

- Detects and characterizes the lesion based on the enhancement pattern on dynamic imaging. For example, adenocarcinomas appear hypodense in the pancreatic phase and the neuroendocrine tumors are characterized by their intense enhancement pattern in the arterial phase.<sup>40-42</sup>
- Helps in staging of the lesion and determining its resectability criteria such as vascular invasion, hepatic and omental metastasis, and regional lymph node involvement.

# Magnetic Resonance Imaging

- Is a problem-solving modality to confirm suspicious lesions on CT or ultrasonography<sup>40</sup>
- Characterizes lesions based on their morphology
- Detects masses in the setting of inflammation in and around the pancreas
- Characterizes pancreatic duct stricture and differentiates benign from malignant ones
- Detects liver lesions and characterizes them in patients with pancreatic neoplasm

# Ultrasonography

Ultrasonography is often the first technique performed when pancreatic adenocarcinoma is suspected. Pancreatic adenocarcinoma is most common in the pancreatic head (65%) and usually manifests as a hypoechoic solid mass. General enlargement from associated pancreatitis is uncommon (15%). Ductal adenocarcinoma shows poor enhancement<sup>36</sup> on all phases of contrast-enhanced ultrasonography. On the contrast-enhanced study this lesion appears as a hypoechoic mass compared with the adjacent normally enhancing pancreatic parenchyma; the margins and size of the lesion are better visualized as is its relationship with peripancreatic arterial and venous vessels for local staging. Contrast-enhanced ultrasonography demonstrates the vascularization of the neoplastic tissue with enhancement seen in the earliest phases of the dynamic study.

On color and power Doppler ultrasonography a "spot pattern" can be demonstrated inside endocrine tumors. However, Doppler "silence" can be present in hypervascular endocrine tumors because of the small size of the lesion or of the tumoral vascular network. On contrast-enhanced ultrasonography, different enhancement patterns can be observed in relation to the dimension of the tumor and tumoral vessels. Endocrine tumors show a rapid intense enhancement in the early contrast-enhanced phases, with exclusion of the necrotic intralesional areas and contrast entrapment in the late phase.<sup>26</sup>

Contrast-enhanced ultrasound examination may improve the identification and characterization of endocrine tumors and also improves locoregional and hepatic staging of endocrine tumors.<sup>26,43</sup>

#### CYSTIC LESIONS

#### Multidetector Computed Tomography

- MDCT with its superior resolution helps in detection of the cystic lesions and their morphologic characterization such as size, presence of calcification, septa, central scar, solid mass wall thickness, and enhancement pattern<sup>44</sup>
- Determination of the status of the pancreatic duct dilatation, stricture, or any communication with cyst
- Categorization of patients into surgical and nonsurgical groups
- For follow-up in patients in whom surgery is not indicated initially
- For postoperative management and follow-up

# Magnetic Resonance Imaging

- Enables better cyst characterization than CT because of superior soft tissue resolution<sup>44</sup>
- For pancreatic duct evaluation, to detect any mural nodules or septations
- For follow-up in patients having higher radiation risk (e.g., those younger than 50 years of age)
- In patients with contraindications for iodinated contrast agents (e.g., patients in renal failure)
- Identifies hemorrhagic complications within the cyst in different stages
- Defines the communication with the pancreatic duct on MRCP images, thus establishing the diagnosis of sidebranch intraductal papillary mucinous tumor of the pancreas in the majority of cases<sup>45,46</sup>

ultrasound characterization of serous cystadenoma, showing

the enhancement of intralesional septa, with better identifica-

is impossible by ultrasonography and is a specific issue for MRI

• Liver lesions can be detected and evaluated in patients

with pancreatic neoplasms. All imaging modalities are

• MRCP is the diagnostic modality of choice for detailed,

Secretin-enhanced MRCP is able both to better assess

pancreatic ducts and to evaluate pancreatic function.

noninvasive evaluation of the pancreatic ducts and cystic

However, demonstration of the absence of communication

tion of the microcystic features of the lesion.44

# Ultrasonography

Serous cystadenomas are composed of glycogen-rich serous fluid, which makes this tumor visible sonographically. Microcystic lesions may have a solid appearance. Further characterization of the cyst is possible by detection an echogenic scar or calcification. Contrast-enhanced ultrasonography improves the

### **Key Points**

- Different diagnostic imaging modalities have been evaluated in assessing pancreatic diseases.
- Ultrasonography, although inexpensive and readily available, is limited by patient body habitus and bowel gas for a complete evaluation of the pancreas.
- MDCT is the modality of choice for the initial evaluation of pancreatic diseases, staging, and presurgical planning.
- MRI shows high contrast resolution in evaluating the pancreatic parenchyma for detection of small lesions and is useful in problem-solving situations.

SUGGESTED READINGS

- Rha SE, Jung SE, Lee KH, et al: CT and MR imaging findings of endocrine tumor of the pancreas according to WHO classification. *Eur J Radiol* 62:371–377, 2007.
- Schima W, Ba-Ssalamah A, Goetzinger P, et al: Stateof-the-art magnetic resonance imaging of pancre-

REFERENCES

- 1. Tunaci M: Multidetector row CT of the pancreas. *Eur J Radiol* 52:18–30, 2004.
- 2. Fenchel S, Boll DT, Fleiter TR: Multislice helical CT of the pancreas and spleen. *Eur J Radiol* 45:S59–S72, 2003.
- Bae KT, Heiken JP, Brink JA: Aortic and hepatic contrast medium enhancement at CT. I. Prediction with a computer model. *Radiology* 207:647– 655, 1998.
- Fenchel S, Fleiter TR, Aschoff AL, et al: Effect of iodine concentration of contrast media on contrast enhancement in multislice CT of the pancreas. *Br J Radiol* 77:821–830, 2004.
- Sahani D, Shah ZK: Soft-organ MDCT imaging: pancreas and spleen. In Saini S, Rubin GD, Kalra MK, editors: *MDCT: a practical approach*, Berlin, 2006, Springer.
- Fishman EK, Jeffrey RB, Jr: Multidetector CT: principles, techniques and clinical applications, Philadelphia, 2004, Lippincott Williams & Wilkins.
- McNulty NJ, Francis IR, Platt JF, et al: Multidetector row helical CT of the pancreas: effect of contrast enhanced multiphasic imaging on enhancement of the pancreas, peripancreatic vasculature, and pancreatic adenocarcinoma. *Radiology* 220:97–102, 2001.
- Nono-Murcia M, Jeffrey RB, Jr, Beaulieu CF, et al: Multidetector CT of the pancreas and bile duct system: value of curved planar reformations. AJR Am J Roentgenol 176:689–693, 2001.
- Raptopoulos V, Prassopoulos P, Chuttani R, et al: Multiplanar CT pancreatography and distal cholangiography with minimum intensity projections. *Radiology* 207:317–324, 1998.
- 10. Thoeni RF, Blankenberg F: Pancreatic imaging: computed tomography and magnetic resonance

atic cancer. Top Magn Reson Imaging 18:421–429, 2007.

and ERCP.48

lesions.

suitable for this purpose.

Sidden CR, Mortele KJ: Cystic tumors of the pancreas: ultrasound, computed tomography, and magnetic resonance imaging features. *Semin Ultrasound CT MR* 28:339–356, 2007.

imaging. Radiol Clin North Am 31:1085-1113,

11. Ferrucci IT: Advances in abdominal MR

imaging. Radiographics 18:1569-1586, 1998.

12. Semelka RC, Ascher SM: MRI of the pancreas:

14. Rofsky NM, Lee VS, Laub G, et al: Abdominal

state of the art. Radiology 188:593-602, 1993.

Siegelman ES, Outwater EK: MR imaging tech-

niques of the liver. Radiol Clin North Am

MR imaging with a volume interpolated breath-

hold examination. *Radiology* 212:876–884, 1999. Hamed MM, Hamm B, Ibrahim ME, et al:

Dynamic MR imaging of the abdomen with

gadopentetate dimeglumine: normal enhance-

ment patterns of the liver, spleen, stomach, and

pancreas. AJR Am J Roentgenol 158:303-307,

a useful tool for evaluating pancreatic disorders.

pancreatography: comparison of 2D single-shot

fast spin-echo and 3D fast spin-echo sequences.

duct: morphologic and functional evaluation

with dynamic MR pancreatography after secre-

Chronic pancreatitis: evaluation of pancreatic

exocrine function with MR pancreatography

after secretin stimulation. Radiology 215:358-

Dynamic pancreatography with magnetic reso-

nance after functional stimulus with secretin in

tin stimulation. Radiology 203:435-441, 1997.

19. Cappeliez O, Delhaye M, Devière J, et al:

20. Manfredi R, Costamagna G, Vecchioli A, et al:

16. Fulcher AS, Turner MA: MR pancreatography:

17. Cova M, Stacul F, Cester G, et al: MR cholangio-

18. Matos C, Metens T, Devière J, et al: Pancreatic

Radiographics 19:5-24, 1999.

Radiol Med 106:178-179, 2003.

1993.

36:263-286, 1998.

13.

15.

1992.

364, 2000.

- Siddiqi AJ, Miller F: Chronic pancreatitis: ultrasound, computed tomography, and magnetic
- sound, computed tomography, and magnetic resonance imaging features. *Semin Ultrasound CT MR* 28:384–394, 2007. Vanbackwoort D: Solid parcreatic masses: benjan
- Vanbeckevoort D: Solid pancreatic masses: benign or malignant. *JBR-BTR* 90:487–489, 2007.

chronic pancreatitis. *Radiol Med* 96:226–231, 1998.

- 21. Nicaise N, Pellet O, Metens T, et al: Magnetic resonance cholangiopancreatography: interest of IV secretin administration in the evaluation of pancreatic ducts. *Eur Radiol* 8:16–22, 1998.
- 22. Manfredi R, Costamagna G, Brizi MG, et al: Dynamic magnetic resonance pancreatography after secretin stimulation: severe chronic pancreatitis vs suspected pancreatic disease. *Radiology* 214:849–855, 2000.
- 23. Mittelstaedt CA: *Abdominal ultrasound*, New York, 1987, Mosby, pp 163–176.
- 24. Weissleder R, Rieumont MJ, Wittenberg J: *Primer of diagnostic imaging*, ed 2, New York, 1997, Mosby, pp 220–228.
- Lev-Toaff AS, Bree RL, Lund PJ, et al: Use of simethicone-coated cellulose suspension to improve pancreatic ultrasound: experience in 55 patients with pancreatic pathology. *Radiology* 209(Suppl):310, 1998.
- D'Onofrio M, Zamboni G, Malagò R, et al: Pancreatic pathology. In Quaia E, editor: *Contrast media in ultrasonography*, Berlin, 2005, Springer-Verlag, pp 335–347.
- Sahani D, Kalva SP, Farrell J, et al: Autoimmune pancreatitis: imaging features. *Radiology* 233: 345–352, 2004.
- Robinson PJA, Sheridan MB: Pancreatitis: computed tomography and magnetic resonance imaging. *Eur Radiol* 10:401–408, 2000.
- Balthazar EJ, Robinson DL, Megibow AJ, et al: Acute pancreatitis: value of CT in determining prognosis. *Radiology* 174:331–336, 1990.
- Luetmer PH, Stephens DH, Ward EM: Chronic pancreatitis reassessment with current CT. *Radiology* 171:353–357, 1989.

#### 464 PART 5 Liver and Pancreas

- Pavone P, Laghi A, Catalano C, et al: The assessment of chronic pancreatitis by magnetic resonance and MR cholangiopancreatography. II. The semeiotics and results. *Radiol Med* 98:373–378, 1999.
- Loren I, Lasson A, Fork T, et al: New sonographic imaging observations in focal pancreatitis. *Eur Radiol* 9:862–867, 1999.
- Baron HT, Morgan ED: The diagnosis and management of fluid collections associated with pancreatitis. Am J Med 102:555–563, 1997.
- Bolondi L, Priori P, Gullo L, et al: Relationship between morphological changes detected by ultrasonography and pancreatic exocrine function in chronic pancreatitis. *Pancreas* 2:222–229, 1987.
- Furukawa N, Muranaka T, Yasumori K, et al: Autoimmune pancreatitis: radiologic findings in three histologically proven cases. J Comput Assist Tomogr 22:880–883, 1998.
- Numata K, Ozawa Y, Kobayashi N, et al: Contrast enhanced sonography of autoimmune pancreatitis: comparison with pathologic findings. J Ultrasound Med 23:199–206, 2004.
- 37. Freeny P, Lawson T: *Radiology of the pancreas*, New York, 1982, Springer-Verlag, p 449.

- Boland GW, O'Malley ME, Saez M, et al: Pancreatic-phase versus portal vein–phase helical CT of the pancreas: optimal temporal window for evaluation of pancreatic adenocarcinoma. *AJR Am J Roentgenol* 172:605–608, 1999.
- 39. Lu DS, Reber HA, Krasny RM, et al: Local staging of pancreatic cancer: criteria for unresectability of major vessels as revealed by pancreatic phase, thin-section helical CT. AJR Am J Roentgenol 168:1439–1443, 1997.
- Ichikawa T, Haradome H, Hachiya J, et al: Pancreatic ductal adenocarcinoma: preoperative assessment with helical CT versus dynamic MR imaging. *Radiology* 193:655–662, 1997.
- Procacci C, Carbognin G, Accordini S, et al: Nonfunctioning endocrine tumors of the pancreas: possibilities of spiral CT characterization. *Eur Radiol* 11:1175–1183, 2001.
- Semelka RC, Cumming MJ, Shoenut JP, et al: Islet cell tumors: comparison of dynamic contrast-enhanced CT and MR imaging with dynamic gadolinium enhancement and fat suppression. *Radiology* 186:799–802, 1993.
- Galiber AK, Reading CC, Charboneau JW: Localization of pancreatic insulinoma: com-

parison of pre- and intraoperative ultrasound with computer tomography and angiography. *Radiology* 166:405–408, 1988.

- 44. Ros PR, Mortele KJ: Imaging features of pancreatic neoplasms. *JBR-BTR* 84:239–249, 2001.
- 45. Manfredi R, Mehrabi S, Motton M, et al: Magnetic resonance (MR) imaging and MR cholangiopancreatography (MRCP) of multifocal intraductal papillary mucinous tumors (IPMT) of the side branches: MR pattern and its evolution. *Radiol Med* 113:414–428, 2008.
- 46. Irie H, Honda H, Aibe H, et al: MR cholangiopancreatography differentiation of benign and malignant intraductal mucin-producing tumors of the pancreas. *AJR Am J Roentgenol* 174:1403– 1408, 2000.
- Bennett GL, Hann LE: Pancreatic ultrasonography. Surg Clin North Am 81:259–281, 2001.
- Procacci C, Schenal G, Dalla Chiara E, et al: Intraductal papillary mucinous tumors: imaging. In Procacci C, Megibow AJ, editors: *Imaging of the pancreas: cystic and rare tumors*, Berlin, 2003, Springer-Verlag, pp 97–137.

# **Solid Pancreatic Masses**

ONOFRIO CATALANO | MELISSA PRICE | DUSHYANT V. SAHANI

# Etiology

The term *solid pancreatic masses*, in its wide meaning, encompasses neoplastic lesions and non-neoplastic masses, ranging from anatomic variants, such as pancreatic head lobulations, to focal inflammatory processes and neoplasms. This chapter will mainly discuss solid pancreatic neoplasms and provide differential diagnoses with other solid lesions, such as variants and focal inflammatory lesions, which are described in detail in other chapters.

The cause of pancreatic neoplasms varies accordingly to their specific histotype and will be discussed in each subsection. Most pancreatic neoplasms occur sporadically, but some are genetically transmitted, and different genes are involved. Usually both environmental factors, such as cigarette smoking and dye exposure, and genetic factors are implicated in a multistep process of progressive genetic deregulation and increased biologic aggressiveness, which can lead to the onset of malignant lesions.<sup>1-3</sup>

# **Prevalence and Epidemiology**

Statistical data regarding the prevalence and incidence of all benign and malignant neoplasms of the pancreas are not available in the literature. Statistical data for invasive pancreatic cancer, derived from the Surveillance Epidemiology and End Results of the National Cancer Institute (http://seer.cancer.gov) show an estimated prevalence percent of 0.008% for all ages, an estimated prevalence percent of 0.041% in the age range 70 to 79 years, and an overall incidence of 11.4 per 100,000 persons. The most commonly encountered solid tumors of the pancreas are adenocarcinomas, endocrine tumors, metastases, and lymphomas. Other tumors, which occur less often, include acinar cell tumors, pancreatoblastomas, and lipomas.<sup>1-3</sup>

# **Clinical Presentation**

Clinical presentation of pancreatic solid lesions is extremely variable and mainly depends on histotype, location, and size of the lesion.

Unless the neoplasm is responsible for hormone overproduction, resulting in specific clinical symptoms at an early stage, the first symptoms of pancreatic neoplasms are often too vague to be considered. Therefore, the majority of patients seek medical attention late in the course of the disease when abdominal pain, jaundice, and weight loss result.<sup>1-4</sup>

# Pathophysiology

Pancreatic neoplasms tend to affect every region of the pancreas but, owing to the higher amount of pancreatic tissue in the head of the organ, this is where tumors tend to occur more often. The site of occurrence may also be influenced by the specific histotype.<sup>1-3</sup>

# Pathology

The pathologic findings are extremely variable from one neoplasm to another, and on this basis the different lesions are differentiated and classified.<sup>1-3</sup>

# Imaging

The imaging techniques for evaluation of solid masses in the pancreas include ultrasonography, contrast-enhanced multidetector computed tomography (MDCT), magnetic resonance imaging (MRI), combined positron emission tomography with CT (PET/CT), endoscopic cholangiopancreatography (ERCP), and endoscopic ultrasonography (EUS). Diagnostic imaging of pancreatic solid lesions is aimed at (1) confirming or excluding the presence of a pancreatic mass; (2) differentiating a benign from a malignant lesion and narrowing the differential diagnosis; (3) staging the neoplastic process, in case it is malignant, and providing a road map for surgery, in case the tumor is considered resectable; and (4) assisting in follow-up of patients after medical and/or surgical treatment.<sup>13,4</sup>

# RADIOGRAPHY

Because of the poor soft tissue resolution and low sensitivity and specificity of conventional and digital radiography, solid lesions of the pancreas are usually not detectable by radiographic studies. Cross-sectional imaging is far more sensitive and specific than conventional radiographic studies.

#### COMPUTED TOMOGRAPHY

MDCT allows the pancreas to be imaged at a high spatial and temporal resolution, within a single breath-hold, with thinslice collimation and multiphasic imaging. Contrast enhancement time is crucial in tumor detection, and when possible it should be planned in accordance with the suspected type of lesion. Usually, pancreatic tumor detection is suboptimal during the arterial phase of enhancement owing to low tumorto-pancreas contrast difference, but in the case of a suspected endocrine neoplasm or renal or breast cancer metastases to the pancreas the arterial phase may be the only one in which the lesion can be detected and characterized. In the case of adenocarcinoma, a dual-phase pancreatic protocol MDCT is considered sensitive for detection and staging of the primary cancer and for evaluation of metastases to the liver and peritoneum (see Chapter 45).<sup>4,5</sup>

#### MAGNETIC RESONANCE IMAGING

MRI is usually used as a second-line imaging modality in patients with high clinical suspicion for a pancreatic tumor or in those with a suspected pancreatic mass and indeterminate finding on high-quality MDCT. MRI, owing to its inherent high soft tissue contrast and resolution, can improve detection of subtle pancreatic lesions even when they are small and do not deform the organ. MRI, through T2-weighted and gadoliniumenhanced T1-weighted sequences, performs better than MDCT in the detection and characterization of liver metastases and peritoneal implants, especially in the setting of the smallest lesions. Regional vascular anatomy can be mapped by threedimensional (3D) contrast-enhanced dynamic MR angiography and reconstructions to assess for vascular involvement. If mangafodipir trisodium is administered, it is taken up by the normal pancreatic parenchyma, which is enhanced on T1-weighted images, in comparison with the relative lack of enhancement of pancreatic masses whose conspicuity is therefore increased. The sensitivity of mangafodipir trisodium-enhanced MRI for detection of pancreatic cancer may reach 100%. Both 2D and 3D MR cholangiopancreatography (MRCP) allow direct noninvasive visualization of the biliary tree and the pancreatic duct. MRCP can demonstrate the "double duct" pattern of obstruction, seen with pancreatic or ampullary tumors. With the administration of secretin (secretin-enhanced MRCP [S-MRCP]), duct distention may be increased, thus improving MRCP quality and lesion conspicuity, allowing a more accurate assessment of pancreatic duct stenosis, and potentially helping to differentiate benign from malignant strictures (see Chapter 45).4-

# ULTRASONOGRAPHY

Transabdominal ultrasonography is a relatively inexpensive, noninvasive, and widely available modality often used as a firstline diagnostic imaging tool for disorders of the abdomen, but it is highly operator dependent, nonreproducible, and limited by abdominal gas and patient body habitus.

EUS, on the other hand, is an expensive technique, not available in every center, and requires highly specialized personnel. It provides high-resolution images of the pancreas and allows lesion biopsy.<sup>4-9</sup>

# NUCLEAR MEDICINE

Nuclear medicine plays a role only (1) in the case of functional endocrine tumors when, using a specific radiopharmaceutical, it can allow the diagnosis to be undertaken and (2) in the study of suspected bony metastases. Otherwise it has no current application in the diagnosis of solid pancreatic neoplasms.

# POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

Although MDCT is characterized by high spatial resolution, differentiating benign from malignant processes is often challenging, mainly in the case of small lesions. On the other hand, fluorodeoxyglucose (FDG)-labeled PET has a high accuracy in discriminating benign from malignant lesions but its spatial resolution is limited, compromising precise anatomic localization. PET/CT integrates morphologic and functional data in a single test, overcoming some of these limitations. Normal pancreatic tissue does not show FDG uptake on PET, and therefore a region of increased uptake in the pancreas is considered abnormal.

PET/CT may be useful in the case of small lesions (<1 cm), which are frequently missed with nonfunctional imaging, and of early tumor recurrence. Because FDG accumulation does not depend on tumor size, cancer can be detected even in normalsized lymph nodes. However, false-negative PET findings can be observed, mostly in patients with insulin-dependent diabetes mellitus; meanwhile, false-positive PET findings can occur in inflammatory benign lesions. New tumor-specific radioisotopes, such as s-receptor ligands and 18F-fluorothymidine (18-FLT) are being used to improve specificity and sensitivity for the detection of primary and metastatic tumors, mainly adenocarcinomas. Carbon-11 (11C)-labeled l-dopa and 11Clabeled 5-hydroxytryptophan are more sensitive and specific radioligands in the setting of functional endocrine pancreatic tumors, but they are less sensitive in detection of nonfunctional neoplasms.4-9

# IMAGING ALGORITHM

The most used diagnostic imaging techniques for solid neoplasms of the pancreas are MDCT and MRCP, which provide high spatial and contrast resolution images and allow dynamic acquisition and postprocessing image reconstruction. Lesion morphology, epicenter location, relationships with the pancreatic duct, and ancillary findings can be evaluated, providing clues for diagnosis, management planning, and preoperative strategy.

MDCT and MRI have been demonstrated to be nearly equally accurate in establishing the diagnosis of malignancy, in characterizing pancreatic lesions, and in their staging.

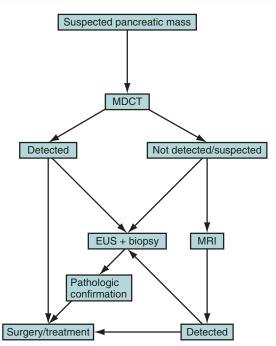
Through MRCP and MDCT images and reconstructions, the entire course of the main pancreatic duct (MPD) can be displayed and its relationships with the lesion can be evaluated. In case the patient is considered a surgical candidate, multiplanar image reconstructions, displaying the extent of the lesions and their anatomic relationships to surrounding structures, can be useful.

The role of PET/CT is still under investigation. An ideal algorithm is summarized in Figure 46-1.<sup>49</sup> The different types of solid lesions of the pancreas will be described in the corresponding sections; the most important features are summarized in Table 46-1.

# **Differential Diagnosis**

Differential diagnosis of solid pancreatic masses is aimed to differentiate benign masses, including anatomic variants, from malignant lesions and to try to characterize the histotype. It relies on a combination of clinical, laboratory, and imaging findings and, in most cases, on information derived from tissue biopsy.

Important clinical factors include age; sex; weight loss; recent onset of diabetes; abdominal pain; jaundice; bloating; gastrointestinal obstruction; thrombophlebitis migrans; diarrhea; depression; history of smoking and of exposure to carcinogenic agents; and family personal history of breast, pancreatic, and endocrine neoplasms; Peutz-Jaegers syndrome; and nonpolyposis familial colon cancer syndrome.



**Figure 46-1** Diagnostic imaging algorithm for solid pancreatic masses. *EUS*, Endoscopic ultrasonography; *MDCT*, multidetector computed tomography; *MRI*, magnetic resonance imaging.

Many laboratory findings and tumor serum markers are available. They include specific hormones, which are overproduced in the case of functional endocrine tumors, or oncologic markers, such as CA 19-9, which is one of the most useful for the diagnosis of adenocarcinoma of the pancreas.<sup>1-4</sup>

Many anatomic variants and pseudolesions may be confused with pancreatic neoplasms. Their differential diagnosis is described in the corresponding sections. Alteration in pancreatic contour, lobulations, and changes in the course and size of the MPD, as well as epicenter, margin, and contrast enhancement characteristics of the lesions are some of the most important imaging features to take into account in the approach to management of pancreatic masses.<sup>4</sup>

# Treatment

## MEDICAL TREATMENT

Medical treatment differs according to the type of cancer and its stage. Its goals are to treat the neoplasm, palliate the patient in the case of untreatable tumors, and improve quality of life.

Patients who are not fit for surgery usually undergo radiation therapy, chemotherapy, or both. Patients with distant metastases are considered ineligible for radiation treatment and undergo chemotherapy alone.<sup>2</sup>

## SURGICAL TREATMENT

Although complete surgical resection remains the best curative treatment for many tumors, including pancreatic adenocarcinoma, currently only a small percentage of patients are recommended for surgical resection, and the small tumors that can undergo curative surgery are the most difficult to detect. The treatment approach is based on tumor histotype, location in the pancreas (e.g., head versus tail), and whether the tumor is resectable or nonresectable at presentation.

Usually, tumors of the pancreatic head are treated with the Whipple procedure, which includes cephalopancreatectomy and duodenectomy, whereas body and tail tumors are treated with distal pancreatectomy and splenectomy.<sup>2</sup>

#### What the Referring Physician Needs to Know: Pancreatic Masses

- Solid lesions may be difficult to differentiate on morphology alone.
- The most important questions in the approach to solid lesions in the pancreas involve differentiation of:
  - Pseudolesions from true lesions
  - Benign versus malignant lesions
  - Adenocarcinomas from nonadenocarcinomas
- Resectable versus nonresectable neoplasms

#### **Key Point**

 Diagnosis of pancreatic masses usually requires correlation of clinical, laboratory, imaging, and pathology data.

# **Specific Lesions**

# ADENOCARCINOMA

#### Etiology

Both environmental and genetic factors are involved in a multistep process of progressive genetic deregulation and increased biologic aggressiveness, which can lead to the onset of malignant lesions.

Cigarette smoking, diets high in meat, and solvent exposure are among the most well-known environmental factors.

Different DNA alterations have been implicated in the onset of pancreatic adenocarcinomas. They cause inactivation of multiple antioncogenes (*CDKN2A*, *TP53*, *SMADH4*), activation of oncogenes (*KRAS*, *HERB2*, *BRAF*), and interference with DNA mismatch repair (*BRCA2*). Multiple mutations coexist in a single adenocarcinoma.<sup>1,2</sup>

# Prevalence and Epidemiology

Pancreatic adenocarcinoma is an invasive malignant epithelial neoplasm with ductal differentiation and without predominance of other types of carcinomas. Its age-adjusted incidence rate is 11 in 100,000, and it constitutes more than 90% of the malignant tumors of the pancreas. Pancreatic adenocarcinoma is one of the most ominous malignancies: it represents the fifth leading cause of cancer death in Western countries, with a poor overall 5-year survival rate of only 4%, which is nearly equal to the incidence rate. Its peak incidence is in the 7th and 8th decades, and it is slightly more common in men (56%).<sup>1-3</sup>

#### Clinical Presentation

Clinical presentation varies according to the site of origin of the cancer and its stage, but many patients recall a history of long-standing abdominal pain, asthenia, reduced appetite, and weight loss. New-onset diabetes mellitus is present in 10% of cases. Painless jaundice is found in 75% at presentation, mostly

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	Clinical History	Abdominal pain radiating to the back Jaundice Weight loss	Endocrinology syndromes may be found. Serum A elevated in 70%	Positive oncologic history	Nonspecific	Serum lipase usually high Hyperlipasemia syndrome in 15%	Acute pancreatitis- like pain, history of alcohol abuse	lgG 4, other autoimmune diseases, response to steroids	
	Peculiar Features	Usually advanced even when small in size	Strongly enhancing lesions	In the setting of widespread malignancy	Lymph node enlargement below renal veins Large homogeneous mass without MPD abnormalities Diffuse enlargement of the gland with loss of its lobular structure	Mn-DPDP uptake	Parenchymal and ductal calcifications	Homogeneous late enhancement Upstream MPD not dilated	
	MPD	Stenosed or obstructed, upstream dilatation	Usually normal	Usually normal	Usually normal	Usually normal	Stenosed, obstructed, normal, dilated	Usually stenosed	
	Enhancement	Poor	Intense, early	Variable, same as that of the primary tumor	Mild, homogeneous	Mild, heterogeneous (cystic areas often coexist)	Homogeneous	Homogeneous, late enhancement	DPDP, DipvridoxvI diphosphate: F, female: 1gG, immunoalobulin G; M, male: MPD, main pancreatic duct: N/A, not applicable.
	Ca <sup>2+</sup>	Rare	22%	Rare	Rare	Common 50%	Common	Rare	reatic duct; N
eoplasms in the Pancreas	Shape/ Borders	Infiltrating	Well defined/ infiltrating	Well defined	Well defined	Well defined	III defined	Well defined	PD. main panc
	Size	Usually <5 cm, mean size 3 cm head location, 5 cm body-tail	>5 cm, unless functional	Usually <5 cm, mean size 4.6 cm	>5 cm, mean size 8 cm	>5 cm, mean size 7 cm	N/A	<5 cm, mean size 3.8 cm	in G: M. male: M
Clinical and Radiologic Features of Solid Ne	Location	Head (75%)	Tail (60%)	Head	Head (80%)	Head/uncinate (60%)	Head (70%)	Head (55%)	G. immunoalobul
logic Featur	Age	7th-8th decades	5th-6th decades	6th decade	4th-8th decades	7th decade	5th-6th decades	7th-8th decades	e: F. female: Ia
and Radio	Sex	L ^ Z	н = Х	μ = Σ	LL ∧ ∑	∑ ∧ ⊥	L ^ E	⊥ ∧ ≥	liphosphate
TABLE 46-1 Clinical a	Neoplasm	Adenocarcinoma	Pancreatic endocrine neoplasm	Metastases	Lymphoma	Acinar cell carcinoma	Alcohol mass-forming pancreatitis	Autoimmune mass-forming pancreatitis	DPDP Dinvridoxvl c

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resulting from cancers arising from the head of the organ. Tumors in the pancreatic body and tail tend to manifest as back pain related to tumor infiltration into the surrounding retroperitoneal structures and nerves. Because of its silent course, late clinical symptoms, and rapid growth, it has been named the "silent killer."<sup>1-3</sup>

## Pathophysiology

Approximately two thirds of pancreatic adenocarcinomas occur in the head of the pancreas; the remainder are found in the body (5% to 15%) or tail (10% to 15%) or diffusely infiltrate the organ (5% to 15%).<sup>1,2</sup>

#### Pathology

It is believed that pancreatic intraepithelial neoplasms (PanINs) may represent its precursors. Normal ductal cells progress to flat hyperplasia (PanIN type 1A), ductal hyperplasia with pseudostratification (PanIN type 1B), hyperplasia with atypia (PanIN type 2), and carcinoma in situ (PanIN type 3). PanIN type 3 is associated with a high risk to evolve into invasive carcinoma.

Resected adenocarcinomas arising in the head of the pancreas, because of the earlier occurrence of clinical symptoms, tend to be smaller at resection (3 cm) than those in the body and tail (5 cm).

Pancreatic adenocarcinomas manifest as poorly defined, firm masses that may focally enlarge the organ and tend to blend with the remaining pancreatic parenchyma. Cystic changes rarely occur secondary to central necrosis or ductal obstruction with retention cyst formation. The disease is associated with an intense desmoplastic reaction, and, because of its ductal origin, it tends to obstruct the pancreatic duct, with subsequent upstream duct dilatation and associated chronic pancreatitis or parenchymal atrophy. If it arises in the pancreatic head, the common bile duct (CBD) can be stenosed with subsequent biliary tree dilatation.

Pancreatic adenocarcinomas tend to infiltrate early into the retroperitoneum, even when smaller than 2 cm, and invade into the surrounding anatomic structures, including nerves and vessels, which are stenosed and/or thrombosed, and to disseminate to the lymph nodes (mainly the superior head, pancreaticoduodenal, hepatoduodenal, perimesenteric, and para-aortic chains), liver, and peritoneum. Therefore, less than 10% to 20% of cancers are deemed surgically resectable, and many of them manifest in an advanced stage at pathologic examination.<sup>1,2</sup>

#### Imaging

The diagnostic imaging approach to pancreatic adenocarcinoma depends on the clinical scenarios: (1) diagnostic imaging proof of the presence or absence of disease for patients with a suspicion of pancreatic cancer, (2) staging for patients with a known pancreatic adenocarcinoma, (3) follow-up of patients with treated adenocarcinoma of the pancreas, and (4) screening of patients at high risk for this tumor. The TNM classification for pancreatic cancer staging is presented in Table 46-2.<sup>4</sup>

**Computed Tomography.** A dual-phase pancreatic protocol MDCT is a sensitive technique for both detection and staging of pancreatic adenocarcinoma. The pancreatic phase allows optimal tumor detection and mapping of the vascular structures; in this phase, the pancreatic adenocarcinoma appears as a low-density lesion compared with the normally enhancing

# TABLE Tumor, Node, Metastasis Classification for 46-2 Pancreatic Cancer Staging

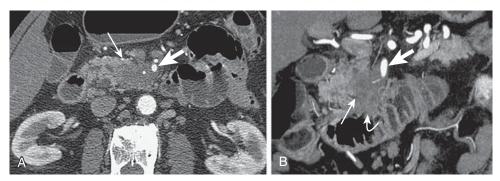
Classification	Description			
T (TUMOR)				
Тх	Primary tumor not assessed			
Tis	Carcinoma in situ			
T1	Tumor is ≤2 cm in maximum diameter and confined to the pancreas			
Т2	Tumor is >2 cm and confined to the pancreas			
Т3	Tumor extends beyond the pancreas but does not involve celiac axis or superior mesenteric artery			
Τ4	Tumor involves either celiac axis or superior mesenteric artery			
N (NODAL INVOLVEMENT)				
Nx	Regional lymph nodes not assessed			
N0	No involvement of regional lymph nodes			
N1	Involvement of regional lymph nodes			
M (METASTASES)				
Mx	Distant metastases not assessed			
MO	No distant metastases			
M1	Distant metastases			

pancreatic parenchyma (Figures 46-2 and 46-3). In the portovenous phase, tumor conspicuity may be reduced but the detection of metastases to the liver and peritoneum, as well as the visualization of portal venous structures, is improved. In approximately 10% of cases it is isoattenuating to pancreatic parenchyma during dynamic contrast imaging and not visible. In these cases, the diagnosis relies on indirect signs, such as focal or diffuse loss of pancreatic parenchyma lobulation, contour deformity, stenosis of the pancreatic duct with upstream ductal dilatation, parenchymal atrophy, stenosis of the distal CBD, and the "double duct" sign (stenosis of both the CBD and the pancreatic duct with subsequent upstream dilatation), which also are useful to support the diagnosis in the case of directly visualized adenocarcinomas (Figures 46-4 to 46-6).

CT sensitivity in tumor detection inversely correlates with tumor size and is influenced by technology; it can be as low as 63% with single-detector scanners and ranges from 88% to 99% with MDCT technology. The assessment of overall tumor resectability with MDCT is accurate, with a negative predictive value of 87%. MDCT is the modality with the highest accuracy in the assessment of vascular invasion. The likelihood of vascular infiltration by pancreatic adenocarcinoma increases as the tumor to vessel circumference contact increases, being less than 3% when the tumor to vessel circumference contact is less than 90 degrees, between 29% and 57% for a contact between 90 and 180 degrees, and more than 80% for a contact of more than 180 degrees. Other imaging criteria for vascular invasion are violation of the fat plane around the vessels, the "tear drop" sign, which refers to a tear drop shape of the portal vein or the superior mesenteric vein, and dilatation of the pancreaticoduodenal veins (see Figures 46-1, 46-2, and 46-7).<sup>4</sup>

**Magnetic Resonance Imaging.** MRI, because of its high soft tissue and contrast resolution, can facilitate detection of subtle pancreatic lesions and small, non–organ-deforming masses;

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**Figure 46-2** Locally invasive pancreatic adenocarcinoma arising from the uncinate process on axial (A) and coronal (B) multidetector computed tomography images, manifesting as a hypodense mass (*thin arrow*), which circumscribes the superior mesenteric artery (*thick arrow*) for more than 180 degrees and invades the duodenum (*curved arrow*, B), rendering the tumor inoperable.

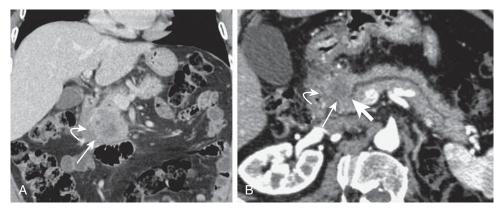
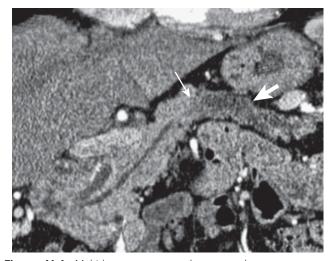


Figure 46-3 Adenocarcinoma of the pancreas shown on coronal (A) and curved reconstructed (B) multidetector computed tomography images. Note a poorly enhancing mass (*thin arrow*) that obstructs the main pancreatic duct (*thick arrow*) and infiltrates the duodenum (*curved arrow*).



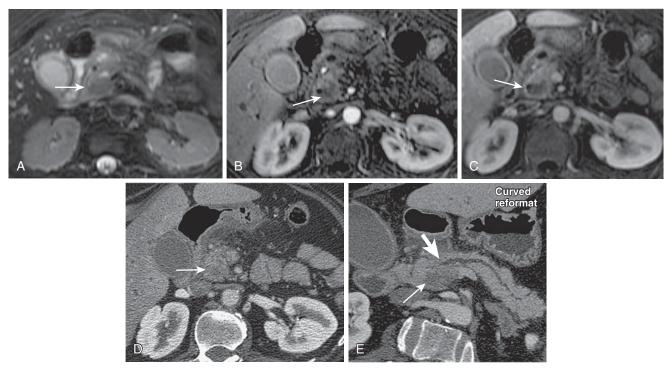
**Figure 46-4** Multidetector computed tomography–pancreatogram image showing abrupt obstruction of the main pancreatic duct with upstream dilatation (*thick arrow*) secondary to a small tumor (*thin arrow*).

therefore, sensitivity and specificity for adenocarcinoma detection with MRI alone are high, at 83% and 98%, respectively. On MRI, pancreatic adenocarcinoma appears hypointense on unenhanced T1-weighted images, particularly if 2D fatsaturated sequences are employed. The lobular architecture is effaced. Because of the different degrees of associated desmoplastic response, adenocarcinomas of the pancreas demonstrate variable signal intensity on T2-weighted images and enhance relatively less than the background pancreatic parenchyma in the early phases of dynamic contrast imaging but show progressive enhancement in the subsequent phases (Figures 46-8 and 46-9). If mangafodipir trisodium is administered, the relative lack of enhancement of the adenocarcinoma, which will appear hypointense compared to normal enhanced parenchyma, leads to increased tumor detection, with a sensitivity that may be close to 100%.

On 2D and 3D MRCP the pancreatic and biliary ducts can be accurately studied and the typical "double duct" sign, often seen with pancreatic or ampullary tumors, can be demonstrated (Figure 46-10). Moreover, S-MRCP, increasing duct distention, improves the quality of the MRCP and the lesion conspicuity; therefore, pancreatic duct stenosis can be better evaluated and duct irregularities demonstrated.

MRI, with a combination of T2- and T1-weighted fatsaturated gadolinium-enhanced images, performs better than MDCT in the detection and characterization of liver lesions and peritoneal implants, especially for the smallest ones, which tend to parallel the signal intensity of the primary cancer.<sup>4,6-10,13-16</sup>

**Ultrasonography.** Although transabdominal ultrasonography is usually the first diagnostic imaging tool in the evaluation of the abdomen, it is highly operator dependent and limited by abdominal gas and patient body habitus. Therefore, despite very



**Figure 46-5** Axial T2-weighted (A), pancreatic phase T1-weighted (B), portovenous phase T1-weighted (C), axial (D), and pancreatographic (E) multidetector computed tomography images show a poorly enhancing pancreatic adenocarcinoma (*thin arrow*) with abrupt obstruction of main pancreatic duct (*thick arrow*, E). The tumor may manifest as hypointense on T2-weighed images, as in this case, which can render it difficult to be detected, unless contrast medium is injected.



**Figure 46-6** Adenocarcinoma of the pancreas. Multidetector computed tomography pancreatogram displays obstruction of the main pancreatic duct with upstream dilatation (*thick arrow*) induced by a poorly defined pancreatic adenocarcinoma (*thin arrow*) along with atrophic parenchyma. The *asterisk* indicates a biliary stent.

few single institution studies that demonstrated ultrasonography to be more accurate than CT in tumor diagnosis and as accurate as CT in staging, a negative ultrasound examination does not reliably rule out a solid pancreatic mass. Adenocarcinoma of the pancreas can appear on ultrasound images as a focal, solid, contour-deforming, hypoechoic mass within the pancreas. The MPD may be dilated and surrounding parenchyma atrophic. Peripancreatic lymph nodes may appear enlarged, and their echogenicity reflects that of the primary cancer.

EUS, on the other hand, provides high-resolution images of the pancreas and allows lesion biopsy. EUS is the most accurate imaging technique for lymph node staging and for detection of duodenal infiltration by the cancer (EUS, 76%; CT, 74%; MRI, 67%).<sup>7</sup>

**Nuclear Medicine.** Nuclear medicine does not play a major role in adenocarcinoma evaluation unless differential diagnosis with functional endocrine tumors or evaluation of bone metastases is required.

**Positron Emission Tomography With Computed Tomography.** PET/CT integrates both functional and morphologic imaging data in a single test. Because the normal pancreas is not visualized on PET, any region of intense FDG uptake is considered abnormal. Initial studies identified pancreatic adenocarcinomas in 95% of patients as discrete foci of increased uptake (Figure 46-11). Lymph node metastases, especially if small (<1 cm in diameter), are frequently missed with CT or ultrasonography and may be responsible for early tumor recurrence after surgery. Because FDG uptake is related to tumor metabolism and not strictly to lesion size, cancer can be detected even in normal-sized lymph nodes. Currently, many new radiopharmaceutical agents are under investigation.<sup>4,17,18</sup>

**Imaging Algorithm.** An imaging algorithm is provided in Figure 46-1; see also Table 46-3.

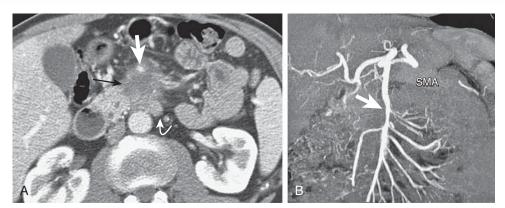
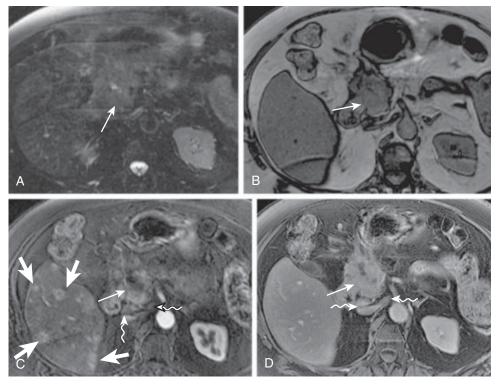


Figure 46-7 Axial (A) and coronal maximum intensity projection (B) multidetector computed tomography images show an advanced adenocarcinoma (*thin arrow*) infiltrating the superior mesenteric artery (SMA) (*thick arrow*) that appears as the "tear drop" sign. Lymph node metastases are present (*curved arrow*).



**Figure 46-8** Infiltrative pancreatic adenocarcinoma as a hypointense lesion (*thin arrows*) on T2-weighted (A) and T1-weighted (B) magnetic resonance images. Note minimal progressive heterogeneous enhancement in pancreatic phase T1-weighted (C) and delayed-phase T1-weighted (D) images. Also noted are multiple hepatic (*thick arrows*) and lymph node (*wavy arrows*) metastases.

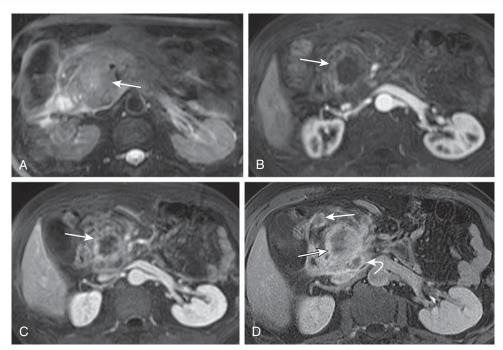
# **Classic Signs: Pancreatic Masses**

- Focal solid pancreatic mass, usually less than 5 cm in diameter
- MPD stenosis/obstruction with upstream dilatation
- CBD dilatation if the tumor is in the pancreatic head
- "Double duct" sign (CBD and MPD dilatation) if the tumor is in the pancreatic head
- Poor enhancement of the mass in the arterial and pancreatic phases of dynamic imaging
- Infiltration into the retroperitoneum
- Lymph node, liver, and peritoneal metastases

# Differential Diagnosis

Clinical data are useful to suspect pancreatic adenocarcinoma and contribute to rule out other conditions. Abdominal pain radiating to the back and partially reduced leaning forward, weight loss, jaundice, a palpable gallbladder, thrombophlebitis migrans, recent onset of diabetes, depression, history of smoking and of exposure to carcinogenic agents, and a family or personal history of breast, colon, and pancreatic neoplasms and of hereditary oncologic syndromes may suggest the occurrence of adenocarcinoma of the pancreas.

Laboratory data, mainly increased serum levels of CA 19-9, may provide some support to the diagnosis, but imaging provides the key to the diagnosis.<sup>1,2</sup>



**Figure 46-9** Advanced pancreatic adenocarcinoma seen on T2-weighted (A) and pancreatic phase (B), portovenous phase (C), and late phase (D) contrast-enhanced T1-weighted magnetic resonance images as a heterogeneously hyperintense infiltrating lesion (*thin arrow*) on T2-weighted imaging and showing poor, heterogeneous, progressive contrast enhancement over time. Peritoneal metastases coexist (*long thin arrow*, D), and necrotic lymph node metastases (*curved arrow*, D) are also noted.

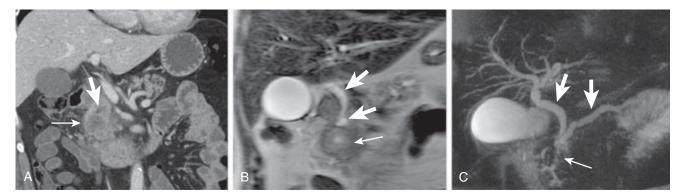


Figure 46-10 Infiltrating pancreatic adenocarcinoma (*thin arrow*) causing obstruction and upstream dilatation of both the main pancreatic duct and the common bile duct (*thick arrows*) and showing the "double duct" sign on coronal multidetector computed tomography (A), coronal steady-state fast spin echo T2-wighted (B) magnetic resonance image, and three-dimensional magnetic resonance cholangiopancreatography (C).

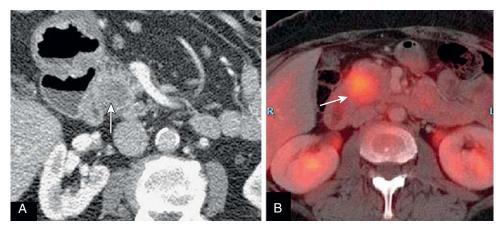


Figure 46-11 Axial multidetector computed tomography (MDCT) (A) and fused positron emission tomography and MDCT (B) images show a pancreatic adenocarcinoma (*arrows*) that avidly takes up fluorodeoxyglucose, highlighting it against normal pancreatic parenchyma.

TABLE 46-3Accuracy,	Limitations, and Pitfalls of Modalities	Used in Imaging of Adenocarc	inoma
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive Nonspecific	Unable to directly visualize soft tissue masses in the pancreas
СТ	89%-99% tumor diagnosis 86%-91% overall locoregional extension 77%-99% vascular invasion 58%-73% lymph node involvement	Radiation exposure	Difficult detection in the setting of background chronic pancreatitis Characterization of small lesions may be difficult.
MRI	82%-91% tumor diagnosis 63%-89% overall locoregional extension 85%-94% vascular invasion 75%-88% lymph node involvement	Patient cooperation High cost	Calcifications not well visualized
Ultrasonography	<70% US 65%-74% (EUS) locoregional extension	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	Detection and characterization of small lesions may be difficult.
Nuclear medicine	Data are not available to specify accuracy. No role at the moment unless in the differential diagnosis with suspected functional endocrine neoplasms or for bone metastases	Poor spatial resolution	
PET/CT	88%-95% tumor diagnosis	Radiation exposure High cost	Diabetes and inflammation may give rise to false results.

CT, Computed tomography; EUS, endoscopic ultrasound; MRI, magnetic resonance imaging; PET, positron emission tomography.

Many anatomic variants may be confused with pancreatic adenocarcinoma. Their differential diagnosis is described in the corresponding sections. Collapsed duodenum or small bowel and duodenal diverticula can be misinterpreted as pancreatic adenocarcinoma, but filling with positive oral contrast agent, air/fluid levels, and enhancement characteristic like that of the intestinal wall suggest the correct diagnosis.

Chronic pancreatitis, usually of alcoholic or autoimmune cause, may manifest as a focal mass clinically and radiologically similar to adenocarcinoma. The differential diagnosis with mass-forming chronic pancreatitis is difficult, and different clinical and imaging findings must be carefully satisfied.

Mass-forming chronic pancreatitis (MFP) tends to blend imperceptibly with surrounding parenchyma in the case of alcoholic MFP and to be better defined in the case of autoimmune MFP, but it has infiltrating margins in the case of adenocarcinoma. MFP tends to enhance more homogeneously and to a higher degree than adenocarcinomas. The MPD is obstructed less often in the case of alcoholic MFP and autoimmune MFP; in the case of MPD stenosis, the length of the affected segment is less than 30 mm in 75% of adenocarcinomas and more than 30 mm in nearly all the cases of autoimmune MFP.

The most reliable differentiating finding is the "duct penetrating" sign, characterized by visualization of the MPD traversing the pancreatic mass, without stenosis and ductal wall irregularities. If this criterion is satisfied, it is highly specific (96%) for MFP. On the other hand, MPD with an irregular wall, while traversing a mass, is not considered predictive of a benign cause. S-MRCP, because of the distention of the pancreatic duct, may potentially help achieve a correct diagnosis.

FDG-PET/CT may be useful to differentiate pancreatic adenocarcinoma, which shows an avid FGD uptake, from MFP, which demonstrates relatively low levels of FDG uptake. New radioisotopes, such as s-receptor ligands and 18F-FLT, are more tumor specific and potentially of better use in the differential diagnosis. Table 46-4 summarizes the most useful differential features (Figures 46-12 to 46-14). Other neoplasms, such as lymphoma, endocrine tumors, and acinar tumors, enter in the differential diagnosis with pancreatic adenocarcinomas (see later discussion). They all tend to spare the MPD, which is not dilated or stenosed; moreover, their size tends to be larger than that of an adenocarcinoma. A lymphoma is usually sharply circumscribed, if focal, and associated with prominent extrapancreatic nodal disease. Endocrine tumors show intense contrast enhancement, and acinar cell tumors are large at presentation and enhance more than adenocarcinomas. Table 46-5 provides a summary of the most useful features to differentiate adenocarcinoma versus nonadenocarcinoma of the pancreas (Figures 46-15 to 46-17).<sup>4,17-20</sup>

# Treatment

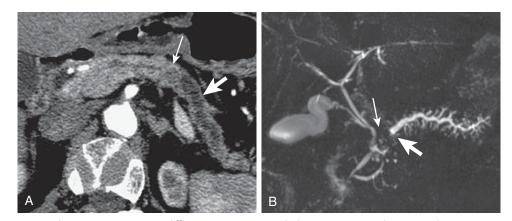
**Medical Treatment.** For locally advanced pancreatic cancer, chemotherapy and radiation therapy, alone or in conjunction, are considered alternatives to surgery. Patients with distant metastases are considered ineligible for radiation therapy and undergo chemotherapy alone, although the traditional chemotherapy regimen for pancreatic adenocarcinoma offers only a small survival advantage and a slight improvement in the quality of life.<sup>1,2</sup>

**Surgical Treatment.** Complete surgical resection remains the best curative treatment for adenocarcinoma of the pancreas, with a 5-year survival rate approaching 20% if performed with curative intent; however, owing to late clinical presentation at an advanced stage, and to the biologic aggressiveness, less than 20% of the cases include surgical intervention and of these most reveal node or liver metastases or local infiltration during surgery. Pancreatic adenocarcinoma is considered unresectable in the case of invasion of major arterial vessels (tumor-to-vessel contiguity >50%) such as the celiac artery, hepatic artery, or superior mesenteric artery; in the case of massive venous invasion into the portal vein or superior mesenteric vein; and in the presence of distant metastasis to the liver, regional lymph nodes, or peritoneum (see Figures 46-1, 46-7, 46-8, 46-15, and 46-18).

# TABLEDifferential Diagnosis of Alcoholic Mass-Forming Pancreatitis, Autoimmune Mass-Forming Pancreatitis, and46-4Adenocarcinoma of the Pancreas

Factor	Alcoholic Mass-Forming Pancreatitis	Autoimmune Mass-Forming Pancreatitis	Adenocarcinoma
Age	6th-7th decades	7th-8th decades	7th-8th decades
Lesion margins	Blending with surrounding parenchyma	Defined (67%)	Infiltrative (82%)
Homogeneity, early contrast enhancement	Common (71%)	Uncommon (25%)	Rare (5%)
Homogeneity, late contrast enhancement	Common (82%)	Usual (100%)	Rare (8%)
MPD obstruction	Uncommon (18%)	Uncommon (11%)	Common (60%)
MPD stenosis >30 mm	Common (50%)	Usual (100%)	22% may be found
Penetrating duct sign	Common (86%)	Common (50%)	Rare
Upstream MPD <4 mm	Uncommon (33%)	Common (67%)	Rare (4%)
Downstream MPD irregularity	Usual (100%)	Uncommon (25%)	Uncommon (25%)
Side branches	Usually dilated (100%)	Commonly dilated (50%)	Uncommonly dilated (37%)
CBD	Normal	Stenosed (>20 mm length)	Stenosed (<20 mm length)
Artery encasement	Absent	Common (57%)	Common (81%)
Pseudocysts	Common	Absent	Rare (retention cysts)
Acute pancreatitis–like pain	Common	Uncommon	Rare
CA 19-9	Normal	May be elevated (33%)	Frequently elevated (77%)
lgG 4	Normal	Increased	Normal
Corticosteroid response	Absent	Present	Absent

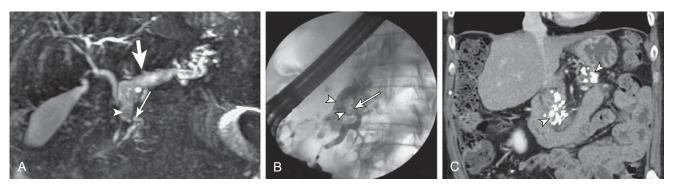
CBD, Common bile duct; IgG, immunoglobulin G; MPD, main pancreatic duct.



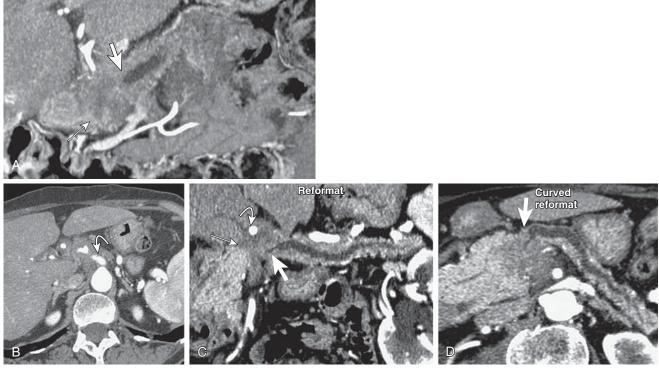
**Figure 46-12** Pancreatic adenocarcinoma in two different patients on multidetector computed tomography pancreatogram (A) and threedimensional magnetic resonance cholangiopancreatography (MRCP) (B) as a small and barely visible lesion (*thin arrow*) causing abrupt narrowing of the main pancreatic duct and upstream dilatation (*thick arrow*). The main pancreatic duct dilatation is better evaluated on MRCP images.



**Figure 46-13** Autoimmune mass-forming chronic pancreatitis manifests as smooth reduction in the main pancreatic duct over a long segment without any features of obstruction within the lesion (*thin arrow*) and absent upstream dilatation (*thick arrow*) in axial pancreatic phase, contrast-enhanced T1-weighted (A) image, three-dimensional magnetic resonance cholangiopancreatography (B), and multidetector computed tomography pancreatogram (C).



**Figure 46-14** Benign stricture (*thin arrow*) secondary to alcoholic chronic pancreatitis appears as smooth narrowing over a short segment along with upstream dilatation of the main pancreatic duct (*thick arrow*) and intraparenchymal and intraductal stones (*arrowheads*) in three-dimensional magnetic resonance cholangiopancreatography (**A**), endoscopic retrograde cholangiopancreatography (**B**), and coronal multidetector computed tomography (**C**) images.



**Figure 46-15** Staging multidetector computed tomography (MDCT) for pancreatic adenocarcinoma in two different patients shows a hypodense heterogeneous mass (*thin arrow*), causing abrupt obstruction of the main pancreatic duct (*thick arrow*) with upstream dilatation on coronal (A), axial (B), and MDCT pancreatograms (C and D) images. Also noted in B and C is atrophy of the corresponding parenchyma and encasement of the superior mesenteric artery (*curved arrows*). Note normal, strong parenchymal enhancement in the pancreatic head, proximal to the tumor.

TABLE <b>46-5</b>				
Charac	teristics	Adenocarcinoma	Nonadenocarcinoma	
Size		Medium-small (3-5 cm)	Large (>5 cm, unless functional pancreatic endocrine neoplasm)	
Necros	is	Rare	Common	
Calcific	ations	Rare	Common	
Enhanc	ement	Poor	Mild-intense	
Signal i	ntensity (T2 weighted)	Low-moderate	Moderate-high	
Main p	ancreatic duct	Stenosed or obstructed, upstream dilatation	Normal or displaced	
Vascula	r Encasement	Common	Rare	

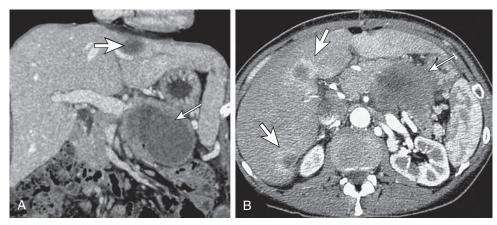


Figure 46-16 Colonic metastases to the pancreas are seen on coronal (A) and axial (B) multidetector computed tomography as a well-defined mass (thin arrow) lacking infiltrative changes, associated main pancreatic duct dilatation, and regional lymphadenopathy. Hepatic metastases are indicated by thick arrows.



**Figure 46-17** Primary pancreatic lymphoma in the region of the head on axial multidetector computed tomography manifests as a large, minimally enhancing homogeneous mass (*thin arrow*) with regional lymphadenopathy (*curved arrows*). However, the main pancreatic duct (*thick arrow*) is of normal caliber despite the size of the lesion.

A tumor with limited invasion into the superior mesenteric vein is still considered resectable.<sup>1,2,4</sup>

# What the Referring Physician Needs to Know: Adenocarcinoma

- Adenocarcinomas of the pancreas are malignant lesions with an incidence that usually peaks in the seventh and eighth decades; the 5-year survival rate is only 4%.
- Because of the nonspecific symptoms when at an early stage, the disease is usually advanced when the tumors are detected.
- Even lesions smaller than 2 cm tend to infiltrate locally and disseminate distally.
- MRI and MDCT plus reformatted imaging are the most accurate noninvasive diagnostic modalities.
- Vascular infiltration can be accurately evaluated noninvasively.

#### Key Points: Adenocarcinoma

- Malignant
- Solid
- Usually less than 5 cm
- Poorly defined
- MPD stenosis within the mass and upstream MPD dilatation
- Poor enhancement
- Retroperitoneal infiltration
- Lymph node, liver, and peritoneal metastases

# **ENDOCRINE TUMORS**

# Etiology

Many different chromosomal losses have been reported in pancreatic endocrine neoplasms (PENs); some of them are associated with more aggressive biologic behavior. Usually, larger PENs harbor more genetic alterations than smaller lesions. PENs usually occur sporadically but also may arise in patients with von Hippel-Lindau syndrome and multiple endocrine neoplasia (MEN).<sup>1,2</sup>

# Prevalence and Epidemiology

PENs are epithelial neoplasms with an organoid growth of cells that resemble pancreatic islet cells or other hormone-producing cells. PENs, which are usually well differentiated, are divided into functional and nonfunctional categories on the bases of associated clinical endocrine paraneoplastic syndrome and are named by the predominantly produced hormone as insulinomas, gastrinomas, VIPomas, glucagonomas, and somatostatinomas. Therefore, in the case of a hormone-secreting PEN, if it is not responsible for any endocrine paraneoplastic syndrome, it falls into the nonfunctional category.

PENs constitute 1% to 2% of pancreatic neoplasms, with the functional category representing between 50% and 85%.

Although PENs may occur at any age, they are found more often between 40 and 60 years of age (mean, 58 years) and at a similar rate between men and women.<sup>1,2</sup>

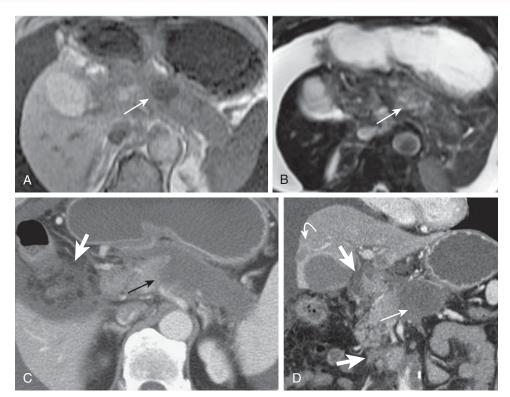


Figure 46-18 An advanced case of adenocarcinoma of the pancreas with peritoneal (*thick arrows*) and liver (*curved arrow*) metastases on axial T1-weighted (A), T2-weighted (B), axial (C), and coronal (D) multidetector computed tomography (MDCT) images appears as a mass (*thin arrow*) in the body of the pancreas. Magnetic resonance imaging is superior to MDCT in detecting the mass when it coexists with postobstructive inflammatory changes.

### **Clinical Presentation**

Clinical presentation varies according to presence or absence of an associated endocrine paraneoplastic syndrome.

Functional PENs are usually small at diagnosis. Nonfunctional PENs tend to be discovered late, when large or locally infiltrating and/or metastatic, with nonspecific features such as abdominal pain, nausea, vomiting, and sometimes jaundice or, in approximately 15% of cases, on imaging studies performed for other reasons, in which case they tend to be small.

Elevated serum levels of chromogranin A are associated with PENs in 70% of cases. Serum hormones do not strictly correlate with hormone type production in the neoplasm as assessed by immunohistochemistry.<sup>1,2</sup>

# Pathophysiology

Sixty percent of PENs present in the tail of the pancreas. Functional PENs occur more often in the head and tail, whereas nonfunctional PENs prefer the tail.<sup>1,2</sup>

#### Pathology

PENs are vascularized neoplasms that present as well circumscribed when small and multinodular, with some features of local invasiveness when large. They may contain areas of hemorrhage and fibrosis. Usually PENs are well differentiated, and most of them are malignant; only lesions less than 5 mm are deemed to be completely benign.

PENs are characterized by uniform nuclei, clear cytoplasm, and secretory granules; they stain positive for neuron-specific enolase and chromogranin A.

A summary of the classification of functional PENs is provided in Table 46-6.  $^{\rm h2}$ 

#### Imaging

PENs may be clinically suspected because of the specific signs and symptoms of the related endocrine paraneoplastic syndrome, may be discovered during workup imaging for nonspecific abdominal complaints or for a suspected malignancy, or may be discovered incidentally during unrelated imaging studies.<sup>1,2</sup>

**Radiography.** As stated earlier, radiography does not play a role in evaluation of PENs.

**Computed Tomography.** The imaging appearance of PENs is strongly influenced by their size at presentation. Because of specific clinical symptoms, functional PENs are investigated early in their course and therefore are small and homogeneous at presentation; meanwhile, nonfunctional neoplasms, owing to the lower index of suspicion, are diagnosed late and manifest larger and nonhomogeneously.

Classically, small PENs manifest as non-contour-deforming masses, isoattenuating to normal pancreas before contrast agent administration, and strongly enhancing during dynamic imaging (Figure 46-19). Sometimes, especially if malignant, they may manifest cystic features, enhance poorly, and contain calcifications. Insulinomas also can appear hyperattenuating before use of a contrast agent.

Large PENs tend to manifest as large heterogeneous masses at baseline and enhance in a nonhomogeneous fashion during dynamic imaging. The degree of heterogeneity parallels their size (Figure 46-20).

In the case of malignant behavior, areas of central necrosis, calcifications, and retroperitoneal invasion can be detected. The imaging features of metastases to regional lymph nodes and to

46-6 Functio	onal Pancreatic Endo	crine Neoplasms			
	Insulinoma	Glucagonoma	Somatostatinoma	Gastrinoma*	VIPoma
Syndrome	Insulinoma syndrome (hypoglycemia)	Glucagonoma syndrome (diabetes, rash, stomatitis, weight loss)	Somatostatinoma syndrome (hypochlorhydria, diabetes, cholelithiasis)	Zollinger-Ellison syndrome (diarrhea, peptic ulcer disease)	Verner-Morrison syndrome (achlorhydria, watery diarrhea, hypokalemia)
Location	Tail (40%), head (30%), body (30%)	Tail (52%), head (26%), body (22%)	Head (63%), tail (27%), body (10%)	Head (55%), tail (27%), body (18%)	Tail (47%), head (23%), body (19%)
Size	<2 cm	7-8 cm	5-6 cm	2-4 cm	4-5 cm
Malignant risk	Low	High	High	High	High
Structure <sup>†</sup>	Homogeneous, solid	Heterogeneous, cystic areas in large lesions	Heterogeneous, cystic areas in large lesions	Homogeneous, solid	Heterogeneous, cystic areas in large lesions
Ca <sup>2+</sup>	Rare	Common	Common		Common
Enhancement	Homogeneous > heterogeneous	Heterogeneous	Heterogeneous	Ring > homogeneous	Heterogeneous
Other features	Hypoglycemia Increased serum insulin and proinsulin	Elevated fasting serum glucagon	Somatostatin	Serum gastrin > 1000 pg/mL Secretin stimulation test	Serum VIP > 60 pg/mL Elevated serum peptide histidine, methionine

\*Gastrinomas often occur in extrapancreatic location in the "gastrinoma triangle" delimited by the hepatic hilum cranially, junction of II and III portion of duodenum inferiorly, and junction of neck-body of the pancreas medially. Gastric wall thickening is frequently multiple. <sup>†</sup>Structural heterogeneity and cystic areas increase with increasing size of the lesions.



Figure 46-19 Functional pancreatic endocrine neoplasm (VIPoma) in the head of the pancreas seen on axial (A) and reconstructed (B and C) multidetector computed tomography images as a lobulated, well-defined strongly enhancing mass (*thin arrow*) with normal main pancreatic duct (*thick arrow*). Note hypertrophic feeding vessels (*curved arrows*).

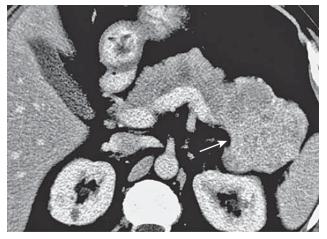
the liver tend to parallel those of the primary tumor and usually enhance early after contrast agent administration.<sup>21-23</sup>

**Magnetic Resonance Imaging.** MRI, owing to its high soft tissue and contrast resolution, can facilitate detection of small, non–organ-deforming masses, especially if strongly enhancing, as in the case of small PENs.

Although PENs, independently of their size, manifest as hypointense on T1-weighted sequences and hyperintense on T2-weighted sequences, in larger lesions there is a higher incidence of hemorrhage, necrosis, and cystic degeneration, which influences their signal intensity. Moreover, lesions smaller than 2 cm display a homogeneous enhancement; meanwhile, larger tumors tend to manifest as a ring-like peripheral enhancement.

On 2D and 3D MRCP, the MPD is not stenosed or obstructed, although large lesions may cause its displacement.<sup>21-23</sup>

**Ultrasonography.** On ultrasonography, PENs tend to manifest as focal, solid, sharply demarcated, hypoechoic masses within



**Figure 46-20** Nonfunctional pancreatic endocrine neoplasm seen on axial multidetector computed tomography as a large, strongly enhancing heterogeneous mass (*arrow*) in the tail of the pancreas.

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the pancreas that tend to markedly enhance after contrast agent administration. The MPD is not dilated.<sup>22</sup>

**Nuclear Medicine.** Nuclear medicine plays a significant role in detection of PENs. Scintigraphy with indium-111 (<sup>111</sup>In)-octreotide, a somatostatin analog, is highly sensitive (67% to 100% of all PENs) and has been proved useful for diagnosis, staging, and follow-up of PENs. Moreover, it helps to identify associated unsuspected lesions.<sup>22,23</sup>

**Positron Emission Tomography With Computed Tomography.** PET/CT and scintigraphy with <sup>111</sup>In-octreotide have complementary roles in the case of PENs. PET/CT may be unable to visualize well-differentiated, slowly growing PENs whose metabolic rate is low, providing false-negative results. These same tumors are those easily detected by scintigraphy with <sup>111</sup>In-octreotide. On the other hand, PET/CT is useful in the case of poorly differentiated PENs that scarcely express somatostatin receptors, for which scintigraphy with <sup>111</sup>In-octreotide is falsely negative (10% to 20%). PET/CT proves particularly useful in the assessment of malignant PENs, poorly differentiated PENs, and metastatic disease.<sup>23</sup> **Imaging Algorithm.** An imaging algorithm is provided in Figure 46-1; see also Table 46-7.

## **Differential Diagnosis**

In the case of functional PENs, clinical and laboratory data are useful to strongly suspect the neoplasms; therefore, diagnostic imaging is requested to confirm the clinical suspicion (Figure 46-21).

In the case of nonfunctional PENs, the nonspecificity of the clinical picture does not help reach an early diagnosis and differentiate against other neoplasms.<sup>1,2</sup>

#### **Classic Signs: Pancreatic Endocrine Tumors**

- Homogeneous solid pancreatic mass less than 5 cm in diameter
- Heterogeneous pancreatic mass more than 5 cm in diameter
- Calcifications
- Strong enhancement in the arterial and pancreatic phases of dynamic imaging
- No MPD stenosis or obstruction

46-7 Accura	cy, Limitations, and Pitfall	s of the Modalities Used in Imaging of Pa	ancreatic Endocrine Tumors
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive Nonspecific	Unable to directly visualize soft tissue masses in the pancreas.
CT	92%	Radiation exposure	Proper contrast-enhancement technique is mandatory to

	72.70		technique is mandatory to visualize small lesions.
MRI	Specific data regarding MRI accuracy are not available; reported sensitivity ranges from 84% to 94%.	Patient cooperation High cost	Calcifications are not well visualized.
Ultrasonography	Specific data regarding accuracy are not available; reported sensitivity ranges from 20% to 86%.	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	Detection and characterization of small lesions may be difficult.
Nuclear medicine	83%	Poor spatial resolution	<sup>111</sup> In-octreotide uptake is reduced in the case of poorly differentiated pancreatic endocrine neoplasms.
PET/CT	Specific data regarding PET/CT accuracy are not available; reported sensitivity ranges from 53% to 57%.	Radiation exposure High cost	FDG uptake is poor in well- differentiated pancreatic endocrine neoplasms.

CT, Computed tomography; FDG, fluorodeoxyglucose; MRI, magnetic resonance imaging; PET, positron emission tomography.



**Figure 46-21** Extrapancreatic gastrinoma seen on coronal (A) and axial (B) multidetector computed tomography images, as a well-defined, intensely enhancing lesion (*arrow*, A) in the pancreatoduodenal groove during the arterial phase. Also noted in the same patient is marked thickening of the gastric folds (*thick arrow*).

Differential diagnosis with anatomic variants and pseudolesions is described in the corresponding sections. The differential diagnosis with other neoplasms of the pancreas mainly includes adenocarcinoma of the pancreas and metastases from renal cancer.

Calcifications (found in 22% of the cases), central necrosis or cystic degeneration, higher signal intensity on T2-weighted images, and lack of MPD obstruction and vascular encasement are features suggestive of PENs. Moreover, in the case of gluca-gonomas and somatostatinomas, metastases to the spleen are characteristic. A negative oncologic history for a renal primary tumor is a useful criterion to rule out intrapancreatic metastases from renal cell carcinoma.<sup>1,2,21-23</sup>

# Treatment

**Medical Treatment.** The role of chemotherapy for metastatic and locally advanced PENs is still debated; it is usually restricted to symptomatic patients, with only some partial responses reported. Octreotide is frequently used to palliate symptoms.<sup>1,2</sup>

**Surgical Treatment.** Surgical resection represents the best curative treatment for solitary PENs; in the case of a single functional PEN, limited pancreatectomy is the treatment of choice. In the setting of PENs associated with multiple endocrine neoplasia type 1, the treatment is particularly complicated, owing to the occurrence of multiple neoplasms in the pancreas and in other organs (Figure 46-22).<sup>1,2</sup>

#### What the Referring Physician Needs to Know: Pancreatic Endocrine Neoplasms

- PENs are deemed benign if less than 5 mm in diameter and harbor malignant potential if larger.
- Peak incidence is usually in the fifth and sixth decades.
- If functional, PENs are suspected at an early stage;
- otherwise, they are usually diagnosed when advanced.
  In the case of malignancy they can infiltrate locally and disseminate distally, by the lymphatic and hematologic
- MRI and MDCT with reformatted imaging are accurate
- noninvasive diagnostic modalities. <sup>111</sup>In-octreotide scintigraphy is highly sensitive in detection of PENs (67% to 100%) and has been proved

useful for diagnosis, staging, and follow-up.

# Key Points: Pancreatic Endocrine Neoplasms

- Potentially malignant or malignant
- Solid
- Usually well defined
- Usually less than 5 cm if functional and more than 5 cm if nonfunctional
- Enhancing
- No MPD stenosis
- Lymph node and liver metastases

# INTRAPANCREATIC METASTASES

#### Etiology

Intrapancreatic metastases usually occur in the setting of widespread malignancies. The pancreas may be secondarily involved through direct invasion or hematogeneous and lymphatic dissemination or be part of systemic hematologic malignancies, such as leukemias and lymphomas.<sup>1,2</sup>

# Prevalence and Epidemiology

Intrapancreatic metastases are rare, accounting for 2% of pancreatic tumors. The mean age at manifestation is 60 years. At autopsy the malignancies most commonly implicated are lung (25%), breast (13%), melanoma (11%), gastric (10%), colorectal (6%), renal (4%), and ovarian (4%).<sup>1</sup>

### **Clinical Presentation**

Intrapancreatic metastases usually occur in the setting of disseminated malignancies. They lack a specific symptomatology, are detected during routine oncologic follow-up, and do not constitute a relevant clinical and management problem.

In less than 8.5% of cases, intrapancreatic metastases are clinically suspected, and in less than 4% they undergo biopsy or resection.<sup>1,2,24,25</sup>

### Pathophysiology

Intrapancreatic metastases may be single (25%) or multiple (75%). In the case of focal involvement, the pancreatic head is the most common location.

# Pathology

The pathologic process of intrapancreatic metastases is extremely variable and reflects that of the primary tumor. Mean size at diagnosis is 4.6 cm.

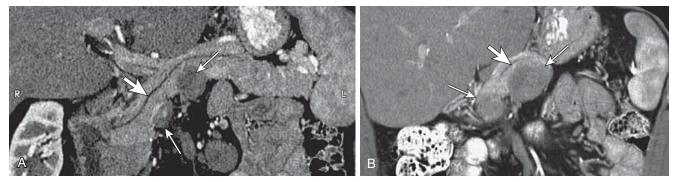


Figure 46-22 Multiple pancreatic endocrine neoplasms seen on multidetector computed tomography (MDCT) pancreatogram (A) and coronal (B) MDCT images, as two well-defined, mildly enhancing solid masses (*thin arrows*) in the body deforming the contour of the organ without causing any obstruction and dilatation of the main pancreatic duct (*thick arrows*).

Renal cell carcinoma metastases, most often of the clear cell type, tend to manifest as solitary, well-circumscribed solid masses with prominent vascularization. They can undergo necrosis, hemorrhage, and cystic degeneration. Lymphomatous involvement of the pancreas, reported in a third of systemic disease cases, occurs more often in the form of a focal mass than a diffuse infiltration.<sup>1</sup>

#### Imaging

Intrapancreatic metastases do not usually pose specific imaging problems because they are discovered during imaging follow-up for a known primary tumor. In the very few cases in which oncologic history is apparently negative, diagnostic imaging is usually inadequate to reach the diagnosis and biopsy or even resection is required.<sup>1,2,24,25</sup>

**Computed Tomography.** There is no imaging feature that is specific for intrapancreatic metastases. Besides the fact that small lesions appear homogeneous whereas large masses display internal heterogeneity, and may contain necrotic areas, these lesions tend to reflect the appearance of their tumor of origin.

Metastases from a hypervascular primary tumor such as breast or clear cell renal cancer strongly enhance during the arterial phase of dynamic imaging (Figure 46-23). Metastases from colorectal cancers tend to enhance poorly and may mimic pancreatic adenocarcinomas (see Figure 46-16).<sup>24,25</sup>

**Magnetic Resonance Imaging.** In the case of intrapancreatic metastases, the information obtained from MDCT also can be provided by MRI, with the added benefits of superior contrast resolution, which could allow the detection of smaller hyper-vascularized metastases and the possibility of identifying chemical shift phenomenon and melanin hyperintensity in the case of intrapancreatic metastases from clear cell renal cancer and melanoma, respectively.<sup>24,25</sup>

#### Positron Emission Tomography With Computed Tomogra-

**phy.** Although there are no specific studies to address PET/CT of intrapancreatic metastases, in our personal experience, and from case reports, they tend to exhibit increased uptake of FDG, highlighting the lesion against the normal background pancreas.

**Imaging Algorithm.** An imaging algorithm is provided in Figure 46-1; see also Table 46-8.

#### **Classic Signs: Intrapancreatic Metastases**

- No specific imaging sign
- History of primary tumor nearly always present
- Usually in the setting of widespread malignancy
- Single or multiple solid pancreatic masses, with 4.5-cm mean diameter
- Baseline and enhancement features paralleling those of the tumor of origin
- Homogeneous if small lesions
- Heterogeneous if large lesions
- Normal MPD
- Normal CBD; dilatation possible if lesion located in pancreatic head

#### Differential Diagnosis

Clinical data are necessary to suspect the metastatic nature of the intrapancreatic lesions and to rule out a pancreatic primary tumor. Clinical history of a primary tumor is found in virtually all patients, with the possible exception of melanoma, which can be unknown to the patient. Pancreatic symptoms are usually absent at presentation or at least overwhelmed by the manifestations of the associated disseminated oncologic disease.<sup>1,2,24,25</sup>

No imaging feature is specific for intrapancreatic metastases. Their imaging appearance varies strongly, according to the primary tumor of origin.

The differential diagnosis from adenocarcinoma of the pancreas is usually prompted by the normal appearance of the MPD and in the case of renal or breast primary tumors by the strong enhancement of the lesions. The most difficult differential diagnosis is with PENs. In these cases, history of a renal or breast primary tumor, absence of endocrinologic abnormalities, and a negative finding on <sup>111</sup>In-octreotide scintigraphy are important differential criteria.<sup>24,25</sup>

## Treatment

**Medical Treatment.** Intrapancreatic metastases are treated with the same chemotherapy regimen used to treat the remaining localizations of the disseminated malignancy.<sup>1,24,25</sup>

**Surgical Treatment.** Surgical resection is not considered in the case of intrapancreatic metastases, unless it is the case of solitary lesions not associated with other metastases.<sup>1,24,25</sup>

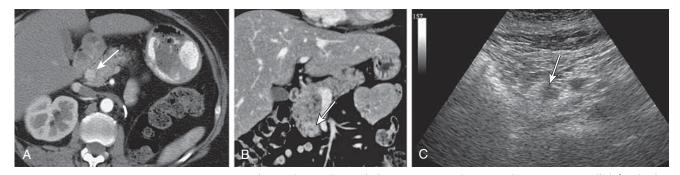


Figure 46-23 Intrapancreatic metastases seen on axial (A) and coronal (B) multidetector computed tomography images, as a well-defined enhancing mass (arrows) in the uncinate process on computed tomography and as a hypoechoic lesion on ultrasonography (C). Note the empty left renal fossa and surgical vascular clip from previous nephrectomy for clear cell renal cancer.

46-8 Accuracy	, Limitations, and Pitfalls of the Modalities	Used in Imaging of Intrapancr	eatic Metastases
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive Nonspecific	Unable to directly visualize soft tissue masses in the pancreas.
СТ	No studies available to specifically address CT accuracy in intrapancreatic metastases	Radiation exposure	Detection and characterization of small lesions may be difficult.
MRI	No studies available to specifically address MRI accuracy in intrapancreatic metastases	Patient cooperation High cost	Calcifications are not well visualized.
Ultrasonography	No studies available to specifically address accuracy in intrapancreatic metastases	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	Detection and characterization of small lesions may be difficult.
Nuclear medicine	Although no studies available to specifically address the accuracy of nuclear medicine in intrapancreatic metastases, role supposed to be poor	Poor spatial resolution	
PET/CT	No studies available to specifically address PET/CT accuracy in intrapancreatic metastases	Radiation exposure High cost	

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

#### What the Referring Physician Needs to Know: Intrapancreatic Metastases

- Intrapancreatic metastases usually occur in the setting of widely spread malignancies.
- They are usually detected incidentally.
- Imaging features reflect those of the primary tumor.
- Small lesions tend to be homogeneous, large ones tend to appear nonhomogeneous.

#### Key Points: Intrapancreatic Metastases

- Multiple or single.
- Solid if small.
- Cystic areas may coexist in the case of large lesions.
- Mean diameter: 4.6 cm.
- Baseline and enhancing features parallel those of the primary tumor.
- No MPD/CBD stenosis.

# PANCREATIC LYMPHOMA

#### Etiology

Pancreatic lymphoma is usually of the non-Hodgkin's type of both B- and T-cell lineage.<sup>1</sup>

# Prevalence and Epidemiology

Primary pancreatic lymphomas are rare, comprising 0.5% of all pancreatic neoplasms, tend to occur in the fourth to eighth decades (mean age, 55 years), and are more common in men (male-to-female ratio, 7:1).<sup>1,2,26-28</sup>

# **Clinical Presentation**

Clinical presentation is not specific, with abdominal pain present in all of the patients. Other symptoms are weight loss and jaundice, and the CA 19-9 value may be elevated.<sup>1</sup>

# Pathophysiology

The most common location is the head of the pancreas (80%).<sup>1,26-28</sup>

# Pathology

Lymphomas may manifest as a mass-forming focal lesion (mean diameter, 8 cm) or as a diffuse replacement of the organ, which appears globally enlarged. In both cases, pancreatic lymphomas tend to diffusely infiltrate the retroperitoneal structures and the gastrointestinal tract, not respecting anatomic boundaries.<sup>1,26-28</sup>

# Imaging

Primary pancreatic lymphoma is rarely clinically suspected, owing to the nonspecificity of the associated symptoms. It is usually discovered during imaging for nonspecific abdominal complaints or for a suspected abdominal malignancy or may be discovered incidentally during unrelated imaging studies.<sup>1</sup>

# Computed Tomography

On MDCT, primary pancreatic lymphoma manifests as a large (usually >7 cm) homogeneous mass or as diffuse enlargement of the gland with effacement of its lobular structure. On baseline CT, lymphomas tend to be hypodense to the pancreas and enhance poorly during dynamic imaging. The MPD is usually not affected. Peripancreatic and infrarenal lymph node enlargement often coexist (see Figure 46-17).<sup>26-28</sup>

# Magnetic Resonance Imaging

Pancreatic lymphomas, despite their size, which can be large at presentation, tend to appear homogeneous. They are hypointense on T1-weighted imaging, are hypointense to isointense on T2-weighted sequences, and tend to enhance poorly and homogeneously during dynamic imaging (Figures 46-24 and 46-25).<sup>26-28</sup>

# Ultrasonography

On transabdominal ultrasonography, primary pancreatic lymphomas may manifest as a large well-defined, hypoechoic

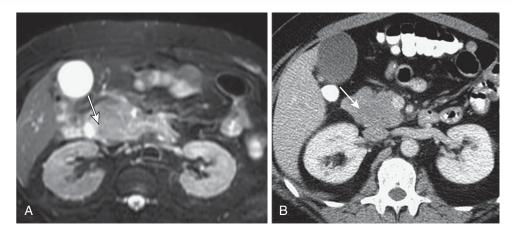


Figure 46-24 Primary pancreatic lymphoma on axial T2-weighted (A) and multidetector computed tomography (B) images seen as a poorly enhancing mass (*arrows*) in the head of the pancreas with internal homogeneity and moderately increased signal on the T2-weighted image.

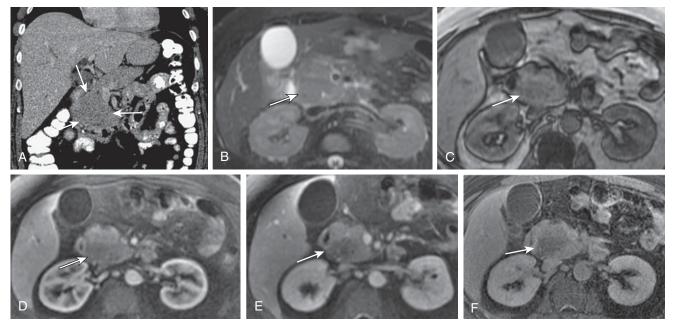


Figure 46-25 Multidetector computed tomography (MDCT) and magnetic resonance images of non-Hodgkin's lymphoma of the pancreas (arrows). Coronal MDCT (A) image shows a mass in the head of the pancreas with lack of main pancreatic duct and intrahepatic bile duct dilatation. The mass is isointense to the pancreas on T2-weighted (B) and T1-weighted (C) images and shows minimal enhancement on gadolinium-enhanced images in the pancreatic phase (D), portovenous phase (E), and delayed phase (F) images.

lesion or as diffuse enlargement of the organ, with reduced echogenicity.  $^{\rm 26\-28}$ 

# Positron Emission Tomography With Computed Tomography

Although there are no specific studies dedicated to PET/CT of primary pancreatic lymphomas, these neoplasms tend to manifest as large focal masses of increased uptake or as a diffusely increased uptake involving the entire pancreas. Usually, FDGavid lymph nodes are discovered in the peripancreatic region.

# Imaging Algorithm

An imaging algorithm is provided in Figure 46-1; see also Table 46-9.

#### **Classic Signs: Pancreatic Lymphoma**

- Solitary mass or diffuse infiltration of the pancreas
- Large diameter, usually greater than 7 cm
- Homogeneity of the lesion despite its large size
- Normal MPD

### **Differential Diagnosis**

In the case of primary pancreatic lymphoma, although clinical data usually are not specific enough to suspect the cause of the intrapancreatic lesion, they are suggestive for nonadeno-carcinoma. Imaging and biopsy are the cornerstones of the diagnosis.<sup>1,2,26-28</sup>

TABLE Accuracy,	Limitations, and Pitfalls of the Modalities	Used in Imaging of Pancreatic	Lymphoma
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive Nonspecific	Unable to directly visualize soft tissue masses in the pancreas.
СТ	No studies are available to specifically address CT accuracy in primary pancreatic lymphoma.	Radiation exposure	Detection and characterization of small lesions may be difficult.
MRI	No studies are available to specifically address MRI accuracy in primary pancreatic lymphoma.	Patient cooperation High cost	
Ultrasonography	No studies are available to specifically address accuracy in primary pancreatic lymphoma.	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	Detection and characterization of small lesions may be difficult.
Nuclear medicine	Although no studies are available to specifically address the accuracy of nuclear medicine in primary pancreatic lymphoma, its role is supposed to be very limited.	Poor spatial resolution	
PET/CT	No studies are available to specifically address PET/CT accuracy in primary pancreatic lymphoma.	Radiation exposure High cost	

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

Primary pancreatic lymphomas must be differentiated from pancreatic adenocarcinoma, PENs, and lymphoma with secondary involvement of the organ. A relatively small pancreatic mass with an obstructed MPD favors adenocarcinoma of the pancreas; in the case of lymphoma the lesion tends to be large at presentation. The MPD is nonobstructed; and if lymph nodes are enlarged, this occurs below the renal veins.

On the other hand, PENs are suspected in the case of more pronounced hyperintensity on T2-weighted sequences, intense arterial contrast enhancement, calcifications, and necrosis. Diffuse lymph node enlargement not limited to the peripancreatic region, but involving other sites, such as the mediastinum and superficial chains, and splenomegaly, hepatomegaly, and changes in the leukocyte count favor secondary involvement. A fine-needle aspiration biopsy is usually required for a definite histologic diagnosis if the just-mentioned signs are not evident.<sup>1,2,26-28</sup>

# Treatment

**Medical Treatment.** Primary pancreatic lymphomas tend to respond well to chemotherapy and/or radiation therapy.<sup>1,26,27</sup>

**Surgical Treatment.** Surgery is not routinely performed in the case of primary lymphoma of the pancreas; it is usually done if a preoperative diagnosis has not been undertaken.<sup>1,26,27</sup>

# What the Referring Physician Needs to Know: Pancreatic Lymphoma

- The clinical presentation is nonspecific.
- The tumor is usually detected incidentally.
- A large homogeneous mass without MPD dilatation is evident.
- Diffuse enlargement of the pancreas with effacement of its lobular architecture occurs.

#### Key Points: Pancreatic Lymphoma

- Solitary lesion or diffuse infiltration
- Large size (>7 cm)
- Homogeneity
- Well demarcated if mass-like
- Low to intermediate signal intensity on T2-weighted imaging
- Mild enhancement
- No MPD stenosis or upstream dilatation

# ACINAR CELL CARCINOMA

# Etiology

Mutations in the adenomatous polyposis coli beta-catenin gene and losses on chromosome 11 have been implicated as etiologic factors in acinar cell carcinoma (ACC).<sup>1</sup>

## Prevalence and Epidemiology

ACC is a rare pancreatic tumor characterized by pancreatic enzyme production by the tumor cells. It accounts for approximately 1% of all adult exocrine pancreatic neoplasms and approximately 15% of all pediatric pancreatic tumors. It occurs more often in women, with its incidence peak in the seventh decade.<sup>1</sup>

#### **Clinical Presentation**

The clinical presentation is variable. Symptoms can be induced by mass effect and/or local infiltration (jaundice, abdominal pain, vomiting, weight loss) or by elevated lipase production in 10% to 15% of cases (polyarthritis and/or subcutaneous fat necrosis). The serum lipase value is elevated in nearly all of the patients, even in the absence of associated symptoms. The serum marker CA 19-9 is increased in 30% of patients.<sup>1,29</sup>

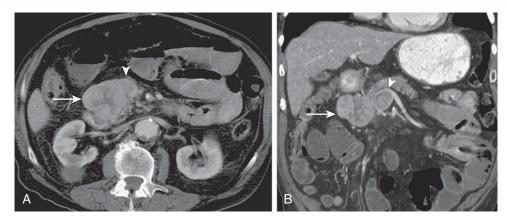


Figure 46-26 Multidetector computed tomography (MDCT) images of acinar cell cancer. Axial (A) and coronal (B) MDCT images show a welldefined, lobulated, predominantly exophytic mass (*arrows*) in the head of the pancreas invading the superior mesenteric vein (*arrowheads*).



Figure 46-27 Acinar cell cancer. Coronal (A and B) and axial (C) multidetector computed tomography images demonstrate a well-defined hypoattenuating mass (*thin arrow*) in the head of the pancreas with mild pancreatic ductal dilatation (*thick arrow*). The presence of mild duct dilatation and lack of parenchymal atrophy despite the critical location and size and of the mass differentiate it from pancreatic adenocarcinoma.

# Pathophysiology

ACC tends to arise more often in the uncinate process and head of the pancreas (60% of cases) as a solitary mass. In approximately 80% of cases this tumor grows exophytically.<sup>1</sup>

# Pathology

ACC manifests as a well-defined solid mass, surrounded by a fibrous pseudocapsule, which can harbor focal areas of discontinuity and infiltration. The mean tumor size at presentation is 7 cm. Large ACCs may exhibit a variable amount of necrosis with cystic degeneration that can encompass even more than 75% of the mass.

Neoplastic cells manifest in an acinar arrangement and acinar differentiation, as demonstrated by zymogen granules and confirmed by immunohistochemistry. Endocrine and ductal components, although commonly present, constitute less than 25% of the mass.<sup>1,29</sup>

#### Imaging

ACC tends to infiltrate locally and metastasize to regional lymph node and hepatic parenchyma ( $\sim$ 50% of cases at presentation). Recurrence is common (79% after curative resection); and although the 5-year survival rate is 5.9%, the median survival is higher than that for adenocarcinoma (19 months).<sup>1,29</sup>

**Computed Tomography.** ACC manifests as a wellcircumscribed, mildly enhancing, predominantly solid mass (Figures 46-26 and 46-27); an enhancing capsule may be demonstrated. Areas of capsular discontinuity and infiltration can be detected. Central necrosis is common (80% of the cases) and may be responsible for a cystic or mixed cystic-solid appearance (Figure 46-28). Calcifications in the form of central punctuate or stellate calcifications or peripheral calcified punctuations or plaques are found in 50% of the cases.<sup>29,30</sup>

**Magnetic Resonance Imaging.** MRI confirms the same imaging findings detected by MDCT, although calcifications are more difficult to appreciate. It is useful to rule out macroscopic intratumoral hemorrhage, a rare finding in ACC.<sup>29,30</sup>

**Ultrasonography.** Transabdominal ultrasonography is usually unable to provide an etiologic diagnosis. Usually, ACC manifests as a large, well-defined hypoechoic solid or mixed solid-cystic mass.

**Positron Emission Tomography With Computed Tomography.** ACC is rare, and currently there are no specific PET/CT studies to address this entity.

**Imaging Algorithm.** An imaging algorithm is provided in Figure 46-1; see also Table 46-10.

#### 46 Solid Pancreatic Masses 487

### Classic Signs: Acinar Cell Carcinoma

- Single, large, predominantly solid pancreatic mass with 7-cm mean diameter
- Tendency to exophytic growth
- Areas of necrosis
- Central and/or peripheral calcifications
- Normal MPD and CBD

#### **Differential Diagnosis**

Hyperlipasemia syndrome, which occurs in less than 15% of the cases and is characterized by coexistence of subcutaneous fat necrosis, polyarthralgias, and serum hyperlipasemia, prompts the search for an ACC.

If hyperlipasemia syndrome is absent, the tumor may be unsuspected or may cause nonspecific symptoms as a result of compression, infiltration, and dissemination. Even in this situation the serum lipase level is commonly elevated and may be useful to support the diagnosis.<sup>1,2,29-30</sup>



**Figure 46-28** Axial multidetector computed tomography image shows a solid and cystic acinar cell tumor (*arrow*) in the head of the pancreas with absence of main pancreatic duct dilatation and parenchymal atrophy.

ACC needs to be differentiated from adenocarcinoma of the pancreas, PENs, and pseudopapillary epithelial neoplasms (SPENs).

Large size at presentation, exophytic growth, calcifications, central necrosis, well-circumscribed appearance, lesion enhancement, and normal size of the MPD are typical for ACCs and rare in adenocarcinomas. Both ACCs and PENs may be large at presentation, display calcifications and central necrosis, and be well circumscribed, but ACCs enhance less than PENs, and take up mangafodipir trisodium. On the other hand, <sup>111</sup>In-octreotide uptake is specific for PENs. Differential diagnosis with SPEN is extremely difficult. SPENs may manifest as central necrosis, be circumscribed by capsule, display calcifications, and enhance as ACCs. SPENs almost invariably manifest as macroscopic hemorrhage, which is less common, although not rare, in ACCs. The most important differentiating features are the occurrence of SPENs in young females and the increased serum level of lipase in ACCs.<sup>1,2,29,30</sup>

## Treatment

**Medical Treatment.** Chemotherapy alone or combined with irradiation is reserved for patients not deemed surgical candidates because of widespread disease at presentation or poor medical condition.<sup>1</sup>

**Surgical Treatment.** Surgical resection is considered the treatment of choice in the case of resectable neoplasms. Large size at presentation, as a result of the expansive grow pattern, is not a contraindication to surgery.<sup>1</sup>

# What the Referring Physician Needs to Know: Acinar Cell Carcinoma

- A solitary, large mass is evident.
- The tumor may infiltrate and metastasize.
- Detection is incidental or symptomatic.
- Mass effect is present.
- Hyperlipasemia syndrome is associated.
- The prognosis is better than with adenocarcinoma.

TABLE 46-10	Accuracy,	Limitations, and Pitfalls of the Modalitie	s Used in Imaging of Acinar Cel	l Carcinoma
Modal	ity	Accuracy	Limitations	Pitfalls
Radiog	graphy	Poor	Insensitive Nonspecific	Unable to directly visualize soft tissue masses in the pancreas.
СТ		Specific data regarding CT accuracy are not available.	Radiation exposure	Detection and characterization of small lesions may be difficult.
MRI		Specific data regarding MR accuracy are not available.	Patient cooperation High cost	Calcifications not well visualized
Ultrasc	bund	Specific data regarding accuracy are not available.	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	Detection and characterization of small lesions may be difficult.
Nuclea	ar medicine	Although specific data regarding the accuracy of nuclear medicine are not available, it currently does not play any role in diagnosis of acinar cell carcinoma.	Poor spatial resolution	
PET/C	Т	Specific data regarding PET/CT accuracy are not available.	Radiation exposure High cost	

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

#### Key Points: Acinar Cell Carcinoma

- Single
- Predominantly solid or cystic
- Mean diameter: 7 cm
- Well circumscribed
- Exophytic growth

#### SUGGESTED READINGS

- Biankin AV, Kench JG, Dijkman FP, et al: Molecular pathogenesis of precursor lesions of pancreatic ductal adenocarcinoma. *Pathology* 35:14–24, 2003.
- Cardenes HR, Chiorean EG, Dewitt J, et al: Locally advanced pancreatic cancer: current therapeutic approach. *Oncologist* 11:612–623, 2006.
- Hines OJ, Reber HA: Pancreatic surgery. Curr Opin Gastroenterol 22:520–526, 2006.

#### REFERENCES

- 1. Hruban RH, Pitman Bishop M, Klimstra DS: Tumors of the pancreas. In Armed Forces Institute of Pathology, editor: *Atlas of tumor pathology*, 4th series, Washington, DC, 2007, Armed Forces Institute of Pathology.
- Yamada T, Alpers DH, Kountz WB, et al: *Textbook of Gastroenterology*, Philadelphia, 2003, Lippincott William & Wilkins.
- 3. Surveillance epidemiology and end results of the National Cancer Institute (SEER) cancer statistics review, 2000-2004, Bethesda, MD, 2008, National Cancer Institute.
- Sahani DV, Shah ZK, Catalano OA, et al: Radiology of pancreatic adenocarcinoma: current status of imaging. J Gastroenterol Hepatol 23:23– 33, 2008.
- Fletcher JG, Wiersema MJ, Farrell MA, et al: Pancreatic malignancy: value of arterial, pancreatic, and hepatic phase imaging with multidetector row CT. *Radiology* 229:81–90, 2003.
- 6. Schima W, Ba-Salamah A, Kolblinger C, et al: Pancreatic adenocarcinoma. *Eur Radiol* 17:638– 649, 2007.
- Soriano A, Castells A, Ayuso C, et al: Preoperative staging and tumor resectability assessment of pancreatic cancer: prospective study comparing endoscopic ultrasonography, helical computed tomography, magnetic resonance imaging, and angiography. Am J Gastroenterol 99:492–501, 2004.
- Irie H, Honda H, Kaneko K, et al: Comparison of helical CT and MR imaging in detecting and staging small pancreatic adenocarcinoma. *Abdom Imaging* 22:429–433, 1997.
- Mehmet Erturk S, Ichikawa T, Sou H, et al: Pancreatic adenocarcinoma: MDCT versus MRI in the detection and assessment of locoregional extension. J Comput Assist Tomogr 30:583–590, 2006.
- Vargas R, Nino-Murcia M, Trueblood W, et al: MDCT in pancreatic adenocarcinoma: prediction of vascular invasion and resectability using

- Necrotic areas in the case of large lesions
- Calcifications
- Mildly enhancing
- No stenosis of MPD or CBD
- Katz MH, Savides TJ, Moossa AR, et al: An evidencebased approach to the diagnosis and staging of pancreatic cancer. *Pancreatology* 5:576–590, 2005.
- Kostakoglu L, Agress H, Jr, Goldsmith SJ: Clinical role of FDG-PET in evaluation of cancer patients. *Radiographics* 23:315–340, 2003.
- Mittendorf EA, Shifrin AL, Inabnet WB, et al: Islet cell tumors. *Curr Probl Surg* 43:685–765, 2006.

Sahani DV, Shah ZK, Catalano OA, et al: Radiology of pancreatic adenocarcinoma: current status of imaging. J Gastroenterol Hepatol 23:23–33, 2008.
Saif MW: Primary pancreatic lymphomas. JOP 7:262–273, 2006.

- Semelka RC, Custodio CM, Cem Balci N, et al: Neuroendocrine tumors of the pancreas: spectrum of appearances on MRI. J Magn Reson Imaging 11:141–148, 2000.
- a multiphasic technique with curved planar reformations. *AJR Am J Roentgenol* 182:419–425, 2004.
- Li H, Zeng MS, Zhou KR, et al: Pancreatic adenocarcinoma: the different CT criteria for peripancreatic major arterial and venous invasion. *J Comput Assist Tomogr* 29:170–175, 2005.
- Mertz HR, Sechopoulos P, Delbeke D, et al: EUS, PET, and CT scanning for evaluation of pancreatic adenocarcinoma. *Gastrointest Endosc* 52:367–371, 2000.
- Birchard KR, Semelka RC, Hyslop WB, et al: Suspected pancreatic cancer: evaluation by dynamic gadolinium-enhanced 3D gradientecho MRI. *AJR Am J Roentgenol* 185:700–703, 2005.
- Schima W, Fugger R, Schober E, et al: Diagnosis and staging of pancreatic cancer: comparison of mangafodipir trisodium-enhanced MR imaging and contrast-enhanced helical hydro-CT. *AJR Am J Roentgenol* 179:717–724, 2002.
- Fulcher AS, Turner MA, Capps GW, et al: Half-Fourier RARE MR cholangiopancreatography: experience in 300 subjects. *Radiology* 207:21–32, 1998.
- Fukukura Y, Fujiyoshi F, Sasaki M, et al: Pancreatic duct: morphologic evaluation with MR cholangiopancreatography after secretin stimulation. *Radiology* 222:674–680, 2002.
- Kostakoglu L, Agress H, Jr, Goldsmith SJ: Clinical role of FDG-PET in evaluation of cancer patients. *Radiographics* 23:315–340, 2003.
- Bares R, Klever P, Hauptmann S, et al: F-18 fluorodeoxyglucose PET in vivo evaluation of pancreatic glucose metabolism for detection of pancreatic cancer. *Radiology* 192:79–86, 1994.
- Ichikawa T, Sou H, Araki T, et al: Ductpenetrating sign at MRCP: usefulness for differentiating inflammatory pancreatic mass from pancreatic carcinomas. *Radiology* 221:107–116, 2001.

- 20. Wakabayashi T, Kawaura Y, Satomura Y, et al: Clinical and imaging features of autoimmune pancreatitis with focal pancreatic swelling or mass formation: comparison with so-called tumor-forming pancreatitis and pancreatic carcinoma. Am J Gastroenterol 98:2679–2687, 2003.
- Noone TC, Hosey J, Firat Z, et al: Imaging and localization of islet-cell tumours of the pancreas on CT and MRI. *Best Pract Res Clin Endocrinol Metab* 19:195–211, 2005.
- Rockall AG, Reznek RH: Imaging of neuroendocrine tumours (CT/MR/US). Best Pract Res Clin Endocrinol Metab 21:43–68, 2007.
- Kaltsas G, Rockall A, Papadogias D, et al: Recent advances in radiological and radionuclide imaging and therapy of neuroendocrine tumours. *Eur J Endocrinol* 151:15–27, 2004.
- 24. Law CH, Wei AC, Hanna SS, et al: Pancreatic resection for metastatic renal cell carcinoma: presentation, treatment, and outcome. *Ann Surg Oncol* 10:922–926, 2003.
- Ghavamian R, Klein KA, Stephens DH, et al: Renal cell carcinoma metastatic to the pancreas: clinical and radiological features. *Mayo Clin Proc* 75:581–585, 2000.
- Nayer H, Weir EG, Sheth S, et al: Primary pancreatic lymphomas: a cytopathologic analysis of a rare malignancy. *Cancer* 102:315–321, 2004.
- 27. Saif MW: Primary pancreatic lymphomas. *JOP* 7:262–273, 2006.
- Psatha EA, Hyslop WB, Woosley JT, et al: Immunoblastic large B-cell lymphoma of the peripancreatic head region: MR findings. *Magn Reson Imaging* 22:1053–1057, 2004.
- Chiou YY, Chiang JH, Hwang JI, et al: Acinar cell carcinoma of the pancreas: clinical and computed tomography manifestations. J Comput Assist Tomogr 28:180–186, 2004.
- Tatli S, Mortele KJ, Levy AD, et al: CT and MRI features of pure acinar cell carcinoma of the pancreas in adults. *AJR Am J Roentgenol* 184: 511–519, 2005.

# **Cystic Lesions of the Pancreas**

ONOFRIO CATALANO | MELISSA PRICE | DUSHYANT V. SAHANI

# Etiology

47

Cystic lesions of the pancreas encompass a wide spectrum of different pathologic entities, ranging from developmental, to inflammatory, to neoplastic cysts. Neoplastic cystic lesions, which are the most important, owing to their profound impact on patient prognosis and the frequent necessity of surgical treatment, are described in detail in this chapter.

Although every pancreatic tumor may undergo central necrosis and manifests predominantly cystic, the term *cystic neoplasm* properly refers to a cyst lined by a neoplastic epithelium, which identifies the tumor as a serous cystic neoplasm (SCN), mucinous cystic neoplasm (MCN), and intraductal papillary mucinous neoplasms (IPMNs). These lesions account for more than 90% of the whole spectrum of cystic neoplasms. The remaining 10% are represented by neoplasms undergoing cystic degeneration, such as solid and pseudopapillary epithelial neoplasms (SPENs), cystic pancreatic endocrine neoplasms (CPENs), acinar cell cystoadenocarcinomas, cystic metastases, and few other even rarer tumors.<sup>1,2</sup>

# Prevalence and Epidemiology

Owing to the increased awareness, improved diagnostic imaging technology, and intensive use of diagnostic imaging, neoplastic cystic lesions of the pancreas have been increasingly diagnosed recently, often at smaller size than in the past and in asymptomatic patients. Therefore, their actual prevalence and size at presentation are not accurately reflected in the literature.

# **Clinical Presentation**

Most neoplastic pancreatic cysts are infrequently associated with any symptomatology, and several are incidentally discovered during imaging for an unrelated medical problem. However, few patients present with symptoms related to mass effect, such as abdominal pain, early satiety, vomiting, and jaundice or with symptoms secondary to obstruction or communication with the pancreatic duct, such as recurrent pancreatitis. Moreover, advanced cystic malignancies may manifest as pain, weight loss, and jaundice and be clinically indistinguishable from pancreatic adenocarcinoma.<sup>1-4</sup>

# Pathophysiology

Although lesions can occur in every portion of the pancreas, some histiotypes tend to have a predilection for specific regions of the organ.

# **Pathology**

Pathologic findings vary greatly, according to the specific type of cystic lesion.

# Imaging

The most commonly encountered neoplastic cystic lesions of the pancreas are represented by SCNs, MCNs, intraductal papillary neoplasms, SPENs, and CPENs.<sup>1-4</sup>

# COMPUTED TOMOGRAPHY

Because of the widespread availability of multidetector computed tomography (MDCT), its capability to image the whole abdomen and pelvis in a single breath-hold, the superb spatial and temporal resolutions, the nearly isotropic voxels obtainable with the current technology, and the robustness to breathing artifact, it is considered the mainstay of diagnostic imaging to assess patients with suspected pancreatic lesions. Moreover, aesthetically pleasing and clinically useful multiplanar reformatted images, including three-dimensional (3D) and angiographic reconstructions of the MDCT data and MDCT-pancreatographic images, facilitate accurate preoperative staging.<sup>1-5</sup>

# MAGNETIC RESONANCE IMAGING

Although many of the new magnetic resonance imaging (MRI) sequences allow faster imaging acquisition, some factors continue to limit its use as a first-line diagnostic tool for imaging of the pancreas. These factors are mainly related to the need for patient cooperation to reduce motion and breathing artifacts, which can severely degrade and compromise the quality of the examination, the reduced availability of the technique, and inherent costs. MRI may be the preferable imaging modality in patients who are allergic to iodinated contrast agents or have renal insufficiency.

Because of an inherent high soft tissue contrast and resolution achieved with MRI, detection of subtle pancreatic lesions and evaluation of their internal details can be enhanced. Similar to CT, 3D contrast-enhanced dynamic MR angiography also can be performed to map the regional vascular anatomy to enable assessment of vascular involvement from the tumor. In addition, MR cholangiopancreatography (MRCP) allows excellent visualization of the entire extrahepatic biliary tract and the pancreatic duct. When MRCP is used in combination with a dynamic MR examination of the pancreas, comprehensive preoperative imaging can be accomplished to facilitate detection and preoperative staging of the pancreatic malignancy.<sup>1-6</sup>

### **ULTRASONOGRAPHY**

Transabdominal ultrasonography is highly operator dependent, nonreproducible, and limited by abdominal gas and patient body habitus. Endoscopic ultrasonography (EUS), on the other hand, provides high-resolution images of the pancreas and detailed assessment of cyst morphology. Moreover, EUS allows both aspiration of cystic fluid and sampling of cyst wall or mural nodules. Cystic fluid analysis can provide relevant insights into the nature of the cyst. Extracellular mucin or high viscosity usually favor mucinous neoplasms, whereas high amylase concentration, indicating a communication with the pancreatic duct, can be observed both in pseudocysts and in IPMNs, with very high levels usually found in the case of pseudocysts. Moreover, tumor markers in the cystic fluid can render the diagnosis of malignancy feasible in selected cases.<sup>1-5</sup>

# NUCLEAR MEDICINE

Nuclear medicine plays a role only in the case of functional endocrine tumors, whereby the use of a specific radiopharmaceutical can allow the diagnosis to be undertaken.

# POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

The role of positron emission tomography with computed tomography (PET/CT) in the evaluation of cystic lesions of the pancreas is still under investigation. Usually, PET/CT is used as an additional imaging functional test to help differentiate benign from malignant neoplasms. In some studies it demonstrated a diagnostic accuracy as high as 83%, but larger studies are needed.<sup>7</sup>

# **IMAGING ALGORITHM**

The most used diagnostic imaging technique for cystic neoplasms of the pancreas are MDCT and MRI/MRCP, which provide high spatial and contrast resolution images and allow dynamic acquisition and postprocessing image reconstruction. Cyst morphology, relationships with the pancreatic duct, and ancillary findings can be evaluated, providing clues for diagnosis, management planning, and preoperative strategy.

MDCT and MRI have been demonstrated to be equally accurate in establishing the diagnosis of malignancy and characterizing pancreatic cystic lesions.

Through MRCP and MDCT images and reconstructions, the entire course of the main pancreatic duct (MPD) can be displayed and its relationships with the cystic lesion can be evaluated. If the patient is considered a surgical candidate, multiplanar image reconstructions displaying the extent of cystic lesions and their anatomic relationships to surrounding structures can be useful.

For selected cases, when MRCP and MDCT pancreatograms have been unable to provide the required information regarding cystic lesion relationships with the MPD, invasive endoscopic retrograde cholangiopancreatography (ERCP) and/or EUS can be performed. The role of PET/CT is still under investigation.<sup>1-6</sup> An ideal algorithm is shown in Figure 47-1; see also

Table 47-1.

The different types of cystic lesions of the pancreas are described in the corresponding sections; the most important features are shown in Table 47-2.

#### What the Referring Physician Needs to Know: Pancreatic Cystic Lesions

- Cysts may be difficult to differentiate on morphology alone.
- Most important answers to be asked in the approach to cystic lesions in the pancreas are differentiation of:
  - True cyst versus pseudocyst
  - Mucinous versus nonmucinous
  - Benign versus malignant lesions

# **Specific Lesions**

# SEROUS CYSTIC NEOPLASMS

# Etiology

Biallelic inactivation of the von Hippel-Lindau (*VHL*) gene has been reported both for the sporadic and the VHL-associated form of SCNs.<sup>1</sup>

### Prevalence and Epidemiology

SCNs, which account for 30% to 39% of all pancreatic cystic neoplasms, are slowly growing, benign lesions with a very low malignant potential. They occur predominantly in women (75%), and patient mean age at presentation is 62 years.<sup>1-5</sup>

#### Clinical Presentation

They are usually incidentally discovered, unless large enough to be responsible for compression of the surrounding organs.<sup>1-5</sup>

# Pathophysiology

SCNs are usually discovered in the head (42%) or body/tail (48%), less often in the proximal body (7%), or diffusely through the pancreas (3%).<sup>1-5</sup>

# Pathology

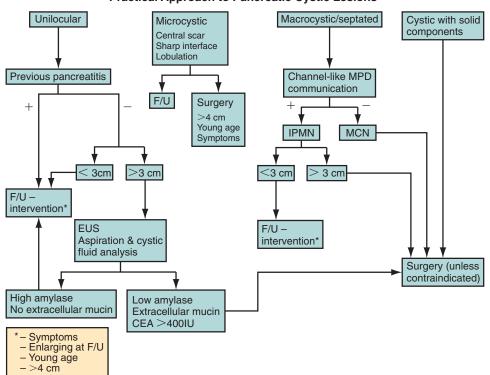
At gross pathologic examination, SCNs manifest as large (average diameter, 2 to 11 cm), well-circumscribed, lobulated cystic masses that lack a capsule or a definite wall. SCNs do not communicate with the pancreatic duct and are devoid of peripheral wall calcifications. Cystic fluid is watery, without mucin.

SCNs are usually microcystic and, less commonly (10%), macrocystic or oligocystic. The classic microcystic SCNs have a "sponge-like" or "honeycomb"-like morphology, characterized by innumerable small cysts of a few millimeters in size. Larger cysts, if present, are less than 2 cm in diameter and peripheral. Microcystic SCNs tend to exhibit a central stellate fibrous scar, a feature considered specific for SCNs; they can manifest as stellate calcifications in about 30% of cases. Macrocystic SCNs are composed of a countable number of larger cysts, between 2 and 7 cm, or even by a single large cyst and usually affect a younger population.

On histopathologic examination, SCNs are lined by a monomorphic epithelium, made up of cuboidal or flat cells, rich in glycogen, that stain with periodic acid–Schiff.<sup>1-5,8,9</sup>

## Imaging

SCNs are usually asymptomatic and incidentally discovered. Less often, in the case of large lesions, they may come to clinical attention because of mass-effect symptoms.<sup>1-5,8,9</sup>



**Practical Approach to Pancreatic Cystic Lesions** 

Figure 47-1 Practical approach to diagnosis of cystic lesions in the pancreas. CEA, Carcinoembryonic antigen; EUS, endoscopic ultrasonography; F/U, follow-up; IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm; MPD, main pancreatic duct.

47-1 Accuracy	, Limitations, and Pitfalls of the Modali	ties Used in Imaging of	Pancreatic Cysts
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive Nonspecific	Unable to directly visualize soft tissue masses in the pancreas.
СТ	<ul> <li>80% malignant from benign lesions</li> <li>100% SCN from MCN</li> <li>90% SCN from IPMN</li> <li>69.8%-81.1% IPMN from other lesions</li> <li>56%-94.5% malignant MCN from benign lesions</li> <li>43% in diagnosing histotype</li> </ul>	Radiation exposure	20% of SCNs, usually when <3 cm, may appear solid on CT. Characterization of small cysts may be difficult. Small mural nodules not easy to be appreciated. Difficulty in discriminating between carcinoma in situ and borderline or benign lesions.
MRI	Similar to CT, but in the case of IPMN higher accuracy than CT in differentiating IPMN from other lesions (86.8%-94.3%) More accurate than CT in evaluation of septa, small mural nodules, and duct communications	Patient cooperation High cost	Calcifications not well visualized. Tumor can masquerade as nodule.
Ultrasonography	Not assessed	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	SCN may manifest as solid lesions in the case of "honeycomb" pattern. In IPMN, communication with main pancreatic duct difficult to appreciate.
Nuclear medicine	No utility unless functional PEN	Poor spatial resolution	
PET/CT	83% in diagnosing malignancy Morphologic plus functional information Data limited; larger studies needed	Radiation exposure High cost	Difficult differentiation of benign from borderline neoplasms.

CT, Computed tomography; IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm; MRI, magnetic resonance imaging; PEN, pancreatic endocrine neoplasm; PET, positron emission tomography; SCN, serous cystic neoplasm.

TABLE Clinical	and Radiologic Fea	atures of Cystic N	Clinical and Radiologic Features of Cystic Neoplasms in the Pancreas	las			
Factor	SCN	MCN	IPMN	SPEN	PEN	Pseudocysts	Cystic Adenocarcinoma
Sex	F > M	ш	M > F	ш	F=M	M > F	M > F
Age*	6th-7th decades	4th-5th decades	6th-7th decades	2nd-3rd decades	5th-6th decades	4th-6th decades	5th-7th decades
Location	Head/body/tail	Tail/body	Head/uncinate	Body/tail	No predilection	Head/tail/body	Head > body/tail
Shape and borders	Lobulated	Oval	Grape-like (branch) Focal or diffuse main pancreatic duct dilatation (main type) Both (combined)	Oval	Oval	Oval	Oval/irregular
Cystic appearance	Microcystic dense stroma	Macrocystic	Macrocystic or cystic with solid component	Cystic with solid component	Cystic with solid component	Unilocular	Cystic with solid component Septa uncommon
Size*	5-11 cm	6-10 cm	1-4 cm (branch type) >5 mm (main type)	5-9 cm	2-10 cm	4-8 cm	4-9 cm
Main pancreatic duct	Normal or rarely compressed	Normal or rarely compressed	Dilated	Normal	Normal	Normal (acute pancreatitis) Dilated (chronic pancreatitis)	Obstructed Upstream dilatation
Calcification	Central stellate in 30%	Peripheral/ septal	Intraductal (or in the case of mucin plug calcification)	Peripheral, nonlaminated	Sometimes	Parenchymal (chronic pancreatitis)	No
Signal intensity	T1 low T2 high	T1 high/low T2 high	T1 low/high T2 high	T1 high T2 high	T1 high/low T2 high	T1 low T2 high	T1 low T2 high
Wall	Occasionally thick	Uniformly thick, variable enhancement		Thick, variable enhancement	Thick, strongly enhancing	Thin, occasionally thick	Thick, variable enhancement
Solid components	No Small (<3 cm) may appear solid	If malignant	lf malignant	Yes	Yes	No	Yes
Clinical history	Noncontributory	Noncontributory	Noncontributory	Noncontributory	± Endocrine syndromes	Pancreatitis	Weight loss Back and abdominal pain Jaundice (head)
*Due to increased · F, Female; IPMN, ir	diagnostic imaging use	e and improved techr icinous neoplasm; <i>M</i> ,	*Due to increased diagnostic imaging use and improved technology, lesions are currently discovered at a younger age and at a smaller size than reported in the literature. F, Female; IPMIN, intraductal papillary mucinous neoplasm; M, male; MCN, mucinous cystic neoplasm; PEN, pancreatic endocrine neoplasm; SCN, serous cystic neoplasm;	discovered at a youn; c neoplasm; PEN, par	ger age and at a sma icreatic endocrine ne	aller size than reported soplasm; SCN, serous	*Due to increased diagnostic imaging use and improved technology, lesions are currently discovered at a younger age and at a smaller size than reported in the literature. F, Female; IPMN, intraductal papillary mucinous neoplasm; M, male; MCN, mucinous cystic neoplasm; PEN, pancreatic endocrine neoplasm; SCN, serous cystic neoplasm; SPEN, solid

Female; IPMN, intraductal papillary mucinous neoplasm; M, male; MCN, mucinous cystic neoplasm; PEŇ, pančreatič endocrine neoplasm; SCN, serous cystic neoplasm; SPEN, solid and pseudopapillary endocrine neoplasm.

**Computed Tomography.** On both MDCT and MRI, the appearance of SCNs is similar to that of gross pathologic findings. Fine external lobulations and a central fibrous scar (Figure 47-2), with a stellate pattern of calcification (Figure 47-3), are suggestive. Enhancement of septa, cyst wall, and the central fibrous scar is best appreciated in the portal and delayed phases of contrast enhancement, respectively. The MPD is normal unless compressed by a large SCN.

On MDCT, 20% of SCNs, as a result of a honeycombed microcystic composition, appear as well-defined, "spongy," soft tissue or mixed density lesions, sharply demarcated from the adjacent structures and difficult to differentiate from a solid pancreatic mass on MDCT.<sup>1-5,8,9</sup>

**Magnetic Resonance Imaging.** The features of SCNs on MRI are very similar to those on MDCT. The main differences are in better detection of calcification on MDCT and improved visualization of cyst internal architecture and contrast enhancement with MRI. In the case of SCNs appearing solid on MDCT, MRI may provide useful insights into the microcystic nature of the lesions, revealing numerous discrete hyperintense cysts with bright signal on T2-weighted sequences and allowing the correct diagnosis to be undertaken (Figure 47-4).<sup>1-5,8,9</sup>

**Ultrasonography.** On transabdominal ultrasonography, owing to the innumerable acoustic interfaces of microcystic SCNs, they can manifest as hyperechoic, lobulated, sharply demarcated



**Figure 47-2** Typical presentation of a serous cystic neoplasm in an axial contrast-enhanced multidetector computed tomography image as a lobulated, microcystic lesion, with a central scar (*arrow*) and radiating septa.

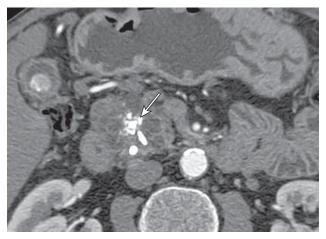
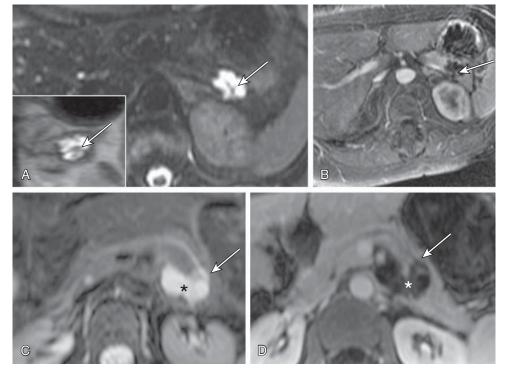


Figure 47-3 Axial multidetector computed tomography image shows the typical serous cystic neoplasm with central stellate calcifications (arrow).

Figure 47-4 A, Axial fat-suppressed T2-weighted magnetic resonance image demonstrates a typical serous cystic neoplasm (SCN) with external lobulations and a hypointense central scar (arrow). B, Note enhancement on postcontrast image. C and D, External lobulations of SCN may mimic branch duct intraductal papillary mucinous neoplasm (asterisk), which can be differentiated by communication with the main pancreatic duct (arrow) and lack of a central scar.



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47-3 Accuracy,	Limitations, and Pitfalls of the Modal	ities Used in Imaging of Serous (	Cystic Neoplasms
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive Nonspecific	Unable to directly visualize soft tissue masses in the pancreas.
СТ	100% SCN from MCN 90% SCN from IPMN	Radiation exposure	20% of SCNs, usually when <3 cm, may appear solid on CT. Characterization of small cysts may be difficult. Thin septa not easily appreciated.
MRI	Although data not available to specify accuracy, no relevant differences are expected between MRI and MDCT.	Patient cooperation High cost	Calcifications not well visualized.
Ultrasonography	Data not available to specify accuracy.	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	SCN may present as solid lesions in the case of "honeycomb pattern."
Nuclear medicine	Data not available to specify accuracy; no current role in diagnosis.	Poor spatial resolution	
PET/CT	Data not available to specify accuracy.	Radiation exposure High cost	

CT, Computed tomography; MCN, mucinous cystic neoplasm; MDCT, multidetector computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; SCN, serous cystic neoplasm.

masses, lacking posterior acoustic enhancement. In the case of macrocystic and oligocystic SCNs, internal septa are visualized.

EUS, which can resolve the fine details of the internal structure of SCNs, is particularly useful in uncertain cases.<sup>1-5,8</sup>

Positron Emission Tomography With Computed Tomogra**phy.** Although there is no currently established role for PET/

CT in the characterization of SCNs, based on our experience these lesions do not take up fluorodeoxyglucose (FDG).

Imaging Algorithm. An imaging algorithm is provided in Figure 47-1; see also Table 47-3.

#### **Classic Signs: Serous Cystic Neoplasms**

- External lobulations
- More than six loculations, each less than 2 cm
- Central scar, with/without stellate calcifications
- Absence of communication with the MPD

# Differential Diagnosis

Clinical data usually are not helpful in discriminating SCNs from other cystic neoplasms of the pancreas. Lobulations, microcysts, and a central scar are present in the classic form of SCN and suggest the diagnosis.

Macrocystic SCNs are usually difficult to differentiate from mucinous cystic tumors, with which they share many morphologic features. However, external lobulations or a central scar support the diagnosis of SCN (Table 47-4 and Figure 47-5).

More than six loculations, a loculation diameter less than 2 cm, a central scar, and absence of channel-like communication with the MPD are useful to differentiate SCNs from branch duct IPMNs (Table 47-5).1-5

# Treatment

Surgical Treatment. SCNs are usually regarded as benign, slowly growing lesions, with an estimated growth of 4 to 12 mm

#### **Differential Features Between Macrocystic** TABLE Serous Cystic Neoplasm and Mucinous 47-4 **Cystic Neoplasm**

	•	
Feature	Macrocystic SCN	MCN
Sex	Female/male (75%/25%)	Female almost exclusively
Age	6th-7th decades	4th-5th decades
Location	Head/body/tail	Body/tail 85%
Shape	Lobulated	Oval
Wall	Absent	Present, usually thick
Number of loculations	>6	<6
Coexisting microcysts (<2 cm)	Present	Absent
Central scar	May be found	Absent
Calcifications	Central if present	Peripheral

MCN, Mucinous cystic neoplasm; SCN, serous cystic neoplasm.

#### **Differential Features Between Serous Cystic** TABLE **Neoplasm and Branch Duct Intraductal** 47-5 **Papillary Mucinous Neoplasm**

Feature	SCN	BD-IPMN
Sex Age Morphology	F/M (75%/25%) 6th-7th decades Lobulated	M > F (60%/40%) 6th-7th decades Uncommonly
Morphology	Lobulated	lobulated
Scar	Central	Absent
Loculations	Smaller	Larger
Main pancreatic duct communication	No	Present

BD-IPMN, Branch duct intraductal papillary mucinous neoplasm; F, female; M, male; SCN, serous cystic neoplasm.

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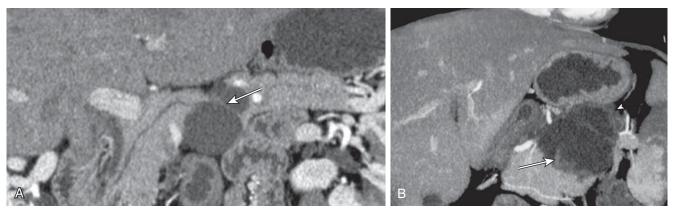


Figure 47-5 Curved reformatted multidetector computed tomography image (A) shows an oligocystic/macrocystic serous cystic neoplasm with characteristic features of external lobulations and central scar (*arrow*) that needs to be differentiated from mucinous cystic neoplasm (B), which lacks external lobulation and shows thick septa (*arrow*) and wall (*arrowhead*).

per year. The decision to operate is often based on size at presentation, patient age, clinical presentation, and location. In younger patients, owing to the increase in size over time, lesions larger than 4 cm are usually resected. In other cases the cysts should be observed with imaging at 6-month intervals for the first year, then annually for a period of 3 years. If the cyst remains stable and the patient is symptom free, no further workup may be needed.<sup>1-5,8,9</sup>

# What the Referring Physician Needs to Know: Serous Cystic Neoplasms

- SCNs are regarded as benign lesions, usually occurring in asymptomatic middle-aged women.
- They may grow over time; therefore, if detected in young patients with a size at presentation of 4 cm or greater, surgery is advocated; in other cases they should be observed by periodic imaging.
- MRI is the most accurate noninvasive diagnostic modality for SCNs.
- Macrocysts are difficult to characterize with imaging; therefore, if lobulations or a central scar is not detected, these patients should undergo EUS and/or biopsy.

#### Key Points: Serous Cystic Lesions

- Benign
- Microcysts
- Lobulations
- Central scar with or without calcification
- Absence of solid components
- No communication with MPD

# MUCINOUS CYSTIC NEOPLASMS

#### Etiology

Closeness of the left primordial gonad to the dorsal pancreatic anlage during the early stages of development, with the possibility that ovarian stroma can be incorporated into the developing pancreatic bud, has been suggested to play a role in the cause of MCNs in the pancreas. This observation could explain the female occurrence and predilection for the tail and body of the pancreas.<sup>1</sup>

# Prevalence and Epidemiology

MCNs account for 10% to 45% of the cystic neoplasms of the pancreas and encompass a spectrum ranging from adenomas to invasive adenocarcinomas. They occur almost exclusively in middle-aged women (mean age, 47 years), with only extremely rare cases reported in men.<sup>1,10</sup>

#### **Clinical Presentation**

MCNs can be diagnosed incidentally in the case of small lesions, or, in the case of larger lesions, they may be responsible for mass-effect symptoms. In the setting of malignant MCNs, jaundice, weight loss, and abdominal pain may be present.<sup>1,10</sup>

# Pathophysiology

MCNs are usually diagnosed in the tail (72%) or body (13%) of the pancreas, and less frequently they replace the organ (9%) or are located in the pancreatic head (6%).<sup>1,2,11-13</sup>

#### Pathology

On gross pathologic examination, MCNs manifest as large (average diameter, 6 to 10 cm), round or oval cystic masses surrounded by a fibrous pseudocapsule, which may contain calcifications. Typically, they are multilocular and macrocystic and occasionally unilocular. Cystic fluid is thick and rich in mucin; hemorrhage may be present. They do not communicate with the pancreatic duct.

Benign MCNs have a smooth internal surface; malignant MCNs contain mural nodules, solid components, and/or papillary projections. Invasive adenocarcinomas are found in 33% of the cases.

On histologic examination, the wall of MCNs contains an ovarian-like stroma that is considered specific for the diagnosis. The epithelial lining exhibits mucin-producing features and may display different degrees of dysplasia, according to which lesions are classified as adenomas, borderline tumors, or carcinomas.<sup>1,2,13</sup>

## Imaging

MCNs are usually asymptomatic and incidentally discovered. Less often, in the case of large lesions or malignant invasive neoplasms, they may come to clinical attention because of mass-effect symptoms or signs and symptoms of pancreatic malignancy.<sup>1,2,12,13</sup> **Computed Tomography.** The complex architecture of the cysts is well depicted on both MDCT and MRI. MCNs manifest as multilocular (fewer than six loculations) macrocystic lesions, with individual compartments larger than 2 cm (Figure 47-6). Hemorrhage and/or debris is uncommonly present. Infrequently, MCNs may manifest as unilocular (Figure 47-7). MCNs do not communicate with the pancreatic duct. Cystic fluid appears hypodense.

Peripheral eggshell or septal calcifications are an infrequent but specific finding for MCNs and are predictive of malignancy.

Findings of wall thickening (see Figure 47-7) or irregularity, mural nodules, papillary projections, and peripheral calcification suggest malignancy.<sup>2,10,11,13-16</sup>

**Magnetic Resonance Imaging.** MRI, by virtue of superior soft tissue and contrast resolution, may better display the internal characteristics of MCN, including thin septa and mural nodules, if present, and their enhancement after administration of gadolinium.

The cystic fluid, owing to the high mucin content, appears hyperintense on T2-weighted sequences and hypointense to minimally hyperintense on T1-weighted sequences. Because of different mucin concentration, it is not unusual to observe differences in signal intensity among the different loculations (Figure 47-8). MRCP is particularly important to rule out communications with the MPD (Table 47-6). Careful scrutiny of 3D MRCP raw data and of thin-section 2D MRCP is required.<sup>2,10,11,13-16</sup>

**Ultrasonography.** At transabdominal ultrasonography, MCNs tend to manifest as round or oval, well-defined, multilocular cystic masses, circumscribed by a wall. The cystic components exhibit a variable degree of hypoechogenicity and through-transmission.

EUS is particularly useful to assess the internal architecture of the lesion, to rule out communications with the pancreatic duct, and to obtain fluid and tissue samplings for subsequent analysis. High extracellular levels of mucin and low amylase levels support the diagnosis of MCNs; a high carcinoembryonic antigen value and a high CA 19-9 are suggestive of malignant behavior.<sup>1,2,15</sup>

**Positron Emission Tomography With Computed Tomography.** Despite the limited data currently available on the role of PET/CT in MCNs, it appears that whereas FDG uptake strongly favors malignancy in cystic lesions, absence of uptake might suggest a benign tumor.

**Imaging Algorithm.** An imaging algorithm is provided in Figure 47-1; see also Table 47-7.

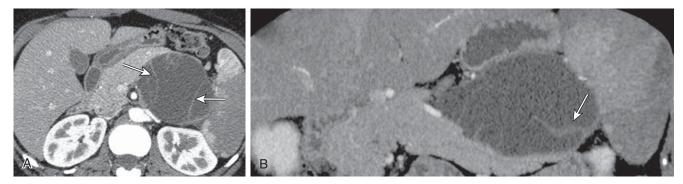


Figure 47-6 Axial (A) and curved reconstructed (B) multidetector images show a typical mucinous cystic neoplasm as a nonlobulated, oval cystic lesion (>2 cm) with enhancing internal septa (arrows). Note the lack of central scar.

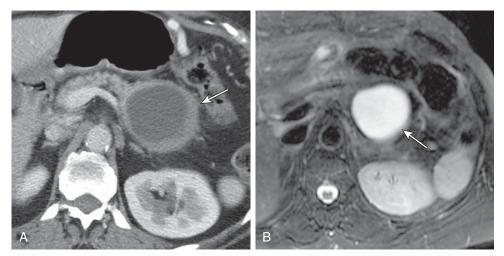


Figure 47-7 Axial multidetector computed tomography (A) and corresponding T2-weighted magnetic resonance image (B) show a thick fibrous wall (*arrows*) that is typical of unilocular mucinous cystic neoplasm.



Figure 47-8 Axial T1-weighted (A) and axial (B) and coronal (C) T2-weighted magnetic resonance images show the typical mucinous cystic neoplasm with internal septations (arrows) that are better appreciated on the T2-weighted images.

# TABLEDifferential Features: Mucinous Cystic Neoplasm, Branch Duct Intraductal Papillary Mucinous Neoplasia,<br/>and Pseudocysts

Feature	MCN	BD-IPMN	Pseudocysts
Sex	Female almost exclusively	M > F (60%/40%)	M > F (68%-78%/32%-22%)
Location	Body/tail only	Head > body/tail	No preferences
Epicenter	Intra/extraparenchymal	Intraparenchymal	Extraparenchymal
Serum amylase	Normal	Normal	Elevated/normal
Loculations	Multilocular, less often oligolocular or unilocular	Multilocular, less often oligolocular or unilocular	Unilocular
Wall	Thick	Nondetectable	Detectable, can be thick in long-lasting cases
Main pancreatic duct communication	Absent	Present Channel-like configuration	Present but rarely seen on imaging Direct opening on pancreatic duct
Cystic fluid content	Mucin	Mucin	Hemorrhagic debris
Parenchyma	Normal	Normal	Often inflammatory changes, calcifications
History of pancreatitis	Negative/uncommon	Negative/uncommon	Positive

BD-IPMN, Branch duct intraductal papillary mucinous neoplasm; F, male; M, male; MCN, mucinous cystic neoplasm.

# TABLE 47-7 Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Mucinous Cystic Neoplasms of the Pancreas

Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive Nonspecific	Unable to directly visualize soft tissue masses in the pancreas.
СТ	100% SCN from MCN 56%-94.5% malignant MCN from benign lesions	Radiation exposure	Characterization of small cysts may be difficult. Thin septa not easy to be appreciated.
MRI	Although data not available to specify accuracy, no relevant differences are expected between MRI and MDCT.	Patient cooperation High cost	Calcifications not well visualized. Tumor can masquerade as nodule.
Ultrasonography	Data not available to specify accuracy.	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	Difficult to rule out communication with main pancreatic duct.
Nuclear medicine	Data not available to specify accuracy; no current role in diagnosis.	Poor spatial resolution	
PET/CT	Data limited; larger studies are needed to specify accuracy. Morphologic plus functional information.	Radiation exposure High cost	Difficult differentiation of benign from borderline neoplasms.

CT, Computed tomography; MCN, mucinous cystic neoplasm; MDCT, multidetector computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; SCN, serous cystic neoplasm.

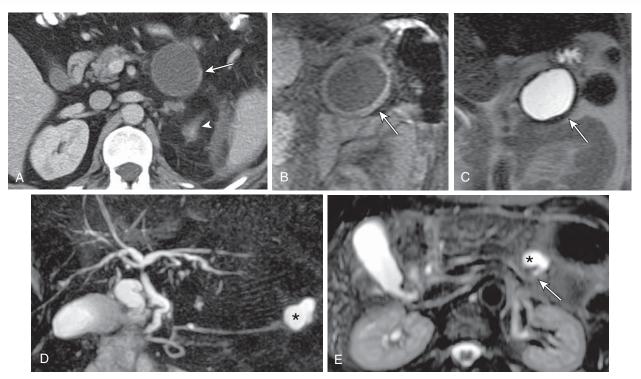


Figure 47-9 A, Axial multidetector computed tomography image demonstrating a pseudocyst in the tail of the pancreas (*thin arrow*) that is predominantly extrapancreatic with adjacent inflammatory changes, indicated by *arrowhead*. These cystic lesions need to be differentiated from mucinous cystic neoplasm, which is an intrapancreatic lesion (*arrows*, B and C) with thick walls and internal septations. Another differential diagnosis for this would be a branch duct intraductal papillary mucinous neoplasm, which is seen as a cystic lesion (*asterisks*, D and E) communicating with the main pancreatic duct (*thin arrow*).

#### **Classic Signs: Mucinous Cystic Neoplasms**

- Oval lesions
- Identifiable wall
- Fewer than six loculations
- Loculations more than 2 cm in diameter
- No communication with the MPD

# **Differential Diagnosis**

The strong association with female sex and middle age at presentation help differentiate MCNs from SCNs and IPMNs. The presence of a capsule and peripheral calcifications and the absence of communication with the pancreatic duct are useful differential signs from IPMNs (see Table 47-5 and Figure 47-9).

Useful differentiating features include oval shape, capsule, and peripheral calcifications; absence of external lobulations; lack of a central scar; and less than six loculations, whose diameter is more than 2 cm (see Table 47-4). Absence of arterially enhancing rim or solid components is useful to exclude a CPEN. Absence of fluid/fluid levels and blood degradation products helps rule out SPEN.\*

#### Treatment

**Surgical Treatment.** Because of the malignant potential and relatively young age at presentation, surgery is advocated in all cases of MCNs, unless contraindicated for other reasons. Patients with MCNs without invasive features have excellent survival, and recurrence is rare.<sup>1,2,12-16</sup>

# What the Referring Physician Needs to Know: Mucinous Cystic Neoplasms

- MCNs occur almost exclusively in young middle-aged women (30 to 50 years).
- All MCNs have malignant potential.
- Solid components, thick septa, and cyst size greater than 5 cm are predictive of malignancy.
- Surgery is indicated because of the relatively good survival, even in the case of invasiveness.

#### Key Points: Mucinous Cystic Neoplasms

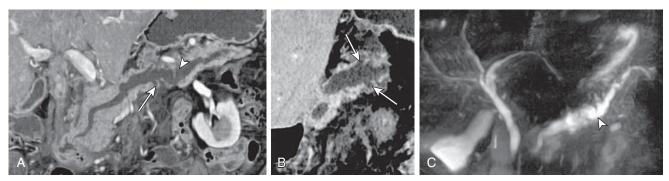
- Capsulated
- Oval
- Multilocular
- Macrocystic
- No communication with MPD
- Malignant behavior suggested by peripheral calcifications, mural nodularity, solid areas, papillary projections, and FDG uptake

# INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

#### Etiology

A large number of different genetic mutations have been reported in IPMNs, including inactivation of tumor suppressor genes, such as *TP53*, and activation of oncogenes, such as *KRAS*.

<sup>\*</sup>References 2, 10, 11, 13, 15, 16.



**Figure 47-10** Multidetector computed tomography (MDCT) pancreatogram (A), MDCT miniP (B), and corresponding two-dimensional magnetic resonance cholangiopancreatography image (C) demonstrate main duct intraductal papillary mucinous neoplasm seen as segmental involvement of the main pancreatic duct in the body and tail of the pancreas (*arrowheads*, A and C) with associated dilated side branches (*arrows*, A and B) and proportional parenchymal atrophy.

Probably a multistep process is involved in the progression from hyperplasia to the invasive carcinoma.<sup>1</sup>

# Prevalence and Epidemiology

IPMNs account for 21% to 33% of all pancreatic cystic neoplasms. They more often affect men (60%), with a mean age at presentation of 65.5 years.

IPMNs are characterized by intraductal papillary growths of mucin-producing neoplastic cells. According to the site of involvement they are classified as main duct (MD) IPMNs, branch duct (BD) IPMNs, and combined IPMNs.<sup>1,2,15-17</sup>

# **Clinical Presentation**

MD-IPMNs are usually symptomatic owing to low-grade pancreatitis, caused by thick mucin occluding the pancreatic duct. Jaundice can be found in the case of malignancy. BD-IPMNs are usually asymptomatic and incidentally detected.<sup>1,2,15-17</sup>

# Pathophysiology

MD-IPMNs usually occur in the head (58%) or body (23%) of the pancreas. In 12% of the cases the pancreas is diffusely involved, and in 7% of the cases the tail is affected. The pancreatic head and the uncinate process are the most common locations (about 60%) for BD-IPMN.<sup>1,2,14-17</sup>

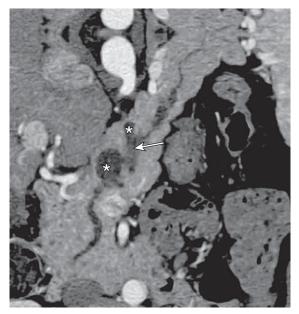
### Pathology

IPMNs tend to progress through an adenoma-carcinoma sequence and can exhibit a wide spectrum of biologic behaviors, ranging from hyperplasia to adenoma to carcinoma in situ to invasive carcinoma, which can coexist in the same patient.

MD-IPMNs usually produce thick mucin with resultant dilatation of the pancreatic duct, either focally or diffusely. In the case of long-standing processes, a low-grade obstruction with associated features of chronic pancreatitis also can result.

BD-IPMNs usually manifest as a single cyst or as grapelike communicating cysts, connected through a channel-like conduit to the pancreatic duct, which may be dilated. Cysts are in the range of 11 to 40 mm (median diameter, 20 mm); they are septated and contain fluid, mucin, and neoplastic cells.

Side-branch and MPD lesions often coexist as independent or combined lesions.  $^{\rm 1,2,15-22}$ 



**Figure 47-11** Multidetector computed tomography pancreatogram clearly shows multiple branch duct intraductal papillary mucinous neoplasms as cystic lesions (*asterisks*) in the pancreas, connected to the main pancreatic duct through-channel–like conduits (*arrow*).

#### Imaging

MD-IPMNs are usually symptomatic, owing to low-grade pancreatitis. BD-IPMNs are usually asymptomatic and incidentally detected.<sup>1,2,15-22</sup>

**Computed Tomography.** On MDCT, MD-IPMNs exhibit diffuse or segmental dilatation of the MPD, usually up to the papilla, absence of a transition point, and proportional atrophy of the parenchyma (Figure 47-10). The duodenal papilla may bulge. BD-IPMNs manifest as one or more lobulated and septated cystic lesions.

Channel-like communication with the pancreatic duct is a requisite for diagnosis, and it can be demonstrated through MDCT-pancreatographic reconstructions (Figure 47-11).

Some imaging features are strong predictors of malignancy, including MPD diameter exceeding 10 mm, nodules, and

invasiveness. Moderate predictors of malignancy are side branch IPMNs greater than 4 cm, thick septa, and irregular walls (Figure 47-12).<sup>1,2,15-23</sup>

**Magnetic Resonance Imaging.** MRI/MRCP in addition to providing the information obtainable through MDCT is characterized by a higher soft tissue and contrast resolution. Therefore, it is particularly useful to demonstrate septa, assess neoplastic mural nodules, and differentiate them from thick mucin or calcification. In fact, although they all manifest as areas of low signal intensity on T2-weighted MR images, only neoplastic mural nodules enhance after gadolinium administration (see Figures 47-12 and 47-13).

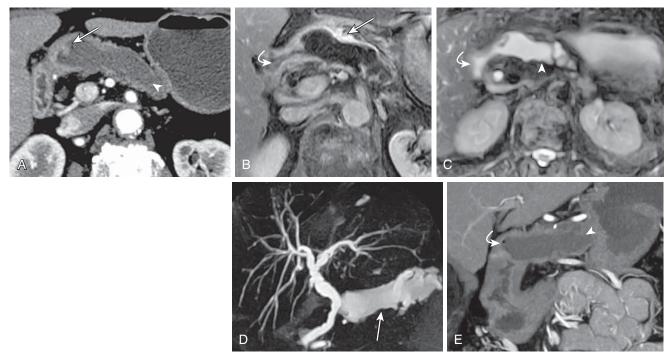
Both MRCP and ERCP can show fine internal details. ERCP, resulting from mucus plugging, may be unable to demonstrate a channel-like communication between a BD-IPMN and the

pancreatic duct (Figure 47-14). Therefore, MRCP is the preferred initial modality to evaluate IPMNs.<sup>1,2,6,14-24</sup>

**Ultrasonography.** Evaluation of BD-IPMNs and MD-IPMNs is usually inadequate on ultrasonography. Imaging differentiation of MD-IPMN from other causes of pancreatic duct dilatation, or BD-IPMN from other pancreatic cystic lesions, is usually difficult. Likewise, papillary projections and mural nodules are difficult to be appreciated.

In the case of large volumes of thick mucin, the pancreatic duct may appear echogenic and indistinguishable from surrounding parenchyma. Therefore, the dilatation of the pancreatic duct may go unrecognized.

In BD-IPMNs, owing to the marked hypoechogenicity of the lesions, their cystic nature is usually demonstrated. On the other hand, communication with MPD is difficult to be ascertained.<sup>15</sup>



**Figure 47-12** Axial contrast-enhanced multidetector computed tomography (MDCT) (A) and three-dimensional magnetic resonance cholangiopancreatography (D) show pancreas divisum with grossly dilated dorsal duct system (*arrowhead*) greater than 10 mm associated with predictors of malignancy such as enhancing mural nodules (*straight arrow*) (axial T1-weighted postcontrast image, B) and thick irregular walls. Also noted is a fistulous communication with the duodenum (*curved arrow*) better appreciated on T2-weighted image (C) and MDCT pancreatogram (E).

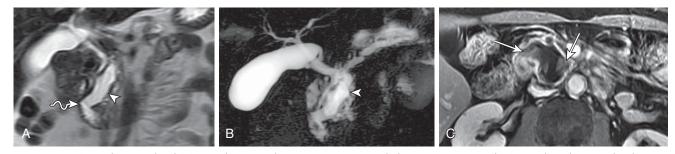


Figure 47-13 Coronal T2-weighted (A), two-dimensional magnetic resonance cholangiopancreatography (B), and axial T1-weighted contrastenhanced (C) images demonstrating main duct diameter greater than 10 mm (*arrowhead*) and solid enhancing components (*arrows*) where the major papilla bulges into duodenum (*wavy arrow*, A). Features are representative of malignant main duct intraductal papillary mucinous neoplasm.

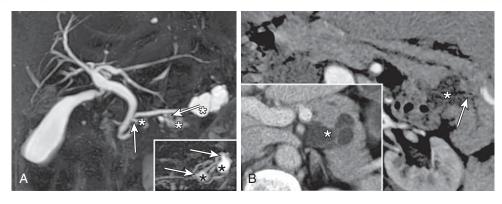


Figure 47-14 Three-dimensional magnetic resonance cholangiopancreatography (A) and reconstructed multidetector computed tomography (B) images show the typical branch duct intraductal papillary mucinous neoplasm (asterisks) as a cystic lesion with a channel-like communication with the main pancreatic duct (arrows). The communications are better appreciated on the reconstructed images seen in the inset.

	, Limitations, and Pitfalls of the Modalit Neoplasms	ies Used in Imaging of Intraduct	al Papillary
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive Nonspecific	Unable to directly visualize soft tissue masses in the pancreas.
СТ	90% SCN from IPMN 69.8%-81.1% IPMN from other lesions	Radiation exposure	Characterization of small cysts may be difficult. Thin septa and small mural nodules not easily appreciated. Difficulty in discriminating between carcinoma in situ and borderline and benign lesions.
MRI	Similar to CT, but in the case of IPMN higher accuracy than CT in differentiating IPMN from other lesions (86.8%-94.3%). More accurate than CT in evaluation of septa, small mural nodules, and duct communications.	Patient cooperation High cost	Calcifications not well visualized. Tumor can masquerade as nodule.
Ultrasonography	Data not available to specify accuracy	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	In IPMN, communication with main pancreatic duct difficult to appreciate.
Nuclear medicine	Data not available to specify accuracy; no current role in diagnosis.	Poor spatial resolution	
PET/CT	Morphologic plus functional information. Data limited; larger studies needed to specify accuracy.	Radiation exposure High cost	Difficult differentiation of benign from borderline neoplasms.

CT, Computed tomography; IPMN, intraductal papillary mucinous neoplasm; PET, positron emission tomography; SCN, serous cystic neoplasm.

Positron Emission Tomography With Computed Tomogra**phy.** The usefulness of PET/CT in the case of IPMNs has not been fully investigated at the present time. According to our experience, malignant IPMNs are more likely to exhibit FDG uptake than their benign counterpart, and this could play a role in management of the lesions in selected cases.

Imaging Algorithm. An imaging algorithm is provided in Figure 47-1; see also Table 47-8.

# **Differential Diagnosis**

In the case of BD-IPMNs, male sex is a useful differential feature from MCNs. In the case of BD-IPMNs, absence of clinically significant previous episodes of pancreatitis is useful to rule out postinflammatory pseudocysts. In MD-IPMNs, absence of

# Classic Signs: Intraductal Papillary Mucinous Neoplasms MD-IPMNs

- Segmental or diffuse dilatation of the pancreatic duct, without areas of stenosis
- Intraductal mural nodules
- Proportional parenchymal atrophy
- Side branch dilatation
- Bulging of duodenal papilla with diffuse IPMN or head/uncinate process IPMN
- BD-IPMNs
  - Grape-like cystic structure
  - Channel-like communication with the pancreatic duct
  - Intraparenchymal location, more often the head/ uncinate process

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alcohol consumption and of malabsorption may be contributing factors to rule out chronic pancreatitis.<sup>1,2,10-16,19-22,24</sup>

Absence of a transition point is a useful imaging criterion to rule out adenocarcinoma of the pancreas and to favor the diagnosis of an MD-IPMN. Absence of parenchymal calcifications and proportional atrophy of the parenchyma are suggestive findings of MD-IPMNs and are useful for the differential diagnosis with chronic pancreatitis (see Table 47-2).

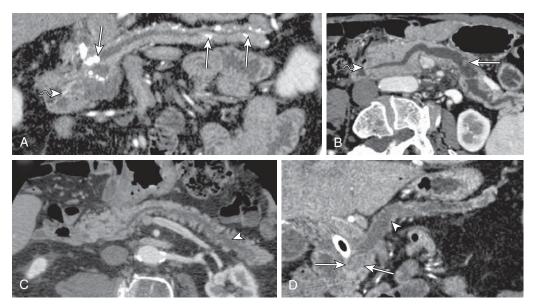
Demonstration of a communication with the pancreatic duct is the most important imaging feature used to differentiate BD-IPMNs from other cystic lesions of the pancreas, including MCNs and SCNs (see Tables 47-5, 47-6, and 47-9 and Figure 47-15).<sup>1,2,10-24</sup>

#### Treatment

**Surgical Treatment.** The management of MD-IPMNs and BD-IPMNs is very different owing to their diverse risk for malignant degeneration and the absence of symptoms in BD-IPMNs.

MD-IPMNs bear a high risk for malignancy (57% to 92%), and in 50% of cases they show invasive features. Despite this, their 5-year survival rate is excellent (80%). Therefore surgery is usually advocated.

BD-IPMNs have lower risks for malignancy: 6% to 46% in lesions less than 3 cm. Moreover, approximately 85% of BD-IPMNs, if devoid of mural nodules, remain stable over



**Figure 47-15** Multiple reformatted multidetector computed tomography images depicting the differential diagnosis for pancreatic duct (PD) dilatation. A, In chronic pancreatitis PD, dilatation is associated with parenchymal atrophy out of proportion to ductal dilatation, ductal calculi (*arrows*), and lack of papillary bulge (*wavy arrow*). In intraductal papillary mucinous neoplasm (IPMN), either diffuse (B) or segmental IPMN (C) PD dilatation manifests as proportional parenchymal atrophy without abrupt PD narrowing. Also in diffuse form, bulging papilla (*wavy arrow*, B) is seen. D, In adenocarcinoma, PD manifests as abrupt change in ductal diameter with a focal stenosis (*arrowhead*) and obstructing mass (*arrows*).

# TABLEDifferential Features: Chronic Pancreatitis, Main Duct Intraductal Papillary Mucinous Neoplasm,47-9Adenocarcinoma of the Pancreas

Feature	Chronic Pancreatitis	MD-IPMN	Adenocarcinoma
Sex	M > F (83%/17%)	M > F (60%/40%)	M > F (57%/43%)
Age	4th-7th decades	6th-7th decades	5th-7th decades
Location	Diffuse	Body/tail > head	Head > body/tail
Duct dilatation	Diffuse	Segmental: Smooth return to normal caliber Diffuse: Entire pancreatic duct until papilla	Dilatation upstream to the transition point
Obstructing mass/ focal stenosis	Absent	Absent If mass present: Small and nonobstructing	Present at site of transition
Intraductal lesions	Absent	Present	Absent
Papilla	Nonbulging	Bulging	Nonbulging
Calcifications	Parenchymal Ductal	Absent (unless coexistent chronic pancreatitis)	Absent
Parenchymal atrophy	Pronounced	Proportional	Mild, unless long lasting

F, Female; M, male; MD, main duct intraductal papillary mucinous neoplasm.

time. Therefore, in the absence of clinical symptoms and of clinical/radiologic signs of malignancy, BD-IPMNs should undergo close observation.

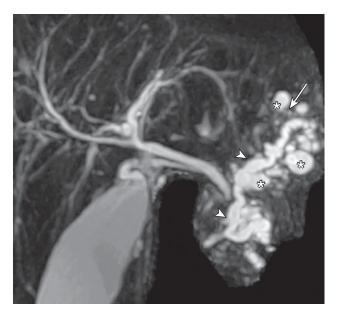
Combined-IPMNs are regarded and treated as MD-IPMNs (Figure 47-16).<sup>1-3,16,17</sup>

# What the Referring Physician Needs to Know: Intraductal Papillary Mucinous Neoplasms

- Because of the high risk for malignancy of MD-IPMNs, surgery is the treatment of choice.
- In the absence of signs of malignancy and of symptoms, BD-IPMNs can be closely observed.
- Combined IPMNs are treated as MD-IPMNs.

#### Key Points: Intraductal Papillary Mucinous Neoplasms

- MD-IPMNs
  - High risk for malignancy
  - Diffusely dilated pancreatic duct without an obstruction point
- BD-IPMNs
  - More benign behavior
  - Cystic lesions communicating with the MPD through a channel-like conduit
- Combined IPMNs
- Treated as MD-IPMNs
- Predictors of malignancy
- Main pancreatic duct diameter exceeding 9 mm, nodules, and invasiveness



**Figure 47-16** Three-dimensional magnetic resonance cholangiopancreatography displays a typical combined intraductal papillary mucinous neoplasm (IPMN) lesion as diffuse dilatation of the main duct (*arrowheads*) and multiple cystic lesions (*asterisks*) as a result of branch duct (BD)-IPMN. Note channel-like communications (*arrow*) between BD-IPMN and main pancreatic duct.

# SOLID AND PSEUDOPAPILLARY EPITHELIAL NEOPLASMS

# Etiology

Mutations in exon 3 of the beta-catenin gene have been found in almost all SPENs, probably interfering with the ubiquitinmediated degradation of beta-catenin proteins.<sup>1</sup>

# Prevalence and Epidemiology

SPENs account for 9% of the cystic neoplasms of the pancreas. They usually have low malignant potential but can be locally aggressive. Metastases, although uncommon, have been reported to the liver and regional lymph nodes. They affect more often nonwhite, young (mean age, 27 years) women (78%).<sup>1-3,25,26</sup>

#### **Clinical Presentation**

Abdominal pain/discomfort and other symptoms related to mass effect are often present.<sup>1-3,25,26</sup>

# Pathophysiology

SPENs usually manifest in the body or tail of the pancreas.<sup>1-3,25,26</sup>

#### Pathology

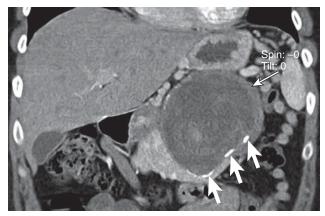
On gross pathologic examination, SPENs manifest as a large (mean diameter, 5 to 9 cm), well-circumscribed mass. At cut section, an admixture of solid, cystic, and papillary components, along with hemorrhagic and necrotic areas, is found. On histologic examination, pseudopapillary architecture is observed.<sup>1-2,25,26</sup>

# Imaging

SPENs are usually symptomatic owing to the large size they reach and the subsequent mass-effect symptoms.<sup>1-3,25,26</sup>

**Computed Tomography.** Because of the different proportion of solid and cystic areas in different tumors, the appearance of a SPEN greatly varies on MDCT from a solid mass to an almost cystic structure. The proportion of solid and cystic components dictates imaging features of SPENs on MDCT.

Peripheral calcifications, although present in a third of lesions on pathologic examination, are uncommonly seen on imaging (Figure 47-17).



**Figure 47-17** Reformatted multidetector computed tomography image showing a typical solid and pseudopapillary epithelial neoplasm (*thin arrow*) as large, ovoid, predominantly cystic lesions in the body and tail of the pancreas. They appear heterogeneous because of the presence of solid, cystic, and hemorrhagic components. The wall can be calcified (*thick arrows*) in up to a third of cases.

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Lesions are ill-defined if aggressive, and eventual liver metastases have morphology similar to that of the primary lesion.<sup>25-27</sup>

**Magnetic Resonance Imaging.** The MRI presentation of SPEN mirrors that observed on MDCT, although enhancement of solid components and internal hemorrhage are better seen. Hemorrhage, when present, can appear hyperintense on both T1- and T2-weighted sequences, and internal fluid/debris levels can be suggestive, although nonspecific, findings.<sup>25-27</sup>

**Positron Emission Tomography With Computed Tomography.** Because of the rarity of the disease and of relatively recent introduction of PET/CT in the clinical setting, the role of PET/ CT in the case of SPENs has not been fully elucidated. According to a few published case reports and our experience, SPENs may show significant uptake of FDG, independently of their biologic behavior.

**Imaging Algorithm.** An imaging algorithm is provided in Figure 47-1; see also Table 47-10.

#### **Classic Signs: Solid and Papillary Epithelial Neoplasms**

- Young women (<30 years)
- Body or tail of pancreas
- Large lesions
- Solid and cystic components

# **Differential Diagnosis**

Young age and female sex are suggestive of SPENs. Fluid/fluid levels and blood degradation products, although not invariably present, are typical of SPENs. CPENs, metastases, and adenocarcinomas of the pancreas enter in the differential diagnosis with SPENs (Figure 47-18 and Table 47-11).

# Treatment

**Medical Treatment.** Medical treatment is reserved for cases of advanced, metastatic SPENs.

**Surgical Treatment.** Because of the tendency of SPENs to infiltrate locally and metastasize distally, the young age at presentation, and a 5-year survival rate of 95%, surgical treatment is advocated in all cases of SPENs, even in the cases of metastatic disease.<sup>25,26</sup>

What the Referring Physician Needs to Know: Solid and Pseudopapillary Epithelial Neoplasms

- Young women (usually <30 years) are affected.
- Even in the case of metastatic or locally advanced disease, surgery is advocated.

#### Key Points: Solid and Pseudopapillary Epithelial Neoplasms

- Young women (usually younger than 30 years of age)
- Heterogeneous appearance
- Variable imaging appearance based on different proportion of solid and cystic areas
- Fluid/fluid levels when hemorrhagic
- Hemorrhagic products

### CYSTIC PANCREATIC ENDOCRINE NEOPLASM

# Etiology

Many different chromosomal losses have been reported in pancreatic endocrine neoplasms (PENs); some of them are associated with more aggressive biologic behavior. Usually larger PENs harbor more genetic alterations than smaller lesions.<sup>1</sup>

# TABLE Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Solid and Pseudopapillary 47-10 Epithelial Neoplasms

Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive Nonspecific	Unable to directly visualize soft tissue masses in the pancreas.
СТ	Data not available to specify accuracy.	Radiation exposure	Characterization of small cysts may be difficult. Thin septa and small mural nodules not easily appreciated.
MRI	Data not available to specify accuracy.	Patient cooperation High cost	Calcifications not well visualized. Tumor can masquerade as nodule.
Ultrasonography	Data not available to specify accuracy.	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	Small lesions may be undetected.
Nuclear medicine	Data not available to specify accuracy.	Poor spatial resolution	
PET/CT	Morphologic plus functional information. Data limited; larger studies needed to specify accuracy.	Radiation exposure High cost	Difficult differentiation of benign from borderline neoplasms.

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

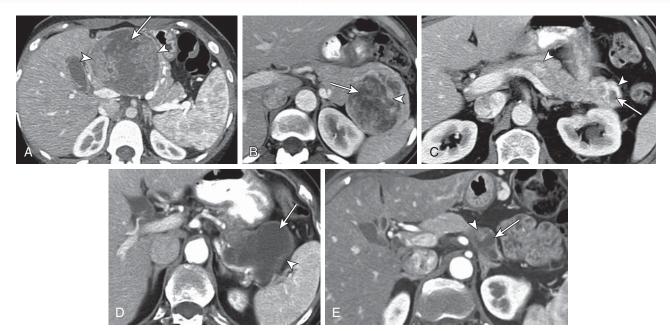


Figure 47-18 Differential diagnosis, axial contrast-enhanced images: solid and pseudopapillary epithelial neoplasm (A), cystic pancreatic endocrine neoplasm (B), cystic metastases (C), oncocytic adenocarcinoma (D), and cystic adenocarcinoma (E). These neoplasms can appear strikingly similar on diagnostic imaging, showing a mixture of cystic (arrows) and solid elements (arrowheads). Age, sex, clinical features, morphology, and pancreatic duct changes can be helpful to narrow the differential diagnosis. Usually, biopsy is necessary.

TABLE	Differential Features Among Solid and Pseudopapillary Endocrine Neoplasia, Pancreatic Endocrine
47-11	Neoplasm, Metastases, and Adenocarcinoma of the Pancreas

Featur	e	SPEN	PEN	Metastases (Kidney, Breast)	Adenocarcinoma
Sex		F > M (78%/22%)	M = F	M/F (33%-85%/67%-15%)	M > F (57%/43%)
Age		2nd-3rd decades	5th-6th decades	5th-7th decades	5th-7th decades
Morph	ology	Solid and cystic- necrotic areas	Rarely necrotic Septa can be present Thick rind	Rarely necrotic Thick rind	Solid, central necrosis may be present. If colloid, is predominantly cystic.
Main p chan	oancreatic duct Iges	Typically absent	Usually absent	Absent/mild prominence	Dilated until obstruction point.
Fluid c	ontent	Hemorrhagic debris (fluid/fluid level, high T1 weighted)	Necrotic	Necrotic	Necrotic
Contra	st enhancement	Moderate	Usually intense	Intense/moderate	Poor
Endoci abno	rine ormalities	Absent	Nonfunctional 70% Functional neoplasms 30%	Absent	Absent
	of previous gnancies	Negative	Negative/positive (MEN)	Positive	Negative

F, Female; M, male; MEN, multiple endocrine neoplasm; PEN, pancreatic endocrine neoplasia; SPEN, solid and pseudopapillary endocrine neoplasia.

# Prevalence and Epidemiology

PENs, in the case of insufficient blood supply, may undergo necrosis, hemorrhage, and cystic degeneration, resulting in cystic PENs (CPENs), which account for 2% of all pancreatic cystic lesions.

CPENs occur at approximately the same rate in men and women, at a mean age of 55 years. They may be single or multiple, and solid PENs may coexist. They may be part of multiple endocrine neoplasia (MEN) syndromes.<sup>1,2,28</sup>

#### **Clinical Presentation**

CPENs can be functional, if associated with hormonal overproduction, or more often nonfunctional. Actually approximately 30% of the nonfunctional endocrine neoplasms manifest cystic.<sup>1,2,28</sup>

# Pathophysiology

These lesions tend to be located in the body or tail of the pancreas.  $^{1,2,28}$ 

# Pathology

CPENs manifest as solid neoplasms with cystic degenerations or as a thick-walled cyst, between 2 and 10 cm (median, 3.7 cm). No correlation has been proved between the proportion of cystic and solid components and the biologic behavior. On histologic examination they match the appearance of the corresponding noncystic PEN.<sup>1,2,28</sup>

### Imaging

CPENs may be functional and come to clinical attention because of hormonal associated symptoms when still at early stages and small at presentation, or they may be nonfunctional and asymptomatic. In the latter case, they can be discovered incidentally or, more often, when large enough to cause mass-effect symptoms.<sup>1,2,28,29</sup>

**Computed Tomography.** On MDCT, CPENs manifest as mixed solid-cystic masses (see Figures 47-18, 47-19, and 47-20) or as well-defined, unilocular cysts with thick walls. Internal septations, if present, tend to be thick. The intense contrast enhancement of the solid portions of the cystic lesions (wall, solid nodules, septations) is the most important differential imaging feature. However, this finding is not invariably present.<sup>2,3,28,29</sup>

**Magnetic Resonance Imaging.** MRI features closely parallel those found on MDCT, with the added benefit of superior soft tissue and contrast resolution.<sup>2,3,28,29</sup>

**Ultrasonography.** When the quality of transabdominal ultrasonography is adequate, CPENs tend to manifest as thick-walled cystic lesions or as solid lesions with cystic areas. In the case of

contrast-enhanced ultrasonography, the solid components exhibit strong enhancement.

**Nuclear Medicine.** Nuclear medicine, using specific radiopharmaceuticals, has a role in the evaluation of functional cystic neoplasms of the pancreas.

**Positron Emission Tomography With Computed Tomography.** Although FDG uptake is poor in well-differentiated neuroendocrine tumors, it is increased in less-differentiated tumors, in lesions with high proliferative activity, and in metastasizing neoplasms. The use of new radiopharmaceuticals, such as <sup>11</sup>C-labeled 5-hydroxytryptophan (5-HTP) and L-dihydroxyphenylalanine (L-DOPA), seems promising in the detection of primary and metastatic PEN.<sup>30</sup>

**Imaging Algorithm.** An imaging algorithm is provided in Figure 47-1; see also Table 47-12.

#### Classic Signs: Cystic Pancreatic Endocrine Neoplasm

- Solid and cystic components, thick rind
- Strongly enhancing solid components

#### Differential Diagnosis

In the case of hyperfunctional tumors, clinical and laboratory data may aid in the final diagnosis.<sup>1-3,28-30</sup> Arterially hyperenhancing rim or solid components, although not invariably present, are suggestive of CPEN (see Table 47-11).<sup>28,29</sup>

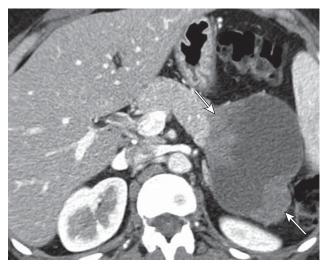
#### Treatment

**Medical Treatment.** Advanced cancers, not amenable to surgical treatment, can be treated with chemotherapy.

# TABLEAccuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Cystic Pancreatic47-12Endocrine Neoplasm

Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive Nonspecific	Unable to directly visualize soft tissue masses in the pancreas.
СТ	Specific data regarding CPEN not available to specify accuracy.	Radiation exposure	Characterization of small cysts may be difficult. Thin septa and small mural nodules not easily appreciated. Difficult discriminating between carcinoma in situ and borderline and benign lesions.
MRI	Specific data regarding CPEN not available to specify accuracy.	Patient cooperation High cost	Calcifications not well visualized. Tumor can masquerade as nodule.
Ultrasonography	Specific data regarding CPEN not available to specify accuracy.	Poor performance in the case of obesity or overlying bowel gas Operator dependent Comprehensive imaging difficult	Small lesions may be undetected.
Nuclear medicine	Specific data regarding CPEN not available to specify accuracy; can be useful in the case of functional CPEN.	Poor spatial resolution	
PET/CT	Specific data regarding CPEN not available to specify accuracy.	Radiation exposure High cost	Difficult differentiation of benign from borderline neoplasms.

CPEN, Cystic pancreatic endocrine neoplasm; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.



**Figure 47-19** Cystic pancreatic endocrine neoplasm (CPEN), classic features. CPEN may manifest as large cystic lesions with solid components (*arrows*), demonstrating arterial enhancement, as shown on this multidetector computed tomography image.

**Surgical Treatment.** Despite the fact that approximately 80% of CPENs are nonmalignant and nonfunctional, they can be locally invasive and also can metastasize to the liver and regional lymph nodes. Therefore, surgery represents the treatment of choice. The 5-year survival rate is 96%.<sup>28,29</sup>

### What the Referring Physician Needs to Know: Cystic Pancreatic Endocrine Neoplasm

- Surgery is the treatment of choice.
- Solid and cystic components are seen.

#### Key Points: Cystic Pancreatic Endocrine Neoplasm

- Occurs in midlife (usually after 50 years of age)
- 70% of nonfunctional tumors
- Solid and cystic areas
- Arterially enhancing solid components and/ or peripheral rind

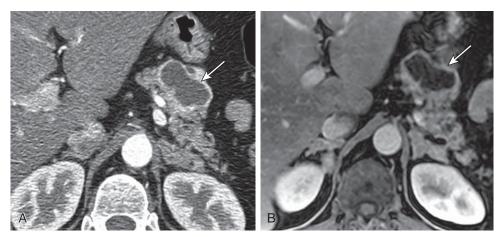


Figure 47-20 Cystic pancreatic endocrine neoplasm (CPEN), classic features. Typically, CPENs (*arrows*) manifest as cystic lesions with thick walls and/or solid components, demonstrating intense arterial enhancement, as shown on multidetector computed tomography (A) and the corresponding magnetic resonance (B) images.

#### SUGGESTED READINGS

- Brugge WR, Lauwers GY, Sahani D, et al: Cystic neoplasms of the pancreas. *N Engl J Med* 351:1218– 1226, 2004.
- Demos TC, Posniak HV, Harmath C, et al: Cystic lesions of the pancreas. *AJR Am J Roentgenol* 179:1375–1388, 2002.
- Lim JH, Lee G, Oh YL: Radiologic spectrum of intraductal papillary mucinous tumor of the pancreas. *Radiographics* 21:323–337, discussion 337–340, 2001.
- Mittendorf EA, Shifrin AL, Inabnet WB, et al: Islet cell tumors. *Curr Probl Surg* 43:685–765, 2006.
- Noone TC, Hosey J, Firat Z, et al: Imaging and localization of islet-cell tumours of the pancreas on CT and MRI. *Best Pract Res Clin Endocrinol Metab* 19:195–211, 2005.
- Sahani D, Prasad S, Saini S, et al: Cystic pancreatic neoplasms evaluation by CT and magnetic resonance cholangiopancreatography. *Gastrointest Endosc Clin N Am* 12:657–672, 2002.
- Sahani DV, Kadavigere R, Soakar A, et al: Cystic pancreatic lesions: a simple imaging-based classification system for guiding management. *Radiographics* 25:1471–1484, 2005.
- Sarr MG, Murr M, Smyrk TC, et al: Primary cystic neoplasms of the pancreas: neoplastic disorders of emerging importance—current state-of-the-art and unanswered questions. *J Gastrointest Surg* 7:417–428, 2003.
- Sheehan MK, Beck K, Pickleman J, et al: Spectrum of cystic neoplasms of the pancreas and their surgical management. *Arch Surg* 138:657–660, discussion 660–662, 2003.
- Tanaka M: Intraductal papillary mucinous neoplasm of the pancreas: diagnosis and treatment. *Pancreas* 28:282–288, 2004.

#### REFERENCES

- Hruban RH, Pitman Bishop M, Klimstra DS: Tumors of the pancreas. In Armed Forces Institute of Pathology, atlas of tumor pathology, 4th series, Washington, DC, 2007, Armed Forces Institute of Pathology, pp 33–376.
- Brugge WR, Lauwers GY, Sahani D, et al: Cystic neoplasms of the pancreas. N Engl J Med 351:1218–1226, 2004.
- 3. Sahani DV, Kadvirere R, Soakar A, et al: Cystic pancreatic lesions: a simple imaging-based classification system for guiding management. *Radiographics* 25:1471–1484, 2005.
- 4. Sheehan MK, Beck K, Pickleman J, et al: Spectrum of cystic neoplasms of the pancreas and their surgical management. *Arch Surg* 138:657– 660, discussion 660–662, 2003.
- Galanis C, Zamani A, Cameron JL, et al: Resected serous cystic neoplasms of the pancreas: a review of 158 patients with recommendations for treatment. J Gastrointest Surg 11:820–826, 2007.
- Irie H, Honda H, Aibe H, et al: MR cholangiopancreatographic differentiation of benign and malignant intraductal mucin-producing tumors of the pancreas. *AJR Am J Roentgenol* 174:1403– 1408, 2000.
- Sperti C, Pasquali C, Decet G, et al: F-18-fluorodeoxyglucose positron emission tomography in differentiating malignant from benign pancreatic cysts: a prospective study. J Gastrointest Surg 9:22–28, discussion 28–29, 2005.
- Goh BK, Tan YM, Yap WM, et al: Pancreatic serous oligocystic adenomas: clinicopathologic features and a comparison with serous microcystic adenomas and mucinous cystic neoplasms. *World J Surg* 30:1553–1559, 2006.
- Carbognin GT, Petrella M, Fuini E, et al: Serous cystic tumors. In Procacci AJ, Megibow AJ, editors: *Imaging of the pancreas: cystic and rare tumors*, Berlin, 2003, Springer, pp 31–55.
- Sarr MG, Murr M, Smyrk TC, et al: Primary cystic neoplasms of the pancreas: neoplastic disorders of emerging importance—current state-of-the-art and unanswered questions. J Gastrointest Surg 7:417–428, 2003.

- Scott J, Martin I, Redhead D, et al: Mucinous cystic neoplasms of the pancreas: imaging features and diagnostic difficulties. *Clin Radiol* 55:187–192, 2000.
- Goh BK, Tan YM, Chung YF, et al: A review of mucinous cystic neoplasms of the pancreas defined by ovarian-type stroma: clinicopathological features of 344 patients. *World J Surg* 30:2236–2245, 2006.
- Zamboni G, Scarpa A, Bogina G, et al: Mucinous cystic tumors of the pancreas: clinicopathological features, prognosis, and relationship to other mucinous cystic tumors. *Am J Surg Pathol* 23:410–422, 1999.
- 14. Suzuki Y, Atomi Y, Sugiyama M, et al: Cystic neoplasm of the pancreas: a Japanese multiinstitutional study of intraductal papillary mucinous tumor and mucinous cystic tumor. *Pancreas* 28:241–246, 2004.
- Biasiutti CF, Venturini F, Pagnotta N, et al: Mucinous cystic tumors. In Procacci AJ, Megibow AJ, editors: *Imaging of the pancreas: cystic and rare tumors*, Berlin, 2003, Springer, pp 57–74.
- Tanaka M, Sawai H, Okada Y, et al: Clinicopathologic study of intraductal papillary-mucinous tumors and mucinous cystic tumors of the pancreas. *Hepatogastroenterology* 53:783–787, 2006.
- Tanno S, Nakano Y, Nishikawa T, et al: Natural history of branch duct intraductal papillarymucinous neoplasms of the pancreas without mural nodules: long-term follow-up results. *Gut* 57:339–343, 2008.
- Lim JH, Lee G, Oh YL: Radiologic spectrum of intraductal papillary mucinous tumor of the pancreas. *Radiographics* 21:323–337, discussion 337–340, 2001.
- Loftus EV, Jr, Oliveres-Pakzad BA, Batts KP, et al: Intraductal papillary-mucinous tumors of the pancreas: clinicopathologic features, outcome, and nomenclature. Members of the Pancreas Clinic, and Pancreatic Surgeons of Mayo Clinic. *Gastroenterology* 110:1909–1918, 1996.
- 20. Pais SA, Attasaranya S, Leblanc JK, et al: Role of endoscopic ultrasound in the diagnosis of

intraductal papillary mucinous neoplasms: correlation with surgical histopathology. *Clin Gastroenterol Hepatol* 5:489–495, 2007.

- Tanaka M: Intraductal papillary mucinous neoplasm of the pancreas: diagnosis and treatment. *Pancreas* 28:282–288, 2004.
- Tanaka M, Kobayashi K, Mizumoto K, et al: Clinical aspects of intraductal papillary mucinous neoplasm of the pancreas. J Gastroenterol 40:669–675, 2005.
- Taouli B, Vilgrain V, Vullierme MP, et al: Intraductal papillary mucinous tumors of the pancreas: helical CT with histopathologic correlation. *Radiology* 217:757–764, 2000.
- Procacci CS, Schenal G, Chiara ED, et al: Intraductal papillary mucinous tumors: imaging. In Procacci C, Megibow AJ, editors: *Imaging of the pancreas: cystic and rare tumors*, Berlin, 2003, Springer, pp 97–137.
- Geers C, Moulin P, Gigot JF, et al: Solid and pseudopapillary tumor of the pancreas: review and new insights into pathogenesis. *Am J Surg Pathol* 30:1243–1249, 2006.
- Hernandez JM, Centeno BA, Kelley ST: Solid pseudopapillary tumors of the pancreas: case presentation and review of the literature. *Am* Surg 73:290–293, 2007.
- Casadei R, Santini D, Calculli L, et al: Pancreatic solid-cystic papillary tumor: clinical features, imaging findings and operative management. *JOP* 7:137–144, 2006.
- Goh BK, Ooi LL, Tan YM, et al: Clinicopathological features of cystic pancreatic endocrine neoplasms and a comparison with their solid counterparts. *Eur J Surg Oncol* 32:553–556, 2006.
- Ligneau B, Lombard-Bohas C, Partensky C, et al: Cystic endocrine tumors of the pancreas: clinical, radiologic, and histopathologic features in 13 cases. *Am J Surg Pathol* 25:752–760, 2001.
- Bombardieri E, Maccauro M, De Deckere E, et al: Nuclear medicine imaging of neuroendocrine tumours. *Ann Oncol* 12(Suppl 2):51–61, 2001.

# **Imaging of Acute Pancreatitis**

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## Etiology

Acute pancreatitis is an acute inflammatory disorder of the pancreas that has numerous causes (Box 48-1). The most common risk factors are chronic alcohol consumption and choledocholithiasis.<sup>1</sup> In 20% of cases no cause can be found.<sup>1</sup>

## **Prevalence and Epidemiology**

In the United States, up to 210,000 patients per year are admitted to a hospital for acute pancreatitis.<sup>2</sup> The spectrum of acute pancreatitis ranges from mild to severe and fatal.

In 1992, the International Symposium on Acute Pancreatitis in Atlanta, Georgia, established a clinical-based classification and defined certain terminologies commonly associated with acute pancreatitis.<sup>3</sup> Acute pancreatitis is classified as mild and severe based on the presence of local complications and organ failure.<sup>3,4</sup> This classification helped identify patients with severe disease who required close monitoring and intensive unit care. Mild acute pancreatitis has a mortality rate of less than 1%, whereas the death rate for severe pancreatitis is much higher— 10% with sterile and 30% with infected pancreatic necrosis.<sup>1</sup>

## **Clinical Presentation**

The hallmark symptom of acute pancreatitis is the acute onset of persistent upper abdominal pain, usually with nausea and vomiting. The pain may radiate to the back, chest, flanks, and lower abdomen. Physical examination findings include fever, hypotension, severe abdominal tenderness, guarding, respiratory distress, and abdominal distention.<sup>2</sup>

## Pathophysiology

The inflammatory process in acute pancreatitis is triggered by the premature activation of pancreatic enzymes with resultant autodigestion of the pancreatic parenchyma. The inflammatory process may remain localized to the pancreas, spread to regional tissues, or even involve remote organ systems, resulting in multiple organ failure and occasionally death.

Mild acute pancreatitis (also known as interstitial or edematous pancreatitis) is more common and is a self-limiting disease with minimal organ dysfunction and an uneventful recovery. Pathologically, the mild form of acute pancreatitis is characterized by interstitial edema and infrequently by microscopic areas of parenchymal necrosis.<sup>3</sup>

Severe acute pancreatitis (also known as necrotizing pancreatitis) occurs in 20% to 30% of all patients and is associated with organ failure and/or local complications, such as necrosis, abscess, or pseudocyst formation.

## **Pathology**

Pathologic findings include macroscopic areas of focal or diffuse pancreatic necrosis, fat necrosis, and hemorrhage in the pancreas and peripancreatic tissues.<sup>3</sup>

## Imaging

Computed tomography (CT) and abdominal ultrasonography are routinely used in the setting of an acute abdomen to identify the source of pain.<sup>5</sup> CT can help confirm the diagnosis of acute pancreatitis and exclude other causes of acute abdomen such as gastrointestinal perforation, acute cholecystitis, acute aortic dissection, and mesenteric artery occlusion, which can clinically mimic acute pancreatitis. In established cases of acute pancreatitis, contrast-enhanced CT is considered the gold standard for evaluating morphologic changes of acute pancreatitis, particularly in the assessment of pancreatic necrosis.<sup>3,6</sup> Magnetic resonance imaging (MRI) with MR cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasonography, and angiography have specific indications in a patient with known acute pancreatitis.

#### RADIOGRAPHY

Plain abdominal radiographs are often normal in patients with acute pancreatitis. Air in the duodenal C-loop, a "sentinel loop" (focally dilated jejunal loop in the left upper quadrant) or the "colon cutoff" sign (distention of the colon to the transverse colon with a paucity of gas distal to the splenic flexure) may be seen on plain radiographs in patients with pancreatitis. However, these findings are never sufficiently enough to confirm the diagnosis.

#### COMPUTED TOMOGRAPHY

#### Role of Computed Tomography in Acute Pancreatitis

CT can establish the diagnosis of acute pancreatitis. It helps determine the underlying cause of acute pancreatitis (identifies choledocholithiasis and biliary ductal dilatation associated with biliary pancreatitis). It grades the severity of the disease and detects complications such as pancreatic necrosis, abscess, or pseudocysts.

#### Optimal Time to Perform Computed Tomography

In established cases of severe acute pancreatitis, contrastenhanced CT helps in grading the severity of the disease and determining the extent of necrosis. Because necrotic areas of pancreatic parenchyma become better defined 2 to 3 days after the onset of symptoms, contrast-enhanced CT performed 48 to 72 hours after the onset of an acute attack gives more reliable information. CT findings can be equivocal if the scan is obtained during the initial 12 hours.<sup>6</sup>

#### Scanning Technique

Multidetector CT scanners allow high-resolution, multiphase imaging of the pancreas performed using short scanning times. Table 48-1 depicts the CT scanning parameters used in our institution.<sup>7</sup>

A single-phase contrast-enhanced CT in the portal venous phase (~70 seconds after the injection of intravenous contrast) is usually adequate to make the diagnosis and assess the complications of acute pancreatitis. Normal pancreatic tissue should demonstrate a homogeneous increase in attenuation to 100 to 150 Hounsfield units (HU) after contrast administration. Lack of enhancement or minimal enhancement (<30 HU) of a portion of the pancreas or the entire pancreas indicates decreased blood perfusion and necrosis.<sup>6</sup> In the absence of pancreatic necrosis, the pancreas and spleen should be similar in attenuation on the portal venous phase.<sup>6</sup>

When vascular complications are suspected, an additional vascular phase can be added to the imaging protocol, which is performed approximately 45 seconds after the injection of the contrast agent. Automated bolus tracking can be used to determine optimal timing of image acquisition. Unenhanced CT

#### BOX 48-1 CAUSES OF ACUTE PANCREATITIS

- Gallstones (45%)
- Alcohol (35%)
- Others (10%)Medications
- Hypercalcemia
- Hypertriglyceridemia
- Duct obstruction (e.g., tumor)
- Post–endoscopic retrograde cholangiopancreatography
- Hereditary
- Trauma
- Viral
- Post cardiac bypass
- Idiopathic (10% to 20%)

may be added to the imaging protocol if there is a strong clinical suspicion of hemorrhage.

#### Imaging Findings

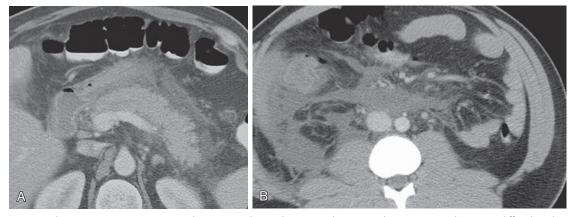
As mentioned earlier, CT is not required in mild, self-limiting cases of acute pancreatitis. In these cases, CT of the pancreas may be normal or the pancreas may be enlarged or low in attenuation, indicating interstitial edema (Figure 48-1, A). The role of CT is primarily in patients with severe acute pancreatitis to assess the degree of pancreatic necrosis and detect complications such as pseudocyst and abscess formation.

The definitions, pathogenesis, and imaging appearance of the different types of fluid collections seen in acute pancreatitis are discussed in this section. These terminologies were standardized by the 1992 International Symposium on Acute Pancreatitis<sup>3</sup> and should be included in the radiology reports.

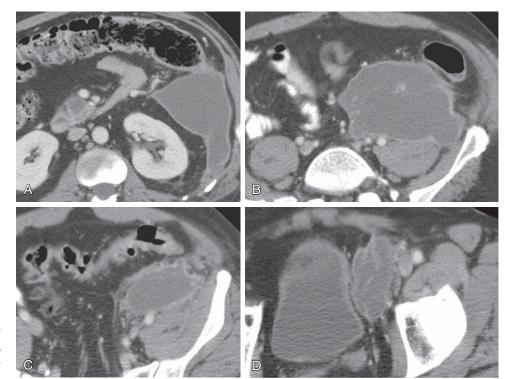
Acute Fluid Collections. Acute fluid collections occur early in the course of acute pancreatitis (within 48 hours). These consist

TABLE 48-1	Computed Tomography Parameters			
Param	eters	Vascular Phase (40-45 sec)	Portal Venous Phase (65-70 sec)	
Intravenous contrast		4-5 cm <sup>3</sup> /s	3 cm <sup>3</sup> /s	
Range		Celiac through entire pancreas	Dome of diaphragm to symphysis pubis	
Autom track	nated bolus king	+ (150-HU threshold in the aorta at the level of celiac artery and 8- to 10-sec diagnostic delay)	+ (55-HU threshold in the right lobe of liver at the level of the right portal vein)	
Slice t	hickness	1-3 mm	5 mm	
Spacin	g	1-3 mm	5 mm	
Kilovo	ltage peak	120-140	120-140	
Milliam	nperage	240-280	240-280	
Time		0.5-0.8 sec	0.5-0.8 sec	
Field c	of view	28	Based on size of patient	

HU, Hounsfield units.



**Figure 48-1** Acute edematous pancreatitis. **A**, Axial contrast-enhanced computed tomography (CT) image showing a diffusely enlarged pancreas and peripancreatic inflammatory fat stranding. **B**, Axial CT image of another patient with mild pancreatitis showing an acute fluid collection inferior to the pancreas. Note that, unlike a pseudocyst, acute fluid collections do not have a well-defined wall.



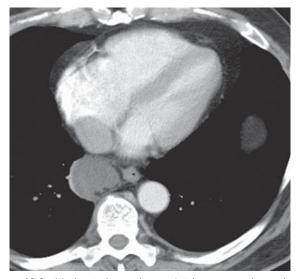
**Figure 48-2** Pancreatic pseudocyst. A to D, Axial contrast-enhanced computed tomography images show a large pseudocyst extending inferiorly from the left pararenal space into the pelvis and left groin.

of enzyme-rich pancreatic juices and lack a wall of fibrous or granulation tissue. These usually occur in or near the pancreas and may dissect in the lesser sac, anterior pararenal spaces (commonly on the left), transverse mesocolon, and mesenteric root (see Figure 48-1, *B*). Acute fluid collections are seen in 30% to 50% of cases and resolve spontaneously in approximately 50% of patients. In the remainder, they can get walled off and progress to become pseudocysts or abscesses.<sup>8,9</sup>

**Acute Pseudocyst.** A pseudocyst is defined as a collection of pancreatic juices enclosed by a wall of fibrous or granulation tissue. Pseudocysts are formed approximately 4 weeks after the onset of acute pancreatitis.<sup>8</sup> On CT, a pseudocyst appears as a well-circumscribed, low-attenuation collection commonly occurring in the vicinity of the pancreas (Figure 48-2). On rare occasions they can be seen in unusual locations such as the mediastinum and groin (Figure 48-3).<sup>10,11</sup> A typical pseudocyst is sterile. If pus is present in the pseudocyst, the lesion is termed a pancreatic abscess.

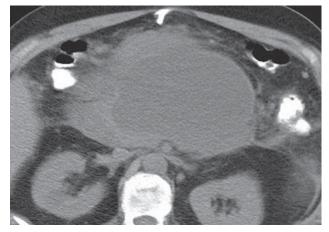
**Pancreatic Abscess.** A pancreatic abscess consists of a circumscribed intra-abdominal collection of pus, usually in proximity to the pancreas, and contains little or no pancreatic necrosis. Like pseudocysts, pancreatic abscesses occur later in the course of severe acute pancreatitis, often 4 weeks or more after the onset.<sup>3</sup> On contrast-enhanced CT, the presence of a thick, irregular wall helps differentiate a pancreatic abscess from a pseudocyst, which generally has a thin, well-delineated wall (Figure 48-4).

**Pancreatic Necrosis.** Pancreatic necrosis is defined as focal or diffuse areas of nonviable pancreatic parenchyma and is typically associated with peripancreatic fat necrosis.<sup>3</sup> On contrastenhanced CT, pancreatic necrosis appears as one or more focal

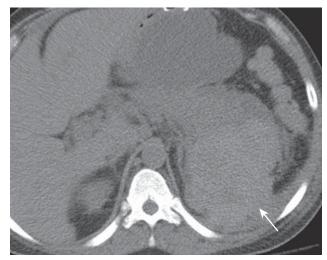


**Figure 48-3** Mediastinal pseudocyst. Axial contrast-enhanced computed tomography image showing an unusual location of a pancreatic pseudocyst in the posterior mediastinum.

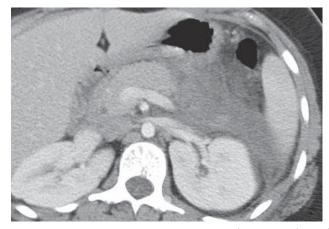
areas of nonenhancing pancreatic parenchyma (Figure 48-5). Pancreatic necrosis is often hemorrhagic because of leakage from small veins and is seen on CT as areas of increased attenuation within the pancreas (Figure 48-6). Retroperitoneal fat necrosis is invariably seen in patients with pancreatic necrosis, but the converse is not true. CT cannot reliably diagnose retroperitoneal fat necrosis, and thus all heterogeneous peripancreatic collections should be considered as areas of fat necrosis until proved otherwise (Figure 48-7).<sup>6</sup>



**Figure 48-4** Pancreatic abscess. Axial computed tomography image of a large thick-walled peripancreatic collection in a patient with severe acute pancreatitis and high fever. Percutaneous needle aspiration of this collection yielded pus.



**Figure 48-6** Severe necrotizing pancreatitis. Axial unenhanced computed tomography image of a patient with necrotizing pancreatitis shows areas of increased attenuation (50 to 60 HU) (*arrow*) suggesting the presence of hemorrhage.

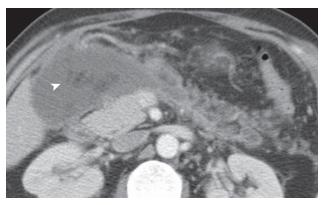


**Figure 48-5** Acute necrotizing pancreatitis. Axial contrast-enhanced computed tomography image demonstrating nonenhancement of the distal body and tail of pancreas, suggesting necrosis. Note that the head and proximal body of the pancreas demonstrate normal enhancement.

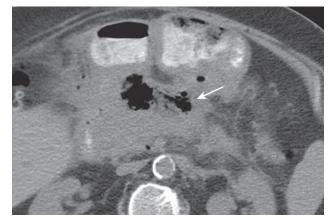
In individuals with fatty infiltration of the pancreas and in those with edematous or interstitial pancreatitis, the decreased enhancement of the pancreas should not be mistaken for pancreatic necrosis.<sup>6</sup> Also, small, focal intrapancreatic fluid collections that are sometimes seen in acute pancreatitis should not be mistaken for focal necrosis. This distinction can be difficult in the absence of prior imaging.<sup>6</sup>

#### Imaging Differentiation of Sterile Versus Infected Necrosis

The differentiation of sterile from infected pancreatic necrosis is important from the management perspective because the latter necessitates necrosectomy.<sup>12-14</sup> The mortality rates increase from 10% in those with sterile necrosis to 30% in the presence of infected necrosis.<sup>1</sup> Distinguishing sterile from infected necrosis based solely on imaging is virtually impossible, the only exception being the presence of gas bubbles within the collection suggesting the presence of infection (Figure 48-8).<sup>6</sup>



**Figure 48-7** Acute pancreatitis with peripancreatic fat necrosis. Collection in the peripancreatic tissue with islands of fat (*arrowhead*) suggests fat necrosis.



**Figure 48-8** Axial unenhanced computed tomography (CT) image of a patient with known necrotizing pancreatitis. During the course of hospitalization, the patient's condition worsened clinically and the patient appeared septic. CT was performed and demonstrated air in the pancreatic bed (*arrow*) diagnostic of infected necrotic tissue.

Percutaneous needle aspiration under CT or ultrasound guidance is helpful in detecting the presence of infection.

#### Computed Tomography Severity Index

Balthazar and colleagues<sup>15,16</sup> graded the severity of acute pancreatitis based on CT findings and described the term *CT severity index* (CTSI). CT grading of acute pancreatitis is depicted in Table 48-2. These investigators reported 0% and 48% mortality and morbidity rates, respectively, in patients who had less than 30% necrosis on CT. Larger areas of necrosis (30% to 50% and >50%) were associated with a morbidity rate of 75% to

TABLE <b>48-2</b>		althazar Grading System and Computed omography Severity Index				
Grade	Grade Description					
А	Normal-appearing	pancreas				
В	Focal or diffuse er	nlargement of the pancre	as			
С	C Pancreatic gland abnormalities accompanied by mild peripancreatic inflammatory changes					
D	Fluid collection in	a single location				
Е	E Two or more fluid collections near the pancreas or gas in or adjacent to the pancreas					
CT Gra	ade Score	Necrosis (%)	Score			
А	0	0	0			
В	1	<30	2			

D 3 >50 6 E 4

2

30-50

4

CT severity index (maximum score 10) – CT grade (0-4) + necrosis (0-6).

Figure 48-9 A and B, Axial computed tomography images of a patient with necrotizing pancreatitis involving the body and tail of the pancreas. Owing to the close proximity of the tail of the pancreas and spleen, the inflammatory process has extended laterally and superiorly to the perisplenic tissues.

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100% and a mortality rate of 11% to 25%.<sup>16</sup> Additionally, patients with a CTSI of 0 to 3 showed a 3% mortality rate and an 8% morbidity rate, whereas in patients with a CTSI of 7 to 10, the mortality and morbidity rates were 17% and 92%, respectively.<sup>15</sup>

#### Extrapancreatic Findings in Acute Pancreatitis

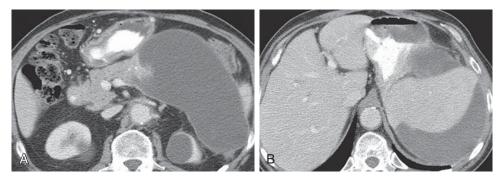
The inflammatory process in pancreatitis can spread into the spleen with formation of an intrasplenic pseudocyst or abscess (Figure 48-9).<sup>17</sup> Splenic infarction can occur as a result of compression of the splenic vessels. Erosion of small intrasplenic vessels can cause parenchymal hemorrhage, resulting in a subcapsular hematoma.

Spread of the inflammatory process to the adjacent liver and gallbladder can produce transient areas of enhancement in the liver, typically seen near the gallbladder fossa and the left lobe of the liver.<sup>18</sup> Likewise, the inflammatory process can extend into the perinephric space, resulting in subcapsular and perirenal fluid collections and pseudocysts (Figure 48-10). Extensive inflammation around the renal vessels can cause renal vein compression and thrombosis. The inflammatory exudates can compress the renal artery, causing asymmetric enhancement of the renal parenchyma.<sup>19</sup>

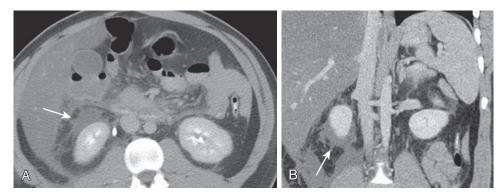
Rarely, direct extension of the inflammatory process or a pseudocyst may inflame or erode the large bowel, resulting in fistula formation and progressive narrowing of the colonic lumen (Figure 48-11).<sup>20</sup> Large bowel involvement may manifest weeks or months after an attack of acute pancreatitis.

#### Vascular Complications

Arterial complications of acute pancreatitis result from the proteolytic effects of the pancreatic enzymes that cause erosion of blood vessels, which often results in pseudoaneurysm formation or free hemorrhage from the erosion site.<sup>21,22</sup> The splenic



**Figure 48-10** Axial (A) and coronal (B) contrast-enhanced CT images in a patient with acute pancreatitis depicting the spread of the inflammatory process to the right perirenal space (arrows).



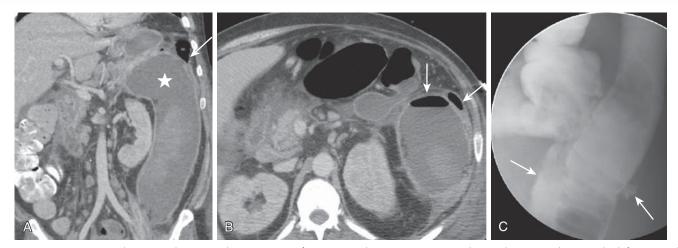


Figure 48-11 A, Coronal computed tomography (CT) image of a patient with severe pancreatitis shows a large pseudocyst in the left pararenal space (star) closely related to the colon (arrow). B, Axial CT image of the same patient performed 10 days later shows new air within the pseudocyst, suggesting either infection or bowel fistulization. C, Water-soluble contrast enema performed the next day shows leakage of contrast agent from the descending colon into the pseudocyst (arrows), indicating that the pseudocyst has eroded the large bowel.

artery, followed by the pancreaticoduodenal and gastroduodenal arteries, are affected most commonly.<sup>21,22</sup> The left gastric, hepatic, and small intrapancreatic arteries are involved less often. Arterial bleeding is one of the most life-threatening complications. On imaging, a pseudoaneurysm can be seen as a completely or partially vascular cystic mass (Figure 48-12).

In addition to arterial complications, venous thrombosis in the portal-mesenteric circulation can occur. In order of frequency, the splenic vein is involved most often, followed by the portal and the superior mesenteric veins (Figure 48-13).

#### ANGIOGRAPHY

If acute hemorrhage or pseudoaneurysm is suspected or diagnosed by contrast-enhanced CT or ultrasonography, a celiac/ superior mesenteric arteriogram should be performed to definitively assess the extent of vascular involvement (Figure 48-14). Once the site of pseudoaneurysm or source of active bleeding is identified, it can be treated by Gelfoam embolization, various coil occlusion devices, or tissue adhesives (e.g., bucrylate).

Complications of celiac/superior mesenteric arteriography and embolization include arterial injury such as thrombosis, dissection, or rupture; distal embolization; ischemia of visceral organs such as the spleen and bowel; coil malpositioning; and rebleeding.

#### MAGNETIC RESONANCE IMAGING

MRI is comparable to CT in the demonstration of morphologic changes associated with acute pancreatitis, including the extent of pancreatic necrosis and peripancreatic fluid collections (Figure 48-15).<sup>23,24</sup> MRI of the pancreas is best performed with a 1.5-tesla (T) MR scanner and phased-array coils. The MRI parameters used in our institution are shown in Tables 48-3 and 48-4.<sup>7</sup>

T2-weighted sequences accurately depict fluid collections, pseudocysts, and hemorrhage. T2-weighted images are more sensitive than CT in demonstration of the contents of fluid collections and therefore in the assessment of the drainability of the collection.<sup>25</sup> T1-weighted images are useful to depict



**Figure 48-12** Splenic artery pseudoaneurysm after an episode of severe acute pancreatitis. Axial contrast-enhanced computed tomography image shows an enhancing structure (*arrow*) in the pancreatic bed with attenuation matching that of the aorta, suggesting a pseudoaneurysm.



**Figure 48-13** Axial contrast-enhanced computed tomography image shows inflammation of the body and tail of pancreas and peripancreatic tissues with splenic vein thrombosis (*arrow*).

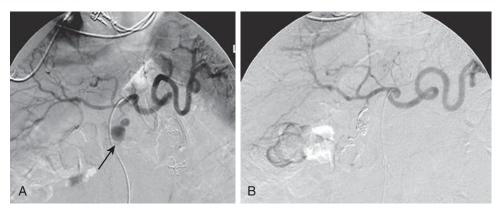
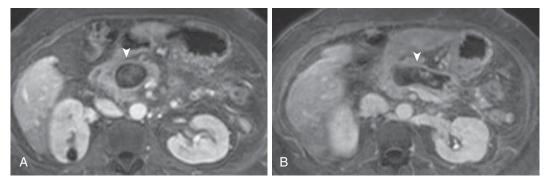


Figure 48-14 A, Celiac artery angiogram performed in a patient with severe acute pancreatitis and upper gastrointestinal hemorrhage demonstrates a pseudoaneurysm (arrow) arising from the gastroduodenal artery. B, After coiling there is complete occlusion of the pseudoaneurysm.



**Figure 48-15** A and B, Gadolinium-enhanced T1-weighted gradient echo images show lack of enhancement of the head and body of the pancreas (*arrowheads*) suggesting the presence of necrosis. Contrast-enhanced magnetic resonance imaging is equivalent to computed tomography for the demonstration of pancreatic necrosis.

TABLE 48-3	Magnetic Resonance Imaging Parameters				
Param	eters	Fast Spin Echo With Fat Saturation	Fast Spin Echo Without Fat Saturation	T1-Weighted Gradient Echo (Spoiled Gradient Recalled)	3D Dynamic Precontrast and Postcontrast
Imagin	ng plane	Axial	Axial	Axial	Axial
TR		4000-4500 ms	2100 ms	200 ms	150 ms
TE		68 ms	60 ms	Minimum	2.4 ms
Flip an	ngle	90 degrees	90 degrees	80 degrees	15 degrees
Field c	of view	36	36	36	36
Matrix		128 × 256	128 × 256	256 × 512	160 × 256
Thickn	ess	3 mm	3 mm	4 mm	4 mm
Gap (n	nm)	0	0	0	Not applicable
Respira	ation	Triggered	Breath-hold	Breath-hold	Breath-hold (three acquisitions)

3D, Three-dimensional; TE, echo time; TR, repetition time.

pancreatic and peripancreatic edema. Dynamic gadoliniumenhanced MRI is useful for depicting viable from nonviable pancreatic parenchyma and identifying vascular complications.

MRCP is highly sensitive and specific for diagnosing choledocholithiasis and hence in establishing the underlying cause of acute pancreatitis (Figure 48-16).<sup>26,27</sup> Also, pancreatic ductal abnormalities such as dilatation, disruption, or leakage, as well as duct communication with a pancreatic pseudocyst, can be well demonstrated by MRCP.<sup>27</sup> Structural abnormalities of the pancreas such as pancreas divisum and anomalous pancreaticobiliary junction with an abnormally long common channel that can cause recurrent attacks of pancreatitis can be depicted by MRCP.<sup>27</sup>

Secretin-enhanced MRCP has proved to be beneficial in improving the visualization of the pancreatic ductal system.<sup>27</sup> Exogenous administration of secretin stimulates secretion of pancreatic juice, notably the fluid and bicarbonate, which consequently results in transient distention of the pancreatic duct. Secretin-enhanced MRCP enhances the ability of MRI to identify structural anomalies such as pancreas divisum and to make the diagnosis of ductal disruption.<sup>28,2</sup>

#### **ULTRASONOGRAPHY**

In a patient with suspected biliary pancreatitis, ultrasound is helpful for the assessment of biliary dilatation and gallbladder and common bile duct stones.

The assessment of the pancreas by ultrasound is limited, secondary to bowel gas and associated paralytic ileus. The ultrasonographic findings in acute pancreatitis can range from a normal-appearing gland, a diffusely enlarged hypoechoic pancreas, or the presence of intrapancreatic or peripancreatic fluid collections, particularly in the lesser sac and anterior pararenal space (Figure 48-17).

The role of endoscopic ultrasonography in the management of acute pancreatitis is limited in everyday practice. There have been reports suggesting it is accurate in identifying common bile duct stones and detecting pancreatic necrosis.<sup>14</sup> Diagnostic endoscopic ultrasonography is helpful before performing therapeutic endoscopic interventions such as cystogastrostomy for the management of pseudocysts.

Figure 48-16 Magnetic resonance cholangiopancreatography per-

formed in a patient with acute pancreatitis demonstrates a stone

causing a filling defect (arrow) in the common bile duct.

#### gallstones in patients with severe gallstone pancreatitis.<sup>30</sup> The morbidity and mortality are reduced with the use of early selective ERCP. ERCP is indicated in patients at risk for or with

ENDOSCOPIC RETROGRADE

**CHOLANGIOPANCREATOGRAPHY** 

evidence of biliary sepsis, cholangitis, biliary obstruction, elevated bilirubin, and worsening and persistent jaundice.

## **IMAGING ALGORITHM**

See Figure 48-18 for an imaging algorithm and also Table 48-5.

ERCP is not used to make the diagnosis of acute pancreatitis. It is used with endoscopic sphincterotomy to extract impacted

#### **Classic Signs**

- Lack of contrast enhancement or minimal contrast enhancement of less than 30 HU indicates pancreatic necrosis.
- If a cystic pancreatic mass demonstrates transient vascular enhancement, a pseudoaneurysm should be suspected.

#### TABLE 48-4 **Magnetic Resonance Cholangiopancreatography Parameters**

	2D S		
Parameters	Thin Section	Thick Section	3D FRFSE
Acquisition plane	Coronal	Coronal	Coronal
TR	Minimum	4849 ms	1717 ms
TE	180 ms	874 ms	500-600 ms
Bandwidth	62.5	31.25	19
Field of view	48	35	36
Matrix	$160 \times 384$	$256 \times 256$	$256 \times 256$
Thickness	5 mm	40 mm	3 mm
Gadolinium	±	±	±

2D, Two-dimensional; 3D, three dimensional; FRFSE, fast-recovery fast spin-echo; SSFSE, single-shot fast spin-echo; TE, echo time; TR, repetition time.

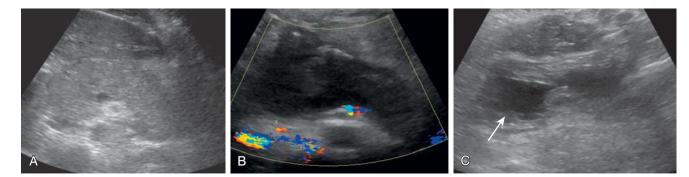
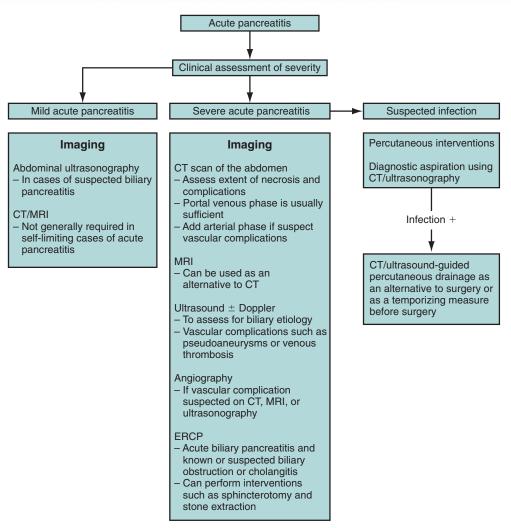


Figure 48-17 A, Transverse ultrasound image shows an enlarged hypoechoic pancreas seen in acute edematous pancreatitis. B, Transverse ultrasound image of a patient with elevated amylase and lipase levels shows a complex fluid collection in the epigastrium conforming to the shape of the pancreas. This patient had extensive pancreatic necrosis on a contrast-enhanced computed tomography scan performed a few days later. Ultrasonography is not very reliable in distinguishing pancreatic necrosis from other fluid collections seen in patients with acute pancreatitis. C, Transverse ultrasound image of a patient with known acute pancreatitis showing a pancreatic/peripancreatic pseudocyst (arrow).



**Figure 48-18** Imaging algorithm for acute pancreatitis. *CT*, Computed tomography; *ERCP*, endoscopic retrograde cholangiopancreatography; *MRI*, magnetic resonance imaging.

TABLE A	Accuracy and Limitations of the Modalities Used in Imaging of Acute Pancreatitis			
Modality		Accuracy	Limitations	
Radiograp CT	ohy	Not very useful Establishing diagnosis Establishing cause Assessing severity and complications Guiding percutaneous interventions	Cannot reliably differentiate sterile from infected necrosis	
MRI		Comparable to CT in assessing pancreatic necrosis and complications Superior to CT in assessing the contents of fluid collections and hence is a better predictor of drainability of collections by percutaneous techniques MRCP useful in assessing choledocholithiasis and pancreatic ducal abnormalities	Long scanning times limit its use in severely ill patients.	
Ultrasono	graphy	Useful in determining the cause of acute pancreatitis, mainly choledocholithiasis and biliary dilatation Portable nature of the modality occasionally helpful in performing simple diagnostic aspirations in critically ill patients	Limited use in assessing severity of pancreatitis	

CT, Computed tomography; MRCP, magnetic resonance cholangiopancreatography; MRI, magnetic resonance imaging.

## **Differential Diagnosis**

The clinical diagnosis of acute pancreatitis is based on abdominal pain, which often radiates to the back and is accompanied by nausea and vomiting. The diagnosis is confirmed by elevation of serum amylase and lipase (more than three times the upper limits of normal).<sup>1</sup> Serum amylase and, less commonly, serum lipase levels can be elevated in many other nonpancreatic disorders (Table 48-6). In equivocal cases, imaging is helpful in establishing the diagnosis of acute pancreatitis.

CT and ultrasonography are useful in confirming the diagnosis of acute pancreatitis and ruling out other intra-abdominal conditions as the cause of pain (Box 48-2).

### Treatment

#### MEDICAL TREATMENT

The severity of pancreatitis is clinically assessed by different scoring systems that assess inflammation and organ failure.<sup>3,6,30</sup> The commonly used Ranson scoring system comprises five clinical criteria measured at admission and six measured after 48 hours.<sup>6,30</sup> The APACHE II monitoring system is considered more reliable, with an accuracy of approximately 75% for the assessment of the severity of pancreatitis at admission.<sup>6,30</sup>

Mild pancreatitis can be managed conservatively with hydration and analgesics.<sup>30</sup> Right upper quadrant ultrasonography to look for gallstones and biliary dilatation make up the standard of care.<sup>30</sup>

table <b>48-6</b>	Common Nonpancreatic Causes of Elevated Amylase and Lipase Levels		
Cause		Amylase	Lipase
Comm Acute Intestin	disease on bile duct obstruction cholecystitis nal ischemia, obstruction, perforation appendicitis		
Gynecologic conditionsNormalEctopic pregnancyAcute salpingitisOvarian cysts and malignanciesRenal insufficiency			Normal
Salivar	y gland disease including mumps		Normal

#### BOX 48-2 CLINICAL MIMICKERS OF ACUTE PANCREATITIS

- Gastritis and peptic ulcer disease
- Esophageal spasm
- Perforated viscus\*
- Intestinal obstruction\*
- Acute cholecystitis\*
- Leaking abdominal aortic aneurysm or acute aortic dissection\*
- Mesenteric ischemia\*

\*Imaging, particularly CT, is useful in establishing the diagnosis.

#### SURGICAL TREATMENT

Surgical management of acute pancreatitis is indicated in two clinical settings: infected necrosis and gallstone pancreatitis. Surgery, consisting of débridement of all devitalized pancreatic and surrounding tissue, is indicated in infected necrosis; its benefit in sterile necrosis is controversial.<sup>14,30</sup> Recent studies suggest that a delayed approach to surgical necrectomy improves outcomes.<sup>14</sup>

#### Endoscopic Interventions

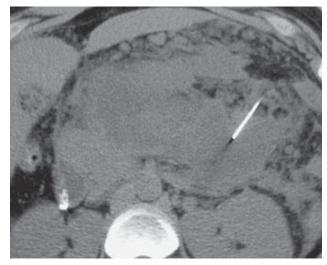
In the acute phase of gallstone-induced pancreatitis, if biliary duct obstruction, biliary sepsis, or cholangitis is suggested, then endoscopic sphincterotomy, biliary calculus removal, and common bile duct drainage are done.<sup>30</sup> Eventually, cholecystectomy is recommended in all cases of biliary pancreatitis to prevent recurrence.<sup>30</sup>

#### Percutaneous Image-Guided Interventions

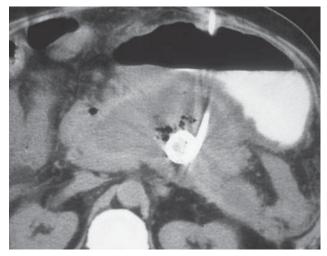
Both diagnostic and therapeutic percutaneous interventions are often performed in patients with acute pancreatitis. Diagnostic aspiration for Gram stain and culture is performed on fluid collections, pseudocysts, or pancreatic necrosis in the case of clinical suspicion of infection (Figure 48-19). Although most pseudocysts regress spontaneously, large (>5 cm), unresolving (>6 weeks) or symptomatic pseudocysts (pain, gastric outlet obstruction, or biliary obstruction) require drainage, which can be done either by percutaneous or endoscopic techniques.<sup>30</sup> Pancreatic abscesses and infected necrosis often require multicatheter drainage either as definitive treatment or as a temporizing measure before surgery (Figure 48-20).<sup>14,30</sup>

CT is commonly used to guide percutaneous interventions. It demonstrates the size, location, and relationship of the collection to the adjacent vasculature and critical organs.

Once a drainage procedure has been performed, follow-up CT is critical in assessing the success of the procedure. Persistent



**Figure 48-19** Axial computed tomography (CT) image of a patient with known necrotizing pancreatitis who developed a high-grade fever. Percutaneous diagnostic aspiration of the necrotic material performed under CT guidance with a 20-gauge Chiba needle yielded pus. CT cannot reliably distinguish sterile from infected pancreatic necrosis, and percutaneous aspiration is often performed when there is a strong clinic cal suspicion of infection.



**Figure 48-20** Axial computed tomography image showing a 14-gauge catheter used to drain extensive pancreatic necrosis. Catheter drainage could be performed as a temporizing measure before definitive surgery for pancreatic necrosis. Large-bore catheters are required if drainage of pancreatic necrosis is attempted.

collections lasting for months may suggest pancreatic ductal communication.

#### What the Referring Physician Needs to Know

- CT of the abdomen helps establish the diagnosis of acute pancreatitis if the diagnosis is equivocal based on clinical presentation or laboratory values. Other causes that mimic acute pancreatitis can be excluded.
- CT is not required in mild, self-limiting cases of acute pancreatitis.
- Contrast-enhanced CT is the gold standard for assessing pancreatic necrosis and other complications of acute pancreatitis.
- Imaging cannot reliably distinguish infected from sterile necrosis. Percutaneous image-guided interventions are helpful if there is suspicion of infection.
- Ultrasonography is helpful in assessing for gallstones and biliary dilatation.
- Gadolinium-enhanced MRI can be used as an alternative to CT for assessing pancreatic necrosis and complications of acute pancreatitis.
- MRCP can be used as a noninvasive alternative to ERCP for evaluation of choledocholithiasis and pancreatic ductal abnormalities.

#### **Key Points**

- Chronic alcohol consumption and gallstones are the leading causes of acute pancreatitis. In 20% of cases the cause may remain unclear.
- The clinical diagnosis of acute pancreatitis is supported by an elevation of the serum amylase and lipase levels in excess of three times the upper limit of normal.
- Appropriate terminology should be used in radiology reports when describing different "fluid collections" that occur in the setting of pancreatitis.
- Contrast-enhanced CT is not required in mild, self-limiting cases of acute pancreatitis.
- Contrast-enhanced CT is considered the gold standard in the assessment of pancreatic necrosis and complications of acute severe pancreatitis.
- The utility of ultrasonography in acute pancreatitis is limited to the evaluation of gallstones and biliary dilatation. Ultrasonography is not very helpful in evaluating pancreatic necrosis.
- MRI can be used as an alternative to CT for the assessment of pancreatic necrosis, especially if the risk for radiation exposure is an issue in younger patients.
- Imaging cannot reliably distinguish infected from sterile necrosis. Diagnostic aspiration under CT or ultrasound guidance is helpful to confirm or rule out infection.
- MRCP is a useful noninvasive method to assess for biliary stones and pancreatic ductal abnormalities.
- Urgent ERCP with sphincterotomy and stone extraction is recommended in cases of gallstone pancreatitis manifesting as cholangitis or biliary ductal obstruction.

#### SUGGESTED READINGS

- Balthazar EJ: Acute pancreatitis: assessment of severity with clinical and CT evaluation. *Radiology* 223:603–613, 2002.
- Banks PA: Practice guidelines in acute pancreatitis. *Am J Gastroenterol* 92:377–386, 1997.
- Fulcher AS, Turner MA: MR pancreatography: a useful tool for evaluating pancreatic disorders. *Radiographics* 19:5–24, 1999.

Saokar A, Rabinowitz CB, Sahani DV: Crosssectional imaging in acute pancreatitis. *Radiol Clin North Am* 45:447–460, 2007. Whiteophysical parentiation acute pancreatities

Whitcomb DC: Clinical practice: acute pancreatitis. *N Engl J Med* 354:2142–2150, 2006.

#### **REFERENCES**

- Whitcomb DC: Clinical practice: acute pancreatitis. *N Engl J Med* 354:2142–2150, 2006.
   Swaroop VS, Chari ST, Clain JE: Severe acute
- pancreatitis. JAMA 291:2865–2868, 2004.
- Bradley EL, 3rd: A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, GA, September 11-13, 1992. Arch Surg 128:586–590, 1993.
- Banks PA: A new classification system for acute pancreatitis. *Am J Gastroenterol* 89:151–152, 1994.
- Rosen MP, Sands DZ, Longmaid HE, 3rd, et al: Impact of abdominal CT on the management of patients presenting to the emergency department with acute abdominal pain. *AJR Am J Roentgenol* 174:1391–1396, 2000.
- Balthazar EJ: Acute pancreatitis: assessment of severity with clinical and CT evaluation. *Radiol*ogy 223:603–613, 2002.
- Saokar A, Rabinowitz CB, Sahani DV: Crosssectional imaging in acute pancreatitis. *Radiol Clin North Am* 45:447–460, 2007.
- Bradley EL, 3rd, Gonzalez AC, Clements JL, Jr: Acute pancreatic pseudocysts: incidence and implications. *Ann Surg* 184:734–737, 1976.

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- 9. Siegelman SS, Copeland BE, Saba GP, et al: CT of fluid collections associated with pancreatitis. *AJR Am J Roentgenol* 134:1121–1132, 1980.
- Yamamura M, Iki K: Mediastinal extension of a pancreatic pseudocyst. *Pancreatology* 4:90, 2004.
- Salvo AF, Nematolahi H: Distant dissection of a pancreatic pseudocyst into the right groin. *Am J Surg* 126:430–432, 1973.
- Buchler MW, Gloor B, Muller CA, et al: Acute necrotizing pancreatitis: treatment strategy according to the status of infection. *Ann Surg* 232:619–626, 2000.
- Buchler P, Reber HA: Surgical approach in patients with acute pancreatitis: is infected or sterile necrosis an indication—in whom should this be done, when, and why? *Gastroenterol Clin North Am* 28:661–671, 1999.
- 14. Shankar S, van Sonnenberg E, Silverman SG, et al: Imaging and percutaneous management of acute complicated pancreatitis. *Cardiovasc Intervent Radiol* 27:567–580, 2004.
- Balthazar EJ, Robinson DL, Megibow AJ, et al: Acute pancreatitis: value of CT in establishing prognosis. *Radiology* 174:331–336, 1990.
- Balthazar EJ, Ranson JH, Naidich DP, et al: Acute pancreatitis: prognostic value of CT. *Radiology* 156:767–772, 1985.

- Fishman EK, Soyer P, Bliss DF, et al: Splenic involvement in pancreatitis: spectrum of CT findings. AJR Am J Roentgenol 164:631–635, 1995.
- Arita T, Matsunaga N, Takano K, et al: Hepatic perfusion abnormalities in acute pancreatitis: CT appearance and clinical importance. *Abdom Imaging* 24:157–162, 1999.
- Mortele KJ, Mergo PJ, Taylor HM, et al: Renal and perirenal space involvement in acute pancreatitis: spiral CT findings. *Abdom Imaging* 25:272–278, 2000.
- Gardner A, Gardner G, Feller E: Severe colonic complications of pancreatic disease. J Clin Gastroenterol 37:258–262, 2003.
- 21. Vujic I: Vascular complications of pancreatitis. *Radiol Clin North Am* 27:81–91, 1989.
- Burke JW, Erickson SJ, Kellum CD, et al: Pseudoaneurysms complicating pancreatitis: detection by CT. *Radiology* 161:447–450, 1986.
- Ward J, Chalmers AG, Guthrie AJ, et al: T2-weighted and dynamic enhanced MRI in acute pancreatitis: comparison with contrast enhanced CT. *Clin Radiol* 52:109–114, 1997.
- 24. Saifuddin A, Ward J, Ridgway J, et al: Comparison of MR and CT scanning in severe acute

pancreatitis: initial experiences. *Clin Radiol* 48:111–116, 1993.

- Morgan DE, Baron TH, Smith JK, et al: Pancreatic fluid collections prior to intervention: evaluation with MR imaging compared with CT and US. *Radiology* 203:773–778, 1997.
- Fulcher AS, Turner MA: MR pancreatography: a useful tool for evaluating pancreatic disorders. *Radiographics* 19:5–24, 1999.
- Matos C, Cappeliez O, Winant C, et al: MR imaging of the pancreas: a pictorial tour. *Radiographics* 22:e2, 2002.
- Fukukura Y, Fujiyoshi F, Sasaki M, et al: Pancreatic duct: morphologic evaluation with MR cholangiopancreatography after secretin stimulation. *Radiology* 222:674–680, 2002.
- Arvanitakis M, Delhaye M, De Maertelaere V, et al: Computed tomography and magnetic resonance imaging in the assessment of acute pancreatitis. *Gastroenterology* 126:715–723, 2004.
- Banks PA: Practice guidelines in acute pancreatitis. Am J Gastroenterol 92:377–386, 1997.

# **Imaging of Chronic Pancreatitis**

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## **Etiology**

Chronic pancreatitis is defined as an ongoing prolonged inflammatory disease characterized by progressive irreversible structural changes resulting in permanent loss of endocrine and exocrine function. The Cambridge classification of 1983 acknowledged that chronic pancreatitis is typically associated with abdominal pain but occasionally can be painless and may recur.<sup>1</sup> According to the revised pancreatic classification of pancreatitis from the Marseille symposium of 1984, acute and chronic pancreatitis are very different diseases and acute pancreatitis only rarely leads to chronic pancreatitis.<sup>2</sup>

Prolonged alcohol abuse is the most common cause (70%) of chronic pancreatitis in the United States. Other causes are familial occurrence with hyperlipidemia, hyperparathyroidism, cystic fibrosis, trauma, cholelithiasis, and pancreas divisum.<sup>3</sup> The familial form of pancreatitis, hereditary pancreatitis, is thought to be inherited in an autosomal dominant fashion with variable penetrance.

Of patients with chronic pancreatitis, 30% to 40% have no apparent underlying cause and are considered to have idiopathic chronic pancreatitis.<sup>4</sup>

Patients with idiopathic chronic pancreatitis have been noted to cluster in a younger group (peak incidence, 15 to 30 years of age) and an older group (peak incidence, 50 to 70 years of age). Autoimmune chronic pancreatitis is an increasingly recognized condition frequently coexisting with other autoimmune diseases such as Sjögren's syndrome and primary sclerosing cholangitis.<sup>5</sup> An independent effect of tobacco smoking on the development of chronic pancreatitis has been suggested by several epidemiologic studies.<sup>6</sup> In certain parts of developing regions such as Africa, India, and South America a particular type of chronic pancreatitis occurs in children and adolescents. It is thought to be caused by dietary toxins and micronutrient deficiencies and results in tropical pancreatitis endemic in these regions (Table 49-1).<sup>7</sup>

## **Prevalence and Epidemiology**

Because of the varied clinical manifestation, recent increase in alcohol consumption, and improved sensitivity of diagnostic tests, the true prevalence of chronic pancreatitis is unknown, although estimates range from 0.04% to 5%.<sup>4</sup> Earlier reports from Copenhagen, the United States, and Mexico City are nearly the same, with the incidence of chronic pancreatitis reported as 4 cases per year per 100,000 inhabitants. Several retrospective studies have reported an annual incidence of 3 to 9 cases per year per 100,000 population.<sup>8</sup>

## **Clinical Presentation**

Chronic abdominal pain is the most frequent presentation in most patients with alcohol-induced disease.<sup>9</sup> The most common

site of pain is the epigastrium, but some individuals report pain in the left or right upper quadrants that radiates to the back. The pain is described as severe, deep, and penetrating and is characteristically relieved by assuming a stooped or jack-knife posture. In some patients there is spontaneous remission of pain as organ failure sets in (burnout).<sup>10</sup>

Exacerbation of pain may be associated with nausea and vomiting. Two patterns of pain have been described in chronic pancreatitis, as follows<sup>11</sup>:

- *Type A:* Short relapsing episodes lasting days to weeks, separated by a pain-free interval
- *Type B:* Prolonged, severe, unrelenting pain

As the disease advances, approximately one fifth of patients present without pain but with pancreatic exocrine (fat and vitamin malabsorption) or endocrine failure, manifesting as steatorrhea, diabetes mellitus, or weight loss.<sup>12,13</sup>

Structural complications of chronic pancreatitis such as pseudocysts and stricture of the common bile duct (CBD) in the pancreatic head are frequently seen. Thrombosis of the splenic or the portal vein with gastric or esophageal varices, arterial pseudoaneurysm formation, pancreatic abscess, ascites, and duodenal obstruction are seen less frequently.

## Pathophysiology and Pathology

The pathophysiology of chronic pancreatitis includes chronic inflammation, irregular and patchy loss of acinar and ductal tissue, glandular atrophy, duct changes, and fibrosis. The pathogenesis of chronic pancreatitis is not well elucidated. Several theories have been developed for alcoholic pancreatitis.

- 1. *Stone and duct obstruction:* Disturbance of acinar and ductular function with formation of intraductal protein plugs, stones, and duct obstruction with subsequent inflammation and fibrosis.
- 2. *Toxic metabolic theory:* Results in early- and late-phase inflammatory responses and production of profibrotic cells, including stellate cells, with progressive lipid deposition, periacinar fibrosis, and inflammatory and fibrotic changes.
- 3. *Oxidative stress theory:* Excess free radicals ultimately result in peroxidation of lipid components of the membrane within the pancreatic acinar cell leading to mast cell degranulation, platelet activation, and an inflammatory response.<sup>14</sup>
- 4. *Necrosis-fibrosis sequence:* Chronic contact of the stones with duct epithelial cells produces ulceration and scarring. Eventually, atrophy and fibrosis result from chronic obstruction of the acini. The necrosis-fibrosis theory emphasizes that acute and chronic pancreatitis represent a spectrum of disease. New research and discoveries about hereditary pancreatitis have supported the necrosis-fibrosis sequence.<sup>15</sup>

49-1 Classification S				
Classification	Risk Factors	Comments		
Toxic-metabolic (70%)	Alcoholic Tobacco smoking Hypercalcemia Hyperlipidemia Chronic renal failure Medications	Associated hyperparathyroidism Example: Phenacetin abuse		
	Toxins	Example: Organotin compounds		
Idiopathic (20%)	Early onset Late onset Tropical Other	Tropical calcific and fibrocalculous pancreatic diabetes		
Others (10%)				
Genetic	Autosomal dominant Autosomal recessive/modifier genes	Cationic trypsinogen gene CFTR mutations, SPINK1 mutations, cationic trypsinogen, alpha-1 antitrypsin deficiency (possible)		
Autoimmune	Isolated autoimmune chronic pancreatitis Syndromic	Sjögren's syndrome, inflammatory bowel disease, primary biliary cirrhosis, sclerosing cholangitis		
Recurrent and severe acute pancreatitis	Postnecrotic Recurrent acute pancreatitis Vascular disease/ischemic Radiation injury	Severe acute pancreatitis		
Obstructive	Pancreas divisum Sphincter of Oddi disorders Duct obstruction Periampullary Duodenal wall cysts Posttraumatic Pancreatic duct scars	Not universally accepted <i>Example</i> : Tumor		

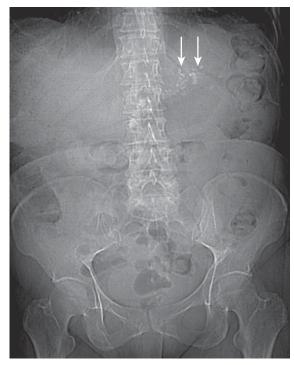
## Imaging

### RADIOGRAPHY

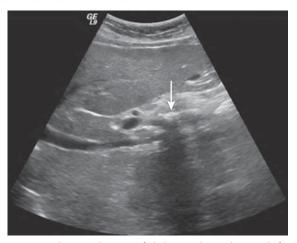
On abdominal radiographs calcifications can be found in 30% to 70% of patients at presentation, which suggests the diagnosis with 95% confidence. Pancreatic calcification is nearly 10% specific but poorly sensitive (30% to 70%) for the diagnosis of chronic pancreatitis. It is important to differentiate parenchymal or ductal calcification from calcified pancreatic cysts or occasionally from heavily calcified peripancreatic vasculature (Figure 49-1).

#### **ULTRASONOGRAPHY**

Transabdominal ultrasonography is a noninvasive, easily accessible imaging modality for evaluation of the pancreas. However, it is limited in its evaluation of the pancreas owing to overlying bowel gas and patient body habitus and is operator dependent. Most ultrasound findings of chronic pancreatitis are not sensitive or specific for the diagnosis. Early diagnosis of chronic pancreatitis is difficult. The size of the gland may be normal, enlarged, or reduced, depending on the amount of active inflammation and fibrosis. Other ultrasound features include altered echotexture of the gland, parenchymal and ductal calcifications, pancreatic duct dilatation and irregularity, biliary dilatation, and, occasionally, pseudocysts.



**Figure 49-1** Diffuse coarse irregular calcification (*arrows*) in the upper abdomen in the expected location of the pancreas suggestive of chronic pancreatitis.



**Figure 49-2** Ultrasound image of abdomen shows dense calcification within pancreatic body (*arrow*) with posterior acoustic shadowing consistent with chronic calcific pancreatitis.

Pancreatic calcifications are a classic ultrasound finding and appear as multiple punctate, hyperechoic foci, which may be focal or distributed throughout the gland, seen in 40% of patients (Figure 49-2).<sup>16</sup> Pancreatic calcification is believed to be the most specific ultrasound finding for chronic pancreatitis.<sup>17</sup> As the disease progresses, the pancreatic parenchyma demonstrates a heterogeneous echotexture with areas of increased and decreased echogenicity. Areas of increased echogenicity result from fibrosis and calcification, whereas areas of decreased echogenicity result from inflammation. The pancreas may be normal in size, enlarged, or atrophic depending on the amount of fibrosis and active inflammation. Most commonly, the gland atrophies in advanced disease. Ultrasound has been described as 97% sensitive for pseudocysts larger than 3 cm. Pancreatic pseudocysts are reported in 25% to 40% of patients.<sup>16</sup> Doppler ultrasonography is useful for vascular complications such as portal and splenic vein thrombosis, varices, and splenic artery pseudoaneurysm.

#### ENDOSCOPIC ULTRASONOGRAPHY

Endoscopic ultrasonography was introduced in the early 1980s, and with advances in its technology it has emerged as a frontline diagnostic tool for detection of early chronic pancreatitis. The proximity of the pancreas to the stomach and duodenum allows acquisition of high-resolution imaging, thus overcoming the limitations of transabdominal ultrasonography—that is, bowel gas and body habitus. The normal pancreas has homogeneous echogenicity with fine granularity and reticulation and increased echogenicity relative to the liver. The margins are smooth without side-branch ectasia. The average pancreatic duct diameter in the body is 1.9 mm, and normal side branches are visible in 32% of patients.

The parenchymal abnormalities demonstrated with endoscopic ultrasonography are heterogeneous echogenicity with hyperechoic foci, prominent interlobular septa appearing as echogenic strands (secondary to fibrosis), hypoechoic foci (1 to 3 mm) resulting from small cystic changes in the parenchyma, lobular outer gland margins, and large echo-poor cavities (>5 mm). The ductal abnormalities include main pancreatic duct (MPD) dilatation more than 3 mm, irregularity, intra-

TABLE <b>49-2</b>	Endoscopic Ultrasound Features of Chronic Pancreatitis		
Paren	chymal Features	<b>Ductal Features</b>	
Gland atrophy		Narrowing	
Hyperechoic foci		Dilation	
Hyperechoic stranding		Irregularity	
Cysts		Calculi	
Lobula	arity	Side branch dilation Hyperechoic walls	

From Stevens T, Conwell DL: Chronic pancreatitis. In Ginsberg GG, Ahmad NA, editors: The clinician's guide to pancreaticobiliary disorders, Thorofare, NJ, 2006, Slack, p 195.

ductal echogenic foci, hyperechoic margins of the pancreatic duct, side-branch ectasia, and intraductal calculi (Table 49-2).<sup>18</sup>

#### COMPUTED TOMOGRAPHY

Contrast-enhanced computed tomography (CT) of the abdomen is the imaging modality of choice in the diagnosis of chronic pancreatitis. The CT features of chronic pancreatitis are scattered coarse parenchymal calcifications, intraductal calcifications, ductal dilatation, and parenchymal atrophy.<sup>18</sup> In a retrospective study by Luetmer and colleagues,<sup>19</sup> pancreatic ductal dilatation was reported in 68%, parenchymal atrophy in 54%, and pancreatic calcification in 50%.

Dilatation of the MPD and side branch ducts is the most common feature of chronic pancreatitis. Ductal dilatation can be smooth, beaded, or irregular; no single pattern is predominant, and more than one pattern can be seen in the same gland. Ductal dilatation is nonspecific as an isolated finding because it is also seen with distal CBD cholangiocarcinoma and pancreatic and ampullary carcinoma.

Altered glandular size is another key finding in chronic pancreatitis. Parenchymal atrophy was seen in 54% in a retrospective study conducted by Luetmer and colleagues.<sup>19</sup> Parenchymal atrophy is frequently seen in association with ductal dilatation. Most patients with exocrine insufficiency have parenchymal atrophy or ductal dilatation.<sup>17</sup> Atrophy, however, is a less sensitive finding in the elderly, in whom it may represent a normal aging process. Occasionally, either focal or diffuse enlargement of the pancreas is present.

A more reliable and the most specific sign of chronic pancreatitis is pancreatic calculi.<sup>19</sup> Intraductal calcifications result in obstruction, ductal ectasia, and periductal fibrosis. Intraductal calculi range in size from microscopic to greater than 1 cm in diameter. Calcifications result from inspissation of pancreatic secretions within the duct and subsequent deposition of calcium carbonate on the intraductal protein plugs. Parenchymal calcifications vary in size and can be fine and stippled to large and coarse. The distribution may be focal, involving only one portion of the gland or diffuse throughout the gland. The head of the pancreas is more prominently involved than the tail.<sup>20</sup> Pancreatic calcifications, when present, are virtually diagnostic of chronic pancreatitis and occur late in the course of the disease. However, in hereditary pancreatitis, calculi are seen early in the course of disease. They are large and rounded, and in the dilated MPD they tend to be arranged in a linear pattern.<sup>21</sup>

CT also has the advantage of detecting complications of chronic pancreatitis. Fluid collections are seen in 30% and may be within the pancreas or adjacent to the pancreas. They may be seen in the retroperitoneum and rarely in distant sites. Extrapancreatic fluid collections are mostly seen in the lesser sac or anterior pararenal spaces. Most fluid collections in chronic pancreatitis are well-encapsulated mature pseudocysts that are present in 25% of cases. Ductal dilatation and intraductal calculi favor chronic pancreatitis as the underlying cause. Unencapsulated fluid collections are seen only with associated superimposed acute pancreatitis. Most pseudocysts resolve spontaneously but can be complicated by hemorrhage, superinfection, and spontaneous rupture.

Dilatation of the MPD is strongly associated. The dilated CBD demonstrates smooth gradual tapering as opposed to the abrupt cutoff shown in malignancy. It is often associated with an inflammatory mass in the pancreatic head.

Arterial pseudoaneurysms (pancreatic duodenal and splenic arteries) and splenic vein thrombosis are the most frequently encountered vascular complications. Pseudoaneurysms are seen near the pancreatic head and splenic hilum. They are caused by destruction of the vascular wall by pancreatic inflammation and appear as rounded areas isoattenuating to vascular structures. They also can be diagnosed with magnetic resonance imaging (MRI) and pulsed Doppler ultrasonography without intravenous administration of a contrast agent.<sup>3</sup> The attenuation is similar to that of hematoma on noncontrast CT.<sup>17</sup> Chronic pancreatitis is also associated with splenic, portal, and superior mesenteric vein thrombosis and accounts for 65% of cases of splenic vein thrombosis. Thrombus is seen as a filling defect in

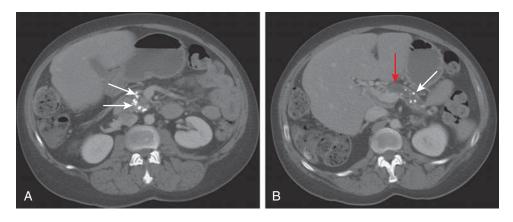
the vein. Venous thrombosis can result in prehepatic portal hypertension with venous collaterals and gastric varices.

Pancreaticopleural fistulas are associated with chronic alcoholic pancreatitis. Patients present with chest symptoms more often than abdominal symptoms. Pancreatic secretions from a ruptured pancreatic duct dissect through the aortic and esophageal hiatus or through the diaphragm and gain access to the pleural cavity and mediastinum.<sup>18</sup> CT and MRI with MR cholangiopancreatography (MRCP) can depict the fistula and ductal anatomy in these patients. Endoscopic retrograde cholangiopancreatography (ERCP) combined with CT can delineate the cause of recurrent pleural effusion and rare complications such as pancreaticobronchial fistula (Figures 49-3 to 49-8).

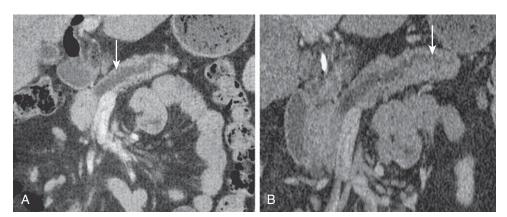
#### ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

ERCP is performed by cannulation of the ampulla of Vater and ingestion of iodinated contrast. ERCP allows visualization of the pancreatic ductal system, including the side branches, and is often considered the gold standard for defining the disease in its early stages.<sup>22</sup>

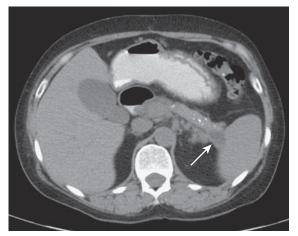
The normal MPD dimension varies between 25 and 95 mm in length. It has the greatest diameter in the pancreatic head, with progressive narrowing toward the tail. The average normal diameter is 3 to 4 mm in the head, 2 to 3 mm in the body, and 1 to 2 mm in the tail. There is progressive increase in the overall diameter with aging as a result of parenchymal atrophy. Normal physiologic narrowing is seen at the junction of the major and minor ducts in the pancreatic head and in the



**Figure 49-3** Chronic pancreatitis. A and B, Computed tomography image shows scattered coarse calcifications (*white arrows*) throughout the pancreas with dilatation of the main pancreatic duct (*red arrow*).



**Figure 49-4** Known cystic fibrosis. A and B, Computed tomography image shows chronic pancreatitis changes with duct dilatation (*arrow*, A) and stricture (*arrow*, B).



**Figure 49-5** Computed tomography image shows chronic pancreatitis changes with a stable pseudocyst in the pancreatic tail (*arrow*).



**Figure 49-6** Computed tomography image shows features of acuteon-chronic pancreatitis with calcification (*arrow*) and small pseudocyst (*arrowhead*) in the pancreatic tail.

and subsequently in the MPD. The ERCP features of chronic pancreatitis include dilatation, irregularity, clubbing, and stenosis of the side branches as well as opacification of small cavities.<sup>23</sup> The MPD demonstrates diffuse duct dilatation, mural irregularity, loss of normal tapering, and multiple segmental areas of stenosis. ERCP also may demonstrate pseudocysts communicating with the main duct. The distal CBD may show elongated smooth compression.<sup>23</sup> Solitary stricture of the MPD caused by pseudocyst is shorter, is smooth, and shows gradual tapering (Table 49-3 and Figure 49-9).<sup>24</sup>

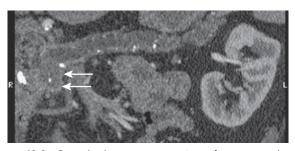
#### MAGNETIC RESONANCE IMAGING

Recent advances in MR technology have contributed significantly to high-resolution noninvasive evaluation of the pancreatic parenchyma before and after intravenous administration of gadolinium, evaluation of the ducts using MRCP with or without secretin administration, and evaluation of pancreatic exocrine function by measuring duodenal fluid volume after secretin administration.

The normal pancreas shows maximum enhancement during the arterial phase after intravenous gadolinium. There is rapid washout during the portal venous and delayed phase when it appears isointense to the liver.<sup>25</sup>

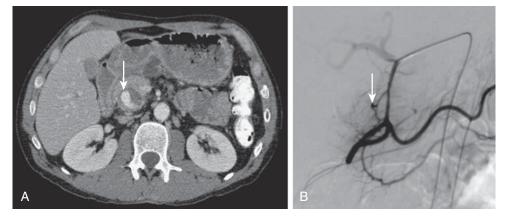
Because of its excellent soft tissue contrast, MRI is sensitive in detecting signal intensity and enhancement abnormalities in early chronic pancreatitis before morphologic changes occur.<sup>26</sup>

Early MRI findings of chronic pancreatitis include a low signal intensity of the pancreas on T1-weighted fat-suppressed images owing to decreased proteinaceous fluid content from chronic inflammation and fibrosis.<sup>26</sup> Also noted is diminished



**Figure 49-8** Curved planar reconstruction of pancreas showing chronic pancreatitis changes with a mass in the head of the pancreas (*arrows*).

Figure 49-7 Gastroduodenal artery pseudoaneurysm in a middle-aged man with chronic pancreatitis and upper gastrointestinal tract hemorrhage. A, Contrast-enhanced computed tomography arteriogram demonstrates pseudoaneurysm (*arrow*) probably originating from gastroduodenal artery. B, Arteriogram of the gastroduodenal artery demonstrates a pseudoaneurysm (*arrow*) originating from the gastroduodenal artery.





**Figure 49-9** Endoscopic retrograde cholangiopancreatography shows diffuse irregular dilatation of the main pancreatic duct secondary to chronic pancreatitis.

## TABLE Classification of Disease Severity on 49-3 Endoscopic Retrograde Pancreatography

L			
	Findings	MPD	Side Branches
	Equivocal	Normal	<3 side branches abnormal
	Mild	Normal	≥3 side branches abnormal
	Moderate	Abnormal	>3 side branches abnormal
	Marked	Abnormal	Moderate disease and one of the following: A large cavity, ductal obstruction, filling defects, severe dilatation, or irregularity

MPD, Main pancreatic duct.

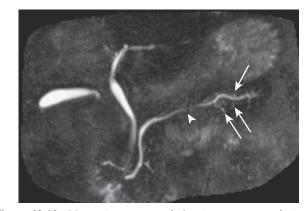
heterogeneous enhancement of the pancreas in the arterial phase and progressive enhancement in the delayed phases.<sup>26</sup> Dilatation of the side branches also occurs. However, CT may demonstrate a normal appearance and enhancement of the pancreas even in advanced disease.

Later in the disease there is evidence of parenchymal atrophy; pseudocyst formation; dilatation, irregularity, and beading of the MPD; and intraductal and parenchymal calcifications.

#### Magnetic Resonance Cholangiopancreatography

MRCP is an excellent noninvasive imaging technique that uses a heavily T2-weighted pulse sequence to selectively display static or slow-moving fluid-filled structures as areas of high intensity.

**Technique.** Three-dimensional (3D) MRCP sequences are obtained using fast recovery sequences or steady-state free precession in suspended respiration or with respiratory gated techniques. The near-isotropic volume data from 3D MRCP are processed using maximum intensity projection (MIP) or volume-rendered technique to display the pancreatic duct and biliary tree (Table 49-4 and Figure 49-10).



**Figure 49-10** Magnetic resonance cholangiopancreatography image from a middle-aged patient with recurrent pancreatitis shows mild prominence of the side ductal branches (*arrows*) and decreased caliber of the long ductal segment (*arrowhead*) suggestive of changes of chronic pancreatitis.

TABLE<br/>49-4Routinely Used Parameters for Two-<br/>Dimensional and Three-Dimensional Magnetic<br/>Resonance Cholangiopancreatography

Technique	TE (ms)	TR	Thickness (mm)
2D MRCP			
Oblique radial SSFSE T2 weighted (14 slices)	500	Minimum	40
Oblique right anterior SSFSE T2 weighted	160	Minimum	5
Oblique left anterior SSFSE T2 weighted	160	Minimum	5
3D MRCP			
3D MRCP fat saturated	500-600	4000	1.4

2D, Two-dimensional; 3D, three-dimensional; MRCP, magnetic resonance cholangiopancreatography; SSFSE, single-shot fast spin echo; TE, echo time; TR, repetition time.

MRCP demonstrates side-branch abnormalities, dilatation and irregularity of the MPD, strictures, and pseudocysts. Intraductal calcifications are seen as filling defects surrounded by intraductal fluid. It clearly shows the site of obstruction and the upstream dilatation of the MPD, and it is highly accurate in the diagnosis of pancreas divisum.<sup>27</sup> In advanced disease, the beaded MPD with marked dilated side branches may result in a "chain of lakes" appearance.<sup>28</sup>

MRCP demonstrates other abnormalities of the duct, including clubbing, sacculation, and ectasia of the side radicles; strictures; ductal obstruction; pseudocysts; and fistula formation. It also has the advantage of demonstrating biliary dilatation secondary to inflammatory stricture or compression of the bile duct.<sup>29</sup>

MRCP has a sensitivity of 60% to 80% and a high specificity of 95.5% to 100% in the diagnosis of filling defects.<sup>30</sup> The images can be viewed on a modern workstation as rotational MIP images, and it is possible to differentiate intraductal lesions within a dilated pancreatic duct from partial volume effects.

#### Functional and Secretin Magnetic Resonance Cholangiopancreatography

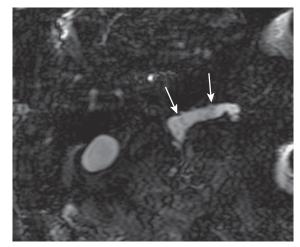
A pharmaceutical agent (SecreFlo, Repligen, Waltham, MA) is now available that allows secretin functional MRCP and exocrine evaluation of the pancreas.

Technique. Intravenous administration of 1 mL of secretin per 10 kg of body weight is followed by thick-slab MRCP in the coronal plane repeated every 15 to 30 seconds for 10 to 15 minutes. The effect of secretin stimulation starts almost immediately after intravenous administration. Measurable dilatation of the MPD is observed mostly within 2 to 6 minutes of secretin injection.<sup>31</sup> Approximately 10 minutes after injection, the caliber of the MPD returns to baseline value as the pancreatic juice flows out through the papilla and progressively fills the duodenum. MRCP after secretin administration shows an increase in caliber of the pancreatic duct in patients with chronic pancreatitis. The normal progressive tapering of the duct toward the tail is lost in patients with severe chronic pancreatitis, and secretin improves the detection of this alteration in duct morphology. The time taken to reach peak pancreatic duct diameter after secretin administration is longer in patients with chronic pancreatitis than in normal patients. Acinar filling is a term used to describe progressive increase in signal intensity of the pancreatic parenchyma and may be a sign of early chronic pancreatitis.32

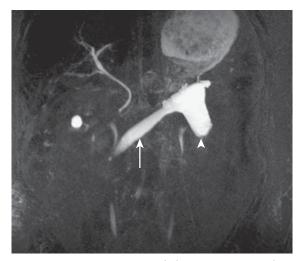
Reports have suggested better visualization of the pancreatic duct after intravenous administration of secretin. In addition, secretin MRCP is also useful for functional evaluation of exocrine pancreas based on quantification of duodenal filling, which with chronic pancreatitis is decreased<sup>31,33</sup> (Figures 49-11 to 49-14).

## POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

<sup>18</sup>Fluorodeoxyglucose (FDG)-labeled positron emission tomography (PET) combined with CT is increasingly being used to differentiate benign from malignant masses. Maldonado and associates<sup>34</sup> described a sensitivity of 100%, specificity of 91%, negative predictive value of 100%, positive predictive value of 96%, and accuracy of 97% in detection of pancreatic lesions.<sup>34</sup>

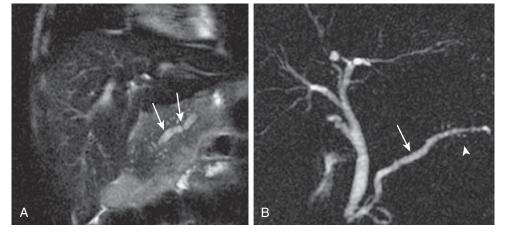


**Figure 49-11** Magnetic resonance cholangiopancreatography image shows diffuse pancreatic duct dilatation related to changes of chronic pancreatitis with multiple filling defects (*arrows*) within the duct representing intraductal calculi.



**Figure 49-12** Magnetic resonance cholangiopancreatography image from a patient with chronic pancreatitis shows dilated pancreatic duct *(arrow)* and pseudocyst *(arrowhead)* communicating through pancreatic duct fistula.

Figure 49-13 Secretin magnetic resonance cholangiopancreatography. A, Dilated irregular duct with alternating areas of dilatations and narrowing (arrows) is seen. B, Early side branch dilatation (arrow and arrowhead) is seen in another case suggestive of changes secondary to chronic pancreatitis.



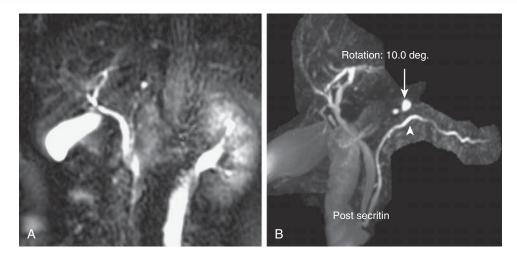
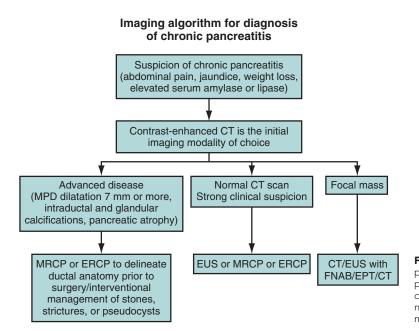


Figure 49-14 Secretin magnetic resonance cholangiopancreatography. A, On pre-secretin view the relation of the cystic structure to the main pancreatic duct is not well demonstrated. B, On post-secretin MRCP the relationship between the pancreatic duct (arrowhead) and pseudocyst (arrow) is well seen and there is no communication of pseudocyst to main duct.



**Figure 49-15** Imaging algorithm for diagnosis of chronic pancreatitis. *CT*, Computed tomography; *EPT*, endoscopic papillotomy; *ERCP*, endoscopic retrograde cholangiopancreatography; *EUS*, endoscopic ultrasound; *FNAB*, fine-needle aspiration biopsy; *MPD*, main pancreatic duct; *MRCP*, magnetic resonance cholangiopancreatography.

FDG-PET/CT also can be used to distinguish pancreatic carcinoma from a focal inflammatory pancreatic mass (Table 49-5).

#### **IMAGING ALGORITHM**

See Figure 49-15 and Table 49-6.

#### **Classic Signs**

- Coarse, focal, or diffuse calcifications
- Ductal dilatation
- Pancreatic atrophy
- Pseudocysts

## TABLESensitivity and Specificity of Various49-5Imaging Modalities

Modality	Sensitivity (%)	Specificity (%)
Plain radiographs	30-70	100
Ultrasonography	60-70	80-90
Endoscopic ultrasonography	97	60
Contrast-enhanced computed tomography	75-90	84-100
MRI/MRCP	85	100
ERCP	71-93	89-100

ERCP, Endoscopic retrograde cholangiopancreatography; MRI/MRCP, magnetic resonance imaging/magnetic resonance cholangiopancreatography.

TABLE         Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Chronic Pancreatitis			
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Not sensitive	
СТ		Radiation	
MRI		Claustrophobia and patient motion High cost	Calcifications difficult to visualize
Ultrasonography		Limited by bowel gas and obesity Operator dependent	Difficulty in differentiating small foci of calcification from small cysts
Nuclear medicine	NA	NA	
PET/CT	NA	Radiation High cost	

CT, Computed tomography; NA, not applicable; PET, positron emission tomography.

## **Differential Diagnosis**

Common upper abdominal pathologic processes include acute pancreatitis, acute cholecystitis, choledocholithiasis, pancreatic tumor, and peptic ulcer disease. A finding on plain radiography and CT of pancreatic calcifications is highly suggestive of chronic pancreatitis. The cardinal CT findings of chronic pancreatitis include MPD dilatation, calcifications, and pancreatic atrophy. Pseudocysts, venous thrombosis, and pseudoaneurysms also can be detected with CT.

Evaluation of pancreatic duct and parenchyma with contrastenhanced MRI and MRCP also offers differentiation of inflammatory and neoplastic masses. Endoscopic ultrasonography has emerged as a first-line modality for evaluation of early chronic pancreatitis and cystic and mass lesions.

## Treatment

### MEDICAL TREATMENT

The medical management of chronic pancreatitis consists of management of abdominal pain and complications and includes the following:

- Analgesics
- Abstinence from alcohol and tobacco
- Nerve blockade
- Pancreatic enzymes with proton-pump inhibitors or histamine-2 blockers
- Insulin
- · Corticosteroids in autoimmune pancreatitis
- Vitamin supplements (A, D, E, K, and B<sub>12</sub>)
- Antidepressants and psychiatric counseling for nonvisceral pain

#### SURGICAL TREATMENT

#### Endoscopy

Endoscopic duct decompression techniques include pancreatic sphincterotomy, removal of intraductal calculi, and placement

of stents. Transampullary or transgastric drainage of pseudocysts can be done.

#### **Decompression Procedures**

Large or symptomatic pseudocysts can be drained through cystenterostomy. Lateral pancreaticojejunostomy may be necessary in disease of the large duct. Sphincterotomy or sphincteroplasty may be needed.

#### Resection

Distal pancreatectomy is done if the disease is confined to the tail of the gland. Otherwise, total pancreatectomy is performed. Whipple's procedure is also an option.

#### What the Referring Physician Needs to Know

- Contrast-enhanced CT is the initial imaging modality of choice.
- Endoscopic ultrasonography is a first-line tool in early chronic pancreatitis and evaluation of cystic and solid masses.
- Contrast-enhanced MRI and MRCP are excellent for noninvasive evaluation of parenchyma, ductal system, and complications of chronic pancreatitis.
- Chronic pancreatitis can manifest as a focal inflammatory mass mimicking pancreatic carcinoma.

#### **Key Points**

- Prolonged alcohol abuse is evident with calcifications, ductal dilatation, atrophy, and a focal mass; carcinoma may be present.
- Imaging modalities of benefit include contrast-enhanced CT, endoscopic ultrasonography, MRI, and secretin MRCP.

#### REFERENCES

 Banks PA: Classification and diagnosis of chronic pancreatitis. J Gastroenterol 42(Suppl 17):148–151, 2007. 2. Singer MV, Gyr K, Sarles H: Revised classification of pancreatitis. Report of the Second International Symposium on the Classification of Pancreatitis in Marseille, France, March 28-30, 1984. *Gastroenterology* 89:683-685, 1985.

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- Lee JK, Sagel SS, Stanley RJ, et al, editors: Computed body tomography with MRI correlation, ed 4, Philadelphia, 2003, Lippincott Williams & Wilkins.
- 4. Steer ML, Waxman I, Freedman S: Chronic pancreatitis. *N Engl J Med* 333:1482–1492, 1995.
- Kim KP, Kim MH, Song MH, et al: Autoimmune chronic pancreatitis. *AJR Am J Roentgenol* 99:1605–1616, 2004.
- Lin Y, Tamakoshi A, Hayakawa T, et al: Cigarette smoking as a risk factor for chronic pancreatitis: a case-control study in Japan. Research Committee on Intractable Pancreatic Diseases. *Pancreas* 21:109–114, 2000.
- Layer P, Singer MV: Non-alcoholic–related etiologies in chronic pancreatitis. In Beger HG, Buchler M, Ditschuneit H, et al, editors: *Chronic pancreatitis*, Berlin, 1990, Springer Verlag, pp 35–40.
- Otsuki M: Chronic pancreatitis in Japan: epidemiology, prognosis, diagnostic criteria, and future problems. *J Gastroenterol* 38:315–326, 2003.
- Layer P, Yamamoto H, Kalthoff L, et al: The different courses of early- and late-onset idiopathic and alcoholic chronic pancreatitis. *Gastroenterology* 107:1481–1487, 1994.
- Warshaw AL, Banks PA, Fernandez-Del Castillo C: AGA technical review: treatment of pain in chronic pancreatitis. *Gastroenterology* 115:765– 776, 1998.
- Ammann RW, Muellhaupt B: The natural history of pain in alcoholic chronic pancreatitis. *Gastroenterology* 116:1132–1140, 1999.
- Haaber AB, Rosenfalck AM, Hansen B, et al: Bone mineral metabolism, bone mineral density, and body composition in patients with chronic pancreatitis and pancreatic exocrine insufficiency. *Int J Pancreatol* 27:21–27, 2000.
- 13. Malka D, Hammel P, Sauvanet A, et al: Risk factors for diabetes mellitus in chronic

pancreatitis. *Gastroenterology* 119:1324–1332, 2000.

- 14. Braganza JM: The pathogenesis of chronic pancreatitis. *Q J Med* 89:243–250, 1996.
- Schneider A, Whitcomb DC: Hereditary pancreatitis: a model for inflammatory diseases of the pancreas. *Best Pract Res Clin Gastroenterol* 16: 347–363, 2002.
- Alpern MB, Sandler MA, Kellman GM, et al: Chronic pancreatitis: ultrasonic features. *Radiology* 155:215–219, 1985.
- Remer EM, Baker ME: Imaging of chronic pancreatitis. *Radiol Clin North Am* 40:1229–1242, 2002.
- Siddiqi AJ, Miller F: Chronic pancreatitis: ultrasound, computed tomography, and magnetic resonance imaging features. *Semin Ultrasound CT MR* 28:384–394, 2007.
- Luetmer PH, Stephens DH, Ward EM: Chronic pancreatitis: reassessment with current CT. *Radiology* 171:353–357, 1989.
- Lesniak RJ, Hohenwalter MD, Taylor AJ: Spectrum of causes of pancreatic calcifications. *AJR Am J Roentgenol* 178:79–86, 2002.
- 21. Kattwinkel J, Lapey A, Di Sant'Agnese PA, et al: Hereditary pancreatitis: three new kindreds and a critical review of the literature. *Pediatrics* 51:55–69, 1973.
- Clain JE, Pearson RK: Diagnosis of chronic pancreatitis. Is a gold standard necessary? Surg Clin North Am 79:829–845, 1999.
- Miller F, Keppke AL, Balthazar E: Pancreatitis. In Laufer I, editor: *Textbook of gastrointestinal radiology*, vol 2, ed 3, Philadelphia, 2007, WB Saunders, pp 1767–1795.
- 24. Axon ATR, Classen M, Cotton PB, et al: Pancreatography in chronic pancreatitis: internal definitions. *Gut* 25:1107–1112, 1984.
- Ito K, Koike S, Matsunaga N: MR imaging of pancreatic diseases. *Eur J Radiol* 38:78–93, 2001.

- Semelka RC, Shoenut JP, Kroeker MA, et al: Chronic pancreatitis: MR imaging features before and after administration of gadopentetate dimeglumine. *J Magn Reson Imaging* 3:79–82, 1993.
- Ward J, Chalmers AG, Guthrie AJ, et al: T2-weighted and dynamic enhanced MRI in acute pancreatitis: comparison with contrast enhanced CT. *Clin Radiol* 52:109–114, 1997.
- Miller FH, Keppke AL, Wadhwa A, et al: MRI of pancreatitis and its complications. II. Chronic pancreatitis. AJR Am J Roentgenol 183:1645– 1652, 2004.
- Leyendecker JR, Elsayes KM, Gratz BI, et al: MR cholangiopancreatography: spectrum of pancreatic duct abnormalities. *AJR Am J Roentgenol* 179:1465–1471, 2002.
- Varghese JC, Masterson A, Lee MJ: Value of MR pancreatography in the evaluation of patients with chronic pancreatitis. *Clin Radiol* 57:393– 401, 2002.
- Cappeliez O, Delhaye M, Deviere J, et al: Chronic pancreatitis: evaluation of pancreatic exocrine function with MR pancreatography after secretin stimulation. *Radiology* 215:358– 364, 2000.
- Matos C, Deviere J, Cremer M, et al: Acinar filling during secretin-stimulated MR pancreatography. AJR Am J Roentgenol 171:165–169, 1998.
- Matos C, Metens T, Deviere J, et al: Pancreatic duct: morphologic and functional evaluation with dynamic MR pancreatography after secretin stimulation. *Radiology* 203:435–441, 1997.
- Maldonado A, Gonzalez F, Tamames S, et al: The role of 18F-FDG PET/CT in the evaluation of pancreatic lesions. *J Nucl Med* 48(Suppl 2):26P, 2007.

# Miscellaneous Pancreatitis

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## Autoimmune Pancreatitis

#### ETIOLOGY

Autoimmune pancreatitis (AIP) is a peculiar form of chronic pancreatitis characterized by a fibroinflammatory process involving multiple organs with characteristic histopathologic and serologic features, association with other autoimmune disorders, and a propensity to respond to corticosteroid therapy (CST).<sup>1-3</sup> Two subtypes of disease have recently been described: type I, also known as lymphoplasmacytic sclerosing pancreatitis, is considered a spectrum of immunoglobulin G4 (IgG4)related systemic disease and represents the predominant form in the United States, Japan, and Korea and is characterized by seropositivity, whereas type II, also known as idiopathic ductcentric pancreatitis, is more commonly seen in Europe and is characterized by seronegativity.4-6 The occurrence of AIP in concordance with other autoimmune disease processes (Box 50-1) as well as pathologic findings have led to acceptance of its immune-mediated causes, possibly in genetically susceptible patients.<sup>3,7,8</sup> For example, 16% to 30% of patients with type II AIP carry or will subsequently be diagnosed with inflammatory bowel disease (IBD).<sup>4,6</sup> Absence of prior attacks of acute pancreatitis or alcohol abuse is a notable feature of this form of pancreatitis.9 Although a benign disease, it often mimics pancreatic malignancy clinically and radiologically.<sup>10</sup>

### PREVALENCE AND EPIDEMIOLOGY

Although there has been an increasing trend in diagnosis of AIP since it was first described in 1961, this trend is thought to be due to increasing awareness of the disease process and prevalence rate of AIP is still unclear.<sup>11</sup> However, certain differences have been observed in the Western and Japanese populations.<sup>4,12</sup> Type I predominantly arises in men over 50 years of age, typically in the sixth and seventh decades, whereas type II predominantly arises in a slightly younger population in the fifth decade without a gender predilection.<sup>4,13,14</sup> However, disease can affect a wide age range, with documented cases even in pediatric populations.<sup>15</sup>

### **CLINICAL PRESENTATION**

Clinical presentation of AIP is generally nonspecific. Symptoms related to pancreatic involvement include vague upper abdominal pain, jaundice, nausea, vomiting, weight loss, steatorrhea, back pain, and exocrine and endocrine dysfunction with type 2 diabetes mellitus arising at or before the onset of AIP.<sup>14,16,17</sup> Patients may present with acute pancreatitis, type II more commonly than type I, although obstructing jaundice is a more

common presentation. Often, up to 75% of older patients will present with obstructive jaundice, making differentiation of pancreatic malignancy difficult.<sup>5</sup> However, most will present with nonspecific or mild symptoms that are overlooked, which results in delay in diagnosis, some to the stage at which changes of chronicity such as atrophy or strictures have set in.<sup>18</sup>

Extrapancreatic manifestations involving the biliary tree, liver, kidney, retroperitoneum, bowel, lungs, lymph nodes, orbits, and salivary glands may occur in 60% of patients, with incidental detection of pancreatic involvement.<sup>2,14,19,20</sup> Aside from known associations with IBD, extrapancreatic manifestations are considered rare in type II AIP and are commonly seen in type I AIP.

Depending on the subtype, the disease may relapse or persist in a milder form for a time before it is diagnosed. Type I AIP has a relapse rate of up to 59%, with most occurring within first 3 years, whereas type II AIP does not appear to relapse.<sup>20</sup>

#### PATHOPHYSIOLOGY

Although the pathophysiology is still largely unknown, it is thought there is an aberrant response to self-antigens that induces cellular and humoral response with resultant chronic inflammation maintained by the complement cascade and IgG4.<sup>21,22</sup> Nearly half of the patients also demonstrate elevated IgE levels and eosinophils, which are typically seen in allergic reactions, and it is unclear if allergic cascade also may be involved in pathogenesis of AIP.<sup>23</sup>

#### PATHOLOGY

#### Laboratory

Obstructive jaundice from pancreatic inflammation can result in elevated levels of bilirubin and other biliary enzymes. Serum amylase and lipase values can be marginally abnormal. The pancreatic tumor marker CA 19-9 can be elevated, and this is probably due to cholestasis.<sup>14</sup> Inflammation of pancreatic acinar, beta, and alpha cells results in exocrine and endocrine dysfunction with reduction in volume and amylase content of pancreatic secretions with normal bicarbonate content as well as reduction in secretion of insulin and glucagon. CST can reverse inflammation affecting beta cells but not the reduction in number, resulting in residual dysfunction.<sup>24,25</sup>

#### Serology

Elevated serum IgG4, is a characteristic feature in type I AIP. Elevated titers of various antibodies such as antinuclear antibodies, rheumatoid factor, anti–carbonic anhydrase antibody, perinuclear antineutrophil cytoplasmic antibody, anti–smooth

muscle antibody, antimitochondrial or antilactoferrin antibody, and variable antibodies to trypsinogen and pancreatic secretory trypsin inhibitor have been variably reported, although none are consistently positive.<sup>3,7,10,14,26</sup> It is unclear if these antibodies are primarily or secondarily produced as a result of inflammatory change. Serum IgG4 is more sensitive than total IgG for diagnosis of type I AIP. It is, however, not specific or diagnostic, because elevated levels have been observed in other forms of acute and chronic pancreatitis, in pancreatic carcinoma, and in individuals without any pancreatic disease (3% to 10%). Also, in the Western population, raised IgG4 levels have been inconsistently observed.<sup>5</sup> A higher IgG4 cutoff value (280 mg/dL, twice the upper limit of normal) is considered highly sensitive and specific (>95%) in distinguishing AIP from pancreatic cancer. Although the positive predictive value of IgG4 is very low (~36%) owing to the low prevalence of disease compared with other conditions with raised IgG4, the negative predictive value is very high (99%).<sup>27,28</sup> Whenever elevated, IgG4 level can be a useful marker to monitor disease activity in type I AIP, and as it is not consistently elevated, it cannot be used solely to diagnose relapse or assess treatment response.<sup>27-30</sup> On the other hand, a high level of CA 19-9 (>100 units/mL) is more suggestive of pancreatic carcinoma. In patients with lower or absent levels of serum IgG4, as is typically the case in type II AIP, the combination of clinical picture, extrapancreatic involvement, and characteristic imaging features are useful. Diagnosis can be confirmed on core biopsies.<sup>27</sup>

#### Gross Pathology

Resection of pancreas affected by AIP could be difficult owing to smoldering, peripancreatic inflammation, and fibrosis with

#### BOX 50-1 AUTOIMMUNE DISORDERS ASSOCIATED WITH AUTOIMMUNE PANCREATITIS

- Diabetes mellitus
  Idiapathia thromboouten
- Idiopathic thrombocytopenic purpuraInflammatory bowel disease
- Rheumatoid arthritis
- Primary sclerosing cholangitis
- Primary biliary cirrhosis
- Sjögren's syndrome

TABLE

• Systemic lupus erythematosus

distortion of surgical planes making dissection difficult and resulting in higher blood loss and longer operating time.<sup>31</sup> On gross inspection, the pancreas is unremarkable but it is firm to rock hard on palpation. No dominant masses or well-circumscribed nodules are detected.<sup>32,33</sup>

#### Histopathology

Depending on the preponderance of involvement, AIP has been subtyped into types I and II.<sup>33,34</sup> Lobular and ductal involvement is often patchy, which hampers definitive diagnosis on needle biopsy. The differences encountered between the two groups are listed in Table 50-1.<sup>33,35,36</sup>

Type I AIP is characterized by dense lymphoplasmacytic infiltration in the pancreatic parenchymal lobules with secondary interlobular and intralobular fibrosis, often characterized by a swirling pattern of fibrosis known as storiform fibrosis. Obliterative endophlebitis is commonly seen.<sup>37,38</sup> Plasma cells are IgG4 positive.<sup>39</sup> Inflammatory infiltrate spills into the peripancreatic soft tissue, resulting in characteristic imaging appearance.

Type II AIP is characterized by ductal epithelial granulocytic infiltration with neutrophilic microabscesses and ulcerations with resultant ductal damage and obliteration. They typically do not stain for IgG4 or IgG4-positive plasma cells, and obliterative endophlebitis is uncommon.<sup>38</sup> Inflammatory infiltrates invade and compress the walls of the pancreatic duct and common bile duct (CBD), resulting in thickening and luminal narrowing. If not treated, chronic inflammation results in fibrosis and stricture.<sup>40,41</sup>

Extrapancreatic lesions, like in type I AIP, reveal lymphoplasmacytic infiltration, fibrosis, IgG4-positive plasma cells, and obliterative endophlebitis and can aid in differentiation of AIP associated sclerosing cholangitis from primary sclerosing cholangitis.<sup>42,43</sup> Renal lesions reveal tubulointerstitial nephritis with lymphoplasmacytic infiltration and fibrosis.<sup>44</sup>

#### Immunoglobulin G4 Immunohistochemistry

Organs affected by type I AIP have a lymphoplasmacytic infiltrate rich in IgG4-positive plasma cells on immunostaining, even in absence of serum IgG4 elevation.<sup>19</sup> Although higher numbers of pancreatic IgG4-positive plasma cells have been identified in AIP compared with pancreatic carcinoma and chronic pancreatitis, this overlap precludes the use of immunostaining as an absolute diagnostic means, particularly when

50-1	Difference in Two Histologic Subtypes of Autoimmune Pancreatitis				
Features		Type I: Lymphoplasmacytic Sclerosing Pancreatitis	Type II: Idiopathic Duct-Centric Pancreatitis		
Gende	er	Male predominance	No gender predominance		
Age		>50 (median seventh decade)	Generally younger than type I, fifth decade		
Population predominance		Predominant form in Asia and North America	More common in Europe		
Pathol	ogy	Predominant lobular and septal Lymphoplasmacytic infiltration Storiform fibrosis Obliterative endophlebitis common	Predominant ductcentric Ductal epithelial granulocytic infiltration Can lead to ductal narrowing Neutrophilic microabscesses and ulceration Obliterative endophlebitis uncommon		
lgG4		Elevated	Typically normal		
Relaps	se	Frequent (up to 59%)	Extremely rare		
	non extrapancreatic ifestation	Salivary glands, liver, kidneys, and retroperitoneum	Association with inflammatory bowel disease		

IgG4, Immunoglobulin G4.

evaluating a biopsy specimen. However, a ratio of IgG4 to IgG of greater than 40% in an involved organ has been suggested by some to be more likely to represent AIP.<sup>45-47</sup> Although it was once thought that the presence of large numbers of IgG4-positive plasma cells supported the diagnosis, type II AIP often will not demonstrate lymphoplasmacytic infiltrates nor elevation in IgG4.<sup>2,4,33</sup>

#### Immunogeneity

Type I AIP demonstrates increased frequency of certain human leukocyte antigen haplotypes, for example, involving the DRB1\*0405 and DQB1\*0401, and DRB1\*0410, substitution of aspartic acid to nonsapartic acid at DQbeta157, and polymorphisms of cytotoxic T lymphocyte–associated protein 4 and Fc receptor–like gene 3.<sup>48-51</sup> Some of these changes have been associated with high relapse rates and may serve as a prognostic indicator in the future.<sup>49</sup>

#### IMAGING

Multiple diagnostic criteria such as the Japan Pancreas Society (Revised proposal, 2006), HISORt (histology, imaging, serology, other organ involvement, and response to therapy) criteria from the Mayo Clinic, Korean criteria, and International Consensus Diagnostic Criteria are currently in use, incorporating imaging, laboratory, serologic features, histopathologic findings with extrapancreatic manifestations, associated disorders, and response to corticosteroids.<sup>2,13,52</sup>

#### Computed Tomography

Computed tomography (CT) is considered the modality of choice for assessing pancreatic and extrapancreatic manifestations of AIP. Focal, multifocal, or, more frequently, diffuse swelling of the pancreas is the most common imaging feature in both types of AIP. Although CT cannot be used to differentiate between two forms, type I tends to demonstrate diffuse swelling whereas type II has the propensity to be more focal. The classic appearance is a diffusely enlarged, sausage-shaped pancreas with sharp borders and a featureless appearance (absent normal pancreatic clefts) with homogeneous attenuation. Although the enhancement pattern varies depending on inflammation and fibrosis, moderate heterogeneous and delayed enhancement is often seen with fibrosis. A peripheral, smooth, well-defined rim of hypoattenuating halo around the pancreatic parenchyma represents fluid, phlegmon/inflammatory exudate, and fibrous tissue (Figure 50-1) with minimal peripancreatic fat stranding.<sup>3</sup> Infrequently, the halo reveals a capsule-like enhancement on delayed phase of contrast enhancement.<sup>53</sup> In type II AIP, ductal injury may lead to pancreatic atrophy with retraction of the pancreatic tail ("tail cutoff") in up to 40% of cases (Figure 50-1 and Figure 50-2).<sup>3,54</sup> Multifocal enlargement of the pancreas occurring concurrently or spaced in time has been noted (Figure 50-2).5

With advanced disease, there may be development of focal mass-like swelling (see Figures 50-2 and 50-3), more commonly in type II AIP.<sup>33</sup> This has been reported more commonly in Western populations and is known as pseudotumorous pancreatitis or inflammatory pancreatic mass; in Japan it is known as tumor-forming pancreatitis.<sup>35,41</sup> Mass-like swellings are often misdiagnosed as chronic alcoholic pancreatitis (which can be distinguished from AIP by presence of necrosis, abscesses, stones, and reparative granulation tissue), and pancreatic

carcinomas and may be surgically resected.<sup>56,57</sup> Homogeneous delayed enhancement may be seen on CT.<sup>3</sup> Distinguishing features of pancreatic carcinoma and AIP are summarized in Table 50-2.

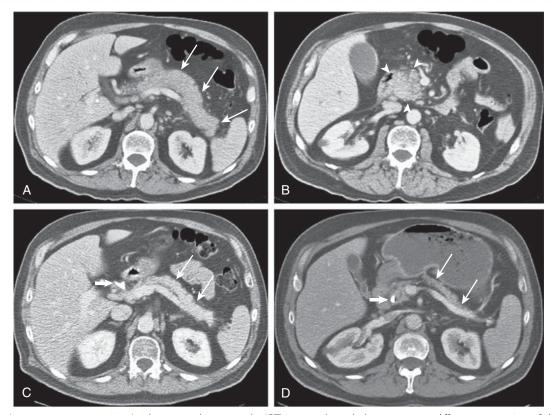
Segmental or diffuse irregularity and narrowing of the pancreatic duct secondary to compression from surrounding inflammation, with or without thickening and enhancement, is



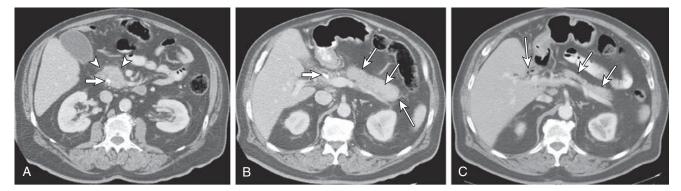
**Figure 50-1** Autoimmune pancreatitis. On this axial computed tomography image the pancreas is diffusely swollen with loss of lobulations. The pancreatic duct is attenuated (not visualized), and the pancreatic tail is retracted (*long arrow*). A smooth rim of hypoattenuation, a "halo" (*short arrows*), is seen around the pancreas. Minimal stranding in seen in the peripancreatic fat (*asterisk*).

TABLE 50-2	Differentiation of Autoimmune Pancreatitis from Pancreatic Malignancy			
Differ Factor	entiation rs	AIP	Pancreatic Cancer	
Serolo	gy	Elevated $IgG_4$	Elevated CA 19-9	
Imaging characteristics		Peripancreatic halo, delayed enhancement, extrapancreatic disease	Low density mass, regional/ metastatic spread, upstream pancreatic atrophy	
Ductal char	acteristics	Long segment or multiple pancreatic ductal strictures, absence of upstream dilatation	Short segment pancreatic ductal stricture with upstream dilatation, duct cutoff	
Histop	bathology	Storiform fibrosis, lymphoplasmacytic infiltrates, obliterative endophlebitis, ductal epithelial granulocytic infiltration	Malignant cells	
Treatn	nent	Steroid responsive	Surgical resection/ chemotherapy	

*IgG4*, Immunoglobulin G4.



**Figure 50-2** Autoimmune pancreatitis. Axial computed tomography (CT) images through the pancreas at different time points of disease process in same patient. A, The pancreas is diffusely swollen and featureless (sausage-shaped) (*arrows*) with attenuated pancreatic duct (not visualized). B, Focal swelling is detected in the pancreatic head (*arrowheads*), with resultant obstruction of the common bile duct requiring biliary drainage. The patient was started on corticosteroid therapy. C, CT image 2 months after treatment reveals significant improvement in the diffuse and focal pancreatic swelling (*arrows*). Biliary stent is seen in situ (*thick arrow*). D, CT image 5 months after the initial evaluation reveals an atrophic pancreas (*arrows*). A biliary stent is seen in situ (*thick arrow*) and was later removed.



**Figure 50-3** Autoimmune pancreatitis (AIP). Axial computed tomography (CT) images at different time points of the disease process in same patient. A, A focal swelling (*arrowheads*) is seen in the head of pancreas with a biliary stent (*thick arrow*) in situ to relieve the obstruction. B, Sausage-shaped enlargement of body and tail of pancreas (*arrows*) with tail cut off (*long arrow*) is also seen. Biliary stent (*thick arrow*) is seen in situ. The focal swelling in the head of pancreas was resected (Whipple's procedure) because of unremitting symptoms and concern for malignancy. Based on histopathologic diagnosis of AIP, the patient was then treated with corticosteroids. C, A follow-up CT examination 3 months later reveals near-complete resolution of swelling of body and tail of pancreas (*arrows*). Air is noted in the biliary tree (postoperative finding) (*long thin arrow*).

seen. The distal CBD may reveal tapered narrowing owing to compression from adjacent pancreatic parenchyma or from involvement of CBD by the disease process; the involved duct also may reveal contrast enhancement. Involvement of the CBD and resulting biliary obstruction often require biliary drainage (see Figures 50-2 and 50-3).<sup>1,58</sup>

Pancreatic swelling, peripancreatic changes, and irregular narrowing of the pancreatic duct usually improve in most, especially if CST is instituted early in the course of disease. Biliary narrowing also improves with CST, allowing withdrawal of biliary drainage tubes.<sup>59</sup> Ductal stricture develops in the absence of timely institution of CST or with a protracted disease course, which may result in irregular upstream dilatation of the pancreatic duct.  $^{60}$ 

Vascular encasement is conspicuously absent, although mass effect on the vessels and narrowing of peripancreatic veins can be seen.<sup>53</sup> Vascular complications such as compression and thrombosis have been reported in 23% of patients.<sup>16</sup>

Occasional pancreatic cysts have been reported; these are known to disappear with or without treatment, without any sequelae.<sup>18</sup> AIP is rarely associated with stone formation, and more so in relapsing cases.<sup>33,61</sup> Pancreatic calcification and ascites are not seen.<sup>1</sup> A long-term, protracted disease course often results in atrophy of the gland (see Figure 50-2).<sup>59</sup>

Extrapancreatic manifestations can occur simultaneously or before or after detection of pancreatic involvement and are listed in Box 50-2.<sup>44,62-64</sup> Extrapancreatic manifestations may be useful in supporting diagnosis in equivocal cases.<sup>18</sup>

Renal lesions are typically parenchymal, predominantly involving the cortex, and are numerous and nonenhancing. However, perirenal tissue, renal sinus, and renal pelvis may be involved. They are detected on contrast-enhanced studies as

#### BOX 50-2 EXTRAPANCREATIC MANIFESTATIONS OF AUTOIMMUNE PANCREATITIS

- Abdominal, cervical, or hilar lymphadenopathy
- Gastric, duodenal, or colonic infiltration
- Interstitial pneumonia
- Orbital pseudotumor
- Renal lesions (35%)
- Retroperitoneal fibrosis (3% to 8%)
- Sclerosing cholangitis (68% to 88%)
- Sialadenitis (12% to 16%)

wedge-shaped, ill-defined, rounded or nodular or diffuse and patchy lesions (Figure 50-4, *A*). Differentials may include pyelonephritis, vascular insult, lymphoma, renal cell carcinoma, or Wegener's granulomatosis. Soft tissue masses in the renal pelvis associated with AIP can resemble urothelial tumors and lymphomas. A perirenal rim of soft tissue and thickening of the renal pelvic wall also can be seen. Renal lesions do not affect renal function in the early stage; however, long-term effects, with or without CST, are not yet clearly known. Eventually, fibrosis in the late stage results in cortical volume loss.<sup>44</sup>

Retroperitoneal fibrosis most commonly appears as a mantle of tissue adjacent to the aorta and other retroperitoneal structures and is morphologically indistinguishable from other causes of retroperitoneal fibrosis (see Figure 50-4, *B*). If untreated, it can also result in hydronephrosis.<sup>62</sup>

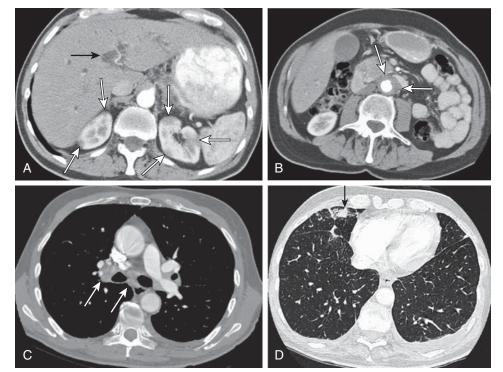
Association of ulcerative colitis with AIP is more frequently observed in the Western population and in a relatively younger age group, commonly in type II AIP.<sup>34,35,63-66</sup> Typical findings of acute, subacute, and chronic inflammatory changes of large bowel are seen on CT.

The incidence of AIP-associated sialadenitis is higher in the Japanese population.<sup>35</sup> Sialadenitis co-occurring with AIP is negative for anti-SSA and anti-SSB antibodies, shows elevated serum IgG4 levels and IgG4-positive plasma cell infiltration in tissue, and is thus different from Sjögren's syndrome. Involved salivary glands (parotid or submandibular) are enlarged, which can be confirmed by scintigraphy.<sup>62</sup>

Abdominal, cervical, and hilar adenopathy have been reported in association with AIP and tends to respond to CST (see Figure 50-4, *C*). Like the halo sign seen in the pancreas, enlarged lymph nodes can demonstrate perinodal halo.

Pulmonary involvement may result in discrete or diffuse nodules or infiltrates (see Figure 50-4, *D*).

Figure 50-4 Autoimmune pancreatitis (AIP). Axial computed tomography images revealing extrapancreatic manifestations of AIP in same patient. A, Multiple, nonenhancing wedge-shaped and nodular, renal cortical lesions (*white arrows*). Note the prominence of the biliary tree (*black arrow*) resulting from involvement of the distal common bile duct by swelling in the head of pancreas. B, A retroperitoneal mantle is seen surrounding the aorta (*arrows*). C, Multiple mediastinal and hilar lymph nodes (*arrows*). D, Parenchymal lesions are seen in the lung (*black arrow*).



## Magnetic Resonance Imaging and Magnetic Resonance Cholangiopancreatography

There is no specific indication for MRI in evaluation of AIP, although MRI is more sensitive and can detect recurrent disease in up to 22% of patients who are clinically and biochemically asymptomatic.<sup>67</sup> MR cholangiopancreatography (MRCP) can be performed as a noninvasive technique in lieu of endoscopic cholangiopancreatography (ERCP) for evaluation and subsequent follow-up of ductal changes.

Involved pancreas appears hypointense on T1-weighted images and hyperintense on T2-weighted images when inflammation is predominant and hypointense when fibrosis predominates (Figure 50-5). Delayed parenchymal enhancement is seen after intravenous administration of gadolinium. The "halo" appears hypointense on T1- and T2-weighted images. Delayed capsule-like enhancement of halo is better appreciated on T1-weighted fat-suppressed gadolinium-enhanced MR images compared with CT.<sup>53,55,60</sup> The pancreatic portion of the CBD can demonstrate delayed wall enhancement. Sometimes, the obliteration of pancreatic duct by the focal or diffuse AIP may be difficult to differentiate from pancreatic cancer.68 More recent work has demonstrated use of ADC values to differentiate AIP from chronic pancreatitis and cancer, most demonstrating lower ADC values in AIP compared to chronic alcoholic pancreatitis or pancreatic cancer.<sup>69</sup> Renal parenchymal and sinus lesions appear hypointense on T1- and T2-weighted imaging.

MRCP can demonstrate findings similar to those seen on ERCP, such as long segment or multisegment stricture of the

main pancreatic duct (MPD) with lack of upstream dilatation of the main or side branches in severe or advanced cases. Although MRCP tends to overestimate ductal narrowing, it may be a viable alternative to ERCP for surveillance of treatment response.<sup>70</sup>

#### Endoscopic Retrograde Cholangiopancreatography

ERCP has an important role in pretreatment and posttreatment evaluation of ductal changes. Moreover, it is of more value than MRCP because it allows simultaneous biliary drainage and ERCP-guided biopsy. Ampullary biopsy with IgG4 staining may be helpful in diagnosis if other imaging and clinical features are less clear.

MPD reveals focal or diffuse irregularity and narrowing without upstream dilatation (Figure 50-6). Segmental involvement of the pancreas with segmental narrowing of the pancreatic duct can mimic carcinoma.<sup>71</sup> Narrowing of the distal CBD with variable proximal dilatation is often observed (Figure 50-7).<sup>1,53</sup> On ERCP the features of sclerosing cholangitis associated with AIP are morphologically difficult to distinguish from primary sclerosing cholangitis or malignancy (Figure 50-8).<sup>18</sup>

#### Ultrasonography

Transabdominal ultrasonography of the pancreas is rarely diagnostic. Moreover, findings on ultrasonography resemble those of other forms of pancreatitis. The swollen portion of the gland appears hypoechoic. Diffusely altered echotexture of the involved pancreas is better appreciated on endoscopic ultrasonography (EUS) with visualization of echogenic interlobular

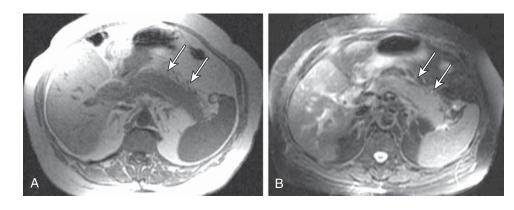


Figure 50-5 Autoimmune pancreatitis. A, Axial T1-weighted magnetic resonance (MR) image reveals swollen body and tail of the pancreas, which appears hypointense. Mild stranding in the peripancreatic fat is also seen (*arrows*). B, Axial T2-weighted fat-suppressed MR image reveals mildly hyperintense pancreas with mild peripancreatic stranding (*arrows*).

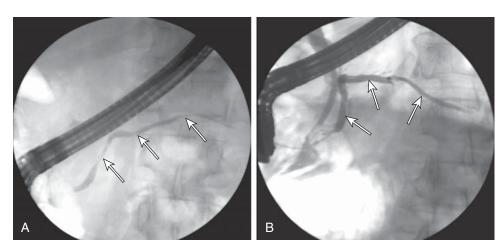


Figure 50-6 Autoimmune pancreatitis. A, Endoscopic retrograde cholangiopancreatography (ERCP) image reveals irregularity and multisegmental narrowing (arrows) of the pancreatic duct. B, ERCP performed 2 months after corticosteroid therapy shows improvement of the narrowing and irregularity (arrows) with normalization of ductal changes.

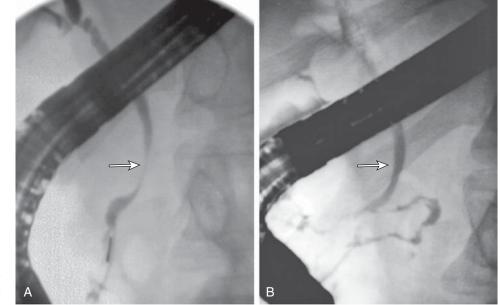
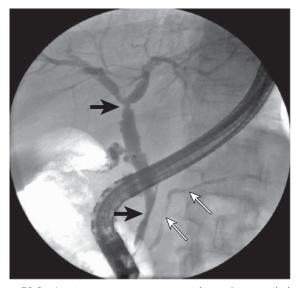


Figure 50-7 Autoimmune pancreatitis. A, Endoscopic retrograde cholangiopancreatography (ERCP) reveals a long segment of narrowing of the distal common bile duct (*arrow*) with mild proximal dilatation. B, ERCP performed 1 month after corticosteroid therapy shows resolution of common bile duct narrowing (*arrow*).



**Figure 50-8** Autoimmune pancreatitis mimicking sclerosing cholangitis. Endoscopic retrograde cholangiopancreatography reveals segments of narrowing in the distal common bile duct and hilar region (*black arrows*). The pancreatic duct also reveals multiple segments of irregular narrowing (*white arrows*).

septa, especially when the gland appears normal or equivocal on CT. This is due to higher sensitivity of EUS and close proximity to the gland.<sup>3</sup> However, the appearance of focal mass-like swelling may be deceptively similar to that of pancreatic carcinoma. EUS-guided fine-needle aspiration serves as a relatively less invasive technique compared to percutaneous image-guided biopsy for further evaluation of these focal mass-like swellings (Figure 50-9). Concentric mural thickening of the distal CBD is visualized with EUS and may be helpful in differentiating from features seen with cholangiocarcinoma, which demonstrates eccentric wall thickening with irregular luminal surface.<sup>10</sup>

#### Nuclear Medicine

Scintigraphy with gallium-67 (<sup>67</sup>Ga) can confirm enlargement of the salivary glands associated with AIP, although it may be difficult to identify if symmetrically enlarged.<sup>62</sup> Hilar adenopathy in AIP reveals increased uptake on <sup>67</sup>Ga scintigraphy, which also disappears after CST.<sup>73</sup>

#### Positron Emission Tomography With Computed Tomography

Increased fluorodeoxyglucose (FDG) uptake in the pancreas and other involved organs in the inflammatory phase of the disease has been reported in up to 100% of patients as opposed to 13% in chronic pancreatitis.<sup>74,75</sup> FDG–positron emission tomography (FDG-PET) can be useful in evaluating disease activity and discovering other hypermetabolic lesions in extrapancreatic locations such as the salivary glands, retroperitoneum, and kidneys. Decreased standardized uptake value is seen with response to CST.<sup>76</sup>

#### Diagnostic and Imaging Algorithm

A diagnostic and imaging algorithm is presented in Figure 50-10.

#### **Classic Signs: Autoimmune Pancreatitis**

- Diffuse pancreatic swelling: "Featureless sausageshaped pancreas"
- Peripancreatic halo
- Minimal peripancreatic stranding
- Diffuse irregular pancreatic ductal attenuation
- No vascular encasement or invasion in presence of focal mass-like swelling
- Extrapancreatic manifestations
- Resolution with CST

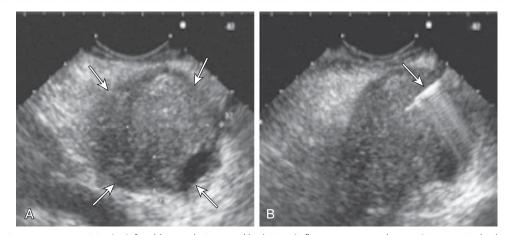
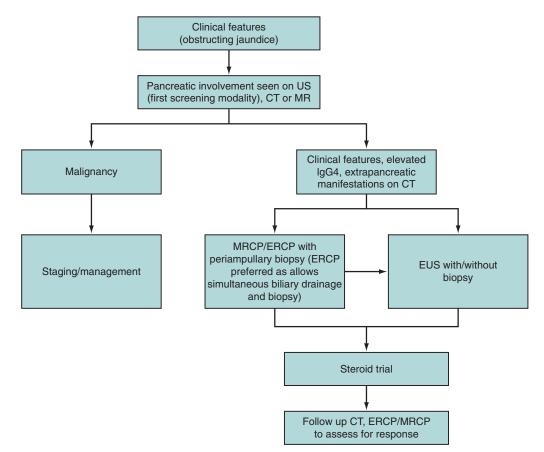


Figure 50-9 Autoimmune pancreatitis. A, A focal hypoechoic mass-like lesion (inflammatory pseudotumor) is seen in the head of the pancreas (arrows) on endoscopic ultrasonography, mimicking a carcinoma. B, Endoscopic ultrasound–guided fine-needle aspiration biopsy (arrow) can be a useful technique to acquire tissue for further evaluation of these lesions.



**Figure 50-10** Imaging algorithm for autoimmune pancreatitis. *CT*, Computed tomography; *ERCP*, endoscopic retrograde cholangiopancreatography; *EUS*, endoscopic ultrasonography; *MRCP*, magnetic resonance cholangiopancreatography; *MRI*, magnetic resonance imaging; *US*, ultrasound.

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#### DIFFERENTIAL DIAGNOSIS

AIP should be differentiated from other pancreatic disorders because changes related to AIP are reversible with CST.<sup>3</sup>

The focal form, particularly involving the head and uncinate process of the pancreas, can mimic pancreatic carcinoma.<sup>3</sup> Focal mass-like swelling associated with AIP enhances like the rest of the pancreas and thus can be differentiated from pancreatic carcinoma, which is generally hypoattenuating in the parenchymal phase. However, this finding alone cannot be relied on for distinguishing AIP from tumor because hypoattenuating focal AIP lesions and isoattenuating pancreatic carcinoma have been reported<sup>3,77</sup> (see Table 50-2). Adequate imaging criteria to differentiate focal AIP from pancreatic carcinoma have not been established; thus, in suspicious cases, those not responding to corticosteroids, and those with persistent intractable symptoms, it is necessary to resort to histopathologic evaluation.<sup>1</sup>

A diffusely enlarged pancreas may morphologically resemble other diffuse disorders such as lymphomas, metastases, or infiltrative processes.

#### TREATMENT

#### Medical Treatment

CST is considered a standard therapy for AIP.<sup>78</sup> Pancreatic, ductal, and extrapancreatic manifestations secondary to the inflammatory component of the disease process, associated clinical symptoms, and laboratory findings, including endocrine and exocrine dysfunction, respond dramatically to CST. However, because AIP is associated with fibrosis, many radiologic changes (ductal changes, focal mass-like swellings, retroperitoneal fibrosis) may improve only partially or remain unchanged after treatment with lack of restoration of normal structure and function, especially when CST is delayed.<sup>14</sup> CST should be used carefully and response objectively assessed; CST should not be a substitute to other investigative parameters.<sup>2</sup> Radiologic response is seen in 2 to 3 weeks. Normalization of radiologic findings can be seen in 4 to 6 weeks. If biliary stenting was done, stent removal is possible within 6 to 8 weeks after starting CST.79

Although duration of the maintenance dose and effect on natural progression of disease is uncertain, therapy can be stopped after 6 to 12 months depending on improvement. Relapses are seen in 6% to 26% (average, 17%) of cases after tapering of corticosteroids or while on maintenance therapy, and these patients may require a second course with a higher dose or a longer maintenance dose of steroids or addition of immunomodulators such as mycophenolate mofetil or azathio-prine.<sup>59,64,81</sup> Use of immunomodulators as a maintenance therapy may be beneficial in patients with relapse.<sup>4</sup> Regular clinical and laboratory follow-up can help detect any recurrence.<sup>64,78</sup> Most recommend routine surveillance of liver function to assess for biliary relapse and starting steroids with evidence of disease as opposed to life-long steroids.<sup>4</sup>

Exocrine and endocrine dysfunction should be individually addressed when possible, as in case of type II diabetes mellitus.<sup>78</sup>

Although spontaneous resolution of acute presentation of disease is known to occur, CST should be instituted because it hastens the resolution of clinical and radiologic features and is likely to prevent progression of fibrosis and its consequential complications.<sup>64,80</sup> If CST does not give a desired response,

as in persistent focal mass-like swelling, reevaluation with additional diagnostic techniques should be sought to exclude malignancy.<sup>78</sup>

To date, there appear to be no significant differences in longterm survival in patients with type I or II AIP.<sup>4</sup> Potential association of this disease with pancreatic cancer is unclear; no studies to date have demonstrated AIP as a predisposing factor to cancer, although theoretical risk for increased risk exists in setting of chronic inflammation and fibrosis.

#### Surgical Treatment

Short-term biliary drainage can be performed with biliary obstruction.<sup>78</sup> Although surgery was used as a primary approach to treat AIP in the past, improved understanding of the disease process has led to a paradigm shift in the management protocol. Surgical resection is now used for focal mass-like swellings or biliary strictures that develop late in the course of disease, which generally do not respond to medical therapy.

#### What the Referring Physician Needs to Know: Autoimmune Pancreatitis

- Awareness of concept of AIP and diverse manifestations.
- Imaging findings in combination with the clinical and serologic parameters should alert the clinician to diagnosis.
- Imaging is an important factor in diagnosis because laboratory and histopathologic findings often may be insufficient and nonspecific.
- There is a propensity for AIP to resemble pancreatic carcinoma clinically and radiologically.
- AIP is often reversible with timely institution of medical therapy.
- Long-term prognosis appears better than for other forms of chronic pancreatitis.

#### **Tumor Lysis Pancreatitis**

Tumor lysis syndrome occurs in patients with lymphoproliferative malignancies treated with chemoradiation therapy or corticosteroids, although spontaneous occurrence has been reported.<sup>82,83</sup> Involvement of the pancreas indistinguishable from other causes of acute pancreatitis has been reported.<sup>84</sup>

## **Eosinophilic Pancreatitis**

Eosinophilic pancreatitis is a systemic manifestation of peripheral eosinophilia, elevated serum IgE levels, and/or eosinophilic infiltrates in other organs.<sup>85</sup> On imaging, it may manifest as diffuse involvement of the pancreas, which histopathologically reveals diffuse, periductal, acinar, and septal eosinophilic infiltrates and eosinophilic phlebitis with arteritis. Focal involvement and pseudocyst formation also may be encountered.<sup>86</sup> It is indistinguishable from other causes of pancreatitis on imaging; clinical and laboratory correlation along with imaging involvement of other organs is necessary for diagnosis.

## **Chemoradiation-Induced Pancreatitis**

Certain chemotherapeutic agents such as pazopanib, sunitinib, sorafenib, and L-asparginase for acute leukemia and, rarely,

radiation therapy have been associated with chemoradiation therapy–induced pancreatitis.<sup>87-90</sup> These forms of pancreatitis are essentially indistinguishable from other forms of pancreatitis on imaging and are often diagnosed based on typical clinical manifestation and lipase elevation and will typically abate once the culprit chemotherapy agent is stopped. Radiation therapy can result, rarely, in malabsorption from chronic pancreatitis with exocrine and endocrine dysfunction.<sup>90</sup>

## **Drug-Induced Pancreatitis**

A variety of medications can induce pancreatitis, indistinguishable from other sources on imaging and diagnosed based on clinical manifestation and lipase elevation. Examples of medications that may cause pancreatitis are shown in Table 50-3.<sup>91</sup>

TABLE 50-3	Drugs Implicated With Pancreatitis		
Antibiotics, antivirals, antifungals		Isoniazid, metronidazole, nelfinavir, Bactrim, cyclosporine, ampicillin	
Analgesics		Acetaminophen, codeine	
Antihypertensives		Captopril, irbesartan, lisinopril, furosemide	
Gastrointestinal drugs		Omeprazole, ranitidine	
Hormones		Estrogen	
Illicit drugs		Cannabis	
Lipid reducing agents		Pravastatin, simvastatin, atorvastatin	
Sedatives		Propofol	
Steroids		Prednisone, prednisolone	

#### SUGGESTED READINGS

- Deshpande V, Mino-Kenudson M, Brugge W, et al: Autoimmune pancreatitis: more than just a pancreatic disease? A contemporary review of its pathology. *Arch Pathol Lab Med* 129:1148–1154, 2005.
- Finkelberg DL, Sahani D, Deshpande V, et al: Autoimmune pancreatitis. N Engl J Med 355:2670– 2676, 2006.
- Kamisawa T, Okamoto A: Prognosis of autoimmune pancreatitis. J Gastroenterol 42(Suppl 18):59–62, 2007.
- Khandelwal A, Shanbhogue AK, Takahashi N, et al: Recent advances in the diagnosis and management of autoimmune pancreatitis. *AJR Am J Roentgenol* 202:1007–1021, 2014.
- Kloppel G, Luttges J, Sipos B, et al: Autoimmune pancreatitis: pathological findings. JOP 6:97–101, 2005.
- Sah RP, Chari ST: Autoimmune pancreatitis: an update on classification, diagnosis, natural history, and management. *Curr Gastroenterol Rep* 14:95–105, 2012.
- Shimosegawa T, Chari S, Frulloni L, et al: International Consensus Diagnostic Criteria for autoimmune pancreatitis. *Pancreas* 40:352–358, 2011.
- Suda K, Takase M, Fukumura Y, et al: Pathology of autoimmune pancreatitis and tumor-forming pancreatitis. J Gastroenterol 42(Suppl 18):22–27, 2007.
- Vlachou PA, Khalili K, Jang HJ, et al: IgG4 related sclerosing disease: autoimmune pancreatitis and extrapancreatic manifestations. *Radiographics* 31:1379–1402, 2011.

#### REFERENCES

- 1. Yang DH, Kim KW, Kim TK, et al: Autoimmune pancreatitis: radiologic findings in 20 patients. *Abdom Imaging* 31:94–102, 2006.
- Chari ST, Smyrk TC, Levy MJ, et al: Diagnosis of autoimmune pancreatitis: the Mayo Clinic experience. *Clin Gastroenterol Hepatol* 4:1010– 1016, quiz 934, 2006.
- Sahari DV, Kalva SP, Farrell J, et al: Autoimmune pancreatitis: imaging features. *Radiology* 233:345–352, 2004.
- Sah RP, Chari ST: Autoimmune pancreatitis: an update on classification, diagnosis, natural history and management. *Curr Gastroenterol Rep* 14:95–105, 2012.
- Kamisawa T, Chari ST, Giday SA, et al: Clinical profile of autoimmune pancreatitis and its histological subtypes: an international multicenter study. *Pancreas* 40:809–814, 2011.
- Sugumar A, Klöppel G, Chari ST: Autoimmune pancreatitis: pathologic subtypes and their implications for its diagnosis. *Am J Gastroenterol* 104:2308–2310, quiz 2311, 2009.
- Okazaki K, Chiba T: Autoimmune related pancreatitis. *Gut* 51:1–4, 2002.
- Yoshida K, Toki F, Takeuchi T, et al: Chronic pancreatitis caused by an autoimmune abnormality: proposal of the concept of autoimmune pancreatitis. *Dig Dis Sci* 40:1561–1568, 1995.
- 9. Weber SM, Cubukcu-Dimopulo O, Palesty JA, et al: Lymphoplasmacytic sclerosing pancreatitis: inflammatory mimic of pancreatic carcinoma. *J Gastrointest Surg* 7:129–137, discussion 137–139, 2003.

- Deshpande V, Mino-Kenudson M, Brugge WR, et al: Endoscopic ultrasound guided fine needle aspiration biopsy of autoimmune pancreatitis: diagnostic criteria and pitfalls. *Am J Surg Pathol* 29:1464–1471, 2005.
- Sarles H, Sarles JC, Muratore R, et al: Chronic inflammatory sclerosis of the pancreas: an autonomous pancreatic disease? *Am J Dig Dis* 6:688–698, 1961.
- Nishimori I, Tamakoshi A, Otsuki M: Prevalence of autoimmune pancreatitis in Japan from a nationwide survey in 2002. J Gastroenterol 42(Suppl 18):6–8, 2007.
- Okazaki K, Kawa S, Kamisawa T, et al: Clinical diagnostic criteria of autoimmune pancreatitis: revised proposal. J Gastroenterol 41:626–631, 2006.
- Kawa S, Hamano H: Clinical features of autoimmune pancreatitis. J Gastroenterol 42(Suppl 18):9–14, 2007.
- Gargouri L, Ponsot P, Viala J, et al: Recurrent autoimmune pancreatitis in a 10 year old boy. J Pediatr Gastroenterol Nutr 48:374–377, 2009.
- Raina A, Yadav D, Krasinskas AM, et al: Evaluation and management of autoimmune pancreatitis: experience at a large US center. *Am J Gastroenterol* 104:2295–2306, 2009.
- Nishimori I, Tamakoshi A, Kawa S, et al: Influence of steroid therapy on the course of diabetes mellitus in patients with autoimmune pancreatitis: findings from a nationwide survey in Japan. *Pancreas* 32:244–248, 2006.

- Nakazawa T, Ohara H, Sano H, et al: Difficulty in diagnosing autoimmune pancreatitis by imaging findings. *Gastrointest Endosc* 65:99– 108, 2007.
- Kamisawa T: IgG4-positive plasma cells specifically infiltrate various organs in autoimmune pancreatitis. *Pancreas* 29:167–168, 2004.
- Sah RP, Chari ST, Pannala R, et al: Differences in clinical profile and relapse rate of type 1 versus type 2 autoimmune pancreatitis. *Gastroenterology* 139:140–148, 2010.
- Okazaki K, Uchida K, Sumimoto K, et al: Autoimmune pancreatitis: pathogenesis, latest developments and clinical guidance. *Ther Adv Chronic Dis* 5:104–111, 2014.
- 22. Watanabe T, Yamashita K, Fujikawa S, et al: Involvement of activation of toll-like receptors and nucleotide-binding oligomerization domainlike receptors in enhanced IgG4 responses in autoimmune pancreatitis. Arthritis Rheum 64: 912–924, 2012.
- Kamisawa T, Anjiki H, Egawa N, et al: Allergic manifestations in autoimmune pancreatitis. Eur J Gastroenterol Hepatol 21:1136–1139, 2009.
- 24. Kamisawa T, Egawa N, Inokuma S, et al: Pancreatic endocrine and exocrine function and salivary gland function in autoimmune pancreatitis before and after steroid therapy. *Pancreas* 27:235–238, 2003.
- Ito T, Kawabe K, Arita Y, et al: Evaluation of pancreatic endocrine and exocrine function in patients with autoimmune pancreatitis. *Pancreas* 34:254–259, 2007.

- Asada M, Nishio A, Uchida K, et al: Identification of a novel autoantibody against pancreatic secretory trypsin. *Pancreas* 33:20–26, 2006.
- 27. Ghazale A, Chari ST, Smyrk TC, et al: Value of serum IgG4 in the diagnosis of autoimmune pancreatitis and in distinguishing it from pancreatic cancer. *Am J Gastroenterol* 102:1646–1653, 2007.
- Hamano H, Kawa S, Horiuchi A, et al: High serum IgG4 concentrations in patients with sclerosing pancreatitis. N Engl J Med 344:732– 738, 2001.
- Pearson RK, Longnecker DS, Chari ST, et al: Controversies in clinical pancreatology: autoimmune pancreatitis: does it exist? *Pancreas* 27:1– 13, 2003.
- Chen RY, Adams DB: IgG4 levels in non-Japanese patients with autoimmune sclerosing pancreatitis. N Engl J Med 346:1919, 2002.
- Hardacre JM, Iacobuzio-Donahue CA, Sohn TA, et al: Results of pancreaticoduodenectomy for lymphoplasmacytic sclerosing pancreatitis. *Ann Surg* 237:853–858, discussion 858–859, 2003.
- Horiuchi A, Kaneko T, Yamamura N, et al: Autoimmune chronic pancreatitis simulating pancreatic lymphoma. *Am J Gastroenterol* 91: 2607–2609, 1996.
- Deshpande V, Mino-Kenudson M, Brugge W, et al: Autoimmune pancreatitis: more than just a pancreatic disease? A contemporary review of its pathology. *Arch Pathol Lab Med* 129:1148– 1154, 2005.
- 34. Zamboni G, Luttges J, Capelli P, et al: Histopathological features of diagnostic and clinical relevance in autoimmune pancreatitis; a study on 53 resection specimens and 9 biopsy specimens. Virchows Arch 455:552–563, 2004.
- Ohara H, Nakazawa T, Ando T, et al: Systemic extrapancreatic lesions associated with autoimmune pancreatitis. *J Gastroenterol* 42(Suppl 18):15–21, 2007.
- Deshpande V, Chicano S, Finkelberg D, et al: Autoimmune pancreatitis: a systemic immune complex mediated disease. *Am J Surg Pathol* 30:1537–1545, 2006.
- Deshpande V, Zen Y, Chan JK, et al: Consensus statement on the pathology of IgG4-related disease. *Mod Pathol* 25:1181–1192, 2012.
- Shinagare S, Shinagare AB, Deshpande V: Autoimmune pancreatitis: a guide for the histopathologist. Semin Diagn Pathol 29:197–204, 2012.
- Okazaki K, Uchida K, Matsushita M, et al: Autoimmune pancreatitis. *Intern Med* 44:1215–1223, 2005.
- Kawaguchi K, Koike M, Tsuruta K, et al: Lymphoplasmacytic sclerosing pancreatitis with cholangitis: a variant of primary sclerosing cholangitis extensively involving pancreas. *Hum Pathol* 22:387–395, 1991.
- Suda K, Takase M, Fukumura Y, et al: Pathology of autoimmune pancreatitis and tumor-forming pancreatitis. *J Gastroenterol* 42(Suppl 18):22–27, 2007.
- 42. Zen Y, Harada K, Sasaki M, et al: IgG4-related sclerosing cholangitis with and without hepatic inflammatory pseudotumor, and sclerosing pancreatitis-associated sclerosing cholangitis: do they belong to a spectrum of sclerosing pancreatitis? *Am J Surg Pathol* 28:1193–1203, 2004.
- Abraham SC, Cruz-Correa M, Argani P, et al: Lymphoplasmacytic chronic cholecystitis and biliary tract disease in patients with lymphoplasmacytic sclerosing pancreatitis. *Am J Surg Pathol* 27:441–451, 2003.
- 44. Takahashi N, Kawashima A, Fletcher JG, et al: Renal involvement in patients with autoimmune

pancreatitis: CT and MR imaging findings. Radiology 242:791-801, 2007.

- 45. Sato Y, Kojima M, Takata K, et al: Systemic IgG4-related lymphadenopathy: a clinical and pathologic comparison to multicentric Castleman's disease. *Mod Pathol* 22:589–599, 2009.
- Cheuk W, Yuen HK, Chu SY, et al: Lymphadenopathy of IgG4-related sclerosing disease. Am J Surg Pathol 32:671–681, 2008.
- Cheuk W, Chan JK: IgG4-related sclerosing disease: a critical appraisal of an evolving clinicopathologic entity. *Adv Anat Pathol* 17:303– 332, 2010.
- Kawa S, Ota M, Yoshizawa K, et al: HLA DRB10405-DQB10401 haplotype is associated with autoimmune pancreatitis in the Japanese population. *Gastroenterology* 122:1264–1269, 2002.
- Park do H, Kim MH, Oh HB, et al: Substitution of aspartic acid at position 57 of the DQβ1 affects relapse of autoimmune pancreatitis. *Gastroenterology* 134:440–444, 2008.
- Umemura T, Ota M, Hamano H, et al: Association of autoimmune pancreatitis with cytotoxic T-lymphocyte antigen 4 gene. *Am J Gastroenterol* 103:588–594, 2008.
- 51. Umemura T, Ota M, Hamano H, et al: Genetic association of Fc receptor-like 3 polymorphisms with autoimmune pancreatitis in Japanese patients. *Gut* 55:1367–1368, 2006.
- Shimosegawa T, Chari S, Frulloni L, et al: International Consensus Diagnostic Criteria for autoimmune pancreatitis. *Pancreas* 40:352–358, 2011.
- Irie H, Honda H, Baba S, et al: Autoimmune pancreatitis: CT and MR characteristics. AJR Am J Roentgenol 170:1323–1327, 1998.
- Deshpande V, Gupta R, Sainani N, et al: Subclassification of autoimmune pancreatitis: a histologic classification with clinical significance. *Am J Surg Pathol* 35:26–35, 2011.
- Mikami K, Itoh H: MR imaging of multifocal autoimmune pancreatitis in the pancreatic head and tail: a case report. *Magn Reson Med Sci* 1:54–58, 2002.
- Takase M, Suda K: Histopathological study on mechanism and background of tumor-forming pancreatitis. *Pathol Int* 51:349–354, 2001.
- Kamisawa T, Egawa N, Nakajima H, et al: Clinical difficulties in the differentiation of autoimmune pancreatitis and pancreatic carcinoma. *Am J Gastroenterol* 98:2694–2699, 2003.
- Kamisawa T, Tu Y, Egawa N, et al: Clinicopathologic study on chronic pancreatitis with diffuse irregular narrowing of the main pancreatic duct. *Nippon Shokakibyo Gakkai Zasshi* 98:15– 24, 2001.
- Kamisawa T, Okamoto A: Prognosis of autoimmune pancreatitis. J Gastroenterol 42(Suppl 18):59–62, 2007.
- 60. Kawaguchi K, Koike M, Tsuruta K, et al: Lymphoplasmacytic sclerosing pancreatitis with cholangitis: a variant of primary sclerosing cholangitis extensively involving pancreas. *Hum Pathol* 22:387–395, 1991.
- Takayama M, Hamano H, Ochi Y, et al: Recurrent attacks of autoimmune pancreatitis result in pancreatic stone formation. *Am J Gastroenterol* 99:932–937, 2004.
- Kamisawa T, Egawa N, Nakajima H, et al: Extrapancreatic lesions in autoimmune pancreatitis. J Clin Gastroenterol 39:904–907, 2005.
- Ohara H, Nakazawa T, Sano H, et al: Systemic extrapancreatic lesions associated with autoimmune pancreatitis. *Pancreas* 31:232–237, 2005.

- 64. Hirano K, Tada M, Isayama H, et al: Long-term prognosis of autoimmune pancreatitis with and without corticosteroid treatment. *Gut* 56:1719–1724, 2007.
- Kamisawa T, Okamoto A, Funata N: Clinicopathological features of autoimmune pancreatitis in relation to elevation of serum IgG4. *Pancreas* 31:28–31, 2005.
- Notohara K, Burgart LJ, Yadav D, et al: Idiopathic chronic pancreatitis with periductal lymphoplasmacytic infiltration: clinicopathologic features of 35 cases. *Am J Surg Pathol* 27:1119– 1127, 2003.
- Manfredi R, Frulloni L, Mantovani W, et al: Autoimmune pancreatitis: pancreatic and extrapancreatic MR imaging-MR cholangiopancreatography findings at diagnosis, after steroid therapy, and at recurrence. *Radiology* 260:428– 436, 2011.
- 68. Muhi A, Ichikawa T, Motosugi U, et al: Massforming autoimmune pancreatitis and pancreatic carcinoma: differential diagnosis on the basis of computed tomography and magnetic resonance cholangiopancreatography, and diffusionweighted imaging findings. *J Magn Reson Imaging* 35:827–836, 2012.
- 69. Kim HJ, Kim YK, Jeong WK, et al: Pancreatic duct "icicle sign" on MRI for distinguishing autoimmune pancreatitis from pancreatic ductal adenocarcinoma in the proximal pancreas. *Eur Radiol* 25:1551–1560, 2015.
- Park SH, Kim MH, Kim SY, et al: Magnetic resonance cholangiopancreatography for the diagnostic evaluation of autoimmune pancreatitis. *Pancreas* 39:1191–1198, 2010.
- Horiuchi A, Kawa S, Hamano H, et al: ERCP features in 27 patients with autoimmune pancreatitis. *Gastrointest Endosc* 55:494–499, 2002.
- Kim KP, Kim MH, Kim JC, et al: Diagnostic criteria for autoimmune chronic pancreatitis revisited. World J Gastroenterol 12:2487–2496, 2006.
- Saegusa H, Momose M, Kawa S, et al: Hilar and pancreatic gallium-67 accumulation is characteristic feature of autoimmune pancreatitis. *Pancreas* 27:20–25, 2003.
- 74. Lee TY, Kim MH, Park do H, et al: Utility of 18F-FDG PET/CT for differentiation of autoimmune pancreatitis with atypical pancreatic imaging findings from pancreatic cancer. AJR Am J Roentgenol 193:343–348, 2009.
- Van Kouwen MC, Jansen JB, Van Goor H, et al: FDG-PET is able to detect pancreatic carcinoma in chronic pancreatitis. *Eur J Nucl Med Mol Imaging* 32:399–404, 2005.
- Nakajo M, Jinnouchi S, Noguchi M, et al: FDG PET and PET/CT monitoring of autoimmune pancreatitis associated with extrapancreatic autoimmune disease. *Clin Nucl Med* 32:282–285, 2007.
- Prokesch RW, Chow LC, Beaulieu CF, et al: Isoattenuating pancreatic adenocarcinoma at multi-detector row CT: secondary signs. *Radiology* 224:764–768, 2002.
- Ito T, Nishimori I, Inoue N, et al: Treatment for autoimmune pancreatitis: consensus on the treatment for patients with autoimmune pancreatitis in Japan. J Gastroenterol 42(Suppl 18):50–58, 2007.
- Ghazale A, Chari ST: Optimizing corticosteroid treatment for autoimmune pancreatitis. *Gut* 56:1650–1652, 2007.
- Chari ST: Current concepts in the treatment of autoimmune pancreatitis. JOP 8:1–3, 2007.
- Kamisawa T, Yoshiike M, Egawa N, et al: Treating patients with autoimmune pancreatitis: results from a long-term follow-up study. *Pancreatology* 5:234–238, discussion 238–240, 2005.

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- 82. Veenstra J, Krediet RT, Somers R, et al: Tumor lysis syndrome and acute renal failure in Burkitt's lymphoma: description of 2 cases and a review of the literature on prevention and management. *Neth J Med* 45:211–216, 1994.
- Jasek AM, Day HJ: Acute spontaneous tumor lysis syndrome. Am J Hematol 47:129–131, 1994.
- Spiegel RJ, Magrath IT: Tumor lysis pancreatitis. Med Pediatr Oncol 7:169–172, 1979.
- 85. Hashimoto F: Transient eosinophilia associated with pancreatitis and pseudocyst formation. *Arch Intern Med* 140:1099–1100, 1980.
- Abraham SC, Leach S, Yeo CJ, et al: Eosinophilic pancreatitis and increased eosinophils in the pancreas. *Am J Surg Pathol* 27:334–342, 2003.
- 87. Amar S, Wu KJ, Tan WW: Sorafenib-induced pancreatitis. *Mayo Clin Proc* 82:521, 2007.
- Li M, Srinivas S: Acute pancreatitis associated with sorafenib. South Med J 100:909–911, 2007.
- McDonald GB: Tirumali N: Intestinal and liver toxicity of antineoplastic drugs. West J Med 140:250–259, 1984.
- Levy P, Menzelxhiu A, Paillot B, et al: Abdominal radiotherapy is a cause for chronic pancreatitis. *Gastroenterology* 105:905–909, 1993.
- Badalov N, Baradarian R, Iswara K, et al: Drug induced acute pancreatitis: an evidence based review. *Clin Gastroenterol Hepatol* 5:648–661, 2007.

# **Diffuse Pancreatic Disease**

HANSOL KIM | NISHA I. SAINANI

## **General Considerations**

Diffuse involvement of the pancreas can occur with various inflammatory, infective, infiltrative, or neoplastic disorders. Any pathologic process that involves the pancreas focally also can cause diffuse involvement (Box 51-1). More common causes of diffuse pancreatic involvement (e.g., pancreatitis) have been discussed previously. This chapter discusses infrequent causes and differential features.

#### IMAGING

Imaging can demonstrate the pattern and extent of pancreatic involvement and other ancillary features, which can suggest and facilitate diagnosis. Although imaging features can overlap, differentiation becomes critical from the management perspective. Please refer to Figure 51-1 for an imaging algorithm of diffuse pancreatic diseases.

#### DIFFERENTIAL DIAGNOSIS

Because of overlapping imaging features, clinical and laboratory parameters are often required to elucidate and reinforce the diagnosis. Imaging can guide invasive techniques (biopsy, fineneedle aspiration) in doubtful cases, aid in further substantiation of diagnosis, and guide in treatment planning. Imaging also plays an important role in screening and posttherapy follow-up to demonstrate resolution, recovery, or recurrence. Please refer to Table 51-1 and Figures 51-2 to 51-5.

#### TREATMENT

Medical management depends on the underlying disease process involving the pancreas and is detailed in the discussion of individual diseases presented in this chapter. Surgical management is generally not recommended for diffuse pancreatic disorders, but palliative measures may be required in some cases.

## What the Referring Physician Needs to Know: General Considerations

- Overlapping imaging features of diffuse pancreatic disease are seen.
- Consideration of clinical, laboratory, and imaging findings are vital for narrowing the differential diagnosis and may help avoid surgery for diagnostic and therapeutic purposes in medically treatable cases.
- Histologic diagnosis is crucial before appropriate medical or surgical therapy is instituted.
- Confirmation of diagnosis can be done by pathologic evaluation of tissue obtained from the pancreatic lesion or other involved organs.

## **Infiltrative Disorders**

## **CYSTIC FIBROSIS**

#### Etiology

Cystic fibrosis is a life-threatening disorder caused by mutation in the cystic fibrosis transmembrane conductance regulator gene (*CFTR*) on chromosome 7.

#### Prevalence and Epidemiology

Cystic fibrosis is an autosomal recessive disorder that is more prevalent in whites, with an incidence of approximately 1 in 2500 (in this population).<sup>1</sup>

#### **Clinical Presentation**

Although predominantly characterized by chronic obstructive lung disease and pancreatic insufficiency, cystic fibrosis is a multiorgan disease affecting the liver, gallbladder, bile ducts, intestines, and the reproductive tract. The clinical and imaging findings vary with severity and duration of disease process in all age groups. Nearly 85% to 90% of patients will present with clinical signs within 1 year of life.<sup>2</sup> Significant loss of pancreatic exocrine cells must be present before development of typical clinical symptoms of insufficiency such as steatorrhea, fat intolerance, failure to thrive, bloating, flatulence, and abdominal pain. Pancreatic function may be preserved in 10% to 15% of patients, and when residual exocrine function is present, patients may present with acute pancreatitis.<sup>3</sup> Endocrine dysfunction is less commonly encountered.

### Pathophysiology

The defective transmembrane ion transport in cystic fibrosis leads to accumulation of thick, viscous pancreatic secretions in the pancreatic ducts, leading to ductal ectasia and acinar atrophy. Inflammatory reaction, progressive fatty replacement, fibrosis, and calcification result, with extensive atrophic change occurring in severe long-standing disease.<sup>4,5</sup> Cyst formation can occur secondary to inspissated secretions obstructing the small pancreatic ducts.<sup>6</sup>

#### Imaging

The patterns of pancreatic involvement include (1) partial fibrofatty replacement of the pancreas, (2) complete fibrofatty replacement with enlargement of pancreas (lipomatous pseudohypertrophy), (3) pancreatic atrophy without evidence of fatty replacement, (4) diffuse pancreatic fibrosis, and (5) pancreatic cystosis.<sup>35</sup> In pancreatic cystosis, cysts are usually multiloculated with individual cysts measuring 0.5 to 12 cm in diameter.<sup>7</sup> Complete fatty replacement of the pancreas is commonly seen, with fat replacement maintaining the shape of the pancreas. This morphologic finding may be evident in older patients and represents late stage of disease, but it also can be seen earlier with severe involvement.<sup>8</sup>

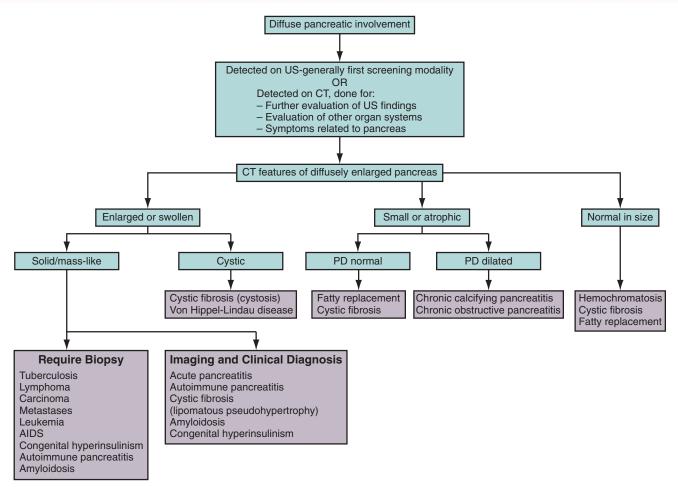


Figure 51-1 Imaging pattern–based algorithm for diffuse pancreatic diseases. AIDS, Acquired immunodeficiency syndrome; CT, computed tomography; PD, pancreatic duct; US, ultrasonography.

#### BOX 51-1 DIFFUSE PANCREATIC DISEASES

#### **INFLAMMATION**

- Acute pancreatitis
- Chronic pancreatitis
  - Chronic calcifying pancreatitis
  - Chronic obstructive pancreatitisAutoimmune pancreatitis
- Autoinninun

#### INFILTRATION

- Cystic fibrosis
- Fatty replacement of pancreas
- Amyloidosis
- Hemochromatosis

#### INFECTION

- Tuberculosis
- Acquired immunodeficiency syndrome

#### NEOPLASM

- Lymphoma
- Leukemia
- Carcinoma
- Metastases

#### MISCELLANEOUS

- Nesidioblastosis (persistent hyperinsulinemic hypoglycemia of infancy, congenital hyperinsulinism)
- Von Hippel-Lindau disease



**Figure 51-2** Acute pancreatitis. Axial computed tomography image reveals a swollen, edematous head and body of pancreas (*arrows*) with peripancreatic fat stranding (*long black arrow at lower left*) and fluid collection (*arrowheads*).

		Imaging Mimics	Lymphoma	Pancreatic CA when associated with focal mass-like lesion	Mass-like lesion of chronic pancreatitis	Acute pancreatitis, pancreatic CA when associated focal mass-like swelling	Carcinoma, Iymphoma, AIDS
		ERCP	I	PD beading, irregular dilatation	Bulging papilla with MD IPMN, PD dilated	PD attenuated or irregular	PD normal, compressed, displaced or stenosed
tes	IMAGING	MR	Enlarged, T1-weighted hypointense, T2-weighted hyperintense	Small or atrophic, MRCP: PD irregularity, beading, dilatation	CA: Hypointense on parenchymal phase of IV contrast, upstream PD dilatation, ± invasion and metastasis MD IPMN: Diffuse PD dilatation ± bulging major papilla	T1 hypointense, T2 hyperintense, sausage shaped, peripancreatic halo, peripancreatic stranding, PD attenuated or inregular, ± CBD involvement, focal mass-like swelling	Enlarged T1 hypointense T2 hyperintense, heterogeneous enhancement
		сī	Enlarged, hypodense Peripancreatic fat stranding and fluid collection	Small or atrophic, irregular ductal dilatation, ± calcification	CA: Hypodense on parenchymal phase of IV contrast, upstream PD ciliatation, ± calcification, ± invasion and metatasis MD IPMN: Diffuse PD ciliatation ± bulging papilla	Enlarged, sausage shaped, peripancreatic halo, peripancreatic stranding, PD attenuated or irregular, ± CBD involvement, focal mass-like swelling	Enlarged, hypodense, heterogeneity as a result of abscess/ calcification/ necrosis, heterogeneous enhancement, peripancreatic edema, peripancreatic, mesenteric, fistulas
		Ultrasonography	Enlarged, hypoechoic	Small or atrophic, irregular ductal dilatation, ± calcification	CA: Hypoechoic lesion, small or atrophic pancreas, upstream PD dilatation and irregularity, ± calcification MD IPMN: Diffuse PD dilatation	Enlarged, hypoechoic	Enlarged, hypoechoic, heterogeneity as a result of abscess/ calcification
		Radiography	Small bowel ileus	Prevertebral calcification	I	I	Calcification in chronic or treated cases
Pancreatic Diseases	Snacific	Laboratory Tests	Serum lipase and amylase	I	1	Serum IgG4	1
Differential Features of Diffuse Pancreatic		Clinical Data	Acute presentation ± history of gallstones and/or alcoholism	Chronic presentation History of gallstones, alcohol, ± exocrine and endocrine insufficiency	Chronic presentation, history of CA or IPMN	Common in males Nonspecific symptoms related to pancreatic involvement	Immigrants, immunocompromised HIV patients Constitutional symptoms, symptoms related to pancreas or other organ system involvement
TABLE Differentia		Disease Process	Acute pancreatitis (see Figure 51-2)	Chronic calcifying pancreatitis (see Figure 51-3)	Chronic obstructive pancreatitis (see Figure 51-4)	Autoimmune pancreatitis (see Figure 51-5)	Tuberculosis (see Figure 51-13)

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		Imaging Mimics	Tuberculosis, carcinoma, lymphoma	Tuberculosis, carcinoma, leukemia, AIDS	Lymphoma Carcinoma Tuberculosis AIDS	Lymphoma, tuberculosis, AIDS
		ERCP	I	PD normal, displaced, narrowed	I	Irregularity or narrowing
	IMAGING	MR	Enlarged T1 hypointense T2 hyperintense, heterogeneous enhancement	Enlarged, T1 hypointense, T2 hyperintense, mild homogeneous enhancement, PD dilatation not a feature, mesenteric and retroperitoneal LN extending below renal vein, invasion of other organs, engulfment of vessels	Enlarged, T1 hypointense, T2 hyperintense, LN, other organ system involvement	Enlarged, T1 hypointense, T2 hyperintense, heterogeneity as a result of necrosis/ calcification, LN, vascular encasement/ invasion, metastases
		cT	Enlarged, hypodense, hemorrhagic necrosis with herpes simplex	Enlarged, hypodense, peripancreatic infiltration, mild homogeneous enhancement, PD dilatation not a feature, mesenteric and retroperitoneal LN extending below renal vein, invasion of other organs, engulfment of vessels Valuable for staging	Enlarged, hypodense, mild enhancement, LN, other organ system involvement	Enlarged, hypodense, heterogeneity as a result of necrosis/ calcification, LN, vascular encasement/ invasion, metastases
		Ultrasonography	Enlarged, hypoechoic	Enlarged, hypoechoic, mesenteric and retroperitoneal LN	Enlarged, hypoechoic, LN, other organ system involvement	Enlarged, hypoechoic, LN, vascular invasion, metastases
e Pancreatic Diseases—cont′d		Radiography	I	Calcification in treated cases	1	I
	Specific	Laboratory Tests	1	I		CA 19-9 for follow-up
Differential Features of Diffuse Pancreatic		Clinical Data	High-risk behavior, IVDA	Systemic symptoms, jaundice less common	Systemic symptoms, jaundice not a feature	Middle-elderly age Systemic symptoms, painless jaundice
TABLE Differentia		Disease Process	AIDS (see Figure 51-14)	Lymphoma (see Figure 51-15)	Leukemia	Carcinoma (see Figure 51-16)

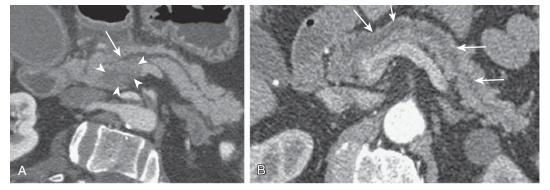
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Lymphoma, carcinoma, tuberculosis	Fatty replacement, VHL	Cystic fibrosis	Fatty replacement	1	I	Cystic fibrosis	
Irregularity or narrowing	I	I	I	I	I	I	common bile du ficiency virus; <i>Ig</i> ( uct; <i>MR</i> , magnet ppel-Lindau dise
Enlarged, T1 hypointense, T2 hyperintense, LN, involvement of other organs	Fatty: T1 and T2 hyperintensity Fibrosis: T1 and T2 hypointensity Cysts: T1 hypointensity, T2 hyperintensity	T1 and T2 hyperintense, prominent lobulations	T1 hypointense and hyperintense, T2 hyperintense	T2 hypointense pancreas and liver	T1 hypointense, T2 hyperintense	Multiple cysts, T1 hypointense, T2 hyperintense ± SCA	CA, carcinoma; CBD, IV, human immunode nopathy); MD, main di capacity; VHL, von Hi
Enlarged, hypodense, occasionally necrosis, LN, involvement of other organs	Size: Normal or atrophic, hypodense as a result of fat/ fibrosis, ± calcification, low-attenuation cystic lesions without solid component	Hypodense, prominent lobulations	Hypodense	Hyperdense pancreas and peripancreatic LN	Enlarged, hypodense	Multiple hypodense cysts with thin wall, $\pm$ calcification throughout pancreas $\pm$ SCA	deficiency syndrome; iopancreatography; H nph nodes (lymphader BC, total iron-binding
Enlarged, hypoechoic, LN, involvement of other organs	Homogeneously or heterogeneously hyperechoic, multiple hypoechoic cysts	Echogenic	Hypoechoic	Normal-appearing pancreas	Enlarged, hypoechoic	Multiple hypoechoic cysts, sometimes solid appearance as a result of multiple interfaces, ± SCA	<ul> <li>e; AIDS, acquired immunc scopic retrograde cholang enous drug abuse; LN, Iyn A, serous cystadenoma; 71</li> </ul>
I		I	I	I	I	I	somal recessives; ERCP, endc s; IVDA, intravestic eatic duct; SC
I	Sweat chloride test	I	I	Serum iron, TIBC, transferrin saturation	Insulin and C peptide	Genetic testing	dominant; AR, auto: M/, diabetes mellitu: alasm; IV, intravenou tography; PD, pancn
Known primary illness, occasionally pancreatic metastaese-first sign Systemic and local symptoms	AR, whites, family histony, exocrine and endocrine dysfunction	Advanced age, DM, metabolic syndrome, Cushing's, long-term use of corticosteroids, chronic pancreatitis	Chronic or hematologic illness	AD, family history, systemic manifestations, endocrine or exocrine pancreatic dysfunction	Recurrent hypoglycemia Insulin and C in infancy peptide	Family history, CNS manifestations, endocrine or exocrine pancreatic dysfunction with severe involvement	, Not available or not relevant; AD, autosomal dominant; AR, autosomal recessive; AIDS, acquired immunodeficiency syndrome; CA, carcinoma; CBD, common bile duct; CNS, central nervous system; CT, computed tomography; DM, diabetes mellitus; ERCP, endoscopic retrograde cholangiopancreatography; HIV, human immunodeficiency virus; IgG4, immunoglobulin G4, IPMN, intraductal papillary mucinous neoplasm; IV, intravenous; IVDA, intravenous drug abuse; LN, lymph nodes (lymphadenopathy); MD, main duct; MR, magnetic resonance; MRCP, magnetic resonance; MRCP, magnetic resonance; MRCP, magnetic resonance cholangiopancreatography; PD, pancreatic duct; SCA, serous cystadenoma; TIBC, total iron-binding capacity; VHL, von Hippel-Lindau disease.
Metastases	Cystic fibrosis (see Figures 51-6 to 51-10)	Fatty replacement (see Figure 51-11)	Amyloidosis	Hemochromatosis (see Figure 51-12)	Nesidioblastosis (congenital hyperinsulinism of infancy)	VHL (see Figures 51-17 and 51-18)	—, Not available or no nervous system; <i>CT</i> , G4; <i>IPMN</i> , intraduct <i>MRCP</i> , magnetic res

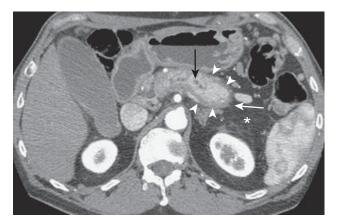
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**Figure 51-3** Chronic calcifying pancreatitis. **A**, Axial computed tomography image shows a small and atrophic pancreas. The pancreatic duct visualized in the region of the body is dilated with an intraductal calcification (*arrow*). **B**, Axial two-dimensional magnetic resonance cholangiopancreatography image in a different patient reveals a beaded irregular pancreatic duct (*arrows*).



**Figure 51-4** Chronic obstructive pancreatitis. Curved reformatted images in two different patients. **A**, A hypodense mass (carcinoma) (*arrowheads*) is seen in the head and uncinate process of the pancreas with abrupt cutoff of the pancreatic duct (*arrow*) and upstream dilatation. The pancreatic parenchyma reveals mild atrophy. **B**, Diffuse dilatation of the pancreatic duct (*arrows*) with mild parenchymal atrophy without any evident mass lesion in this case of main duct intraductal papillary mucinous neoplasm.

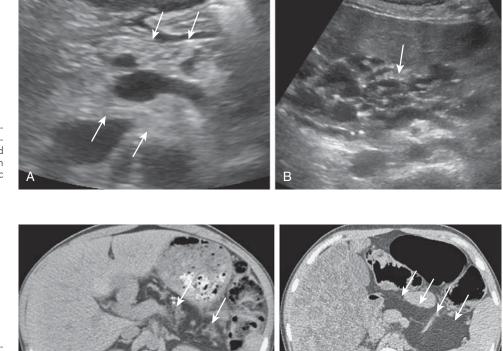


**Figure 51-5** Autoimmune pancreatitis. Axial computed tomography image reveals a swollen pancreas with a peripancreatic hypodensity (halo) (*arrowheads*), minimal peripancreatic stranding (*asterisk*), irregularity of the pancreatic duct (*vertical black arrow*), and retraction of the pancreatic tail (*white arrow*).

**Radiography.** Calcifications may be seen in the late stage of the disease.

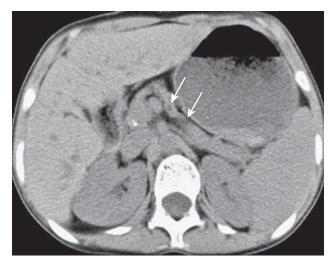
**Ultrasonography.** On ultrasonography, the involved pancreas reveals homogeneously or heterogeneously increased echogenicity (Figure 51-6, A). The pancreas may be normal or small in size, and the typical fine lobular echotexture of the pancreas is gradually lost. Pancreatic cystosis is seen as multiple, thin-walled, anechoic, multiloculated cysts scattered throughout the pancreas with interspersed hyperechoic pancreatic parenchyma (see Figure 51-6, B). Ultrasonography is not sensitive for detecting and estimating the extent of pancreatic involvement.<sup>9</sup>

**Computed Tomography.** Fatty replacement of the pancreas (Figure 51-7) and fibrosis appears hypodense on computed tomography (CT); measurement of Hounsfield units will differentiate the two processes. A small atrophic pancreas can be seen (Figure 51-8). Calcification, when present, is better appreciated on CT.<sup>6</sup> The cystic lesions appear as well-defined



**Figure 51-6** Cystic fibrosis. Ultrasound images reveal hyperechoic pancreatic parenchyma (*arrows*, **A**) and diffuse cystosis of the pancreas with interspersed echogenic pancreatic parenchyma (*arrow*, **B**).

**Figure 51-7** Cystic fibrosis. Axial computed tomography images demonstrate fatty changes in the pancreas with interspersed residual pancreatic parenchyma (*arrows*, **A**) and complete replacement of pancreas by fat (*arrows*, **B**).



**Figure 51-8** Cystic fibrosis. Axial computed tomography image reveals atrophy of the pancreas with a few small cystic lesions seen in the proximal body (*arrows*).

low-attenuation structures without any solid portions or excrescences (Figure 51-9).

**Magnetic Resonance Imaging and Magnetic Resonance Cholangiopancreatography.** Fatty changes reveal hyperintense signal Figure 51-10), whereas areas of fibrosis show as hypointense signal on T1- and T2-weighted images. Cysts appear as hypointense on T1-weighted images and hyperintense on T2-weighted images. Although magnetic resonance imaging (MRI) is more sensitive in detection of additional small cysts compared to CT or ultrasound, no additional clinically important information is added.<sup>9</sup> Exocrine dysfunction and appearance on MR may not correlate, and a normalappearing pancreas can be seen in patients with dysfunction.<sup>10</sup> Beading, strictures, poststenotic dilatation, and obstruction of pancreatic duct also may be present and are best characterized on magnetic resonance cholangiopancreatography (MRCP).

# **Classic Signs: Cystic Fibrosis**

R

- Fatty replacement
- Cystic changes
- Calcifications
- Fibrosis
- Atrophy
- Ductal stenosis and beading

#### **Differential Diagnosis**

With cystic changes, differential diagnosis may include cystic pancreatic neoplasms, polycystic kidney disease, and von Hippel-Lindau syndrome. With diffuse fatty change, lipomatosis may be indistinguishable, although clinical findings of recurrent respiratory infections, age, exocrine and endocrine dysfunction, family history, and positive sweat chloride test can aid in diagnosis.

#### Treatment

**Medical Treatment.** Lifelong pancreatic enzyme replacement and insulin therapy are mainstays of treatment in patients with endocrine or exocrine insufficiency.<sup>11</sup>

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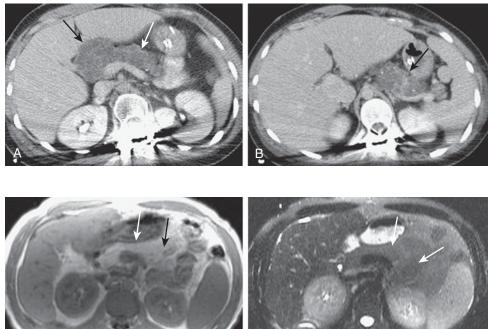


Figure 51-9 Cystic fibrosis. Axial computed tomography images reveal diffuse pancreatic cystosis involving the head, neck, body (black and white arrows, A) and tail of the pancreas (black arrow, B).

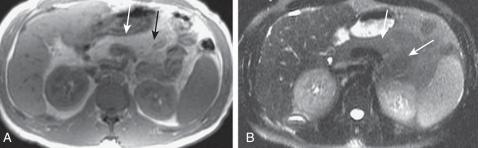


Figure 51-10 Cystic fibrosis. Axial T1-weighted (A) and T2-weighted fatsuppressed (B) magnetic resonance images reveal near-complete fatty replacement of pancreas (arrows), appearing isointense to the retroperitoneal fat.

Surgical Treatment. End-stage lung disease is treated with bilateral lung transplantation. Excess primary digestive tract malignancies have been reported, and use of immunosuppressive therapy after transplant and exogenous growth hormone can secondarily trigger pancreatic malignancies in patients with cystic fibrosis requiring surgical management.<sup>12-</sup>

#### What the Referring Physician Needs to Know: **Cystic Fibrosis**

- Genetic testing can result in early diagnosis and treatment.
- Although less common, pancreatitis can occur in those with preserved exocrine function.
- Asymptomatic patients can be observed with ultrasonography.
- Exocrine pancreatic dysfunction may not become clinically apparent until 98% to 99% of pancreatic parenchyma is damaged.
- Pancreatic insufficiency may lead to an earlier pseudomonal colonization of airways.
- Noninvasive imaging can be useful for quantitative evaluation of morphologic changes in the pancreas and in monitoring the progression of disease, before clinical decline becomes apparent.

# FATTY REPLACEMENT (LIPOMATOSIS) **OF PANCREAS**

#### Etiology

Fatty replacement of the pancreas is commonly seen with obesity and aging. Metabolic syndrome, characterized by obesity, dyslipidemia, glucose intolerance, hypertension, and

proinflammatory or prothrombotic state, is thought to have high association with fatty replacement.<sup>15</sup> Other associated conditions include Cushing's syndrome, adult-onset diabetes mellitus, chronic pancreatitis, hereditary pancreatitis, alcoholic hepatitis, malnutrition, Shwachman-Diamond syndrome, and long-term use of corticosteroids.6

# **Clinical Presentation**

Fatty replacement does not cause clinical symptoms. Clinical presentation is according to the primary disease process.

### Pathology

Mature adipocytes and bands of fibrous tissue replace the pancreatic tissue with sparing of acini and islets of Langerhans.<sup>12</sup>

# Imaging

Ultrasonography. The pancreatic gland appears echogenic on ultrasound examination.

Computed Tomography. Uniform or patchy fatty replacement can be readily identified on CT, which reveals separation of pancreatic parenchyma with prominence of lobulations interspersed with fat. With patchy involvement, the spared regions can be mistaken as pseudotumors. Associated atrophy of the pancreas may be seen to a variable degree, particularly in elderly individuals (Figure 51-11). Massive enlargement of the pancreas due to fatty replacement is known as lipomatous pseudohypertrophy.<sup>16</sup>

Magnetic Resonance Imaging. Fatty replacement of the gland appears hyperintense on T1- and T2-weighted imaging and will suppress on fat-saturated sequences. MRI may be helpful in distinguishing patchy fatty infiltration and pseudotumor appearance of the residual normal pancreas, whereas

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**Figure 51-11** Fatty replacement of pancreas. A and B, Axial computed tomography images in two different elderly patients aged 75 and 84 years, respectively, show variable degree of fatty replacement with prominent pancreatic lobulations and mild atrophy.

true pancreatic adenocarcinoma will rarely demonstrate presence of fat.

# Classic Signs: Fatty Replacement (Lipomatosis) of Pancreas

- Fatty replacement
- Prominent lobules

### **Differential Diagnosis**

Clinical diagnosis gives an insight to the cause of fatty replacement. In the presence of clinical diagnosis and imaging findings, no other diagnostic studies are required.

#### Treatment

No medical treatment is required or available. Sometimes lipomatous pseudohypertrophy can be mistaken as pancreatic mass and taken for surgical resection. Fatty replacement is reversible in obesity after weight reduction, in treated Cushing's syndrome, and with discontinuation of corticosteroids.<sup>6</sup>

#### What the Referring Physician Needs to Know: Fatty Replacement (Lipomatosis) of Pancreas

 Knowledge of lipomatosis helps recognize this condition and avoids mistaking this benign process from other treatable disorders.

#### AMYLOIDOSIS

# Etiology

Amyloidosis is a systemic disorder characterized by abnormal protein folding and extracellular deposition of insoluble fibrillar proteins. Three forms have been defined, with the primary form representing deposition of light-chain immunoglobulins secondary to plasma cell dyscrasias; the secondary form arising as a result of chronic diseases such as rheumatoid, sarcoid, or diabetes; and the familial form representing the autosomal dominant form of the disease with formation of abnormal proteins.

#### **Clinical Presentation**

Patients can present with exocrine or endocrine dysfunction or abdominal pain, in addition to the signs and symptoms of associated systemic illness.

#### Pathology

The pancreas can be involved in primary amyloidosis or, more commonly, as a part of amyloidosis secondary to chronic systemic disease processes. Affinity to Congo red with apple green birefringence under polarized light microscopy are pathognomonic for all amyloidosis.<sup>17</sup>

#### Imaging

Although literature on characteristic imaging findings on pancreatic amyloidosis is scarce, pancreatic involvement can be focal or diffuse.

**Ultrasonography.** The diffusely involved gland appears enlarged and hypoechoic on ultrasound.<sup>18</sup> Often, there is increased affinity to deposition of calcium and punctate calcifications can be seen.<sup>19</sup>

**Computed Tomography.** The diffusely involved gland appears enlarged and hypodense on CT.<sup>18</sup> Similarly, punctate calcifications can be seen.<sup>19</sup>

**Magnetic Resonance Imaging.** The involved gland appears hypointense or hyperintense on T1-weighted imaging and hyperintense on T2-weighted imaging.<sup>18</sup> Diffuse heterogeneous enhancement may be seen.<sup>19</sup>

# Differential Diagnosis

Differential diagnosis for diffuse involvement of the pancreas includes autoimmune pancreatitis, lymphoma, and acute pancreatitis. Involvement of other organ systems can indicate the diagnosis in secondary amyloidosis. Histopathologic evaluation with Congo red and immunostaining of tissue is required for differentiation from other clinical entities.

#### Treatment

Medical management involves treatment of the systemic disease process in secondary forms of amyloidosis.

# What the Referring Physician Needs to Know: Amyloidosis

 Although amyloidosis is a rare cause of diffuse pancreatic involvement, this disease should be considered when chronic or hematologic illnesses coexist.

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## **HEMOCHROMATOSIS**

## Etiology

Hemochromatosis is a disorder of excessive iron accumulation.

## Prevalence and Epidemiology

Hereditary hemochromatosis is prevalent in Northern European descent and is less common in blacks, Hispanics, and Asian-Americans. The disease is five times more common in men, and they usually experience symptoms at an earlier age. Because women lose iron with menstruation and pregnancy, they tend to store less iron than men. After menopause or hysterectomy, the risk for women is the same as that for men.

#### **Clinical Presentation**

Pancreatic involvement manifests as abdominal pain, in addition to the other systemic manifestations of hemochromatosis owing to involvement of heart, skin, liver, thyroid, joints, and other organ systems. Patients will typically present with abdominal pain, fatigue, joint pain, and loss of libido, among other symptoms related to iron deposition in multiple organs.

### Pathophysiology

Hemochromatosis can be primary/hereditary or secondary. Hereditary hemochromatosis is an autosomal dominant disorder resulting from excessive absorption of iron; secondary hemochromatosis results from excessive ingestion of iron or from multiple transfusions. Hereditary hemochromatosis is mainly caused by a defect in the *HFE* gene, which helps regulate the amount of iron absorbed from food. The two common mutations involving the *HFE* gene are *C282Y* and *H63D*. Juvenile and neonatal hemochromatosis, two additional forms, are caused by a mutation in a gene called hemojuvelin.<sup>20</sup>

#### Imaging

**Radiography.** Radiographs have no role in evaluation of pancreatic hemochromatosis. Joint involvement can be separately imaged.

**Ultrasonography.** Ultrasonography is noncontributory in most pancreatic cases. Liver involvement may be seen as an altered echotexture or as heterogeneity.

**Computed Tomography.** CT characteristically reveals increased density in the pancreas and adjacent peripancreatic lymph nodes, although no correlation has been found between the amount of increased density and pancreatic dysfunction or

insufficiency.<sup>21</sup> Unopacified vessels may give a spurious impression of low-density masses in the pancreas, which can be resolved by contrast administration.<sup>22</sup>

**Magnetic Resonance Imaging.** Pancreatic involvement is uncommon without cirrhosis. On T2-weighted gradient recalled echo MRI, the liver and pancreas reveal markedly diminished signal intensity compared with that of skeletal muscles (Figure 51-12). Hypointense signal also can be seen on spin echo T2-weighted images, although this sequence is less sensitive. The splenic signal is normal in primary hemochromatosis.<sup>23</sup> On chemical shift in-phase and out-of-phase imaging, reversal of signal drop is seen in comparison to when there is intracytoplasmic fat, with signal drop out seen on in-phase imaging with iron deposition. Quantification of the liver iron content can be performed using T2-weighted gradient recalled echo images. By calculating the ratio of signal intensity of liver to that of fat, mounting iron overload can be serially evaluated.<sup>24</sup>

# **Classic Signs: Hemochromatosis**

- Hyperdense on CT (pancreas and lymph nodes)
- Hypointense on T2-weighted gradient recalled echo MRI

### **Differential Diagnosis**

Systemic involvement of the heart, skin, liver, joints, thyroid, and other organ systems supports the imaging diagnosis. Findings of elevated serum iron concentration, total iron-binding capacity, and transferrin saturation values are characteristic. Liver biopsy is the gold standard for diagnosis.

# Treatment

**Medical Treatment.** Regular phlebotomy is effective in removing excess iron from the body.

**Surgical Treatment.** No surgical management is recommended. However, patients developing hepatic cirrhosis secondary to hemochromatosis are at increased risk for hepatocellular carcinoma, which may require surgical management.

# Infections

## **TUBERCULOSIS**

#### Etiology

Pancreatic tuberculosis is a rare disease entity caused by *Mycobacterium tuberculosis*.

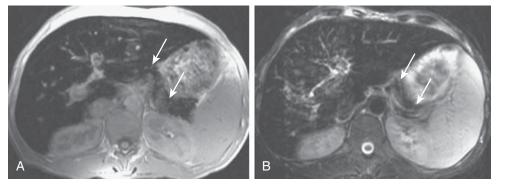


Figure 51-12 Hemochromatosis. Axial T1-weighted (A) and T2-weighted fatsuppressed gradient recalled echo (B) magnetic resonance imaging reveals diffusely hypointense pancreas (*arrows*) and liver, compared with the muscles, secondary to iron deposition. Spleen is shown as normal signal intensity.

# What the Referring Physician Needs to Know: Hemochromatosis

- Early identification of disease and appropriate treatment can prevent progression to irreversible pancreatic insufficiency and liver cirrhosis.
- Genetic testing can be done for early identification.
- Spleen is spared in primary form.
- In secondary form, pancreatic involvement occurs only once the reticuloendothelial system becomes saturated with iron (bone marrow, spleen, and liver).
- Imaging is performed to determine organ involvement, monitor response to treatment, and diagnose and manage complications such as hepatic cirrhosis and hepatocellular carcinomas.

#### Prevalence and Epidemiology

An increased incidence of tuberculosis is being documented in developed countries owing to immigration, human immunodeficiency virus (HIV) pandemic with worldwide resurgence of *M. tuberculosis*, and other immunocompromise conditions. Sporadic cases are also noted with the propensity to involve malnourished or homeless people or those living in overcrowded situations.<sup>25</sup>

#### **Clinical Presentation**

Because of the propensity to involve multiple organ systems, the clinical presentation of tuberculosis varies. Pancreatic involvement can result in moderate intensity, intermittent or persistent vague upper abdominal pain, obstructive jaundice, portal vein obstruction, acute or chronic pancreatitis, gastrointestinal bleeding, ventral abdominal wall fistula, and lymphadenopathy. Constitutional signs and symptoms related to tuberculosis or symptoms of tuberculosis elsewhere in the body (i.e., lungs, brain) may or may not be present, although a significant proportion of patients will demonstrate involvement of the abdominal cavity alone, without extraabdominal sites of disease.<sup>26-28</sup>

# Pathophysiology

Within the abdomen, mesentery, small bowel, peritoneum, liver, and spleen are common sites of involvement. Tuberculosis of the pancreas usually occurs as a complication of miliary tuberculosis and immunodeficiency; isolated or primary involvement of the pancreas is exceedingly rare. The rarity of occurrence of pancreatic tuberculosis has been attributed to antibacterial pancreatic factors. Diagnosis is suggested by relevant clinical history or evidence of tuberculosis elsewhere in the body.<sup>25</sup>

#### Pathology

Lymphatic, hematogenous, and direct extension from adjacent involved organs are the modes theorized to result in pancreatic involvement. The gland may be diffusely involved by caseating granulomas, or there may be a combination of granulomas and inflammation. Pancreatic tuberculosis can cause biliary obstruction by compression of the bile duct by lymphadenopathy or by direct involvement of the duct itself.<sup>29</sup> HIV-infected patients often develop well-formed caseating granulomas because tuberculosis tends to occur before advanced immunocompromise develops.<sup>30</sup>

# Imaging

Although focal involvement of pancreas is more common, diffuse involvement has been reported.

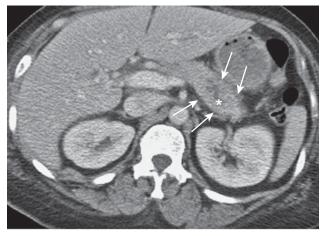
**Radiography.** Evidence of pulmonary tuberculosis may be seen on chest radiographs. Abdominal radiographs may reveal calcifications within chronic or treated granulomas of abdominal organs.<sup>29</sup>

**Ultrasonography.** Diffusely involved gland appears enlarged and hypoechoic, although heterogeneity secondary to necrosis, abscess formation, and calcification may be evident, which can be difficult to differentiate from pancreatic carcinoma.<sup>29</sup>

**Computed Tomography.** On noncontrast CT, involved gland appears enlarged and hypodense and can at times mimic pancreatic malignancy. Focal areas of necrosis or calcification may result in a heterogeneous appearance (Figure 51-13). On contrast-enhanced CT, the lesion reveals peripheral enhancement with a nonenhancing central necrotic component. Areas of central enhancement may result in a multiloculated appearance. Peripancreatic edema or collections may be seen. Peripancreatic, mesenteric, or periportal lymphadenopathy is more readily identified on CT. Lymphadenopathy may be homogeneous or may reveal necrotic foci. Fistulas (interbowel loop or enterocutaneous), when present, are also better appreciated on CT.<sup>29</sup>

**Magnetic Resonance Imaging.** On MRI, the involved gland appears hypointense on T1-weighted imaging and hyperintense or heterogeneous on T2-weighted imaging, with heterogeneous enhancement after intravenous contrast agent administration.<sup>31</sup>

**Positron Emission Tomography With Computed Tomography.** Fluorodeoxyglucose with positron emission tomography (FDG-PET) reveals increased tracer uptake, resulting in a falsepositive diagnosis of malignancy. PET-CT can be helpful in identifying the region of interest for CT-guided biopsy or aspiration to improve diagnostic sensitivity. PET/CT can be used to



**Figure 51-13** Tuberculosis. Axial computed tomography image through the pancreas demonstrates diffuse enlargement of the body and tail. The involved pancreas is mildly enhancing peripherally (*arrows*) with a central hypodense nonenhancing area secondary to necrosis (*asterisk*).

assess treatment response in patients with persistent or increasing size of tuberculoma. It is suggested persistent FDG uptake is likely representative of disease not responsive to treatment and may require change in medications or prolonged therapy.<sup>32</sup>

**Endoscopic Retrograde Cholangiopancreatography.** Endoscopic retrograde cholangiopancreatography (ERCP) reveals a normal pancreatic duct, or there may be compression, displacement, or stenosis.<sup>33</sup>

#### **Classic Signs: Tuberculosis**

- Necrosis and abscess formation
- Peripancreatic, mesenteric, and periportal lymphadenopathy
- Heterogeneous enhancement
- Bowel involvement
- Fistulas

# **Differential Diagnosis**

Imaging features are nonspecific and may resemble those of other inflammatory or neoplastic lesions of the pancreas. A search for associated findings, such as ileocecal mural thickening or lymphadenopathy in the peripancreatic tissues and mesentery, as well as local and constitutional signs and symptoms, assists in raising the clinical suspicion and confirming the diagnosis.<sup>34</sup> Histologic diagnosis is crucial before appropriate medical therapy can be instituted. Confirmation of diagnosis usually requires pathologic evaluation of the tissue obtained from a pancreatic lesion or peripancreatic lymph nodes, which can be obtained via CT- or ultrasound-guided percutaneous or surgical biopsy.

The aspirate should be stained for acid-fast bacilli and cultured for *M. tuberculosis.* Image-guided percutaneous aspiration and biopsy has a reported sensitivity of less than 50% for pancreatic tuberculosis; surgical biopsy is hence sometimes essential, especially when image-guided biopsy results are negative in a setting of high clinical and radiologic suspicion.<sup>25</sup> Acidfast staining of pathologic material demonstrates organisms in 20% to 40% of cases, and culture is approximately 77% sensitive. Polymerase chain reaction (PCR) assay has proved useful in identifying *M. tuberculosis* in pathologic material, although the results offer no information regarding drug susceptibility and therefore it is best used as an adjunct to standard culture.<sup>25</sup>

Few investigators have successfully used endoscopic ultrasound-guided fine-needle aspiration for definitive histologic and bacteriologic diagnosis of pancreatic tuberculosis, with one study demonstrating sensitivity of 76%.<sup>28</sup> This technique along with PCR shows promise in a minimally invasive technique for improving the diagnostic accuracy of pancreatic tuberculosis.<sup>28,35</sup>

#### Treatment

**Medical Treatment.** Patients with pancreatic tuberculosis typically respond well to conventional antituberculous therapy with rifampin, isoniazid, ethambutol, and pyrazinamide. Abscesses, particularly large ones, require aspiration to accelerate the response. Prognosis is poor, however, in patients with HIV infection.<sup>36</sup>

Surgical Treatment. Patients with biliary obstruction need either endoscopic or surgical relief because ductal narrowing

might persist despite treatment with antituberculous therapy.<sup>37</sup> Ultrasound or CT can be used to observe patients with pancreatic tuberculosis to assess response to treatment.<sup>38</sup>

# What the Referring Treating Physician Needs to Know: Tuberculosis

- Pancreatic tuberculosis can be treated with antituberculous therapy with good results.
- Sometimes may be confused with pancreatic malignancy.
- Early diagnosis of pancreatic tuberculosis is important to avoid unnecessary diagnostic or therapeutic procedures.
- Imaging plays an important role for noninvasive characterization, guidance of biopsy, and assessing treatment response.

# ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

#### Etiology

In patients with acquired immunodeficiency syndrome (AIDS), opportunistic infections (Box 51-2), drug-induced inflammation, or neoplasms may affect the pancreas, in addition to the disorders seen in the general population. Multiple antiviral medications, such as zidovudine, efavirenz, didanosine, and protease inhibitors are known to cause acute and chronic pancreatitis, some by inducing hyperlipidemia.<sup>39</sup>

# **Clinical Presentation**

In addition to constitutional symptoms of AIDS, pancreatic involvement may manifest with signs and symptoms indistinguishable from those of other causes of pancreatitis. Although it is unclear if cases of acute pancreatitis in HIV-seropositive individuals are related to malnutrition or to the HIV, they have a higher incidence of acute pancreatitis compared to the general population.<sup>39,40</sup>

#### BOX 51-2 OPPORTUNISTIC INFECTIONS AFFECTING PANCREAS IN ACQUIRED IMMUNODEFICIENCY SYNDROME

#### BACTERIA

- Mycobacterium tuberculosis
- Mycobacterium avium-intracellulare complex (MAC)

#### FUNGI

- Cryptococcus neoformans
- Candida
- Histoplasma capsulatum
- Aspergillus

#### PROTOZOA

- Toxoplasma gondii
- Pneumocystis jiroveci
- Cryptosporidium
- Microsporidia
- Leishmania

#### VIRUS

- Cytomegalovirus
- Herpes simplex
- Herpes zoster

# Pathology

Multiple organ systems can be involved. Pancreatic involvement may vary from asymptomatic to fulminant pancreatitis and is most commonly part of a disseminated disease process.

# Imaging

Involvement of the pancreas in AIDS is more often diffuse (Figure 51-14). In one study, 25% of patients demonstrated abnormalities on ultrasound and 33% demonstrated abnormalities on CT, including focal or diffuse enlargement of the pancreas, ductal dilatation, and pseudocyst and abscess formation.<sup>41</sup> Typically, ultrasonography or CT reveals an enlarged or boggy pancreas with cytomegalovirus infection.<sup>42</sup> Hemorrhagic necrotic lesions are seen with herpes simplex pancreatitis.<sup>43</sup>

**Ultrasonography and Computed Tomography.** The involved gland is indistinguishable from other forms of pancreatitis. Abnormal ductal dilatation or abscess or psuedocyst formation can be seen.

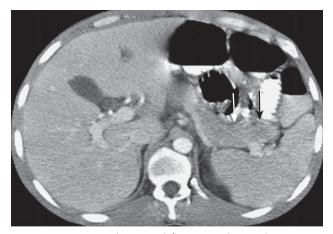
**Magnetic Resonance Imaging.** The involved gland is hypointense on T1-weighted images, hyperintense on T2-weighted images, and indistinguishable from that of other forms of pancreatitis.

#### **Classic Signs: Acquired Immunodeficiency Syndrome**

- Enlarged boggy pancreas with cytomegalovirus infection
- Hemorrhagic necrosis with herpes simplex infection

### **Differential Diagnosis**

Clinical diagnosis of AIDS is of utmost importance to raise suspicion of pancreatic involvement. Extrapancreatic sites of involvement should be sought. Histologic evaluation may be necessary for organism-specific diagnosis. Special stains for mycobacteria, fungi, and viral inclusions after biopsy and serologic tests are required for diagnosis.



**Figure 51-14** Acquired immunodeficiency syndrome. The pancreas is diffusely swollen and hypodense (arrows) on this axial computed tomography image. *Mycobacterium bovis* was cultured from the pancreatic aspirate.

# Treatment

Medical management includes supportive therapy and treatment of the underlying disease process and inciting cause.

#### What the Treating Physician Needs to Know: Acquired Immunodeficiency Syndrome

- Recognition of AIDS-related pancreatic involvement is important for appropriate management.
- Antiretroviral therapy may be the cause of pancreatitis.
- Appearance is indistinguishable from that of other causes of pancreatitis.

# **Neoplasms**

# LYMPHOMA

#### Etiology

Lymphomatous involvement of the pancreas can be primary or secondary.

#### Prevalence and Epidemiology

Primary pancreatic lymphoma is a rare extranodal manifestation of non-Hodgkin's lymphoma (NHL). Secondary involvement of the pancreas is more common compared to primary involvement in NHL, although both are considered extremely rare. Only 0.2% to 2% of patients with NHL have primary involvement of the pancreas. Primary and secondary forms may be distinguished by extrapancreatic involvement. A relatively higher incidence (5%) is seen with AIDS-related NHL.<sup>44</sup> In Hodgkin's lymphoma, pancreatic involvement is considered extremely rare. Because of the absence of a capsule, adjacent lymph node involvement may be difficult to distinguish from pancreatic infiltration.<sup>45</sup>

## **Clinical Presentation**

Manifesting symptoms of pancreatic lymphoma are usually nonspecific and include abdominal pain, abdominal mass, weight loss, nausea, vomiting, jaundice, and acute pancreatitis.<sup>44</sup> Abdominal pain and pancreatic mass without associated jaundice is a clinical manifestation commonly associated with pancreatic lymphoma and can be valuable in distinguishing these lesions from carcinomas or at least in raising suspicion of an unusual neoplasm.<sup>46</sup>

## Pathophysiology

The majority of primary pancreatic lymphomas are the B-cell type, although T-cell types have been reported in the Japanese literature.<sup>47</sup> Most are intermediate- to high-grade NHLs, with diffuse large cell tumors being the predominant histotype.<sup>46</sup> Diagnostic criteria for primary pancreatic involvement include a predominant pancreatic mass with gross involvement of only peripancreatic lymph nodes, no hepatic or splenic involvement, no palpable superficial or mediastinal lymph nodes, and a normal leukocyte count.<sup>48</sup> Secondary involvement of the pancreas occurs by extension of peripancreatic lymphadenopathy to the adjacent gastrointestinal tract.<sup>44,46</sup>

#### Imaging

The morphologic manifestation of pancreatic lymphoma on imaging may be in the form of a localized, well-circumscribed mass, or a diffuse enlargement of the pancreas. Primary pancreatic lymphoma may sometimes be indistinguishable from primary pancreatic adenocarcinoma and further evaluation with biopsy is warranted.

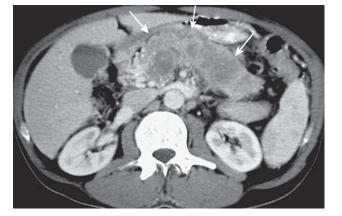
**Radiography.** Calcifications can be seen in treated disease.<sup>49</sup>

**Ultrasonography.** On ultrasonography, pancreatic involvement, whether focal or diffuse, appears homogeneously hypoechoic. Involved peripancreatic lymph nodes are isoechoic to the pancreatic lesion. Typically, peripancreatic vasculature is engulfed by pancreatic lymphoma and patency can be evaluated using color Doppler imaging. On endoscopic ultrasonography, the wall of the common bile duct appears hyperechoic, contrasting to the adjacent hypoechoic pancreatic parenchyma.<sup>46</sup>

**Computed Tomography.** CT by far is the most common imaging modality used for detection and staging of pancreatic lymphoma. The lesions are predominantly homogeneous and hypodense to the musculature, although areas of heterogeneity may sometimes be seen (Figure 51-15). Infiltration and stranding of peripancreatic fat may be seen. The lesions reveal poor homogeneous enhancement and occasional heterogeneous enhancement may be seen after contrast administration.<sup>46</sup>

Diffuse infiltrating pattern with enlargement and irregular infiltration of the peripancreatic fat may mimic acute pancreatitis on imaging. However, clinical presentation is never similar to acute pancreatitis and is disproportionate to the extensive pancreatic involvement, even in the presence of abnormal laboratory parameters. Pancreatic ductal dilatation is not marked, despite invasion. Invasion of the retroperitoneum, upper abdominal organs, and gastrointestinal tract and the presence of mesenteric or retroperitoneal lymphadenopathy extending below the renal veins are also signs favoring lymphoma. Calcification and necrosis in an untreated case weighs against lymphoma. The engulfment, rather than stenosis or occlusion of peripancreatic vessels, which characteristically differentiates lymphoma from pancreatic carcinoma, can be appreciated on CT angiography, although stenosis or occlusion of the superior mesenteric, splenic, or portal vein has been seen in minority of cases.49

Magnetic Resonance Imaging. Often used as a problemsolving tool, the diffusely involved gland appears hypointense



**Figure 51-15** Lymphoma. Axial computed tomography image reveals a diffusely enlarged and predominantly hypodense pancreas (*arrows*) with mild heterogeneous enhancement.

on T1-weighted imaging and hypointense or hyperintense on T2-weighted imaging, with mild to moderate homogeneous enhancement. Peripancreatic lymphadenopathy has signal intensity similar to that of the pancreas. Ductal involvement can be assessed with MRCP, whereas MR angiography can help evaluate peripancreatic vasculature.

**Endoscopic Retrograde Cholangiopancreatography.** On endoscopic retrograde cholangiopancreatography (ERCP), the Wirsung duct may be normal, displaced, or narrowed in patients with pancreatic lymphoma. This is in contrast to carcinoma, which causes stenosis with moderate to severe upstream dilatation. Although biliary obstruction may be seen, jaundice occurs in fewer than half of the cases of pancreatic lymphoma.

**Positron Emission Tomography With Computed Tomography.** Lymphomas reveal avid FDG uptake, and PET/CT is crucial in staging and posttreatment follow-up.

# Classic Signs: Lymphoma

- Abdominal pain and mass without associated jaundice
- Predominantly homogeneous
- Infiltration of peripancreatic fat
- Lack of pancreatic ductal dilatation
- Lack of calcification and necrosis in untreated cases
- Retroperitoneal lymphadenopathy extending below renal veins
- Engulfment rather than stenosis of vessels

### **Differential Diagnosis**

Clinical presentation can be overlapping with other pancreatic neoplasms, but absence of jaundice is an important diagnostic clue to differentiate lymphoma from carcinoma. Pancreatic lymphoma also can manifest with diffuse enlargement of the gland with peripancreatic fat stranding, findings indistinguishable from those of acute pancreatitis. However, clinical symptoms will be less pronounced.

Imaging plays an important role in the diagnosis and staging of pancreatic lymphoma. Treatment and prognosis of lymphoma significantly differ from those of pancreatic carcinoma, which is the main differential diagnosis. CT- or ultrasoundguided biopsy of a pancreatic mass can be performed for pathologic evaluation, which serves as a gold standard in distinguishing pancreatic lymphoma from carcinoma. Surgery is reserved for cases in which the diagnosis cannot be established by less invasive methods.<sup>49,50</sup>

#### Treatment

**Medical Treatment.** Chemotherapy with CHOP (cyclophosphamide, hydroxydaunomycin, vincristine [Oncovin], prednisolone) regimen is the treatment of choice; irradiation or immunotherapy drugs (e.g., rituximab) are used as adjuncts to chemotherapy in advanced cases.<sup>46</sup>

**Surgical Treatment.** Relief of biliary obstruction can be achieved by endoscopic or percutaneous stent insertion or with surgical procedures such as choledochojejunostomy, tumor debulking, or a palliative Whipple procedure, which is no longer performed for this indication.<sup>46</sup>

#### What the Referring Physician Needs to Know: Lymphoma

- The prognosis of pancreatic lymphoma is much better than the dismal survival rate of pancreatic carcinoma.
- Most pancreatic lymphomas respond well to chemotherapy.
- Imaging diagnosis and staging play a crucial role in management.

# LEUKEMIA

# Etiology

Leukemia-associated extramedullary disease can occur as lymphoid or myeloid lesions. Extramedullary myeloid lesions are more common and are called *granulocytic sarcomas*. Granulocytic sarcomas can involve virtually any organ system but has particular predilection for soft tissues, bones, skin, lymph nodes, and periosteum.<sup>51</sup> Although granulocytic sarcomas are rare, patients may present with extramedullary relapse of leukemia within the pancreas.<sup>52</sup>

### Prevalence and Epidemiology

Pancreatic disease may be seen with preexisting hematologic disease, which suggests the diagnosis, or the pancreas may be the primary site of involvement.<sup>53</sup>

### **Clinical Presentation**

Presentation is similar to that of other pancreatic neoplastic processes. Associated systemic manifestations may be present. Although patients may be asymptomatic, cholestatic jaundice and pancreatitis may occur.<sup>54</sup>

### Pathology

In addition to the pancreas, lymph nodes, bones, periosteum, skin, soft tissue, kidney, liver, central nervous system (CNS), mediastinum, testicles, and other organ systems may be involved.

### Imaging

Three morphologic patterns of pancreatic leukemia have been described: (1) well or ill-circumscribed focal form, (2) diffuse infiltrative form, and (3) combination of nodular and diffuse infiltrative form. Leukemic involvement of the pancreas is by and large indistinguishable from that of pancreatic lymphoma on imaging. As seen in lymphomas, the pancreatic duct is not commensurately dilated. Likewise, the common bile duct may be involved, but jaundice is not a common feature. Lymphadenopathy may or may not be seen with pancreatic leukemia.<sup>53</sup>

**Radiography.** Radiographic manifestations of skeletal involvement may be a clue to diagnosis.

**Ultrasonography and Computed Tomography.** The involved gland appears hypoechoic on ultrasonography and hypodense on CT with poor contrast enhancement.

**Magnetic Resonance Imaging.** The involved gland appears hypointense on T1-weighted images and hyperintense on T2-weighted images.

### **Differential Diagnosis**

Clinical features and systemic manifestations are a clue to diagnosis. Associated widespread extramedullary multiorgan

#### Classic Sign: Leukemia

- Overlapping features with lymphoma
- Often lacks bulky peripancreatic lymphadenopathy

involvement with pathologic evaluation of tissue facilitates appropriate diagnosis.

# Treatment

Pancreatic involvement responds to antileukemic therapy.

#### What the Referring Physician Needs to Know: Leukemia

- Because extramedullary involvement of leukemia is known to be highly responsive to systemic antileukemic therapy, consideration of this rare diagnosis is important for management, especially to avoid unnecessary surgery.
- Although leukemia is rare, patients may present with primary relapse of leukemia within the pancreas with diffuse pancreatic enlargement, obstructive jaundice, and pancreatitis.

# CARCINOMA

# Etiology

Diffuse involvement of the pancreas with a carcinomatous process is rare. The cause remains the same as for a focal disease process.

### Prevalence and Epidemiology

Pancreatic carcinoma appears as a focal mass, most commonly in the head of the pancreas. However, the gland can be diffusely involved in 21% of cases.

# **Clinical Presentation**

Clinical features are similar to those associated with focal involvement of the gland (see corresponding chapter on pancreatic carcinoma).

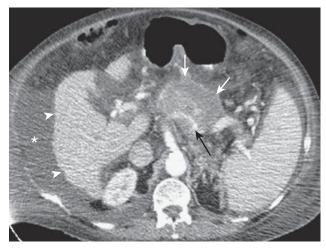
# Pathology

Two or more segments (head, neck, body, tail) or the whole pancreas may be involved. Pathologic features are similar to those of focal involvement of gland.

### Imaging

**Ultrasonography.** Diffusely involved gland appears homogeneously hypoechoic, although areas of heterogeneity may be seen secondary to necrosis and calcification.

**Computed Tomography.** On CT, attenuation values are not significantly different from those of the uninvolved pancreas. Focal areas of hypoattenuation may be seen, secondary to either necrosis or focal areas of ductal obstruction with dilatation (Figure 51-16). Focal areas of increased density can be seen as a result of calcification.<sup>55,56</sup> After intravenous contrast administration, the lesion appears hypoenhancing compared to rest of the normal enhancing pancreatic parenchyma. Distant metastatic lesions to the liver, peripancreatic and para-aortic lymph nodes, and vascular encasement, when present, can suggest a



**Figure 51-16** Carcinoma. Axial computed tomography image reveals a heterogeneously enhancing diffuse mass lesion (*arrows*) encasing the splenic artery (*long arrow*). Also noted are shrunken liver (*arrowheads*) and ascites (*asterisk*) in this patient with cirrhosis.

neoplastic process and facilitate differentiation of pancreatic carcinoma from other lesions. Lymphomas tend to engulf the vessels, whereas carcinomas encase or infiltrate the vessels.<sup>56</sup> Diffuse obscuration of the posterior pancreatic fat plane is a finding favoring pancreatitis rather than diffuse carcinoma.<sup>57</sup>

**Magnetic Resonance Imaging.** Diffusely involved gland appears homogeneously or heterogeneously hypointense on T1-weighted images and hyperintense on T2-weighted images. Calcification cannot be appreciated on MRI. The gland reveals heterogeneous enhancement after intravenous administration of gadolinium. MRCP may reveal irregular ductal narrowing, which is considered rare in lymphoma.

**Positron Emission Tomography With Computed Tomography.** PET/CT plays an important role in staging and posttreatment follow-up.

#### **Classic Signs: Carcinoma**

- Heterogeneous appearance
- Necrosis and calcification
- Irregular ductal dilatation
- Metastases
- Lymphadenopathy
- Vascular encasement and infiltration

#### Differential Diagnosis

Clinical features may resemble other neoplastic or nonneoplastic processes. However, the presence of jaundice with weight loss with or without abdominal pain and a mass should be viewed with a high level of clinical suspicion, especially in middle-aged and elderly patients. Correlation with biomarkers such as CA 19-9 may be helpful. Histologic confirmation is generally required and can be obtained by image-guided percutaneous biopsy. Several different sites must be sampled to improve diagnostic accuracy and avoid false-negative findings, which can result from scattered distribution of tumor cells and associated inflammatory and fibrotic changes.<sup>56</sup>

### Treatment

**Medical Treatment.** Palliative medical management is required.

**Surgical Treatment.** There are no surgical recommendations for a diffusely involved gland. Palliative procedures for relieving ductal obstruction can be performed.

#### What the Referring Physician Needs to Know: Carcinoma

- Diagnosis of pancreatic carcinoma holds a poor prognosis.
- Imaging features may overlap with other pancreatic neoplastic processes, such as lymphoma, which has a better outcome.
- Compared to lymphoma, ductal involvement is more common.
- Appropriate diagnosis and staging with imaging and histology are mandatory.

#### **METASTASES**

#### Etiology

Pancreatic metastases are not as rare as they were once thought to be and must be considered in the differential diagnosis of pancreatic neoplasms, even years after treatment of primary malignancy.<sup>58</sup>

#### Prevalence and Epidemiology

Most common primary lesions metastasizing to the pancreas include lung, breast, renal, hepatobiliary, gastrointestinal, prostate, malignant melanomas, and, rarely, osteosarcomas or Ewing's sarcomas.<sup>59</sup> Occasionally, pancreatic metastasis is the first sign of a malignant disease.<sup>60</sup> The hematogenous route is presumed to be the mode of spread to the pancreas.<sup>61</sup>

#### **Clinical Presentation**

Clinical presentations of pancreatic metastases include abdominal pain, back pain, weight loss, jaundice secondary to biliary obstruction, gastrointestinal obstruction, upper gastrointestinal bleeding, melena, and acute pancreatitis, or patients may be asymptomatic and incidentally discovered on a staging CT examination.<sup>62</sup>

# Pathology

Metastatic foci in other organs and the primary lesion should be sought. In general, the pathologic findings are similar to those of focal pancreatic metastases.

#### Imaging

Pancreatic metastases may manifest as focal lesions, multifocal nodularity, or diffuse enlargement of the gland.<sup>62</sup> On imaging, diffuse pancreatic metastasis is generally morphologically indistinguishable from other diffuse primary neoplasms.<sup>60</sup> Likewise, no distinguishing features of pancreatic metastasis have been found on ERCP.<sup>63</sup> Occasionally, pancreatic metastases can cause severe pancreatitis with necrosis, making it difficult to differentiate from hemorrhagic necrotizing pancreatitis.<sup>64</sup>

**Radiography.** Associated skeletal metastases may be seen on radiographs.

**Ultrasonography and Computed Tomography.** Appearance is indistinguishable from those of other pancreatic neoplasms.

**Magnetic Resonance Imaging.** Involved gland appears hypointense on T1-weighted images and hyperintense on T2-weighted images.

**Positron Emission Tomography With Computed Tomography.** Pancreatic metastases reveal increased FDG uptake. PET/ CT helps in elucidating the extent of the disease process.

#### **Classic Signs: Metastases**

- Overlapping imaging features with other pancreatic neoplasms
- May occasionally mimic fulminant form of pancreatitis

## **Differential Diagnosis**

Clinical manifestations may support but do not contribute significantly to the diagnosis. Confirmation with biopsy is mandatory when metastasis is suspected or when the lesions do not reveal any distinguishing features.<sup>61</sup> Although CT-guided biopsy is a common approach, its accuracy (43%) has been found to be less than that of careful analysis of the same CT scan (76%) for diagnosis of cancer.<sup>65</sup> Moreover, doubt remains regarding the safety of biopsy procedures owing to the possibility of malignant cells seeding along the biopsy tract. Endoscopic ultrasound–guided biopsy is a relatively lesser invasive and promising technique, found to be as much as 80% sensitive.<sup>66</sup>

#### Treatment

Medical Treatment. Palliative management is recommended.

**Surgical Treatment.** No surgical management is available for diffusely involved gland. Palliative procedures for relieving ductal obstruction can be performed.

#### What the Referring Physician Needs to Know: Metastases

- Although diffuse involvement of the pancreas by a metastatic process is rare, this diagnosis should be kept in mind because it prevents curative resection.
- The primary site and other metastatic foci need to be elucidated before initiation of palliative therapy.
- Although rare, a single metastatic focus within the pancreas may arise without evidence of other sites of metastatic disease and years from prior therapy.

# **Miscellaneous Disorders**

## NESIDIOBLASTOSIS (PERSISTENT HYPERINSULINEMIC HYPOGLYCEMIA OF INFANCY, CONGENITAL HYPERINSULINISM)

#### Etiology

Nesidioblastosis is a common cause of recurrent hypoglycemia arising from hyperfunctioning pancreatic islets of Langerhans and can lead to irreversible brain damage.

## Prevalence and Epidemiology

Most cases are sporadic, but familial cases have been reported.

#### **Clinical Presentation**

Presentation is within the first year of life in 70% of cases with symptoms of hypoglycemia, including sweating, seizure, pallor, motor abnormalities, and macrosomia.<sup>67</sup> Although commonly seen in infants, nesidioblastosis may be seen in adults as well, with predilection to morbidly obese patients undergoing bariatric surgery.

#### Pathophysiology

Genetic studies have revealed various different mutations in genes encoding the adenosine triphosphate–sensitive potassium channels in the cell membranes of beta cells, suggesting underlying functional disorder rather than an increase in number of beta cells.<sup>68</sup> Severity of symptoms depends on specific mutations. In diffuse form, the pancreas is studded with abnormally shaped, enlarged beta islet cells, with enlarged and hyperchromatic nuclei and ductuloinsular complexes. On the other hand, in the focal form, islet cells in the surrounding pancreas are normal.<sup>69</sup>

#### Imaging

Morphologically, nesidioblastosis may manifest as focal (40%) or diffuse (50%) forms. The diffuse form is seen on imaging as a generalized enlargement of the pancreas.<sup>70</sup> Although distinguishable by histologic examination, differentiation by clinical and biochemical parameters is difficult. However, use of F-18 fluoro-dihydroxyphenyalanine (F-DOPA) PET has emerged as a method to differentiate the two forms with accuracy of 96% and with 100% accuracy in localizing the lesion.<sup>71,72</sup>

Ultrasonography. Diffusely involved gland appears hypoechoic.

**Computed Tomography.** Diffuse enlargement and a homogeneously hypodense gland may resemble the CT appearance of other diffuse disease processes.

**Magnetic Resonance Imaging.** The gland appears hypointense on T1-weighted images and hyperintense on T2-weighted images.

**Nuclear Studies.** Cases of localized uptake of indium-111 (<sup>111</sup>In)pentreotide have been reported on somatostatin receptor scintigraphy, which may confuse between insulinoma and nesidioblastosis and patients may end up going to surgery for resection.<sup>73</sup>

**Positron Emission Tomography With Computed Tomography.** The role of F-DOPA PET/CT has been evaluated in the preoperative differentiation between focal or diffuse form of hyperinsulinism and has become an important alternative or complementary investigational tool to pancreatic venous catheterization, which was previously the only study available for differentiation of the two forms.<sup>74</sup>

#### Classic Signs: Nesidioblastosis (Persistent Hyperinsulinemic Hypoglycemia of Infancy)

- Focal or diffuse: Commonly homogeneously enlarged gland
- Sometimes nesidioblastosis can demonstrate features similar to insulinoma such as uptake of <sup>111</sup>In-pentreotide.

### Differential Diagnosis

Clinical symptoms of hypoglycemia in the appropriate age group should raise clinical suspicion. Confirmation of diagnosis with histologic evaluation and now with F-DOPA PET/CT is essential for management planning.

#### Treatment

Although medical therapy may be tried, such as diazoxide, octreotide, calcium antagonists, and glucocorticoids, surgical resection of the involved gland is the management of choice. Surgical treatment of diffuse hyperinsulinism involves near-total pancreatectomy, whereas focal hyperinsulinism can be treated with partial pancreatectomy.

What the Referring Physician Needs to Know: Nesidioblastosis (Congenital Hyperinsulinism of Infancy)

- In neonates with characteristic clinical findings, the main differentiation is not with other lesions but between focal and diffuse forms.
- Histologic examination, although a gold standard for confirmation of diagnosis, involves an invasive technique.
- F-18 DOPA- PET/CT can be used to noninvasively distinguish the two forms.

# VON HIPPEL-LINDAU DISEASE

#### Etiology

Von Hippel-Lindau disease (VHL) is an autosomal dominant hereditary multisystem syndrome caused by germline mutations of the *VHL* tumor suppressor gene.<sup>75</sup>

#### Prevalence and Epidemiology

Pancreatic involvement in VHL varies from 17% to 77%. The pancreas may be the only organ involved in 7.6% of cases.<sup>76,77</sup>

#### Clinical Presentation

Age at the onset of VHL varies and depends on the expression of the disease within the individual or within the family and the intensity with which asymptomatic lesions are sought.<sup>78</sup> More often, diagnosis of VHL is made as a result of manifestations of CNS involvement. Pancreatic involvement rarely results in presenting symptoms. Pancreatic cysts are usually detected incidentally during screening or workup for other abnormalities.<sup>78</sup> However, identification of multiple pancreatic and renal cysts without a prior history of pancreatic inflammation should raise the suspicion and lead to genetic testing for VHL rather than other invasive investigations.<sup>79</sup> Extensive pancreatic involvement can result in exocrine and endocrine dysfunction.

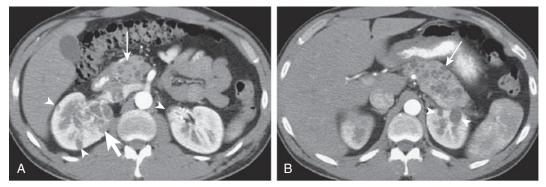
#### Pathology

VHL is a multisystem disorder involving the pancreas, kidneys, adrenals, epididymis, and CNS. The most common pancreatic lesions are single or multiple cysts (90%), and less commonly nonfunctional neuroendocrine tumors, adenocarcinomas, and serous cystadenomas. Discrete cysts in the pancreas with or without calcified foci are seen early in the course of disease. These gradually increase in number, ultimately replacing the entire pancreatic parenchyma and resulting in pancreatic insufficiency. In severe cases, pancreatic parenchyma may be difficult to distinguish. Solid pancreatic lesions (nonfunctional neuroendocrine tumors or pancreatic adenocarcinomas) are known to be associated with severe cystic disease and often arise within the pancreatic head.<sup>80</sup> The multisystem involvement includes cancers of the CNS (retinal and craniospinal hemangioblastomas, endolymphatic sac tumors), pheochromocytomas, benign cysts, and tumors of the pancreas, kidneys, and epididymis. CNS and renal cell carcinomas are major causes of death.<sup>76,77</sup> Unlike typical neuroendocrine tumors that tend to metastasize frequently, pancreatic neuroendocrine tumors in VHL tend to grow slowly and fewer than 10% will metastasize with increased propensity to metastasize when greater than 3 cm in size.<sup>80</sup>

#### Imaging

**Ultrasonography.** Multiple cystic lesions are seen as welldefined hypoechoic lesions with thin walls. Severe involvement is seen as complete cystic replacement of the pancreas. Serous cystadenomas, when present, appear microcystic and sometimes solid because of the multiple acoustic interfaces caused by innumerable microscopic cysts. Distinguishing serous cystadenomas from multiple cysts may sometimes be difficult, which is, however, not clinically important unless they cause symptoms.<sup>78</sup>

**Computed Tomography.** Multiple cysts appear as thin-walled hypodense structures on CT, with poorly defined or nonenhancing walls (Figure 51-17). Diffusely replaced pancreas may be mistaken for a tumor. Calcification is commonly seen



**Figure 51-17** Von Hippel-Lindau disease. Axial computed tomography images through the head (A) and body-tail (B) of the pancreas reveal multiple thin-walled cystic lesions in the pancreas (*arrows*) and kidneys (*arrowheads*). Incidental note is made of a complex cystic lesion in the right kidney (*large arrow*, A), which was proved at biopsy to be renal cell carcinoma.

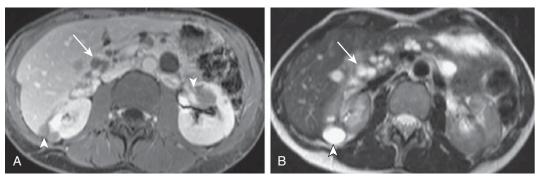


Figure 51-18 Von Hippel-Lindau disease. Contrast-enhanced axial T1- (A) and T2-weighted fat-suppressed (B) gradient recalled echo magnetic resonance imaging reveals multiple cysts in the pancreas (arrows) and kidneys (arrowheads).

throughout the pancreas and is well appreciated on CT. It may be relatively easier to discriminate serous cystadenoma on CT, which appears as focal enlargement of the pancreas and has a microcystic appearance with or without a central scar and calcification.<sup>78,81</sup> Pancreatic neuroendocrine tumors are usually well circumscribed, less than 3.0 cm, hypodense, hypervascular, and homogeneously enhancing and predominantly arise within the pancreatic head.<sup>80</sup>

**Magnetic Resonance Imaging.** MRI does not offer any significant additional advantage except for detecting few more cystic lesions and better characterization of these lesions (Figure 51-18).<sup>78</sup> Neuroendocrine tumors are typically hypointense relative to pancreatic parenchyma on T1-weighted image, slightly hyperintense on T2-weighted image, hypervascular, and homogeneously enhancing and can contain necrosis or calcifications.<sup>80</sup> If typical characteristics are not seen, such as rapid growth, heterogeneous enhancement, and size greater than 3.0, more aggressive treatment may be necessary to prevent metastatic disease.

#### Classic Signs: Von Hippel-Lindau Disease

- Multiple cysts in pancreas and kidneys
- Solid lesions of pancreas and kidneys

# **Differential Diagnosis**

A correct and early diagnosis of VHL is vital for patient management and detection of asymptomatic relatives.<sup>79</sup> Screening

#### SUGGESTED READINGS

- Beazley RM, Cohn I, Jr: Pancreatic cancer. CA Cancer J Clin 31:346–358, 1981.
- Choi EK, Byun JH, Lee SJ, et al: Imaging findings of leukemic involvement of the pancreaticobiliary system in adults. AJR Am J Roentgenol 188:1589– 1595, 2007.
- Falk RH, Comenzo RL, Skinner M: The systemic amyloidoses. N Engl J Med 337:898–909, 1997.
- Fishman RS, Bartholomew LG: Severe pancreatic involvement in three generations in von Hippel-Lindau disease. *Mayo Clin Proc* 54:329–331, 1979.
- Katz DS, Hines J, Math KR, et al: Using CT to reveal fat-containing abnormalities of the pancreas. *AJR Am J Roenteenol* 172:393–396, 1999.
- Ladas SD, Vaidakis E, Lariou C, et al: Pancreatic tuberculosis in non-immunocompromised patients: reports of two cases and a literature review. Eur J Gastroenterol Hepatol 10:973–976, 1998.
- Merkle EM, Bender GN, Brambs H: Imaging findings in pancreatic lymphoma: differential aspects. *AJR Am J Roentgenol* 174:671–675, 2000.

in families affected by VHL permits timely genetic counseling and early identification of potentially life-threatening sequelae. Screening programs should minimally include evaluation of the eyes, CNS, and abdomen. Accurate, noninvasive imaging of the CNS and abdomen should begin in the early or middle teens. Abdominal ultrasonography, although an attractive screening tool owing to low cost and the absence of ionizing radiation, is insensitive for isolated pancreatic cysts and small renal and pancreatic tumors. Contrast-enhanced CT of the abdomen is the preferred modality for initial evaluation of pancreatic lesions. Follow-up screening, especially in younger individuals (younger than16 years of age) at risk for VHL can be performed using ultrasonography. MRI has a limited role in screening for VHL because of its expense.<sup>82</sup>

# Treatment

Solid neoplasms of pancreas and kidney, especially the malignant lesions, need to be surgically treated. Serous cystadenomas may require surgical resection when causing symptoms.

#### What the Referring Physician Needs to Know: Von Hippel-Lindau Disease

- Early screening can result in timely recognition of life-threatening manifestations.
- Typical neuroendocrine tumors of the pancreas in VHL are located within the head of the pancreas, less than 3.0 cm, very slow growing, and hypervascular. If solid lesion grows rapidly, is larger than 3.0 cm, and heterogeneously enhancing, aggressive management should be considered.
  - Merkle EM, Boaz T, Kolokythas O, et al: Metastases to the pancreas. *Br J Radiol* 71:1208–1214, 1998.
  - Miller FH, Gore RM, Nemcek AA, Jr, et al: Pancreaticobiliary manifestations of AIDS. AJR Am J Roentgenol 166:1269–1274, 1996.
  - Patel S, Bellon EM, Haaga J, et al: Fat replacement of the exocrine pancreas. *AJR Am J Roentgenol* 135:843–845, 1980.
  - Robertson MB, Choe KA, Joseph PM: Review of the abdominal manifestations of cystic fibrosis in the adult patient. *Radiographics* 26:679–690, 2006.

#### REFERENCES

- Dodge JA, Morison S, Lewis PA, et al: Incidence, population, and survival of cystic fibrosis in the UK, 1968-85. UK Cystic Fibrosis Survey Management Committee. *Arch Dis Child* 77:493– 496, 1997.
- 2. Bornstein MN, Sokol RJ, Abman SH, et al: Pancreatic insufficiency, growth, and nutrition in infants identified by newborn screening as having cystic fibrosis. *J Pediatr* 120:533–540, 1991.
- 3. Ferrozzi F, Bova D, Campodonico F, et al: Cystic fibrosis: MR assessment of pancreatic damage. *Radiology* 198:875–879, 1996.
- 4. Oppenheimer EH, Esterly JR: Pathology of cystic fibrosis: review of the literature and comparison with 146 autopsied cases. *Perspect Pediatr Pathol* 2:241–278, 1975.
- 5. Tham RT, Heyerman HG, Falke TH, et al: Cystic fibrosis: MR imaging of the pancreas. *Radiology* 179:183–186, 1991.
- 6. Liu P, Daneman A, Stringer DA, et al: Pancreatic cysts and calcification in cystic fibrosis. *Can Assoc Radiol J* 37:279–282, 1986.
- Agrons GA, Corse WR, Markowitz RI, et al: From the archives of AFIP: Gastrointestinal manifestations of cystic fibrosis: radiologicpathologic correlation. *Radiographics* 16:871– 893, 1996.
- Daneman A, Gaskin K, Martin DJ, et al: Pancreatic changes in cystic fibrosis: CT and sonographic appearances. *AJR Am J Roentgenol* 141:653–655, 1983.
- 9. Berrocal T, Pajares MP, Zubillaga AF: Pancreatic cystosis in children and young adults with cystic fibrosis: sonographic, CT, and MRI findings. *AJR Am J Roentgenol* 184:1305–1309, 2005.
- Ferrozzi F, Bova D, Campodonico F, et al: Cystic fibrosis: MR assessment of pancreatic damage. *Radiology* 198:875–879, 1996.
- Liou TG, Adler FR, Cahill BC, et al: Survival effect of lung transplantation among patients with cystic fibrosis. JAMA 286:2683–2689, 2001.
- 12. Penn I: De novo malignances in pediatric organ transplant recipients. *Pediatr Transplant* 2:56–63, 1998.
- Ibrahim YH, Yee D: Insulin-like growth factor-I and cancer risk. *Growth Horm IGF Res* 14:261– 269, 2004.
- Neglia JP, FitzSimmons SC, Maisonneuve P, et al: The risk of cancer among patients with cystic fibrosis. N Engl J Med 332:494–499, 1995.
- Meng K, Lee CH, Seremi F: Metabolic syndrome and ectopic fat deposition. *Acad Radiol* 17:1302– 1312, 2010.
- Matsumoto S, Mori H, Miyake H, et al: Uneven fatty replacement of the pancreas: evaluation with CT. *Radiology* 194:453–458, 1995.
- 17. Sipe JD, Benson MD, Buxbaum JN, et al: Nomenclature 2014: amyloid fibril proteins and clinical classification of the amyloidosis. *Amyloid* 21:221–224, 2014.
- Segovia Garcia C, Quilez Barrenechea JI, Vidales Arechaga L, et al: Pancreatic involvement in primary amyloidosis: radiologic findings. *Eur Radiol* 12:774–778, 2002.
- 19. Onur MR, Yalmz M, Poyraz AK, et al: Pancreatic islet cell amyloidosis manifesting as a large pancreas. *Korean J Radiol* 13:94–97, 2012.
- Erdman RA, Vandersall JH: Effect of rumen protein degradability on milk yield of dairy cows in early lactation. J Dairy Sci 66:1873– 1880, 1983.
- 21. Long JA, Jr, Doppman JL, Nienhus AW, et al: Computed tomographic analysis of beta-thalassemic

syndromes with hemochromatosis: pathologic findings with clinical and laboratory correlations. *J Comput Assist Tomogr* 4:159–165, 1980.

- Haaga JR, Lanzieri CF, Gilkeson RC: The pancreas. In Haaga JR, editor: Computed tomography and magnetic resonance imaging of the whole body, ed 4, Philadelphia, 2003, Elsevier, pp 1395–1485.
- 23. Hayes AM, Jaramillo D, Levy HL, et al: Neonatal hemochromatosis: diagnosis with MR imaging. *AJR Am J Roentgenol* 159:623–625, 1992.
- Gandon Y, Guyader D, Heautot JF, et al: Hemochromatosis: diagnosis and quantification of liver iron with gradient-echo MR imaging. *Radiology* 193:533–538, 1994.
- Woodfield JC, Windsor JA, Godfrey CC, et al: Diagnosis and management of isolated pancreatic tuberculosis: recent experience and literature review. *ANZ J Surg* 74:368–371, 2004.
- De Backer AI, Mortele KJ, Bomans P, et al: Tuberculosis of the pancreas: MRI features. *AJR Am J Roentgenol* 184:50–54, 2005.
- Hulnik DH, Megibow AJ, Naidich DP, et al: Abdominal tuberculosis: CT evaluation. *Radiology* 157:199–204, 1985.
- Song TJ, Lee SS, Park DH, et al: Yield of EUSguided FNA on the diagnosis of pancreatic/ peripancreatic tuberculosis. *Gastrointest Endosc* 69:484–491, 2009.
- 29. Schapiro RH, Maher MM, Misdraji J: Case records of the Massachusetts General Hospital: case 3-2006—a 63-year-old woman with jaundice and a pancreatic mass. *N Engl J Med* 354:398–406, 2006.
- Pitchenik AE, Fertel D: Medical management of AIDS patients: tuberculosis and nontuberculous mycobacterial disease. *Med Clin North Am* 76:121–171, 1992.
- 31. De Backer AI, Mortele KJ, Bomans P, et al: Tuberculosis of the pancreas: MRI features. *AJR Am J Roentgenol* 184:50–54, 2005.
- Park IN, Ryu JS, Shim TS: Evaluation of therapeutic response to tuberculoma using F-18 FDG positron emission tomography. *Clin Nucl Med* 33:1–3, 2008.
- Fischer G, Spengler U, Neubrand M, et al: Isolated tuberculosis of the pancreas masquerading as a pancreatic mass. *Am J Gastroenterol* 90:2227– 2230, 1995.
- 34. Takhtani D, Gupta S, Suman K, et al: Radiology of pancreatic tuberculosis: a report of three cases. *Am J Gastroenterol* 91:1832–1834, 1996.
- 35. Itaba S, Yoshinaga S, Nakamura K, et al: Endoscopic ultrasound-guided fine-needle aspiration for the diagnosis of peripancreatic tuberculous lymphadenitis. J Gastroenterol 42:83–86, 2007.
- 36. Eyer-Silva WA, de Sa CA, Pinto JF, et al: Pancreatic tuberculosis as a manifestation of infection with the human immunodeficiency virus. *Clin Infect Dis* 16:332, 1993.
- Iwai T, Kida M, Kida Y, et al: Biliary tuberculosis causing cicatricial stenosis after oral antituberculosis therapy. *World J Gastroenterol* 12:4914–4917, 2006.
- Teo LL, Venkatesh SK, Ho KY: Clinics in diagnostic imaging. *Singapore Med J* 48:687–692, quiz 692, 2007.
- Trivedi CD, Pitchumoni CS: Drug induced pancreatitis, an update. J Clin Gastrogenterol 39:709– 716, 2005.
- 40. Oliveira NM, Ferreira FAY, Yonamine RY, et al: Antiretroviral drugs and acute pancreatitis in HIV/AIDS patients: is there any association? A

literature review. *Einstein (Sao Paulo)* 12:112-119, 2014.

- Cappell MS, Marks M: Acute pancreatitis in HIV-seropositive patients: a case control study of 44 patients. Am J Med 98:243–248, 1995.
- Joe L, Ansher AF, Gordin FM: Severe pancreatitis in an AIDS patient in association with cytomegalovirus infection. *South Med J* 82:1444– 1445, 1989.
- Drew WL, Buhles W, Erlich KS: Herpesvirus infections (cytomegalovirus, herpes simplex virus, varicella-zoster virus): how to use ganciclovir (DHPG) and acyclovir. *Infect Dis Clin North Am* 2:495–509, 1988.
- 44. Saif MW, Khubchandani S, Walczak M: Secondary pancreatic involvement by a diffuse large B-cell lymphoma presenting as acute pancreatitis. *World J Gastroenterol* 13:4909–4911, 2007.
- Shirkhoda A, Ros PR, Farah J, et al: Lymphoma of the solid abdominal viscera. *Radiol Clin North Am* 28:785–799, 1990.
- Behrns KE, Sarr MG, Strickler JG: Pancreatic lymphoma: is it a surgical disease? *Pancreas* 9:662–667, 1994.
- Nishimura R, Takakuwa T, Hoshida Y, et al: Primary pancreatic lymphoma: clinicopathological analysis of 19 cases from Japan and review of the literature. *Oncology* 60:322–329, 2001.
- Dawson IM, Cornes JS, Morson BC: Primary malignant lymphoid tumours of the intestinal tract: report of 37 cases with a study of factors influencing prognosis. *Br J Surg* 49:80–89, 1961.
- Prayer L, Schurawitzki H, Mallek R, et al: CT in pancreatic involvement of non-Hodgkin lymphoma. Acta Radiol 33:123–127, 1992.
- Arcari A, Anselmi E, Bernuzzi P, et al: Primary pancreatic lymphoma: a report of five cases. *Haematologica* 90:ECR09, 2005.
- Wang GX, Liao JL, Zhang D, et al: Relapse of acute lymphoblastic leukemia in the pancreas after bone marrow transplant. *World J Pediatr* 1–3, 2014. Web.
- Neiman RS, Barcos M, Berard C, et al: Granulocytic sarcoma: a clinicopathologic study of 61 biopsied cases. *Cancer* 48:1426–1437, 1981.
- Matsueda K, Yamamoto H, Doi I: An autopsy case of granulocytic sarcoma of the porta hepatis causing obstructive jaundice. J Gastroenterol 33:428–433, 1998.
- Ramanathan S, Prakash M, Khandelwal N: Concurrent pancreatic and renal leukemic cell infiltration. *Indian J Hematol Blood Transfus* 30:S57–S59, 2014.
- Kaplan JO, Isikoff MB, Barkin J, et al: Necrotic carcinoma of the pancreas: "the pseudopseudocyst." J Comput Assist Tomogr 4:166–167, 1980.
- Wittenberg J, Simeone JF, Ferrucci JT, Jr, et al: Non-focal enlargement in pancreatic carcinoma. *Radiology* 144:131–135, 1982.
- Mendez G, Jr, Isikoff MB, Hill MC: CT of acute pancreatitis: interim assessment. AJR Am J Roentgenol 135:463–469, 1980.
- Z'graggen K, Castillo CF, Rattner DW, et al: Metastases to the pancreas and their surgical extirpation. Arch Surg 133:413–418, 1998.
- Rubin E, Dunham WK, Stanley RJ: Pancreatic metastases in bone sarcomas: CT demonstration. J Comput Assist Tomogr 9:886–888, 1985.
- Charnsangavej C, Whitley NO: Metastases to the pancreas and peripancreatic lymph nodes from carcinoma of the right side of the colon: CT findings in 12 patients. AJR Am J Roentgenol 160:49–52, 1993.

- Rumancik WM, Megibow AJ, Bosniak MA, et al: Metastatic disease to the pancreas: evaluation by computed tomography. *J Comput Assist Tomogr* 8:829–834, 1984.
- 62. Muranaka T, Teshima K, Honda H, et al: Computed tomography and histologic appearance of pancreatic metastases from distant sources. *Acta Radiol* 30:615–619, 1989.
- 63. Swensen T, Osnes M, Serck-Hanssen A: Endoscopic retrograde cholangiopancreatography in primary and secondary tumours of the pancreas. *Br J Radiol* 53:760–764, 1980.
- Niccolini DG, Graham JH, Banks PA: Tumorinduced acute pancreatitis. *Gastroenterology* 71:142–145, 1976.
- Rodriguez J, Kasberg C, Nipper M, et al: CT-guided needle biopsy of the pancreas: a analysis of diagnostic accuracy. *Am J Gastroenterol* 87:1610–1613, 1992.
- Giovannini M, Seitz JF, Monges G, et al: Fineneedle aspiration cytology guided by endoscopic ultrasonography: results in 141 patients. *Endoscopy* 27:171–177, 1995.
- Aynsley-Green A, Hussain K, Hall J, et al: Practical management of hyperinsulinism in infancy. Arch Dis Child Fetal Neonatal Ed 82:F98–F107, 2000.
- Clayton PT, Eaton S, Aynsley-Green A, et al: Hyperinsulinism in short-chain L-3-hydroxyacyl-CoA dehydrogenase deficiency reveals the importance of beta-oxidation in insulin secretion. *J Clin Invest* 108:457–465, 2001.

- Suchi M, MacMullen C, Thornton PS, et al: Histopathology of congenital hyperinsulinism: retrospective study with genotype correlations. *Pediatr Dev Pathol* 6:322–333, 2003.
- Fournet JC, Mayaud C, de Lonlay P, et al: Unbalanced expression of 11p15 imprinted genes in focal forms of congenital hyperinsulinism: association with a reduction to homozygosity of a mutation in *ABCC8* or *KCNJ11. Am J Pathol* 158:2177–2184, 2001.
- Ribeiro MJ, De Lonlay P, Delzescaux T, et al: Characterization of hyperinsulinism in infancy assessed with PET and 18F-fluoro-L-DOPA. *J Nucl Med* 46:560–566, 2005.
- Hardy OT, Hernandez-Pampaloni M, Saffer JR, et al: Diagnosis and localization of focal congenital hyperinsulinism by 18F-fluorodopa PET scan. J Pediatr 150:140–145, 2007.
- 73. Ferrario C, Stoll D, Boubaker A, et al: Diffuse nesidioblastosis with hypoglycemia mimicking an insulinoma: a case report. *J Med Case Rep* 6:332, 2012.
- 74. Subramaniam RM, Karantanis D, Peller PJ: [18F]Fluoro-L-dopa PET/CT in congenital hyperinsulinism. J Comput Assist Tomogr 31:770–772, 2007.
- Kim WY, Kaelin WG: Role of VHL gene mutation in human cancer. J Clin Oncol 22:4991– 5004, 2004.
- 76. Mohr VH, Vortmeyer AO, Zhuang Z, et al: Histopathology and molecular genetics of multiple

cysts and microcystic (serous) adenomas of the pancreas in von Hippel-Lindau patients. *Am J Pathol* 157:1615–1621, 2000.

- Hammel PR, Vilgrain V, Terris B, et al: Pancreatic involvement in von Hippel-Lindau disease. The Groupe Francophone d'Étude de la Maladie de von Hippel-Lindau. *Gastroenterology* 119: 1087–1095, 2000.
- Choyke PL, Glenn GM, Walther MM, et al: von Hippel-Lindau disease: genetic, clinical, and imaging features. *Radiology* 194:629–642, 1995.
- Elli L, Buscarini E, Portugalli V, et al: Pancreatic involvement in von Hippel-Lindau disease: report of two cases and review of the literature. *Am J Gastroenterol* 101:2655–2658, 2006.
- Marcos HB, Libutti SK, Alexander HR, et al: Neuroendocrine tumors of the pancreas in von-Hippel-Lindau disease: a spectrum of appearances at CT and MR imaging with histopathologic comparison. *Radiology* 225:751–758, 2002.
- Bergmann LS, Russell JC, Gladstone A, et al: Cystadenomas of the pancreas. *Am Surg* 58:65– 71, 1992.
- Choyke PL, Filling-Katz MR, Shawker TH, et al: von Hippel-Lindau disease: radiologic screening for visceral manifestations. *Radiology* 174:815– 820, 1990.

# **Dilated Bile Ducts**

MICHAEL CHEW | SURABHI BAJPAI | PETER F. HAHN

# **Etiology**

Biliary dilatation can occur as a result of biliary obstruction, from an altered functional state (e.g., after cholecystectomy or with sphincter of Oddi dysfunction), or uncommonly as a result of a choledochal cyst. The role of imaging is to identify a bile duct obstruction and define its level and cause. The cause may be intraluminal, mural, or extrinsic (Figure 52-1). Cholangiographic and cross-sectional modalities provide complementary information, and both are required to investigate biliary dilatation.

The pattern of biliary dilatation depends on the cause and level of abnormality within the biliary tree. The biliary tract may be involved diffusely or focally, or dilatation may be multifocal. Adenocarcinoma of the pancreatic head or a stone in the distal common bile duct (CBD) results in generalized intrahepatic and extrahepatic bile duct dilatation to the level of obstruction. Peripheral cholangiocarcinoma may cause segmental dilatation of the intrahepatic bile ducts. Sclerosing cholangitis and Caroli's disease typically cause multifocal dilatation of intrahepatic bile ducts.

There are numerous causes of benign and malignant bile duct dilatation. Benign causes include the following:

- Choledocholithiasis: Stones in the bile ducts or cystic duct (Mirizzi's syndrome)
- Benign stricture resulting from:
  - Previous surgery (e.g., cholecystectomy), trauma, instrumentation, or irradiation
  - Inflammation: Primary sclerosing cholangitis (PSC), pancreatitis, previous passage of a stone, or previous perforated duodenal ulcer; and infection
  - Miscellaneous: Crohn's disease, cystic fibrosis with liver involvement, and eosinophilic cholecystitis
- Extrinsic compression: Liver cyst, aneurysm (Figure 52-2)
- Benign neoplasms: Biliary cystadenoma (Figure 52-3), ampullary adenoma, intraductal papillary mucinous adenoma of the bile ducts
- Congenital anomaly: Choledochal cyst (Figure 52-4), Caroli's disease

Malignant causes of bile duct dilatation include the following:

- Pancreatic head carcinoma
- Cholangiocarcinoma
- Ampullary carcinoma
- Gallbladder carcinoma
- Hepatocellular carcinoma
- Malignant mucinous neoplasm of the pancreas or bile duct
- Lymphoma (Figure 52-5)
- Metastatic disease

In this chapter, we discuss an approach to biliary dilatation, emphasizing the distinguishing features of benign and malignant causes. We describe some common benign causes of bile duct dilatation. Malignant and benign neoplasms that can cause bile duct dilatation and choledochal cysts are discussed separately.

# **Prevalence and Epidemiology**

Bile duct dilatation can be arbitrarily defined as a common duct diameter greater than 6 mm and an intrahepatic duct diameter greater than 3 mm (Figure 52-6).<sup>1</sup> There is some increase in size of the normal extrahepatic duct with increasing age.

The most common cause of benign biliary dilatation is choledocholithiasis. In Western society, cholesterol stones are the most common type; in Southeast Asia, pigment stones are more common. Parasitic infection of the bile ducts is endemic in Southeast Asia. This precipitates hepatolithiasis and can be complicated by recurrent pyogenic cholangitis.

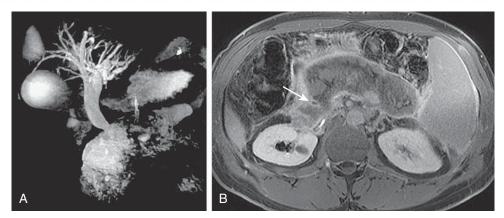
The exact prevalence of iatrogenic biliary stricture is unclear. Bile duct injury complicates 3 to 7 per 1000 laparoscopic cholecystectomies.<sup>2</sup> Biliary stricture is the most common late complication of hepatobiliary surgery.

The most common malignant cause of bile duct dilatation is pancreatic adenocarcinoma, followed by cholangiocarcinoma. Seventy percent of pancreatic adenocarcinomas involve the head of the pancreas,<sup>3</sup> where they may cause CBD dilatation in addition to pancreatic duct dilatation. The incidence of cholangiocarcinoma is at least four times less than pancreatic carcinoma. Cholangiocarcinoma complicates several benign diseases of the bile ducts, including choledochal cysts, PSC, and parasitic liver infestation. Thus, malignant and benign causes of biliary dilatation may coexist and differentiating one from the other may be problematic.

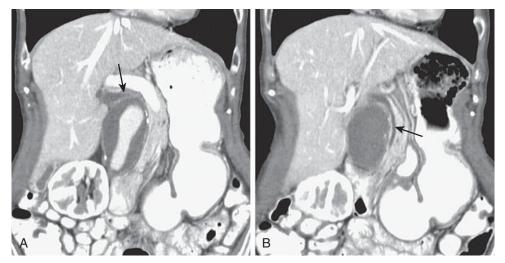
# **Clinical Presentation**

All causes of bile duct dilatation lead to cholestatic symptoms once obstruction becomes severe enough. The classic symptoms and signs are jaundice, pruritus, pale stools, and dark urine. Typically, choledocholithiasis is associated with acute intermittent right upper quadrant pain and transient jaundice. Malignant causes of bile duct obstruction, such as carcinoma of the head of the pancreas, are often initially painless or manifest as dull pain, and jaundice is progressive. Occasionally, patients with bile duct strictures may develop manifestations of chronic cholestasis: xanthomas, anorexia, nausea, vomiting, weight loss, and deficiencies of calcium and fat-soluble vitamins.

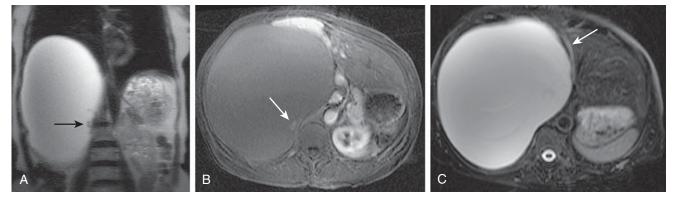
Patients with biliary obstruction typically have elevated serum alkaline phosphatase and gamma-glutamyl transpeptidase levels. These enzymes are disproportionately elevated compared with serum transaminases. In more severe cases of biliary obstruction, total and conjugated bilirubin values are increased.



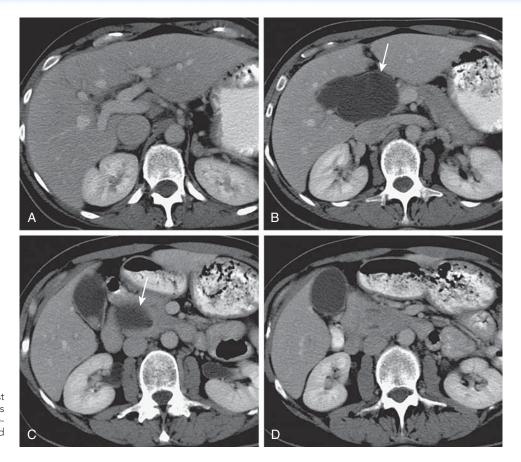
**Figure 52-1** Necrotizing pancreatitis. A, magnetic resonance cholangiopancreatography (maximal intensity projection) image demonstrates marked intrahepatic and extrahepatic duct dilatation to the level of the pancreas, which shows as high T2 signal intensity and is amorphous. B, Postcontrast axial T1-weighted image shows a nonenhancing necrotic mass replacing most of the pancreas and compressing the common bile duct (*arrow*).



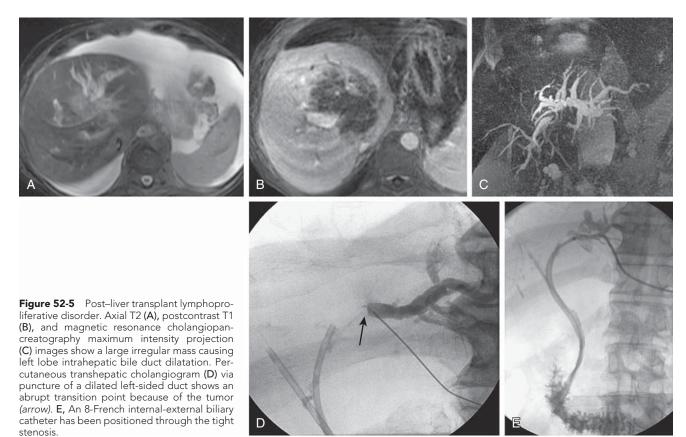
**Figure 52-2** Mild biliary dilatation secondary to extrinsic compression of the common bile duct by an abdominal aortic aneurysm. A 66-year-old woman presented with weight loss and elevated alkaline phosphatase level. A and B, Coronal reformatted computed tomography images show mild compression of the bile duct (*arrows*) by a 4.8-cm infrarenal abdominal aortic aneurysm.

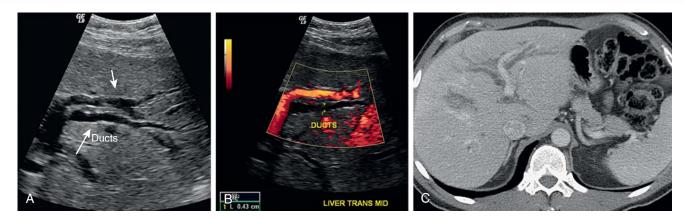


**Figure 52-3** Biliary cystadenoma causing mild intrahepatic bile duct dilatation as a result of extrinsic compression. Coronal single-shot fast spin echo (A), postcontrast axial flexible appearance modeling environment (B), and axial T2-weighted fast spin echo (C) magnetic resonance images show a large cystic lesion with enhancing papillary projections (*arrows*, A and B), causing mild intrahepatic bile duct dilatation (*arrow*, C).



**Figure 52-4** A to D, Postcontrast axial computed tomography sections of the abdomen show a type 1 chole-dochal cyst (*arrow*). A stone is noted within the gallbladder.





**Figure 52-6** Intrahepatic duct dilatation. **A**, Transverse ultrasound image of the left lobe of the liver shows a dilated bile duct (*long arrow*) posterior to a portal vein branch (*short arrow*). **B**, Color Doppler ultrasound image shows flow within the portal vein branch. **C**, Computed tomography image at the same axial level.

Patients with elevated levels of alkaline phosphatase and direct hyperbilirubinemia without biliary dilatation have intrahepatic cholestasis with blockage of biliary capillaries as a result of hepatocyte swelling.

Complete or partial bile duct obstruction leads to bile stasis. This can be complicated by ascending cholangitis and stone formation. Ascending cholangitis can be recurrent and lifethreatening: the classic clinical manifestation is fever and rigors, jaundice, and right upper quadrant abdominal pain (Charcot's triad). Patients also may have altered mental status and hypotension (Reynolds' pentad). Benign causes of bile duct obstruction are more likely to cause ascending cholangitis than malignant causes.

# Pathophysiology

Certain variants in bile duct anatomy, particularly around the gallbladder fossa, may lead to inadvertent bile duct injury and subsequent bile duct dilatation. The right posterior duct is frequently aberrant. It may drain via the cystic duct, and if this is not recognized at the time of cholecystectomy, bile leak and obstruction can occur.

The anatomy of the junction of the distal CBD and main pancreatic duct is slightly variable. In 60% of cases there is a true common channel at the ampulla of Vater. In 38% of cases there is a "double-barreled" opening at the apex of the papilla. In 2% there are separate duodenal openings for the two canals.<sup>4</sup> Diseases that cause both bile and pancreatic duct dilatation either involve the common channel (e.g., ampullary carcinoma) or are large enough to involve both ducts (e.g., pancreatic carcinoma). Lesions that arise from the wall of bile duct (e.g., cholangiocarcinoma) or are eccentric to the common channel (e.g., duodenal carcinoma) are more likely to manifest as bile duct dilatation without pancreatic duct dilatation. Pancreas divisum or a residual duct of Santorini to the minor papilla may spare the pancreatic duct from dilatation by some periampullary lesions.<sup>5</sup>

# Pathology

The pathogenic basis of bile duct dilatation varies. Choledocholithiasis usually is due to bile stasis and supersaturation of one of the constituents of bile. Benign bile duct strictures are



**Figure 52-7** Endoscopic retrograde cholangiopancreatography shows a benign postoperative stricture (*arrow*) 2 months after liver transplant with end-to-end bile duct anastomosis.

often precipitated by an injurious agent that incites an inflammatory response, which is followed by fibrosis. Ischemia plays a role in the development of some strictures (e.g., after liver transplantation [Figure 52-7]), and some strictures are idiopathic (e.g., PSC).

Choledochal cysts are congenital anomalies secondary to an intrinsic weakness in the wall of the bile ducts. Caroli's disease is an autosomal recessive inherited condition in which there is abnormal embryologic remodeling of bile ducts.

# Imaging

The role of imaging is to establish the presence of biliary dilatation and determine the level and cause of obstruction. Associated dilatation of the pancreatic duct and gallbladder are noted. Stones, masses, and strictures are searched for, as well as complications of these diseases: cholangitis, pancreatitis, stones, cirrhosis, liver abscess, and cholangiocarcinoma. If a malignant cause is found, suitability for resection is determined and staging is performed.

#### RADIOGRAPHY

Of all imaging modalities, endoscopic retrograde cholangiography (ERC) and percutaneous transhepatic cholangiography (PTC) can evaluate the bile ducts with the highest spatial resolution. They are, therefore, the gold standard for detecting stones, evaluating strictures, and localizing bile duct leaks. When the bile ducts are obstructed, the ducts closest to the site of injection are best demonstrated. ERC best evaluates the pancreaticobiliary junction and distal ducts, and PTC best evaluates the proximal intrahepatic ducts (see Figure 52-5). Two additional advantages of ERC are that the ampulla of Vater can be directly visualized and manometry can be performed. A potential pitfall of ERC is failure to recognize complete obstruction of a lobar or segmental bile duct. In this scenario, the obstructed ducts are absent from the cholangiogram because they are not opacified, and this absence may be difficult to appreciate, with the remaining ducts seeming complete.

ERC and PTC have a therapeutic as well as a diagnostic role. Removal of stones and sphincterotomy can be performed via ERC, external or internal-external drainage catheters can be inserted during PTC, and biliary dilation and insertion of stents can be performed by both approaches.

Endoscopic retrograde cholangiopancreatography (ERCP) has a complication rate of 1% to 5%. Moderate to severe pancreatitis is seen in 0.7%; the mortality rate associated with the procedure is approximately 0.2%.<sup>6</sup>

Complications of PTC include cholangitis, sepsis, hemobilia, hemorrhage, and bile leak. The reported complication rate for PTC is approximately 2%. When percutaneous biliary drainage is performed, the complication rate rises to 5% to 7%. Factors that increase the likelihood of complications include poor preprocedure clinical status, coagulopathy, cholangitis, stones, and malignant, proximal, and multiple duct obstruction.<sup>7</sup>

Cholangiography is highly sensitive for detecting bile duct stones and strictures. Stones are typically smooth filling defects. Other less common intraluminal filling defects include neoplasms (which can appear papillary, irregular, or smooth and demonstrate attachment to the bile duct wall), hemorrhage, sludge, and infected debris (Figure 52-8).

Strictures may be due to a pathologic process of the bile duct wall and/or surrounding tissues. The cholangiogram should be interpreted in conjunction with cross-sectional imaging, because this provides complementary information, in particular, identification of a mass.

The classic cholangiographic features of a malignant stricture are irregular contour, abrupt transition (>1 cm), shouldered margins, asymmetry, and associated irregular or papillary intraluminal filling defects (Figure 52-9). Benign strictures classically have a long transition and are smooth, gently tapered, and concentric (Figure 52-10). Unfortunately, biliary strictures often are not classic in their appearance and the specificity of cholangiography for differentiating between benign and malignant disease is poor.<sup>8</sup>

#### COMPUTED TOMOGRAPHY

Multidetector computed tomography (MDCT) with intravenous contrast can produce high spatial resolution, with multi-

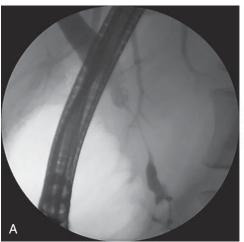


**Figure 52-8** Endoscopic retrograde cholangiopancreatography shows multiple filling defects in the common duct, a combination of stones and hemorrhage. Multiple stones are seen within the gallbladder.



**Figure 52-9** Malignant-appearing stricture of cholangiocarcinoma that has an irregular contour is asymmetric and has an abrupt transition.

phase images that accurately assess the presence of biliary dilatation and detect and evaluate obstructing masses. The sensitivity of both CT and magnetic resonance imaging (MRI) for detection of pancreatic carcinoma is improved by scanning in the pancreatic phase.<sup>9</sup> The pancreatic phase improves tumor conspicuity, maximizes the tumor-to-pancreas attenuation difference, and permits adequate arterial and mesenteric venous opacification for characterization of vascular invasion.<sup>10</sup> The high spatial resolution of CT is particularly useful for local



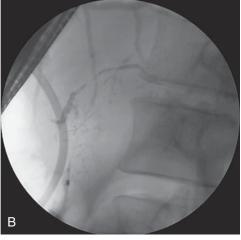


Figure 52-10 Inflammatory bile duct stricture in autoimmune pancreatitis. Long, smooth, benign-appearing stricture (A) involving the common duct, with multiple pancreatic duct strictures (B). Three weeks later (not shown) there was dramatic improvement after corticosteroid therapy, balloon dilatation, and stenting of the common bile duct stricture.

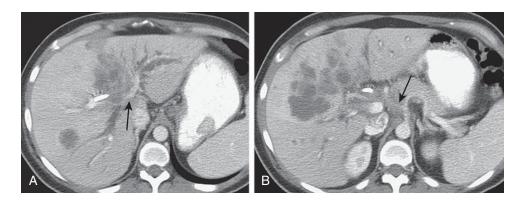


Figure 52-11 Advanced hilar cholangiocarcinoma (Klatskin's tumor) with hepatic metastases on postcontrast axial computed tomography images of the abdomen. The tumor is invading the hepatic parenchyma, the portal vein (arrow, A), and the celiac axis (arrow, B).

staging of malignancies such as pancreatic adenocarcinoma and cholangiocarcinoma (Figure 52-11). CT or MRI can detect features that suggest a tumor is not suitable for resection; in cholangiocarcinoma, for example, these include hepatic parenchymal invasion; involvement of second-order bile duct branches in both lobes of the liver; vascular invasion or encasement of the proper hepatic artery, both right and left hepatic arteries, or main portal vein; extensive regional lymphadenopathy; and distant metastases.<sup>11</sup>

CT without cholangiographic contrast is less sensitive than MRI for detection of choledocholithiasis. CT cholangiography using iodinated contrast agents such as intravenous meglumine iotroxate (which is taken up by the liver and excreted in bile) depicts bile duct stones more accurately. In one study, the sensitivity and specificity of CT cholangiography for detecting choledocholithiasis were, respectively, 87% and 96%, compared with 80% and 88% for magnetic resonance cholangiopancreatography (MRCP).<sup>12</sup> However, several characteristics of cholangiographic contrast agents have limited their use: their biliary excretion is diminished in patients with elevated bilirubin levels or liver insufficiency, they can worsen renal impairment, and have a higher rate of adverse reactions compared with other iodinated contrast agents.

Dual-energy CT (DECT), an innovation that allows concurrent scanning with x-ray beams of different energies, is being explored for improved detection and characterization of pancreatic cancer. Virtual monoenergetic CT images and iodinespecific images generated after DECT acquisition have been shown to improve the conspicuity of isoattenuating pancreatic masses and depict small tumors that are difficult to identify on single-energy (120 kVp) CT images.<sup>13</sup>

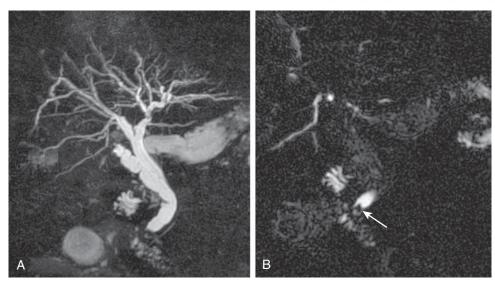
#### MAGNETIC RESONANCE IMAGING AND MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY

MRI, including MRCP, is extremely accurate in identifying the presence and level of biliary obstruction. It has a sensitivity of 92% for diagnosing stones and 88% for detecting malignant obstruction (with >90% specificity in each case).<sup>14</sup>

MRCP does not require exogenous contrast agents. It uses heavily T2-weighted sequences to image bile and pancreatic secretions within their ducts. The most common sequences used are a multiple-section three-dimensional fast spin echo sequence with respiratory triggering and a single-section (thick slab) half-Fourier rapid acquisition with relaxation enhancement (RARE) sequence performed during a single breath-hold. Multiple-section acquisitions are usually postprocessed and displayed as maximum intensity projection (MIP), multiplanar reformatted images. These postprocessed images provide a useful overview of the pattern of biliary dilatation on one image. However, they may obscure small filling defects that are apparent on the thin-section source images (Figure 52-12). Therefore, both source and postprocessed images should be

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Figure 52-12 Magnetic resonance cholangiopancreatography of choledocholithiasis. A, Maximum intensity projection image shows intrahepatic and extrahepatic bile duct dilatation and suggests narrowing at the ampulla. B, Source image reveals that, in fact, a small stone (*arrow*) in the distal common bile duct is the cause of the bile duct dilatation.



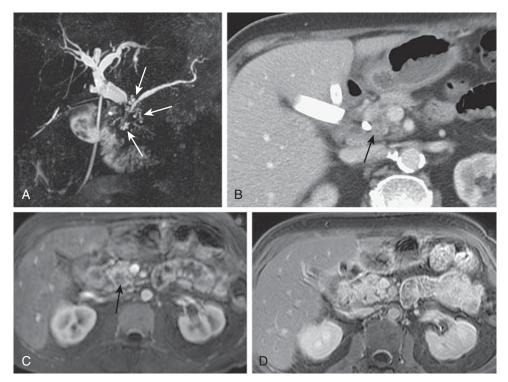


Figure 52-13 Pancreatic head adenocarcinoma. A, Magnetic resonance cholangiopancreatography shows double duct sign and dilatation of pancreatic duct side branches (arrows), suggesting adenocarcinoma of the pancreatic head. B, Post-intravenous contrast computed tomography shows the carcinoma as a low-density lesion (arrow). C, However, the mass is most conspicuous in the arterial phase postcontrast T1-weighted image as a hypointense mass (arrow). D, It is difficult to visualize in the delayed phase.

reviewed. In addition, fluid within bowel can obscure the bile and pancreatic ducts on MIP and thick slab images, but this is rarely a problem on thin-section source images.

MRCP allows visualization of the bile ducts above and below the point of obstruction, a potential advantage over techniques using contrast (ERC and PTC). MRI is the most sensitive modality for the detection of a mass causing bile duct obstruction, owing to its superior contrast and temporal resolution. For instance, pancreatic adenocarcinoma is usually T1 hypointense, and fat-saturated T1-weighted images have been shown to improve its conspicuity.<sup>15-17</sup> Pancreatic carcinoma is often well visualized as a hypointense mass in pancreatic phase postcontrast images, because it tends to be less vascular than normal glandular tissue and this phase provides superior tumor-togland attenuation difference (Figure 52-13).<sup>10,17,18</sup> Cholangiocarcinoma also may be hypointense on T-weighted imaging but characteristically shows delayed enhancement (at 1 to 5 minutes) because of intratumoral fibrosis, a feature that may be seen on MRI or CT (Figure 52-14).<sup>19</sup>

Depiction of the contour of strictures by MRCP is inferior to that with ERCP because MRCP has poorer spatial resolution.<sup>20</sup>

The ampulla may be difficult to assess on MRCP for a variety of reasons, including interference from adjacent intraluminal

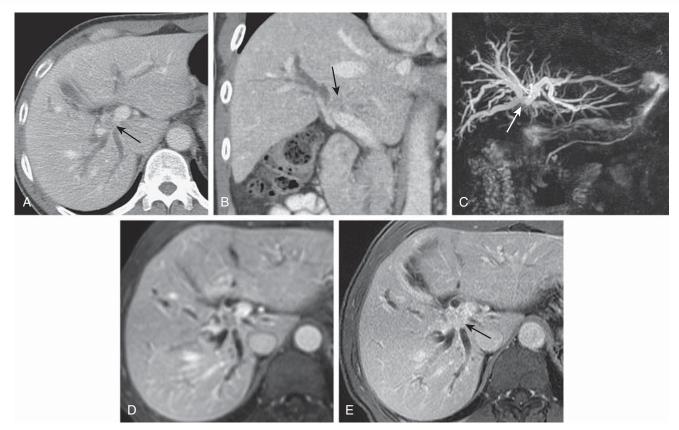


Figure 52-14 Klatskin's tumor. Axial (A) and coronal (B) postcontrast computed tomography images show low-density tumor (arrows) at the confluence of the right and left hepatic ducts suggestive of cholangiocarcinoma (Klatskin's tumor). Magnetic resonance cholangiopancreatography maximum intensity projection (C), axial early arterial phase (D), and delayed high-resolution (E) magnetic resonance images show abrupt transition point of bile duct caliber (arrow, C) at the confluence of the right and left hepatic ducts, where the cholangiocarcinoma shows characteristic delayed enhancement (arrow, E).

gas, duodenal diverticula, duodenal wall contractions,<sup>21</sup> and nondistention of the duodenal lumen. ERCP and endoscopic ultrasonography may image the distal CBD with greater resolution and accuracy.<sup>22</sup>

# ULTRASONOGRAPHY

Transabdominal ultrasonography is often the initial imaging investigation for evaluating clinically suspected bile duct obstruction. It is readily available and sensitive for detecting biliary dilatation, gallbladder stones, and cholecystitis. It does not require contrast agents or prolonged patient immobility (Figure 52-15). Overall, it is not as reliable as other modalities for determining the cause and level of bile duct obstruction. The main technical limitation is that bowel gas often obscures the distal CBD (Figure 52-16).

The sensitivity for detecting Klatskin's tumors by ultrasound is highly variable, ranging from 21% to 96%, and appears highly dependent on operator experience and expertise.<sup>23,24</sup> Ultrasonography using microbubble intravenous contrast material has been reported to improve detection and staging of malignant hilar masses compared with routine ultrasonography.<sup>25</sup>

Endoscopic ultrasonography with fine-needle aspiration cytology can be useful for differentiating benign and malignant causes of bile duct obstruction at the level of the biliary confluence and in the head of the pancreas.

### NUCLEAR MEDICINE

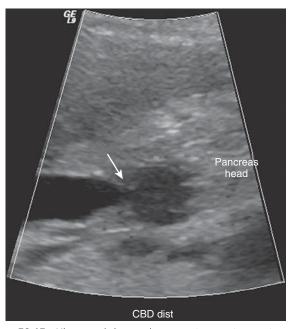
Hepatic iminodiacetic acid scan (HIDA) can help determine the clearance of bile across a stricture or surgical anastomosis, thus providing a functional assessment of the severity of bile duct narrowing with upstream dilatation. Complete biliary obstruction is suggested if the small intestine is not visualized in 60 minutes. HIDA scans do not show biliary dilatation or the site and cause of bile duct obstruction.

# POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

The role of positron emission tomography with CT (PET/CT) in the workup of patients with biliary obstruction is still evolving as evidence of its accuracy with different tumors accumulates.

PET/CT has a role in staging of patients with malignant causes of bile duct obstruction. In assessing cholangiocarcinoma, for instance, PET/CT is more accurate than CT alone for diagnosing regional lymph node metastases and distant metastases.<sup>26</sup> However, PET/CT does not appear to be more accurate at diagnosing the primary tumor than CT and MRI/MRCP.

It is unclear whether certain types of cholangiocarcinoma are more likely to be PET negative; some studies have found



**Figure 52-15** Ultrasound-detected pancreatic mass in a patient with known non-small cell lung carcinoma and biliary dilatation. Longitudinal view of the common bile duct shows abrupt termination of a dilated duct secondary to a hypoechoic pancreatic head mass (*arrow*), presumably a lung metastasis or primary pancreatic adenocarcinoma. The patient had an iodine contrast allergy, and this lesion was not visible on noncontrast computed tomography.

PET to be less helpful in infiltrating-type cholangiocarcinoma,<sup>27,28</sup> whereas others have found no significant difference in PET detection of mass-forming, periductal-infiltrating, and intraductal types.<sup>26</sup> For cholangiocarcinoma that is shown to be PET positive, PET/CT is useful for detecting metastatic and recurrent disease and assessing response to treatment.

In the setting of PSC, PET/CT may play a role in differentiating between benign and malignant strictures.<sup>29</sup>

# IMAGING ALGORITHM

Because of its availability, relatively low cost, lack of ionizing radiation, and high sensitivity for detecting bile duct dilatation, ultrasonography is the initial investigation for obstructive jaundice (Table 52-1). If bile duct dilatation is present and choledocholithiasis is detected, the patient will usually have an ERC for confirmation of the diagnosis and stone removal. If there is biliary dilatation without a clear cause or with a mass or stricture, CT or, preferably, MRI/MRCP is performed. Subsequently, ERC may be performed to remove stones, further evaluate a stricture, or place a stent across a narrowed duct. PTC is usually performed after failed ERCP.

# **Differential Diagnosis**

Considerable overlap exists between the symptoms associated with benign and malignant causes of obstructive jaundice. Progressive painless jaundice in an older patient with weight loss is suggestive of malignancy. Jaundice with a palpable enlarged gallbladder usually is not due to stones (Courvoisier's law)

# **Classic Signs: Dilated Bile Ducts**

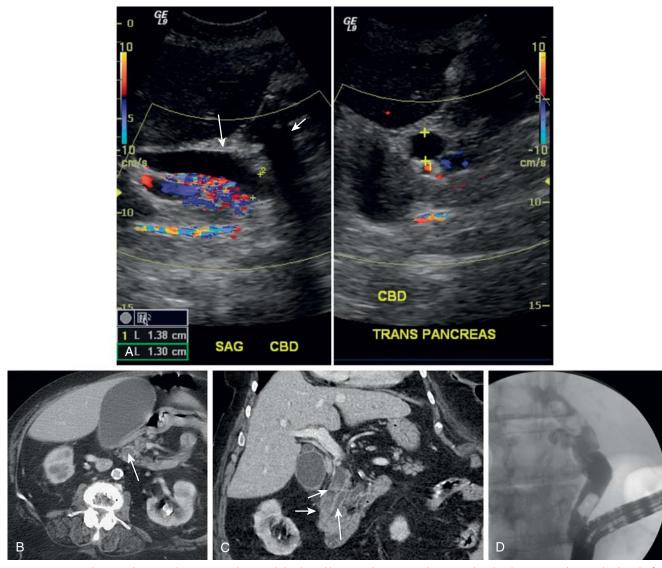
- "Tram track" appearance: Describes intrahepatic bile duct dilatation on ultrasonography—parallel echogenic lines of the dilated bile duct and adjacent portal vein branch are seen coursing through the liver.
- "Double duct" sign: Refers to dilatation of both the CBD and main pancreatic duct. This is classically seen in pancreatic adenocarcinoma (62%) but also can be seen in ampullary carcinoma (52%) and chronic pancreatitis.<sup>4</sup>
- "Target" sign: Describes the appearance of a stone within a bile duct, surrounded by a rim of hypodense bile. A slightly eccentrically positioned stone may give rise to a "crescent" sign.
- "Central dot" sign of Caroli's disease: The central enhancing fibrovascular bundle containing a portal vein surrounded by a focally dilated intrahepatic bile duct cyst.<sup>30</sup>

and is therefore also suggestive of malignancy (Figure 52-17). Younger patients with intermittent sharp pain are more likely to have a benign cause of biliary dilatation.

The differential diagnosis of biliary dilatation depends on the level of obstruction, unifocality or multifocality, and the presence of a stone, stricture, or mass.

Bile duct dilatation to the level of the ampulla of Vater is one pattern of dilatation that has a wide differential diagnosis. When no mass is seen, the differential diagnosis includes ampullary carcinoma or adenoma, inflammatory or fibrotic ampullary stenosis, dysfunction of the sphincter of Oddi, and an impacted or recently passed stone. The presence of a mass is suggestive of a periampullary neoplasm-carcinoma of the ampulla, pancreas, bile duct, or duodenum. MRI and ERCP are the most useful modalities for assessing ampullary obstruction. MRI may detect very small parenchymal tumors and show their relation to the pancreatic and bile ducts. If pancreatic sidebranch dilatation is seen in the setting of a "double duct" sign, this is highly suggestive of pancreatic adenocarcinoma.<sup>4</sup> In cases in which the degree of duct dilatation is of indeterminant significance, dynamic, time-resolved MRCP can be performed after pharmacologic stimulation of the pancreas with secretin. This provides a functional assessment in which significant obstruction at the ampulla leads to prolonged and exaggerated pancreatic dilatation. ERCP allows direct visualization of the ampulla, biopsy of a lesion, manometry, and endoscopic ultrasonography.

Another pattern of biliary dilatation—intrahepatic segmental dilatation—has a vastly different differential diagnosis. It may be caused by a mass such as peripheral cholangiocarcinoma, in which case the bile ducts tend to be irregular, distorted, and slightly enlarged. Marked multifocal saccular or fusiform dilatation of the intrahepatic bile ducts is seen in Caroli's disease (Figure 52-18). Recurrent pyogenic cholangitis shares many of the features of Caroli's disease—marked bile duct dilatation, strictures, stones, and superimposed cholangiocarcinoma; however, the biliary dilatation of recurrent pyogenic cholangitis is rarely saccular (Figure 52-19). Segmental intrahepatic bile duct dilatation can also be seen in PSC. However, in this disease the dilatation tends to be mild and



**Figure 52-16** A, Ultrasound image showing extrahepatic bile duct dilatation (*long vertical arrow*). The distal common duct in the head of the pancreas is not visualized owing to shadowing from overlying bowel gas (*short arrow*). Computed tomography (CT) reveals the cause of duct dilatation, choledocholithiasis. B, Axial postcontrast CT scan shows a stone (*arrow*), slightly denser than bile, in the extrahepatic bile duct within the head of the pancreas. The rim of surrounding hypodense bile creates a "target" appearance. C, Coronal reformatted image shows that there are multiple stones (*short arrows*) in the distal common bile duct and a dilated pancreatic duct (*long arrow*). D, Endoscopic retrograde cholangiopancreatography also shows multiple stones in the common duct. *CBD*, Common bile duct; *SAG*, sagittal.

fusiform, with the predominant feature being bile duct stricture (Figure 52-20).

# Treatment

Treatment options and prognosis of neoplasms and choledochal cysts are discussed in other chapters. In general, for pancreatic adenocarcinoma and cholangiocarcinoma, surgical resection with negative resection margins is the only chance for cure. Adjuvant radiation therapy and chemotherapy have not been shown to improve survival in cholangiocarcinoma. Options for palliation include biliary drainage procedures, radiation, chemotherapy, and photodynamic therapy.

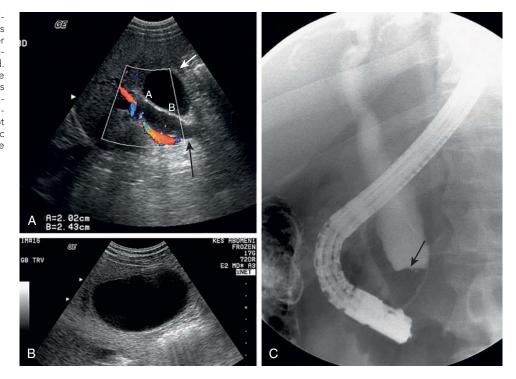
# What the Referring Physician Needs to Know: Dilated Bile Ducts

- Is bile duct dilatation present?
- What is the level of obstruction and what is the cause? Is there a stone, stricture, or mass?
- Are there complications of bile duct obstruction (e.g., hepatic abscess, biloma, ascending cholangitis, cholangiocarcinoma)?
- If a malignant cause is found, staging should be performed to determine if the patient is a surgical candidate or needs medical therapy alone.

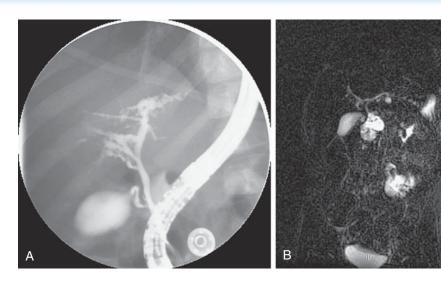
TABLE   Accuracy,	Limitations, and Pitfalls of the Mod	alities Used in Imaging of Dilated E	Bile Ducts	
Modality	Accuracy	Limitations	Pitfalls	
Radiography (ERC and PTC)	High spatial resolution Gold standard for choledocholithiasis and strictures Cytology sampling can be performed during ERC. Potential for therapy (e.g., stent placement)	Ionizing radiation Invasive Potential complications: Pancreatitis, cholangitis, bile duct leak, hemorrhage Ducts beyond the point of obstruction may be poorly visualized.	Failure to recognize complete obstruction of a lobar or segmental bile duct	
СТ	<ul> <li>Adderately accurate for detection of stones and masses and staging of malignancy</li> <li>Choledocholithiasis:</li> <li>CT without contrast: 70% sensitivity</li> <li>CT cholangiogram: 90% sensitivity, &gt;90% specificity</li> <li>Assessment of resectability of cholangiocarcinoma is 60%-75%.</li> </ul>	<ul><li>Cholangiographic contrast agents may worsen renal impairment and cause adverse reactions.</li><li>Biliary excretion is decreased with elevated bilirubin levels and liver insufficiency.</li><li>Fibrosis or inflammation may be indistinguishable from malignancy.</li></ul>	Stones isodense to surrounding bile or tissue may not be detected. Local staging of malignancy is incorrect owing to inability to differentiate tumor from fibrosis/ inflammation.	
MRI/MRCP	After ERC, MRI/MRCP is the most accurate modality for detection of stones and strictures. Choledocholithiasis: >90% sensitivity, >90% specificity. Most accurate test for detecting masses Detection of malignant obstruction: >80% sensitivity, >90% specificity	Less availability Claustrophobia Inferior spatial resolution compared with conventional cholangiography	Surgical material (e.g., metallic clips and stents) and biliary gas (e.g., after biliary-enteric anastomosis) may cause artifacts and may create difficulties with interpretation. Intraductal air may mimic stones in the coronal plane: Axial scans demonstrate nondependent positioning of air.	
Transabdominal ultrasonography	Choledocholithiasis: 22%-75% sensitivity	Bowel gas often obscures the distal common bile duct.	1 5	
Nuclear medicine	Hepatic iminodiacetic acid scan (HIDA) provides functional assessment of the severity of bile duct stricture.	Does not demonstrate the site or cause of bile duct obstruction		
PET/CT	Evolving role. Improves staging of malignant bile duct obstruction In cholangiocarcinoma, more accurate than CT alone for diagnosing regional lymph node and distant metastases	Cholangiocarcinoma: Unclear whether PET/CT improves accuracy of diagnosing the primary tumor over CT and MRI/MRCP		

CT, Computed tomography; ERC, endoscopic retrograde cholangiography; MRI, magnetic resonance imaging; MRCP, magnetic resonance cholangiopancreatography; PET, positron emission tomography; PTC, percutaneous transhepatic cholangiography.

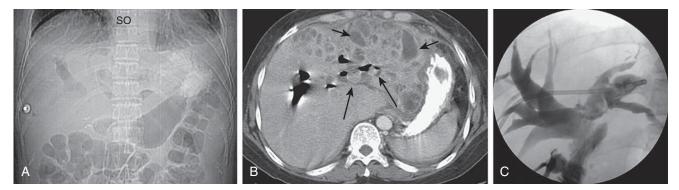
Figure 52-17 Ampullary adenocarcinoma. Ultrasonography demonstrates bile duct (*long arrow*) and gallbladder (*short arrow*) dilatation. The distal common bile duct was not well visualized. The patient was jaundiced, and the gallbladder was palpable; Courvoisier's law states that the cause is not gallstones. C, Endoscopic retrograde cholangiopancreatography shows an abrupt cutoff at the ampulla by an eccentric mass lesion (*arrow*) that proved to be ampullary carcinoma.



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**Figure 52-18** Caroli's disease with multiple areas of focal intrahepatic bile duct dilatation. A, Endoscopic retrograde cholangiopancreatography. B, Magnetic resonance cholangiopancreatography.



**Figure 52-19** Recurrent pyogenic cholangitis. A, Scout film shows marked fusiform dilatation of the intrahepatic bile ducts with pneumobilia. B, Postcontrast axial computed tomography of the abdomen shows intrahepatic bile duct stones (*long arrows*) and abscess formation (*short arrows*). C, Injection of an abscess drainage catheter 5 years later shows communication of the liver abscess with markedly dilated bile ducts. Debris is seen within the left-sided ducts. No significant stricture of the biliary-enteric anastomosis is seen at this time.

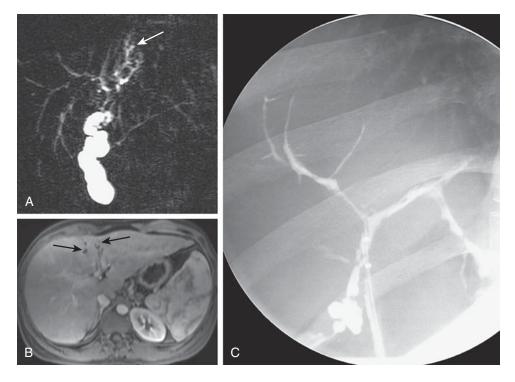


Figure 52-20 Sclerosing cholangitis with strictures and segmental biliary dilatation (arrows) in segment IV. A, Magnetic resonance cholangiopancreatography. B, Postcontrast T1weighted magnetic resonance image. C, Strictures are best seen on endoscopic retrograde cholangiopancreatography (ERCP), but the dilated ducts are not filled on ERCP.

# **Specific Lesions**

# **CHOLEDOCHOLITHIASIS**

#### Etiology

The formation of gallstones is due to bile stasis and supersaturation of solutes, such as cholesterol and bilirubin.

#### **Epidemiology and Definitions**

Choledocholithiasis can be due to stones formed within the bile ducts (primary) or within the gallbladder, subsequently migrating to the bile ducts (secondary). Primary choledocholithiasis is usually secondary to an underlying ductal abnormality such as biliary stricture or choledochal cyst.

In the developed world, most stones are cholesterol stones. These are more common in females and with increased dietary fat intake. In underdeveloped parts of Southeast Asia, brown pigment stones are more common, and these are formed in chronically infected bile ducts.

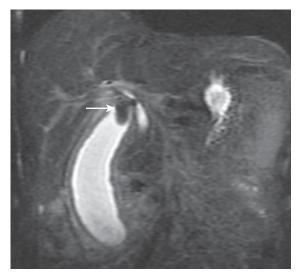
#### **Clinical Presentation**

Choledocholithiasis can manifest as symptoms of biliary obstruction, biliary colic, cholangitis, or pancreatitis. Bile duct stones may be asymptomatic.

Mirizzi's syndrome, resulting from a stone impacted in the cystic duct or neck of the gallbladder exerting pressure on the common hepatic duct, usually manifests as jaundice and cholangitis (Figure 52-21). Repeated episodes of inflammation can lead to formation of a stricture (type I) or pressure necrosis leading to the formation of a cholecysto-choledochal fistula (type II).

# Pathophysiology

Gallstones can be classified into cholesterol and pigment stones. Pigment stones can be further classified into brown and black stones.



**Figure 52-21** Mirizzi's syndrome. Coronal fat-saturated T2-weighted magnetic resonance image shows an impacted stone (*arrow*) in the neck of the gallbladder that is causing acute cholecystitis with gallbladder distention, extrinsic compression of the common hepatic duct, and mild biliary dilatation (the latter feature was seen better on thick-slab magnetic resonance cholangiopancreatography [not shown]).

Pure cholesterol stones are uncommon; most cholesterol stones have calcium salts in their nidus. Cholesterol stones are usually formed within the gallbladder, and their pathogenesis involves several steps: supersaturation of cholesterol in bile, crystal nucleation, gallbladder dysmotility, and alterations in gallbladder absorption.

Black pigment gallstones are often associated with hemolytic conditions or cirrhosis. In hemolytic states, bile becomes supersaturated with unconjugated bilirubin, a breakdown product of red cells. These gallstones usually form within the gallbladder and are not associated with infected bile.

Brown pigment stones are typically found within infected bile ducts. Bacterial glucuronidase converts soluble conjugated bilirubin glucuronide to free bilirubin, which precipitates with calcium.

#### Imaging

Cholangiography is considered the gold standard for detection of bile duct stones. On a cholangiogram, stones usually appear as smooth filling defects. Occasionally, a stone may cause complete obstruction of a branch of the biliary tree, and this abnormality may be difficult to appreciate (Figure 52-22).

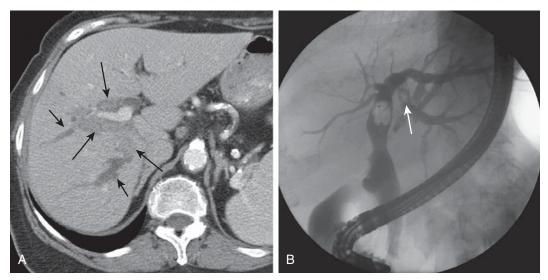
**Computed Tomography.** CT has 70% to 80% sensitivity for stones. Direct visualization of a stone within a bile duct depends on differential density between the stone and surrounding bile or soft tissue. Stones are usually denser than surrounding bile or ampullary soft tissue, especially if they are calcified (Figure 52-23).

Optimal technique for detecting stones includes obtaining oblique coronal reformatted images, using thin collimation (2.5 to 5.0 mm), adjusting window settings to a moderately narrow range (~150 Hounsfield units) around a level matched to the density of bile, and magnifying the image. Stones that are isodense to bile will not be detectable by CT.

Intravenous contrast can be helpful because it may reveal subtle duct dilatation and improve delineation of a stone. Conversely, it may obscure a small stone if the enhancing bile duct mucosa is of a density similar to that of the stone. Orally, contrast agents can obscure small stones near the ampulla of Vater, so if there is clinical suspicion of choledocholithiasis, water or neutral-density contrast media rather than barium can be administered.

**Magnetic Resonance Imaging and Magnetic Resonance Cholangiopancreatography.** Stones appear as areas of signal void within high signal intensity bile on MRCP. MRI has a sensitivity and specificity for choledocholithiasis of over 90%. Very small stones are more difficult to detect on MRCP, with one study showing a decrease in sensitivity from 100% to 64% when stones larger and smaller than 3 mm were compared.<sup>31</sup> Nevertheless, MRI/MRCP is a reasonably accurate, noninvasive test that may avert the need for more invasive procedures such as ERC.

**Ultrasonography.** Sensitivity of transabdominal ultrasonography for choledocholithiasis varies (22% to 75%), depending on the technical skill of the operator and the position of the stone: the distal CBD is often obscured by duodenal or colonic gas. Visualization of the distal CBD may be improved by scanning in the right lateral decubitus or erect right posterior oblique position, aiming to decrease the amount of air in the



**Figure 52-22** Recurrent pyogenic cholangitis with numerous right lobe intrahepatic bile duct stones (*long arrows*, **A**) readily seen on computed tomography (CT) but difficult to detect on endoscopic retrograde cholangiography because they are causing complete branch bile duct obstruction. The obstructed ducts are also seen on CT but not endoscopic retrograde cholangiopancreatography (ERCP) (*short arrows*, **A**). A small left intrahepatic duct stone is seen on ERCP (*arrow*, **B**); balloon trawling is being performed.

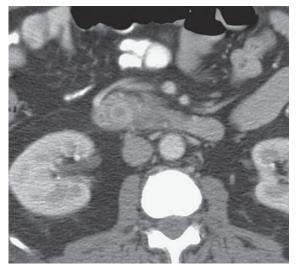


Figure 52-23 Computed tomography showing a peripherally calcified stone at the ampulla of Vater.

gastric antrum and duodenum.<sup>32</sup> Stones appear as echogenic foci with or without shadowing. The differential diagnosis for nonshadowing stones includes soft tissue masses and sludge. Endoscopic ultrasonography is more accurate for the diagnosis of choledocholithiasis but more invasive.

# **Differential Diagnosis**

The differential diagnosis of a filling defect in a dilated bile duct includes neoplasms (e.g., biliary adenoma, papilloma, papillary mucinous neoplasm, and cholangiocarcinoma, papillary type), sludge, blood clot, parasites (Figure 52-24), and gas.

## Treatment

**Medical Treatment.** Stones can be removed from the extrahepatic bile duct during ERCP with a balloon catheter or stone basket and sphincterotomy. The success rate for stone removal from the CBD is 85% to 95%. Endoscopic stone extraction may not be possible if stones are numerous, large, impacted, or intrahepatic. Altered postsurgical anatomy, duodenal diverticula, and biliary strictures also may make this approach difficult. Complications, including cholangitis, pancreatitis, perforation, and bleeding, occur in 5% to 8% of cases.<sup>33</sup>

**Surgical Treatment.** Classification of CBD stones into primary and secondary is important because treatment differs. Treatment of primary stones involves a drainage procedure such as choledochoenterostomy or sphincteroplasty in addition to removal of stones. Secondary stones can be treated by removal of stones and cholecystectomy.

Laparoscopic exploration of the CBD for choledocholithiasis is 75% to 95% successful in clearing all stones.<sup>34</sup> Laparoscopically, the bile duct can be explored via the cystic duct or a choledochotomy. Transcystic duct exploration is suitable for cases of fewer than six to eight stones that are smaller than 9 mm and within the CBD (below the cystic duct). Choledochotomy is generally performed when stones are in the common hepatic or intrahepatic ducts, when stones number more than six to eight, or when they are larger than 1 cm. Choledochotomy is contraindicated in common ducts with a diameter of less than 6 mm because of the potential for postoperative narrowing.<sup>35</sup> Occasionally, if other methods of bile duct stone removal fail, open CBD exploration is performed.

### POSTOPERATIVE BILE DUCT STRICTURES

#### Etiology

Most benign biliary strictures follow surgery in the upper abdomen, most commonly cholecystectomy and CBD exploration.

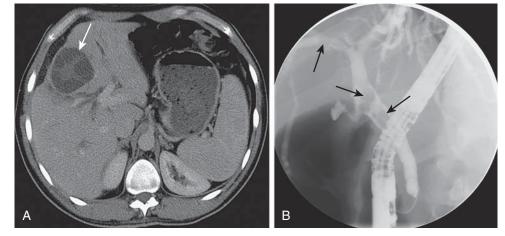


Figure 52-24 A, Hepatic hydatid cyst (arrow) with rupture into the bile ducts. B, Filling defects (infected material) (arrows) seen within the intrahepatic and extrahepatic bile ducts are causing biliary dilatation.

# What the Referring Physician Needs to Know: Choledocholithiasis

- ERCP is the most accurate test for detecting choledocholithiasis. In addition, stones can be removed during ERCP.
- MRI/MRCP is a noninvasive, alternative investigation for choledocholithiasis with sensitivity and specificity both over 90%.
- The number, size, and location of stones within the bile ducts, and the diameter of the CBD, are important for surgical planning of stone removal.
- Factors that predispose to stone formation, such as biliary strictures, are important to identify, because they need to be reversed to prevent future stone formation.

Strictures also can develop after hepatic resection and gastrectomy and at biliary-enteric or end-to-end bile duct anastomoses.

## Prevalence and Epidemiology

The exact incidence of bile duct injury after surgery is unclear. The rate of bile duct injury after laparoscopic cholecystectomy (3 to 7/1000) is higher than after open cholecystectomy (1 to 2/1000).<sup>36</sup>

# **Clinical Presentation**

Most patients present in the early postoperative period. However, 30% of patients present more than 6 months after surgery and patients can present years later. In the acute postoperative setting, patients with bile duct injury may present with rising bilirubin and alkaline phosphatase levels or with symptoms of bile leak.

Patients with postoperative biliary stricture who present months or years after surgery often have symptoms of mild or recurrent cholangitis with cholestatic liver function tests. Less commonly, they may have painless jaundice or advanced biliary cirrhosis.

## Pathophysiology

Failure to recognize aberrant drainage of the right hepatic duct via the cystic duct can lead to injury of the aberrant duct at cholecystectomy (Figure 52-25). Inadequate visualization or perception error at cholecystectomy, more common when performed laparoscopically, may lead to the CBD being confused with the cystic duct and mistakenly clipped. The precise location of a bile duct injury or stricture, in particular its relation to the hepatic duct confluence, is important for surgical management.

#### Pathology

Ischemia can play a role in the formation of bile duct strictures. Dissection around the bile duct during cholecystectomy or bile duct anastomosis can damage the blood supply to the bile ducts (Figure 52-26). Ischemia, bile leak, infection, and direct mechanical injury can lead to inflammation and subsequent fibrosis and scarring.

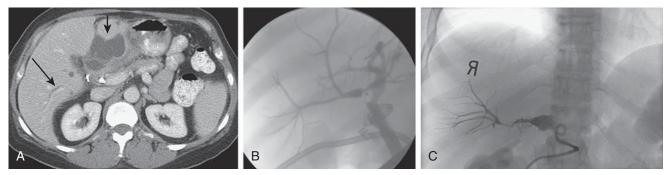
#### Imaging

**Radiography.** PTC is often more useful than ERCP because it provides information about the proximal biliary tree needed for planning reconstructive bile duct surgery. In cases of complete obstruction, the proximal dilated bile ducts will not be demonstrated by ERC (Figure 52-27). PTC can be followed by percutaneous catheter drainage of the obstructed bile ducts.

**Computed Tomography.** In early postoperative presentations, CT is the preferred investigation. It can identify associated bile leak or intra-abdominal collection, confirm bile duct dilatation, and demonstrate the level of obstruction.

**Magnetic Resonance Imaging and Magnetic Resonance Cholangiopancreatography.** MRI/MRCP accurately and noninvasively delineates the bile ducts above and below the level of obstruction and defines the level and length of bile duct stricture or injury. Hepatobiliary contrast agents can detect and localize bile duct leaks on MRCP. Assessment is less reliable if there is a stent within the bile duct or artifact from surgical clips. Also, if there is decompression of the biliary tree, for example, in the setting of bile duct leak treated by percutaneous peritoneal catheter drainage, bile duct injury is more difficult to evaluate and its length may be overestimated.<sup>37</sup>

**Nuclear Medicine.** Radionuclide biliary scanning (technetium-99m–iminodiacetic acid scintigraphy) can be used to confirm an associated bile leak.



**Figure 52-25** A, Post–laparoscopic cholecystectomy bile duct injury with biloma (*short arrow*) and segmental bile duct dilatation (involving the posterior right hepatic lobe) (*long arrow*). **B**, Endoscopic retrograde cholangiopancreatography does not reveal the leak or bile duct dilatation. (A drainage catheter had been inserted into the biloma and is projected over the common duct.) **C**, Injection of the drainage catheter shows communication with the dilated posterior right lobe bile ducts, indicating injury to an aberrant duct previously draining via the cystic duct.



**Figure 52-26** Percutaneous transhepatic cholangiography showing benign smooth stricture at biliary-enteric anastomosis (after Whipple procedure).

# Treatment

**Medical Treatment.** The exact nature of bile duct injury or stricture should be determined by cholangiography before balloon dilatation or surgical repair.

Percutaneous and endoscopic balloon dilatation of biliary strictures is an alternative to surgical repair. Balloon dilatation is most effective for short-segment strictures of the main bile ducts. Strictures usually require repeated (usually two to four) treatments.

The success rate of percutaneous balloon dilatation at 2 to 6 years is 70% to 90%,<sup>38</sup> similar to surgical results. Complications include hemobilia, cholangitis, and bile leaks (20% of patients).

The success of endoscopic balloon dilatation in the treatment of postoperative bile duct strictures is also similar to that of surgery, approximately 80% at 4-year follow-up. **Surgical Treatment.** Definitive surgical management aims to restore adequate bile flow into the upper gastrointestinal tract, usually via a tension-free anastomosis. Surgical operations include end-to-end repair, Roux-en-Y hepatico-jejunostomy, and choledocho-jejunostomy. If the injured or strictured length of bile duct is greater than 1 cm or close to the hepatic duct confluence, an end-to-end anastomosis is generally avoided. Successful long-term outcome is achieved in 70% to 90% of patients at 4- to 10-year follow-up.<sup>38</sup> Long-term follow-up is needed after surgery or balloon dilatation because strictures can recur years later.

## What the Referring Physician Needs to Know: Postoperative Bile Duct Strictures

- Is there biliary dilatation? What is the level of obstruction?
- In patients originally treated for malignancy, is the stricture benign or does it signal recurrence?
- What is the severity and location of the bile duct stricture? Does it involve the hepatic duct confluence?
- Is there an aberrant bile duct drainage pattern?
- Is there a collection, bile leak, or biloma?

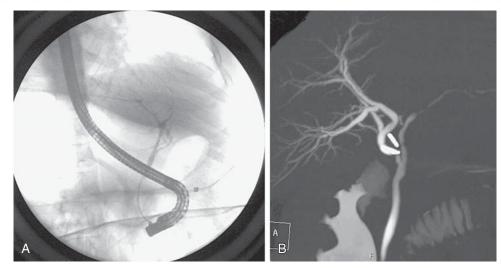
# PRIMARY SCLEROSING CHOLANGITIS

# Etiology, Prevalence, and Epidemiology

PSC is a chronic cholestatic disease of unknown cause characterized by inflammation, fibrosis, and destruction of intrahepatic and extrahepatic bile ducts. Although the cause of PSC is unknown, genetic and immunologic factors appear to play a role. PSC affects men more commonly than women (2:1). It is associated with ulcerative colitis in 50% to 70% of cases. Conversely, 3.0% to 7.5% of patients with ulcerative colitis will develop PSC.<sup>39</sup> Less commonly, PSC is associated with pancreatitis, diabetes, and autoimmune diseases such as retroperitoneal fibrosis, Riedel's thyroiditis, and Crohn's disease.

#### **Clinical Presentation**

PSC typically manifests as jaundice in the fourth or fifth decades. This may be accompanied by right upper quadrant pain, pruritus, fever, weight loss, and fatigue. Symptoms are characteristically cyclical, but over time the disease is progressive.



**Figure 52-27** A, Endoscopic retrograde cholangiopancreatography after inadvertent surgical clipping of right hepatic duct during cholecystectomy. There are too few ducts because the right-sided ducts are completely unopacified. B, Computed tomography cholangiogram shows the dilated right intrahepatic ducts.

Cholestatic liver function tests are seen, with alkaline phosphatase elevated disproportionately compared with serum bilirubin (which often fluctuates in conjunction with the clinical symptoms).

PSC may be complicated by biliary cirrhosis (50%) and cholangiocarcinoma (10%).<sup>40</sup> Patients with PSC have a 5-year survival of 88%; and from the time of diagnosis, the average life expectancy is 11.9 years.<sup>41</sup>

# Pathophysiology

PSC can be classified into large and small duct PSC, visible by cholangiography and microscopy, respectively. Large duct disease most commonly affects the confluence of the right and left hepatic ducts and common hepatic duct (98% to 99%). There is some involvement of the remainder of the extrahepatic ducts in 80% of cases. The intrahepatic ducts are almost always affected. The gallbladder wall is affected in approximately 15% of patients.

## Pathology

PSC is characterized by fibrosing inflammation of the bile ducts, usually both intrahepatic and extrahepatic. The classic findings of PSC are fibrous obliteration of intrahepatic ducts with associated cholangiectasis. Bile duct destruction is patchy, nonsuppurative, and nongranulomatous. There may be periportal edema and bile duct proliferation secondary to large bile duct obstruction. Liver injury results from chronic hepatitis and bile duct obstruction and can range from mild portal hepatitis to cirrhosis. Because the disease is typically patchy, biopsy specimens are often nondiagnostic of PSC.

#### Imaging

Cholangiography can be diagnostic of PSC. Cross-sectional imaging can detect features of biliary dilatation and occasionally wall thickening and complications such as cholangiocarcinoma and cirrhosis.

**Radiography.** ERC often establishes the diagnosis of PSC. Alternating strictures and dilatations of the intrahepatic and

extrahepatic bile ducts (beading) are seen (Figure 52-28). Strictures are usually the predominant feature; duct dilatation is mild and proportionately less than the degree of stricture. For this reason, PTC may be technically difficult. ERC and liver biopsy are used to follow disease progression.

Strictures can vary in length from 1 mm (band strictures) to several centimeters. There may be obliteration of the peripheral intrahepatic bile ducts, giving the biliary tree a "pruned" appearance; this usually indicates that cirrhosis has developed. Rarely, diverticular outpouchings from the bile ducts may be seen; these have a high specificity for PSC. Bile duct walls are often irregular.

**Computed Tomography and Magnetic Resonance Imaging.** Segmental bile duct dilatation, wall thickening, and enhancement may be seen on CT and MRI. There may also be nonspecific T2 high signal in the porta hepatis as a result of inflammation of the hilar bile ducts and features of fibrosis and cirrhosis.

**Ultrasonography.** Areas of biliary dilatation and common duct wall thickening can be demonstrated by ultrasonography. Intrahepatic bile duct wall thickening is usually more subtle but can be detected by experienced sonographers.

#### **Classic Signs: Primary Sclerosing Cholangitis**

- "Beading": Alternating strictures and dilatations
- "Pruning": Peripheral obliteration of the bile ducts
- Diverticular outpouchings from the bile ducts
- Band strictures

#### **Differential Diagnosis**

The most important differential diagnosis of PSC is cholangiocarcinoma. Multicentric or metastatic cholangiocarcinoma can have a cholangiographic appearance similar to that of PSC, and cholangiocarcinoma complicates 15% of cases of PSC. It is difficult to detect this complication early.

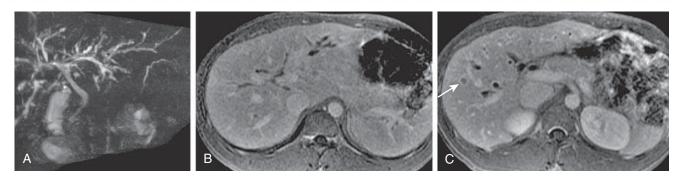


Figure 52-28 Primary sclerosing cholangitis. Magnetic resonance three-dimensional maximum intensity projection (A), and portal venous phase postcontrast T1-weighted (B and C) images show features of sclerosing cholangitis, multiple irregularly dilated intrahepatic ducts, strictures, and bile duct enhancement (arrow, C).



Figure 52-29 Sclerosing cholangitislike picture. Patient on chemotherapy for metastatic breast carcinoma. Endoscopic retrograde cholangiopancreatography (A) shows numerous strictures and multifocal areas of dilatation. No metastases are seen on computed tomography (B).

Imaging features that suggest cholangiocarcinoma rather than PSC include the following:

- More marked biliary dilatation
- A dominant or progressive stricture in the setting of PSC, especially if there is associated clinical deterioration
- An intraluminal or extraluminal mass
- Mural thickening of the extrahepatic bile ducts greater than 5  $\rm mm^{42}$
- Increased uptake of fluorodeoxyglucose (FDG) on PET/ CT (with a standard uptake value >3.6) in hilar strictures<sup>29</sup>

If there is clinical or cholangiographic suspicion of cholangiocarcinoma, cross-sectional imaging should be performed; this can confirm a neoplasm in 50% to 80% of cases. Diagnosis can be confirmed by biopsy of a mass or endoscopic cytology brushings of a suspicious stricture, although the latter has only 50% sensitivity.

Other mimics of the radiographic appearance of PSC include cholangitis secondary to intra-arterial chemotherapy (5-fluorouracil), cholangiopathy related to acquired immunodeficiency syndrome (AIDS), and autoimmune hepatitis or pancreatitis (Figure 52-29).

Intra-arterial 5-fluorouracil therapy, used for treating hepatic metastases of colorectal carcinoma, can be complicated by segmental strictures of variable length with mild upstream biliary dilatation. The hilar regions are preferentially involved by stricture with relative sparing of the distal CBD and peripheral intrahepatic ducts.<sup>43</sup> The gallbladder and cystic duct are more commonly involved than in PSC. Pathologically, dense fibrosis of the bile ducts and surrounding hepatic parenchyma has been reported. However, some strictures are reversible after the cessation of therapy.

AIDS-related cholangitis may be indistinguishable from PSC, with multiple intrahepatic and extrahepatic biliary strictures being the predominant feature. Other features include filling defects in the bile ducts (25%) resulting from polypoidal granulation tissue, mural thickening of bile ducts and gallbladder, and associated papillary stenosis. The clinical setting is the key to making the diagnosis—the condition is an uncommon manifestation of AIDS, most likely secondary to opportunistic infection by *Cryptosporidium*, cytomegalovirus, or both. In addition to symptoms of cholangitis, patients may have abdominal pain and diarrhea from cryptosporidial enteritis.

Autoimmune pancreatitis may cause biliary strictures that are longer (see Figure 52-10) and that tend to cause more upstream biliary dilatation than strictures of PSC.<sup>44</sup> Typically, corticosteroids have a beneficial effect on the strictures of autoimmune pancreatitis but minimal impact on those of PSC.<sup>45</sup>

#### Treatment

**Medical Treatment.** No known medical therapy is effective in improving outcome in patients with PSC. Endoscopic or percutaneous dilatation of dominant strictures is often performed. **Surgical Treatment.** Surgical options include resection of strictures involving the extrahepatic bile duct with long-term transhepatic stenting and liver transplantation.<sup>35</sup> Liver transplantation is recommended for patients with biliary cirrhosis or symptomatic severe intrahepatic duct strictures. Liver

transplantation decreases the risk for cholangiocarcinoma and improves life expectancy. The 5-year survival and graft survival rates are 85% and 72%, respectively. Preoperative detection of cholangiocarcinoma significantly worsens the outcome of liver transplantation.

### What the Referring Physician Needs to Know: Primary Sclerosing Cholangitis

- Cholangiography plays a key role in diagnosing and monitoring the progress of PSC.
- Cholangiocarcinoma and biliary cirrhosis are the main long-term complications of PSC.
- Features that suggest the development of cholangiocarcinoma in the setting of PSC include clinical deterioration, a dominant or progressive stricture, marked biliary dilatation, a mass, common duct thickening greater than 5 mm, and increased FDG uptake on PET/CT.

#### **Key Points**

- A patient with abdominal pain, fever, and jaundice (Charcot's triad) has ascending cholangitis until proved otherwise.
- Patients with duct dilatation and ascending cholangitis need prompt bile duct decompression and intravenous antibiotic coverage.
- In the workup of patients with clinical cholestasis, imaging should establish the presence of biliary dilatation and

define the level, cause, and complications of biliary obstruction.

- Cross-sectional imaging, in particular MRI, best identifies obstructing masses.
- Cholangiography (ERC, PTC, and MRCP) is best at evaluating bile duct stones and strictures.

#### SUGGESTED READINGS

Kim JH, Kim MJ, Chung JJ, et al: Differential diagnosis of periampullary carcinomas at MR imaging. *Radiographics* 22:1335–1352, 2002.

Mulholland MW, Lillemoe KD, Doherty GM, et al: Greenfield's surgery: scientific principles and prac*tice*, ed 4, Philadelphia, 2005, Lippincott Williams & Wilkins.

- Romagnuolo J, Bardou M, Rahme E, et al: Magnetic resonance cholangiopancreatography: a meta-analysis of test performance in suspected
- biliary disease. Ann Intern Med 139:547-557, 2003.
- Zein CO, Lindor KD: Primary sclerosing cholangitis. Semin Gastrointest Dis 12:103–112, 2001.

## REFERENCES

- Bowie JD: What is the upper limit of normal for the common bile duct on ultrasound: how much do you want it to be? *Am J Gastroenterol* 95:897–900, 2000.
- Hall JG, Pappas TN: Current management of biliary strictures. J Gastrointest Surg 8:1098– 1110, 2004.
- Molinari M, Helton W, Espat NJ: Palliative strategies for locally advanced unresectable and metastatic pancreatic cancer. Surg Clin North Am 81:651–665, 2001.
- Kim JH, Kim MJ, Chung JJ, et al: Differential diagnosis of periampullary carcinomas at MR imaging. *Radiographics* 22:1335–1352, 2002.
- Soto JA, Alvarez O, Lopera JE, et al: Biliary obstruction: findings at MR cholangiography and cross-sectional MR imaging. *Radiographics* 20:353–366, 2000.
- Loperfido S, Angelini G, Benedetti G, et al: Major early complications from diagnostic and therapeutic ERCP: a prospective multicenter study. *Gastrointest Endosc* 48:1–10, 1998.
- Burke DR, Lewis CA, Cardella JF, et al: Quality improvement guidelines for percutaneous transhepatic cholangiography and biliary drainage. *J Vasc Interv Radiol* 14:S243–S246, 2003.
- Rosch T, Meining A, Fruhmmorgen S, et al: A prospective comparison of the diagnostic accuracy of ERCP, MRCP, CT and EUS in biliary stricture. *Gastrointest Endosc* 55:870–876, 2002.

- 9. Tabuchi T, Itoh K, Ohshio G, et al: Tumor staging of pancreatic adenocarcinoma using early and late-phase helical CT. *AJR Am J Roent-genol* 173:375–380, 1999.
- Fletcher JG, Wiersema MJ, Farrell MA, et al: Pancreatic malignancy: value of arterial, pancreatic, and hepatic phase imaging with multi-detector row CT. *Radiology* 229:81–90, 2003.
- 11. Slattery JM, Sahani DV: What is the current state-of-the-art imaging for detection and staging of cholangiocarcinoma? *Oncologist* 11: 913–922, 2006.
- 12. Okada M, Fukada J, Toya K, et al: The value of drip infusion cholangiography using multidetector-row helical CT in patients with choledocholithiasis. *Eur Radiol* 15:2140–2145, 2005.
- Agrawal MD, Pinho DF, Kulkarni NM, et al: Oncologic applications of dual-energy CT in the abdomen. *Radiographics* 34:589–612, 2014.
- Romagnuolo J, Bardou M, Rahme E, et al: Magnetic resonance cholangiopancreatography: a meta-analysis of test performance in suspected biliary disease. *Ann Intern Med* 139:547–557, 2003.
- Semelka RC, Ascher SM: MR imaging of the pancreas. *Radiology* 188:593–602, 1993.
- Mitchell DG: MR imaging of the pancreas. Magn Reson Imaging Clin N Am 3:51–71, 1995.

- Semelka RC, Kroeker MA, Shoenut JP, et al: Pancreatic disease: prospective comparison of CT, ERCP, and 1.5-T MR imaging with dynamic gadolinium enhancement and fat suppression. *Radiology* 181:785–791, 1991.
- Vellet AD, Romano W, Bach DB, et al: Adenocarcinoma of the pancreatic ducts: comparative evaluation with CT and MR imaging at 1.5 T. *Radiology* 183:87–95, 1992.
- Guthrie JA, Ward J, Robinson PJ: Hilar cholangiocarcinomas: T2 weighted spin-echo and gadolinium-enhanced FLASH MR imaging. *Radiology* 201:347–355, 1996.
- Mehta SN, Reinhold C, Barkun AN: Magnetic resonance cholangiopancreatography. *Gastrointest Endosc Clin N Am* 7:247–270, 1997.
- David V, Reinhold C, Hochman M, et al: Pitfalls in the interpretation of MR cholangiopancreatography. *AJR Am J Roentgenol* 170:1055–1059, 1998.
- Cannon ME, Carpenter SL, Elta GH, et al: EUS compared with CT, magnetic resonance imaging, and angiography and the influence of biliary stenting on staging accuracy of ampullary neoplasms. *Gastrointest Endosc* 50:27–33, 1999.
- Hann L, Greatrex KV, Bach AM, et al: Cholangiocarcinoma at the hepatic hilus: sonographic findings. *AJR Am J Roentgenol* 168:985–989, 1997.

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- Robledo R, Muro A, Prieto ML: Extrahepatic bile duct carcinoma: US characteristics and accuracy in demonstration of tumors. *Radiology* 198:869–873, 1996.
- Khalili K, Metser U, Wilson SR: Hilar biliary obstruction: preliminary results with Levovistenhanced sonography. *AJR Am J Roentgenol* 180: 687–693, 2003.
- 26. Kim JY, Kim MH, Lee TY, et al: Clinical role of 18F-FDG PET-CT in suspected and potentially operable cholangiocarcinoma: a prospective study compared with conventional imaging. *Am J Gastroenterol* 102:1–7, 2007.
- Jadvar H, Henderson RW, Conti PS: [F-18]Fluorodeoxyglucose positron emission tomography and positron emission tomography: computed tomography in recurrent and metastatic cholangiocarcinoma. J Comput Assist Tomogr 31:223– 228, 2007.
- Anderson CD, Rice MH, Pinson CW, et al: Fluorodeoxyglucose PET imaging in the evaluation of gallbladder carcinoma and cholangiocarcinoma. J Gastrointest Surg 8:90–97, 2004.
- Reinhardt MJ, Strunk H, Gerhardt T, et al: Detection of Klatskin's tumor in extrahepatic bile duct strictures using delayed 18F-FDG PET/ CT: preliminary results for 22 patient studies. J Nucl Med 46:1158–1163, 2005.
- Levy AD, Rohrmann CA, Jr, Murakata LA, et al: Caroli's disease: radiologic spectrum with pathologic correlation. *AJR Am J Roentgenol* 179:1053–1057, 2002.

- Mendler MH, Bouillet P, Sautereau D, et al: Value of MR cholangiography in the diagnosis of obstructive diseases of the biliary tree: a study of 58 cases. *Am J Gastroenterol* 93:2482–2490, 1998.
- Laing FC: The gallbladder and bile ducts. In Rumack CM, Wilson SR, Charboneau JW, editors: *Diagnostic ultrasound*, ed 2, St. Louis, 1998, Mosby, pp 187–193.
- Freeman M, Nelson D, Sherman S, et al: Complications of endoscopic biliary sphincterotomy. N Engl J Med 335:909, 1996.
- 34. Rhodes M, Sussman L, Cohen L, et al: Randomized trial of laparoscopic exploration of common bile duct versus postoperative endoscopic retrograde cholangiography for common bile duct stones. *Lancet* 351:159–161, 1998.
- Mulholland MW, Lillemoe KD, Doherty GM, et al: Greenfield's surgery: scientific principles and practice, ed 4, Philadelphia, 2005, Lippincott Williams & Wilkins, p 996.
- Hall JG, Pappas TN: Current management of biliary strictures. J Gastrointest Surg 8:1098– 1110, 2004.
- Hoeffel C, Azizi L, Lewin M, et al: Normal and pathologic features of the postoperative biliary tract at 3D MR cholangiopancreatography and MR imaging. *Radiographics* 26:1603– 1620, 2006.
- 38. Lillemoe KD: Biliary strictures and sclerosing cholangitis. In Greenfield LJ, editor: Surgery,

scientific principles and practice, Philadelphia, 2001, Lippincott Williams & Wilkins.

- Zein CO, Lindor KD: Primary sclerosing cholangitis. Semin Gastrointest Dis 12:103–112, 2001.
- De Groen PC, Gores GJ, LaRusso NF, et al: Biliary tract cancers. N Engl J Med 341:1368– 1378, 1999.
- Wiesner RH: Current concepts in primary sclerosing cholangitis. *Mayo Clin Proc* 69:969–982, 1994.
- Schulte SJ, Baron RL, Teefey SA, et al: CT of the extra-hepatic bile ducts: wall thickness and contrast enhancement in normal and abnormal ducts. *AJR Am J Roentgenol* 154:79–85, 1990.
- Shea WJ, Jr, Demas BD, Goldberg HI, et al: Sclerosing cholangitis associated with hepatic arterial FUDR chemotherapy: radiographichistologic correlation. *AJR Am J Roentgenol* 146: 717–721, 1986.
- Nakazawa T, Ohara H, Sano H, et al: Cholangiography can discriminate sclerosing cholangitis with autoimmune pancreatitis from primary sclerosing pancreatitis. *Gastrointest Endosc* 60:937–944, 2004.
- Kloppel G, Luttges J, Lohr M, et al: Autoimmune pancreatitis: pathological, clinical and immunological features. *Pancreas* 27:14–19, 2003.

# **Tumors of the Gallbladder**

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# **Etiology**

The precise cause of gallbladder carcinoma is unknown, but cholelithiasis and pancreaticobiliary malformations are major risk factors. Gallstones and reflux of pancreaticobiliary enzymes are thought to result in chronic repetitive inflammation of the gallbladder mucosa that, over time, may undergo malignant transformation into invasive carcinoma.<sup>1</sup>

# Prevalence and Epidemiology

Gallbladder carcinoma is the most common primary biliary tract cancer and sixth most common gastrointestinal malignancy. It typically affects older patients (>65 years), with a female and Native American/Hispanic predominance. Associated conditions include chronic cholecystolithiasis; large (>3 cm) or cholesterol-type gallstones; gallbladder wall calcification ("porcelain gallbladder"); large (>1 cm) gallbladder polyps; obesity; anomalous pancreaticobiliary junctions and choledochal cystic disorders; chronic cholangitic infection by *Salmonella* or *Helicobacter*; inflammatory bowel disease and familial adenomatous polyposis; use of tobacco, estrogens, isoniazid, or methyldopa; and occupational exposures to rubber, petroleum, heavy metals, and radon.<sup>2,3</sup>

# **Clinical Presentation**

Signs and symptoms are nonspecific. In early stages, symptoms can mimic those of cholelithiasis or cholecystitis with right upper quadrant abdominal pain. Advanced disease can lead to significant biliary obstruction with resulting weight loss, hepatomegaly, jaundice, ascites, and less frequently bowel obstruction.

Most cases are advanced stage at diagnosis or less commonly incidentally discovered postoperatively. Poor prognostic factors include tumor invasion and metastatic spread at the time of diagnosis. When tumors are detected early, surgical resection can be curative.

On physical examination, classic signs include a painless enlarged gallbladder in the right upper quadrant (Courvoisier's sign), periumbilical (Sister Mary Joseph node), or left supraclavicular (Virchow's node) lymphadenopathy, and pelvic seeding palpable on digital rectal examination (Blumer's shelf).<sup>2,4,5</sup>

# Pathophysiology

The gallbladder is a saccular organ located between the right and left hemilivers, just below segments IV and V. Sixty percent of tumors occur in the fundus, 30% in the body, and 10% in the neck (Figure 53-1). Cancers disseminate via lymphatic spread to the porta hepatis, peripancreatic, and retroperitoneal nodes and via hematogenous spread to the lungs, liver, and bones. Direct local spread can lead to intraperitoneal seeding or infiltration of adjacent tissues. The American Joint Committee on Cancer Staging Tumor, Node, Metastasis (TNM) classification system is most commonly used for staging (Figure 53-2).<sup>24,5</sup>

# Pathology

The gallbladder has three microscopic layers: mucosa, muscularis, and adventitia, or serosa. Serosa is found on the free surface of the gallbladder, and a layer of adventitia is present at liver interfaces. The muscularis layer consists of contractile smooth muscle, surrounded by a perimuscular connective tissue sheath. The mucosa consists of lamina propria and simple columnar epithelium lining the gallbladder lumen. There is no muscularis mucosa or submucosa separating the muscularis and mucosa layers, leading to easier spread of tumor into the adjacent liver and peritoneum.

Ninety percent of gallbladder cancers are adenocarcinomas that originate from glandular cells in the gallbladder lining. Subtypes include papillary and mucinous tumors. The papillary type is least aggressive and has the best prognosis. Other histologic types include squamous cell, adenosquamous, small cell, neuroendocrine, and sarcomatoid. Occasionally, metastases from melanoma, renal, and breast carcinoma can involve the gallbladder. Histologic grade also affects outcome, with poorly differentiated tumors portending a worse prognosis.

Benign tumors of the gallbladder include adenomas, villous papillomas, paragangliomas, and granular cell tumors. Adenomas are uncommon lesions that result from chronic inflammation and/or cholelithiasis.<sup>5-7</sup>

# Imaging

Gallbladder carcinoma manifests either as an intraluminal polypoid or sessile mass, gallbladder wall thickening, or a large extraluminal mass invading surrounding organs. Most tumors are seen in the fundus or body, with fewer in the neck or cystic duct. Irregular mural thickening and gallbladder calculi may also be present.

# RADIOGRAPHY

Plain radiography has limited value in gallbladder carcinoma. Abdominal films may show porcelain gallbladder, calcified gallstones, vague or punctate tumor calcification, and occasionally pneumobilia from a gallbladder-enteric fistula (Figure 53-3). Invasive procedures such as endoscopic retrograde cholangiography (ERCP) or percutaneous transhepatic cholangiography (PTC) can show bile duct narrowing and/or nonvisualization of the gallbladder secondary to obstruction (Figure 53-4). A malignant-appearing stricture of the midportion of the common bile duct (CBD) should raise suspicion for a gallbladder carcinoma.<sup>8,9</sup>



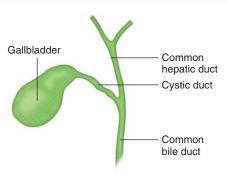
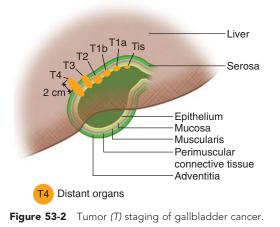


Figure 53-1 Anatomy of the gallbladder.





**Figure 53-3** Abdominal radiography of gallbladder carcinoma demonstrates thick circumferential calcification in the right upper quadrant consistent with a porcelain gallbladder, a major risk factor for development of gallbladder carcinoma.



**Figure 53-4** Endoscopic retrograde cholangiography demonstrates a high-grade stricture of the mid–common bile duct and nonopacification of the gallbladder, highly suggestive of gallbladder cancer.

# COMPUTED TOMOGRAPHY

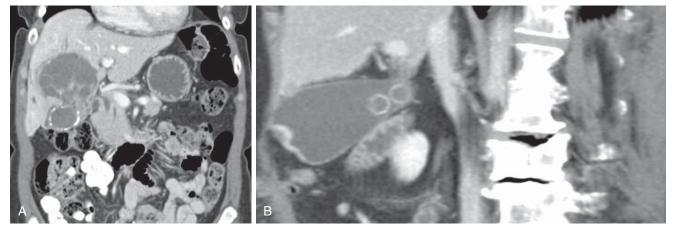
Computed tomography (CT) can detect gallbladder masses and wall thickening. Tumors are visualized as hypodense masses that enhance heterogeneously, occasionally filling the entire lumen (the "jam-packed gallbladder"). Focal or diffuse wall thickening also can be seen, often with abnormally avid or persistent enhancement. Porcelain gallbladder, calcified gallstones, and/or biliary dilatation also may be present. Advanced tumors may manifest with hepatoduodenal ligament lymphadenopathy and invasion of the liver, bile ducts, duodenum, stomach, pancreas, and/or kidneys. Metastasis may be noted in distant organs (Figure 53-5).<sup>9-12</sup>

# MAGNETIC RESONANCE IMAGING

Findings on magnetic resonance imaging (MRI) are similar to those of CT, with superior assessment of local disease extension and tumor composition because of better soft tissue contrast. Tumors generally appear hyperintense on T2-weighted and isointense to hypointense on T1-weighted images. When gadolinium is administered, tumors enhance heterogeneously and peripherally (Figure 53-6). Magnetic resonance cholangiopancreatography (MRCP) provides superior visualization of the biliary system for assessing obstruction (Figure 53-7). Highresolution three-dimensional T1-weighted gradient echo postcontrast MR images delineate vascular detail for surgical planning. More recently, hepatobiliary contrast agents have been advocated to improve detection of liver invasive disease.<sup>9-13</sup>

# ULTRASONOGRAPHY

Transabdominal ultrasonography is the most common imaging modality for gallbladder carcinoma, leveraging low cost, easy accessibility, and noninvasive evaluation. It is more sensitive than CT for detecting gallstones and assessing biliary dilatation.



**Figure 53-5** Computed tomography (CT) can detect gallbladder masses, gallstones, biliary dilatation, and local invasion or distant metastasis. Coronal contrast-enhanced CT (A) demonstrates a porcelain gallbladder and gallbladder mass directly invading the liver. Coronal contrast-enhanced CT (B) in a different patient demonstrates an avidly enhancing mass along the gallbladder fundus and two calcified gallstones.

However, evaluation of the distal common bile duct can be limited by overlying gastroduodenal air. Ultrasonography cannot reliably be used for staging owing to limited visualization of lymph nodes, intraperitoneal disease, and distant metastases. Nonspecific sonographic signs of gallbladder carcinoma include wall thickening, intraluminal or extraluminal masses, and large polyps. Early-stage lesions are small with homogeneous echotexture, whereas advanced lesions are more complex with necrotic areas and mixed echogenicity. Color Doppler imaging often shows foci of increased vascularity. Gallstones, wall calcification, and tumefactive sludge are frequently present and can obscure small tumors. Ultrasonography can be helpful in distinguishing adenomyomatosis. Metastases and biliary dilatation may be visualized in the liver. Endoscopic ultrasonography provides more accurate assessment of the gallbladder wall, bile ducts, and regional lymphadenopathy but is invasive (Figure 53-8).<sup>9-12</sup>

## NUCLEAR MEDICINE

Cholescintigraphy using technetium-99m (<sup>99m</sup> Tc)–diisopropyl iminodiacetic acid (HIDA) is used to image the liver, gallbladder, and bile ducts. Nonopacification of the gallbladder is a nonspecific sign of cystic duct obstruction, most commonly in the setting of acute cholecystitis, but can also be seen with gallbladder carcinoma.<sup>9-12</sup>

# POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

<sup>18</sup>F-fluorodeoxyglucose (FDG) positron emission with computed tomography (PET/CT) may show foci of increased uptake (standard uptake value >2.5) in the gallbladder wall or fundus (Figure 53-9). Whole-body scanning allows for identification of distant metastases.

## IMAGING ALGORITHM

Patients presenting with right upper quadrant abdominal pain should initially be screened with ultrasonography (Table 53-1). Advanced symptoms such as hepatomegaly, jaundice, and ascites should raise concern for a hepatobiliary malignancy, prompting further imaging. Both CT and MRI are used to characterize gallbladder tumors. CT best demonstrates calcification and distant metastases, whereas MRI is used to characterize tumor composition, detect fibrosis and hemorrhage, and delineate local soft tissue invasion. MRCP provides a noninvasive assessment of the bile ducts. Whole-body PET/CT can be used to evaluate the metabolic activity of suspected tumors and detect metastases.

#### **Classic Signs**

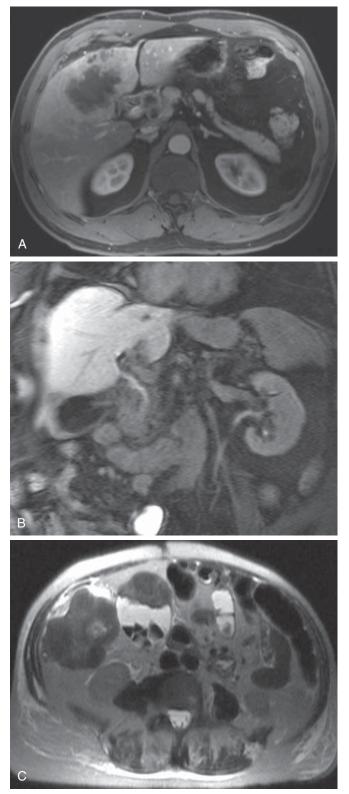
- Porcelain gallbladder on abdominal radiography, ultrasonography, and CT
- "Jam-packed gallbladder" on CT and MRI

# **Differential Diagnosis**

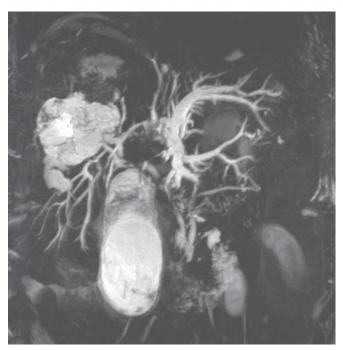
Clinical symptoms of gallbladder cancer overlap with many other hepatobiliary syndromes. The differential diagnosis includes other gallbladder disorders such as cholelithiasis, cholecystitis, gallbladder mucocele, and gallbladder volvulus; bile duct diseases such as cholangitis, choledocholithiasis, choledochal cysts, and cholangiocarcinoma; liver disorders such as cirrhosis, primary liver cancer, or metastases; and pancreatic diseases such as pancreatitis or neoplasm.

Laboratory tests such as carbohydrate antigen 19-9 (CA 19-9), carcinoembryonic antigen, alkaline phosphatase, and bilirubin are nonspecific indicators for malignancy and hepatobiliary disease.

Nonspecific signs on imaging can confound the diagnosis of gallbladder cancer. Calcification and pneumobilia on plain radiography can be seen in a variety of hepatobiliary and gastrointestinal conditions. Inflammation, radiation changes, and benign lesions can mimic tumors on CT and MRI. Xanthogranulomatous cholecystitis is particularly difficult to distinguish from gallbladder carcinoma, given its similar imaging features of wall thickening and fibrosis, regional lymphadenopathy, and surrounding tissue involvement. Hepatoduodenal lymphadenopathy is a finding also present in lymphoma and



**Figure 53-6** Magnetic resonance imaging (MRI) provides higher soft tissue contrast and aids in assessing the presence of a gallbladder mass, associated biliary ductal dilation, gallstones, liver invasion, and local lymph node spread. Axial T1-weighted postcontrast MRI (A) demonstrates a peripherally enhancing, centrally necrotic mass invading the liver from the gallbladder, with necrotic porta hepatis lymphadenopa-thy. Coronal T1-weighted postcontrast MRI with a hepatobiliary contrast agent (B) demonstrates to better advantage subtle local invasion of the liver adjacent to a mass in the gallbladder fundus in a different patient. Axial T2-weighted MRI (C) demonstrates a fundal gallbladder mass and gallstones.



**Figure 53-7** Magnetic resonance cholangiopancreatography demonstrates a large gallbladder mass and necrotic liver metastasis result in biliary ductal obstruction.

gastrointestinal carcinoma, and gallbladder fossa invasion is seen in hepatic tumors and melanoma.

On ultrasonography, adenomyomatosis can manifest as focal wall thickening ("hourglass gallbladder" if in the wall of the midbody) and "comet tail" reverberation artifacts as a result of intramural cholesterol deposits. Diffuse gallbladder wall thickening is also seen in cholecystitis, hepatitis and cirrhosis, hypoalbuminemia, and heart failure. Tumefactive sludge, benign polypoid lesions, porta hepatis nodes, and metastases may also mimic primary cancer.

Any source of biliary obstruction can produce abnormal results on cholescintigraphy. With PET/CT, inflammatory lesions and metastases can show increased FDG uptake indistinguishable from that of primary gallbladder cancer.<sup>8</sup>

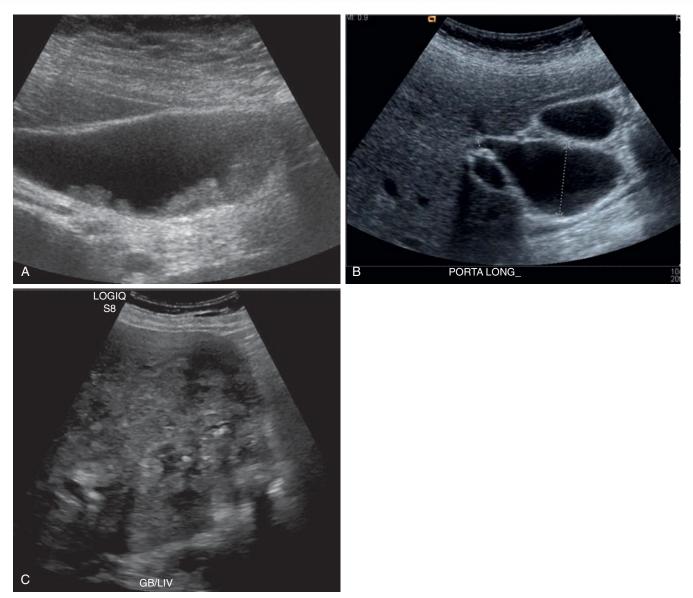
# Treatment

## MEDICAL TREATMENT

There is no definitive medical therapy for gallbladder cancer. Chemotherapy (5-fluorouracil, gemcitabine, cisplatin, capecitabine), radiation therapy, or both may be used for preoperative downstaging, postoperative tumor control, and palliation of advanced disease.<sup>14,15</sup>

## SURGICAL TREATMENT

Operative resection is the only curative treatment for gallbladder cancer. Surgery is high risk and generally contraindicated in the presence of advanced local invasion or distant metastasis. Palliative biliary decompression may be considered in inoperable patients.



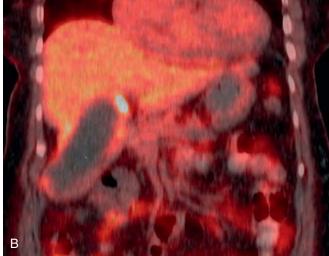


# TABLE 53-1 Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Tumors of the Gallbladder

Modality	Accuracy	Limitations	Pitfalls
Radiography	Limited	Low sensitivity	Other hepatobiliary diseases
СТ	Good	Small tumors	Cholecystitis, benign lesions
MRI	Excellent	Motion artifact	Inflammation, hematomas
Ultrasonography	Fair	Low spatial resolution, small field of view, operator dependent	Cholecystitis, adenomyomatosis, benign lesions
Nuclear medicine	Poor	Nonspecific	Other causes of biliary obstruction
PET/CT	Same as CT	Carcinoid and indolent tumors	Inflammation, metabolic disturbances

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.





**Figure 53-9** Whole-body positron emission tomography with computed tomography demonstrates fluorodeoxyglucose-avid foci in the gallbladder wall.

Operative approaches are determined by the extent of tumor spread. For early-stage tumors, open cholecystectomy is performed to avoid peritoneal seeding. More advanced disease requires extended cholecystectomy with partial liver resection and regional lymphadenectomy. Bile duct excision also may be indicated, particularly if jaundice is present. Surrounding organ invasion may necessitate more radical operations. If laparoscopic approaches have been used and resection margins are positive, port-site resection is done to preclude tract seeding and micrometastasis. Prophylactic resection with cholecystectomy is recommended for porcelain gallbladder, gallstones greater than 3 cm, and polyps that are greater than 1 cm, enlarging, symptomatic, or associated with coexisting biliary disease. Focal resection is also recommended for choledochal cysts and pancreaticobiliary maljunction, owing to the increased risk for developing gallbladder cancer.<sup>7,15-17</sup>

### What the Referring Physician Needs to Know

- Clinical signs and symptoms of gallbladder cancer are nonspecific, resulting in delayed diagnosis and subsequently poor prognosis.
- Imaging enables sensitive detection and accurate characterization of gallbladder carcinoma, facilitating early diagnosis and intervention.
- Various radiologic modalities can be used for preoperative surgical planning and postoperative monitoring of gallbladder disease.

### **Key Points**

- Gallbladder carcinoma is associated with chronic cholecystolithiasis, porcelain gallbladder, gallbladder polyps, biliary disorders, and a variety of environmental exposures.
- Clinical signs and symptoms of gallbladder carcinoma are nonspecific and can be seen in a wide range of hepatobiliary disorders.
- Gallbladder carcinoma manifests as an intraluminal polypoid or extraluminal invasive mass, often with irregular mural thickening. Gallstones, tumefactive sludge, wall calcification, and biliary obstruction/ dilatation are common.
- Plain radiography, cholangiography, and cholescintigraphy have limited applications in gallbladder carcinoma.
- Ultrasonography is the most common imaging modality for gallbladder carcinoma but is limited by low spatial resolution and a small field of view.
- Overall, CT and MRI are the most accurate imaging modalities for characterizing gallbladder cancer. CT is best for demonstrating calcification and identifying distant metastases, whereas MRI is used to characterize tumor composition, detect enhancement/fibrosis/ hemorrhage, and delineate local soft tissue invasion.
- Whole-body PET/CT shows foci of increased uptake in the gallbladder and can identify distant metastases.
- Surgery is the definitive treatment for gallbladder cancer but is contraindicated in advanced disease. Preventive cholecystectomy is recommended for conditions that predispose to gallbladder cancer.

### **SUGGESTED READINGS**

- Daines WP, Rajagopalan V, Grossbard ML, et al: Gallbladder and biliary tract carcinoma: a comprehensive update. II. Oncology 18:1049–1059, 2004.
- Gore RM, Yaghmai V, Newmark GM, et al: Imaging benign and malignant disease of the gallbladder. *Radiol Clin North Am* 40:1307–1323, 2002.
- Heller SL, Lee VS: MR imaging of the gallbladder and biliary system. *Magn Reson Imaging Clin North Am* 13:295–311, 2005.
- Levy AD, Murakata LA, Abbott RM, et al: From the archives of the AFIP. Benign tumors and tumorlike lesions of the gallbladder and extrahepatic

bile ducts: radiologic-pathologic correlation. Armed Forces Institute of Pathology. *Radiographics* 22:387–413, 2002.

- Levy AD, Murakata LA, Rohrmann CA: Gallbladder carcinoma: radiologic-pathologic correlation. *Radiographics* 21:295–314, 2001.
- Miller G, Schwartz LH, D'Angelica M: The use of imaging in the diagnosis and staging of hepatobiliary malignancies. *Surg Oncol Clin North Am* 16:343–368, 2007.
- Oikarinen H: Diagnostic imaging of carcinomas of the gallbladder and the bile ducts. *Acta Radiol* 47:345–358, 2006.
- Rajagopalan V, Daines WP, Grossbard ML, et al: Gallbladder and biliary tract carcinoma: a comprehensive update. I. Oncology 18:889–896, 2004.
- Reid KM, Ramos-De la Medina A, Donohue JH: Diagnosis and surgical management of gallbladder cancer: a review. J Gastrointest Surg 11:671– 681, 2007.
- Rodríguez-Fernández A, Gómez-Río M, Medina-Benítez A, et al: Application of modern imaging methods in diagnosis of gallbladder cancer. J Surg Oncol 93:650–664, 2006.

#### REFERENCES

- Goldin RD, Roa JC: Gallbladder cancer: a morphological and molecular update. *Histopathol*ogy 55:218–229, 2009.
- 2. Donohue JH: Present status of the diagnosis and treatment of gallbladder carcinoma. *J Hepatobiliary Pancreat Surg* 8:530–534, 2001.
- 3. Hundal R, Shaffer EA: Gallbladder cancer: epidemiology and outcome. *Clin Epidemiol* 6:99– 109, 2014.
- Rajagopalan V, Daines WP, Grossbard ML, et al: Gallbladder and biliary tract carcinoma: a comprehensive update. I. Oncology 18:889–896, 2004.
- 5. Gourgiotis S, Kocher HM, Solaini L, et al: Gallbladder cancer. *Am J Surg* 196:252–264, 2008.
- Levy AD, Murakata LA, Rohrmann CA: Gallbladder carcinoma: radiologic-pathologic correlation. *Radiographics* 21:295–314, 2001.
- 7. Cariati A, Piromalli E, Cetta F: Gallbladder cancers: associated conditions, histological

types, prognosis, and prevention. *Euro J Gastroenterol Hepatol* 26:562–569, 2014.

- Gore RM, Yaghmai V, Newmark GM, et al: Imaging benign and malignant disease of the gallbladder. *Radiol Clin North Am* 40:1307– 1323, 2002.
- 9. Oikarinen H: Diagnostic imaging of carcinomas of the gallbladder and the bile ducts. *Acta Radiol* 47:345–358, 2006.
- Rodríguez-Fernández A, Gómez-Río M, Medina-Benítez A, et al: Application of modern imaging methods in diagnosis of gallbladder cancer. J Surg Oncol 93:650–664, 2006.
- Miller G, Schwartz LH, D'Angelica M: The use of imaging in the diagnosis and staging of hepatobiliary malignancies. *Surg Oncol Clin North Am* 16:343–368, 2007.
- 12. Furlan A, Ferris JV, Hosseinzadeh K, et al: Gallbladder carcinoma update: multimodality imaging evaluation, staging, and treatment

options. AJR Am J Roentgenol 191:1440–1447, 2008.

- Hwang J, Kim YK, Choi D, et al: Gadoxetic-acid enhanced MRI for T-staging of gallbladder carcinoma: emphasis on liver invasion. *Br J Radiol* 87:20130608, 2014.
- de Aretxabala X, Roa I, Berrios M, et al: Chemoradiotherapy in gallbladder cancer. J Surg Oncol 93:699–704, 2006.
- Daines WP, Rajagopalan V, Grossbard ML, et al: Gallbladder and biliary tract carcinoma: a comprehensive update. II. *Oncology* 18:1049–1059, 2004.
- Reddy SK, Clary BM: Surgical management of gallbladder cancer. Surg Oncol Clin North Am 18:307–324, 2009.
- Hueman MT, Vollmer CM, Pawlik TM: Evolving treatment strategies for gallbladder cancer. *Ann Surg Oncol* 16:2101–2115, 2009.

# **Intrahepatic Bile Duct Tumors**

ANUP SHETTY | RICHARD TSAI | VAMSIDHAR R. NARRA

# **Etiology**

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The exact pathogenesis of bile duct carcinoma has not been described, but predisposing factors include long-standing inflammation, parasitic infestation, toxin and drug exposures, and genetic abnormalities. It is believed that repeated inflammation leads to chronic bile duct injury with formation of premalignant lesions. DNA alterations secondary to genetic mutations, bile salt exposure, or other carcinogens can predispose to biliary epithelial proliferation and subsequent tumorigenesis. Intrahepatic cholangiocarcinoma and hepatocellular carcinoma likely arise from a common progenitor cell based on experiments in patients with chronic liver disease.<sup>1</sup>

# **Prevalence and Epidemiology**

Intrahepatic cholangiocarcinoma is the second most common primary hepatic cancer after hepatocellular carcinoma. Patients are older (50 to 60 years), with a male preponderance. Survival rates are initially high (50% at 1 year), but because of early metastasis, decline quickly (5% to 15% at 5 years). Established risk factors for the development of bile duct cancer include a family history of hepatic fibrosis, choledochal cysts, parasitic infestation (e.g., *Clonorchis sinensis*), biliary stones, cholangitis, inflammatory bowel disease, chronic pancreatitis, thorium dioxide [Thorotrast] exposure, and certain medications. Factors that predispose specifically to intrahepatic cholangiocarcinoma include chronic hepatitis C virus infection, nonalcoholic liver disease, smoking, and obesity.<sup>2</sup>

# **Clinical Presentation**

Symptoms of cholangiocarcinoma result from biliary obstruction. Thus, intrahepatic tumors manifest late in the course of disease. Patients develop jaundice and pruritus and may also complain of acholic stools and bilirubinuria. Other symptoms resulting from liver dysfunction also may be the presenting symptom.

Prolonged biliary obstruction is associated with cholangitis, cirrhosis, renal dysfunction, and progressive malnutrition.

Intrahepatic cholangiocarcinoma metastasizes early, with a poor prognosis, and early surgical resection is the only chance for curative treatment.<sup>3-7</sup>

# Pathophysiology

The liver consists of bile-secreting hepatocytes draining into bile canaliculi, which merge into hepatic ductules to form the intrahepatic main right and left hepatic ducts. These converge just outside the liver to form the common hepatic duct (Figure 54-1). Bile duct tumors are classified as extrahepatic (87% to 92%) or intrahepatic (8% to 13%). Intrahepatic tumors develop in the small ductal branches within the liver. Morphologically, intrahepatic cholangiocarcinomas may exhibit mass-forming (most common), intraductal-growing, periductal-infiltrating, or combined growth patterns.

The majority of intrahepatic cholangiocarcinomas are solitary, well-circumscribed tumors. Tumors may be peripherally or centrally located. A single hepatic duct is involved in 8% to 13% of cases. Satellite nodules surrounding the main tumor occur in approximately 65% of patients. Ten percent of tumors have a diffuse multicentric distribution with no dominant mass.

Cholangiocarcinomas most commonly disseminate via perineural invasion and lymphatics with involvement of the cystic and common bile duct nodes in 15% of patients. Hematogenous spread is extremely rare. Tumors also can directly infiltrate adjacent liver or cause peritoneal seeding.

Staging of intrahepatic cholangiocarcinoma is performed using the American Joint Committee on Cancer Staging Tumor, Node, Metastasis (TNM) system of classification (Table 54-1).<sup>7,8-21</sup>

# Pathology

Benign biliary tumors such as adenomas, hamartomas, cystadenomas, and papillomas are extremely rare compared with malignant cholangiocarcinomas.

Histologically, the majority (95%) of malignant cancers are mucin-secreting adenocarcinomas with varying levels of differentiation. Pathologic subtypes include scirrhous, nodular, and papillary cancers. The scirrhous type creates fibrotic annular thickenings with low cellularity and is generally seen in the proximal ducts and hilum.

Microscopic findings of anisonucleosis and distended intracytoplasmic lumina support the diagnosis of bile duct cancer. Immunohistochemical staining for carcinoembryonic antigen (CEA), carbohydrate antigens (CA 50 and CA 19-9), and mucins may facilitate diagnosis. The pathologic findings of cholangiocarcinoma and metastatic adenocarcinoma of unknown origin can be especially difficult to differentiate. Cytokeratin (CK) 7 suggests a gastric or colorectal primary, and CK-20 suggests cholangiocarcinoma. Mutations in the *KRAS* oncogene are seen in intrahepatic and perihilar tumors. Studies have also identified mutations in the *TP53* tumor suppressor gene, *c-erb* oncogene, chromosomes 5 and 17, epidermal growth factors, and nuclear antigens.<sup>9,22</sup>

# Imaging

Bile duct tumors are variable in location and morphology and may require multiple modalities for complete characterization. In general, intrahepatic tumors are larger than their

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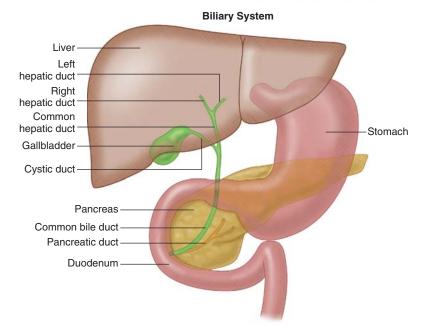


Figure 54-1 Anatomy of the hepatobiliary system.

TABLE 54-1	American Joint Committee on Cancer Staging Tumor, Node, Metastasis Classification, and Staging for Intrahepatic Bile Duct Cancers		
TNM	Definition	Tumor Location	
ТΧ		Primary tumor cannot be assessed	
TO		No evidence of primary tumor	
Tis		Intramucosal carcinoma (intraductal tumor)	
T1		Solitary tumor without vascular invasion	
T2a		Solitary tumor with vascular invasion	
T2b		Multiple tumors, with or without vascular invasion	
Т3		Tumor perforating the visceral peritoneum or involving the local extrahepatic structures by direct invasion	
T4		Tumor with periductal invasion	
NX		Regional lymph nodes cannot be assessed	
N0		No regional lymph node metastasis	
N1		Regional lymph node metastasis present	
M0		No distant metastasis	
M1		Distant metastasis	

From Edge SB, Byrd DR, Compton CC, et al: American Joint Committee on Cancer (AJCC) cancer staging manual, ed 7, New York, 2010, Springer, p 207.

TNM, Tumor, node, metastasis.

extrahepatic counterparts and more conspicuous on imaging. Imaging is also used to evaluate vascular and ductal anatomy, secondary signs of obstruction, and metastatic disease.

# RADIOGRAPHY

Conventional radiography has a limited role in the evaluation of bile duct carcinoma. Intrahepatic tumors may contain calci-



**Figure 54-2** Percutaneous transhepatic cholangiography demonstrates a partially obstructive stricture of the mid–left hepatic duct, with contrast distending the inferior left hepatic duct. A stent was placed to relieve the obstruction.

fications or produce pneumobilia. Digital subtraction angiography (DSA) is infrequently used for assessment of the hepatic vasculature. Cholangiography allows for evaluation of biliary disease and can be performed via transhepatic or endoscopic approaches. Endoscopic retrograde cholangiopancreatography (ERCP) is used for assessment of distal tumors, whereas percutaneous transhepatic cholangiography is used to assess proximal lesions (Figure 54-2).<sup>9,10</sup>

#### COMPUTED TOMOGRAPHY

Large exophytic tumors are easily seen with computed tomography (CT), whereas small or diffuse tumors may be difficult to visualize. Intraluminal polypoid tumors and exophytic tumors appear as lobulated, hypoattenuating masses with variable enhancement. Infiltrating tumors may be high attenuating



**Figure 54-3** On computed tomography, an exophytic peripheral cholangiocarcinoma in the right hepatic lobe appears as a large, lobulated, hypoattenuating mass with heterogeneous internal and peripheral rim enhancement. In comparison, intraluminal polypoid or diffusely infiltrating tumors can be difficult to detect in the absence of biliary obstruction. Delayed contrast-enhanced imaging may be helpful to detect irregular biliary wall thickening and/or enhancement.

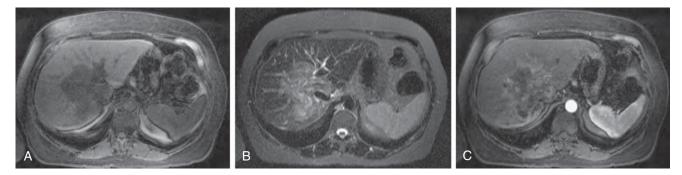
and distributed throughout the bile ducts. Peripheral biliary dilatation may be seen, secondary to intrahepatic obstruction. Capsular retraction of the liver and intra-abdominal lymphadenopathy also can be evaluated. CT angiography (CTA) is useful for assessment of the hepatic vasculature (Figure 54-3).<sup>10-16</sup>

## MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) evaluates intrahepatic and periductal tumors more accurately than CT. Tumors appear isointense to hypointense on T1-weighted images. Continuous rim enhancement and progressive centripetal enhancement can be seen. Lesions are often hyperintense on T2-weighted imaging, with central hypointensity and delayed enhancement reflective of fibrosis (Figure 54-4). Multiphase three-dimensional postcontrast imaging can accurately demonstrate the tumor extent and vascular involvement. Magnetic resonance cholangiopancreatography (MRCP) is useful in the detection of intrahepatic biliary ductal dilation resulting from the primary mass and ductal thickening. Benign ductal thickening appears circumferential and smooth, whereas malignant lesions tend to be eccentric and nodular (Figure 54-5). MRI can be helpful in differentiating intrahepatic cholangiocarcinoma from metastatic adenocarcinomas of unknown primary.<sup>10-16,2</sup>

## ULTRASONOGRAPHY

Transabdominal ultrasonography demonstrates intraductalgrowing tumors more readily than periductal-infiltrating or exophytic mass-forming tumors. Tumor masses are generally



**Figure 54-4** A to C, On magnetic resonance imaging, tumors appear isointense to hypointense on T1-weighted images. Delayed gadolinium enhancement can be seen but is a nonspecific sign. Lesions are often hyperintense on T2-weighted images, with central hypointensity reflective of fibrosis.

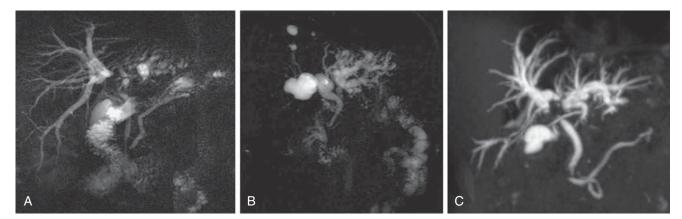
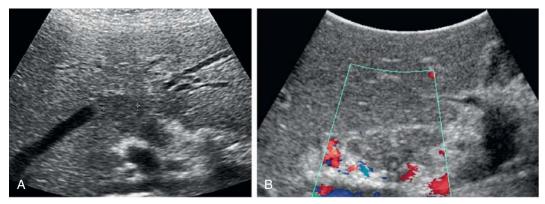


Figure 54-5 A to C, Magnetic resonance cholangiopancreatography is useful in the detection of intrahepatic bile duct strictures.



**Figure 54-6** A, On ultrasonography, tumor masses are generally hyperechoic but also may appear hypoechoic or heterogeneous. Intraluminal polypoidal tumors are visualized more readily than diffuse sclerosing or exophytic tumors. B, Doppler imaging may demonstrate vascular encasement or thrombosis.

hyperechoic but may also appear hypoechoic or heterogeneous. Peripheral biliary dilatation secondary to intrahepatic obstruction may be seen. Doppler imaging may demonstrate vascular encasement or thrombosis (Figure 54-6). Contrast-enhanced ultrasonography is more accurate with late-phase washout being a specific finding.

Endoscopic and intraductal ultrasonography can provide more accurate local assessment than the transabdominal approach. However, both are invasive techniques with limited fields of view. <sup>10-16,21</sup>

## NUCLEAR MEDICINE

Cholangiocarcinoma cells have receptors for somatostatin that inhibit tumor growth. Uptake may be observed with gallium scans. Cholescintigraphy using technetium-99m (<sup>99m</sup>Tc)-diisopropyl iminodiacetic acid (HIDA) scan may reveal sites of biliary obstruction. Sulfur colloid scans show intrahepatic cholangiocarcinomas as cold liver lesions, owing to dysfunctional hepatocyte uptake.<sup>10-16</sup>

# POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

Positron emission tomography with computed tomography (PET/CT) may be helpful in evaluating cholangiocarcinoma superimposed on other biliary conditions. PET demonstrates focal increased uptake of 18F-fluorodeoxyglucose (FDG), with a standardized uptake value (SUV) that is relatively higher for malignant versus benign lesions (SUV > 3.6 vs. 2.5). Wholebody scans are valuable for identifying distant metastases (Figure 54-7).

#### **IMAGING ALGORITHM**

Transabdominal ultrasonography is the first-line imaging examination in patients with jaundice or right upper quadrant pain (Table 54-2). Ultrasonography can visualize intrahepatic tumors, but CT and MRI are necessary for accurate staging and evaluation of extrahepatic lesions. Percutaneous transhepatic cholangiography, ERCP, or MRCP may be required to identify diffuse sclerosing tumors throughout the bile ducts. DSA, CTA, and MRI demonstrate the relationship of tumors to the surrounding vasculature. PET/CT helps to evaluate cholangiocarcinoma in the setting of preexisting biliary disease and can detect distant metastases.

# **Differential Diagnosis**

Clinical symptoms of cholangiocarcinoma overlap with many hepatobiliary syndromes. The differential diagnosis includes other biliary diseases, gallbladder disorders, hepatic dysfunction, primary cancer or metastases, and pancreatic disease.

Laboratory tests such as CA 19-9 and CEA are nonspecific indicators of malignancy. However, high levels of CA19-9 portends poor survival after attempted surgical resection. Elevated levels of bilirubin, alkaline phosphatase, and gammaglutamyltransferase are reflective of obstructive biliary processes. In intrahepatic cholestasis, the alkaline phosphatase level is generally less than three times the upper limit of normal.

On ultrasonography, CT, and MRI, benign tumors and strictures can have an appearance similar to that of cholangiocarcinoma. Primary sclerosing cholangitis may be indistinguishable from diffuse infiltrating cholangiocarcinomas. Primary sclerosing cholangitis classically manifests as alternating stenoses and dilatations in the intrahepatic and extrahepatic bile ducts, creating a "beaded" appearance. Strictures have a gradual, tapered morphology, as opposed to the abrupt narrowing characteristic of malignant processes. In contrast, cholangiocarcinoma originates as a tumor mass within the peripheral or central (Klatskin tumor) bile ducts. This leads to proximal bile duct obstruction with intrahepatic biliary dilatation and normal extrahepatic bile ducts. Metastases may spread to lymph nodes and extrabiliary organs. In the Western hemisphere, cholangiocarcinoma is most commonly secondary to primary sclerosing cholangitis, and malignant transformation should be suspected if there is radiographic evidence of asymmetric thickening of the bile duct wall with duct dilatation, soft tissue mass with rapid growth, vascularity, or necrosis; encasement; invasion; and lymphadenopathy. In the presence of vascular involvement, contrast-enhanced CT and MRI may demonstrate transient hepatic attenuation/intensity differences, which are not typical of primary sclerosing cholangitis.

Distinguishing intrahepatic cholangiocarcinoma from metastatic adenocarcinoma may be challenging for the radiologist and pathologist. Immunohistochemical staining with CK-20

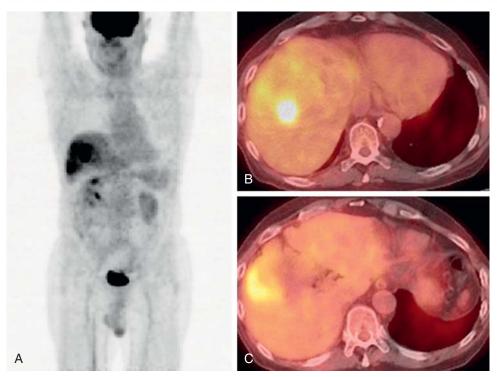


Figure 54-7 A to C, Whole-body positron emission tomography with computed tomography can evaluate cholangiocarcinoma superimposed on other biliary conditions and identifies distant metastases. (Courtesy Jerold Wallis, Mallinckrodt Institute of Radiology, St. Louis, MO.)

TABLE 54-2				
Modal	ity	Accuracy	Limitations	Pitfalls
Radiog	Iraphy	Limited	Low sensitivity	Other hepatobiliary diseases
СТ		Fair	Diffuse and intraluminal tumors	Hepatocellular carcinoma, metastatic adenocarcinoma, benign lesions
MRI		Good	Diffuse and intraluminal tumors	Metastatic adenocarcinoma, benign lesions, ductal thickening
Ultrasc	nography	Fair	Low spatial resolution, small field of view, operator dependent	Benign tumors, cholangitis
Nuclea	ır medicine	Poor	Nonspecific, low spatial resolution	Benign disease, trauma, abscesses, choledocholithiasis
PET/C	Г	Fair	Limited tumor detection, misregistration, unable to stage tumor for resection	Inflammation, metabolic disturbances

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

and CK-7 has increased accuracy, but the pathologist still relies on imaging findings. Fortunately, MR findings of capsular retraction, diffuse heterogeneous enhancement with progressive lesional enhancement, and porta hepatis lymphadenopathy favor cholangiocarcinoma. Ring enhancement (not to be mistaken for peritumoral enhancement) and greater number of lesions favors metastatic adenocarcinoma. Differentiation between these two entities is critical because cholangiocarcinoma is primarily a surgical lesion and metastatic adenocarcinoma is treated with chemotherapy. Often, pathologic examination is needed for differentiation.

Combined hepatocellular-cholangiocarcinoma tumors share overlapping pathologic and imaging features of hepatocellular carcinoma and cholangiocarcinoma. These biphenotypic tumors should be considered when imaging features of a lesion overlap. For example, a mass with arterial phase hyperenhancement and washout with additional features of capsular retraction and associated intrahepatic biliary ductal dilation should make the radiologist suspicious for a biphenotypic tumor.

Any cause of bile duct obstruction, including benign tumors and choledocholithiasis, can yield an abnormal HIDA scan. With PET/CT, inflammatory lesions and metastases can show increased FDG uptake indistinguishable from that shown with primary cholangiocarcinoma.<sup>17,18,23-25</sup>

# Treatment

# MEDICAL TREATMENT

Nonsurgical procedures should be reserved for patients at high operative risk and/or with unresectable tumors. Interventional biliary procedures can be performed endoscopically or percutaneously. Endoscopic approaches are used for distal tumors, whereas percutaneous techniques are preferred for proximal lesions. Strategies to relieve biliary obstruction include internal-external drains, internal endoprostheses, metallic stents, balloon dilatation, and sphincterotomy. These procedures also can offer palliation in the face of unresectable or metastatic disease.

Radiation therapy can be delivered via intracavitary brachytherapy, external-beam radiation, radioimmunotherapy, or charged particle irradiation. Chemotherapy also may be administered by systemic administration, transarterial chemoembolization, or percutaneous injection. Photodynamic therapy, which uses laser-activated photosensitizing agents, is frequently effective. Chemical sympathectomy with alcohol or sclerosing agents is used to relieve pain.<sup>4,7,19,20</sup>

## SURGICAL TREATMENT

Surgical resection is the only curative treatment for cholangiocarcinoma. Resection rate is approximately 20% for intrahe-

## **Key Points**

- Cholangiocarcinoma is associated with congenital hepatic fibrosis or cysts, parasitic infestation, hepatobiliary inflammation and lithiasis, inflammatory bowel disease, chronic pancreatitis, metabolic and inherited diseases, occupational exposures, and certain toxins and medications. Factors that predispose specifically to intrahepatic cholangiocarcinoma include chronic hepatitis C virus infection, nonalcoholic liver disease, smoking, and obesity.
- Clinical signs and symptoms of cholangiocarcinoma are nonspecific and can be seen in a wide range of hepatobiliary disorders.
- Intrahepatic cholangiocarcinoma may manifest as massforming, intraductal-growing, or periductal infiltrating lesions. Biliary obstruction, dilatation, or both and tumor calcification may be seen.

patic tumors. Diffuse carcinomatosis, metastases, and organ or vascular invasion are operative contraindications.

Intrahepatic tumors are treated via local or lobar liver excision. Larger tumors may necessitate extended right/left hepatectomy or central liver resection. The remaining liver parenchyma must contain a functional portal vein, hepatic artery, and bile duct. With diffuse intrahepatic tumors, orthotopic liver transplantation may be considered. However, recurrence after resection is common.<sup>4,7,20-25</sup>

## What the Referring Physician Needs to Know

- Clinical signs and symptoms of cholangiocarcinoma are nonspecific, so a high index of suspicion is necessary.
- Imaging enables sensitive detection and accurate characterization of cholangiocarcinoma, facilitating early diagnosis and intervention.
- Various radiologic modalities can be used for the preoperative surgical planning and postoperative monitoring of biliary disease.
- Plain radiography and nuclear medicine have limited applications in cholangiocarcinoma.
- Ultrasonography, CT, and MRI are the preferred imaging modalities for nodular cholangiocarcinomas.
   Ultrasonography can help identify intrahepatic tumors, but CT and MRI are necessary to stage and further characterize extrahepatic lesions.
- Invasive and MR cholangiography are used to identify diffuse sclerosing tumors throughout the bile ducts.
- Whole-body PET/CT evaluates cholangiocarcinoma superimposed on other biliary conditions and can identify distant metastases.
- Surgery is the definitive treatment for cholangiocarcinoma but is contraindicated in advanced disease. The success of surgical therapy depends on tumor location and extent, with intrahepatic tumors having a worse prognosis.

## **SUGGESTED READINGS**

- Choi H, Loyer EM, Charnsangavej C: Neoplasms of the liver and the bile ducts. Semin Roentgenol 39:412–427, 2004.
- Han JK, Choi BI, Kim AY, et al: Cholangiocarcinoma: pictorial essay of CT and cholangiographic findings. *Radiographics* 22:173–187, 2002.
- Khan SA, Thomas HC, Davidson BR, et al: Cholangiocarcinoma. *Lancet* 366:1303–1314, 2005.
- Lee WJ, Lim HK, Jang KM, et al: Radiologic spectrum of cholangiocarcinoma: emphasis on

#### unusual manifestations and differential diagnoses. *Radiographics* 21:S97–S116, 2001.

- Oikarinen H: Diagnostic imaging of carcinomas of the gallbladder and the bile ducts. *Acta Radiol* 47:345–358, 2006.
- Singh P, Patel T: Advances in the diagnosis, evaluation and management of cholangiocarcinoma. *Curr Opin Gastroenterol* 22:294–299, 2006.
- Slattery JM, Sahani DV: What is the current stateof-the-art imaging for detection and staging of
- cholangiocarcinoma? *Oncologist* 11:913–922, 2006.
- Stroszczynski C, Hunerbein M: Malignant biliary obstruction: value of imaging findings. *Abdom Imaging* 30:314–323, 2005.
- Zech CJ, Schoenberg SO, Reiser M, et al: Crosssectional imaging of biliary tumors: current clinical status and future developments. *Eur Radiol* 14:1174–1187, 2004.

#### REFERENCES

- 1. Hassid VJ, Orlando FA, Awad ZT, et al: Genetic and molecular abnormalities in cholangiocarcinogenesis. *Anticancer Res* 29:1151–1156, 2009.
- Shin HR, Oh JK, Masuyer E, et al: Epidemiology of cholangiocarcinoma: an update focusing on risk factors. *Cancer Sci* 101:579–585, 2010.
- Gatto M, Bragazzi MC, Semeraro R, et al: Cholangiocarcinoma: update and future perspectives. *Dig Liver Dis* 42:253–260, 2010.
- Aljiffry M, Walsh MJ, Molinari M: Advances in diagnosis, treatment and palliation of cholangiocarcinoma: 1990-2009. World J Gastroenterol 15:4240–4262, 2009.
- Singh P, Patel T: Advances in the diagnosis, evaluation and management of cholangiocarcinoma. *Curr Opin Gastroenterol* 22:294–299, 2006.
- Sandhu DS, Roberts LR: Diagnosis and management of cholangiocarcinoma. *Curr Gastroenterol Rep* 10:43–52, 2008.

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- Blechacz B, Gores GJ: Cholangiocarcinoma: advance in pathogenesis, diagnosis, and treatment. *Hepatology* 48:308–321, 2008.
- Yamasaki S: Intrahepatic cholangiocarcinoma: macroscopic type and stage classification. *J Hepatobiliary Pancreat Surg* 10:288–291, 2003.
- Chung YE, Kim MJ, Park YN, et al: Varying appearances of cholangiocarcinoma: radiologicpathologic correlation. *Radiographics* 29:683– 700, 2009.
- Choi BI, Lee JM, Han JK: Imaging of intrahepatic and hilar cholangiocarcinoma. *Abdom Imaging* 29:548–557, 2004.
- Choi JY, Kim MJ, Lee JM, et al: Hilar cholangiocarcinoma: role of preoperative imaging with sonography, MDCT, MRI, and direct cholangiography. *AJR Am J Roentgenol* 191:1448–1457, 2008.
- Han JK, Choi BI, Kim AY, et al: Cholangiocarcinoma: pictorial essay of CT and cholangiographic findings. *Radiographics* 22:173–187, 2002.
- Sainani NI, Catalano OA, Holalkere NS, et al: Cholangiocarcinoma: current and novel imaging techniques. *Radiographics* 28:1263– 1287, 2008.

- 14. Zech CJ, Schoenberg SO, Reiser M, et al: Crosssectional imaging of biliary tumors: current clinical status and future developments. *Eur Radiol* 14:1174–1187, 2004.
- Gakhal MS, Gheyi VK, Brock RE, et al: Multimodality imaging of biliary malignancies. Surg Oncol Clin N Am 18:225–239, 2009.
- Miller G, Schwartz LH, D'Angelica M: The use of imaging in the diagnosis and staging of hepatobiliary malignancies. *Surg Oncol Clin N Am* 16:343–368, 2007.
- Menias CO, Surabhi VR, Prasad SR, et al: Mimics of cholangiocarcinoma: spectrum of disease. *Radiographics* 28:1115–1129, 2008.
- Lee WJ, Lim HK, Jang KM, et al: Radiologic spectrum of cholangiocarcinoma: emphasis on unusual manifestations and differential diagnoses. *Radiographics* 21:S97–S116, 2001.
- Hopfner M, Schuppan D, Scherubl H: Targeted medical therapy of biliary tract cancer: recent advances and future perspectives. World J Gastroenterol 14:7021–7032, 2008.
- Shimoda M, Kubota K: Multi-disciplinary treatment for cholangiocellular carcinoma. World J Gastroenterol 13:1500–1504, 2007.

- Baheti AD, Tirumani SH, Rosenthatl NH, et al: Diagnosis and management of intrahepatic cholangiocarcinoma: a comprehensive update for the radiologist. *Clin Radiol* 69:e463–e470, 2014.
- 22. Al Ansari N, Kim BS, Srirattanapong S, et al: Mass-forming cholangiocarcinoma and adenocarcinoma of unknown primary: can they be distinguished on liver MRI? *Abdom Imaging* 39:1228–1240, 2014.
- Hatzaras I, Schmidt C, Muscarella P, et al: Elevated CA 19-9 portends poor prognosis in patients undergoing resection of biliary malignancies. *HPB (Oxford)* 12:134–138, 2010.
- Fowler KJ, Sheybani A, Parker RA, 3rd, et al: Combined hepatocellular and cholangiocarcinoma (biphenotypic) tumors: imaging features and diagnostic accuracy of contrast-enhanced CT and MRI. AJR Am J Roentgenol 201:332–339, 2013.
- Shetty AS, Fowler KJ, Brunt EM, et al: Combined hepatocellular-cholangiocarcinoma: what the radiologist needs to know about biphenotypic liver carcinoma. *Abdom Imaging* 39:310– 322, 2014.

# **Extrahepatic Bile Duct Tumors**

ANUP SHETTY | RICHARD TSAI | VAMSIDHAR R. NARRA

# Etiology

The exact pathogenesis of bile duct carcinoma has not been described, but predisposing factors are similar to those causing intrahepatic bile duct neoplasms. It is believed that long-standing inflammation causes metaplasia and, finally, carcinogenesis.<sup>1</sup>

# Prevalence and Epidemiology

Tumors of the biliary tract constitute 2% of all cancers found at autopsy. The vast majority of bile duct tumors are extrahepatic (87% to 92%). Patients are typically older than those with intrahepatic bile duct tumors (60 to 70 years of age vs. 50 to 60 years), and there is a slight male preponderance. Survival rates are high (50% at 1 year, 39% at 5 years), reflecting the slow course of the disease and better prognosis than intrahepatic tumors as a result of later metastases. Established risk factors for the development of bile duct cancer are similar to those for intrahepatic biliary tumors and include causes of biliary inflammation such as choledochal cysts, parasitic infestation, biliary stones, inflammatory bowel disease; inherited disorders such as alpha-1 antitrypsin deficiency; toxic exposures such a thorium dioxide; and certain medications (e.g., isoniazid).<sup>2</sup>

# **Clinical Presentation**

In general, cholangiocarcinomas are slow growing and locally infiltrative and they metastasize late. Extrahepatic and perihilar tumors have a more indolent clinical course than intrahepatic tumors, with a better prognosis after complete resection.

Symptoms of cholangiocarcinoma result from biliary obstruction with subsequent cholestasis and hyperbilirubinemia. Thus, extrahepatic and perihilar tumors manifest early in the course of disease. Patients develop jaundice and pruritus and may also report acholic (clay-colored) stools and bilirubinuria (dark urine).

Other symptoms include increased bleeding and bruising, right upper quadrant or epigastric pain, and diarrhea. Prolonged biliary obstruction is associated with complications such as cholangitis, cirrhosis, renal dysfunction, and progressive malnutrition. On physical examination, hepatomegaly may be present. With tumors distal to the cystic duct takeoff, a painless enlarged gallbladder may be identified (Courvoisier's sign).<sup>3-7</sup>

# Pathophysiology

The liver consists of bile-secreting hepatocytes draining into bile canaliculi, which merge into hepatic ductules to form the biliary tree. The main right and left hepatic ducts drain their respective lobes and converge just outside the liver to form the common hepatic duct. The convergence of the left and right hepatic ducts is extrahepatic. The common hepatic duct is then joined by the cystic duct to form the common bile duct (CBD). The CBD continues inferiorly, joining the pancreatic duct at the ampulla of Vater to drain into the second part of the duodenum (Figure 55-1).

Bile duct tumors are classified as extrahepatic (87% to 92%) or intrahepatic (8% to 13%). Extrahepatic tumors occur in the major bile ducts, whereas intrahepatic tumors develop in smaller ductal branches within the liver. Tumors located at the hepatic duct bifurcation are the least common and are termed perihilar or Klatskin's tumors. Morphologically, extrahepatic biliary tumors may exhibit exophytic, polypoid, infiltrating, or combined growth patterns.

The extrahepatic biliary tree is divided into proximal, middle, and distal regions, with anatomic divisions at the level of the cystic duct and upper duodenum. Of bile duct tumors, 50% to 75% are localized in the upper third, 10% to 25% in the middle third, and 10% to 20% in the lower third. Among proximal extrahepatic tumors, 10% to 26% involve the confluence of the ducts (Klatskin's tumor). Among distal tumors, the common hepatic duct is involved in 14% to 37%, the cystic duct in 6%, and the ampulla of Vater in 0.2% of cases.

Cholangiocarcinomas most commonly disseminate via the lymphatic system. Extrahepatic tumors spread to the cystic and CBD nodes in 32% of cases, the celiac nodes in 16% of cases, and the peripancreatic and superior mesenteric nodes on rare occasions. Hematogenous spread to the liver, peritoneum, and lungs is extremely rare. Direct extension of tumor results in infiltration of adjacent liver in 23% of cases and in peritoneal seeding in 9% of cases.

Staging of extrahepatic cholangiocarcinoma is performed using the American Joint Committee on Cancer Staging Tumor, Node, Metastasis (TNM) system of classification (Table 55-1). Klatskin's tumors are categorized using the Bismuth classification (Table 55-2 and Figure 55-2).<sup>7,8</sup>

# **Pathology**

Rarely, extrahepatic bile duct tumors may represent adenomas, hamartomas, cystadenomas, and papillomas, but the vast majority are malignant cholangiocarcinomas. Lesions are thought to develop through an adenoma-carcinoma sequence, stimulated by recurrent biliary obstruction and inflammation with resulting cholestasis.

Histologically, the majority (95%) of malignant cancers are mucin-secreting adenocarcinomas with varying levels of differentiation like their intrahepatic counterpart. Nonsecretory apudomas have occasionally been reported in the hilar region.

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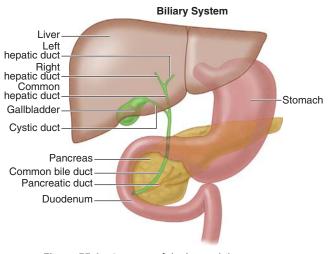


Figure 55-1 Anatomy of the hepatobiliary system.

Pathologic subtypes include scirrhous, nodular, and papillary cancers. Extrahepatic scirrhous tumors can be seen in the hilum. The nodular variety forms irregular strictures in the ductal walls and is most common in the distal ducts and ampulla. Papillary tumors are typically intraluminal, highly vascular and friable, and most commonly seen in the intrahepatic ducts.

Microscopic findings of extrahepatic cholangiocarcinomas mirror intrahepatic cholangiocarcinoma and anisonucleosis, and distended intracytoplasmic lumens support the diagnosis of bile duct cancer. Histologically dedifferentiated tumors have a worse prognosis. Immunohistochemical staining for carcinoembryonic antigen (CEA) and CA19-9 may facilitate diagnosis. Experimental studies have also identified mutations in the *TP53* tumor suppressor gene, *c-erb* oncogene, chromosomes 5 and 17, epidermal growth factors, and nuclear antigens.

Tumors located distal to the cystic and pancreatic ducts also may disrupt the functions of the gallbladder and pancreas, respectively.<sup>9</sup>

# Imaging

Bile duct tumors are highly variable in location and morphology and may require multiple imaging studies for complete characterization. In general, extrahepatic tumors are smaller than their intrahepatic counterparts and more difficult to identify with imaging. Imaging is also used to evaluate vascular and ductal anatomy, secondary signs of obstruction, and metastatic disease.

#### RADIOGRAPHY

Conventional radiography has a limited role in the evaluation of bile duct carcinoma. Extrahepatic tumors may produce extrinsic compression of the stomach and/or duodenum on upper gastrointestinal barium studies. Cholangiography allows for evaluation of biliary disease and can be performed via transhepatic or endoscopic approaches. Percutaneous transhepatic cholangiography (PTC) is used for assessment of proximal lesions, whereas endoscopic retrograde cholangiopancreatography (ERCP) permits visualization of distal tumors. "Apple core" strictures may be seen with circumferential CBD lesions.

TABLE 55-1	Tumor, No	Joint Committee on Cancer Staging ode, Metastasis Classification and r Extrahepatic Bile Duct Cancers
	A: STAGING	FOR PERIHILAR BILE DUCT TUMORS
TNM	Definition	Tumor Location
ΤX		Primary tumor cannot be assessed
TO		No evidence of primary tumor
Tis		Carcinoma in situ
T1		Tumor confined to the bile duct, with extension up to the muscle layer or fibrous tissue
T2a		Tumor invades beyond wall of the bile duct to surrounding adipose tissue
T2b		Tumor invades adjacent hepatic parenchyma
Т3		Tumor invades unilateral branches of the portal vein or hepatic artery
Τ4		Tumor invades main portal vein or its branches bilaterally; or the common hepatic artery; or the second-order biliary radicals bilaterally; or unilateral second-order biliary radicals with contralateral portal vein or hepatic artery involvement
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Regional lymph node metastasis (including nodes along the cystic duct, common bile duct, hepatic artery, and portal vein)
N2		Metastasis to periaortic, pericaval, superior mesentery artery, and/or celiac artery lymph nodes
MO		No distant metastasis
M1		Distant metastasis

From Edge SB, Byrd DR, Compton CC, et al: American Joint Committee on Cancer (AJCC) Cancer Staging Manual, ed 7, New York, 2010, Springer, pp 223, 231.

TNM, Tumor, node, metastasis.

TABLE 55-2	Bismuth Classification for Tumors of the Hepatic Duct Bifurcation	
Туре	Involvement	
1	Common hepatic duct	
П	Bifurcation without secondary intrahepatic ducts	
IIIA	Right secondary intrahepatic duct	
IIIB	Left secondary intrahepatic duct	
IV	Bilateral secondary intrahepatic ducts	
V	Junction of common bile duct and cystic duct	

In ampullary tumors, dilation of the common bile and pancreatic ducts creates a "double duct" sign (Figure 55-3; see also Figure 55-8).<sup>9,10</sup>

### COMPUTED TOMOGRAPHY

CT is most useful for nodular mass-like tumors, whereas diffuse sclerosing tumors are more difficult to visualize. Nodular

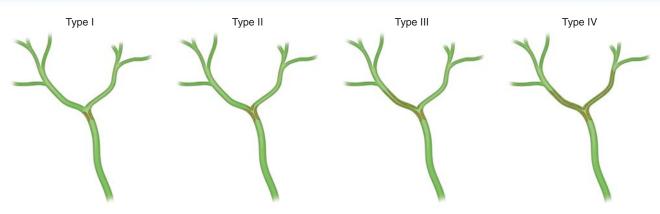
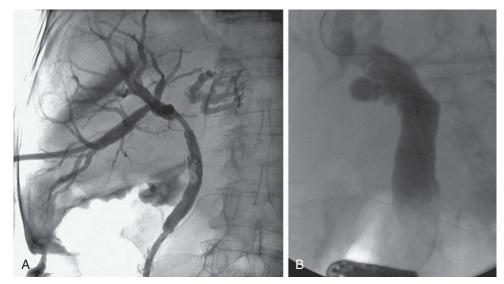


Figure 55-2 Bismuth classification for tumors of the hepatic duct bifurcation.



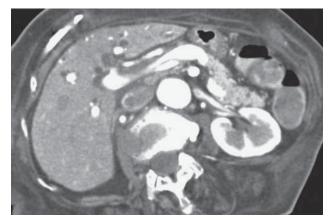
**Figure 55-3 A**, Endoscopic retrograde cholangiography (ERCP) demonstrates high-grade strictures of the inferior left hepatic and superior common bile ducts, consistent with multifocal cholangiocarcinoma. Circumferential luminal narrowing is suggestive of infiltrative variant. **B**, Coneddown ERCP image in a different patient demonstrates nodular filling defects in the superior common bile duct, consistent with intraluminal polypoid cholangiocarcinoma.

tumors manifest as lobulated, hypoattenuating masses with variable enhancement. Infiltrating tumors grow along the bile ducts and may have high attenuation.

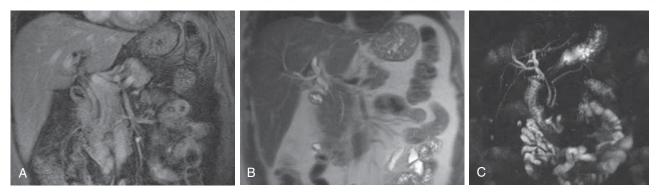
Secondary signs of obstruction are often present, including upstream biliary dilatation, ductal collapse distal to the tumor, and lobar or segmental atrophy. A contracted gallbladder is seen in proximal tumors, whereas a dilated gallbladder suggests a more distal lesion. Vascular involvement and intra-abdominal lymphadenopathy also can be evaluated. CT angiography (CTA) is useful for assessment of the mesenteric vasculature (Figure 55-4).<sup>10-16</sup>

#### MAGNETIC RESONANCE IMAGING

MRI evaluates periductal and hilar tumors more accurately than CT. Tumors appear isointense to hypointense on T1-weighted images. Delayed gadolinium enhancement can be seen but is a nonspecific sign. Lesions are often hyperintense on T2-weighted imaging, with central hypointensity reflective of fibrosis (Figures 55-5 and 55-6). MR angiography (MRA)



**Figure 55-4** On computed tomography, intraluminal polypoid cholangiocarcinoma is present within the superior common bile duct. The lesion appears hypodense as a result of the early phase of contrast imaging. Intrahepatic biliary dilatation is secondary to obstruction. Additional metastases are seen within the liver, portal vein, and inferior vena cava.



**Figure 55-5** On magnetic resonance, coronal T1-weighted fat saturation (A), T2-weighted fat saturation (B), and magnetic resonance cholangiopancreatography maximum intensity projection images (C), show an enhancing, T2 hypointense, extrahepatic mass circumferentially involving the mid to inferior common duct with invasion of the surrounding pancreatic head and duodenum.

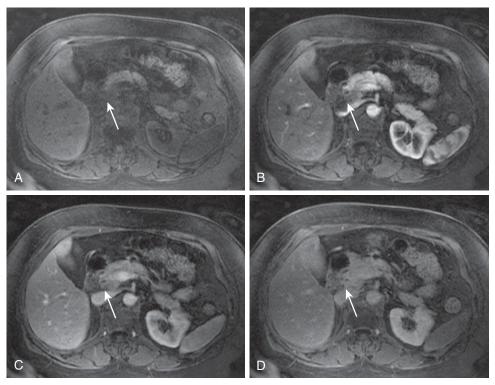


Figure 55-6 In the same patient as in Figure 55-5, transaxial magnetic resonance imaging shows proximal intrahepatic and extrahepatic duct dilatation. T1-weighted, fat-saturation, precontrast (A), arterial phase (B), portal venous phase (C), and 5-minute delay images (D), of the extrahepatic cholangiocarcinoma mass (arrow) shows progressive enhancement on delayed images.

effectively demonstrates the mesenteric circulation. MR cholangiopancreatography (MRCP) is useful in the detection of ductal strictures. Benign ductal thickening appears circumferential and smooth, whereas malignant lesions tend to be eccentric and nodular (Figure 55-7).<sup>10-16</sup>

## ULTRASONOGRAPHY

Transabdominal ultrasonography demonstrates nodular tumors more readily than diffuse sclerosing tumors. Tumor masses can have a variety of appearances, but are most commonly hyperechoic. Secondary signs of obstruction, such as intrahepatic biliary dilatation, extrahepatic ductal collapse, and lobar or segmental atrophy, can be demonstrated. Doppler imaging may demonstrate vascular encasement or thrombosis. In Klatskin's tumors, segmental dilatation and nonunion of the right and left hepatic ducts are observed. Visualization of distal tumors is difficult, owing to overlying bowel gas and subcutaneous fat (Figure 55-8).

Endoscopic ultrasonography (EUS) and intraductal ultrasonography (IDUS) can provide more accurate local assessment than the transabdominal approach. However, both are invasive techniques with limited fields of view.<sup>10-16</sup>

#### NUCLEAR MEDICINE

Cholangiocarcinoma cells have receptors for somatostatin, which inhibit tumor growth. Radionuclide scanning with octreotide, a somatostatin analog, is able to detect most cholangiocarcinomas. Uptake also may be observed with gallium scans. Cholescintigraphy using technetium-99m (<sup>99m</sup>Tc)-diisopropyl iminodiacetic acid (HIDA) scan can reveal sites of biliary obstruction.<sup>10-16</sup>

### POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

Positron emission tomography (PET)/CT may be helpful in evaluating cholangiocarcinoma superimposed on other biliary



**Figure 55-7** Magnetic resonance cholangiopancreatography is useful in the detection of extrahepatic bile duct strictures.

conditions. It demonstrates focal increased uptake of 18F-fluorodeoxyglucose (FDG), with a standardized uptake value that is relatively higher for malignant versus benign lesions (standardized uptake value > 3.6 vs. 2.5). Whole-body scans are valuable for identifying distant metastases.

## IMAGING ALGORITHM

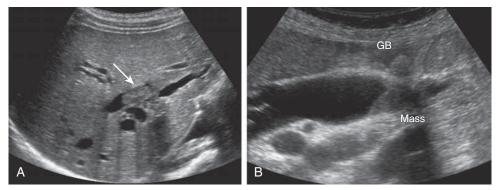
Transabdominal ultrasonography is the first-line imaging examination in patients with jaundice or right upper quadrant pain (Table 55-3). Ultrasonography visualizes most intrahepatic tumors, whereas CT and MRI are used to characterize extrahepatic lesions. PTC, ERCP, or MRCP may be required to identify diffuse sclerosing tumors throughout the bile ducts. DSA, CTA, and MRA demonstrate the relationship of tumors to the surrounding vasculature. PET/CT and PET/MR also can aid in detecting cholangiocarcinoma metastases.

#### **Classic Signs**

- Apple core strictures on ERCP and MRCP
- Double duct sign on CT, MR, ERCP, and MRCP (Figure 55-9)

# **Differential Diagnosis**

Clinical symptoms of cholangiocarcinoma overlap with many other hepatobiliary syndromes. The differential diagnosis includes other biliary diseases such as primary sclerosing cholangitis and choledocholithiasis, gallbladder neoplasms, liver disorders such as primary cancer or metastases, and pancreatic diseases such as abscesses and neoplasms. The location of

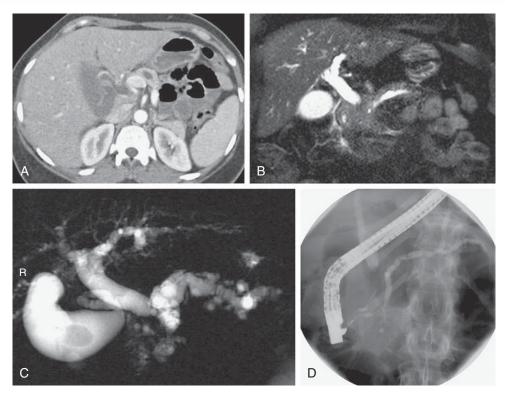


**Figure 55-8** A and B, On ultrasonography, tumor masses are generally hyperechoic but may also appear hypoechoic or heterogeneous (*arrow*). Nodular and proximal tumors are visualized more readily than infiltrating and distal tumors. *GB*, Gallbladder.

# TABLE 55-3 Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Extrahepatic Bile Duct Tumors

Modality	Accuracy	Limitations	Pitfalls
Radiography	Limited	Low sensitivity	Other hepatobiliary diseases
CT	Good	Diffuse and intraluminal tumors	Benign lesions
MRI	Excellent	Distant metastases	Benign lesions, ductal thickening
Ultrasonography	Fair	Low spatial resolution, small field of view, operator dependent	Benign tumors, cholangitis
Nuclear medicine	Poor	Nonspecific, low spatial resolution	Benign disease, trauma, abscesses, choledocholithiasis
PET/CT	Good	Limited tumor detection, misregistration	Inflammation, metabolic disturbances

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission control.



**Figure 55-9** In ampullary tumors, dilation of the common bile and pancreatic ducts creates a "double duct" sign on computed tomography (A), magnetic resonance imaging (B), magnetic resonance cholangiopancreatography (C), and endoscopic retrograde cholangiopancreatography (D). (Courtesy Christine Menias, Mayo Institute, Scottsdale, AZ.)

malignant biliary stricture can offer a differential diagnosis (Table 55-4).

Laboratory tests such as CA 19-9 and CEA are nonspecific indicators of malignancy. Abnormalities in blood counts are nonspecific, but may be seen in biliary tumors. Elevated liver function tests are reflective of an obstructive biliary process. In extrahepatic cholestasis, the alkaline phosphatase level is generally greater than three times the upper limit of normal but alanine and aspartate transaminase values are not increased.

On ultrasonography, CT, and MRI, benign tumors and strictures can have an appearance similar to that of cholangiocarcinoma. In particular, primary sclerosing cholangitis causing alternating stenosis and dilatation in extrahepatic bile ducts and can mimic extrahepatic biliary neoplasm. Benign strictures have a gradual, tapered morphology, as opposed to the abrupt narrowing characteristic of malignant processes. There are no predominant masses, although irregular thickening of ductal walls may be present. In contrast, extrahepatic cholangiocarcinoma originates as a tumor mass involving the common hepatic or bile duct. The resulting outflow obstruction produces diffuse intrahepatic and proximal extrahepatic ductal dilation, without the skip lesions seen in primary sclerosing cholangitis. In addition, the region of the common duct distal to the obstructing lesion is spared. Metastases may spread to lymph nodes and extrabiliary organs. Cholangiocarcinoma can arise in areas affected by primary sclerosing cholangitis, and malignant transformation should be suspected if there is evidence of a soft tissue mass with rapid growth, vascularity, or necrosis; encasement, invasion, or obstruction of vessels and bile ducts;

# TABLEDifferential Diagnosis of Malignant55-4Biliary Strictures

Location	Differential Diagnosis	
Proximal duct	Klatskin's tumor	
Mid duct	Gallbladder tumor	
Distal common duct	Pancreatic tumor or ampullary tumor	

lymphadenopathy; and/or distant metastases. Vascular and parenchymal involvement by a tumor may produce heterogeneous patterns of organ enhancement on CT and MRI.

Any source of bile duct obstruction can yield an abnormal HIDA scan. With PET/CT, inflammatory lesions and metastases can demonstrate increased FDG uptake indistinguishable from primary cholangiocarcinoma.<sup>17,18</sup>

# Treatment

#### MEDICAL TREATMENT

Nonsurgical procedures should be reserved for patients at high operative risk or with unresectable tumors.

As described in the intrahepatic biliary tumor section, interventional biliary procedures are used to provide palliative care for obstructive symptoms. Strategies to relieve biliary obstruction include internal-external drains, internal endoprostheses, metallic stents, balloon dilatation, and sphincterotomy via an endoscopic or percutaneous approach.

Radiation therapy can be delivered via intracavitary brachytherapy, external-beam irradiation, radioimmunotherapy, or charged particle irradiation. Chemotherapy also may be administered by systemic administration, transarterial chemoembolization, or percutaneous injection. Photodynamic therapy, which uses laser-activated photosensitizing agents, is frequently effective. Hormone therapies, including somatostatin analogs, cholecystokinin, and cholecystokinin antagonists, are currently being investigated. Chemical sympathectomy with alcohol or sclerosing agents is used to relieve pain.<sup>4-7,19,20</sup>

## SURGICAL TREATMENT

Surgical resection is the best treatment for cholangiocarcinoma, improving both prognosis and survival. In patients who cannot be resected, liver transplant also can offer a curative treatment. Resection rate is approximately 60% for extrahepatic and 40% for hilar tumors. Diffuse carcinomatosis, metastases, and organ/ vascular invasion are operative contraindications.

Extrahepatic tumors are managed with bile duct resection and reanastomosis. A Roux-en-Y hepaticojejunostomy is performed for mid-ductal tumors, whereas distal tumors are treated via Whipple's resection or pylorus-preserving pancreaticoduodenectomy.

Klatskin's tumors are treated with local or lobar liver excision. For larger tumors, extended right/left hepatectomy or central liver resection may be necessary. The remaining liver parenchyma must contain a functional portal vein, hepatic artery, and bile duct. However, recurrence after resection is common, and even benign tumors may undergo malignant transformation.

In patients who are found to have unresectable disease or metastases at surgical exploration, prophylactic or palliative surgical bypass should be performed. Options include bile duct stenting, biliary anastomosis, and gallbladder grafts.<sup>4-7,20-25</sup>

#### What the Referring Physician Needs to Know

- Clinical signs and symptoms of cholangiocarcinoma are nonspecific, so a high index of suspicion is necessary.
- Imaging enables sensitive detection and accurate characterization of cholangiocarcinoma, facilitating early diagnosis and intervention.
- Various radiologic modalities can be used for the preoperative surgical planning and postoperative monitoring of biliary disease.

## **Key Points**

- Cholangiocarcinoma is associated with congenital hepatic fibrosis or cysts, parasitic infestation, hepatobiliary inflammation and lithiasis, inflammatory bowel disease, chronic pancreatitis, metabolic and inherited diseases, occupational exposures, and certain toxins and medications.
- Clinical signs and symptoms of cholangiocarcinoma are nonspecific and can be seen any obstructive biliary process.
- Extrahepatic cholangiocarcinoma may manifest as a nodular mass or diffuse sclerosing tumor. Biliary dilatation or collapse and liver atrophy may be seen.
- The location of a malignant biliary stricture can offer a differential diagnosis.
- Ultrasonography, CT, and MRI are the preferred imaging modalities for nodular cholangiocarcinomas.
   Ultrasonography identifies intrahepatic tumors, whereas CT and MRI are used to characterize extrahepatic lesions.
- Invasive and MR cholangiography are used to identify diffuse sclerosing tumors throughout the bile ducts.
- Whole-body PET/CT evaluates cholangiocarcinoma identify distant metastases.
- Surgery is the definitive treatment for cholangiocarcinoma but is contraindicated in advanced disease. The success of surgical therapy depends on tumor location and extent, with extrahepatic tumors having a better prognosis.

#### SUGGESTED READINGS

- Han JK, Choi BI, Kim AY, et al: Cholangiocarcinoma: pictorial essay of CT and cholangiographic findings. *Radiographics* 22:173–187, 2002.
- Khan SA, Thomas HC, Davidson BR, et al: Cholangiocarcinoma. *Lancet* 366:1303–1314, 2005.
- Lee WJ, Lim HK, Jang KM, et al: Radiologic spectrum of cholangiocarcinoma: emphasis on unusual manifestations and differential diagnoses. *Radiographics* 21:S97–S116, 2001.
- Levy AD, Murakata LA, Abbott RM, et al: From the archives of the AFIP. Benign tumors and tumorlike lesions of the gallbladder and extrahepatic
- bile ducts: radiologic-pathologic correlation. Armed Forces Institute of Pathology. *Radiographics* 22:387–413, 2002.
- Lim JH, Lee WJ, Takehara Y, et al: Imaging of extrahepatic cholangiocarcinoma. *Abdom Imaging* 29:565–571, 2004.
- Oikarinen H: Diagnostic imaging of carcinomas of the gallbladder and the bile ducts. *Acta Radiol* 47:345–358, 2006.
- Singh P, Patel T: Advances in the diagnosis, evaluation and management of cholangiocarcinoma. *Curr Opin Gastroenterol* 22:294–299, 2006.
- Slattery JM, Sahani DV: What is the current state-ofthe-art imaging for detection and staging of cholangiocarcinoma? Oncologist 11:913–922, 2006.
- Stroszczynski C, Hunerbein M: Malignant biliary obstruction: value of imaging findings. Abdom Imaging 30:314–323, 2005.
- Zech CJ, Schoenberg SO, Reiser M, et al: Crosssectional imaging of biliary tumors: current clinical status and future developments. *Eur Radiol* 14:1174–1187, 2004.

#### REFERENCES

- Hassid VJ, Orlando FA, Awad ZT, et al: Genetic and molecular abnormalities in cholangiocarcinogenesis. *Anticancer Res* 29:1151–1156, 2009.
- Shin HR, Oh JK, Masuyer E, et al: Epidemiology of cholangiocarcinoma: an update focusing on risk factors. *Cancer Sci* 101:579–585, 2010.
- Gatto M, Bragazzi MC, Semeraro R, et al: Cholangiocarcinoma: update and future perspectives. *Dig Liver Dis* 42:253–260, 2010.
- Aljiffry M, Walsh MJ, Molinari M: Advances in diagnosis, treatment and palliation of cholangiocarcinoma: 1990-2009. World J Gastroenterol 15:4240–4262, 2009.
- Singh P, Patel T: Advances in the diagnosis, evaluation and management of cholangiocarcinoma. *Curr Opin Gastroenterol* 22:294–299, 2006.
- Sandhu DS, Roberts LR: Diagnosis and management of cholangiocarcinoma. *Curr Gastroenterol Rep* 10:43–52, 2008.
- Blechacz B, Gores GJ: Cholangiocarcinoma: advances in pathogenesis, diagnosis, and treatment. *Hepatology* 48:308–321, 2008.
- Chung YE, Kim MJ, Park YN, et al: Staging of extrahepatic cholangiocarcinoma. *Eur Radiol* 18:2182–2195, 2008.
- Chung YE, Kim MJ, Park YN, et al: Varying appearances of cholangiocarcinoma: radiologicpathologic correlation. *Radiographics* 29:683– 700, 2009.

- Lim JH, Lee WJ, Takehara Y, et al: Imaging of extrahepatic cholangiocarcinoma. *Abdom Imaging* 29:565–571, 2004.
- Choi JY, Kim MJ, Lee JM, et al: Hilar cholangiocarcinoma: role of preoperative imaging with sonography, MDCT, MRI, and direct cholangiography. *AJR Am J Roentgenol* 191:1448–1457, 2008
- Han JK, Choi BI, Kim AY, et al: Cholangiocarcinoma: pictorial essay of CT and cholangiographic findings. *Radiographics* 22:173–187, 2002.
- Sainani NI, Catalano OA, Holalkere NS, et al: Cholangiocarcinoma: current and novel imaging techniques. *Radiographics* 28:1263–1287, 2008.
- Zech CJ, Schoenberg SO, Reiser M, et al: Crosssectional imaging of biliary tumors: current clinical status and future developments. *Eur Radiol* 14:1174–1187, 2004.
- Gakhal MS, Gheyi VK, Brock RE, et al: Multimodality imaging of biliary malignancies. Surg Oncol Clin N Am 18:225–239, 2009.
- Miller G, Schwartz LH, D'Angelica M: The use of imaging in the diagnosis and staging of hepatobiliary malignancies. *Surg Oncol Clin N Am* 16:343–368, 2007.
- Menias CO, Surabhi VR, Prasad SR, et al: Mimics of cholangiocarcinoma: spectrum of disease. *Radiographics* 28:1115–1129, 2008.

- Lee WJ, Lim HK, Jang KM, et al: Radiologic spectrum of cholangiocarcinoma: emphasis on unusual manifestations and differential diagnoses. *Radiographics* 21:S97–S116, 2001.
- Hopfner M, Schuppan D, Scherubl H: Targeted medical therapy of biliary tract cancer: recent advances and future perspectives. *World J Gastroenterol* 14:7021–7032, 2008.
- Shimoda M, Kubota K: Multi-disciplinary treatment for cholangiocellular carcinoma. World J Gastroenterol 13:1500–1504, 2007.
- Boutros C, Somasundar P, Espt NJ: Extrahepatic cholangiocarcinoma: current surgical strategy. Surg Oncol Clin N Am 18:269–288, 2009.
- Ito F, Cho CS, Rikkers LF, et al: Hilar cholangiocarcinoma: current management. *Ann Surg* 250:210–218, 2009.
- Patel T, Singh P: Cholangiocarcinoma: emerging approaches to a challenging cancer. Curr Opin Gastroenterol 23:317–323, 2007.
- Aljiffry M, Abdulelah A, Walsh M, et al: Evidence-based approach to cholangiocarcinoma: a systematic review of the current literature. J Am Coll Surg 208:134–147, 2009.
- Schwartz JJ, Hutson WR, Gayowski TJ, et al: Liver transplantation for cholangiocarcinoma. *Transplantation* 88:295–298, 2009.

# **Diffuse Gallbladder Wall Thickening**

AVINASH KAMBADAKONE | DUSHYANT V. SAHANI

Diffuse gallbladder wall thickening is commonly encountered in diagnostic settings. The ability of ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) to directly visualize the thickened gallbladder wall ascertains the importance of this condition.<sup>1</sup> Ultrasound is the initial imaging technique for evaluation of suspected gallbladder disease.<sup>1</sup> CT plays the role of a problem-solving tool in inconclusive ultrasound examinations, in staging of diseases, and as the initial modality in cases of acute abdomen.<sup>1</sup> MRI is emerging as a modality of choice in the evaluation of pain, jaundice, and gallbladder masses.<sup>2,3</sup> The current widespread use of abdominal CT and MRI has resulted in the detection of causes of gallbladder wall thickening.<sup>4</sup>

Diffuse gallbladder wall thickening is a nonspecific finding.<sup>1</sup> It is the most common finding in either acute calculus or acalculus cholecystitis. Although a thickened gallbladder wall is considered a hallmark feature of acute cholecystitis, it can be encountered in a wide variety of disease processes such as gallbladder cancer and extracholecystic benign conditions such as hepatitis, heart failure, hypoalbuminemia, and acute severe pyelonephritis. It can be found in both symptomatic and asymptomatic patients.<sup>1</sup>

# Normal Gallbladder Wall

The normal gallbladder wall is composed of four layers: the mucosa, lamina propria, an irregular muscle layer, and serosa of loose connective tissue.<sup>5</sup>

On ultrasonography, the normal gallbladder wall appears as a pencil-thin echogenic line.<sup>1</sup> Sonographic depiction of gallbladder wall thickening depends on the degree of gallbladder distention, and pseudo-thickening can occur in the postprandial state.<sup>1</sup> A thickened gallbladder wall measures more than 3 mm and has a layered appearance.

On CT, the normal gallbladder wall is visible as a thin rim of soft tissue density that enhances after injection of a contrast agent. The thickened gallbladder wall on CT frequently contains a hypodense layer of subserosal edema that mimics pericholecystic fluid.

On MRI, the gallbladder wall shows an inner layer of low signal intensity representing mucosal and muscular layers and outer layer of high signal intensity of the serosa on high-resolution T2-weighted images.<sup>2,3,5</sup> However, these layers may not be discernible in the nonthickened normal gallbladder wall on half-Fournier acquisition single-shot turbo spin echo (HASTE) images. The portion of the gallbladder wall adjacent to liver is not identified as a separate structure owing to its lower signal intensity on T2-weighted images.<sup>2</sup> On T1-weighted

images, the wall has intermediate signal intensity and enhances uniformly after the administration of gadolinium-based contrast material.<sup>2</sup> Because of similar enhancement of the gallbladder wall and the liver parenchyma, the portion of the wall adjacent to the liver is not well appreciated.<sup>2</sup>

# **Thickened Gallbladder Wall**

Although its thickness depends on the degree of gallbladder distention, 3 mm is regarded as the upper limit of normal; and mural thickening is defined as a transverse wall measurement of 4 mm or greater.

On CT, the thickened gallbladder wall is of soft tissue density.<sup>4</sup> It may manifest as a layered, "sandwich-like" appearance formed by an inner enhancing layer of mucosa and an outer enhancing layer of serosa with an intervening hypodense layer made up of subserosal edema, or it may have a halo of low-attenuation subserosal edema surrounding the enhancing mucosa.<sup>4</sup> Occasionally, the enhanced mucosa of the thickened gallbladder wall surrounded by pericholecystic fluid.<sup>4</sup> The differentiation of the halo of edema from pericholecystic fluid is possible on CT by demonstrating small enhancing punctate structures within the edematous wall.<sup>4</sup> The focal pericholecystic fluid also can be differentiated from the diffusely thickened gallbladder wall. Ultrasonography may be required at times to exclude these simulations.<sup>4</sup>

On MRI, four different patterns of gallbladder wall thickening have been described based on the definition of the gallbladder layers.<sup>5</sup>

- *Type 1* refers to a well-demarcated two-layered appearance with an inner layer showing thin uniform and low signal intensity and an outer layer demonstrating thick high signal intensity.
- *Type 2* refers to an ill-defined two-layered pattern with a broadened or interrupted inner layer and a heterogeneous outer layer showing intermediate signal intensity.
- *Type 3* is characterized by the presence of multiple high signal intensity cystic spaces within a thickened wall; layering may or may not be evident.
- *Type 4* incorporates diffuse nodular wall thickening without layering and with a homogeneous low signal intensity.

A wide variety of conditions can cause diffuse gallbladder wall thickening. Gallbladder wall thickening from conditions intrinsic to the gallbladder are referred to as primary, whereas wall thickening resulting from conditions not related to gallbladder disease are considered secondary (Box 56-1 and Figure 56-1).

#### BOX 56-1 VARIOUS CONDITIONS CAUSING **DIFFUSE GALLBLADDER** WALL THICKENING

## **PRIMARY CAUSES**

- Acute cholecystitis
  - Acute calculus cholecystitis
- Acute acalculus cholecystitis Gangrenous cholecystitis
- Emphysematous cholecystitis
- Chronic cholecystitis
- Adenomyomatosis
- Xanthogranulomatous cholecystitis
- Gallbladder carcinoma

#### SECONDARY CAUSES

- Systemic disease
- Liver dysfunction
- Congestive heart failure
- Renal failure
- Hypoalbuminemic states
- Extracholecystic inflammatory process
  - Acute hepatitis
  - Peritonitis
  - Acute pancreatitis
  - Acute pyelonephritis
- Others Peptic ulcer
- Infectious mononucleosis, typhoid
- Acquired immunodeficiency syndrome cholangiopathy Pregnancy
- Total parenteral nutrition

# Primary Gallbladder Wall Thickening

### ACUTE CHOLECYSTITIS

#### Etiology

Acute Calculus Cholecystitis. Mechanical obstruction of the cystic duct by gallstones (90% of cases) or on rare occasions by helminths (Ascaris, Clonorchis) may occur.<sup>1,4,6</sup> Risk factors include female sex, obesity or rapid weight loss, certain drugs, pregnancy, and increasing age.

Acute Acalculus Cholecystitis. Acute acalculus cholecystitis frequently occurs in those who are critically ill from trauma, sepsis, or burns, presumably because of increased bile viscosity from fasting and taking medication that causes cholestasis.<sup>1,</sup> Other risk factors include vascular disease, systemic vasculitides, human immunodeficiency virus infection, diabetes mellitus, acute renal failure, immunosuppression, prolonged fasting, and total parenteral nutrition.

#### Prevalence and Epidemiology

Acute cholecystitis is defined as acute inflammation of the gallbladder. It is the fourth most common cause of hospital admissions for patients presenting with an acute abdomen. Acute acalculus cholecystitis accounts for 2% to 12% of cholecystitis.<sup>1,4,6</sup>

#### **Clinical Presentation**

Acute Calculus Cholecystitis. Acute calculus cholecystitis is right upper quadrant pain increasing in frequency and intensity, radiating to the interscapular area or shoulder, and increasing with deep inspiration. The pain is often accompanied by nausea, vomiting, and loss of appetite. Fever with chills and rigor also occur.<sup>1</sup>

On physical examination, right upper quadrant tenderness and guarding are noted. Murphy's sign is the characteristic physical finding in these patients and is considered highly sensitive (97%) and predictive (93%) of calculus cholecystitis. Murphy's sign refers to pain elicited by palpation in the right upper quadrant during mid-inspiration.

Acute Acalculus Cholecystitis. Acute acalculus cholecystitis mostly affects patients with prolonged fasting or protracted immobility and those experiencing hemodynamic instability.4,

Pyrexia may be the only symptom, and up to 75% of patients may have no symptoms referable to the right upper quadrant. This disorder can occur as a manifestation of acquired immunodeficiency syndrome (AIDS) cholangiopathy, usually caused by pathogens such as Cryptosporidium followed by microsporidia such as Enterocytozoon bieneusi.

## Pathophysiology

Acute Calculus Cholecystitis. The initial event in acute calculus cholecystitis is obstruction of the cystic duct by a gallstone. The trapped concentrated bile has an irritant effect on the gallbladder wall, in turn causing increased secretions. This leads to a series of events resulting in increased intraluminal pressure, gallbladder distention, and wall edema that progress to cause venous and lymphatic obstruction, ischemia, and necrosis. Bacterial colonization, perforation, and abscess formation soon ensue. The bile is sterile in early stages, and infection occurs as a secondary event. Bile cultures are positive in only 20% to 75% of patients, and the organisms most commonly cultured are enteric bacteria, including Escherichia coli, Klebsiella, and Enterococcus.<sup>1</sup>

If untreated, acute cholecystitis is complicated by hemorrhage, necrosis, empyema, and perforation.<sup>6</sup> The complications include gangrenous cholecystitis, which complicates 2% to 38% of patients with acute cholecystitis and has increased incidence of perforation and resultant peritonitis. Perforation of the gallbladder wall is present in 3% to 10% of patients. Emphysematous cholecystitis is a rare complication most commonly seen in elderly diabetic men secondary to infection of the gallbladder wall with gas-forming organisms such as Clostridium welchii and Escherichia coli.

Acute Acalculus Cholecysitis. The pathogenesis of acute acalculus cholecystitis is multifactorial, with gallbladder stasis, paresis, and ischemia considered to play a role. The concentrated and stagnant bile along with reduced gallbladder perfusion leads to chemical and ischemic injury of the gallbladder epithelium, resulting in cholecystitis. Cholecystectomy specimens demonstrate impaired gallbladder microcirculation, possibly resulting from splanchnic vasoconstriction and intravascular coagulation. Infection is a secondary event complicating the ischemic injury.<sup>1,4,</sup>

#### Imaging

The combination of prolonged, constant right upper quadrant pain and tenderness with fever is highly suggestive of acute cholecystitis. Leukocytosis, increased neutrophils, and band

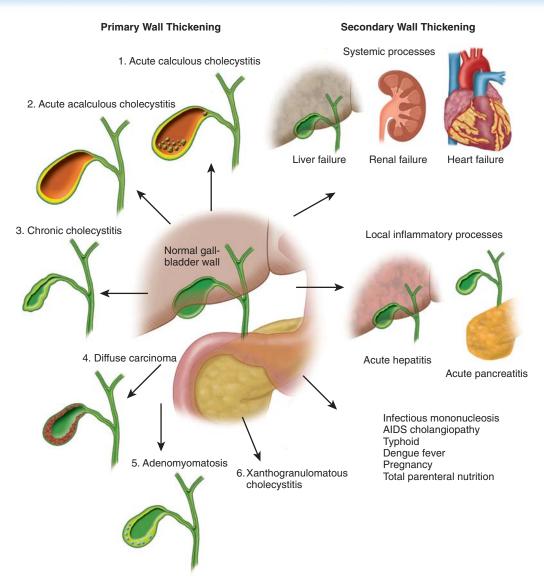


Figure 56-1 The various causes of diffuse gallbladder wall thickening. AIDS, Acquired immunodeficiency syndrome.

forms are usually present. Occasional elevated levels of liver transaminases or bilirubin can occur.

**Radiography.** The role of conventional radiography in the evaluation of acute cholecystitis is limited (Table 56-1). Gall-stones may be visualized occasionally. In patients with emphysematous cholecystitis, intraluminal or intramural air within the gallbladder may be seen.<sup>10</sup> Staging of emphysematous cholecystitis on conventional radiography is as follows<sup>10</sup>:

- Stage 1: Gas within the gallbladder lumen
- *Stage 2:* Gas within the gallbladder wall
- Stage 3: Gas within the pericholecystic tissues

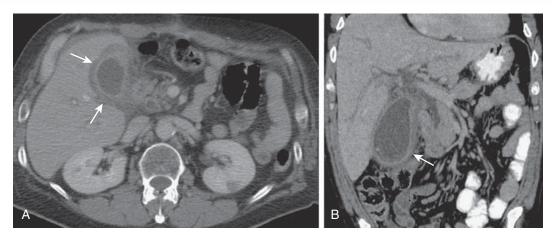
**Computed Tomography.** CT is used for the evaluation of patients with acute right upper quadrant complaints with inconclusive ultrasound findings or with a perplexing clinical presentation when acute cholecystitis is not the first diagnostic choice.

*Acute Calculus Cholecystitis.* The most common CT finding in acute cholecystitis is gallbladder wall thickening and gallstones and is noted in 75% of cases (Figure 56-2). Indistinct interface of the gallbladder wall and the juxtaposed liver is regarded as highly suggestive of acute cholecystitis.<sup>1,4,6-9,11-15</sup>

Pericholecystic stranding, which represents inflammatory changes within the fat surrounding the gallbladder, is another CT feature. Extensive changes may cause reactive mural thickening and edema in the adjacent colon or duodenum (see Figure 56-2).<sup>1,4,6-9,11-15</sup>

Transient focal hyperattenuation in the hepatic parenchyma adjacent to the inflamed gallbladder is probably related to hepatic arterial hyperemia. The thick gallbladder wall may mimic pericholecystic fluid, particularly if the gallbladder lies oblique to the axial plane of imaging.

Major criteria for acute calculus cholecystitis include calculi, thickened wall, pericholecystic fluid, and subserosal edema. Minor criteria are gallbladder distention and gallbladder sludge.



**Figure 56-2** Acute calculus cholecystitis. Axial (A) and coronal (B) contrast-enhanced computed tomography images in a febrile 45-year-old woman with right upper quadrant abdominal pain show diffuse wall thickening and enhancement with marked distention of the gallbladder (*arrows*, A). Associated pericholecystic stranding is also seen with mild wall thickening of the adjacent transverse colon on the coronal image (*arrow*).

TABLE 56-1	Accuracy,	Limitations, and Pitfalls of th	ne Modalities Used in Imaging of Acute Cho	olecystitis
Modal	ity	Accuracy	Limitations	Pitfalls
Radiog	Iraphy	Data not available to specify accuracy	Insensitive Nonspecific	Unable to directly visualize the soft tissues of gallbladder
СТ		Accuracy: 94%	Radiation exposure Not ideal in pregnant patients Murphy's sign cannot be elicited as in ultrasonography.	CT misses 20% of gallstones because they have the same density as bile
MRI		Sensitivity: 95%	Not preferred in critically ill patients	
Ultraso	nography	Sensitivity: 48%-100% Specificity: 64%-100%	Inability to image cystic duct Decreased sensitivity for choledocholithiasis Air within gallbladder may be mistaken for calcifications	Gallbladder sludge in acute calculus cholecystitis may mimic gallbladder carcinoma
Nuclea	r medicine	Accuracy: 92% Gold standard for diagnosis of acute cholecystitis	Reduced specificity in the presence of hepatic impairment, parenteral nutrition, or patient fasting Does not give information about nonobstructing cholelithiasis and cannot detect other pathology	False-negative and false-positive results
PET/C	Г	Data not available to specify accuracy	Decreased sensitivity in patients with diabetes	Differentiation from gallbladder cancer not always possible

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

The presence of one major and two minor criteria helps to make the diagnosis.

Acute Acalculus Cholecystitis. Major CT criteria include gallbladder mural thickening ( $\geq 4$  mm), pericholecystic fluid, subserosal edema in the absence of ascites, intramural gas, or sloughed mucosa. Minor criteria are a distended gallbladder and hyperdense bile.<sup>9</sup> Presence of two major criteria or one major and two minor criteria suggests the diagnosis.

*Gangrenous Cholecystitis.* Lack of mural enhancement, a greater degree of gallbladder distention, and wall thickening are features of gangrenous cholecystitis (Figure 56-3). Discontinuous and/or irregular mucosal enhancement has been described. Pericholecystic abscess is another specific sign of mural necrosis indicating gangrenous cholecystitis, a severe form of acute cholecystitis.

A hyperdense gallbladder wall on unenhanced CT has been reported as a sign of acute gangrenous cholecystitis. Because mucosa is prone to ischemia, mucosal necrosis and hemorrhage result in high density that is detectable on CT. Other additional features include the presence of intraluminal membranes and an irregular wall.

*Emphysematous Cholecystitis.* The presence of gas in the gallbladder wall represents another variant of acute cholecystitis known as *emphysematous cholecystitis* (Figure 56-4). Gas also may appear within the gallbladder lumen and pericholecystic tissue. CT has a critical role in detecting the gas because it mimics calcifications or cholesterol deposits on ultrasonography. CT is the most sensitive and specific imaging modality for identifying gas within the gallbladder lumen or wall. The presence of pneumoperitoneum indicates perforation, which requires emergent surgical intervention.

**Magnetic Resonance Imaging.** Sensitivity of MRI for the diagnosis and differentiation of acute cholecystitis is 95%. The common MRI features include wall thickening ( $\geq$ 4 mm) and distended gallbladder (long axis dimension >8 cm and short axis dimension >4 cm) (Figure 56-5). The type 2 layered pattern of wall thickening is seen. Other features include wall

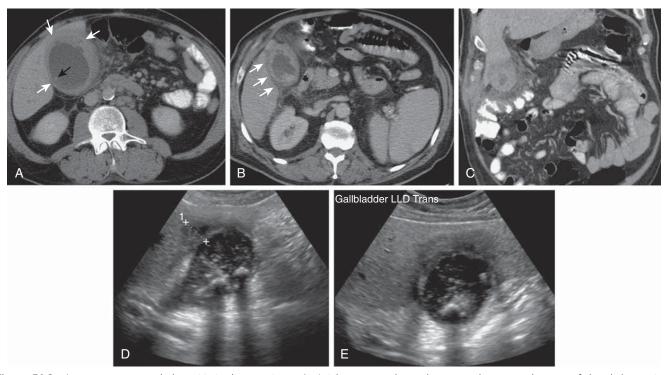
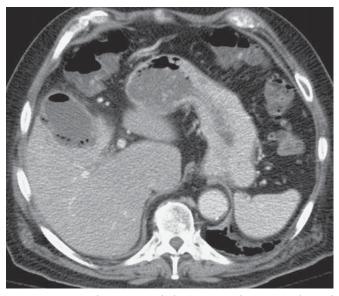


Figure 56-3 Acute gangrenous cholecystitis in three patients. A, Axial contrast-enhanced computed tomography scan of the abdomen in a 74-year-old man shows marked distention of the gallbladder with asymmetric wall thickening and areas of absent mural enhancement (*thin white arrow*). Small irregular nonenhancing foci are noted within the thickened wall, suggesting necrosis (*shorter white arrows*). A slender intraluminal membrane is also seen (*black arrow*). B, Axial contrast-enhanced computed tomography scan in a 56-year-old woman shows marked irregularity of the gallbladder wall with irregular mural enhancement and break in the mucosal lining (*arrows*). C, Coronal reformatted image from the same patients shows marked pericholecystic fat stranding and thickening of the adjacent colonic wall at the hepatic flexure. Also seen is the thickening and loss of definition of the adjacent lateral abdominal wall muscles. Transverse (D) and sagittal (E) ultrasonograms obtained in a 63-year-old woman show irregular gallbladder wall thickening (*within calipers*, D) with intraluminal sludge, membranes, and gallstones.



**Figure 56-4** Emphysematous cholecystitis. Axial contrast-enhanced CT scan of the abdomen in a 48-year-old patient with diabetes shows multiple pockets of intramural gas and an intraluminal air/fluid level. Mild pericholecystic fat stranding is seen.

irregularity or defect and intraluminal membranes that are irregular or have intraluminal linear soft tissue signal intensities. On gadolinium administration there is gallbladder wall enhancement with increased transient pericholecystic hepatic enhancement that is best seen during the hepatic arterial dominant phase. Mural striation representing a layered pattern of gallbladder wall with different alternating signal intensities sometimes can be seen. Increased transient pericholecystic hepatic enhancement is highly specific and helps in differentiation from chronic cholecystitis.<sup>1-3,5,16</sup>

Pericholecystic fat signal intensity changes are seen as decreased signal intensity on T1-weighted images and as increased signal on T2-weighted images. Pericholecystic fluid is seen as a high signal intensity collection on T2-weighted images.

Gas in the wall or lumen is seen as signal void gas bubbles in the gallbladder wall or lumen on T1-weighted or T2-weighted images. Air/fluid levels sometimes can be seen.

#### Ultrasonography

Acute Calculus Cholecystitis.\* Diffuse gallbladder wall thickening (≥4 mm) and a distended gallbladder (long axis

<sup>\*</sup>References 1, 6, 7, 11, 15, 17.

dimension >8 cm and short axis dimension >4 cm) are seen (Figure 56-6). The presence of gallstones is the most common and sensitive finding, particularly the presence of an obstructing stone at the gallbladder neck or cystic duct.

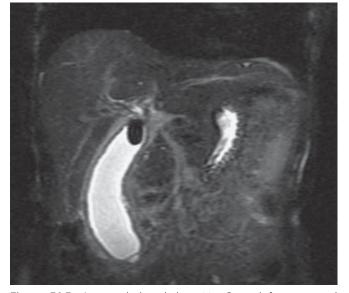
On ultrasonography, a positive Murphy's sign refers to maximal tenderness elicited by pressure over the sonographically located gallbladder during inspiration. Pericholecystic fat inflammation and/or fluid are secondary findings. Hyperemia of the gallbladder wall demonstrated on color and power Doppler imaging improves the accuracy of ultrasound in diagnosing acute cholecystitis.

*Acute Acalculus Cholecystitis.* The imaging features of acalculus cholecystitis are similar to those of acute cholecystitis except for the absence of gallstones and the presence of gallbladder sludge (Figure 56-7).

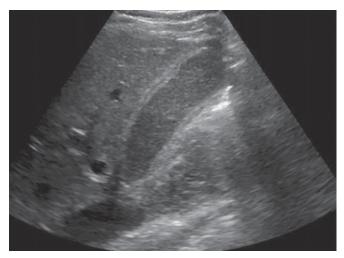
*Gangrenous Cholecystitis.* Gangrenous cholecystitis is characterized by asymmetric gallbladder wall thickening or the presence of intraluminal membranes (see Figure 56-3). Murphy's sign is negative in up to 66% of cases because of denervation of the gallbladder wall.

*Emphysematous Cholecystitis.* Ultrasonography demonstrates highly echogenic reflectors with low-level posterior shadowing and reverberation artifact ("dirty shadowing") emanating from the gallbladder lumen (see Figure 56-6). The "champagne sign" refers to the finding of small, nonshadowing echogenic foci rising up from the dependent portions of the gallbladder lumen, similar to effervescing bubbles in a glass of champagne.<sup>10,11</sup>

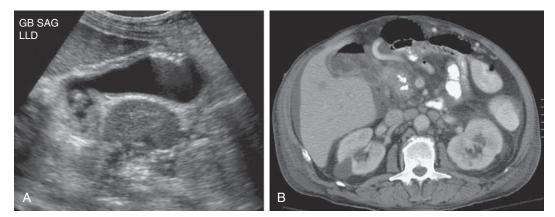
**Nuclear Medicine.** Biliary scintigraphy is the gold standard for diagnosis of acute cholecystitis resulting from cystic duct obstruction. Cholescintigraphy using technetium-99m (<sup>99m</sup>Tc)-diisopropyl iminodiacetic acid, also known as a *hepatobiliary iminodiacetic acid* (HIDA) scan, is 86% to 100% sensitive and



**Figure 56-5** Acute calculus cholecystitis. Coronal fat-suppressed T2-weighted magnetic resonance image in a 47-year-old woman shows distended gallbladder with diffuse wall thickening and a rounded low signal intensity calculus seen lodged at the gallbladder neck.



**Figure 56-7** Acute acalculus cholecystitis. Sagittal ultrasound image in a 45-year-old woman with sepsis shows distended gallbladder filled with echogenic sludge and diffuse wall thickening. No calculus was identified on the scan.



**Figure 56-6** Acute calculus cholecystitis with emphysematous change. A, Sagittal ultrasound image of the abdomen in a 42-year-old man with right upper quadrant pain shows a distended gallbladder with wall thickening and a calculus seen at the gallbladder neck. Multiple tiny echogenic reflectors corresponding to gas bubbles are seen along the antidependent portion of the gallbladder wall with "comet tail" artifact. B, Axial contrast-enhanced computed tomography scan confirmed the presence of gas within the gallbladder. Significant fat stranding and fluid collections are seen in the pericholecystic region. *GB*, Gallbladder; *SAG*, sagittal.

94% to 100% specific for acute cholecystitis with an accuracy of 92%.  $^{6.7,11,14,18}$ 

HIDA scan criteria for acute cholecystitis include persistent nonvisualization of the gallbladder 3 hours after administration of a radiotracer or 30 minutes after morphine sulfate augmentation. Filling of the gallbladder within 60 minutes can occur and is a false-negative finding. False-negative rates are decreased by administering morphine. A false-positive result is nonvisualization of the gallbladder in the absence of obstruction. This can occur in patients who are fasting, are receiving total parenteral nutrition, or have severe liver disease.

The role of HIDA scan in acute acalculus cholecystitis is debatable.

In emphysematous cholecystitis, there is nonvisualization of the gallbladder, along with a region of increased hepatic activity adjacent to the gallbladder fossa ("rim sign").

**Positron Emission Tomography With Computed Tomogra-phy.** On positron emission tomography (PET), acute cholecystitis is seen as a hypermetabolic lesion with a ringlike radiotracer uptake in the gallbladder area.<sup>19</sup>

#### **Classic Signs: Acute Cholecystitis**

- Diffuse gallbladder wall thickening (≥4 mm) with gallstones
- Positive sonographic Murphy's sign
- Pericholecystic fat stranding and fluid collections
- Irregular wall thickening with lack of mural enhancement or discontinuous mucosal enhancement with intraluminal membranes (suggestive of gangrenous cholecystitis)
- Air within the gallbladder wall or lumen
- Champagne sign on ultrasonography for emphysematous cholecystitis
- Persistent nonvisualization of the gallbladder 3 hours after administration of radiotracer on hepatobiliary scintigraphy

## **Differential Diagnosis**

The differential diagnosis includes choledocholithiasis, pancreatitis, peptic ulcer disease, acute hepatitis, liver abscess, liver neoplasm with complications, pneumonia, and heart disease. Sympathetic thickening of the gallbladder wall secondary to an acute inflammatory process in the right upper quadrant, including acute pancreatitis, perforated duodenal ulcer, hepatitis, right-sided diverticulitis, and even acute right-sided pyelonephritis can cause confusion with acute cholecystitis.<sup>7</sup>

#### Treatment

**Medical Treatment.** Medical treatment includes restriction of oral intake, intravenous fluid and electrolyte resuscitation, and parenteral (narcotic) analgesia. Indomethacin and diclofenac have been reported to reduce the rate of progression of acute cholecystitis. Intravenous antibiotic therapy is often administered.

## **Surgical Treatment**

*Acute Calculus Cholecystitis.* Open/laparoscopic cholecystectomy is performed.

*Acute Acalculus Cholecystitis.* Open cholecystectomy is the traditional approach for surgical treatment of acalculus cholecystitis. Percutaneous cholecystostomy is the treatment of

choice in critically ill and elderly patients as both a diagnostic and therapeutic procedure.<sup>1</sup>

## CHRONIC CHOLECYSTITIS

## Etiology

Chronic cholecystitis is often associated with cholelithiasis.<sup>8,20,21</sup> It is a result of chronic irritation of the gallbladder wall by recurrent attacks of cholecystitis secondary to transient obstruction by gallstones.<sup>1,8,20-22</sup>

## Prevalence and Epidemiology

Chronic cholecystitis is the most common form of gallbladder disease and refers to chronic low-grade inflammation of the gallbladder. Women are more often affected than men. The disorder usually occurs in the fifth to sixth decades.<sup>8,20-22</sup>

Long-standing chronic cholecystitis may develop mural calcification and is referred to as a "porcelain" gallbladder. Porcelain gallbladder has a prevalence of 0.06% to 0.8% in cholecystectomy specimens.<sup>8,20,21,23</sup> It is strongly associated with gallbladder cancer, with an incidence ranging from 12% to 61%.<sup>8,20,21,23</sup>

#### Clinical Presentation

Intermittent or constant right upper quadrant pain is the most specific symptom, and the attacks are sudden in onset.<sup>8,20,21,23</sup> The pain is due to progressive increase in tension within the gallbladder wall secondary to obstruction of the cystic duct. The pain is located in the epigastrium and the right upper abdomen and may radiate to the shoulder or the back. The pain lasts for 30 to 60 minutes or occasionally several hours. Episodes can be precipitated by heavy meals or fatty foods. Other nonspecific symptoms include nausea, belching, bloating, flatulence, or a feeling of upper abdominal fullness.<sup>8,20,21,23</sup>

#### Pathophysiology

The characteristic finding of chronic cholecystitis is fibrosis, which leads to a shrunken, contracted gallbladder.<sup>8,20-23</sup> The gallbladder wall mucosa is usually intact.

On histologic examination, mononuclear cell infiltration is seen in the wall with subserosal fibrosis and edema. The term *porcelain gallbladder* is used to describe the bluish discoloration and brittle consistency of the gallbladder wall.<sup>8,20,21,23</sup>

#### Imaging

**Radiography.** Fifteen to twenty percent of gallstones contain enough calcium to be visible on plain radiographs (Table 56-2). A porcelain gallbladder is seen as a round opacity with a rim and internal amorphous calcifications in the region of the gallbladder.<sup>23</sup>

**Computed Tomography.** The CT appearance is a contracted gallbladder with soft tissue density wall thickening and gallstones (Figure 56-8).<sup>24</sup> Differentiation from gallbladder carcinoma is essential. On dynamic CT, the thin inner wall layer will be isoattenuating to the adjacent hepatic parenchyma on arterial and portovenous phases.<sup>24</sup> In gallbladder carcinoma, the inner wall layer is thicker and shows intense enhancement in the arterial phase becoming isoattenuating in the portovenous phase.<sup>24</sup> A porcelain gallbladder is identified by the presence of a thick layer of nonuniform calcifications coating the inner wall of the gallbladder (Figure 56-9).

## E Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Chronic Cholecystitis

56-2					
Modality	Accuracy	Limitations	Pitfalls		
Radiography	Data not available to specify accuracy	Insensitive Nonspecific	Unable to directly visualize the soft tissues of gallbladder		
СТ	Data not available to specify accuracy	Radiation exposure	Gallstones not visualized in 20% of cases		
MRI	Data not available to specify accuracy	Is not accurate for visualization of gallstones			
Ultrasonography	94% <sup>27</sup>	Does not allow reliable differentiation between calcifications (gallstones and porcelain gallbladder) and air within the gallbladder Technical limitations occur in obese patients	Gallbladder sludge may mimic malignancy		
Nuclear medicine	Accuracy: 73%	Reduced specificity in the presence of hepatic impairment or parenteral nutrition or when patient is fasting Does not give information about nonobstructing cholelithiasis and cannot detect other pathologic processes			
PET/CT	Data not available to specify accuracy	Decreased sensitivity in diabetic patients	Differentiation from gallbladder cancer not always possible		

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.



**Figure 56-8** Chronic calculus cholecystitis. Axial contrast-enhanced computed tomography scan in an 86-year-old man with recurrent right upper quadrant pain and dyspeptic symptoms shows a contracted gallbladder with wall thickening and two large gallstones within it.

**Magnetic Resonance Imaging.** The gallbladder appears small and contracted with an irregular and thickened wall. A type 1 layered pattern of gallbladder wall thickening is demonstrated.<sup>5</sup> Gallstones may be present.

After gadolinium administration the wall enhances less intensely than in acute cholecystitis.<sup>16</sup> The wall enhancement is smooth, slow, and prolonged.<sup>16</sup>

The type 1 pattern of gallbladder wall thickening is seen on MRI as two distinct layers, with the inner layer showing thin, uniform, and low signal intensity and the outer layer showing thick, high signal intensity.<sup>5</sup> Other findings include mural striation, increased gallbladder dimension, pericholecystic fluid, and pericholecystic fat signal intensity changes.<sup>16</sup>

**Ultrasonography.** On ultrasonography a thick-walled contracted gallbladder with gallstones may be seen. The gallbladder



**Figure 56-9** Porcelain gallbladder. Axial contrast-enhanced computed tomography scan in a 78-year-old woman shows thick linear calcifications along the gallbladder wall and high density bile within the lumen.

is not distended, and Murphy's sign and hyperemia in the wall are not present.

**Nuclear Medicine.** Hepatobiliary scintigraphy is normal in 28% to 90% of patients with chronic cholecystitis, particularly in asymptomatic patients. In symptomatic patients with chronic cholecystitis there is stasis of concentrated thick bile in the diseased gallbladder, mainly in the cystic duct, which precludes gallbladder visualization.<sup>25</sup> Visualization of bowel activity before gallbladder visualization during the first hour of the study suggests chronic cholecystitis. When used in conjunction with other imaging and clinical findings, the nuclear scintigraphic findings increase the overall accuracy of diagnosis of chronic cholecystitis.

**Positron Emission Tomography With Computed Tomography.** On PET there is an increased focus of activity in the region of gallbladder and lower edge of liver with a rim of intense activity and central photopenia.<sup>26,27</sup>

#### **Classic Signs: Chronic Cholecystitis**

- Thickened gallbladder wall
- Contracted gallbladder
- Gallstones
- Porcelain gallbladder
- Visualization of bowel activity before gallbladder visualization on hepatobiliary scintigraphy

## **Differential Diagnosis**

Other causes of acute upper abdominal pain should be included in the differential diagnosis, including gastroesophageal reflux disease, acute pancreatitis, peptic ulcer disease, or irritable bowel syndrome.<sup>20</sup> Other causes of primary gallbladder wall thickening should be considered, and the diagnosis of chronic cholecystitis is made based on the presence of diffuse gallbladder wall thickening, gallstones, and contracted gallbladder.

#### Treatment

**Medical Treatment.** Medical methods are aimed at dissolving the gallstones; these include the following:

- Oral dissolution agents: Ursodeoxycholic acid and chenodeoxycholic acid
- Extracorporeal shock wave lithotripsy with oral dissolution agents
- Contact dissolution with methyl tert-butyl ether

Diet therapy emphasizing a low-fat diet may be successful in patients with recurrent attacks of cholecystitis.

#### **Surgical Treatment**

*Chronic Cholecystitis.* The treatment of choice is elective laparoscopic or open cholecystectomy.

**Porcelain Gallbladder.** Because patients with porcelain gallbladder have a high incidence of gallbladder carcinoma, a prophylactic cholecystectomy is recommended.

## XANTHOGRANULOMATOUS CHOLECYSTITIS

## Etiology

Chronic gallbladder infection associated with gallstones, and obstruction to gallbladder outflow is the primary cause.<sup>17,28-37</sup> The principal characteristic is thickening of the gallbladder wall with a tendency to adhere to neighboring organs, even leading to fistula formation.

## Prevalence and Epidemiology

Xanthogranulomatous cholecystitis (XGC) is an unusual variant of chronic cholecystitis characterized pathologically by the presence of grayish yellow nodules or streaks in the gallbladder wall that are mainly caused by lipid-laden macrophages.<sup>17,34</sup> The presence of nonspecific features such as gallbladder wall thickening and calculi on imaging makes its identification and differentiation from gallbladder carcinoma difficult.<sup>17,37</sup>

XGC is an uncommon form of chronic cholecystitis similar to xanthogranulomatous pyelonephritis and accounts for 0.7% to 13.2% of gallbladder disease. It more commonly affects women in the fourth to seventh decades.<sup>17,37</sup> An association with gallbladder adenocarcinoma is seen in up to 20% of cases.<sup>17,28-35</sup> Association with biliary ductal carcinoma is also reported.

## **Clinical Presentation**

The clinical presentation of XGC is similar to that of acute or chronic cholecystitis.<sup>17,28-35</sup> Frequently encountered features are vomiting, upper right quadrant pain, positive Murphy's sign on ultrasonography, and leukocytosis.<sup>17,28-35</sup> Repeated episodes of biliary colic or pancreatitis commonly occur. Clinical findings on physical examination and laboratory results are nonspecific and are not helpful in differentiating this disease from other causes. Complications include a perforated gallbladder, abscess formation, or enterobiliary fistula.

#### Pathophysiology

XGC is caused by chronic infection and calculi in association with bile stasis. Recurrent inflammation and calculi incite degeneration and necrosis of the gallbladder wall, which subsequently leads to intramural abscess formation and eventual replacement by xanthogranulomas.<sup>37</sup> Inspissations of bile and mucin in Rokitansky-Aschoff sinuses lead to their subsequent rupture and inflammation.

Chronic stages are characterized by fibrous reaction and scarring from healing of the inflammatory reaction, and the histiocytes have a granular cytoplasm containing yellow-brown ceroid pigment.<sup>30,32</sup>

## Pathology

Chronic inflammation causes persistent thickening of the gallbladder wall and adhesions to adjacent tissues and organs. Grossly there is a large or small contracted gallbladder usually associated with cholelithiasis, irregular wall thickening, and poorly demarcated nodules of varying size in the outer layers of the gallbladder wall with ulceration of the mucosal surface.<sup>37</sup>

On microscopy, nodular or poorly demarcated areas of foamy histiocytes, foreign body giant cells with chronic inflammatory cells, and surrounding vascular fibroblastic reaction are noted.<sup>31</sup>

Bile cultures are often positive for the organisms noted in acute cholecystitis, such as *E. coli, Enterococcus, Klebsiella*, and *Staphylococcus*.<sup>17</sup>

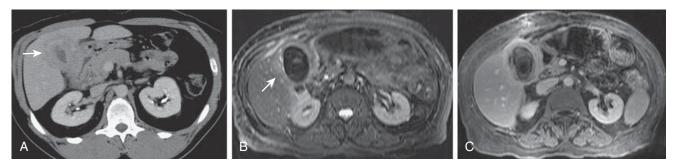
## Imaging

Significant overlap exists between the radiographic appearances of XGC, acute/chronic cholecystitis, and gallbladder carcinoma.<sup>17,28-34</sup>

**Radiography.** The role of conventional radiography in the evaluation of xanthogranulomatous cholecystitis is limited (Table 56-3).

**Computed Tomography.** Cholelithiasis may be evident. Diffuse uneven thickening of the gallbladder wall is the most frequent finding (Figure 56-10).<sup>4,17,28,29,34</sup> A hypoattenuating band occasionally can be seen around the thickened gallbladder wall. Intramural calcification similar to porcelain gallbladder also can be seen. Diffuse or focal intramural low-attenuation areas are seen within the gallbladder wall.<sup>4,17,28,29,34</sup>

On contrast-enhanced scans, continuous enhancement of the mucosal line is seen that corresponds to both the mucosal and muscular layer. This corresponds well to the presence of an



**Figure 56-10** Xanthogranulomatous cholecystitis. **A**, Axial contrast-enhanced computed tomography scan in a 64-year-old man presenting with 4 months of right upper quadrant pain and tenderness showed diffuse enhancing irregular gallbladder wall thickening and an ill-defined hypodense band at the periphery (*arrow*). The inflammatory lesion is seen to penetrate the serosal layer and infiltrate into the pericholecystic space with indistinct margin of the liver and gallbladder. **B**, Axial T2-weighted magnetic resonance (MR) image in a 63-year-old woman shows asymmetric gallbladder wall thickening with small intramural hyperintense areas. The interface between the gallbladder wall and the liver is indistinct (*arrow*). **C**, Contrast-enhanced T1-weighted MR image in the same patient as in **B** shows heterogeneous enhancement of the gallbladder wall with nonenhancing areas within corresponding to the hyperintense regions seen on T2-weighted images. These regions correspond to the areas of intramural necrosis/ abscess.

TABLE         Accuracy           56-3         Accuracy	, Limitations, and Pitfalls of the Mo	dalities Used in Imaging of Xanthogr	anulomatous Cholecystitis
Modality	Accuracy	Limitations	Pitfalls
Radiography	Data not available to specify accuracy	Insensitive Nonspecific	Unable to directly visualize the soft tissues of gallbladder
СТ	Sensitivity: 78-83%, Specificity: 82%-100% Accuracy: 69%-91% for differentiation of XGC from gallbladder cancer	The low soft tissue contrast resolution of CT may not be able to detect small intramural hypoattenuating areas	Significant overlap of CT features of XGC and gallbladder cancer
MRI	Data not available to specify accuracy		Significant overlap of MRI features of XGC and gallbladder cancer
Ultrasonography	Data not available to specify accuracy	Limited depiction of surrounding inflammatory changes and extension into adjacent organs	
Nuclear medicine	Data not available to specify accuracy	Does not allow specific diagnosis	
PET/CT	Data not available to specify accuracy	Decreased sensitivity in patients with diabetes	False-positive result mimicking malignancy

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; XGC, xanthogranulomatous cholecystitis.

epithelial layer. Focal disruption of the mucosal line is also seen, although less frequently compared with gallbladder carcinoma.<sup>4,17,28,29,34</sup> In general, the enhancement is diffuse and heterogeneous in XGC compared with gallbladder carcinoma.\*

Pericholecystic fat infiltration is also reported. Extension of the inflammatory process into the liver is common and manifests as either an ill-defined hypoattenuating mass or abnormalities of parenchymal enhancement. Biliary tree obstruction is also reported and is due to the presence of choledocholithiasis or concurrent cholangiocarcinoma. Mild lymphadenopathies in the portacaval space, along the hepatoduodenal ligament, also can occur.<sup>36</sup> Goshima and associates<sup>38</sup> showed five CT findings, including diffuse gallbladder wall thickening, a continuous mucosal line, intramural hypoattenuating nodules in the thickened walls, absence of macroscopic hepatic invasion, and absence of intrahepatic biliary ductal dilatation were significantly different between XGC and gallbladder cancer. Using a combination of at least three of these five CT findings, a high degree of sensitivity (83%), specificity (100%), and accuracy (91%) can be achieved in the differentiation of XGC from gall-bladder cancer.<sup>38</sup>

Magnetic Resonance Imaging. Diffuse wall thickening with contrast enhancement and inhomogeneous signal intensity can be seen (see Figure 56-10). There is low signal intensity of the wall on T1-weighted images and moderately high signal intensity on T2-weighted images. Small intramural abscesses may occur. Multiple intramural hyperintense regions are seen on T2-weighted images that do not show contrast enhancement on postgadolinium T1-weighted images.<sup>2,35</sup> Histopathologically these areas represent areas of necrosis or abscess formation. Another distinguishing feature for XGC on MRI is the presence of hypointense nodules in the gallbladder wall on T1-weighted images that demonstrate higher signal on *in-phase* images than out-of-phase chemical shift images, suggesting the presence of fat content.39 There are early reports on the value of diffusion weighted imaging in differentiating XGC from gallbladder cancer.4

<sup>\*</sup>References 17, 28, 29, 32, 34, 36.

Few high-intensity areas are seen on T2-weighted images, which show strong enhancement at late phase on postcontrast T1-weighted images. These consist of abundant proliferation of foamy cells.

There is loss of a well-defined fat plane between the gallbladder and liver.

Early enhancement of the hepatic parenchyma on dynamic studies is seen in the liver bed. The early enhancement is caused not only by increased cystic venous drainage but also by inflammatory changes in the adjacent hepatic parenchyma.<sup>2,3</sup>

**Ultrasonography.** Diffuse thickening of the gallbladder wall is evident. The gallbladder wall is typically echogenic but can be sonolucent (or isoechoic) and rarely hypoechoic. The characteristic feature is the presence of oval or flat hypoechoic nodules or bands within the gallbladder wall. The hypoechoic nodules represent the lipid-containing xanthogranulomas.<sup>17,3</sup>

A curvilinear hypoechoic halo within the gallbladder wall sometimes has been reported.<sup>28</sup> Associated features such as gallstones or gallbladder sludge are often present.

The soft tissue interface between the gallbladder wall and the liver is frequently maintained, but if it is lost, the differentiation from gallbladder carcinoma becomes difficult.

#### Positron Emission Tomography With Computed Tomogra-

**phy.** XGC can show increased activity on <sup>18F</sup>fluorodeoxyglucose (FDG)-labeled PET (FDG-PET) and mimic malignancy, yielding a false-positive result.<sup>41</sup>

#### Classic Signs: Xanthogranulomatous Cholecystitis

- Gallbladder wall thickening with surrounding hypoechoic/hypodense band
- Multiple intramural hypoattenuating nodules that are hyperintense on T2-weighted images
- Continuous line of mucosal enhancement of gallbladder wall with early adjacent hepatic parenchymal enhancement
- Gallbladder sludge and gallstones

#### **Differential Diagnosis**

The differential diagnosis includes acute cholecystitis, chronic cholecystitis, and gallbladder carcinoma.

#### Treatment

Medical Treatment. No medical treatment is recommended for this condition.

Surgical Treatment. Open cholecystectomy is the treatment of choice for XGC.33 Partial cholecystectomy may be performed in patients in whom adhesions are extensive or for those with extensive surrounding infiltration. Laparoscopic cholecystectomy may be ineffective owing to the presence of extensive adhesions and the infiltrative nature of the disease.<sup>3</sup>

An extended operation including hepatic resection or pancreaticoduodenectomy may be required in cases in which the pathologic process infiltrates into the liver tissue or adjacent organs.<sup>33</sup> The condition has also been related to difficult cholecystectomy.

Patients with XGC usually have a longer hospital stays and more postoperative complications, including bile leak, bile

peritonitis, bleeding, hepatic abscess, wound infection, and cholangitic stenosis.<sup>33</sup> These complications are largely related to difficulty in stripping the gallbladder, the mode of operation, and the physical condition of the patient.

#### GALLBLADDER MALIGNANCY

## Etiology

Gallbladder Carcinoma. Cholelithiasis is a well-established risk factor present in 70% to 90% of patients with gallbladder carcinoma. Porcelain gallbladder is seen in 10% to 25% of patients with gallbladder carcinoma. Other risk factors include female sex, age, postmenopausal status, cigarette smoking, chronic Salmonella typhi infection, exposure to chemicals used in rubber and metal fabricating industries, and biliary disorders such as choledochal cysts and primary sclerosing cholangitis.\*

Lymphoma of Gallbladder. Lymphoma is rare and represents primary non-Hodgkin lymphoma from mucosa-associated lymphoid tissue or may be secondary to systemic disease.<sup>2,44</sup>

## Prevalence and Epidemiology

Primary carcinoma of gallbladder is an uncommon malignancy with distinctive demographic and geographic distribution. It is the sixth most common gastrointestinal malignancy, following cancer of the colon, pancreas, stomach, liver, and esophagus.<sup>4</sup>

Incidental detection of gallbladder carcinoma has been reported in 1% to 3% of cholecystectomy specimens. Detection of gallbladder malignancy occurs in the late stage of the disease because of the lack of early or specific symptoms.

It is three times more common in women than men and is a disease of the elderly, with a peak incidence in the eighth decade and commonly manifesting at approximately 72 years of age.<sup>8,20,21,42,</sup>

#### Clinical Presentation

The most common manifesting symptom is right upper quadrant pain. Other features include jaundice, a palpable right upper quadrant mass, nausea and vomiting, anorexia, and weight loss.

Five different clinical syndromes are used to describe the presentation of patients with gallbladder cancer.<sup>20</sup>

- Chronic cholecystitis (40% to 45%): Postprandial right upper quadrant pain with a recent change in quality and frequency of pain
- Acute cholecystitis (15% to 20%): Short duration of pain with vomiting, fever, tenderness
- Malignant biliary obstruction (30% to 35%): Jaundice, weight loss, and right upper quadrant pain
- Nonbiliary malignancy (25% to 30%): Anorexia and weight loss in the absence of jaundice
- Other gastrointestinal problems (~5%): Gastrointestinal bleeding or obstruction

#### Pathophysiology

Gallstones cause chronic irritation and inflammation of the gallbladder, which leads to mucosal dysplasia and subsequent carcinoma.<sup>8,20,21,42</sup>

<sup>\*</sup>References 8, 14, 20, 21, 24, 42, 43.

Adenocarcinoma accounts for 75% to 85% of cases.<sup>8,20,21,42,43</sup> Other histologic types include adenosquamous carcinoma, squamous carcinoma, small cell carcinoma, and carcinoid of the gallbladder. The most common type is infiltrative adenocarcinoma. Thirty percent of cases are poorly differentiated, and 12% are of papillary variety; 12% are mucinous cancers, and 7% are of the adenosquamous or squamous variant.

Diffuse gallbladder wall thickening is a less frequent occurrence. Invasion of the adjacent liver parenchyma occurs in 70% of the cases.

Venous spread occurs into segment IV.<sup>8,20,21,42</sup> Direct invasion into segments IV and V, stomach, duodenum, colon, anterior abdominal wall, and common hepatic duct is common. Intraductal or perineural spread is also possible. Implants of the peritoneal surfaces can lead to intra-abdominal carcinomatosis, ascites, and invasion into an adjacent hollow organ, leading to biliary-enteric fistulas.

Gallbladder carcinoma spreads lymphatically to the lymph nodes around the cystic duct, common bile duct, and pancreaticoduodenal region, followed later by the para-aortic region. It occurs early in the disease course and is likely to be present in approximately 50% of the cases at the time of diagnosis. More distant sites often involved include mediastinal, bronchial, or supraclavicular lymph nodes.

#### Tumor, Node, Metastasis Staging

The TNM classification for staging of gallbladder tumors is shown in Table 56-4.

#### Imaging

Abnormal laboratory parameters include hyperbilirubinemia and an elevated serum alkaline phosphatase level. Tumor markers include elevated serum carcinoembryonic antigen or carbohydrate antigen 19-9 (CA 19-9).<sup>8,20,21,42</sup>

**Radiography.** Calcified gallstones or a porcelain gallbladder may be present. Rarely, calcification precipitating in mucus within the glandular tissue may also be visible (Table 56-5). Abnormal collections of gas in the right upper quadrant may be visible on radiographs when tumor invades into adjacent bowel and fistula has formed.  $^{\rm 42}$ 

**Computed Tomography.** Diffuse gallbladder wall thickening secondary to tumor infiltration and inflammatory change is a common and late manifestation of advanced gallbladder carcinoma. Diffuse or focal gallbladder wall thickening is seen in 20% to 30% of cases of gallbladder carcinoma. The most common appearance is that of a mass replacing the gallbladder and seen in 40% to 65% of cases. An intraluminal polypoid mass is seen in 15% to 25% of patients.

Wall thickening is the most diagnostically challenging pattern because it mimics the other common acute and chronic inflammatory conditions of the gallbladder. Pronounced wall thickening (i.e., >1 cm) with mural irregularity and marked asymmetry suggests carcinoma (Figure 56-11). Associated findings such as biliary dilatation, invasion of adjacent structures, and liver and

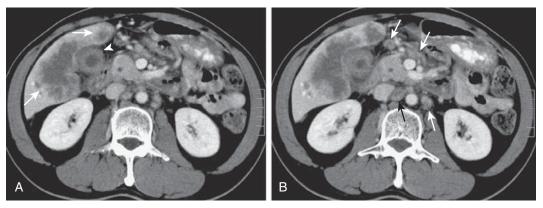
TABLE <b>56-4</b>	American Joint Committee on Cancer Staging Tumor, Node, Metastasis Classification for Gallbladder Carcinoma			
Stage	Description			
T1	Tumor confined within the muscular layer			
T2	Tumor extends beyond the muscular layer into the perimuscular connective tissue			
Т3	Tumor invading liver <2 cm and/or one other adjacent organ such as stomach, duodenum, colon, or pancreas			
Τ4	Tumor invading into liver >2 cm or invaded the main portal vein or hepatic artery or has invaded more than one organ or structure beyond the liver			
N1	Cystic and pericholedochal nodes			
N2	Posterior pancreaticoduodenal, retroportal, and celiac nodes			
M1	Distant metastases and involvement of intercaval nodes			
From American Joint Committee on Concer Staning TNM				

From American Joint Committee on Cancer Staging TNM Classification Manual.

TABLE 56-5Accuracy,						
Modality	Accuracy	Limitations	Pitfalls			
Radiography	Data not available to specify accuracy	Insensitive Nonspecific	Unable to directly visualize the soft tissues of gallbladder			
СТ	68%-84% <sup>42,47</sup>	Not reliable in accurate detection and characterization lymph nodes Not sensitive in detection of small peritoneal implants Not accurate in detection of recurrence	Significant overlap of CT features of XGC and gallbladder cancer			
MRI	Data not available to specify accuracy	Not sensitive for detection of direct ductal invasion Reliable identification of gallstones and porcelain gallbladder not possible	Significant overlap of CT features of XGC and gallbladder cancer			
Ultrasonography	Data not available to specify accuracy	Operator dependent Poor gallbladder distention precludes accurate evaluation Not accurate for evaluation of nodal metastases				
Nuclear medicine	Data not available to specify accuracy	Not the preferred modality for diagnosis				
PET/CT	81%	Decreased sensitivity in patients with diabetes	False-positive results with XGC			

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; XGC, xanthogranulomatous cholecystitis. From Edge SB, et al: American Joint Committee on Cancer (AJCC) Cancer Staging Manual, ed 7, New York, 2010, Springer.

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**Figure 56-11** Gallbladder carcinoma. A, Axial contrast-enhanced computed tomography scan of abdomen in 78-year-old man presenting with right upper quadrant pain and weight loss shows diffuse irregular gallbladder wall thickening (*arrowhead*) and necrotic liver metastases (*arrows*). B, Axial image also shows multiple enlarged lymph nodes with heterogeneous enhancement in the perihepatic, peripancreatic, and para-aortic regions (*arrows*).

nodal metastases may help in establishing the correct diagnosis and differentiating it from chronic cholecystitis.

Metastatic nodes in the foramen of Winslow, the superior pancreaticoduodenal region, and the posterior pancreaticoduodenal region are most commonly demonstrated by CT. Nodal masses around the distal common bile duct and pancreatic head may mimic pancreatic head carcinoma.<sup>1,4,24,42,43</sup>

Gallbladder lymphoma may manifest as diffuse gallbladder wall thickening and enlarged lymph nodes at the porta hepatis.<sup>2,44</sup>

**Magnetic Resonance Imaging.** Diffuse nodular wall thickening without layering is evident, and the wall shows homogeneous low signal intensity (type 4 pattern).<sup>5</sup> Wall thickening greater than 1 cm and asymmetric thickening are highly suggestive of carcinoma.<sup>2,3,5,42</sup>

The tumor is heterogeneously hyperintense to the liver on T2-weighted images and isointense to hypointense on T1-weighted images.<sup>2,3,5,42</sup>

All gallbladder cancers show enhancement after administration of gadolinium-based contrast material. On dynamic contrast-enhanced imaging, the outer margin of enhancement is irregular. This helps in differentiation from chronic cholecystitis, in which the outer wall of enhancement is smooth. The late phases of enhancement are less specific.<sup>2,3,5,42</sup>

The most common appearance of gallbladder carcinoma is a large mass in the gallbladder fossa replacing the gallbladder, with extension into the liver and adjacent organs.<sup>2,3,5,42</sup> The mass demonstrates heterogenous hyperintense signal on T2-weighted images and shows early and prolonged enhancement after gadolinium administration.

Gadolinium-enhanced fat-suppressed T1-weighted images are useful in diagnosing tumor extent, direct invasion of surrounding organs, liver metastases, and involvement of critical vascular structures such as portal vein and hepatic artery.<sup>2,3,5,42</sup> Small peritoneal implants are better appreciated on delayed gadolinium-enhanced fat-suppressed T1W images.<sup>2,3,5,42</sup>

Gallbladder lymphoma manifests as wall thickening, and tumor is hypointense on T1-weighted images and hyperintense on T2-weighted images.<sup>2</sup>

**Ultrasonography.** The diffusely thickened gallbladder wall has irregular margins and a heterogeneous echotexture.<sup>42</sup> Echogenic

foci and acoustic shadowing may be seen and are related to coexisting gallstones, gallbladder wall calcification, or tumoral calcification.<sup>42</sup> Specific patterns of wall echogenicity such as submucosal echolucency, echolayering, mural edema, and intramural echolucencies are helpful in excluding the cancer in the presence of gallbladder wall thickening.\*

Features helping differentiate malignancy from acute or XGC include adjacent structure invasion, secondary bile duct dilatation, and liver or nodal metastases.

**Nuclear Medicine.** There is no role for cholescintigraphy in the evaluation of gallbladder carcinoma.

**Positron Emission Tomography With Computed Tomography.** Gallbladder cancers show intense focal FDG uptake that is more intense than the uptake of liver.<sup>26</sup> Delayed FDG-PET is more helpful in the evaluation of malignancy compared with early FDG-PET.<sup>26</sup>

#### **Classic Signs: Gallbladder Malignancy**

- Diffuse irregular nodular wall thickening (>1 cm)
- Nodal metastases, biliary dilatation, and adjacent organ invasion
- Gallstones

#### Differential Diagnosis

The differential diagnosis includes acute or chronic cholecystitis, XGC, and diffuse gallbladder wall thickening secondary to noninflammatory causes including heart failure, cirrhosis, hepatitis, hypoalbuminemia, renal failure, and cholecystitis. Gallbladder carcinoma is differentiated from these conditions by the presence of irregular wall thickening, lymphadenopathy, hepatic metastases, and biliary obstruction. A thicker and more irregular wall is more suggestive of gallbladder cancer than chronic cholecystitis.

In XGC (Table 56-6), significant overlap can occur both clinically and radiologically between its features and those of

<sup>\*</sup>References 1, 14, 36, 42, 43, 45 to 47.

TABLEDifferentiating Features Among Xanthogranulomatous Cholecystitis, Gallbladder Carcinoma,56-6and Adenomyomatosis

Differentiating Features	XGC	Gallbladder Carcinoma	Adenomyomatosis
Luminal surface enhancement	Present	Absent	Can be present
Mucosal line	Continuous	Disrupted	
Intramural low-attenuation nodules	Present	Absent	$\pm$ (cystic areas)
Hypoechoic nodules and band	Present	Absent	Absent
Very high signal areas on T2-weighted imaging	Present	Absent	Present
"Pearl necklace" sign on MRCP	Absent	Absent	Pathognomonic
Hepatic metastases	Absent	Present	Absent
Lymphadenopathy	Less likely	More likely	Absent
Intramural diverticula	Absent	Absent	Present

MRCP, Magnetic resonance cholangiopancreatography.

gallbladder carcinoma. The presence of a continuous mucosal line and of intramural hypoattenuating nodular lesions in the former helps in the diagnosis.

In adenomyomatosis there is regular wall thickening with anechoic or echogenic foci in the gallbladder wall on ultrasonography, which aids in the differentiation from gallbladder carcinoma.

#### Treatment

The prognosis of most patients with cancer of the gallbladder is poor. Those in whom the tumor is confined to the gallbladder wall have a better prognosis.

Surgery is the only potentially curative therapy for resectable tumors.<sup>20</sup> Patients with advanced cancers or with significant comorbidities are candidates for biliary enteric bypass or endoscopic or percutaneous drainage as palliation for obstruction.

T1 tumors are treated with cholecystectomy. Invasive gallbladder cancers (stages II and III) are associated with increasing incidence of regional nodal metastases and should be treated with extended cholecystectomy, which includes resection of at least a 2-cm margin of liver beyond the palpable or ultrasonographic extent of tumor.

Treatment of extensive tumors includes the following<sup>20</sup>:

- Palliation of obstructive jaundice with either an endoscopic or percutaneously placed biliary stent
- Percutaneous celiac ganglion nerve block to reduce pain
- Chemotherapy and external-beam or intraoperative radiation therapy

#### ADENOMYOMATOSIS

#### Etiology

Adenomyomatosis is an acquired, benign, and degenerative condition of the gallbladder mostly seen in adults. It is characterized by epithelial proliferation, muscular hypertrophy, and intramural diverticula (Rokitansky-Aschoff sinuses), which could be segmental or diffuse.<sup>2-5,14,22,48-52</sup>

#### Prevalence and Epidemiology

Adenomyomatosis of the gallbladder is relatively common, with a reported incidence of 2.8% to 5%. It has been observed in 2% to 9% of the cholecystectomy specimens. Adenomyomatosis of the gallbladder is more common in women than in men.

#### **Clinical Presentation**

Most patients with adenomyomatosis remain asymptomatic, and the diagnosis is usually an incidental finding on either imaging or histopathologic examination of surgical gallbladder specimens. Symptomatic patients present with reports of persistent right upper quadrant pain, and 90% have coexistent gallstones.

#### Pathology

Proliferation of the gallbladder epithelium occurs that extends downward into the crypts, into the thickened muscularis, or beyond into the outer layer of connective tissue. There also is associated muscular hypertrophy that results in gallbladder wall thickening, which can be diffuse, segmental, or localized (Figure 56-12).

A Rokitansky-Aschoff sinus within the thickened muscular layer of the gallbladder is the characteristic finding of adenomyomatosis. Microscopic examination shows extension of epithelium into the mucosal invaginations of the muscle. The invaginations are lined by a single layer of tall columnar epithelial cells similar to the surface-lining epithelium. Cystic spaces within the wall may be grossly visible, and stones may be present within them.

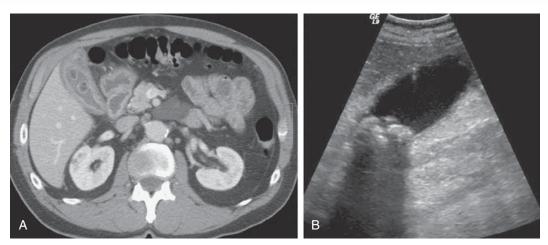
#### Imaging

**Radiography.** Opacification of the Rokitansky-Aschoff sinus is depicted on drip-infusion cholecystographic images, specifically in the diffuse type of adenomyomatosis, and is called the "pearl necklace" sign.

**Computed Tomography.** Diffuse gallbladder wall thickening with mural enhancement is evident. Biliary sludge and calculi are seen as high-attenuation intraluminal material on nonenhanced CT scans. Intramural fluid attenuation and nonenhancing areas suggestive of Rokitansky-Aschoff sinuses are seen within the gallbladder wall. The ability of CT to delineate the Rokitansky-Aschoff sinuses is limited because of insufficient spatial and contrast resolution (Table 56-7).

**Magnetic Resonance Imaging.** On MRI, diffuse gallbladder wall thickening with mural enhancement is seen. The type 3 pattern of wall thickening is evident and consists of multiple

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**Figure 56-12** Adenomyomatosis. **A**, Axial contrast-enhanced computed tomography scan of the abdomen in a 73-year-old man with dyspepsia shows diffuse gallbladder wall thickening, ill-defined intramural low-attenuation areas, and gallstones. **B**, Sagittal ultrasound image in a 67-year-old man shows wall thickening and gallstones. Few echogenic foci are seen within the gallbladder wall mimicking intramural air. Histopathologic examination showed adenomyomatosis. The echogenic foci correspond to calculi within Rokitansky-Aschoff sinuses.

TABLE 56-7	Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Adenomyomatosis					
Modal	ity	Accuracy	Limitations	Pitfalls		
Radiog	raphy	Data not available to specify accuracy	Insensitive Nonspecific	Unable to directly visualize the soft tissues of gallbladder		
СТ		75% <sup>49</sup>	Decreased sensitivity in detection of Rokitansky-Aschoff sinuses secondary to insufficient contrast and spatial resolution			
MRI		93% <sup>49</sup>	Restricted evaluation in the presence of thick bile or stones	Presence of unusually thick bile in adenomyomatosis may cause pseudolesions on MRI		
Ultraso	nography	66% <sup>49</sup>	Restricted visibility as a result of intestinal gas and coexistent stones			
Nuclear medicine		Data not available to specify accuracy				
PET/CT	Г	Data not available to specify accuracy	Decreased sensitivity in diabetic patients			
		1 1 1 1 1 1 1 1 1 1 1 1				

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

cystic spaces of high signal intensity in the thickened wall regardless of whether the thickened wall is present.

The characteristic feature is the presence of multiple intramural cystic spaces, some of which may contain signal void as a result of the presence of calculi. The cystic spaces are hyperintense on T2-weighted images and hypointense on T1-weighted images and are nonenhancing.

The pearl necklace sign is described on MR cholangiopancreatography (MRCP). It refers to a curvilinear arrangement of multiple small, rounded, high signal intensity foci representing Rokitansky-Aschoff sinuses within the thickened wall of gallbladder. This sign is highly specific for adenomyomatosis and helps in differentiation from carcinoma of the gallbladder.

**Ultrasonography.** Diffuse gallbladder wall thickening is evident with intramural diverticula seen as anechoic spaces or as echogenic foci that may have acoustic shadows or reverberation artifacts. Intramural diverticula containing bile appear anechoic, whereas diverticula containing sludge, stones, or papillary projections appear echogenic with associated acoustic shadowing or reverberation artifact. The frond-like mucosal projections within diverticula, with their multiple interfaces of varying acoustic impedances, are the likely cause of the reverberation or "comet tail" artifacts. When the entire gland is involved the lumen may be collapsed.

**Nuclear Medicine.** Hepatobiliary cholescintigraphy has no role in the routine evaluation of adenomyomatosis.

**Positron Emission Tomography With Computed Tomography.** Sometimes adenomyomatosis shows increased activity on FDG-PET, owing to an inflammatory reaction.

#### **Classic Signs: Adenomyomatosis**

- Diffuse gallbladder wall thickening with intramural cystic spaces
- Pearl necklace sign on MRCP

#### Differential Diagnosis

Patients are usually asymptomatic. However in the presence of symptoms, the manifestation is similar to that of any other gallbladder disease.

In emphysematous cholecystitis,<sup>10,11</sup> a common differentiating factor is comet tail reverberation artifact. The air within the wall in emphysematous cholecystitis can produce a similar artifact; however, patients with emphysematous cholecystitis are usually ill, in contrast to those with adenomyomatosis.

#### Treatment

**Medical Treatment.** This is a benign condition and requires no specific treatment.

**Surgical Treatment.** Cholecystectomy is indicated for patients with symptomatic cases of gallbladder adenomyomatosis without cholelithiasis.

No clear-cut role exists for the treatment of asymptomatic cases. Nevertheless, prophylactic laparoscopic cholecystectomy may be justified considering the uncertain nature of the disease and the difficult differentiation from malignant lesions.

#### Secondary Gallbladder Wall Thickening

#### **ETIOLOGY**

Systemic causes include liver dysfunction (cirrhosis), congestive heart failure, hypoalbuminemic states, and renal failure. An extracholecystic inflammatory process such as acute hepatitis, peritonitis, acute pancreatitis, and acute pyelonephritis may cause gallbladder wall thickening. Other causes include infectious mononucleosis, opportunistic infections, or secondary neoplastic infiltration (Kaposi's sarcoma and primary lymphoma) in patients with AIDS, and trauma.<sup>14,53</sup>

#### PREVALENCE AND EPIDEMIOLOGY

In patients with secondary wall thickening, a cholecystectomy is unwarranted and gallbladder wall thickening will usually return to normal after correction of its extrinsic cause.<sup>1,4,53</sup>

#### **CLINICAL PRESENTATION**

The clinical presentation is related to the primary condition causing secondary gallbladder involvement. Generally, there are no symptoms localized to the right upper quadrant.

#### PATHOPHYSIOLOGY

Systemic diseases, such as liver dysfunction (cirrhosis), heart failure, or renal failure, may lead to diffuse gallbladder thickening. The exact pathophysiologic mechanism leading to edema of the gallbladder wall in these diverse conditions is uncertain. It has been postulated that elevated portal venous pressure, elevated systemic venous pressure, decreased intravascular osmotic pressure, or a combination of these factors could lead to gallbladder wall thickening. Liver cirrhosis, hepatitis, and congestive right heart failure are relatively frequent causes. The factors leading to the development of gallbladder wall thickening in cirrhosis include ascites, decreased systemic vascular resistance, and portal hypertension.<sup>1,4,53</sup>

Extracholecystic inflammation may secondarily involve the gallbladder, thereby causing wall thickening as a result of the direct spread of the primary inflammation or, less frequently, an immunologic reaction. Gallbladder wall thickening may be

caused by any inflammation that extends to the region of the gallbladder, but only a few entities are regularly encountered, including hepatitis, pancreatitis, and pyelonephritis.<sup>14,53</sup>

#### IMAGING

The gallbladder wall thickening is more severe than expected from clinical presentation.

#### Radiography

Conventional radiography has no role to play in the diagnostic evaluation of patients with secondary gallbladder wall thickening.

#### Computed Tomography

Regular diffuse gallbladder wall thickening is seen. Additional findings of extravascular volume overload may be seen, such as pleural or pericardial effusions, ascites, dependent subcutaneous edema, and distended inferior vena cava. Patients with congestive heart failure will demonstrate pulmonary congestion in the lung bases.<sup>1,4,53</sup>

When gallbladder wall thickening occurs secondary to spread of adjacent inflammatory process, CT features identifying the primary inflammatory lesion are seen resembling those of pancreatitis, appendicitis, and pyelonephritis.

Traumatic perforation of gallbladder may manifest on CT with mural thickening and high-density fluid content within the gallbladder representing hemobilia and pericholecystic stranding along the tract of invasion.

#### Magnetic Resonance Imaging

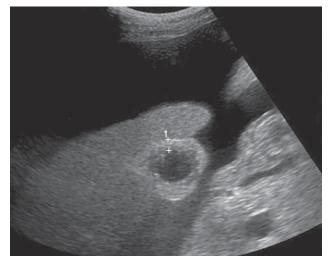
Diffuse regular gallbladder wall thickening is seen.

#### Ultrasonography

Diffuse gallbladder wall thickening is seen (Figure 56-13).

#### Nuclear Medicine

Hepatobiliary cholescintigraphy has a limited role but can be used to rule out acute cholecystitis.



**Figure 56-13** Diffuse gallbladder wall thickening in cirrhosis. Sagittal ultrasound image in a 68-year-old man shows diffuse regular gallbladder wall thickening and gross ascites.

#### DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes systemic diseases and local inflammatory processes that can cause gallbladder wall thickening, acute and chronic cholecystitis, and XGC.

#### What the Referring Physician Needs to Know

#### Acute Cholecystitis

- Ultrasonography is the initial imaging in patients with suspected acute cholecystitis.
- CT is an excellent second choice for the evaluation of suspected acute cholecystitis.
- Hepatobiliary scintigraphy is highly accurate in the diagnosis of acute cholecystitis and is reserved for patients with indeterminate ultrasound or CT findings.
- Imaging features suggestive of perforation, necrosis, abscess formation, and emphysematous change in a setting of acute cholecystitis necessitates emergent cholecystectomy.

#### **Chronic Cholecystitis**

- Correlation of the imaging finding of a stone-containing, slightly thick-walled gallbladder with clinical history is critical.
- Porcelain gallbladder has high association with gallbladder carcinoma, and the patient should undergo prophylactic cholecystectomy.
- Chronic cholecystitis can have overlapping imaging features with gallbladder carcinoma.

#### Xanthogranulomatous Cholecystitis

- Preoperative identification of XGC and its differentiation from gallbladder carcinoma is essential for proper surgical management.
- Open cholecystectomy is preferred over the laparoscopic method owing to the presence of extensive adhesions and pericholecystic extension.

#### TREATMENT

There is no treatment for gallbladder thickening except treatment of the primary cause.

- Association with gallbladder carcinoma is seen in 20% of cases, and the differentiation between the two entities may be difficult on imaging at times.
- XGC can show increased activity on FDG-PET and yield a false-positive result for gallbladder carcinoma.

#### Gallbladder Malignancy

- Diffuse irregular gallbladder wall thickening is present in 20% to 30% of gallbladder carcinoma and can mimic other acute and chronic inflammatory conditions of the gallbladder.
- CT is the initial imaging investigation of choice for diagnosis and staging of gallbladder carcinoma.

#### Adenomyomatosis

- Adenomyomatosis of the gallbladder is an incidental finding on imaging.
- The imaging features of adenomyomatosis can be distinctive enough to allow confident diagnosis; however, findings of gallbladder wall thickening and enhancement are nonspecific.

#### Secondary Gallbladder Wall Thickening

- Gallbladder wall thickening can occur in a variety of systemic and inflammatory conditions without direct involvement of the gallbladder.
- Correlation with clinical presentation is important to rule out primary involvement and prevent unnecessary intervention.

#### **Key Points**

#### Acute Cholecystitis

- Four "Fs" of acute calculus cholecystitis: Fat, female, forty, and fertile
- Acute acalculus cholecystitis is seen in critically ill patients with prolonged fasting, immobility, and hemodynamic instability.
- Acute calculus cholecystitis presents as diffuse gallbladder wall thickening, tense gallbladder distention, and an obstructing stone in the gallbladder neck or cystic duct.
- Nonvisualization of the gallbladder 3 hours after the radiotracer administration in cholescintigraphic scanning is highly suggestive of acute cholecystitis.
- Gangrenous cholecystitis is characterized by irregular wall thickening, areas of gallbladder wall nonenhancement, and intraluminal membranes.
- Emphysematous cholecystitis is characterized by air within the gallbladder lumen or gallbladder wall.

#### **Chronic Cholecystitis**

 Chronic cholecystitis is the most common form of gallbladder disease and refers to chronic low-grade inflammation of the gallbladder.

- There is diffuse gallbladder wall thickening with gallstones.
- Porcelain gallbladder is characteristic of calcific chronic cholecystitis and has a strong association with gallbladder cancer.

#### Xanthogranulomatous Cholecystitis

- XGC is an unusual variant of chronic cholecystitis characterized pathologically by the presence of lipid-laden macrophages.
- It affects women more commonly in the fourth to seventh decades.
- On CT, diffuse gallbladder wall thickening is evident with diffuse or focal areas of low attenuation within the gallbladder wall.
- There is diffuse heterogeneous enhancement of the gallbladder wall with continuous enhancement of the mucosal line.

#### Gallbladder Malignancy

• Gallbladder carcinoma is an uncommon malignancy of the gastrointestinal tract affecting women in the eighth decade of life.

#### Key Points-cont'd

- Gallstones and porcelain gallbladder are well-established risk factors.
- The various imaging appearances of gallbladder carcinoma include focal or diffuse wall thickening, polypoidal intraluminal lesion, or an infiltrating mass replacing the gallbladder.
- Presence of adjacent organ invasion and liver or nodal metastases helps in differentiation from other inflammatory conditions mimicking it.

#### Adenomyomatosis

 Adenomyomatosis is an acquired, benign, and degenerative condition of the gallbladder mostly seen in adults.

- It is characterized by epithelial proliferation, muscular hypertrophy, and intramural diverticula.
- On imaging, diffuse gallbladder wall thickening may be present with intramural cystic spaces that can occasionally be filled with calculi.
- The pearl necklace sign is a characteristic imaging finding seen on T2-weighted MRI or MRCP and is seen as a curvilinear arrangement of multiple small, rounded, high signal intensity foci within the thickened gallbladder wall.
- Secondary Gallbladder Wall Thickening
- Diffuse gallbladder wall thickening in the absence of gallstones or symptoms referable to the right upper quadrant can occur.

#### REFERENCES

- van Breda Vriesman AC, Englebrecht MR, Smithius RH, et al: Diffuse gallbladder wall thickening: differential diagnosis. *AJR Am J Roentgenol* 188:495–501, 2007.
- Catalano OA, Sahani DV, Kalva SP, et al: MR imaging of the gallbladder: a pictorial essay. *Radiographics* 28:135–155, quiz 324, 2008.
- Elsayes KM, Oliveira EP, Narra VR, et al: Magnetic resonance imaging of the gallbladder: spectrum of abnormalities. *Acta Radiol* 48:476– 482, 2007.
- 4. Zissin R, Osadchy A, Shapiro-Feinberg M, et al: CT of a thickened-wall gallbladder. *Br J Radiol* 76:137–143, 2003.
- Jung SE, Lee JM, Lee K, et al: Gallbladder wall thickening: MR imaging and pathologic correlation with emphasis on layered pattern. *Eur Radiol* 15:694–701, 2005.
- Yusoff IF, Barkun JS, Barkun AN: Diagnosis and management of cholecystitis and cholangitis. *Gastroenterol Clin North Am* 32:1145–1168, 2003.
- Hanbidge AE, Buckler PM, O'Malley ME, et al: From the RSNA refresher courses: imaging evaluation for acute pain in the right upper quadrant. *Radiographics* 24:1117–1135, 2004.
- Hermann R, Vogt D, Chung R: Biliary system. In Davis J, Sheldon G, editors: Surgery: a problem solving approach, St. Louis, 1995, Mosby, pp 1514–1557.
- Jacobs JE, Birnbaum BA: Abdominal computed tomography of intensive care unit patients. *Semin Roentgenol* 32:128–141, 1997.
- Grayson DE, Abbott RM, Levy AD, et al: Emphysematous Infections of the abdomen and pelvis: a pictorial review. *Radiographics* 22:543– 561, 2002.
- 11. Alobaidi M, Gupta R, Jafri SZ, et al: Current trends in imaging evaluation of acute cholecystitis. *Emerg Radiol* 10:256–258, 2004.
- Bennett GL, Rusinek H, Lisi V, et al: CT findings in acute gangrenous cholecystitis. AJR Am J Roentgenol 178:275–281, 2002.
- Fidler J, Paulson EK, Layfield L: CT evaluation of acute cholecystitis: findings and usefulness in diagnosis. *AJR Am J Roentgenol* 166:1085–1088, 1996.
- Gore RM, Yaghmai V, Newmark GM, et al: Imaging benign and malignant disease of the gallbladder. *Radiol Clin North Am* 40:1307– 1323, vi, 2002.
- 15. Paulson EK: Acute cholecystitis: CT findings. Semin Ultrasound CT MR 21:56–63, 2000.

- Altun E, Semelka RC, Elias J, Jr, et al: Acute cholecystitis: MR findings and differentiation from chronic cholecystitis. *Radiology* 244:174–183, 2007.
- Parra JA, Acinas O, Bueno J, et al: Xanthogranulomatous cholecystitis: clinical, sonographic, and CT findings in 26 patients. *AJR Am J Roentgenol* 174:979–983, 2000.
- Kitazono MT, Colletti PM: FDG-PET imaging of acute cholecystitis. *Clin Nucl Med* 31:23–24, 2006.
- Kao CH: Ring-like FDG uptake in acute cholecystitis. *Clin Nucl Med* 28:162–163, 2003.
- Ahrendt S, Pitt H: Biliary tract. In Townsend C, Jr, Beauchamp RD, Evers MB, editors: Sabiston textbook of surgery: the biological basis of modern surgical practice, Philadelphia, 2004, Saunders, pp 1597–1641.
- Ferrell L: Gallbladder and extrahepatic bile ducts. In Weidner N, Cote RJ, Suster S, et al, editors: *Modern Surgical Pathology*, vol 1, Philadelphia, 2003, WB Saunders, pp 981–998.
- Levy AD, Murakata LA, Abbott RM, et al: Benign tumors and tumorlike lesions of the gallbladder and extrahepatic bile ducts: radiologicpathologic correlation. Armed Forces Institute of Pathology. *Radiographics* 22:387–413, 2002.
- 23. Liang HP, Cheung WK, Su FH, et al: Porcelain gallbladder. J Am Geriatr Soc 56:960–961, 2008.
- 24. Yun EJ, Cho SG, Park S, et al: Gallbladder carcinoma and chronic cholecystitis: differentiation with two-phase spiral CT. *Abdom Imaging* 29:102–108, 2004.
- Al-Sheikh W, Hourani M, Barkin JS, et al: A sign of symptomatic chronic cholecystitis on biliary scintigraphy. *AJR Am J Roentgenol* 140:283–285, 1983.
- Koh T, Taniguchi H, Yamaguchi A, et al: Differential diagnosis of gallbladder cancer using positron emission tomography with fluorine-18-labeled fluoro-deoxyglucose (FDG-PET). *J Surg Oncol* 84:74–81, 2003.
- Matolo NM, Stadalnik RC, McGahan JP: Comparison of ultrasonography, computerized tomography, and radionuclide imaging in the diagnosis of acute and chronic cholecystitis. *Am* J Surg 144:676–681, 1982.
- Casas D, Peres-Andres R, Jimenez JA, et al: Xanthogranulomatous cholecystitis: a radiological study of 12 cases and a review of the literature. *Abdom Imaging* 21:456–460, 1996.
- Chun KA, Ha HK, Yu ES, et al: Xanthogranulomatous cholecystitis: CT features with emphasis

on differentiation from gallbladder carcinoma. *Radiology* 203:93–97, 1997.

- Dao AH, Wong SW, Adkins RD, Jr: Xanthogranulomatous cholecystitis: a clinical and pathologic study of twelve cases. *Am Surg* 55:32–35, 1989.
- Duber C, Störkel S, Wagner PK, et al: Xanthogranulomatous cholecystitis mimicking carcinoma of the gallbladder: CT findings. J Comput Assist Tomogr 8:1195–1198, 1984.
- Fligiel S, Lewin KJ: Xanthogranulomatous cholecystitis: case report and review of the literature. Arch Pathol Lab Med 106:302–304, 1982.
- Guzman-Valdivia G: Xanthogranulomatous cholecystitis: 15 years' experience. World J Surg 28:254–257, 2004.
- Houston JP, Collins MC, Cameron I, et al: Xanthogranulomatous cholecystitis. Br J Surg 81: 1030–1032, 1994.
- Shuto R, Kiyosue H, Komatsu E, et al: CT and MR imaging findings of xanthogranulomatous cholecystitis: correlation with pathologic findings. *Eur Radiol* 14:440–446, 2004.
- Ros PR, Goodman ZD: Xanthogranulomatous cholecystitis versus gallbladder carcinoma. *Radiology* 203:10–12, 1997.
- Kim PN, Ha HK, Kim YH, et al: US findings of xanthogranulomatous cholecystitis. *Clin Radiol* 53:290–292, 1998.
- Goshima S, Chang S, Wang JH, et al: Xanthogranulomatous cholecystitis: diagnostic performance of CT to differentiate from gallbladder cancer. *Eur J Radiol* 74:e79–e83, 2010.
- Zhao F, Lu PX, Yan SX, et al: CT and MR features of xanthogranulomatous cholecystitis: an analysis of consecutive 49 cases. *Eur J Radiol* 82: 1391–1397, 2013.
- 40. Kang TW, Kim SH, Park HJ, et al: Differentiating xanthogranulomatous cholecystitis from wall-thickening type of gallbladder cancer: added value of diffusion-weighted MRI. *Clin Radiol* 68:992–1001, 2013.
- Oe A, Kawabe J, Torii K, et al: Distinguishing benign from malignant gallbladder wall thickening using FDG-PET. *Ann Nucl Med* 20:699– 703, 2006.
- Levy AD, Murakata LA, Rohrmann CA, Jr: Gallbladder carcinoma: radiologic-pathologic correlation. *Radiographics* 21:295–314, questionnaire, 549–555, 2001.
- Oikarinen H: Diagnostic imaging of carcinomas of the gallbladder and the bile ducts. *Acta Radiol* 47:345–358, 2006.

- 44. Orton DF, Saigh JA: CT of Hodgkin's lymphoma limited to the gallbladder. *Abdom Imaging* 21:238–239, 1996.
- 45. Wibbenmeyer LA, Sharafuddin MJ, Wolverson MK, et al: Sonographic diagnosis of unsuspected gallbladder cancer: imaging findings in comparison with benign gallbladder conditions. *AJR Am J Roentgenol* 165:1169–1174, 1995.
- Puylaert JB, Coerkamp EG: [Tumors in the gallbladder: a possible differentiation between malignant and benign tumours]. *Ned Tijdschr Geneeskd* 151:1653, 2007. author reply 1653.
- Kim SJ, Lee JM, Lee JY, et al: Accuracy of preoperative T-staging of gallbladder carcinoma using MDCT. AJR Am J Roentgenol 190:74–80, 2008.
- Yoshimitsu K, Honda H, Jimi M, et al: MR diagnosis of adenomyomatosis of the gallbladder and differentiation from gallbladder carcinoma: importance of showing Rokitansky-Aschoff sinuses. *AJR Am J Roentgenol* 172:1535–1540, 1999.
- Yoshimitsu K, Honda H, Aibe H, et al: Radiologic diagnosis of adenomyomatosis of the gallbladder: comparative study among MRI, helical CT, and transabdominal US. J Comput Assist Tomogr 25:843–850, 2001.
- Maldjian PD, Ghesani N, Ahmed S, et al: Adenomyomatosis of the gallbladder: another cause for a "hot" gallbladder on 18F-FDG PET. AJR Am J Roentgenol 189:W36–W38, 2007.
- 51. Haradome H, Ichikawa T, Sou H, et al: The pearl necklace sign: an imaging sign of adenomyomatosis of the gallbladder at MR cholangiopancreatography. *Radiology* 227:80–88, 2003.
- Boscak AR, Al-Hawary M, Ramsburgh SR: Best cases from the AFIP: adenomyomatosis of the gallbladder. *Radiographics* 26:941–946, 2006.
- 53. Kaftori JK, Pery M, Green J, et al: Thickness of the gallbladder wall in patients with hypoalbuminemia: a sonographic study of patients on peritoneal dialysis. *AJR Am J Roentgenol* 148: 1117–1118, 1987.

# **Focal Gallbladder Wall Thickening**

AVINASH KAMBADAKONE | DUSHYANT V. SAHANI

Focal gallbladder wall thickening is often an imaging diagnosis and encompasses a wide variety of differential diagnoses. Polypoid lesions of the gallbladder form an important group of conditions that are included in the differential diagnosis of focal gallbladder wall thickening and can be divided into neoplastic and non-neoplastic groups (Figure 57-1). The neoplastic group includes adenomas, leiomyomas, neurofibromas, and gallbladder carcinoma. The non-neoplastic group includes lesions such as cholesterol polyps, inflammatory polyps, adenomyoma, and focal xanthogranulomatous cholecystitis (XGC) (Box 57-1).

#### Gallbladder Adenoma

#### ETIOLOGY

57

The majority of gallbladder adenomas are associated with cholelithiasis (50% to 65%).<sup>1,2</sup> An increased incidence of gallbladder adenomas and biliary tract adenomas are seen in familial adenomatous polyposis and Peutz-Jeghers syndrome.<sup>3,4</sup>

#### PREVALENCE AND EPIDEMIOLOGY

Gallbladder adenomas are uncommon lesions, found in 0.5% of cholecystectomy specimens.<sup>1,2</sup> A small proportion of the gallbladder adenomas can progress to carcinoma, and approximately 10% are multiple.<sup>1,5</sup>

#### **CLINICAL PRESENTATION**

Gallbladder adenomas are usually asymptomatic and incidentally discovered. Large adenomas or sometimes small adenomas can obstruct the cystic duct and cause right upper quadrant pain.<sup>1</sup>

#### PATHOPHYSIOLOGY

The most common variant is a tubular adenoma. They appear as polypoid structures that project into the gallbladder lumen and may be sessile or pedunculated and generally less than 2 cm.

#### IMAGING

Gallbladder polyps with a stalk and a diameter less than 10 mm are predominantly benign.<sup>6</sup> Sessile polyps and those greater than 10 mm in diameter have a higher likelihood of harboring malignancy and are often an indication for elective cholecystectomy.<sup>2,6</sup> Adenomas obstructing the cystic duct may lead to gallbladder hydrops or cholecystitis.

#### Computed Tomography

Gallbladder adenomas are seen as intraluminal soft tissue masses that are isoattenuating or hypoattenuating relative to the liver on contrast-enhanced CT (Table 57-1). These intraluminal masses are difficult to distinguish from noncalcified gallstones on CT, and ultrasonography often helps.<sup>1,7</sup>

#### Magnetic Resonance Imaging

Polyps are usually seen as homogeneous and low to intermediate signal intensity on T1- and T2-weighted images.<sup>6</sup> Contrast enhancement is seen on delayed images.<sup>6</sup>

#### Ultrasonography

The lesions appear as smoothly marginated, intraluminal polypoid masses with an occasional lobulated or cauliflower-like contour (Figure 57-2).<sup>1,2</sup> There is a homogenous hyperechoic echotexture, but the echogenicity decreases with increasing size and large adenomas may have a heterogeneous appearance.<sup>1,2</sup>

The adjacent gallbladder wall characteristically maintains a normal thickness of less than 3 mm.<sup>1</sup> Focal gallbladder wall thickening adjacent to a polypoid mass increases the probability of malignancy.

Gallstones are common in patients with gallbladder adenomas.<sup>1</sup>

#### Positron Emission Tomography With Computed Tomography

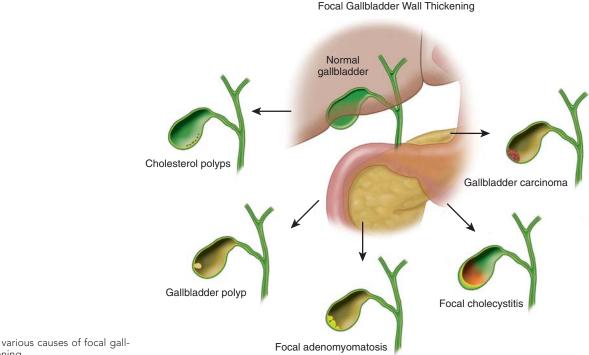
Positron emission tomography (PET) is not usually indicated in the diagnosis of adenomas. However, it has a potential application in ruling out malignancy within a polypoid lesion in the gallbladder.

#### Classic Signs: Gallbladder Adenoma

- A smoothly marginated polypoid, sessile, or
- pedunculated lesion projects into the gallbladder lumen.
- Cholelithiasis is a common association.

#### DIFFERENTIAL DIAGNOSIS

These lesions are usually asymptomatic and thus detected incidentally. Adenomas obstructing the cystic duct may present with symptoms of acute cholecystitis (see Chapter 56). Gallstones are differentiated based on mobility and adherence to the gallbladder wall. Gallbladder carcinoma has a heterogeneous internal architecture with mucosal irregularity, adjacent parenchymal liver invasion, biliary duct dilatation, metastases, and lymphadenopathy.



**Figure 57-1** The various causes of focal gallbladder wall thickening.

#### BOX 57-1 VARIOUS CONDITIONS CAUSING FOCAL GALLBLADDER WALL THICKENING

#### NEOPLASTIC LESIONS

- Benign
- Adenoma
- Leiomyoma
- Neurofibroma
- Malignant
- Gallbladder carcinomaMetastases
- Ivietastase

#### NON-NEOPLASTIC LESIONS

- Cholesterol polyps
- Acute cholecystitis
- Xanthogranulomatous cholecystitis
- Adenomyomatosis
- Gastric and pancreatic rests

#### TREATMENT

Because of their malignant potential, cholecystectomy is recommended for gallbladder adenomas larger than 10 mm.

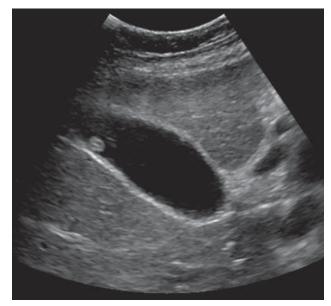
### **Cholesterol Polyps**

#### ETIOLOGY

These benign lesions are uncommonly associated with cholelithiasis and cholesterolosis.<sup>1</sup>

#### PREVALENCE AND EPIDEMIOLOGY

Cholesterol polyps are benign lesions with no malignant potential that account for approximately 50% of the polypoid lesions



**Figure 57-2** Tubular adenoma of the gallbladder in a 56-year-old woman with epigastric discomfort. Transverse ultrasound image shows an echogenic, rounded polyp attached to the gallbladder wall.

in the gallbladder.<sup>1</sup> They predominantly occur in women in their fifth or sixth decades.

#### **CLINICAL PRESENTATION**

Usually asymptomatic, these polyps are typically found in patients who are being evaluated for epigastric discomfort and right upper quadrant pain.<sup>1</sup>

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#### ABLE Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Gallbladder Adenoma

37-1			
Modality	Accuracy	Limitations	Pitfalls
Radiography	Data not available to specify accuracy	Insensitive Nonspecific	Unable to directly visualize the soft tissues of gallbladder
СТ	Data not available to specify accuracy	Radiation exposure Not ideal in pregnant patients	CT may not differentiate noncalcified gallstones from adenomas
MRI	Data not available to specify accuracy	Expensive	
Ultrasonography	Data not available to specify accuracy	Operator dependent	Differentiation from gallstones adherent to the wall may be difficult
Nuclear medicine	Data not available to specify accuracy No role in imaging of adenomas		
PET/CT	Data not available to specify accuracy	Decreased sensitivity in patients with diabetes	Differentiation from gallbladder cancer is not always possible

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

TABLE 57-2							
Modal	ity	Accuracy	Limitations	Pitfalls			
Radiog	graphy	Data not available to specify accuracy	Insensitive Nonspecific	Unable to directly visualize the soft tissues of gallbladder			
СТ		Data not available to specify accuracy	Radiation exposure Not ideal in pregnant patients	Identification is difficult because the polyps have attenuation similar to bile Differentiation from floating stones and tumefactive sludge can be difficult.			
MRI		Data not available to specify accuracy	Expensive				
Ultrasc	onography	Data not available to specify accuracy	Operator dependent				
Nuclea	ar medicine	Data not available to specify accuracy No role in imaging of adenomas					
PET/C	Т	Data not available to specify accuracy	Decreased sensitivity in patients with diabetes				

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

#### PATHOLOGY

The cholesterol polyps are composed of lipid-laden macrophages and are covered by normal gallbladder epithelium that can invaginate and form gland-like structures.<sup>1</sup> They can be single or multiple and usually are less than 10 mm in diameter.<sup>1</sup>

#### IMAGING

Cholesterol polyps are incidental findings on imaging (Table 57-2).

#### Computed Tomography

On unenhanced scans, cholesterol polyps are often not identifiable because they have attenuation values similar to those of bile. These polyps show enhancement on contrast-enhanced computed tomography (CT) and often appear as floating within the lumen of gallbladder because the thin stalk is not detected on CT and hence are mistaken for noncalcified stones or tumefactive sludge.

#### Ultrasonography

Small polyps are seen as round or slightly lobulated, brightly echogenic masses attached to a gallbladder wall with no posterior acoustic shadowing (Figure 57-3).<sup>1</sup>

Larger polyps are less echogenic and are characterized by aggregations of echogenic foci within.<sup>1</sup> The presence of these echogenic aggregates within the large polyps is helpful in differentiating cholesterol polyps from benign adenomas and malignant tumors.<sup>1</sup> Large cholesterol polyps can mimic gall-bladder carcinoma.<sup>8</sup>

#### **Classic Signs: Cholesterol Polyps**

- On ultrasonography, cholesterol polyps are seen as single or multiple nodular brightly echogenic masses attached to the gallbladder wall.
- Posterior acoustic shadowing is not present.
- Cholesterol polyps show enhancement on contrastenhanced CT and are seen as floating within the gallbladder lumen.

#### DIFFERENTIAL DIAGNOSIS

Cholesterol polyps are usually asymptomatic. Gallstones adherent to the gallbladder wall are echogenic and show posterior acoustic shadowing. These are often mistaken for cholesterol polyps. Tumefactive sludge forms another differential diagnosis but can be discerned by the difference in morphology as shown with a change in position of the patient.

Adenomas are smooth, lobulated or rounded masses with a homogeneous echotexture and an identifiable stalk in





Figure 57-3 Ultrasound appearance of cholesterol polyps. Longitudinal (A) and transverse (B) ultrasound images of the gallbladder in a 48-yearold woman with right upper quadrant pain show multiple small echogenic cholesterol polyps (arrows) adherent to the gallbladder wall.

pedunculated polyps. Gallbladder carcinoma is evident by its heterogeneous internal architecture with mucosal irregularity, adjacent parenchymal liver invasion, biliary duct dilatation, metastases, and lymphadenopathy.

#### TREATMENT

Small cholesterol polyps are conservatively treated with follow-up. Large polyps mimicking gallbladder carcinoma may require cholecystectomy to rule out malignancy.

#### Focal Xanthogranulomatous Cholecystitis

ETIOLOGY, PREVALENCE AND EPIDEMIOLOGY, CLINICAL PRESENTATION, PATHOPHYSIOLOGY, AND PATHOLOGY

See Chapter 56, Diffuse Gallbladder Wall Thickening.

#### IMAGING

In addition to the nonspecific clinical presentation, leukocytosis is present.

#### Radiography

The role of conventional radiography in the evaluation of XGC is limited.

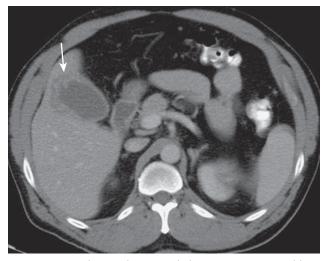
#### Computed Tomography

Focal or diffuse wall thickening is the hallmark of XGC on cross-sectional images.<sup>9-18</sup> Wall thickening is usually in the range of 3 to 25 mm, and the wall thickening may be well defined or ill defined (Figure 57-4).

Low-attenuation bands or nodules are visualized within the thickened gallbladder wall, which represent abscesses of foci of xanthogranulomatous inflammation. The enhancement pattern of the focal process is similar to that of diffuse XGC.

The wall margin with the liver may be indistinct, and extension of inflammatory process into the liver may give a masslike appearance. CT depicts the infiltration of the focal mass into the adjacent soft tissues and fat planes better than ultrasonography. Focal pericholecystic fat infiltration may be seen at times.

Biliary dilatation when present is usually secondary to intraductal stones, hepatoduodenal ligament adenopathy, or coexistent malignancy of the gallbladder or bile duct.



**Figure 57-4** Xanthogranulomatous cholecystitis in a 56-year-old man. Axial contrast-enhanced computed tomography scan of the abdomen shows irregular gallbladder wall thickening at the fundus with mucosal irregularity and extension into the surrounding hepatic parenchyma (*arrow*).

#### Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) features of focal XGC are similar to the diffuse process and are localized to a portion of the gallbladder wall.

#### Ultrasonography

Focal wall thickening with hypoechoic bands or nodules within the thickened gallbladder wall is seen.<sup>9-18</sup> The hypoechoic nodules have been shown to represent abscesses or foci of xanthogranulomatous inflammation. Extension of the inflammatory process into the adjacent liver results in loss of well-defined fat plane between the gallbladder and liver. Other ultrasonographic findings include disruption of the mucosal line, pericholecystic fluid, stones, and intrahepatic biliary dilatation.

#### Positron Emission Tomography With Computed Tomography

XGC can show increased activity on <sup>18F</sup>Fluorodeoxyglucoselabeled PET (FDG-PET) and mimic malignancy, yielding a false-positive result.

#### DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes acute cholecystitis, chronic cholecystitis, and gallbladder carcinoma (see Chapter 56).

#### TREATMENT

See Chapter 56, Diffuse Gallbladder Wall Thickening.

#### Adenomyoma

#### **ETIOLOGY**

See Chapter 56, Diffuse Gallbladder Wall Thickening.

#### PREVALENCE AND EPIDEMIOLOGY

See Chapter 56, Diffuse Gallbladder Wall Thickening. The three variants of adenomyomatous hyperplasia are localized (or fundal), segmental, and diffuse. The localized variant is the most common variant and is also known as adenomyoma.<sup>1,7,19-21</sup>

#### **CLINICAL PRESENTATION**

See Chapter 56, Diffuse Gallbladder Wall Thickening.

#### PATHOLOGY

On gross pathologic examination, adenomyoma characteristically appears as a well-formed semilunar or crescent-shaped mass in the gallbladder fundus.<sup>1,7</sup> The segmental variant is characterized by focal circumferential thickening in the gallbladder wall typically located in the body of the gallbladder, giving it an hourglass configuration on gross inspection.<sup>1,7</sup>

The risks for malignancy associated with adenomyomas are related to the presence of stones, chronic inflammation, and meta-plastic changes rather than adenomyomatous hyperplasia.<sup>1,7</sup>

#### IMAGING

#### Radiography

Calcification of the intramural sludge, cholesterol, or stones present in the Rokitansky-Aschoff sinuses can occur in longstanding adenomyomatosis. These calcifications may be visible on abdominal radiographs as nondependent calcific opacities in the right upper quadrant.<sup>1</sup>

#### Computed Tomography

The localized or focal variant of adenomyomatous hyperplasia appears as a mass of soft tissue attenuation or focal wall thickening in the gallbladder fundus (Figure 57-5). When visualized, the Rokitansky-Aschoff sinus appears as a small cystic structure with water density within the thickened wall. Small calcific densities within these sinuses also may be visualized.<sup>22</sup>

#### Magnetic Resonance Imaging

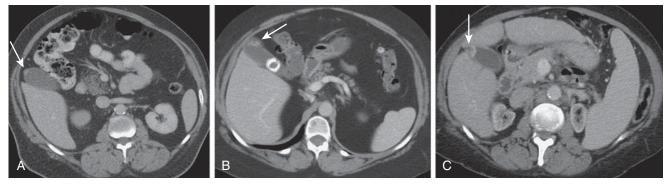
Focal gallbladder wall thickening or focal mass is seen with features similar to those of diffuse adenomyomatosis. Multiple intramural cystic spaces are seen within a focal mass that appear hypointense on T1-weighted images and hyperintense on T2-weighted images. Signal void may be seen within the cystic spaces when intracystic calculi are present. The sinuses at times may show high signal intensity on T1-weighted images, when they are filled with thick bile concretion or debris. The visualization of Rokitansky-Aschoff sinuses on T2-weighted MRI has been reported to be useful in differentiation of adenomyomatous hyperplasia from gallbladder carcinoma.

On gadolinium administration, the focal mass shows enhancement while the cystic spaces are nonenhancing. A "diamond ring" appearance may be seen on transverse sections because of the ringlike distribution of the hyperintense cystic structures around the gallbladder wall on T2-weighted images.<sup>22</sup>

#### Ultrasonography

Focal adenomyomas appear as focal gallbladder wall thickening with intramural diverticula that may be anechoic or contain echogenic foci.<sup>1,7,21-23</sup>

The ultrasonographic hallmark of adenomyomatous hyperplasia is a V-shaped or "comet tail" reverberation artifact emanating from the echogenic gallbladder wall foci.<sup>1,7,21-23</sup> This comet tail artifact is helpful when differentiating this lesion from gallbladder carcinoma. Occasionally, this artifact may be mistaken for air within the gallbladder lumen or wall (emphysematous cholecystitis), which can have a similar appearance. Whereas the dirty shadow of air is more linear in configuration, the reverberation artifacts of adenomyoma are V shaped.<sup>1,7,21-23</sup>



**Figure 57-5** Adenomyoma of the gallbladder in three different patients. A to C, Axial contrast-enhanced computed tomography images of the abdomen show focal wall thickening of the gallbladder at the fundus (*arrows*). The small cystic areas of water attenuation are best seen in B and C within the focal wall thickening and represent the Rokitansky-Aschoff sinuses filled with bile.

#### Nuclear Medicine

Hepatobiliary scintigraphy has no role in the routine evaluation of adenomyomatosis.

# Positron Emission Tomography With Computed Tomography

Adenomyomatosis normally does not show increased activity on FDG-PET. However, the presence of inflammatory reaction may sometimes lead to increased activity on FDG-PET.

#### **Classic Signs: Adenomyoma**

- A focal wall thickening or mass with intramural cystic spaces is seen.
- Reverberation artifact, or comet tail artifact, emanating from the cystic spaces is an important sign on ultrasonography.

#### DIFFERENTIAL DIAGNOSIS

Patients are usually asymptomatic. However, if symptoms do occur, the presentation is similar to that of any other gallbladder disease. See a more detailed discussion in Chapter 56.

#### Treatment

This benign condition requires no specific treatment (see Chapter 56).

#### Gallbladder Carcinoma

# ETIOLOGY, PREVALENCE AND EPIDEMIOLOGY, CLINICAL PRESENTATION

See Chapter 56, Diffuse Gallbladder Wall Thickening.

#### PATHOLOGY

Gallbladder carcinomas are epithelial in origin, and 90% of these are adenocarcinomas.<sup>24-26</sup> Thirty to forty percent of gallbladder

carcinomas present as intraluminal polypoidal lesions. Adenocarcinomas usually result in localized thickening of the gallbladder wall after causing it to bulge into the lumen. Papillary adenocarcinomas are usually sessile with a cauliflower-like appearance.

Infiltrating carcinomas with submucosal spread can appear as focal wall thickening with nodularity and induration of the gallbladder wall.<sup>24-26</sup> Sixty percent of the tumors originate in the gallbladder fundus, 30% in the body, and 10% in the neck.<sup>24-26</sup>

#### IMAGING

Focal wall thickening may represent an early stage of gallbladder cancer.<sup>26</sup> On imaging, focal thickening is difficult to differentiate from an area of fibrosis associated with chronic cholecystitis or an area of adenomatous hyperplasia.<sup>26</sup> In addition, focal thickening can be easily obscured by shadowing from overlying gallstones or missed because of their small size.<sup>26</sup>

Gallbladder carcinoma manifesting as an intraluminal mass can have appearances similar to those of benign tumors, polyps (cholesterol or inflammatory), tumefactive sludge, and blood clots.<sup>26</sup>

For detailed discussion, see Chapter 56, Diffuse Gallbladder Wall Thickening.

#### Radiography

See Chapter 56, Diffuse Gallbladder Wall Thickening.

#### Computed Tomography

Focal wall thickening seen in gallbladder carcinoma can be confused with appearances of more common inflammatory conditions of the gallbladder. However, the presence of pronounced wall thickening (>1 cm) with associated mucosal irregularity suggests malignancy.<sup>24-29</sup>

Polypoid carcinoma exhibits a well-defined, round or oval shape and may be hypoattenuating or isoattenuating on CT. These polypoid masses enhance homogenously and the adjacent gallbladder wall shows thickening, which enhances in the venous phase. CT also readily depicts subtle extension of the tumor beyond the wall of the gallbladder.

Other features indicating malignancy, such as lymphadenopathy, invasion into hepatic parenchyma, biliary dilatation, and presence of liver metastases, can be seen (Figure 57-6).

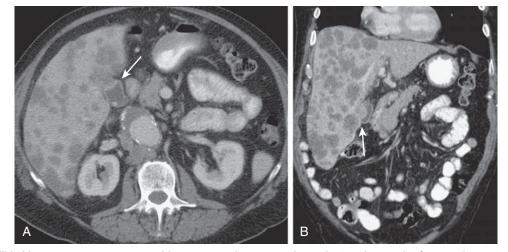
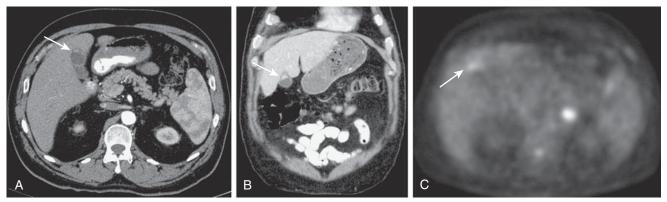


Figure 57-6 Gallbladder carcinoma in a 69-year-old woman. Axial contrast-enhanced (A) and coronal reformatted (B) computed tomography images of the abdomen show a focal gallbladder carcinoma (arrows) adjacent to the gallbladder fossa invading into the adjacent hepatic parenchyma and with associated extensive hepatic metastases.



**Figure 57-7** Melanoma metastases to the gallbladder wall in a 51-year-old man. Axial contrast-enhanced (A) and coronal reformatted (B) computed tomography images show the metastatic focus (*arrows*) appearing as a focal enhancing mass in the fundus protruding into the gallbladder lumen. C, Transaxial fluorodeoxyglucose (FDG)-positron-emission tomography image shows increased FDG uptake within the focal enhancing mass (*arrow*).

#### Magnetic Resonance Imaging

MRI is routinely used to differentiate between gallbladder carcinoma and inflammatory conditions causing focal gallbladder wall thickening.<sup>24-28,30</sup> Gallbladder carcinoma shows focal nodular wall thickening with mucosal irregularity. The tumor appears hypointense on T1-weighted images and hyperintense on T2-weighted images compared with the liver parenchyma. Illdefined early enhancement is typical of gallbladder carcinoma on dynamic imaging. Malignant polypoid lesions larger than 1 cm demonstrate early and prolonged enhancement, whereas benign lesions demonstrate early enhancement with subsequent washout.

#### Ultrasonography

Focal gallbladder wall thickening or focal polypoid mass is seen with overlying mucosal irregularity and heterogenous echotexture. It is possible to differentiate gallbladder carcinoma from sludge, nonshadowing calculi, and blood clot based on motion in real time.

#### Positron Emission Tomography with Computed Tomography

Gallbladder carcinomas show increased FDG uptake on PET and are useful in the differentiation from benign lesions. FDG-PET has a sensitivity of 75%, specificity of 87.5%, and an accuracy of 81.3% for detection of gallbladder carcinoma.

#### DIFFERENTIAL DIAGNOSIS

Other malignant lesions causing focal mass or gallbladder wall thickening include lymphoma and metastases. Gallbladder

#### Classic Signs: Gallbladder Carcinoma

- Focal gallbladder wall thickening occurs with surface nodularity and mucosal irregularity.
- Nodal metastases, biliary dilatation, and invasion of adjacent hepatic parenchyma may occur.
- Gallstones can be present.

wall metastases can occur from melanoma, breast cancer, gastric cancer, renal cell carcinoma, hepatocellular carcinoma, and lung cancer. Gallbladder metastases can manifest as polypoid lesions or infiltrative wall thickening.<sup>31</sup> Whereas ade-nocarcinomas metastasizing to gallbladder manifest as infiltrative wall thickening, nonadenocarcinomatous metastases manifest as polypoid lesions.<sup>31</sup> Melanoma is the most common cause and accounts for 50% to 60% of all reported cases. The ultrasound appearance of melanoma metastases is that of single or multiple hyperechoic masses greater than 1 cm in diameter and attached to the gallbladder wall. The lesions show enhancement on contrast-enhanced CT (Figure 57-7). The characteristic MR feature helps in confirming the diagnosis. Melanoma metastases show high signal intensity on T1-weighted imaging.<sup>32</sup>

#### TREATMENT

See Chapter 56, Diffuse Gallbladder Wall Thickening.

#### What the Referring Physician Needs to Know

#### Gallbladder Adenoma

- Gallbladder adenomas are incidental findings on imaging.
- Adenomas obstructing the cystic duct can manifest as acute cholecystitis.
- Adenomas have malignant potential and can harbor foci of adenocarcinoma.
- Sessile gallbladder adenomas and those greater than 10 mm should raise the suspicion of malignancy and should be treated with cholecystectomy.
- Polypoid lesions less than 10 mm should be periodically followed with ultrasonography to look for features of malignancy such as an increase in size, thickening, and nodularity of the gallbladder wall, the presence of parenchymal hepatic invasion, lymphadenopathy, and biliary duct dilatation.
- Other risk factors for malignancy in gallbladder adenomas are age (>60 years) and cholelithiasis.<sup>7</sup>

#### What the Referring Physician Needs to Know-cont'd

#### **Cholesterol Polyps**

- These benign asymptomatic lesions are detected as incidental findings on imaging.
- Ultrasonography is the most sensitive imaging tool for detection and characterization of cholesterol polyps.

#### Adenomyoma

• Adenomyomatosis of the gallbladder is an incidental finding on imaging.

#### **Key Points**

#### Gallbladder Adenoma

- Gallbladder adenomas are incidental findings.
- Cholelithiasis is frequently associated.
- Obstruction of cystic duct can lead to gallbladder hydrops or acute cholecystitis.
- Adenomas manifest as smoothly marginated, polypoidal, sessile, or pedunculated lesions projecting into the gallbladder lumen.
- Sessile adenomas and those greater than 10 mm have a higher risk for malignancy.

#### **Cholesterol Polyps**

- These asymptomatic incidental lesions account for 50% of polypoid lesions of the gallbladder.
- On ultrasonography, they appear as single or multiple nodular echogenic masses adherent to the gallbladder wall with no posterior acoustic shadowing.

#### Focal Xanthogranulomatous Cholecystitis

- Focal XGC is a variant of chronic cholecystitis characterized pathologically by the presence of lipidladen macrophages.
- Focal gallbladder wall thickening with focal lowattenuation bands or nodules within the gallbladder wall are evident on CT.

• The imaging features of adenomyomatosis can be distinctive enough to allow confident diagnosis; however, findings of gallbladder wall thickening and enhancement are nonspecific.

#### Gallbladder Carcinoma

- Focal gallbladder wall thickening or a focal mass is one of the common manifestations of gallbladder carcinoma.
- CT is the initial imaging investigation of choice for diagnosis and staging of gallbladder carcinoma.
- Focal heterogeneous enhancement of the gallbladder wall with continuous enhancement of the mucosal line can be seen.

#### Adenomyoma

- Adenomyomatosis is an acquired, benign, and degenerative condition of the gallbladder mostly seen in adults.
- It is characterized by epithelial proliferation, muscular hypertrophy, and intramural diverticula.
- Adenomyomatosis can be focal, diffuse, or segmental.
- On imaging, focal gallbladder wall thickening or a mass is seen with intramural cystic spaces that can occasionally be filled with calculi.
- Reverberation or a comet tail artifact emanating from the focal mass or wall thickening is a specific sign.

#### Gallbladder Carcinoma

- The various imaging appearances of gallbladder carcinoma include focal or diffuse wall thickening, polypoidal intraluminal lesion, or an infiltrating mass replacing the gallbladder.
- The presence of adjacent organ invasion or liver or nodal metastases helps its differentiation from other inflammatory conditions mimicking it.

#### SUGGESTED READINGS

- Catalano OA, Sahani DV, Kalva SP, et al: MR imaging of the gallbladder: a pictorial essay. *Radiographics* 28:135–155, quiz 324, 2008.
- Elsayes KM, Oliveira EP, Narra VR, et al: Magnetic resonance imaging of the gallbladder: spectrum of abnormalities. *Acta Radiol* 48:476–482, 2007.
- Gore RM, Yaghmai V, Newmark GM, et al: Imaging benign and malignant disease of the gallbladder. *Radiol Clin North Am* 40:1307–1323, vi, 2002.
- Levy AD, Murakata LA, Abbott RM, et al: From the archives of the AFIP: benign tumors and tumorlike lesions of the gallbladder and extrahepatic bile ducts—radiologic-pathologic correlation. Armed Forces Institute of Pathology. *Radiographics* 22:387–413, 2002.
- Oikarinen H: Diagnostic imaging of carcinomas of the gallbladder and the bile ducts. *Acta Radiol* 47:345–358, 2006.
- Rooholamini SA, Tehrani NS, Razavi MK, et al: Imaging of gallbladder carcinoma. *Radiographics* 14:291–306, 1994.
- Yoon JH, Cha SS, Han SS, et al: Gallbladder adenomyomatosis: imaging findings. *Abdom Imaging* 31:555–563, 2006.

#### REFERENCES

- 1. Levy AD, Murakata LA, Abbott RM, et al: From the archives of the AFIP: benign tumors and tumorlike lesions of the gallbladder and extrahepatic bile ducts—radiologic-pathologic correlation. Armed Forces Institute of Pathology. *Radiographics* 22:387–413, 2002.
- Kumagai Y, Kotanagi H, Ishida H, et al: Gallbladder adenoma: report of a case with emphasis on contrast-enhanced US findings. *Abdom Imaging* 31:449–452, 2006.
- 3. Wada K, Tanaka M, Yamaguchi K, et al: Carcinoma and polyps of the gallbladder associated with Peutz-Jeghers syndrome. *Dig Dis Sci* 32:943–946, 1987.
- Walsh N, Qizilbash A, Banerjee R, et al: Biliary neoplasia in Gardner's syndrome. Arch Pathol Lab Med 111:76–77, 1987.
- Turrini R, Lanzani G, Salmi A: [Gallbladder adenoma with focal adenocarcinoma: a case report]. *Recenti Prog Med* 98:506–508, 2007.
- Elsayes KM, Oliveira EP, Narra VR, et al: Magnetic resonance imaging of the gallbladder: spectrum of abnormalities. *Acta Radiol* 48:476– 482, 2007.
- Terzi C, Sokmen S, Seckin S, et al: Polypoid lesions of the gallbladder: report of 100 cases with special reference to operative indications. *Surgery* 127:622–627, 2000.
- 8. Kaido T, Kano M, Suzaki S, et al: Large cholesterol polyp of the gallbladder mimicking

#### 636 PART 6 Gallbladder, Bile Ducts, and Spleen

gallbladder carcinoma. *Abdom Imaging* 29:100–101, 2004.

- 9. Casas D, Perez-Andres R, Jimenez JA, et al: Xanthogranulomatous cholecystitis: a radiological study of 12 cases and a review of the literature. *Abdom Imaging* 21:456–460, 1996.
- Chun KA, Ha HK, Yu ES, et al: Xanthogranulomatous cholecystitis: CT features with emphasis on differentiation from gallbladder carcinoma. *Radiology* 203:93–97, 1997.
- Dao AH, Wong SW, Adkins RB, Jr: Xanthogranulomatous cholecystitis: a clinical and pathologic study of twelve cases. *Am Surg* 55:32–35, 1989.
- 12. Duber C, Stökel S, Wagner PK, et al: Xanthogranulomatous cholecystitis mimicking carcinoma of the gallbladder: CT findings. *J Comput Assist Tomogr* 8:1195–1198, 1984.
- Fligiel S, Lewin KJ: Xanthogranulomatous cholecystitis: case report and review of the literature. Arch Pathol Lab Med 106:302–304, 1982.
- Houston JP, Collins MC, Cameron I, et al: Xanthogranulomatous cholecystitis. Br J Surg 81:1030–1032, 1994.
- Parra JA, Acinas O, Bueno J, et al: Xanthogranulomatous cholecystitis: clinical, sonographic, and CT findings in 26 patients. *AJR Am J Roentgenol* 174:979–983, 2000.
- Guzman-Valdivia G: Xanthogranulomatous cholecystitis: 15 years' experience. World J Surg 28:254–257, 2004.

- Hsu C, Hurwitz JL, Schuss A, et al: Radiology-Pathology Conference: Xanthogranulomatous cholecystitis. *Clin Imaging* 27:421–425, 2003.
- Ros PR, Goodman ZD: Xanthogranulomatous cholecystitis versus gallbladder carcinoma. *Radiology* 203:10–12, 1997.
- Maldjian PD, Ghesani N, Ahmed S, et al: Adenomyomatosis of the gallbladder: another cause for a "hot" gallbladder on 18F-FDG PET. AJR Am J Roentgenol 189:W36–W38, 2007.
- Yoshimitsu K, Honda H, Aibe H, et al: Radiologic diagnosis of adenomyomatosis of the gallbladder: comparative study among MRI, helical CT, and transabdominal US. J Comput Assist Tomogr 25:843–850, 2001.
- Yoshimitsu K, Honda H, Jimi M, et al: MR diagnosis of adenomyomatosis of the gallbladder and differentiation from gallbladder carcinoma: importance of showing Rokitansky-Aschoff sinuses. *AJR Am J Roentgenol* 172:1535– 1540, 1999.
- Yoon JH, Cha SS, Han SS, et al: Gallbladder adenomyomatosis: imaging findings. *Abdom Imaging* 31:555–563, 2006.
- 23. Haradome H, Ichikawa T, Sou H, et al: The pearl necklace sign: an imaging sign of adenomyomatosis of the gallbladder at MR cholangiopancreatography. *Radiology* 227:80–88, 2003.
- 24. Levy AD, Murakata LA, Rohrmann CA, Jr: Gallbladder carcinoma: radiologic-pathologic

correlation. *Radiographics* 21:295–314, questionnaire, 549-255, 2001.

- Oikarinen H: Diagnostic imaging of carcinomas of the gallbladder and the bile ducts. *Acta Radiol* 47:345–358, 2006.
- Rooholamini SA, Tehrani NS, Razavi MK, et al: Imaging of gallbladder carcinoma. *Radiographics* 14:291–306, 1994.
- Gore RM, Yaghmai V, Newmark GM, et al: Imaging benign and malignant disease of the gallbladder. *Radiol Clin North Am* 40:1307– 1323, vi, 2002.
- Yun EJ, Cho SG, Park S, et al: Gallbladder carcinoma and chronic cholecystitis: differentiation with two-phase spiral CT. *Abdom Imaging* 29:102–108, 2004.
- Kim SJ, Lee JM, Lee JY, et al: Accuracy of preoperative T-staging of gallbladder carcinoma using MDCT. AJR Am J Roentgenol 190:74–80, 2008.
- Catalano OA, Sahani DV, Kalva SP, et al: MR imaging of the gallbladder: a pictorial essay. *Radiographics* 28:135–155, quiz 324, 2008.
- Choi WS, Kim SH, Lee ES, et al: CT findings of gallbladder metastases: emphasis on differences according to primary tumors. *Korean J Radiol* 15:334–345, 2014.
- Takayama Y, Asayama Y, Yoshimitsu K, et al: Metastatic melanoma of the gallbladder. *Comput Med Imaging Graph* 31:469–471, 2007.

# **58**

# Gallbladder and Bile Duct Functional Imaging

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#### **Technical Aspects**

Functional imaging of the gallbladder and bile ducts is a valuable tool, providing critical information for the management of conditions of the biliary system. Modern functional techniques are noninvasive and can permit earlier and improved disease characterization resulting in appropriate and timely patient care.

Ultrasonography is typically used as the initial modality for assessment of the biliary tree because it is fast, inexpensive, and noninvasive. Although highly sensitive in the evaluation of the gallbladder, ultrasound is limited in assessment of the extrahepatic biliary tree and intrahepatic bile ducts in the absence of biliary dilatation. T2-weighted magnetic resonance cholangiopancreatography (MRCP) is an MR technique performed with fast and heavily T2-weighted sequences providing optimal, noninvasive depiction of the fluid-containing biliary tree and requires no contrast. However, functional assessment of the biliary tree is based on evaluation of morphologic changes such as biliary duct dilatation, stricture, or filling defects. Additionally, MRCP does not allow objective evaluation of partial or complete obstruction of bile flow.

Oral cholecystography or cholescintigraphy allow noninvasive functional assessment of the gallbladder and the biliary tree (see later discussion). However, both oral cholecystography and cholescintigraphy have been gradually replaced by functional MR cholangiography (fMRC) and computed tomography (CT) cholangiography. Both the latter techniques require administration of contrast agents, which are eliminated via the biliary ducts, and have the potential to provide comprehensive evaluation of both the anatomy and function of the gallbladder and biliary tree.

#### FUNCTIONAL MAGNETIC RESONANCE CHOLANGIOGRAPHY

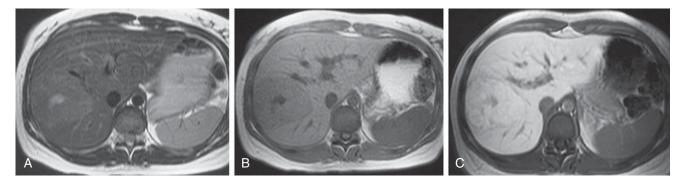
fMRC is an MR technique performed with hepatobiliary contrast agents. Hepatobiliary contrast agents with liver-specific properties have been developed primarily to increase the accuracy of MRI in the detection and characterization of focal liver lesions; however, the biliary excretion of these agents have since been explored to provide functional information about the biliary tracts.

Exclusive distribution to the hepatocellular compartment can be obtained using contrast agents that, when injected by slow infusion, accumulate within the hepatocytes and cause an increase in the proton relaxation rate. Mangafodipir trisodium (Mn-DPDP, Teslascan, GE Health, Milwaukee, WI) is a hepatobiliary MR imaging contrast agent that consists of manganese bound to dipyridoxyl diphosphate. As a result of its five unpaired electrons, manganese is moderately paramagnetic, resulting in high signal intensity on T1-weighted images. Dipyridoxyl diphosphate has a chemical structure similar to that of vitamin  $B_6$ . After intravenous injection, mangafodipir trisodium is taken up by functioning hepatocytes through vitamin  $B_6$ receptors. Extrahepatic uptake is observed when some of the manganese dissociates from its ligand within the blood circulation. The free manganese is then available for uptake into parenchymal cells, particularly those of the liver, pancreas, kidneys, and adrenals, in which metabolism of this metal takes place.

In Europe, mangafodipir trisodium is infused slowly (2 to 3 mL/min over a 10- to 20-minute period) at a dosage of 5-10 µmol/kg, whereas in the United States a faster injection (~1 minute) is employed. The maximum tissue enhancement is observed at the end of the infusion after approximately 20 minutes and lasts for around 4 hours. The liver parenchyma enhances significantly after mangafodipir trisodium administration, whereas tumors of nonhepatocytic origin show little or no enhancement, resulting in increased lesion conspicuity (Figure 58-1). Several studies have shown improved lesion detection on images obtained after infusion of mangafodipir trisodium.<sup>1</sup> Many hepatocellular lesions, on the other hand, show enhancement, thereby resulting in decreased tumor-liver contrast-to-noise ratio (Figure 58-2). Uptake of mangafodipir trisodium, and therefore enhancement, by both benign and malignant hepatic neoplasms of hepatocellular origin limits their accurate differentiation and therefore represents a major shortcoming of this agent.<sup>2</sup> One important advantage of this contrast agent is its biliary excretion, which is obtained in the same time window after the injection as that for the enhancement of the liver parenchyma. This excretion reflects the functionality of the hepatocytes and makes the bile bright on T1-weighted sequences. The high signal intensity of the biliary system during excretion of the contrast agent produces excellent contrast with the liver parenchyma and hepatic vessels in the background. Thus, it is possible to use T1-weighted gradient recalled echo three-dimensional (3D) images for high-resolution imaging of the biliary ducts. Source images from the 3D data set are reviewed, and maximum intensity projection (MIP) images are generated with and without a restricted volume. In March 2004, manufacturing of mangafodipir in the United States had been suspended by GE Health but resumption of manufacturing is expected, although its manufacturing continues in the other countries.



Figure 58-1 Liver metastases from colon carcinoma. Spin echo T2-weighted magnetic resonance image (A) shows a hyperintense lesion with central necrotic changes. Gradient recalled echo T1-weighted images before (B) and after (C) administration of mangafodipir trisodium. After administration of the contrast agent there is an increase of the contrast ratio owing to the lack of uptake of the agent by the lesion.



**Figure 58-2** Focal nodular hyperplasia. Spin echo T2-weighted magnetic resonance (MR) image (A) shows a hyperintense lesion with a central scar. Gradient recalled echo T1-weighted MR images before (B) and after (C) administration of mangafodipir trisodium. After administration of the contrast agent the lesion is hyperintense with a decrease of the contrast ratio owing to uptake of the agent by the lesion.

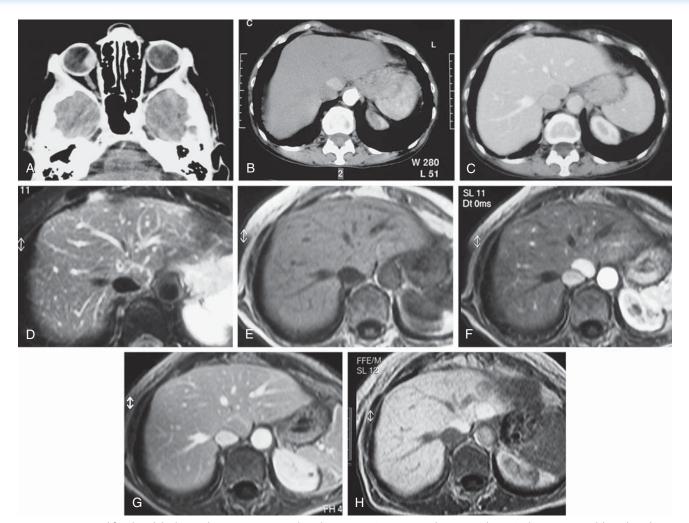
Other contrast agents demonstrate combined perfusion and hepatocyte-selective properties. Such compounds distribute initially to the vascular-interstitial compartment in a manner analogous to that of the conventional, extracellular contrast agents. Thereafter, a fraction of the injected dose is taken up into the hepatocytes, causing an increase of the signal intensity of the hepatic tissue. Agents of this type include gadobenate dimeglumine (Gd-BOPTA) and gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA).

Gd-BOPTA is a chelate of gadolinium and benzyloxypropionictetraacetic acid. It was approved for use in the United States in December 2004 and has been used in Europe for several years. Gd-BOPTA is a second-generation gadolinium chelate that combines the properties of a conventional extracellular gadolinium agent with those of an agent targeted specifically to the liver.<sup>3</sup> Two features that distinguish Gd-BOPTA from the conventional gadolinium chelates are a capacity for weak and transient interaction with serum albumin and an elimination profile that sees roughly 96% of the injected dose excreted renally via glomerular filtration; the remaining 2% to 4% is taken up by functioning hepatocytes and eliminated in the bile via the hepatobiliary pathway. Whereas the former feature confers on Gd-BOPTA a twofold greater T1 relaxation rate in vivo, the latter leads to a marked and long-lasting enhancement of the signal intensity of normal liver parenchyma, resulting in an additional, delayed imaging window beginning 40 minutes after Gd-BOPTA administration.<sup>4</sup> Studies have shown that although Gd-BOPTA behaves in an analogous way to

conventional gadolinium agents during the dynamic phase of contrast enhancement, in the delayed phase it improves the impact of MRI for the detection of focal liver lesions<sup>5</sup> and may also contribute to the improved characterization of detected lesions, particularly lesions demonstrating atypical enhancement on dynamic imaging (Figure 58-3).<sup>6</sup>

Gd-EOB-DTPA exploits the carrier used by hepatocytes for the uptake of bilirubin.<sup>7</sup> In a manner analogous to that of Gd-BOPTA, this contrast agent distributes initially to the vascular-interstitial compartment after injection. However, whereas only 2% to 4% of the injected dose of Gd-BOPTA is thereafter taken up by hepatocytes and eliminated in the bile, in the case of Gd-EOB-DTPA some 50% of the injected dose is taken up and eliminated via the hepatobiliary pathway after approximately 60 minutes. The maximum increase of liver parenchyma signal intensity is observed approximately 20 minutes after injection and lasts for approximately 2 hours.<sup>8</sup> During the perfusion phase the dynamic enhancement patterns seen after injection of Gd-EOB-DTPA are similar to those seen with Gd-DTPA, whereas during the hepatobiliary phase Gd-EOB-DTPA-enhanced images have been shown to yield a statistically significant improvement in the detection rate of metastases, hepatocellular carcinomas, and focal nodular hyperplasia compared with unenhanced and Gd-DTPA-enhanced images.

Also with these contrast agents, it is possible to analyze their biliary excretion with T1-weighted gradient recalled echo 3D images. There are no available data comparing the two contrast



**Figure 58-3** Atypical focal nodular hyperplasia in a patient with melanoma. A, On computed tomography (CT) a lesion compatible with melanoma is visible in the right eye. B and C, CT of the liver—arterial (B) and portal (C) phases—shows a hypervascular lesion with washout in the portal phase in the caudate lobe that is suggestive of liver metastasis from melanoma. D to H, On magnetic resonance imaging the lesion is isointense both on T2-weighted (D) and unenhanced T1-weighted gradient recalled echo (E) images. During dynamic imaging after injection of gadobenate dimeglumine, the lesion is hypervascular on the arterial phase (F), with washout in the portal phase (G). At the hepatobiliary phase, 2 hours after the injection (H), both the liver and the lesion are hyperintense owing to contrast uptake.

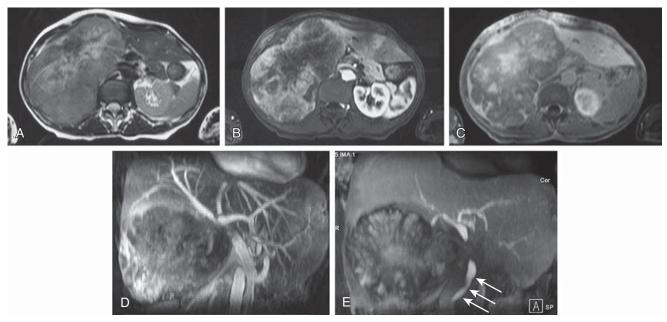
agents in their biliary excretion, although the greater percentage of biliary excretion of Gd-EOB-DTPA should give a better contrast of the biliary ducts. However, in practical comparison with normal patients, no significant differences can be appreciated, whereas in patients with liver-impaired function, the biliary excretion of Gd-BOPTA is very low.<sup>10</sup>

A major advantage of these contrast agents compared to mangafodipir trisodium is the possibility to use them for dynamic imaging of the liver. Thus, in addition to arterial and portal phase imaging for detection and characterization of liver lesions, hepatic arterial and portal vein status can be evaluated. Vascular assessment, together with parenchymal imaging and functional biliary imaging, can provide a comprehensive evaluation of hepatic disease ("one-stop shopping technique" (Figure 58-4). If T2-weighted MRC and fMRC have to be performed in the same sitting, it is advisable to perform fMRC sequences after T2-weighted MRC sequences, to avoid T2 shortening effects related to the excretion of the hepatobiliary contrast agent in the biliary tree.<sup>9</sup>

#### COMPUTED TOMOGRAPHY CHOLANGIOGRAPHY

CT cholangiography is performed after intravenous drip infusion of a biliary contrast agent that is excreted by the biliary system and induces opacification of the gallbladder and the biliary tree after at least 15 to 20 minutes. High spatial resolution CT is commonly performed, with thin sections (1 to 2 mm thickness), to allow high-resolution multiplanar reformation (MPR) images and 3D postprocessed images.

CT cholangiography has shown potential for the depiction of biliary tree anatomy. Some authors have reported better biliary tract visualization with CT cholangiography than T2-weighted MRC or fMRC, either alone or in combination in potential living donors,<sup>11</sup> because it may provide better depiction of second-order biliary branching. Additionally, CT cholangiography is an inexpensive and widely available technique compared with fMRC. However, there are factors limiting its application in routine clinical evaluation.



**Figure 58-4** Fibrolamellar hepatocellular carcinoma. A, Turbo spin echo T2-weighted image. A large hyperintense lesion with central necrotic changes can be appreciated in the right lobe. B and C, During dynamic imaging after injection of gadobenate dimeglumine, the lesion is hypervascular on the arterial phase (B), with washout in the portal phase (C). The data of the portal phase were reviewed, and maximum intensity projection (MIP) images of the portal vein were generated (D), showing involvement of the main trunk of the portal vein. At the hepatobiliary phase, 2 hours after the injection (E), MIP image shows clear evidence of the main biliary ducts, which appear hyperintense owing to the presence of contrast agent in the bile. The common bile duct is not recognizable at the level of the lesion because of involvement, but the passage of bile in the lower segment is still maintained (arrows).

### TABLEPros and Cons of Functional Magnetic Resonance Cholangiography and Computed Tomography58-1Cholangiography for Functional Imaging of the Gallbladder and the Biliary Tree

Imaging Type	Pros	Cons
fMRC	Noninvasive No exposure to ionizing radiation Good anatomic depiction of biliary tree anatomy 3D postprocessing possible Functional evaluation possible Higher experience than CT cholangiography	More expensive than CT cholangiography State-of-art MR scanners not widely available
CT cholangiography	Noninvasive Good anatomic depiction of biliary tree anatomy Functional evaluation possible MPR and 3D postprocessing possible	Risk for adverse reactions to biliary contrast agent High exposure to ionizing radiation Availability of biliary contrast agents Limited experience

3D, Three-dimensional; CT, computed tomography; fMRC, functional magnetic resonance cholangiography; MPR, multiplanar reformation; MR, magnetic resonance.

CT cholangiography contrast agents reportedly have a higher rate of adverse reactions, compared with hepatobiliary contrast agents for fMRC, suggesting the need for premedication of all patients with antihistaminic drugs before the examination. High spatial resolution CT with isotropic voxel reconstruction should be performed for multiplanar reconstructions to optimally depict biliary anatomy that could increase radiation dose. Furthermore, high spatial resolution images are improving with recent state-of-the art MRI.

Although CT cholangiography has been evaluated and is in clinical use in Asia and Europe, its application in routine clinical evaluation is still limited. CT cholangiography in routine clinical evaluation is confined to selected cases, and experience with this technique is lower than with other functional imaging techniques.

### **Pros and Cons**

See Table 58-1.

#### **Normal Anatomy**

The gallbladder and cystic duct develop from a diverticulum that develops in the caudal portion of the primitive hepatic duct. Within 3 months of gestation, the entire biliary system and gallbladder have canalized to form a continuous lumen. Bile capillaries communicate with biliary canaliculi creating a small passage between two contiguous hepatocytes; they encircle the hepatic lobule and open into the interlobular bile ducts. They join with other ducts and form segmental ducts in the left and right lobes of the liver (anterior and posterior segmental ducts), which fuse, respectively, into the main left and right hepatic ducts (LHD and RHD).

The main LHD and RHD normally converge and form the common hepatic duct (CHD), which passes for approximately 4 cm between the layers of the lesser omentum, where it is joined at an acute angle by the cystic duct and thus forms the common bile duct (CBD). The CBD consists of supraduodenal, retroduodenal, pancreatic, and intraduodenal segments; its terminal portions, the terminal portion of pancreatic ducts, and their common channel are encircled by the muscular structure of the sphincter of Oddi.

The gallbladder is a thin-walled, musculomembranous sac that generally holds 20 to 30 mL and generally measures 7 to 10 cm in length and 3 cm in width. It is located in a fossa on the inferior surface of the right lobe of the liver. It is divided into a fundus, projecting beyond the anterior margin of the liver, body, and neck, and converges into the cystic duct.

Bile is the liquid flowing in the biliary system that is composed of three major components: cholesterol, bile salts, and bilirubin. It is continuously formed in the liver, but its flow into the duodenum is regulated by periodic relaxation of the sphincter of Oddi, and then it accumulates in the hepatic duct and in the CBD when this sphincter is contracted. As pressure in the CBD increases to 50 to 70 mm H<sub>2</sub>O, bile flows into the cystic duct and accumulates in the gallbladder. In the gallbladder, bile concentrates as a result of H<sub>2</sub>O absorption and manifests as increased viscosity, compared with the hepatic bile, owing to mucin secretion from the gallbladder wall. Gallbladder emptying is mainly the result of hormonal stimuli. When gastric contents reach the duodenum, cholecystokinin (CCK) is released from the duodenal wall, causing the gallbladder to contract and the sphincter of Oddi to relax, allowing bile to empty. In addition, CCK allows the cystic duct and sometimes the CBD to contract. Coordination of gallbladder and sphincter of Oddi function also may be influenced by nerve bundles that connect the gallbladder and the sphincter of Oddi via the cystic duct.

# Pathophysiology and Pathologic Correlation

A wide range of pathologic conditions directly or indirectly affect the biliary tree and the gallbladder in adult patients, as well as in neonatal or young patients, with a wide range of clinical outcome. Some of those pathologic conditions result in altered physiology of the biliary tree and gallbladder, as well as in altered physiology of bile. The role of functional imaging, with particular focus on fMRC, in a range of pathologic conditions affecting the gallbladder and the biliary tree is described.

#### **BILIARY ANATOMY**

The anatomy of the biliary tree is highly variable, and 24% to 57% of individuals have variant biliary patterns.<sup>12,13</sup> Accurate preoperative assessment of the anatomy of biliary tree is essential for the surgeon to identify variant biliary anatomy, which is critical for hepatobiliary surgeries especially because of the increased number of adult-to-adult liver transplantations performed in which the right hepatic lobe of the living donor is transplanted into the recipient.<sup>14</sup> Particularly relevant are the variations of the biliary tree anatomy involving the drainage of the RHDs, mainly the right posterior one. Normally, the union of the anterior duct (from segments V and VIII) and the

posterior duct (from segments VI and VII) forms the RHD, which joins the LHD. The RHD and LHD converge into the CHD, which joins the cystic duct coming from the gallbladder to form the CBD. Most of the variations occur in the RHD, typically including the anomalous insertion of the right posterior duct (draining segments VI and VII) into the LHD, the CHD, or the CBD.<sup>12</sup> In living adult-to-adult liver transplantations, therefore, variants of the biliary anatomy may increase the risk for postoperative complications, including bilary leaks and strictures, in both the donor and the recipient,<sup>13</sup> and reliable preoperative assessment of any variant in biliary tree anatomy is critical for the safety of donors and to improve the selection of suitable candidates.<sup>13,14</sup>

Intraoperative cholangiography, which has been traditionally used for mapping the biliary anatomy in transplant surgery, increases operative time. Endoscopic retrograde cholangiopancreatography (ERCP) is an invasive technique with a major complication rate of 1.4% to 3.2%.15 T2-weighted MRC has been shown to be accurate in the identification of biliary abnormalities and variant extrahepatic biliary anatomy but may be inadequate for evaluation of a nondilated biliary tree. fMRC performed after the administration of a hepatobiliary contrast agent can be used for optimal depiction of biliary tree anatomy using T1-weighted 3D gradient recalled echo sequences with a nearly isotropic voxel size. Because of the high contrast and spatial resolution of T1-weighted imaging in fMRC, it is possible to use volume-rendering algorithms for multiplanar reconstructions that facilitate the depiction of the complex orthogonal relationships among biliary ducts, which may be critical for distinguishing between biliary trifurcation (with which single duct-to-duct anastomosis might still be performed in a recipient, as surgeons prefer) and right posterior duct draining into the LHD (which precludes single duct-to-duct anastomosis; Figure 58-5).14 In the 108 patients studied by Lee and colleagues,14 the addition of mangafodipir trisodiumenhanced volumetric MRC to conventional T2-weighted MRC significantly improved identification of biliary anatomic variants, particularly right biliary duct variants, the detection of which can be critical in living adult-to-adult transplantation of the right lobe of the liver. However, the new T2-weighted



**Figure 58-5** Biliary anatomic variants. Right posterior duct draining into the left hepatic duct. Maximum intensity projection images of three-dimensional gradient recalled echo T1-weighted sequence 2 hours after the injection of gadobenate dimeglumine. The right posterior duct drains (*arrow*) into the left hepatic duct.

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sequences with free-breathing and navigator technique have high-resolution capability, which competes with that of fMRC, although they lack in functional information.

#### **BILIARY LEAKS**

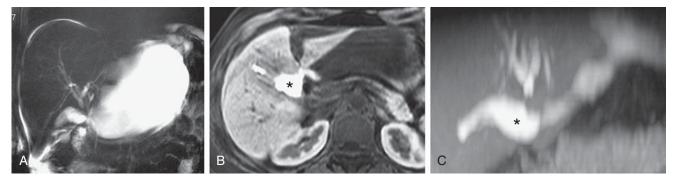
The increased number of hepatobiliary surgical procedures, such as laparoscopic cholecystectomies and liver transplantations, have been associated with an increase in postoperative biliary complications, which are a major cause of morbidity and mortality.<sup>16</sup> Injuries after cholecystectomy include leaks at the cystic duct, from the gallbladder bed, from an accessory cystic duct, or from a tear in a main bile duct. Injuries after hepatic surgery may include bile leaks from the site of a biliary anastomosis, a dislodged or removed external drainage tube, or a bile duct damaged after surgery or trauma; they are the most frequent acute biliary complications during the first few weeks after liver transplantation. Accurate diagnosis has become crucial for these patients, but they often have multiple investigations (ultrasonography, CT, hepatobiliary scintigraphy, and ERCP) and there is often a delay in making the diagnosis.<sup>17</sup> Hepatobiliary scintigraphy is a highly sensitive and specific functional test, but in 81% of patients it does not allow documentation of the leak location.<sup>1</sup>

T2-weighted MRC does not provide functional information<sup>17,18</sup> but only shows indirect evidence of bile leakage (e.g., peritoneal fluid or loculated fluid collections) instead of directly depicting it. Furthermore, this technique may be limited by its inability to differentiate in some cases bile leaks from common findings of the postoperative period, such as ascites, perihepatic fluid collections, and soft tissue edema. fMRC can provide both anatomic and functional assessment of the biliary tree.<sup>17</sup> When a bile leak is present, free extravasation of a hepatobiliary contrast agent is seen on T1-weighted imaging at fMRC in the delayed phase. Thus, fMRC allows direct visualization of biliary leaks and their sites (Figure 58-6), as well as the identification of bile collections (biloma), after surgery (Figure 58-7) or trauma (Figure 58-8 and 58-9).<sup>16</sup>

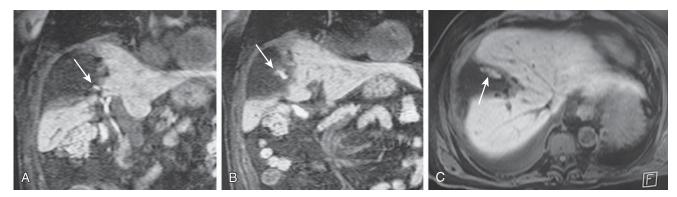
Furthermore, fMRC may detect biliary leaks that do not communicate with the central biliary tree and thus are not detected on ERCP (Luschka's ducts, strictures, stones), because it is an anterograde technique.<sup>17</sup> fMRC with hepatobiliary contrast agents is highly recommended when biliary leak is clinically suspected, but findings at T2-weighted MRC or ERCP are negative.

#### **BILIARY DRAINAGE**

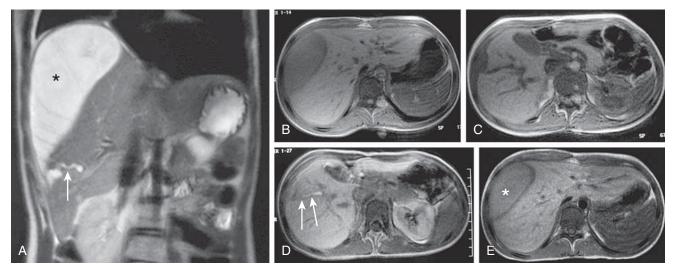
T2-weighted MRC is widely used in the assessment of the gallbladder and biliary tree, owing to its successful depiction of anatomic detail, but it may have shortcomings in the assessment of biliary drainage. Some studies report the use of T2-weighted



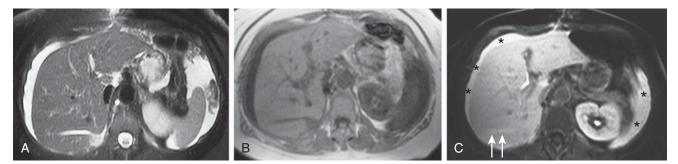
**Figure 58-6** Bile leaks from the site of a biliary anastomosis. **A**, T2-weighted half-Fourier acquisition single-shot turbo spin echo (HASTE) sequence. The identification of the biliary leak is hampered by the fluid in the stomach. After administration of mangafodipir trisodium, a collection of bile (*asterisks*) can be appreciated at the level of the anastomosis on the gradient recalled echo T1-weighted image (**B**), whose relationship with the bile ducts is better appreciated with maximum intensity projection images (**C**). (*Courtesy Alfonso Ragozzino, MD, Radiology Department, Ospedale SM Grazie, Pozzuoli, Italy.*)



**Figure 58-7** Biloma after partial liver resection. A to C, T1-weighted gradient recalled echo images after injection of mangafodipir trisodium. A small collection of hyperintense bile resulting from the presence of the contrast agent can be observed (*arrows*) at the level of the hepatic resection.



**Figure 58-8** Biloma after trauma. A, Coronal T2-weighted magnetic resonance (MR) sequence. A large subcapsular fluid collection (*asterisk*) with a small hepatic lesion (*arrow*) can be appreciated in the right lobe of the liver in a young girl. B to E, Axial gradient recalled echo T1-weighted MR images before (B and C) and after (D and E) administration of gadobenate dimeglumine. After enhancement, the small hepatic lesion (*arrows*, D) in the right lobe of the liver is hyperintense, owing to the presence of bile leakage. The biloma becomes hyperintense (*asterisk*, E) after contrast agent administration owing to the persistence of communication with the bile leak. (*Courtesy Luigi Grazioli, MD, Radiology Department, Civic Hospital Brescia, Brescia, Italy.*)



**Figure 58-9** Biliary ascites after trauma. **A**, Axial T2-weighted sequence. A fluid collection in the peritoneal area with a small hepatic lesion in the right lobe of the liver can be appreciated in a 59-year-old woman. Axial gradient recalled echo T1-weighted images before (**B**) and after (**C**) administration of gadobenate dimeglumine. After enhancement, the small hepatic lesion (*arrows*, **C**) in the right lobe of the liver is hyperintense, owing to the presence of bile leakage. The ascites becomes hyperintense (*asterisks*, **C**) after contrast agent administration as a result of the communication with the bile leak.

MRC under CCK stimulation or fatty meal and suppressed fluid signal of duodenum by an iron agent.<sup>19</sup> In the latter study, T2-weighted MRC thick-slab imaging was repeated on the same volume every 30 seconds for 40 minutes, allowing assessment of bile drainage into the duodenum by the increase of its signal intensity over time. fMRC provides assessment of biliary drainage into the duodenum, by the direct visualization of the bile, which manifests as high signal intensity in T1-weighted sequences, owing to the biliary excretion of hepatobiliary contrast agents. The visualization of an excreted contrast agent in the biliary tree and duodenum provides more easily interpretable functional information regarding biliary drainage and the rate of biliary excretion.<sup>20</sup> Although there are no established norms for rates of hepatobiliary contrast agent excretion, fMRC can be extremely useful in the evaluation of biliary drainage in patients with and without a surgically bypassed biliary system.<sup>20</sup>

#### SPHINCTER OF ODDI DYSFUNCTION

Sphincter of Oddi dysfunction includes a heterogeneous group of clinical pain syndromes caused by dysmotility or stenosis of the sphincter, leading to reduced transphincteric flow of bile or pancreatic juice. The diagnosis of sphincter of Oddi dysfunction is based on clinical signs (impaired liver function), imaging signs (extrahepatic duct >12 mm), and functional signs (delayed emptying of contrast agent, more than 45 minutes after ERCP).<sup>20</sup> Manometry, although still considered the gold standard, is an invasive procedure. T2-weighted MRC is a noninvasive technique that can reliably assess for imaging signs related to sphincter of Oddi dysfunction; it provides an optimal identification of biliary tree dilatation, which is an indirect sign of altered biliary drainage. However, T2-weighted MRC provides no useful information about functional signs related to sphincter of Oddi dysfunction, such as delayed biliary drainage, leading to a relatively low specificity and sensitivity. There is some evidence that secretin-stimulated T2-weighted MRC could improve performance of standard T2-weighted MRC for the assessment of a patient with suspected sphincter of Oddi dysfunction, because it could improve the selection of patients most likely to benefit from endotherapy.<sup>21</sup> fMRC provides optimal identification of imaging signs related to sphincter of Oddi dysfunction, such as biliary tree dilatation, owing to the



**Figure 58-10** Sphincter of Oddi dysfunction in a young man who presented with subtle cholestasis and episodic gastric pain. **A**, T2-weighted magnetic resonance cholangiography is normal; the dynamic acquisition never displayed completely the sphincter area. **B** and **C**, After administration of gadolinium-ethoxybenzyl-diethylenetetraminepentaacetic acid, the bile ducts and the gallbladder are filled and appear normal at 30 (**B**) and 45 (**C**) minutes. No contrast medium is displayed in the duodenum. (*Courtesy Celso Matos, MD, Radiological Department, Hospital Erasme, Brussels, Belgium.*)

high spatial and contrast resolution of 3D T1-weighted imaging. In addition, fMRC provides the objective assessment of biliary drainage, with reliable identification of any delayed hepatobiliary contrast agent drainage (Figure 58-10).

#### DIAGNOSIS OF COMPLETE OBSTRUCTION

T2-weighted MRC can suggest the diagnosis of biliary obstruction by the optimal depiction of a dilated biliary tract. However, fMRC may provide better diagnosis of complete biliary obstruction compared with T2-weighted MRC alone, owing to the hepatobiliary contrast agent physiology. Fayad and associates<sup>18</sup> showed that fMRC increased the average diagnostic accuracy for CBD obstruction over standard MRC alone. In early obstruction, biliary ducts may be of normal caliber and missed with T2-weighted MRC. In cases of resolved prior obstructions, biliary ducts may remain dilated and misdiagnosed as new or recurrent obstructions.<sup>20</sup>

#### **STENT PATENCY**

T2-weighted MRC can only indirectly suggest stent patency by the visualization of normal proximal biliary ducts. However, the direct visualization of internal bile lumen may be difficult by T2-weighted MRC, also owing to susceptibility to artifact formation in different stent types. In contrast, fMRC allows the direct visualization of biliary contrast within a plastic stent providing convincing evidence of stent patency.

#### **STRICTURES**

T2-weighted MRC provides depiction of biliary anatomy, owing to the high signal intensity of the bile in heavily T2-weighted sequences. Thus, optimal depiction of biliary ducts is achieved when they contain bile and especially when dilated. It can be difficult, then, to differentiate a segment of nondistended duct from a strictured segment by T2-weighted MRC, and additional examination providing functional assessment of biliary ducts might be required. ERCP may solve such doubtful findings of T2-weighted MRC.ERCP has a great advantage over T2-weighted MRC because of the ability of the contrast agent to distend the ducts with a suspected stricture. However, ERCP is an invasive technique and complications related to the procedure have been reported.<sup>15</sup> Cholescintigraphy is able to provide functional assessment of biliary ducts, but strictures are uncommonly visualized and the diagnosis of partial obstruction is not made in up to 50% of patients with this technique.<sup>22</sup>

fMRC provides functional assessment of biliary ducts by the biliary excretion of hepatobiliary contrast agent. Thus, the presence or absence of hepatobiliary contrast agent in the bile duct with a suspected stricture may objectively account for the presence or absence of a biliary stricture, respectively. Furthermore, the high contrast and spatial resolution of fMRC imaging is supposed to overcome some of the artifacts of T2-weighted MRC related to flow and vascular pseudolesions that mimic filling defects and strictures. The addition of fMRC sequences after administration of a hepatobiliary contrast agent to the T2-weighted MRC is advisable in the workup of a patient with suspected biliary stricture, because it may improve the diagnosis in doubtful cases (Figure 58-11). As reported in the experience by Fayad and associates,<sup>18</sup> better sensitivity in the diagnosis of strictures was achieved when fMRC was performed in combination with T2-weighted MRC than alone and the primary role of fMRC in evaluating strictures may therefore relate to the functional assessment of drainage rather than the morphology of the stricture. The combination of T2-weighted MRC with fMRC is suggested for a comprehensive evaluation of biliary strictures.

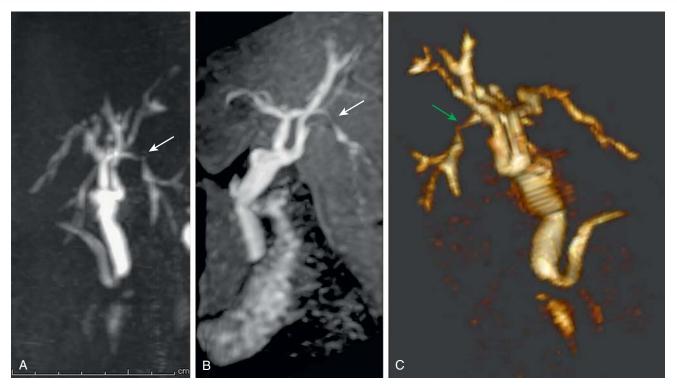
#### ACUTE CHOLECYSTITIS

The role of T2-weighted MRC in the assessment of acute cholecystitis relies mainly on the detection of impacted calculi in the cystic duct or gallbladder neck, which constitutes the most important cause of acute cholecystitis. However, associated findings other than gallstones are not commonly assessed by T2-weighted MRC.

The potential advantage of fMRC over T2-weighted MRC can be related to its ability to provide functional assessment of biliary dynamics.

When there is high clinical suspicion of cystic duct obstruction and findings at T2-weighted MRC are equivocal or negative, fMRC can provide definitive diagnosis. If in delayed scanning (up to 60 minutes) there is no opacification by hepatobiliary contrast agent of the gallbladder but normal opacification of the CBD and bowel (Figure 58-12) acute cholecystitis is present.

Again as demonstrated by Fayad and associates,<sup>18</sup> fMRC alone or in combination with T2-weighted MRC showed significantly increased diagnostic confidence for the detection of



**Figure 58-11** A patient presented with clinical suspicion of primary sclerosing cholangitis (PSC). A and B, Stricture (arrows) of the posterior biliary duct of the right lobe of the liver is suspected on T2-weighted magnetic resonance cholangiography. C, Stricture of the posterior biliary duct (arrow) of the right lobe is objectively confirmed by functional magnetic resonance cholangiography, and the patient was diagnosed with PSC at an early stage.



**Figure 58-12** Biliary stone in the neck of the gallbladder in a patient with clinical suspicion of acute cholecystitis. **A**, T2-Weighted images show hyperintense bile in the fundus as well as in the neck of the gallbladder; no objective assessment of biliary dynamics is possible. **B** and **C**, Delayed T1-weighted scanning after administration of a hepatobiliary contrast agent (gadobenate dimeglumine) shows no opacification of the body and the fundus of gallbladder but normal opacification of the neck of the gallbladder, as well as of the cystic duct and the common bile duct; assessment of biliary dynamics is provided, with objective identification of obstruction at the level of the gallbladder neck (arrows).

acute and chronic cholecystitis, compared with T2-weighted MRC alone.

Kim and coworkers<sup>23</sup> compared T2-weighted MRC, fMRC with mangafodipir trisodium, and hepatobiliary scintigraphy in patients having acute cholecystitis clinically and at ultrasonography who were undergoing surgery. They noted that in all patients biliary dynamics depicted at fMRC agreed completely with those depicted at hepatobiliary scintigraphy and concluded that fMRC, when combined with T2-weighted MRC, provides not only morphologic but also reliable functional information.

#### **BILIARY DUCT CALCULI**

ERCP has been traditionally considered the gold standard for diagnosing bile duct stones, with the great advantage of its easy conversion from a diagnostic imaging technique to a therapeutic interventional procedure. However, it is an invasive technique, with a morbidity rate of 1% to 7% and a mortality rate of 0.1% to 0.2%,<sup>24</sup> requiring an experienced operator, because technical failure occurs in approximately 4% of patients.<sup>24</sup>

T2-Weighted MRC has been increasingly performed in the past years as an alternative to ERCP, because it is a noninvasive

technique, with a reported diagnostic accuracy comparable to that of ERCP in the evaluation of choledocholithiasis and even better than ERCP for the diagnosis of intrahepatic duct stones.<sup>25</sup> However, difficulties can occur with T2-weighted MRC in the detection of biliary tract calculi, when the calculi are only partially outlined or they are not outlined at all by the hyper-intense bile.

The complementary role of fMRC in the identification of biliary tract calculi when performed in addition to T2-weighted MRC has been investigated in some studies, but results are controversial.

According to Sheppard and associates, T2-weighted MRC is more reliable than fMRC in identifying biliary tract calculi.<sup>20</sup> They attributed different performances to the different temporal resolution between the sequences of the two techniques. T2-weighted MRC sequences are less prone to patient-breathing artifact because of short acquisition times (3 to 4 seconds for thick-slab T2-weighted turbo spin echo and at 1 second per slice for thin-slice half-Fourier acquisition single-shot turbo [HASTE] sequences) and navigator technique for T2-weighted MRC-triggered sequences. 3D T1-weighted fMRC sequences can take 15 to 25 seconds and are more prone to breathing misregistration artifact, with the result that pathologic process can be missed.<sup>20</sup> Furthermore, poor mixing of contrast and bile can result in pseudo-filling defects, which can be mistaken for calculi. Fayad and associates<sup>18</sup> also reported a decreased sensitivity with fMRC (82%) compared with T2-weighted MRC (91%) or a combination of the two techniques (91%) for detection of biliary ductal filling defects.

In contrast, Kim and coworkers<sup>25</sup> observed no significant differences between T2-weighted MRC and fMRC for diagnosing common duct stones, but higher diagnostic accuracy and detection sensitivity with combined imaging (T2-weighted MRC and fMRC) than with the T2-weighted MRC alone. Additionally, the complex anatomy of biliary tree (with small-caliber bile ducts or with multiple branching bile ducts) and the presence of adjacent vascular structures (with low signal intensity) may mimic the presence of biliary calculi on T2-weighted MRC images. More studies are required to better investigate the

additional value of fMRC technique for biliary calculi assessment. However, from preliminary evidence, fMRC may be suggested when interpretation of T2-weighted MRC is controversial (Figure 58-13), because it may provide additional information for better assessment of biliary tract calculi.

#### **BILIARY ATRESIA**

Biliary atresia is a progressive obliterative cholangiopathy that occurs in neonates. Prenatal or perinatal insults to the biliary tree may result in complete obstruction of the lumina of the extrahepatic biliary trees and sclerosis of the intrahepatic bile ducts. The obstruction of the bile flow results in cholestasis, hepatic fibrosis, cirrhosis, and hepatic failure within 2 years and may require liver transplantation in children. However, the natural progression of biliary atresia can be favorably altered by means of early recognition and by performing hepatic portoenterostomy.

The diagnosis of biliary atresia relies on the demonstration of a fibrotic extrahepatic biliary tree at exploratory laparotomy or intraoperative cholangiography. However, no single noninvasive imaging technique is currently available to reliably exclude biliary atresia when neonatal cholestasis is suspected.

The ultrasound finding of a triangular cord sign that is cranial to the portal vein bifurcation is a simple and useful diagnostic tool for early detection of biliary atresia. However, the absence of a triangular cord sign does not exclude the possibility of biliary atresia<sup>26</sup> and anatomic delineation of the biliary system provided by ultrasonography is limited.

Hepatobiliary scintigraphy has high sensitivity (100%) but lower specificity (75%) for the diagnosis of biliary atresia, which can be diagnosed only if the scan shows no intestinal radioactivity in a patient with hypocholic to acholic stools, but it cannot be excluded if there is no intestinal radioactivity.

T2-weighted MRC is a reliable technique for visualization of biliary anatomy in neonates and small infants and can be used to depict the major biliary structures and thus exclude biliary atresia as the cause of neonatal cholestasis. However, Norton and colleagues<sup>27</sup> reported both false-positive and false-negative



Figure 58-13 Pseudo-filling defects of the common bile duct (CBD) in a young woman who presented with subtle cholestasis. A, On T2-weighted magnetic resonance cholangiography (MRC), two filling defects in the CBD can be appreciated; the presence of small biliary calculi is suggested. B, Maximum intensity projection coronal gradient recalled echo T1-weighted image obtained in the hepatobiliary phase 2 hours after administration of gadobenate dimeglumine shows no evidence of filling defects in the CBD. Without functional MRC, filling defects of the CBD detected at T2-weighted MRC could have been mistaken for calculi.

findings for T2-weighted MRC, which achieved an overall accuracy of only 82%. The insufficient production or secretion of bile resulting from other severe cholestatic diseases and movement artifacts related to breathing (infants cannot hold their breath), may account for a number of false-positive or false-negative results in T2-weighted MRC.

fMRC may serve as a "one-stop shopping" imaging examination for biliary atresia, providing functional information similar to that of hepatobiliary scintigraphy and morphologic information similar to that of T2-weighted MRC, CT, and ultrasonography. Furthermore, it provides superior contrast between biliary ducts (opacified with hepatobiliary contrast agent) and background tissue and higher spatial resolution, with better capabilities for multiplanar reformatted images compared with those achievable with T2-weighted MRC.

In the study by Ryeom and associates,<sup>28</sup> fMRC with mangafodipir trisodium enabled identification of neonatal cholestasis in 19 patients without biliary atresia with no false-positive results and in 4 patients with biliary atresia with no falsenegative results.

#### **Key Points**

- fMRC and CT cholangiography allow a comprehensive evaluation of both the anatomy and function of the gallbladder and the biliary tree.
- Both are based on administration of a contrast agent, which is eliminated via the biliary ducts.
- Hepatobiliary contrast agents for fMRC belong to two different classes: ones with exclusive distribution to the hepatocellular compartment (mangafodipir trisodium [Mn-DPDP]) and ones that demonstrate combined perfusion and hepatocyte-selective properties (gadobenate dimeglumine [Gd-BOPTA] and gadoliniumethoxybenzyl-diethylenetetraminepentaacetic acid [Gd-EOB-DTPA]).
- Biliary contrast agents for CT cholangiography have a higher risk for adverse reactions compared with conventional contrast agents for CT or with hepatobiliary contrast agents for fMRC.
- High-resolution MPR images and 3D postprocessed images are commonly used for the evaluation of fMRC and CT cholangiography images.

- fMRC and CT cholangiography are comparable for the depiction of biliary tree anatomy, and both allow evaluation of function, but some shortcomings have limited routine clinical application of CT cholangiography.
- Recently, an increased number of adult-to-adult liver transplantations has focused efforts on the accurate preoperative assessment of the biliary tree anatomy, which is essential for the surgeon to prevent any variant in biliary anatomy.
- A wide range of pathologic conditions affect the biliary tree and the gallbladder and may result in the altered physiology of the biliary tree and gallbladder as well as in the altered physiology of bile and may benefit from functional imaging; these include biliary leaks, altered biliary drainage, sphincter of Oddi dysfunction, obstruction of biliary ducts or stents, biliary strictures, acute cholecystitis, biliary duct calculi, and biliary atresia.

#### SUGGESTED READINGS

Fayad LM, Kamel IR, Mitchell DG, et al: Functional MR cholangiography: diagnosis of functional abnormalities of the gallbladder and biliary tree. *AJR Am J Roentgenol* 184:1563–1571, 2005.

Gandhi SN, Brown MA, Wong JG, et al: MR contrast agents for liver imaging: what, when, how. *Radiographics* 26:1621–1636, 2006. Hoeffel C, Azizi L, Lewin M, et al: Normal and pathologic features of the postoperative biliary tract at 3D MR cholangiopancreatography and MR imaging. *Radiographics* 26:1603–1620, 2006.Kirchin MA, Pirovano GP, Spinazzi A: Gadobenate dimeglumine (Gd-BOPTA): an overview. *Invest Radiol* 33:798–809, 1998. Sheppard D, Allan L, Martin P, et al: Contrastenhanced magnetic resonance cholangiography using mangafodipir compared with standard T2W MRC sequences: a pictorial essay. *J Magn Reson Imaging* 20:256–263, 2004.

#### REFERENCES

- Wang C: Mangafodipir trisodium (MnDPDP)enhanced magnetic resonance imaging of the liver and pancreas. *Acta Radiol Suppl* 415:1–31, 1998.
- Rofsky NM, Weinreb JC, Bernardino ME, et al: Hepatocellular tumors: characterization with Mn-DPDP–enhanced MR imaging. *Radiology* 188:53–59, 1993.
- Kirchin MA, Pirovano GP, Spinazzi A: Gadobenate dimeglumine (Gd-BOPTA): an overview. *Invest Radiol* 33:798–809, 1998.
- Spinazzi A, Lorusso V, Pirovano G, et al: Multihance clinical pharmacology: biodistribution and MR enhancement of the liver. *Acad Radiol* 5(Suppl 1):S86–S89, 1998.
- Petersein J, Spinazzi A, Giovagnoni A, et al: Focal liver lesions: evaluation of the efficacy of gadobenate dimeglumine in MR imaging—a multicenter phase III clinical study. *Radiology* 215:727–736, 2000.
- Grazioli L, Morana G, Federle MP, et al: Focal nodular hyperplasia: morphologic and functional information from MR imaging with gadobenate dimeglumine. *Radiology* 221:731–739, 2001.
- Schuhmann-Giampieri G: Liver contrast media for magnetic resonance imaging: interrelations between pharmacokinetics and imaging. *Invest Radiol* 28:753–761, 1993.
- 8. Hamm B, Staks T, Mühler A, et al: Phase I clinical evaluation of Gd-EOB-DTPA as a hepatobiliary

MR contrast agent: safety, pharmacokinetics, and MR imaging. *Radiology* 195:785–792, 1995.

- Vogl TJ, Kümmel S, Hammerstingl R, et al: Liver tumors: comparison of MR imaging with Gd-EOB-DTPA and Gd-DTPA. *Radiology* 200:59–67, 1996.
- Grazioli L, Morana G, Caudana R, et al: Hepatocellular carcinoma: correlation between gadobenate dimeglumine–enhanced MRI and pathologic findings. *Invest Radiol* 35:25–34, 2000.
- 11. Yeh BM, Breiman RS, Taouli B, et al: Biliary tract depiction in living potential liver donors: comparison of conventional MR, mangafodipir trisodium-enhanced excretory MR, and multidetector row CT cholangiography—initial experience. *Radiology* 230:645–651, 2004.

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- 12. Puente SG, Bannura GC: Radiological anatomy of the biliary tract: variations and congenital abnormalities. *World J Surg* 7:271–276, 1983.
- Nakamura T, Tanaka K, Kiuchi T, et al: Anatomical variations and surgical strategies in right lobe living donor liver transplantation: lessons from 120 cases. *Transplantation* 73:1896– 1903, 2002.
- Lee VS, Krinsky GA, Nazzaro CA, et al: Defining intrahepatic biliary anatomy in living liver transplant donor candidates at mangafodipir trisodium-enhanced MR cholangiography versus conventional T2-weighted MR cholangiography. *Radiology* 233:659–666, 2004.
- Masci E, Toti G, Mariani A, et al: Complications of diagnostic and therapeutic ERCP: a prospective multicenter study. *Am J Gastroenterol* 96:417– 423, 2001.
- Hoeffel C, Azizi L, Lewin M, et al: Normal and pathologic features of the postoperative biliary tract at 3D MR cholangiopancreatography and MR imaging. *Radiographics* 26:1603–1620, 2006.
- 17. Vitellas KM, El-Dieb A, Vaswani K, et al: Using contrast-enhanced MR cholangiography with IV mangafodipir trisodium (Teslascan) to evaluate bile duct leaks after cholecystectomy: a prospective study of 11 patients. *AJR Am J Roentgenol* 179:409–416, 2002.

- Fayad LM, Holland GA, Bergin D, et al: Functional magnetic resonance cholangiography (fMRC) of the gallbladder and biliary tree with contrast-enhanced magnetic resonance cholangiography. J Magn Reson Imaging 18:449–460, 2003.
- Inoue Y, Komatsu Y, Yoshikawa K, et al: Biliary motor function in gallstone patients evaluated by fatty-meal MR cholangiography. J Magn Reson Imaging 18:196–203, 2003.
- Sheppard D, Allan L, Martin P, et al: Contrastenhanced magnetic resonance cholangiography using mangafodipir compared with standard T2W MRC sequences: a pictorial essay. J Magn Reson Imaging 20:256–263, 2004.
- 21. Pereira SP, Gillams A, Sgouros SN, et al: Prospective comparison of secretin-stimulated magnetic resonance cholangiopancreatography with manometry in the diagnosis of sphincter of Oddi dysfunction types II and III. *Gut* 56:809–813, 2007.
- Thrall JH, Zeissman HA: Hepatobiliary system. In Gay S, editor: *Nuclear medicine*, St. Louis, 1995, Mosby, pp 199–204.
- Kim KW, Park M-S, Yu J-S, et al: Acute cholecystitis at T2-weighted and manganese-enhanced T1-weighted MR cholangiography: preliminary study. *Radiology* 227:580–584, 2003.

- Bilbao MK, Dotter CT, Lee TG, et al: Complications of endoscopic retrograde cholangiopancreatography (ERCP): a study of 10,000 cases. *Gastroenterology* 70:314–320, 1976.
- Kim TK, Kim BS, Kim JH, et al: Diagnosis of intrahepatic stones: superiority of MR cholangiopancreatography over endoscopic retrograde cholangiopancreatography. *AJR Am J Roentgenol* 179:429–434, 2002.
- 26. Kanegawa K, Akasaka Y, Kitamura E, et al: Sonographic diagnosis of biliary atresia in pediatric patients using the "triangular cord" sign versus gallbladder length and contraction. *AJR Am J Roentgenol* 181:1387–1390, 2003.
- Norton KI, Glass RB, Kogan D, et al: MR cholangiography in the evaluation of neonatal cholestasis: initial results. *Radiology* 222:687–691, 2002.
- Ryeom HK, Choe BH, Kim JY, et al: Biliary atresia: feasibility of mangafodipir trisodiumenhanced MR cholangiography for evaluation. *Radiology* 235:250–258, 2005.

# **Focal Splenic Lesions**

MIN JU KIM | KYOUNG WON KIM

### **Splenic Cysts**

#### NON-NEOPLASTIC AND NONPARASITIC SPLENIC CYSTS

#### Etiology

Non-neoplastic and nonparasitic splenic cysts are classified into primary (i.e., epithelial, true) and secondary (i.e., pseudocysts, false) cysts, depending on the presence or absence of the internal epithelial lining. Primary or epithelial cysts are considered congenital or developmental in origin. Trauma is the most likely etiologic factor of pseudocysts or secondary cysts, and other causes are considered to be infarction, infection, and pancreatitis.<sup>1</sup>

#### Prevalence and Epidemiology

Splenic cysts are uncommon and are usually found incidentally on imaging studies. In one series the incidence at autopsy was 7.6 per 10,000.<sup>2</sup> Epithelial cysts are less common and are mainly seen in children and young adults (Figures 59-1 and 59-2). Pseudocysts constitute 75% to 80% of the splenic cysts (Figures 59-3 and 59-4).<sup>3</sup>

#### **Clinical Presentation**

The majority of splenic cysts are asymptomatic, but large cysts may produce nonspecific symptoms such as mild pain, fullness, or discomfort in the left upper quadrant; dyspnea; anorexia; nausea; and vomiting. Although uncommon, acute complications, such as hemorrhage, rupture, or infection, may be the manifesting features. Physical examination may be normal or reveal a left upper quadrant mass with or without tenderness. Results of routine laboratory tests are usually normal.

#### Pathophysiology

Splenic cysts are usually solitary but can be multiple; 65% are subcapsular, and 80% are unilocular.<sup>4</sup> Cases have been described in accessory spleens as well.

#### Pathology

Primary splenic cysts have an internal-lining epithelium and can be further subdivided into mesothelial, epidermoid, and dermoid cysts. Mesothelial cysts are considered to be derived from infolding of peritoneal mesothelium or collections of peritoneal mesothelial cells trapped within the splenic sulci during embryogenesis. Epidermoid cysts are lined with squamous epithelium and are thought to develop from metaplasia within mesothelial cysts. The stratified epithelium lining these cysts has immunoreactivity for carcinoembryonic antigen and CA 19-9, and these markers may be elevated in the serum as well. Dermoid cysts are extremely rare, with only a few cases reported, and contain skin adnexa and squamous epithelium. Macroscopically, a glistening inner surface with marked trabeculation is often noted (see Figures 59-1 and 59-2). The wall of pseudocysts is composed of dense fibrous tissue, which is often calcified, with no epithelial lining. These cysts contain a mixture of blood and necrotic debris.<sup>1,5</sup>

#### Imaging

Although smaller size, internal debris, and calcifications within the fibrous wall are all favorable imaging features that aid in distinguishing false from true cysts, nevertheless both true and false cysts can possess cyst wall calcifications, trabeculations, peripheral septations, and debris (e.g., cholesterol crystals or breakdown products after hemorrhage) (Tables 59-1 and 59-2).<sup>3</sup>

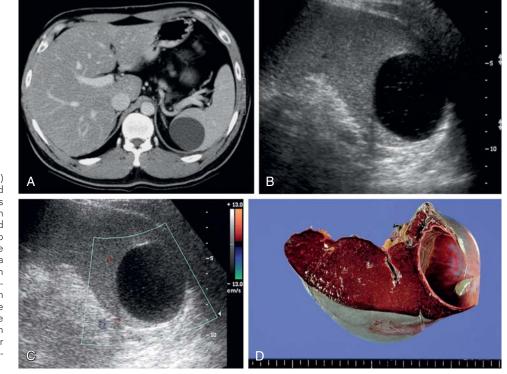
**Radiography.** Splenic cysts are often large enough to cause splenomegaly and displacement of adjacent organs. Curvilinear or plaque-like calcification is seen on plain radiographs in 5% of true cysts and in 38% of false cysts (see Figure 59-3).<sup>4</sup>

**Computed Tomography.** Splenic cysts are typically round, well-defined lesions with smooth margins, attenuation near that of water, and a thin or imperceptible wall on computed tomography (CT) (see Figures 59-1 and 59-2). Septa may be noted, and rim calcification is seen in 14% of the true cysts and in 50% of false cysts (see Figures 59-3 and 59-4).<sup>4</sup> Typically, there is no rim enhancement on a postcontrast scan. Epithelial cysts occurring in an intrapancreatic accessory spleen are frequently misdiagnosed as cystic tumor of the pancreas. In such cases, the presence of thin, compressed splenic parenchyma surrounding the cyst may be noted, suggesting the correct diagnosis (see Figure 59-2).

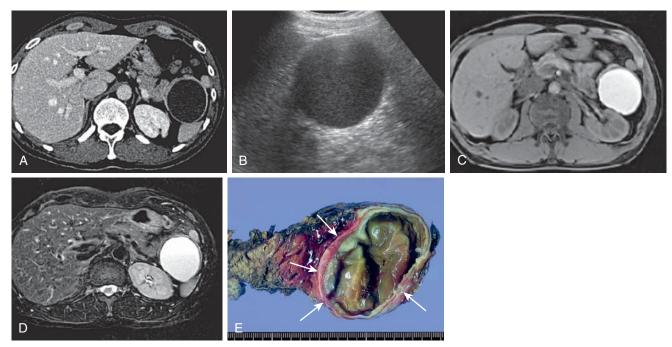
**Magnetic Resonance Imaging.** Although splenic cysts typically have signal intensity equal to that of water on both T1- and T2-weighted magnetic resonance imaging, the signal intensity on T1-weighted images may be increased, whereas the signal intensity on T2-weighted images remains high, depending on the composition of the cystic fluid (see Figure 59-2).<sup>1</sup> A rim of hypointensity may be caused by calcified wall or hemosiderin deposit at the cyst wall (see Figure 59-3).<sup>4</sup>

**Ultrasonography.** On ultrasonography, typical splenic cysts appear as round, homogeneous, anechoic lesions with marked posterior echo enhancement and with a smooth, thin wall (see Figures 59-1 and 59-2). However, sometimes they appear as a more complex picture attributed to thin septations, irregular

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**Figure 59-1** Epithelial (mesothelial) splenic cyst. **A**, Axial contrast-enhanced computed tomography scan reveals a well-defined spherical lesion with smooth margin, imperceptible wall, and attenuation near that of water. No rim enhancement is noted. **B**, Oblique axial ultrasound image demonstrates a round, homogeneously anechoic lesion with marked posterior echo enhancement. **C**, Color Doppler ultrasonogram shows avascularity of the lesion. **D**, The patient underwent splenectomy. The cut surface of the gross specime shows a smoothly marginated unilocular splenic cyst with a thin wall. Histopathologic diagnosis was a mesothelial cyst.



**Figure 59-2** Epithelial (epidermoid) cyst in an intrapancreatic accessory spleen. A, Axial contrast-enhanced computed tomography scans show a round, unilocular low-attenuation lesion around the pancreas tail. Also noted is another accessory spleen in the left anterior aspect of the cyst. **B**, Oblique coronal ultrasound image shows fine granular echo of the cyst contents and posterior acoustic enhancement. **C**, On axial fat-suppressed T1-weighted magnetic resonance imaging, the signal of the cyst contents appears hyperintense. **D**, Hyperintense signal of the cyst contents and fluid/fluid level is demonstrated on an axial fat-suppressed T2-weighted image. **E**, The patient underwent splenectomy. The gross specimen shows the cystic mass (*arrows*) with a glistening inner surface and some trabeculation. Histopathologic diagnosis was an epidermoid cyst in an intrapancreatic accessory spleen.

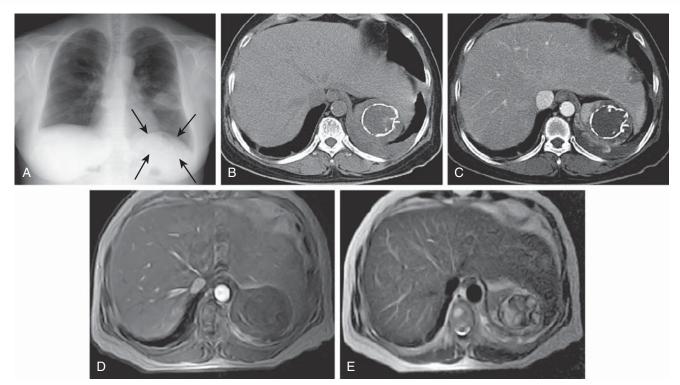


Figure 59-3 Splenic pseudocyst. A, Chest radiograph shows coarse, eggshell-like calcification (arrows) in the left upper quadrant. B, On noncontrast computed tomography (CT), dense, irregular, and discontinuous rim-like calcification is seen in the upper pole of the spleen. C, Axial contrast-enhanced CT scan shows a low-attenuation mass with irregular boundary and dense internal rim-like calcification. Note the incidental findings of hepatic hemangioma in the left lateral segment. D and E, The cystic lesion has profound low signal intensity on the T1-weighted magnetic resonance image (D) and heterogeneous high signal intensity on the T2-weighted image (E). Also noted is a dark signal intensity rim attributed to the calcification.

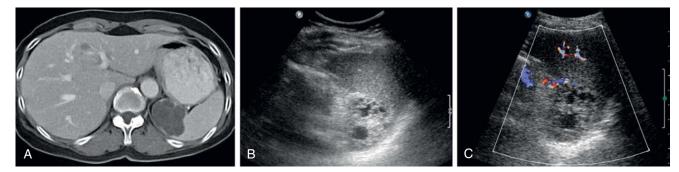


Figure 59-4 Splenic pseudocyst. A, Axial contrast-enhanced computed tomography scan shows a well-demarcated, spherical low-attenuation mass. Also noted are the peripheral curvilinear calcifications (arrows). B, A round, mixed echoic lesion is seen with marked posterior echo enhancement on this oblique coronal ultrasound image. The heterogeneous echo pattern of the cyst contents may reflect internal debris or hemorrhage. C, Color Doppler ultrasonogram demonstrates avascularity of the lesion.

TABLE 59-1						
Moda	lity	Accuracy	Limitations	Pitfalls		
Radiog	graphy	Poor	Insensitive Nonspecific	Unable to directly visualize splenic abnormality		
СТ		Availability of source literature limited for specifying and	Radiation exposure Adverse effect of contrast agent	Imaging findings of splenic lesions overlap on noncontrast and postcontrast CT		
MRI		comparing accuracy of different imaging modalities for evaluation	High cost Patient cooperation	Imaging findings of splenic lesions overlap		
Ultraso	onography	of splenic abnormality	Operator dependent	Imaging findings of splenic lesions overlap		
Nuclea	ar medicine		Poor spatial resolution	Nonspecific		
PET/C	Т	Useful to differentiate, malignant from benign lesion (larger study is needed)	Radiation exposure High cost	False-negative result in splenic metastasis of non–FDG-avid tumors False-positive result in splenic granulomatous disease such as sarcoidosis and tuberculosis		

CT, Computed tomography; FDG, fluorodeoxyglucose; MRI, magnetic resonance imaging; PET, positron emission tomography. Document téléchargé de ClinicalKey.fr par Faculte de Medecine de Tunis août 30, 2016. Pour un usage personnel seulement. Aucune autre utilisation n'est autorisée. Copyright ©2016. Elsevier Inc. Tous droits réservés.

### TABLE 59-2 Summary of Clinical and Imaging Features of Focal Splenic Lesions

L	59-2 Juin	9-2 Summary of Chincal and Imaging Features of Focal Spienic Lesions					
	Lesion	General Features	СТ	MRI	Ultrasonography	Clinical Features	Imaging Features
	Cyst	Location: Lower pole, subcapsular Most unilocular Age: True cyst—children or young adults; pseudocyst —<40 yr	Contrast- enhanced: no rim enhancement of the water attenuation, round lesion Rim Ca <sup>2+</sup> : 14% of the true cysts and 50% of pseudocysts	Τ1 ↓, Τ2 ↑	Round, homogeneous, anechoic lesions with marked posterior echo enhancement	No history of underlying malignancy or pancreatitis and/or recent travel to or living in endemic area of <i>Echinococcus</i> A remote history of trauma to the left upper quadrant	Nonspecific cystic lesion
	Hemangioma	Asymptomatic <2 cm Frequently solitary Age: 35-55 years	Nonenhanced CT: Punctuate or peripheral curvilinear Ca <sup>2+</sup> Contrast- enhanced CT: Variable	Τ1 ↓↔, Τ2 ↑	Well-defined echogenic solid or complex cystic mass	Nonspecific	Nonspecific
	Hamartoma	Location: Midportion Often solitary	Isoattenuating relative to normal spleen Heterogeneous enhancement	T1 ↓↔, T2 ↔↑ Early phase: Diffusely heterogeneous enhancement Delayed images: More uniform homogeneous enhancement	Solid homogeneous lesion Color Doppler imaging: Hypervascularity	Nonspecific	Relatively similar feature of the normal spleen Delayed phase of dynamic study: More uniform Color Doppler imaging: Hypervascularity
	Lymphangiom	a Location: Subcapsular Age: In children	Single or multiple thin-walled, low-attenuation masses with sharp margins	T1 ↓↑ (bleeding, proteinaceous content), T2 ↑ Enhancing septa	Well-defined anechoic cystic lesions	Nonspecific	Nonspecific cystic lesion
	Littoral cell angioma	Multiple splenic lesions in patients with hypersplenism Rare	Multiple lesions of similar size, homogeneous enhancement on delayed phase	T1 ↓↔, T2 ↑ Mild heterogeneous enhancement on arterial phase, and homogeneous enhancement on delayed phase	Variable and includes mottled echotexture without discrete lesions	Hypersplenism	Delayed phase: Homogeneously isoattenuating lesion Multiple Splenomegaly
	Angiosarcoma	Very rare Vigorous prognosis Diffuse involvement common Older patients	Noncontrast CT: Hyperdense area as a result of hemorrhage and Ca <sup>2+</sup> Contrast- enhanced CT: Heterogeneous enhancement	T1, T2: Variable signal intensity, resulting from blood products and necrosis	A complex mass with heterogeneous echotexture	Massive splenomegaly Hemoperitoneum secondary to spontaneous rupture (>30%)	Massive enlarged spleen with heterogeneous enhancement Hemoperitoneum
	Lymphoma	Most common splenic malignant tumor Splenomegaly not always a reliable sign of splenic involvement	Variable: Splenomegaly without mass, solitary mass, multifocal lesions, or diffuse miliary nodular infiltration	Dynamic study (↓ on 30 sec, ↔ on 2 min), superparamagnetic particles (↑), and diffusion weighted imaging (↑) can improve the evaluation of splenic involvement of lymphoma	Variable	Nonspecific	Nonspecific
	Metastasis	Metastases uncommon Poor prognosis Solitary or multiple (most common) nodular lesions or diffuse infiltrating lesions	Multiple low-attenuation masses, sometimes solitary	Τ1↓, Τ2↑	Variable	History of underlying malignancy No evidence of fever	Nonspecific

 $Ca^{2+}$ , Calcification;  $\downarrow$ , low signal intensity;  $\leftrightarrow$ , iso-signal intensity;  $\uparrow$ , high signal intensity; CT, computed tomography; *MRI*, magnetic resonance imaging.

Document téléchargé de ClinicalKey.fr par Faculte de Medecine de Tunis août 30, 2016. Pour un usage personnel seulement. Aucune autre utilisation n'est autorisée. Copyright ©2016. Elsevier Inc. Tous droits réservés. cyst wall, heterogeneous echo pattern from internal debris or hemorrhage (see Figure 59-4), and cyst wall calcifications with bright echo and distal shadowing.

**Nuclear Medicine.** Technetium-99m (<sup>99m</sup>Tc)-sulfur colloid scintigraphy shows a defect with thin, rim-like uptake in the periphery.<sup>4</sup>

#### Differential Diagnosis

The number of diseases that may appear as cystic lesions in the spleen on imaging is extensive. The differentiation between primary and secondary cysts and the differentiation of them from cystic tumors, echinococcal cysts (see later discussion), and abscesses may be difficult radiologically because the findings commonly overlap. The clinical presentation, a history of underlying malignancy or pancreatitis, and or recent traveling to or living in an endemic area of *Echinococcus* can help narrow the differential diagnoses. A remote history of trauma to the left upper quadrant often can be ascertained.<sup>3</sup>

The evidence of daughter cysts or similar coexisting cystic lesions in other organs such as liver, lungs, brain, and musculoskeletal system are favored for echinococcal cysts. Therefore, imaging survey of these organs may be helpful in suspicious cases. Because cystic metastases to the spleen commonly come from breast and ovarian cancer, followed by melanoma, it may be helpful to survey these organs radiologically to elucidate the possible primary lesions.

#### Treatment

**Medical Treatment.** Secondary cysts, especially those associated with pancreatitis, may resolve spontaneously. However, some will require percutaneous or operative drainage.<sup>6</sup>

**Surgical Treatment.** Surgery may be indicated in cases of large symptomatic, mostly primary, cysts. Spleen-conserving surgery may be possible in some cases (e.g., epidermoid cysts arising in accessory spleen).

## What the Referring Physician Needs to Know: Splenic Cysts

- Cystic splenic lesions encompass various abnormalities, such as neoplasms (including cystic metastases), abscesses, as well as non-neoplastic and nonparasitic cysts.
- Clinical findings and history may help narrow the differential diagnosis.

#### **Benign Splenic Tumors**

Both benign and malignant primary tumors are rare in the spleen. Among benign tumors, hemangioma is the most common benign primary neoplasm. Other less common benign neoplasms include hamartoma, lymphangioma, littoral cell angioma, hemangioendothelioma, and hemangiopericytoma (see Tables 59-1 and 59-2).<sup>1</sup>

#### HEMANGIOMA

#### Etiology

Splenic hemangiomas are considered congenital in origin, arising from sinusoidal epithelium.<sup>7</sup>

#### Prevalence and Epidemiology

Although rare, hemangiomas are the most common benign primary neoplasm of the spleen (Figures 59-5 to 59-8), with a prevalence ranging from 0.3% to 14% in autopsy series.<sup>7,8</sup> They are found most often in adults 35 to 55 years of age and have no sex predilection. Diffuse hemangiomatosis of the spleen is a rare benign vascular condition occurring as a manifestation of systemic angiomatosis. Associations with Klippel-Trenaunay-Weber, Turner's, Kasabach-Merritt–like, and Beckwith-Wiedemann syndromes have been reported.<sup>1,9</sup>

#### **Clinical Presentation**

Patients with hemangiomas are generally asymptomatic and have an excellent prognosis. However, large hemangiomas may occasionally manifest as a mass in the left upper quadrant, pain, or splenomegaly. Spontaneous rupture has been reported.<sup>8</sup> Anemia, thrombocytopenia, coagulopathy (Kasabach-Merritt syndrome), and high-output congestive heart failure may rarely occur with large hemangiomas with vast blood flow. Coagulopathy is probably due to sequestration of red blood cells and platelets and to consumption of clotting factors in hemangiomas.

#### Pathophysiology

Most asymptomatic hemangiomas are smaller than 2 cm, but they can sometimes be huge. Splenic hemangiomas are frequently solitary but may be multiple and also can be diffuse when they manifest as a part of systemic angiomatosis.<sup>1</sup>

#### Pathology

Histopathologically, splenic hemangioma consists of a nonencapsulated proliferation of vascular channels, lined by a single layer of endothelium and filled with blood. These blood-filled spaces are separated by thin fibrous septa or splenic pulp tissue. The size of vascular spaces in splenic hemangiomas varies, ranging from capillary to, most frequently, cavernous. In diffuse angiomatosis, neoplastic vascular channels may replace the whole spleen. Grossly, splenic hemangiomas will appear as bluered spongelike nodules in the spleen (see Figure 59-5). Smaller hemangiomas, both capillary and cavernous, tend to be solid, whereas large cavernous lesions can develop thrombosis, infarction, fibrosis, and pseudocystic degeneration caused by necrosis. Calcium deposits may be present in the fibrotic area of the mass or in the periphery of the intratumoral cystic spaces.<sup>7</sup>

#### Imaging

The radiologic appearance of hemangioma ranges from solid to cystic, depending on the gross morphology. Typically, cavernous hemangiomas have a combination of solid and cystic components (see Figure 59-6).

**Radiography.** On radiographs, large hemangiomas may manifest as a mass in the left upper quadrant or as splenomegaly. When present, multiple small punctuate calcifications or peripheral curvilinear calcifications may be noted.<sup>7</sup>

**Computed Tomography.** On unenhanced CT scans, hemangiomas appear as hypoattenuating or isoattenuating, wellmarginated masses, sometimes with punctuate or peripheral curvilinear calcifications. Contrast-enhancement patterns can be variable; although strong homogeneous enhancement may

**Figure 59-6** Splenic hemangiomas. A, Axial unenhanced computed tomography (CT) scan shows variable-sized multiple low-attenuation masses in the spleen. B and C, Contrast-enhanced CT scans during the arterial (B) and portal venous (C) phases demonstrate mild and gradual enhancement of the lesions. D, Oblique coronal ultrasonogram shows solid and cystic appearance of the lesions, seen as hyperechoic and anechoic compartments. E, Color Doppler ultrasonogram shows the hypervascularity in the solid portion of the splenic masses.

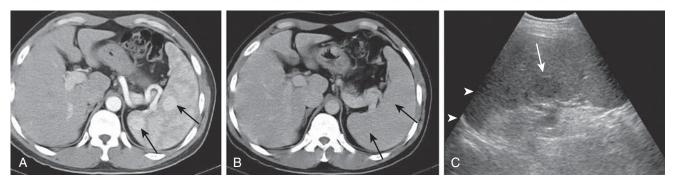
be seen immediately after the contrast administration (see Figure 59-7), also only low-grade enhancement may be noted compared with strong contrast enhancement of the parent spleen (see Figures 59-5 and 59-6). The area of degeneration remains hypoattenuating relative to normal spleen until the delayed phase.

D

Figure 59-5 Splenic hemangiomas. A, Axial contrast-enhanced computed tomography (CT) scan during the arterial phase shows multiple low-attenuation nodules (arrows) in the spleen. B, On portal venous phase CT, diffuse low-grade enhancement of the lesions (arrows) is appreciated. C, Oblique coronal ultrasound image shows hyperechogenicity in one of the lesions (arrows). D, The patient underwent splenectomy. The cut surface of the gross specimen shows a well-demarcated purple-red mass (arrow-heads). Histopathologic diagnosis was

splenic cavernous hemangioma.

**Magnetic Resonance Imaging.** Splenic hemangiomas are mildly low to isointense on T1-weighted images and mildly to moderately hyperintense on T2-weighted images. Contrast-enhancement patterns are similar to those of CT. Compared with hepatic hemangiomas, splenic hemangiomas generally do not demonstrate well-defined peripheral nodules on early



**Figure 59-7** Splenic hemangiomas. **A**, Axial contrast-enhanced computed tomography (CT) scan during the arterial phase shows two nodular lesions (*arrows*) with homogeneous and intense contrast enhancement. **B**, The tumors appear as nearly isoattenuating lesions (*arrows*) compared with the surrounding spleen parenchyma on the delayed-phase CT. **C**, The lesion is hypoechoic (*arrow*) on an oblique coronal ultrasound image. The patient underwent splenectomy. Histopathologic diagnosis was splenic hemangioma.

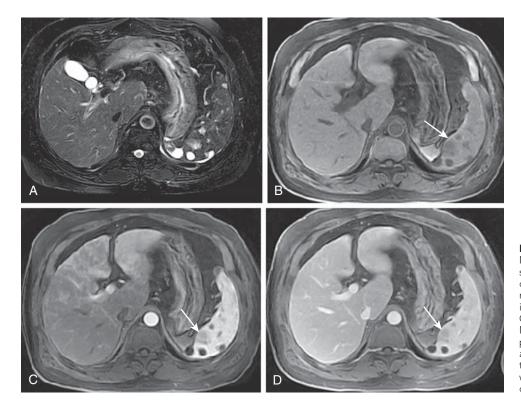


Figure 59-8 Splenic hemangiomas. Multiple nodules (arrow, B) in the spleen are seen as high signal intensity on the T2-weighted magnetic resonance (MR) image (A) and as low signal intensity on the T1-weighted image (B). Gadolinium-enhanced T1-weighted MR images during the arterial (C) and portal venous (D) phases reveal mild and prolonged enhancement in one of the lesions (arrows). The patient underwent splenectomy. Histopathologic diagnosis was splenic hemangioma.

postgadolinium-enhanced images (see Figure 59-8).<sup>10</sup> Again, this characteristic is thought to reflect the differences in vascular supply to the background organ (spleen vs. liver) rather than inherent differences between splenic and hepatic hemangiomas.

**Ultrasonography.** On ultrasonography, a hemangioma may manifest as a well-defined intrasplenic or pedunculated echogenic solid or complex cystic mass (see Figure 59-6). However, it also can appear as a low-echoic lesion (see Figure 59-7). Echogenic calcifications with acoustic shadowing may be present.<sup>7</sup>

Nuclear Medicine. Traditionally, it has been noted that a <sup>99m</sup>Tc-labeled red blood cell scan demonstrates a perfusion

defect and persistent filling on the early and delayed blood pool images, respectively.<sup>4</sup> Nuclear medicine has little role in evaluation of splenic hemangiomas in clinical practice.

**Positron Emission Tomography With Computed Tomography.** Most benign splenic tumors such as hemangiomas or hamartomas are expected to be non–fluorodeoxyglucose (FDG)-avid lesions.<sup>11</sup>

#### HAMARTOMA

#### Etiology

Splenic hamartoma is thought to be congenital in origin, reflecting a focal developmental disturbance in the spleen. However, it also has been proposed that splenic hamartoma may be a neoplasm or possibly a posttraumatic lesion.<sup>7</sup>

#### Prevalence and Epidemiology

Hamartomas are rare benign lesions and are found without age or sex predilection. Review of autopsy series has shown that the prevalence of splenic hamartoma is less than 1%.<sup>7</sup>

#### **Clinical Presentation**

Most patients with splenic hamartomas have no symptoms, and these lesions are usually found incidentally at radiologic studies. Larger lesions may manifest as a palpable mass, splenomegaly, or, rarely, rupture.<sup>4,7</sup>

Hamartomas of the spleen have been associated with hamartomas elsewhere in the body and have been reported in cases of tuberous sclerosis and Wiskott-Aldrich–like syndrome. The association of splenic hamartoma with tuberous sclerosis lends support to the hamartomatous nature of the latter condition. In addition, an association of splenic hamartoma with malignancy has been suggested.<sup>7</sup>

#### Pathophysiology

Hamartomas are most likely to occur in the midportion of the spleen, arising from the anterior or posterior aspect of the convex surface (Figures 59-9 to 59-11).<sup>10</sup> They are most often solitary but may manifest as multiple nodules, and lesions up to 19 cm have been reported.

#### Pathology

Histopathologically, splenic hamartomas are composed of a mixture of unorganized vascular channels lined by endothelial cells and surrounded by fibrotic cords of predominant splenic red pulp with or without (lymphoid) white pulp.<sup>5,7</sup> Grossly, splenic hamartomas are usually well-circumscribed, solid

bulging nodular lesions that tend to compress the adjacent parenchyma. Their gross appearance is typically dark red (see Figure 59-9) to grayish white. Despite their well-defined appearance at gross examination, however, hamartomas do not appear well defined at microscopic analysis. Their expansile growth compresses the surrounding red pulp.

#### Imaging

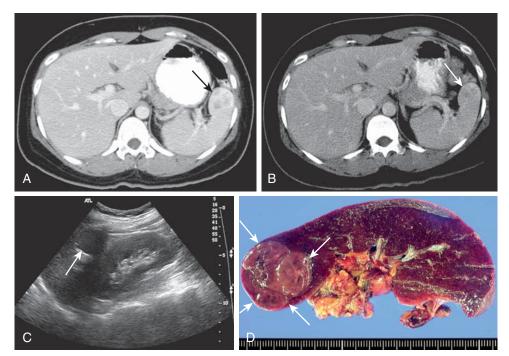
**Radiography.** Splenomegaly may be the only finding of splenic hamartomas on plain radiography, when they are large enough to be visualized.

**Computed Tomography.** Although splenic hamartomas may be seen as heterogeneously enhancing lesions on postcontrast CT scans (see Figure 59-9), they often can appear as nearly isoattenuating lesions compared with normal spleen before and after enhancement with a contrast agent (see Figure 59-10) and, therefore, can be difficult to detect; in such cases, a contour abnormality may be the only finding present. They can also appear as hypoattenuating lesions.

**Magnetic Resonance Imaging.** Splenic hamartomas generally exhibit mildly low-signal to iso-signal intensity and moderately high signal intensity on T1- and T2-weighted images, but they may show heterogeneous signal intensity partly because of the varying-sized cystic spaces. If the amount of fibrous tissue is substantial, hamartomas may have regions of low signal intensity on T2-weighted images. The contrast-enhancement pattern is similar to that evident on CT (see Figure 59-11).

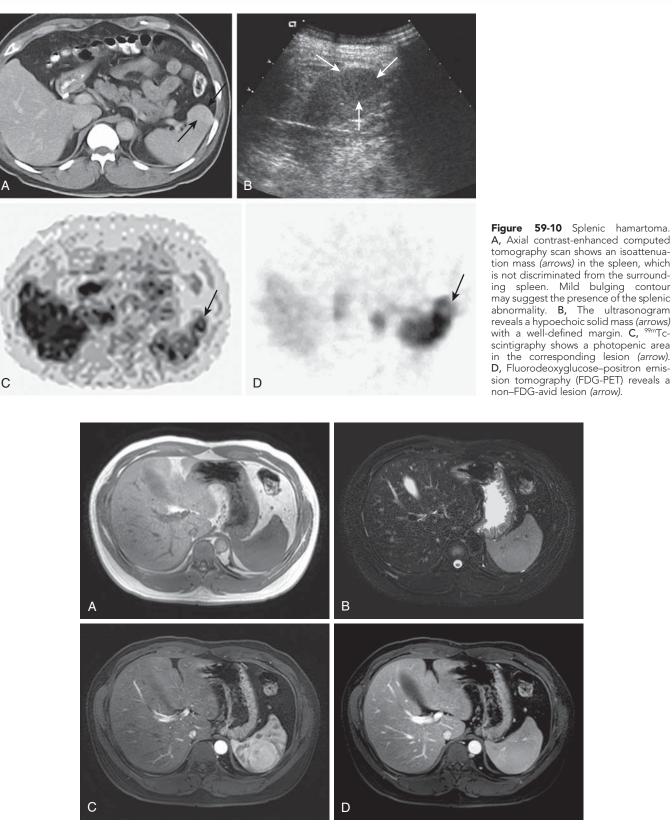
**Ultrasonography.** It has been reported that ultrasonography is more sensitive than CT in detection of splenic hamartomas. The typical appearance is a solid-looking, homogeneous hyperechoic lesion relative to the adjacent normal splenic

Figure 59-9 Splenic hamartoma. A, Axial contrast-enhanced computed tomography scan during the arterial phase shows a heterogeneously enhancing mass (arrow) in the anterior pole of the spleen. B, On delayed phase, this lesion (arrow) shows as an isoattenuated to slightly hyperattenuated mass. C, The lesion is seen as a hypoechoic mass (arrow) on an oblique coronal ultrasound image. D, The patient underwent splenectomy. The cut surface of the specimen reveals a well-circumscribed, dark-red solid nodular lesion (arrows). Histopathologic diagnosis was splenic cavernous hamartoma



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**Figure 59-11** Splenic hamartoma. Axial T1-weighted (A), T2-weighted (B), early contrast-enhanced (C), and late contrast-enhanced (D) magnetic resonance images show a round splenic lesion (arrows) with iso-signal to slightly low signal intensity on T1- and T2-weighted images (A and B), heterogeneous character, good enhancement on arterial phase image (C), and more uniform enhancement on the portal phase image (D) The patient underwent ultrasonography-guided biopsy. Histopathologic diagnosis was splenic hamartoma. (From Yang DM, Kim SW, Kim MJ: Spleen. In Lim JH, Kim PN, Han JG, editors: Abdominal radiology, Seoul, 2015, Ilchokak, 2015, p 665, Figure 9-29. The Korean Society of Abdominal Radiology.)

parenchyma, but some may be seen as isoechoic or low echoic (see Figures 59-9 and 59-10). Color Doppler imaging may reveal the hypervascularity of the lesion.<sup>7</sup>

**Angiography.** Although the typical hypervascularity of the red pulp within the hamartoma may produce several angiographic findings, such as tumor vessels with aneurysmal dilatation, arteriovenous shunts, vascular lakes, and tumor blush, this examination is seldom performed for diagnostic purposes currently because of the advances in noninvasive imaging methods.<sup>7</sup>

Positron Emission Tomography With Computed Tomography. Most benign splenic tumors such as hamartomas are

expected to be non-FDG-avid lesions (see Figure 59-10).<sup>11,12</sup>

#### LYMPHANGIOMA

#### Etiology

There is no firm consensus as to the exact origin of splenic lymphangioma, which may represent a hamartomatous rather than a neoplastic lesion. Others have proposed a unified concept of lymphangioma and cystic hygroma as being a congenital developmental defect.

#### Prevalence and Epidemiology

Figure 59-12 Splenic lymphangioma.

Splenic lymphangioma is a relatively rare benign tumor with various clinical manifestations that range from an asymptomatic incidental lesion to a large symptomatic mass requiring surgery. Most splenic lymphangiomas occur in children, and adult cases are reported less frequently.<sup>7</sup> Lymphangiomatosis is a syndrome in which multiple organs are involved.

Lymphangiomas are either solitary or multiple or may replace the spleen in a condition called lymphangiomatosis.<sup>4</sup> Therefore, in a young patient with splenic lymphangioma, the diagnostic evaluation should be extended to include extrasplenic organs.

#### **Clinical Presentation**

In patients with splenic lymphangiomas there is a close relationship between the occurrence of symptoms and splenic size. Larger lesions cause symptoms such as left upper quadrant pain, nausea, and abdominal distention. More extensive or larger lymphangiomas of the spleen may be complicated by bleeding, consumptive coagulopathy, hypersplenism, and portal hypertension.<sup>7</sup>

#### Pathophysiology

Splenic lymphangiomas cover a broad spectrum, which includes solitary lesions (Figure 59-12), multiple lesions, and diffuse lymphangiomatosis (Figure 59-13). They often involve the capsule and trabeculae of the spleen, where lymphatics are normally concentrated, in contrast to the random localization seen with hemangiomas. Of the solitary subcapsular focal lesions, lymphangioma is the most common, when focal splenic infarction is excluded. With larger multifocal lesions, the tumors are separated by distinct residual splenic tissue. Lymphangiomas can be divided into three types according to the size of the vascular channels: capillary, cavernous, and cystic.<sup>7</sup>

#### Pathology

At gross examination, splenic lymphangiomas have thick fibrous walls with an internal morphology characterized by fibrous trabeculae (see Figure 59-12). Hyalinization and

**Figure 59-13** Splenic lymphangiomatosis. A, Unenhanced computed tomography (CT) scan reveals a moderately enlarged spleen and multiple low-attenuation masses. B, Axial contrast-enhanced CT scan obtained during the portal venous phase shows multiple, well-circumscribed low-attenuation nodules disseminated throughout the spleen. C, The patient underwent splenectomy. The cut surface of the gross specimen shows numerous small foci of lymphangiomatous lesions disseminated throughout the spleen. Histopathologic diagnosis was a splenic lymphangioma.

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calcification of the fibrous connective tissue may be present. Microscopically, these tumors consist of a single layer of flattened endothelium-lined spaces, filled with eosinophilic proteinaceous material instead of blood as seen in hemangiomas. When the histologic characteristics are not clear, the endothelial origin of the cyst may be established with immunohistochemical techniques that demonstrate reactivity for factor VIII.<sup>7</sup>

#### Imaging

Splenic lymphangiomas typically show cystlike appearances on cross-sectional imaging studies (see Table 59-2).

**Radiography.** Splenomegaly may be the only finding of splenic lymphangiomas on plain radiography, when they are large enough.

**Computed Tomography.** On CT scans, lymphangiomas appear as single or multiple, thin-walled, low-attenuation masses with sharp margins that are typically subcapsular. No significant contrast enhancement is typically seen (see Figure 59-12). Curvilinear peripheral mural calcifications may be noted.<sup>7</sup>

**Magnetic Resonance Imaging.** On T1- and T2-weighted MRI, the cystic lesions of variable sizes that correspond to the dilated lymphatic spaces typically have hypointensity and hyperintensity relative to the surrounding parenchyma. However, the T1 signal intensity may be high, resulting from internal bleeding or the presence of large amounts of intracystic proteinaceous content. The intervening septa appear as hypointense bands on both T1- and T2-weighted MRI, corresponding to the presence of fibrous connective tissue.<sup>7</sup> Moderate to intense septal enhancement is seen on a postcontrast study during the late phase.<sup>10</sup>

**Ultrasonography.** On ultrasonography, splenic lymphangiomas appear as well-defined anechoic cystic lesions with occasional internal septations and intralocular echogenic debris. Tiny echogenic calcifications may be noted. Color Doppler ultrasonography can demonstrate the vasculature along the cyst walls.<sup>7</sup>

**Nuclear Medicine.** Nuclear medicine currently has no role in the evaluation of splenic lymphangiomas.

#### Positron Emission Tomography With Computed Tomogra-

**phy.** Splenic lymphangiomas are expected to be non-FDG-avid lesions.

#### LITTORAL CELL ANGIOMA

#### Etiology

Littoral cell angioma of the spleen is a rare vascular tumor arising from littoral cells, which line the splenic sinus of the red pulp.

#### Prevalence and Epidemiology

Littoral cell angiomas may occur at any age and have no gender predilection. Although these tumors were originally thought to be benign, their biologic behavior has not been firmly established because there have been several reports of littoral cell angioma with malignant features. Also, an association between littoral cell angioma and other malignancies, including colorectal, renal, and pancreatic adenocarcinoma and meningioma, has been described.<sup>7,10</sup>

#### **CLINICAL PRESENTATION**

Typically, patients with littoral cell angioma present with anemia or thrombocytopenia. Other systemic symptoms such as fever, chills, weakness, fatigue, and pain have been reported. At physical examination, splenomegaly is noted. In most patients, splenectomy is performed because symptomatic hematologic problems are present and the imaging findings are nonspecific.<sup>7</sup>

#### Pathophysiology

Littoral cell angioma varies in size from minute foci to large nodules almost completely replacing the splenic tissue.

#### Pathology

Littoral cell angioma is a neoplasm with characteristic morphologic and immunophenotypic features distinguished from the other vascular splenic tumors.<sup>7</sup> Microscopically, it is composed of anastomosing vascular channels resembling splenic red pulp sinuses. Immunohistochemically, the neoplastic cells express both endothelial (factor VIII) and histiocytic (KP-1, lysozyme) markers.<sup>5</sup>

#### Imaging

There is a remarkable uniformity to the clinical characteristics and radiologic findings, and littoral cell angioma usually manifests as multiple splenic lesions in patients with hypersplenism. All modalities including ultrasonography, CT, and MRI usually demonstrate splenomegaly and multiple lesions of similar size and appearance (see Table 59-2).

**Radiography.** Splenic littoral cell angioma may appear as splenomegaly on plain radiography.

**Computed Tomography.** Littoral cell angioma typically manifests as multiple hypoattenuating lesions on CT, but lesions with this appearance have a broad differential diagnosis, including other primary splenic neoplasms, lymphoma, infection, and systemic diseases, such as sarcoidosis. However, on delayed phase contrast-enhanced images, littoral cell angiomas homogeneously enhance and become isoattenuating relative to the remaining splenic parenchyma, a finding that may help limit the differential diagnosis. No capsular calcification or tiny cystic spaces associated with the nodular lesions seen on histologic examination are identified at CT. There is no significant abdominal adenopathy, which is typically seen in patients with splenic metastasis and lymphoma, in patients with littoral cell angioma.<sup>7</sup>

**Magnetic Resonance Imaging.** MRI shows the tumor to be multiple with regular well-defined margins and mildly low signal to isointensity on T1-weighted images, moderately high signal intensity on T2-weighted images, mild heterogeneous enhancement on arterial phase imaging, and homogeneous enhancement on delayed phase imaging.<sup>10</sup>

**Ultrasonography.** The ultrasonographic pattern of littoral cell angioma is variable.

**Positron Emission Tomography With Computed Tomography.** Further studies are warranted to evaluate the role of FDG-PET/CT in the differentiation of littoral cell angiomas of the spleen from other ominous splenic malignancies.

#### INFLAMMATORY PSEUDOTUMOR/ MYOFIBROBLASTOMA

#### Etiology

The cause of inflammatory pseudotumor is unclear. It has been speculated that this lesion represents a reactive tumor-like condition secondary to the infectious or autoimmune disorder. However, now this lesion generally is considered neoplastic and has been redesignated as myofibroblastic tumor.<sup>5,6</sup>

#### Prevalence and Epidemiology

The exact nature of myofibroblastic tumor is unclear. Although it is rare and generally considered benign, it is potentially a locally aggressive lesion. Most patients are adults.<sup>6</sup>

#### **Clinical Presentation**

There is either absence of or vague systemic symptoms of fever and malaise with a mass.<sup>6</sup>

#### Pathophysiology

Myofibroblastic tumors are usually solitary but may be multiple.

#### Pathology

Grossly, this lesion is well defined, with a great size range from a few centimeters to up to 12 cm (Figure 59-14). Microscopically, the lesion consists of inflammatory (lymphocytes, plasma cells, eosinophils, and histocytes) and spindle cells with varying amounts of granulomatous reaction, fibrosis, and necrosis. The spindle cells have an immunophenotype interpreted as myofibroblastic. The predominant growth pattern may be sclerotic, xanthogranulomatous, or plasma cell granuloma type. Central coagulation necrosis is frequently seen, in association with a neutrophilic infiltration.

#### Imaging

**Radiography.** Large lesions may displace the adjacent organs on plain radiographs.

**Computed Tomography.** On noncontrast CT, myofibroblastic tumors are usually heterogeneously hypodense. Peripheral and

stippled calcification has been reported.<sup>7</sup> On contrast-enhanced CT, mild to moderate and prolonged enhancement can be demonstrated with the lesions remaining hypodense or isodense relative to normal spleen (see Figure 59-14).

**Magnetic Resonance Imaging.** Myofibroblastic tumors are seen as slightly hypointense and slightly hyperintense lesions compared with background spleen on T1- and T2-weighted images.<sup>6</sup>

**Ultrasonography.** On ultrasonography, myofibroblastic tumors may be seen as hypoechoic masses.<sup>6</sup>

**Positron Emission Tomography With Computed Tomography.** On FDG-PET/CT, myofibroblastic tumors may exhibit increased uptake of FDG owing to the activation of macrophages.

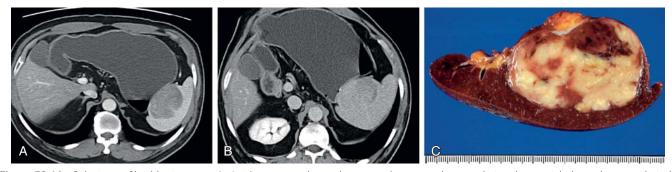
#### Differential Diagnosis

Many of the benign splenic tumors are incidentally found on imaging studies in asymptomatic patients or those with nonspecific symptoms. Because the most important aspect in the diagnosis of benign splenic tumors is the differentiation of the lesions from the more ominous abnormalities such as lymphoma and metastasis, careful physical examination is warranted to search for the palpable lymphadenopathy in the abdomen and other regions. History or current evidence of underlying malignancy should be assessed as well.

Benign splenic tumors may be confidently diagnosed when they have typical findings on radiologic multimodalities studies. However, when the diagnosis is uncertain on radiologic studies, patients should be referred for FDG-PET. Most benign splenic tumors, except myofibroblastic tumors, are expected to be non– FDG avid.

#### Treatment

**Medical Treatment.** When a noninvasive diagnosis of benign splenic tumor is confident in asymptomatic patients, they may be safely observed without treatment. However, if benignancy of the splenic mass cannot be ascertained, percutaneous biopsy may be indicated and should be performed only after careful assessment of the patient's clotting function, because of the high incidence of complications.



**Figure 59-14** Splenic myofibroblastic tumor. **A**, Axial contrast-enhanced computed tomography scan during the arterial phase shows a relatively well-defined solitary mass with heterogeneous hypoattenuation in the spleen. **B**, On delayed phase imaging, this mass becomes more isodense relative to the normal spleen. **C**, The patient underwent splenectomy. The cut surface of the gross specimen shows a well-defined solitary mass having a heterogeneous internal compartment, including fibrotic and hemorrhagic foci. Histopathologic diagnosis was myofibroblastic tumor of the spleen.

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**Surgical Treatment.** Splenectomy may be indicated for the treatment of benign splenic tumors when a diagnosis is uncertain and other ominous splenic abnormalities cannot be excluded, when a biological behavior of the lesion is uncertain, and when patients are symptomatic. The evolution after splenectomy is usually benign in such patients.

# What the Referring Physician Needs to Know: Benign Splenic Tumors

- Benign splenic tumors may be confidently diagnosed noninvasively when they have typical findings on multimodality imaging studies and consistent clinical findings.
- When benignancy of the splenic mass cannot be ascertained from radiologic studies and FDG-PET, percutaneous biopsy may be helpful in patients without coagulopathy.

# **Malignant Splenic Tumors**

#### ANGIOSARCOMA

#### Etiology

Unlike hepatic angiosarcoma, splenic angiosarcoma has no documented strong predisposition to exposure to carcinogens such as thorium dioxide (Thorotrast), vinyl chloride, or arsenic. There have been case reports of splenic angiosarcoma associated with previous chemotherapy for lymphoma and radiation therapy for breast cancer.<sup>7</sup>

#### Prevalence and Epidemiology

Primary angiosarcoma of the spleen is very rare, but it represents the most common nonhematolymphoid malignant tumor of the spleen. It is found more frequently in older patients. There is no apparent gender predilection.<sup>7</sup>

#### **Clinical Presentation**

The most common manifesting signs and symptoms are abdominal pain (83%), fever (10%), splenomegaly, malaise, and weight loss. Clinical complaints may be accompanied by hematologic disturbance such as anemia, thrombocytopenia, or other coagulopathy, presumed to be attributed to damage to blood elements in the neoplastic vessels. Patients with splenic angiosarcoma also may present with signs and symptoms of hemoperitoneum secondary to spontaneous rupture, which has been reported in up to 30% of patients. Metastatic disease is common at the time of presentation and typically involves the liver (70%), lungs, bone, bone marrow, and lymphatic system. Prognosis is poor, and most patients with splenic angiosarcomas die within 1 year of diagnosis.<sup>4,7</sup>

#### Pathophysiology

Patients with splenic angiosarcoma typically have massive splenomegaly. Diffuse involvement of the spleen is common, and in such cases the tumor may replace the entire splenic parenchyma. Although the tumor may manifest as a solitary mass, it is a less common finding. Histologically, splenic angiosarcoma appears to arise from splenic sinus endothelial cells, and this hypothesis has been supported by immunohistochemical studies.

#### Pathology

Grossly, cut specimens usually reveal poorly defined nodular masses that are purple or red (Figure 59-15). There are frequently prominent areas of hemorrhage and necrosis within the tumor. The histologic features of splenic angiosarcomas are similar to those of angiosarcomas in other locations. Microscopically, the tumor consists of disorganized anastomosing vascular channels lined by atypical endothelial cells with a high mitotic rate.<sup>4,7</sup> Sometimes the tumor cells have an epithelioid appearance. Immunohistochemically, the tumor cells exhibit endothelial markers and frequently histiocytic markers as well.

#### Imaging

On cross-sectional imaging studies, angiosarcomas appear as either solitary or multiple nodular masses in an enlarged spleen, composed of a heterogeneous compartment including the area of hemorrhage or necrotic degeneration (see Table 59-2).

**Radiography.** Splenomegaly may be the finding of angiosarcoma of spleen on plain radiograph.

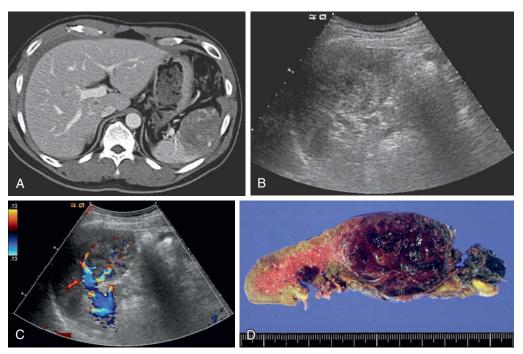
**Computed Tomography.** Angiosarcomas may have hyperdense area on unenhanced CT because of hemorrhage and dystrophic calcific deposits. In cases of spontaneous rupture, intraperitoneal hemorrhage will appear hyperattenuating on unenhanced images in the intrasplenic, subcapsular, or perisplenic area. Contrast-enhanced CT reveals heterogeneous enhancement within the tumor (see Figure 59-15). When there is a substantial active bleeding at the time of CT examination, an extravasation of the intravenous contrast agent may be noted on postcontrast scan, a finding that necessitates emergent surgery. CT also plays the principal role for the evaluation of hypervascular metastasis to the liver as well as metastatic disease to the lungs, bones, and lymphatic system.<sup>7</sup>

**Magnetic Resonance Imaging.** The MRI appearance of splenic angiosarcoma reflects the hemorrhagic nature of the tumor. Areas of increased and decreased signal intensity may be seen on both T1- and T2-weighted images, attributed to the blood products and necrosis. Areas of low signal intensity on MR images have also been shown to represent hemosiderin deposition. Contrast-enhanced MRI reveals heterogeneous enhancement within the tumor.<sup>7</sup>

**Ultrasonography.** On ultrasonography, splenic angiosarcoma most commonly appears as a complex mass with heterogeneous echotexture. Anechoic areas within the mass are frequently identified and likely reflect areas of necrosis and hemorrhage. Increase of color Doppler flow may be seen in the solid echogenic portions of the tumor (see Figure 59-15).<sup>7</sup>

**Nuclear Medicine.** Nuclear medicine does not play a role in evaluation of splenic angiosarcomas.

**Positron Emission Tomography With Computed Tomography.** Although increased uptake of FDG has been noted in angiosarcomas of the pleura and chest wall, further experience is needed to ascertain the role of FDG in evaluation of splenic angiosarcomas.



**Figure 59-15** Splenic angiosarcoma. **A**, Axial contrast-enhanced computed tomography scan demonstrates a large contour bulging mass in the spleen. The mass is predominantly seen as low attenuation, but multiple small foci of strong contrast enhancement are scattered within the lesion. Also noted is hyperdense ascites in the perisplenic area, suggesting the possibility of focal rupture. **B**, Oblique coronal sonogram reveals a complex, heterogeneous echo pattern of the mass. **C**, Color Doppler ultrasonogram reveals the hypervascularity of the mass. **D**, The patient underwent splenectomy. The cut surface of the gross specimen shows a poorly defined nodular purple mass. Histopathologic diagnosis was angiosarcoma of the spleen.

#### LYMPHOMA

#### Etiology

Although the cause for the vast majority of lymphoma is unknown, genetic abnormalities have been postulated. Some viruses (e.g., Epstein-Barr virus) may cause some lymphomas.

#### Prevalence and Epidemiology

Lymphoma is by far the most common malignant tumor of the spleen, and splenic lymphoma can be classified as either primary or secondary lymphomatous involvement. Most splenic lymphomas represent secondary involvement, and it is challenging for the oncologists and radiologists to assess whether the spleen is involved in patients with lymphoma, to determine the type of therapy administered. Staging laparotomy with splenectomy reveals splenic involvement in 39% of patients with Hodgkin's disease (HD).<sup>13</sup> Similarly, 30% to 40% of patients with non-Hodgkin's lymphoma (NHL) have splenic involvement at the time of initial presentation. Primary splenic lymphoma, without nodal disease, is uncommon and occurs in only 1% of all cases of NHL.<sup>14</sup>

#### **Clinical Presentation**

Patients with both primary splenic lymphoma and lymphoma with splenic involvement commonly present with nonspecific systemic symptoms, including fever, weight loss, night sweats, and malaise. Abdominal pain, left upper quadrant mass, or splenomegaly may occur, but these are also nonspecific findings.

The spleen is enlarged in 84% of patients with primary splenic lymphoma, which can manifest both clinically and at

physical examination similar to splenic abscess. Splenic lymphomas sometimes become secondarily infected, which results in abscess formation.<sup>3</sup> Patients with secondary splenic involvement tend to have diffuse nodal enlargement as well. These nodes are often palpable on physical examination. Rarely, splenic lymphoma may be complicated by nontraumatic splenic rupture.<sup>13</sup>

#### Pathology

Four distinct gross pathologic patterns of splenic involvement in lymphoma have been described: (1) homogeneous enlargement without masses, (2) miliary nodules (<5 mm in diameter) (Figure 59-16), (3) multiple masses of various size (1 to 10 cm), and (4) a large solitary mass (>5 cm). High-grade NHL (e.g., large cell lymphoma) especially in an advanced stage and HD in an advanced or later stage are more likely to show the last two patterns of disease. Primary splenic lymphoma usually manifests as a mass or masses rather than splenomegaly alone.<sup>4</sup> However, the spleen may appear normal at gross pathologic examination, with tumor cells seen only microscopically.<sup>15</sup> The white pulp is usually involved first in both primary and secondary lymphoma. Primary splenic lymphoma typically represents NHL of B-cell origin.

#### Imaging

Currently, the need for exploratory staging laparotomy with splenectomy is essentially eliminated. CT is the premier imaging technique for diagnosing and staging lymphoma as well as for evaluating tumor volume and monitoring response to therapy. FDG-PET surpasses CT for these purposes, and large comparative studies are warranted for further validation. On the other

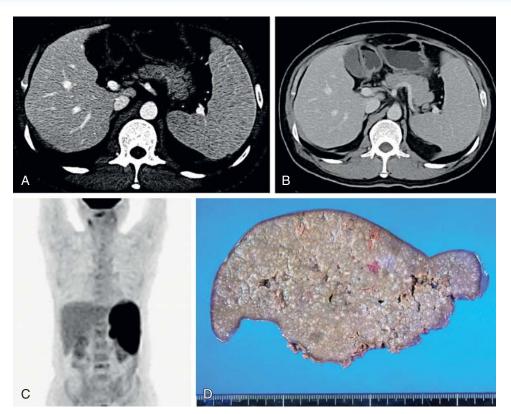


Figure 59-16 Splenic lymphoma. A, Axial contrast-enhanced computed tomography (CT) scan shows an enlarged spleen with diffuse miliary nodular infiltration. B, On the portal venous phase, CT shows more homogeneous enhancement of the spleen, and the miliary lesion seen on A is not discriminated. C, Fluorodeoxyglucosepositron emission tomography reveals strongly increased glucose metabolism in the spleen. D, The patient underwent splenectomy. The cut surface of the gross specimen shows diffuse miliary nodular infiltration throughout the spleen. Histopathologic diagnosis was diffuse large B-cell lymphoma.

hand, CT also provides a cross-sectional display for planning radiation therapy ports (see Table 59-2).

**Radiography.** Mild to moderate splenomegaly may be present with or without mass effect on the adjacent organs. The splenic size correlates with the risk for splenic involvement by lymphoma: in most cases, massive splenomegaly in a patient with HD or NHL means a high probability of splenic involvement.<sup>15</sup> However, splenomegaly is not always a reliable sign of lymphomatous involvement, because markedly enlarged spleens can occur without lymphomatous involvement and because approximately one third of patients with splenic HD may have a normal-sized spleen.<sup>13</sup>

**Computed Tomography.** The CT appearances of splenic lymphoma mirror the variety of pathologic appearances and can be categorized into (1) splenomegaly without a discrete mass, (2) solitary mass (Figure 59-17), (3) multifocal lesions (Figure 59-18), and (4) diffuse miliary nodular infiltration (see Figure 59-16).<sup>13</sup> However, although CT is the premier imaging technique for diagnosing and staging lymphoma, it is not a perfect method for splenic lymphoma, because it may show normal-appearing spleen in spite of lymphomatous involvement. Greater accuracy in diagnosing splenic lymphoma may be obtained by demonstrating adenopathy in the splenic hilum.<sup>15</sup> Lymphoma may become cystic secondary to massive internal necrosis. When necrosis is present, attenuation is similar to that of water and differentiation from other cystic entities such as abscesses may be difficult.<sup>3</sup>

Magnetic Resonance Imaging. Conventional unenhanced MRI has only limited success in imaging lymphomatous

involvement of the spleen, because normal spleen and lymphomatous tissue may have similar T1 and T2 relaxation times.<sup>10,13</sup> Areas of necrosis or old hemorrhage within lymphomas are easier to detect because of substantially increased T2 values.<sup>3</sup> However, in some instances, focal lymphomatous deposits may be seen as low signal intensity compared with background spleen on T2-weighted images (see Figure 59-18), which is a feature distinguishing lymphomas from other focal splenic lesions that usually have an isointense or high signal.

Gadolinium-enhanced MRI may surpass CT for the evaluation of splenic involvement of lymphoma. Foci of lymphomatous involvement are seen as focal lesions of low signal intensity in a background of arciform-enhancing or uniformly enhancing spleen. It has been reported that acquisition of enhanced images within the first 30 seconds after contrast agent injection is critical because foci of lymphoma equilibrate early, becoming isointense with normal splenic tissue within 2 minutes. Superparamagnetic particles can improve the evaluation of splenic involvement of lymphoma. Although these particles are selectively taken up by the reticuloendothelial system cells and homogeneously decrease the signal intensity of the splenic parenchyma, malignant cells do not take up superparamagnetic particles. Therefore, splenic lymphoma remains hyperintense compared with the normal spleen, increasing the contrast resolution between tumor and spleen.<sup>10</sup> Recently, several investigators proposed that MRI using diffusion weighted imaging is reasonable accurate in the detection of splenic lymphomatous involvement, although there remains a diagnostic challenge in cases of diffuse lymphomatous infiltration in normal-sized spleen.<sup>16,17</sup>

**Ultrasonography.** On ultrasonography, splenic lymphoma typically appears as a diffuse or focal hypoechoic pattern (see

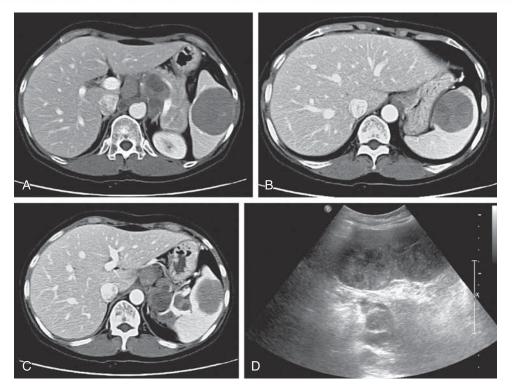


Figure 59-17 Splenic lymphoma. Axial contrast-enhanced computed tomography scans during the arterial (A) and portal venous (B) phases show multiple large splenic masses, with typical hypovascularity. C, Also noted is associated lymphadenopathy in the suprapancreatic area. D, Splenic masses are seen as heterogeneous, hypoechoic lesions on ultrasonography.

Figure 59-17). Abnormal ultrasound textures may be found in 4% to 15% of patients with HD and NHL. Patients with lowgrade HD and NHL tended to have diffuse infiltration of the splenic parenchyma with small nodules. High-grade NHL usually shows focal lesions larger than 3 cm in diameter. The lesions may occasionally appear nearly anechoic (see Figure 59-18), with apparent septa-like structures mimicking an abscess. A hypoechoic lesion with scattered echogenic foci is a less common feature of lymphoma, and echogenic patterns are rare.<sup>13</sup>

**Nuclear Medicine.** <sup>99m</sup>Tc-sulfur colloid scintigraphy has an accuracy rate of 54% to 64% for the diagnosis of lymphoma, and the typical appearance is one or more zones of decreased tracer uptake within the spleen. However, such a finding is obviously nonspecific. Also, detection of small lesions is not successful owing to the limited spatial resolution.<sup>13</sup>

**Positron Emission Tomography With Computed Tomography.** FDG-PET surpasses CT for evaluating the spleen during initial staging of lymphoma (see Figure 59-16). Detecting lymphomatous involvement of the spleen with FDG-PET depends on identifying increased glucose metabolism by tumor cells. There can be apparent metabolic changes when there is diffuse or focal tumor infiltration, regardless of whether frank morphologic changes are present.<sup>18</sup>

Lymphoma Related to Acquired Immunodeficiency Syndrome. Lymphomas that are related to acquired immunodeficiency syndrome (AIDS) are highly aggressive tumors with relatively undifferentiated histologic subtypes, including both NHL and HD. Patients typically have an advanced stage of disease at the time of presentation. The prognosis is poor because of both the lymphoma and other manifestations of AIDS. AIDS-related lymphomas more commonly manifest as focal splenic lesions than lymphomas without AIDS. Focal splenic involvement is demonstrated on CT in 10% of cases of AIDS-related HD and 26% of cases of AIDS-related NHL. Splenomegaly and lymphadenopathy are quite common in patients with AIDS-related lymphoma but not pathognomonic for lymphoma, because they can be caused by Kaposi's sarcoma, mycobacterial or fungal infection, and reactive hyperplasia as well. Image-guided fine-needle aspiration biopsy permits a specific diagnosis to be made.<sup>14</sup>

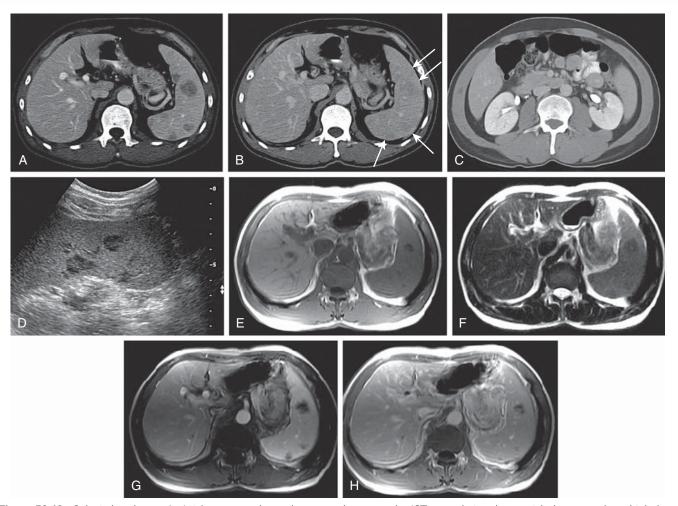
#### **METASTASIS**

#### Etiology

Common primary cancers that metastasize to the spleen include carcinomas of the breast, lung, ovary, stomach, pancreas, liver, and colon, as well as melanoma. In one large series, melanoma was most frequent, defined as the percentage of each tumor that metastasized to the spleen, followed by breast, ovary, and lung.<sup>14,19</sup>

#### Prevalence and Epidemiology

Despite high vascularity of the spleen, metastatic tumors are uncommon. Several theories for this have been proposed, including the natural rhythmic contraction of the spleen squeezing tumor emboli out, the antineoplastic properties of lymphoid-rich splenic parenchyma, and the lack of afferent lymphatics to bring in metastatic tumor.<sup>20</sup> Splenic metastasis generally occurs in patients with widespread metastatic disease, indicating a poor prognosis. However, in one large series, isolated splenic lesions were seen in 52% of patients with splenic metastases (Figures 59-19 and 59-20). These



**Figure 59-18** Splenic lymphoma. A, Axial contrast-enhanced computed tomography (CT) scan during the arterial phase reveals multiple lowattenuation masses in the spleen. B, On portal venous phase CT, multiple masses become more isodense lesions (*arrows*), relative to the normal spleen. Lymphomatous nodules are more confidently found on the arterial phase image than the portal venous phase image in this case. C, Multiple enlarged lymph nodes in the aortocaval space and in the mesentery are noted. D, The splenic lesions are seen as nearly anechoic lesions with septa-like structures on an ultrasonogram. Characteristically, the lymphomatous splenic nodules are seen as low signal intensity on both T1-weighted (E) and T2-weighted (F) magnetic resonance (MR) images. T1-weighted MR images after gadolinium administration also demonstrate multiple hypointense masses during the arterial phase (G) and decrease of lesional conspicuity during the portal venous phase (H).

metastases are believed to arise from hematogeneous spread of disease via splenic arterial blood flow. Less commonly, metastases may spread to the spleen via the splenic vein in patients with portal hypertension or via the lymphatics in a retrograde fashion.<sup>14</sup>

#### **Clinical Presentation**

Because splenic metastases usually occur late in the course of disease with widespread involvement of other organs, clinical findings are those of progressed malignancies and there is no unique clinical feature associated with splenic metastases. In patients with isolated splenic metastases, the manifesting symptom may be left upper quadrant mass or pain when the spleen is enlarged and replaced with tumor. Rupture is rare but may precipitate an abdominal emergency.<sup>14</sup>

#### Pathophysiology

One third of intrasplenic metastases are microscopic nodules, and the other two thirds are grossly visible at autopsy.<sup>19</sup> Splenic

metastases may be solitary (30% to 40%) or multiple (50% to 60%) nodular lesions or diffuse infiltrating lesions (8% to 10%).

#### Pathology

Grossly, the spleen is usually seen to be normal in size with multiple small discrete nodules or as a solitary large mass (see Figure 59-19). At microscopic examination, the appearance of metastases varies depending on the tumor of origin. Many metastases in the spleen are cystic, secondary to rapid growth, resulting in autoinfarction, internal necrosis, or both.<sup>3</sup>

#### Imaging

**Radiography.** Mild to moderate splenomegaly may be present with or without mass effect on the adjacent organs.

**Computed Tomography.** Splenic metastases are typically multiple masses of decreased attenuation compared with the normal spleen and sometimes may be solitary (see Figures

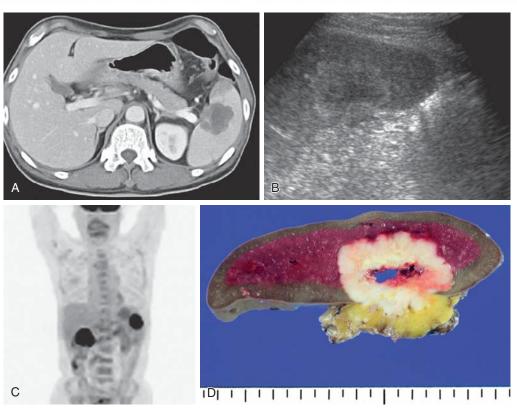
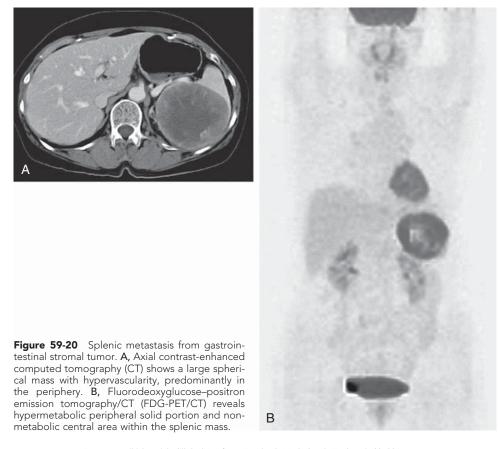


Figure 59-19 Splenic metastasis from colon cancer. A, Axial contrast-enhanced computed tomography (CT) shows lobulating contoured lowattenuation mass in the spleen. Note the wedge-shaped low-attenuation lesion in the subcapsular portion of the spleen, suggestive of splenic infarction. B, Oblique axial sonogram reveals heterogeneous echo pattern of the lesion, with hyperechoic periphery and hypoechoic center. C, Fluorodeoxyglucosepositron emission tomography/CT (FDG-PET/CT) demonstrates strongly increased glucose metabolism in the spleen as well as hepatic flexure of the colon, the primary site. D, The patient underwent splenectomy as well as right hemicolectomy. The cut surface of the gross specimen shows a whitish splenic mass with infiltrative margin. Histopathologic diagnosis was isolated splenic metastasis from carcinoma of the colon.



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#### 668 PART 6 Gallbladder, Bile Ducts, and Spleen

59-19 and 59-20 and Table 59-2). They may appear solid or occasionally cystic. Other lesions may be infiltrative and have lower attenuation than normal splenic tissue, mimicking lymphoma. CT is helpful in identifying any enhancing components of the lesion that favor the diagnosis of malignancy (Figure 59-21). A cystic mass may show enhancement of the periphery and septum. Calcifications of metastases are rare unless the primary tumor is a mucinous adenocarcinoma. Common primary tumors that produce cystic splenic metastases include melanoma and carcinomas of the ovary, breast, and endometrium.<sup>14</sup>

**Magnetic Resonance Imaging.** Splenic metastases are typically seen as low and high signal intensity on T1- and T2-weighted images. The presence of blood products from hemorrhage or other paramagnetic substances, such as melanin within melanomas, may result in high signal intensity on T1-weighted images.<sup>3</sup> In some instances, metastatic tumors have similar signal intensities to normal spleen and, in such cases, conventional MRI may have limited value in



**Figure 59-21** Axial contrast-enhanced computed tomography shows cystic splenic metastasis from ovarian cancer, seen as a heterogeneous mass with cystic and solid components.

detection and size estimation of the metastatic diseases. Gadolinium-enhanced MRI may improve lesion detection by acquiring early postenhanced images. Furthermore, the use of superparamagnetic iron oxide improves detection of splenic metastases, because the signal drop of the splenic parenchyma results in an increase of contrast resolution between metastatic tumor and spleen. Similarly, in patients with transfusion-related iron overload, metastatic disease can be more conspicuously seen as high signal intensity lesions on T2-weighted images against profound low signal intensity of the surrounding spleen with iron deposition.<sup>1,10,20</sup>

**Ultrasonography.** Splenic metastases vary in ultrasonographic appearance from hypoechoic to hyperechoic. Although there is no correlation between the radiologic features of the metastases and the primary tumor type, large lesions tend to appear more complex than smaller ones (see Figure 59-19). A target type with a hypoechoic halo is not a common pattern (~10%) in splenic metastases, in contrast to hepatic metastases.

**Nuclear Medicine.** <sup>99m</sup>Tc-sulfur colloid scintigraphy has currently no role for workup of splenic metastasis because of a low sensitivity and specificity.<sup>14</sup>

**Positron Emission Tomography With Computed Tomography.** FDG-PET surpasses radiologic studies such as CT and MRI in characterizing splenic lesions as benign and malignant (see Figures 59-19 and 59-20), and a recent study reported the accuracy of 100% for this purpose.<sup>12</sup> However, although it is generally accepted that PET/CT has a high negative predictive value for malignancy, it should be kept in mind that splenic metastasis of non–FDG-avid tumors such as some renal or thyroid cancers may result in false-negative findings.<sup>12</sup> Also, splenic granulomatous disease (e.g., sarcoidosis, tuberculosis, *Brucella*) may appear as FDG-avid splenic lesions, mimicking malignancy.<sup>11,12</sup>

#### Direct Invasion of the Spleen

Direct invasion of the spleen by adjacent malignant tumor is uncommon but may occur from a large gastric or colonic cancer, pancreatic tail cancer (Figure 59-22), renal cell

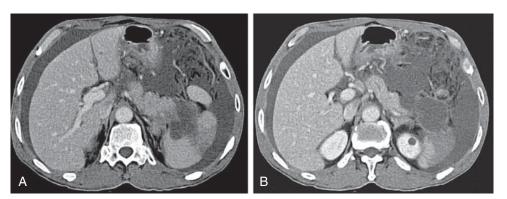
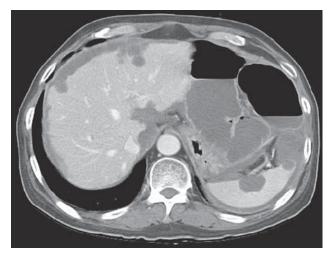


Figure 59-22 Direct splenic invasion of pancreatic tail cancer. A and B, Axial contrast-enhanced computed tomography scans show a lobulated contoured, low-density mass replacing the pancreas tail and abutting the splenic hilum.

carcinoma of the left kidney, or malignant tumor of left adrenal origin, in decreasing order of frequency. Peripancreatic or splenic hilar lymph node metastases from various tumors may secondarily invade the spleen as well.<sup>14</sup>

#### Peritoneal Implants to the Surface of the Spleen

Serosal implants on the spleen are seen in patients with peritoneal carcinomatosis from ovarian cancer, gastrointestinal adenocarcinoma, and pancreatic cancer. CT typically shows scalloping of the surface of the spleen associated with solid and cystic components (Figure 59-23). Either psammomatous or dense calcifications may be noted in a case of mucinous adenocarcinoma. Serosal implants may occasionally indent the splenic parenchyma and mimic intrasplenic masses.<sup>14</sup>



**Figure 59-23** Axial contrast-enhanced computed tomography scan shows multiple serosal implants on the spleen as well as on the liver, scalloping the surface and indenting the parenchyma, in a patient with pseudomyxoma peritonei.

#### Treatment

**Medical Treatment.** Because splenic metastases usually occur late in the course of the disease, only conservative and palliative medical management may be indicated in most patients.

**Surgical Treatment.** Surgery may be occasionally indicated in patients with isolated splenic metastasis.

#### OTHER SPLENIC MALIGNANCIES

Rarely, other primary malignant tumors of mesenchymal origin, including fibrosarcoma, leiomyosarcoma, malignant teratoma, and malignant fibrous histiocytoma, may occur in the spleen. Because of the rarity of these lesions, radiologic features have been rarely reported in the literature. It has been reported that malignant fibrous histiocytoma arising in the spleen may appear as a bulky mass with areas of extensive necrosis.<sup>6</sup>

#### What the Referring Physician Needs to Know: Malignant Splenic Tumors

- Although there may be considerable overlap between imaging findings of benign and malignant lesions, sometimes radiologic studies enable the diagnosis of malignant splenic tumors, practically with no need for further investigation.
- Because FDG-PET is highly accurate in characterizing splenic lesions as benign and malignant, it can be helpful in problematic cases.
- Because FDG-PET also may result in false-positive and false-negative diagnoses, a complementary approach using multimodality imaging and FDG-PET/CT may aid in reaching a correct diagnosis.

#### **Key Points**

#### Splenic Cysts

- Sharp demarcation and smooth margin
- Nearly imperceptible wall and avascularity
- Contents having water density, signal, and echo, if uncomplicated

#### **Benign Splenic Tumors**

- Hemangioma: Well-defined solitary or multiple masses with a combination of solid and cystic appearances and variable enhancement pattern on postcontrast studies
- Hamartoma: Well-circumscribed, solid mass with hypervascularity, seen as heterogeneously enhancing lesion or isoattenuating lesion compared with background spleen on postcontrast studies
- Lymphangioma: Sharply marginated solitary or multiple cystic lesions with scanty vascularity only in the wall and septum, typically in subcapsular location
- Littoral cell angioma: Typically multiple nodular lesions of similar size and appearance in patients with splenomegaly and hypersplenism

• Inflammatory pseudotumor/myofibroblastoma: Heterogeneously hypodense mass with mild to moderate and prolonged contrast enhancement and increased uptake of FDG

#### Malignant Splenic Tumors

- Angiosarcoma: Solitary or multiple nodular hypervascular masses composed of a heterogeneous compartment including the area of hemorrhage or necrotic degeneration, sometimes with rupture
- Lymphoma: Variable appearances on radiologic studies such as (1) splenomegaly without a discrete mass,
  (2) solitary hypovascular mass, (3) multifocal lesions, and
  (4) diffuse miliary nodular infiltration; occasionally low signal intensity lesion on T2-weighted images; invariably increased FDG uptake on PET
- Metastasis: Late in the course of disease with widespread metastasis or sometimes isolated to the spleen; typically multiple or sometimes solitary; solid hypovascular lesion compared with the normal spleen; possible cystic changes; invariably increased FDG uptake on PET

#### SUGGESTED READINGS

- Abbott RM, Levy AD, Aguilera NS, et al: From the archives of the AFIP: primary vascular neoplasms of the spleen—radiologic-pathologic correlation. *Radiographics* 24:1137–1163, 2004.
- Bhatia K, Sahdev A, Reznek RH: Lymphoma of the spleen. Semin Ultrasound CT MR 28:12–20, 2007. De Schepper AM, Vanhoenacker F, de Beeck BO,
- et al: Vascular pathology of the spleen. II. Abdom Imaging 30:228–238, 2005.

#### REFERENCES

- 1. Robertson F, Leander P, Ekberg O: Radiology of the spleen. *Eur Radiol* 11:80–95, 2001.
- 2. Doolas A, Nolte M, McDonald OG, et al: Splenic cysts. J Surg Oncol 10:369–387, 1978.
- Urrutia M, Mergo PJ, Ros LH, et al: Cystic masses of the spleen: radiologic-pathologic correlation. *Radiographics* 16:107–129, 1996.
- 4. Vos PM, Barnard SA, Cooperberg PL: Benign and malignant lesions of the spleen. In Gore RM, Levine MS, editors: *Textbook of Gastrointestinal Radiology*, ed 4, Philadelphia, 2015, Saunders, pp 1923–1964.
- 5. Rosai J: Spleen. In *Surgical Pathology*, ed 9, St. Louis, 2004, Mosby, pp 2019–2045.
- Warshauer DM, Hall HL: Solitary splenic lesions. Semin Ultrasound CT MR 27:370–388, 2006.
- Abbott RM, Levy AD, Aguilera NS, et al: From the archives of the AFIP: primary vascular neoplasms of the spleen: radiologic-pathologic correlation. *Radiographics* 24:1137–1163, 2004.
- 8. Husni EA: The clinical course of splenic hemangioma with emphasis on spontaneous rupture. *Arch Surg* 83:681–688, 1961.

- Elsayes KM, Narra VR, Mukundan G, et al: MR imaging of the spleen: spectrum of abnormalities. *Radiographics* 25:967–982, 2005.
- Kamaya A, Weinstein S, Desser TS: Multiple lesions of the spleen: differential diagnosis of cystic and solid lesions. Semin Ultrasound CT MR 27:389–403, 2006.
- Metser U, Even-Sapir E: The role of 18F-FDG PET/ CT in the evaluation of solid splenic masses. *Semin Ultrasound CT MR* 27:420–425, 2006.
- 9. Elsayes KM, Narra VR, Mukundan G, et al: MR imaging of the spleen: spectrum of abnormalities. *Radiographics* 25:967–982, 2005.
- Bilaj F, Rivero H, Firat Z, et al: Spleen. In Semelka RC, editor: *Abdominal-pelvic MRI*, ed 2, Hoboken, NJ, 2006, Wiley, pp 637–675.
- Metser U, Even-Sapir E: The role of 18F-FDG PET/CT in the evaluation of solid splenic masses. Semin Ultrasound CT MR 27:420–425, 2006.
- Metser U, Miller E, Kessler A, et al: Solid splenic masses: evaluation with 18F-FDG PET/CT. *J Nucl Med* 46:52–59, 2005.
- Taylor MA, Kaplan HS, Nelsen TS: Staging laparotomy with splenectomy for Hodgkin's disease: the Stanford experience. *World J Surg* 9:449– 460, 1985.
- Kawashima A, Urban BA, Fishman EK: Malignant lesions of the spleen. In Gore RM, Levine MS, editors: *Textbook of Gastrointestinal Radiology*, ed 2, Philadelphia, 2000, Saunders, pp 1904–1914.
- Freeman JL, Jafri SZ, Roberts JL, et al: CT of congenital and acquired abnormalities of the spleen. *Radiographics* 13:597–610, 1993.

- Robertson F, Leander P, Ekberg O: Radiology of the spleen. *Eur Radiol* 11:80–95, 2001.
- Urrutia M, Mergo PJ, Ros LH, et al: Cystic masses of the spleen: radiologic-pathologic correlation. *Radiographics* 16:107–129, 1996.
- Warshauer DM, Hall HL: Solitary splenic lesions. Semin Ultrasound CT MR 27:370–388, 2006.
- Littooij AS, Kwee TC, Barber I, et al: Accuracy of whole-body MRI in the assessment of splenic involvement in lymphoma. 2015 Feb 13. pii: 0284185115571657 [Epub ahead of print].
- Kwee TC, Vermoolen MA, Akkerman EA, et al: Whole body MRI, including diffusion-weighted imaging, for staging lymphoma: comparison with CT in a prospective multicenter study. *J Magn Reson Imaging* 40:26–36, 2014.
- Rini JN, Leonidas JC, Tomas MB, et al: 18F-FDG PET versus CT for evaluating the spleen during initial staging of lymphoma. J Nucl Med 44:1072–1074, 2003.
- Berge T: Splenic metastases: frequencies and patterns. Acta Pathol Microbiol Scand [A] 82:499–506, 1974.
- Kamaya A, Weinstein S, Desser TS: Multiple lesions of the spleen: differential diagnosis of cystic and solid lesions. *Semin Ultrasound CT* MR 27:389–403, 2006.

# 0 Diffuse Splenic Lesions

MIN JU KIM | KYOUNG WON KIM

### Normal Variants and Congenital Anomalies

The spleen begins to develop during the fifth week of embryogenesis when mesenchymal cells aggregate between the two leaves of the dorsal mesogastrium to form a lobulated embryonic spleen. Rotation of the stomach and growth of the dorsal mesogastrium translocate the spleen from the midline to the left side of the abdominal cavity. The left aspect of the mesogastrium fuses with the peritoneum over the left kidney. Then, rotation of the dorsal mesogastrium establishes a mesenteric connection (the splenorenal ligament) between the spleen and the left kidney. The gastrosplenic ligament is the portion of dorsal mesentery between the spleen and the stomach.<sup>1</sup>

The fetal spleen is normally lobulated. Although such lobulations generally disappear before birth, they may persist along the medial part of the spleen. The notches or clefts on the superior border of the adult spleen are remnants of the grooves that originally separated the fetal lobules. These clefts can be sharp and are occasionally as deep as 2 to 3 cm. They may be erroneously interpreted as splenic laceration in patients with abdominal trauma. The differential points are ancillary findings such as subcapsular hematoma, hemoperitoneum, or a jagged linear area of parenchymal defect.<sup>1,2</sup>

#### ACCESSORY SPLEEN

#### Etiology

During embryogenesis a failure of the embryonic splenic buds to unite within the dorsal mesogastrium and an extreme lobulation of the spleen with pinching off of splenic tissue may result in accessory spleens.<sup>1</sup>

#### Prevalence and Epidemiology

An accessory spleen denotes a congenital focus of heterotopic, healthy splenic tissue that is separate from the main splenic body. It is the most common congenital anomaly of the spleen and is detected in 10% to 30% of patients at autopsy and in approximately 16% on computed tomography (CT).<sup>3</sup>

#### **Clinical Presentation**

The vast majority of accessory spleens are incidentally discovered without clinical significance, and recognizing them is important so as not to misdiagnose an accessory spleen as lymphadenopathy or as a tumor arising from adjacent organs. In patients with hematologic and autoimmune disorders, the presence of accessory spleens should be noted before planning splenectomy to guide surgeons to remove all functional splenic tissue at surgery, because a remnant accessory spleen after the surgery may evoke relapse of the disorder. An accessory spleen may be noted as a source of "preservable" splenic tissue in the case of rupture of the main splenic body.<sup>3</sup>

#### Pathophysiology

Accessory spleens are commonly located near the splenic hilum or adjacent to the pancreatic tail (Figure 60-1). However, an accessory spleen also may occur along the splenic vessels, in the gastrosplenic or splenorenal ligament, within the pancreas tail, in the gastric wall, in the greater omentum or the mesentery, or even in the pelvis or scrotum.<sup>1</sup>

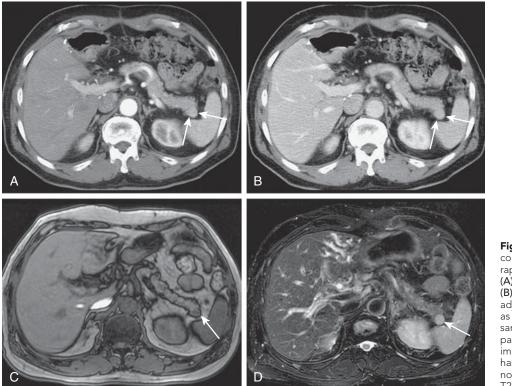
Accessory spleens are usually approximately 1 cm in diameter (see Figure 60-1) but vary from microscopic deposits not visible on CT to over 4 cm in diameter.<sup>4,5</sup>

#### Imaging

When a small accessory spleen is typically located in the splenic hilum there is no confusion at cross-sectional imaging. However, those in atypical locations may be misdiagnosed as various entities according to the location. It is worthwhile to compare their imaging characteristics with those of a normal spleen because accessory spleens invariably exhibit the same features as a normal spleen on various imaging modalities (Tables 60-1 and 60-2; see also Figures 60-1 and 60-2). After splenectomy a remnant accessory spleen can be hypertrophied, occasionally mimicking enlarged lymph nodes or another mass (Figure 60-3). In all confusing cases, technetium-99m sulfur colloid (<sup>99m</sup>Tc-SC) scintigraphy is helpful because it can demonstrate functional activity of the splenic tissue.<sup>1</sup>

**Radiography.** Accessory spleens are usually not detected by conventional radiographic studies.

**Computed Tomography.** CT features of accessory spleens are quite characteristic. They appear as round or ovoid masses with well-defined borders, typically near the splenic hilum or adjacent to the pancreatic tail. Accessory spleens have similar density



**Figure 60-1** Accessory spleen. Axial contrast-enhanced computed tomography scans during the arterial phase (A) and the portal venous phase (B) show an accessory spleen (*arrows*) adjacent to the pancreatic tail, seen as a well-defined nodule with the same enhancement pattern as the parent spleen. On magnetic resonance imaging, an accessory spleen (*arrow*) has a signal intensity similar to that of normal spleen on T1-weighted (C) and T2-weighted (D) images.

TABLEAccuracy60-1Accuracy	, Limitations, and Pitfalls of	Modalities Used in Imaging of	Diffuse Splenic Lesions	
Modality	Accuracy	Advantages	Limitations	Pitfalls
Radiography	Poor	Limited	Insensitive Nonspecific	Unable to directly visualize splenic abnormality
СТ	Up to 95% in a case of trauma-related lesion Data of the rest are not available to specify accuracy.	Initial modality of most splenic abnormalities, especially trauma-related lesion	Radiation exposure Adverse effect of contrast agent	Multiple, tiny, diffusely scattered nodules not easy to be detected
MRI	Data are not available to specify and compare accuracy of different imaging modalities for evaluation of splenic abnormality	May be additional clue in the difficult case for differentiation	Ineffective in hemodynamically unstable patients High cost Patient cooperation	Small lesions may not be detected
Ultrasonography		May be additional clue in the difficult case for differentiation Useful screening method for the splenic injury especially in hemodynamically unstable patient and pediatric patient	Operator dependent	Small lesions may not be detected
Nuclear medicine		Helpful to identify the splenic functional activity of the suspected lesion such as splenosis, accessory spleen, and wandering spleen	Poor spatial resolution	Nonspecific
PET/CT			Radiation exposure High cost	Nonspecific

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

TABLE Clinical	Clinical and Radiologic Features of Diffuse Sp	of Diffuse Splenic Lesions				
Lesion	Characteristics	cī	MR	Ultrasonography	Distinguishing Clinical Features	Distinguishing Imaging Findings
Accessory spleen	Most common: Congenital anomaly Size: 1 cm Locations: Splenic hilum, adjacent to the pancreas tail	Similar density/signal intensity (T14, T2f)/echogenicity, and contrast- enhancement pattern as normal spleen on unenhanced and postcontrast images	y (T14, T21)/echogenicity, ormal spleen on unenhanc	, and contrast- ied and postcontrast	Underlying malignancy (-) Splenic injury or prior splenectomy (-) Normal visceral situs	Typical findings → straightforward diagnosis
Wandering spleen	Absence of the spleen in its normal position and a soft tissue mass resembling the spleen located somewhere else Location: Left mid abdomen Age: 20-40 years Sex: F > M	No spleen in left subphrenic area Comma-shaped spleen-like mass somewhere else Splenic torsion: Lower attenuation than liver and "rim" sign	A little additional value of MRI	Splenic infarction: Less echogenic Color Doppler: Absence of blood flow	Nonspecific	Absence of the spleen in its normal location and presence of a comma-shaped abdominal or pelvic mass
Polysplenia	Multiple spleens or a multilobed spleen Interrupted IVC with continuation to azygos vein Liver: Midline; gallbladder: central location Anomalies of branching pattern of portal vein an Truncated pancreas Abnormalities of bowel rotation Age: Early childhood because of the various carc Sex: F > M	Multiple spleens or a multilobed spleen Interrupted IVC with continuation to azygos vein Liver: Midline; gallbladder: central location Anomalies of branching pattern of portal vein and biliary tree Truncated panceas Anormalities of bowel rotation Age: Early childhood because of the various cardiac anomalies Sex: F > M	ee lies		Related to the cardiac disease Young patient	Multiple spleens or a multilobed spleen Interrupted IVC with continuation to azygos vein
ASPLENIA	Absence of splenic tissue on ultrasonography/CT/ lpsilateral position of IVC/hepatic veins and aorta Liver: Midline; gallbladder: central location Anomalies of branching pattern of portal vein anc Truncated pancreas Abnormalities of bowel rotation Very high mortality rate >95% in their first year of Sex: M > F	Absence of splenic tissue on ultrasonography/CT/splenic scan psilateral position of IVC/hepatic veins and aorta Liver: Midline; gallbladder: central location Anomalies of branching pattern of portal vein and biliary tree Truncated pancreas Abnormalities of bowel rotation Very high mortality rate >95% in their first year of life because of severe congenital heart disease Sex: M > F	an ee use of severe congenital h	eart disease	Splenectomy and trauma (-), and abnormal situs of various organs in thorax and abdomen Related to the cardiac disease	Absence of splenic tissue on ultrasonography/CT/ splenic scan lpsilateral position of IVC/hepatic veins and aorta
INFECTIOUS AN Bacterial infection	INFECTIOUS AND INFLAMMATORY LESIONS Bacterial Cause: Hematogenous, infection trauma, infarction Organism: Aerobic (60%)	Lesion with a low-density center surrounded by a thick, irregular, dense rim	Rarely performed	Poorly defined, hypoechoic or anechoic lesions with irregular boundary	Findings of fever, chills, and leukocytosis helpful	Containing gas: Discriminating finding, but rare
Fungal infection	Most common cause: Candida, Aspergillus Size: 5-10 mm Distribution: Diffuse dissemination	Multiple, rounded, low density, small lesion with ring-like enhancement	MR superior to CT Multiple small nodules T1↓ ↔ T2↑	"Bull's-eye" pattern: Typical splenic candidiasis	Immunocompromised patients Fever and splenomegaly Nonspecific, sometimes	Diffusely disseminated small nodules: Nonspecific Differential diagnosis: Tuberculosis, sarcoidosis, lymphoma, and metastases
Mycobacterial infection	Hematogenous or lymphatic spread, usually from the lung Miliary form, usually	Miliary or multiple small nodules of low density Abdominal lymphadenopathy or peritonitis	Few reports	Tuberculomas: Decreased or mixed echogenicity	Indolent fever, immunocompetence, malignancy (–) and pulmonary abnormality	Diffusely disseminated small nodules: Nonspecific

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60 Diffuse Splenic Lesions 673

Continued

TABLE Clinica	Clinical and Radiologic Features of Diffuse	of Diffuse Splenic Lesions-	cont'd			
Lesion	Characteristics	c	MR	Ultrasonography	Distinguishing Clinical Features	Distinguishing Imaging Findings
Echinococcosis	Echinococcus granulosus Systemic and intraperitoneal spread from ruptured liver cyst	Spherical, well-defined water-attenuation lesions	Well-defined rounded mass with water-attenuation signal intensity (T1 ↓, T2^)	Anechoic or mixed echogenic, round lesion	A patient from an endemic area with positive serologic tests	Daughter cysts
Sarcoidosis	Multisystem disease Mediastinal and hilar lymph nodes Splenomegaly or multiple small lesions	Normal or enlarged spleen Multiple low-attenuation nodules (1 mm-3 cm)	т14, т24	Diffuse increase of splenic echogenicity and splenomegaly	Extraabdominal sarcoidosis and an elevated angiotensin- converting enzyme level	↓ Signal intensity on T2-weighted MRI
VASCULAR LESIONS	SNOIS					
Splenic infarction	Most common causes: Embolic occlusion from cardiovascular disease (usually elderly patients) and local thrombosis from hematologic diseases (age <40 yr)	Peripheral wedge-shaped, sharply demarcated area of low attenuation	Of various signal intensity according to age of infarctions	Color Doppler imaging: Absence of blood flow	High-fever (–) Episode of trauma (–)	Peripheral wedge- shaped, sharply demarcated area Differential diagnosis: Splenic abscess, tumor, laceration, and cyst
Splenic venous thrombosis	Most common cause: Pancreatitis	Noncontrast CT: High- attenuation lesion Contrast-enhanced CT: Intraluminal, low- attenuation filling defect adjacent to the venous wall, gastrointestinal varices, splenomegaly	Acute thrombus: T11, T21	Acute thrombus: Echogenic Color Doppler ultrasonography: Absence of color flow in cases of total occlusion	History of pancreatitis and variceal bleeding	Imaging findings are almost always typical, pinpointing the diagnosis
Splenic artery aneurysm	Most incidentally detected Rupture of splenic artery aneurysm is a rare, but life-threatening complication. Sex: F > M	Round to saccular or fusiform dilatation of the splenic artery, with or without peripheral calcification, sometimes with mural thrombus	Various signal intensity according to flow alteration and the extent of the mural thrombus	Anechoic mass with or without peripheral calcification Color Doppler imaging proves the vascular lesion	Asymptomatic, usually	Imaging findings are almost always typical, pinpointing the diagnosis
Trauma- related lesions	Most common injured organ after blunt trauma	Best imaging modality for screening of splenic injury Accuracy > 95% Useful for acute hematoma, laceration, active bleeding, pseudoaneurysms, arteriovenous fistula, and posttraumatic infarction	Little role in splenic trauma because of long scanning time	Useful method for the screening of splenic injury, especially in hemodynamically unstable patient and pediatric patient	Episode of trauma: Important clinical data	Splenic cleft may mimic splenic laceration; from lateral surface, fill-in enhancement from periphery on dynamic study
Splenosis	Heterotopic splenic implants anywhere Multiple Size: Various	Same echogenicity, density, and signal intensity as normal spleen on ultrasonography, CT, and MRI On dynamic study, similar enhancement pattern as normal spleen	and signal intensity as no MRI hancement pattern as no	mal spleen on rmal spleen	History of splenic trauma or splenectomy is an important clue. Underlying malignancy (-)	<sup>99</sup> mTc-sulfur colloid scintigraphy is helpful to identify the splenic functional activity of the suspected lesion
Splenomegaly	Most common cause: Portal hypertension	Craniocaudal measurement of 13-14 cm	of 13-14 cm		Clinical presentation: Various	Size measurement, roughly
↔, Iso-signal inte MR, magnetic r	↔, Iso-signal intensity; ↓, Iow signal intensity; ↑, high signal intensity; (−), absence of history; <sup>99m</sup> Tc, technetium-99m; CT, computed tomography; F, female; NC, inferior vena cava; M, male; MR, magnetic resonance; MRI, magnetic resonance imaging.	high signal intensity; (–), absen iance imaging.	ce of history; <sup>99m</sup> Tc, techne	etium-99m; CT, computed tc	omography; F, female; IVC, in	nferior vena cava; <i>M</i> , male;

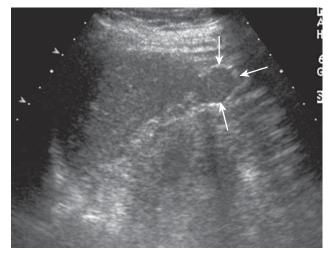
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and contrast-enhancement pattern as a normal spleen on unenhanced and postcontrast CT (see Figure 60-1).<sup>3</sup>

**Magnetic Resonance Imaging.** On various MR pulse sequences, accessory spleens have the same signal intensities as those of normal spleen (dark on T1-weighted image and bright on T2-weighted and diffusion weighted images) (see Figure 60-1).<sup>3</sup>

**Ultrasonography.** Sonographically, accessory spleens have the same echogenicity and echotexture as the main splenic body (see Figure 60-2).<sup>1</sup>

**Nuclear Medicine.** The diagnosis of splenic tissue not in its normal anatomic location is best made by <sup>99m</sup>Tc-SC scintigraphy, which is highly sensitive and specific for splenic and hepatic tissue.<sup>3</sup>



**Figure 60-2** Accessory spleen. Oblique coronal ultrasound image of the left upper quadrant shows an accessory spleen (*arrows*), inferior to the main splenic body, producing the same echogenicity as the main spleen.

#### **Classic Signs: Accessory Spleen**

- Typical location near the splenic hilum or adjacent to the pancreatic tail
- Same features and enhancement pattern as normal spleen on various imaging modalities

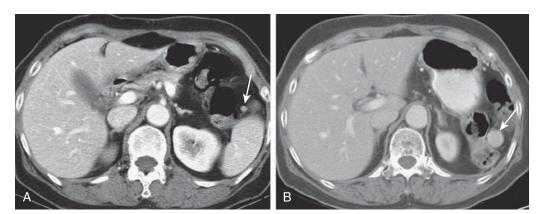
#### Differential Diagnosis

The differential diagnosis of accessory spleen includes splenosis, polysplenia, peritoneal metastatic implants, lymphadenopathy, and a tumor arising from adjacent organs. The clinical history of previous splenic injury or prior splenectomy permits differentiation of splenosis from other disorders. It is helpful for discrimination of polysplenia that there is bilateral "leftsidedness" of abdominal viscera and cardiovascular anomalies. A previous clinical history of an underlying malignancy such as ovarian cancer or pancreatic cancer helps in differentiating an accessory spleen from peritoneal metastases, lymphadenopathy, and malignant tumor from adjacent organs.

Contrast enhancement of the lesion similar to the spleen on CT, magnetic resonance imaging (MRI), and ultrasonography and intense uptake of tracer by accessory spleens on nuclear scintigraphy permit differentiation of this anomaly from other disorders. The most common location of accessory spleen is the splenic hilum and around the pancreatic tail, whereas splenosis can develop anywhere, including the abdomen, the pelvis, and even the chest. When accessory spleen is located in the pancreas tail, it is important to make a differential diagnosis from neuroendocrine tumor of the pancreas that may appear as a small hypervascular lesion. It has been suggested that diffusion weighted MRI may help differentiate intrapancreatic accessory spleen from solid pancreas tumors, because splenic tissue is usually hyperintense on diffusion weighted images with high b-value.<sup>6</sup>

#### Treatment

Accessory spleens are normal variants. Treatment is not necessary.



**Figure 60-3** Hypertrophy of accessory spleen. **A**, Axial contrast-enhanced computed tomography (CT) shows a small accessory spleen (*arrow*) anterior to the main splenic body. **B**, The patient underwent distal pancreatectomy and splenectomy for the treatment of cystic pancreatic tumor (mucinous cystadenoma, not shown). On follow-up CT 3 years after the splenectomy, the remnant accessory spleen is hypertrophied to approximately 2 cm. Typical location, smooth margin, homogeneity, and good enhancement are the diagnostic clues of accessory spleen, and it should not be misdiagnosed as lymph node metastasis or a peritoneal seeding nodule in patients with malignancy and desmoid tumor.

#### WANDERING SPLEEN

#### Etiology

Wandering or ectopic spleen refers to migration of the spleen from its normal site in the left upper quadrant to a more caudal location in the abdominal cavity, owing to laxity or maldevelopment of the supporting (gastrosplenic and splenorenal) ligaments. Congenital wandering spleen is characterized by the absence or underdevelopment of one or both of these ligaments, resulting in a long pedicle containing the splenic vessels and, frequently, the pancreatic tail. The acquired form occurs secondary to weakened supporting ligaments from the hormonal effects of pregnancy, abdominal wall laxity, and other causes such as splenomegaly. The long pedicle renders the spleen hypermobile, predisposing it to torsion.<sup>3,4</sup> Also, wandering spleen is more susceptible to trauma.<sup>7</sup>

#### Prevalence and Epidemiology

This anomaly is quite rare, with an incidence of less than 0.5% in several large series of splenectomies. It is usually found between the ages of 20 and 40 years and is more common in women. Children make up one third of all cases, with boys and girls younger than the age of 10 years equally affected. The assumed cause in this age group is a congenital defect.<sup>3,4</sup>

#### **Clinical Presentation**

Adult patients with wandering spleen most commonly present with nonspecific abdominal pain associated with a palpable abdominal mass, whereas children most commonly present often with acute abdominal pain. Presumably, pain occurs when there is pressure on the vascular pedicle of the spleen or when torsion develops. Acute splenic torsion may produce clinical signs of acute pancreatitis.

Persistent torsion of greater than 180 degrees may lead to splenic infarction and an acute abdomen. Intermittent and chronic torsion may be related to splenic venous congestion, causing splenomegaly, hypersplenism, fundal gastric varices, and even acute gastrointestinal hemorrhage.<sup>1,3</sup>

#### Pathology

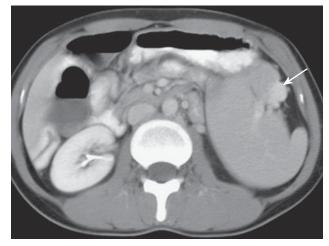
Wandering spleen manifests as a mobile mass in the left (Figure 60-4) or central abdomen. It is most commonly located anterior to the left kidney, and the left kidney may be elevated. Splenic flexure of the colon may be medial and anterior to its usual location, or it may be interposed between the diaphragm and the spleen. The stomach may be displaced into the splenic fossa and appear inverted.<sup>1</sup>

#### Imaging

The most characteristic radiologic finding of wandering spleen is absence of the spleen in its normal position and a soft tissue mass resembling the spleen located somewhere else in the abdomen. The most common location of the spleen is in the left mid abdomen<sup>3</sup> (see Figure 60-4).

**Radiography.** In patients with wandering spleen, plain radiographs may depict a mobile masslike contour in the left or central abdomen, with a changing location at supine and erect positions.<sup>1</sup>

**Computed Tomography.** Wandering spleen is easily diagnosed on CT when there is no spleen in the left subphrenic area and



**Figure 60-4** Wandering spleen. Axial contrast-enhanced computed tomography shows incorrect location of the spleen in the left midabdomen, which is the most common location of the wandering spleen. Typical comma-shaped appearance of the spleen is noted as well as normal splenic vessels (*arrow*) in the laterally fronted splenic hilum.

typically a comma-shaped spleen-like mass is found somewhere else in the abdomen (see Figure 60-4).

In addition, CT is valuable for the diagnosis of splenic torsion. The twisted splenic pedicle containing splenic vessels, surrounding fat, and sometimes the pancreatic tail may produce the "whirl" sign, representing splenic torsion. In such cases, the splenic parenchyma with congestion or infarction has attenuation considerably lower than that of the liver, more than the usual difference of approximately 10 Hounsfield units (HU). An area of infarction is apparently seen as a perfusion defect on contrast-enhanced CT.

The rim sign, defined as the high density of the splenic capsule compared with the parenchyma, is another CT finding of splenic infarction, which can be noted on both precontrast and postcontrast scans. This finding is probably due to collateral circulation through the short gastric and pancreatic arteries and/or the short gastric and left gastric veins.<sup>3,7</sup>

**Magnetic Resonance Imaging.** MRI may also demonstrate absence of the spleen in the left subphrenic area and a spleen-like mass somewhere else. Although there have been only a few reports on the additional value of MRI in the diagnosis of wandering spleen and splenic torsion up to now, this examination may confer certain advantages over CT in the future, owing to its superior tissue characterization as well as its lack of ionizing radiation.<sup>8</sup>

**Ultrasonography.** Ultrasonography may show an abnormal location of the spleen as well. Splenic infarction may cause the spleen to appear less echogenic than normal. Color Doppler ultrasonography may demonstrate the absence of blood flow in the spleen and a high resistive index in the splenic artery in cases of torsion of a wandering spleen.<sup>1</sup>

**Nuclear Medicine.** <sup>99m</sup>Tc-SC scintigraphy is the time-honored method for diagnosing wandering spleen. It depicts the abnormal location of the spleen, which may migrate on sequential studies. A decubitus view may be added to show splenic motion. The absence of uptake in a previously demonstrated wandering spleen indicates torsion.<sup>1</sup>

#### **Classic Signs: Wandering Spleen**

- Absence of the spleen in its normal location
- A comma-shaped abdominal or pelvic mass

#### Differential Diagnosis

When patients with wandering spleen present with acute splenic torsion, physical examination is difficult because of acute pain and clinical signs often mimic those of acute pancreatitis. Also, often the initial impression may be a twisted ovarian cyst, appendicitis, or cholecystitis.<sup>1</sup>

When there is a typical comma-shaped abdominal or pelvic mass with absence of the spleen from its normal location, the diagnosis of wandering spleen on cross-sectional imaging studies can be straightforward.<sup>3,9</sup> However, in the case of torsion, further diagnostic information on splenic perfusion and viability should be assessed on imaging studies because this information is important for the surgeon, to determine whether splenopexy or splenectomy is the treatment of choice.<sup>7</sup> When the differential diagnosis of wandering spleen from space-occupying lesion is, rarely, difficult, <sup>99m</sup>Tc-SC scintigraphy may help for differentiation.

#### Treatment

For patients without presenting symptoms of torsion, surgical intervention is not advised.<sup>9</sup> In the torsion of wandering spleen, conservative treatment has been employed in selected cases but is not recommended.<sup>7</sup>

The treatment of choice for wandering spleen, especially in young children, is fixation of the spleen (splenopexy). In the presence of splenic infarction, splenectomy is required.<sup>7,9</sup>

#### POLYSPLENIA AND ASPLENIA SYNDROMES

#### Etiology

Polysplenia and asplenia syndromes represent two major categories in a spectrum of anatomic abnormalities known as visceral heterotaxia. Embryologically altered timing in the development of embryonic body curvature has been postulated as the cause of these visceroatrial sinus abnormalities: accelerated curvature causing polysplenia syndrome and delayed curvature causing asplenia syndrome.<sup>1</sup>

As a cause of embryologic abnormality, genetic mutation in some genes has been reported recently in patients with heterotaxia. Environmental factors also may contribute to heterotaxia.<sup>10</sup>

#### Prevalence and Epidemiology

Polysplenia syndrome is a multisystemic congenital abnormality characterized by multiple small splenic masses and features of left isomerism. On the contrary, asplenia syndrome refers to congenital absence of the spleen and right isomerism.

Polysplenia syndrome is usually diagnosed in early childhood because of the various and, often, severe cardiac anomalies. There is a female predilection in polysplenia syndrome. Most patients of polysplenia syndrome with severe cardiac anomalies die by the age of 5 years. However, when patients with polysplenia syndrome have a normal heart or only a minor cardiac defect, they reach adulthood asymptomatically without complication and the anomalies may be incidentally found on imaging studies. Therefore, the true incidence and mortality of this disorder are uncertain. Asplenia syndrome is found in 1 in 40,000 live births and occurs predominantly in males. Congenital heart disease complicates this anomaly in 99% to 100% of patients, accounting for a very high mortality rate of up to 95% in the first year of life.<sup>1,3</sup>

#### **Clinical Presentation**

The mode of clinical manifestation in polysplenia and asplenia syndromes is usually related to the associated cardiac disease. In childhood or adulthood cases of polysplenia syndrome with no or minimal cardiac abnormality, the abdominal visceral abnormalities generally do not produce any symptoms, but bowel malrotation may cause obstruction and pain because of infarction.<sup>1</sup>

#### Pathology

There is a spectrum of abdominal visceral anomalies as well as cardiopulmonary anomalies in polysplenia and asplenia syndromes.

**Spleen.** In the polysplenia syndrome, multiple discrete spleens (Figure 60-5) are considered the hallmark of the disorder. However, the number of splenic masses varies, ranging from many very small spleens to a multilobular spleen with tiny accessory spleens. The spleens may be either left-sided or right-sided and are always seen on the same side as the stomach along the greater curvature. Rarely, one of the multiple spleens may be complicated by torsion with subsequent infarction.

In the asplenia syndrome, the spleen is absent or rarely rudimentary (Figure 60-6).<sup>1,3</sup>

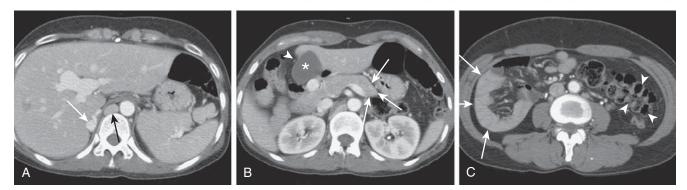
**Liver, Gallbladder, and Biliary Tract.** The liver is mostly situated in the midline, extending symmetrically to both sides of the upper abdomen in both polysplenia and asplenia syndromes. The gallbladder has a central location when the liver is in the midline, and anomalies also may affect the branching pattern of the portal vein (see Figure 60-5) and the biliary tree. Biliary atresia may be associated as well.<sup>1,3</sup>

**Pancreas.** Both polysplenia and asplenia syndromes may accompany a truncated pancreas (see Figure 60-5), also referred to as short pancreas. Cross-sectional images show only the pancreatic head or the pancreatic head and a small pancreatic body.<sup>1,3</sup>

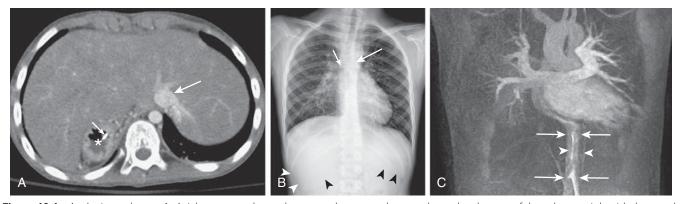
**Gastrointestinal Tract.** The stomach may be right-sided or left-sided in both polysplenia and asplenia syndromes. There may be abnormalities of bowel rotation; the small bowel is right-sided and the colon is left-sided (see Figure 60-5). An inverse relationship between the superior mesenteric artery and the superior mesenteric veins is also frequently noted.<sup>11</sup>

**Venous System.** The most common venous anomaly associated with polysplenia syndrome is interruption of the inferior vena cava (IVC) with azygos or hemiazygos continuation, occurring in 65% to 80% of individuals with polysplenia (see Figure 60-5). Caudad to the caval interruption, the IVC may be right or left of the aorta or may be duplicated. The hepatic segment of the IVC is often absent, and the hepatic veins drain directly into the right atrium. A preduodenal portal vein is another common venous anomaly.<sup>3</sup>

In asplenia syndrome, IVC interruption with azygos continuation or hemiazygos may be encountered but is very rare.



**Figure 60-5** Polysplenia syndrome. A, Axial contrast-enhanced computed tomography (CT) image shows multiple spleens in the left upper quadrant. There is an aberrant collateral vessel (*white arrow*) posterior to the hepatic bare area and engorgement of the azygos vein (*black arrow*), resulting from an interruption of the inferior vena cava. Also noted is the portal vein variation with total ramification of the intrahepatic portal branches from the right-sided umbilical segment. B, CT image shows a truncated pancreas, with only the presence of the pancreatic head and small body and with abrupt termination without a tail (*arrows*). Also noted is a slightly left-sided gallbladder (*asterisk*) compared with the fissure for the ligamentum teres (*arrowhead*). C, Intestinal malrotation is also appreciated, with right-sided small bowel (*arrows*) and left-sided colon (*arrowheads*).



**Figure 60-6** Asplenia syndrome. A, Axial contrast-enhanced computed tomography scan shows the absence of the spleen, a right-sided stomach (*asterisk*), and midline location of the large liver. A Levin tube (*small arrow*) is inserted in the stomach. Also noted is the abnormal location of the inferior vena cava (*large arrow*) in left juxtaposition to the aorta. **B**, Chest radiograph shows bilaterally symmetric bronchial trees with right isomerism. The main bronchus (*long arrow*) of the left lung is as short as the right main bronchus (*short arrow*). The shadow of the liver (*arrowheads*) is noted in both right upper and left upper quadrants of the abdomen. **C**, Magnetic resonance angiography depicts a left ipsilateral position of the aorta (*arrows*) and the inferior vena cava (*arrowheads*). The patient underwent a Fontan operation for complex congenital heart disease, including pulmonary stenosis.

An ipsilateral location of the aorta and IVC has been reported to be a consistent finding in asplenia. However, this finding is not always present in all patients. The abdominal aorta may be located slightly to the right of midline and the IVC slightly to the left to midline along their entire lengths (see Figure 60-6).<sup>11</sup>

**Cardiac and Pulmonary System.** Most patients with polysplenia or asplenia syndrome have cardiac abnormalities. In comparison with asplenia syndrome, serious cardiac malformation is less common in patients with polysplenia syndrome. Patients with polysplenia syndrome have a high frequency of bilateral bilobed lungs and bilateral hyparterial bronchi (pulmonary artery courses over ipsilateral bronchus). In most patients with asplenia, the lungs are bilaterally trilobed and the bronchi are located over the ipsilateral pulmonary artery (eparterial bronchi).<sup>1,10,12</sup>

#### Imaging

**Radiography.** Heart size in asplenia syndrome is usually normal or small on chest radiography. Cardiac enlargement mostly indicates cardiac valvular disease. A symmetric liver

shadow (see Figure 60-6) and ectopic location of gastric gas may be noted as well. A right-sided bronchial pattern (see Figure 60-6) and a minor fissure may be present bilaterally. Both pulmonary arteries project anterior to the trachea on lateral chest radiographs. Superior mediastinal widening may result from a bilateral superior vena cava.

Radiographic findings in patients with polysplenia syndrome depend on which heart defect is present. If there is an interruption of the IVC, the shadow of this vessel is absent on the lateral chest radiograph and the extension via the enlarged azygos vein may cause mediastinal widening in the frontal view. In polysplenia, bilateral symmetric bilobes with usually bilaterally hyparterial bronchi may be seen.<sup>1,10</sup>

**Computed Tomography.** Analyzing the shape and location of the heart, liver, gallbladder, bowel, and spleen on contrast-enhanced CT is useful in determining the situs abnormalities.<sup>1</sup>

**Magnetic Resonance Imaging.** Like CT, abdominal MRI can be helpful to evaluate abdominal situs abnormalities. In addition, MRI may be a useful diagnostic tool for diagnosing cardiovas cular anomalies in polysplenia and especially asplenia syndromes.  $^{\rm 12}$ 

**Ultrasonography.** Although limited in that it is operatordependent, ultrasonography may demonstrate the abdominal situs abnormalities without radiation hazard and intravenous use of a contrast agent and even in critically ill patients.<sup>1</sup>

**Nuclear Medicine.** Spleen scans using various agents including <sup>99m</sup>Tc-SC and tagged red blood cells are used in detecting splenic tissue. However, with advances in cross-sectional radiologic studies, these radioisotope studies are less frequently used than previously. Moreover, even in the presence of multiple spleens in polysplenia syndrome, splenic function may not be normal, which limits the value of radioisotope studies.<sup>10</sup>

#### **Differential Diagnosis**

The differential points of asplenia or polysplenia from splenectomy and splenosis are the previous history of splenectomy and splenic rupture after abdominal trauma.

#### Treatment

Treatment planning depends on the wide spectrum of polysplenia and asplenia syndrome. In contrast to polysplenia, asplenic patients need prophylactic antibiotics. Cardiac malformations may require surgical correction.

## Infectious and Inflammatory Lesions

#### **BACTERIAL INFECTION**

#### Etiology

A pyogenic splenic abscess is most commonly caused by the hematogenous spread of infection (75%), followed by penetrating trauma (15%), and prior splenic infarction (10%). Approximately 60% of pyogenic splenic abscesses are due to aerobic organisms, such as *Staphylococcus*, *Streptococcus*, *Escherichia coli*, and *Salmonella*. Anaerobic organisms are found in 6% to 18% of cases, with *Bacteroides* being the most common.<sup>13,14</sup>

#### Prevalence and Epidemiology

Although splenic abscess was once considered rare, its frequency of occurrence has grown over the decades as a result of an increasing number of immunosuppressed patients because of aggressive chemotherapy, bone marrow or organ transplantation, and acquired immunodeficiency syndrome (AIDS). Immunosuppressed patients make up 24% to 34% of patients with splenic abscesses.<sup>14</sup>

#### **Clinical Presentation**

Fewer than half of patients with splenic abscesses classically present with fever and chills, left upper quadrant pain and tenderness, and splenomegaly. Left pleural effusion and consolidation may be found in one third of patients. Laboratory findings are nonspecific, with leukocytosis the most common. Complications such as rupture and subsequent subphrenic abscess and peritonitis may result from a delayed diagnosis and have a high mortality rate.<sup>14</sup>

#### Pathology

There is no site of predilection of splenic abscesses, but multiple lesions are typically centrally located.<sup>15</sup> Splenic abscesses appear solitary and unilocular (65%), solitary and multilocular (8%), or multiple (27%).

Grossly, splenic abscess can be seen to have irregular borders and no capsule or pseudocapsule. At microscopic examination, suppuration or liquefactive necrosis can be seen, depending on the time course, within the abscess.<sup>13</sup>

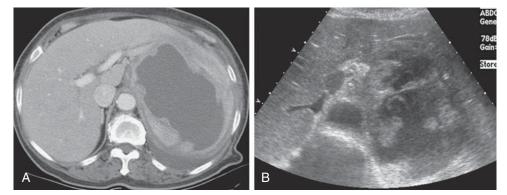
#### Imaging

**Radiography.** The most frequent plain radiographic finding in patients with splenic abscess is a left pleural effusion. Mottled air and extraluminal air/fluid levels in the left upper quadrant also may be seen, but these findings are rarely encountered.<sup>14</sup>

**Computed Tomography.** With its high sensitivity (96%), CT is the noninvasive diagnostic method of choice for splenic abscesses. On CT, pyogenic splenic abscess appears as a lesion with a low-density center (fluid, necrotic tissue, or pus) surrounded by a thick, irregular, dense rim (Figure 60-7). Although CT can be diagnostic if the intrasplenic fluid collection contains gas, gas is present in only a small number of splenic abscesses (Figure 60-8). Splenic abscess also can contain septa that vary in thickness from 1 to 10 mm.<sup>14</sup> A wedge-shaped abscess may be seen in patients with endocarditis and associated septic emboli.<sup>15</sup>

**Magnetic Resonance Imaging.** MRI is rarely performed in patients with suspected splenic abscesses because CT is highly sensitive, and the condition of many patients is not considered clinically stable.<sup>14</sup> MRI shows the abscess as a lesion of fluid signal intensity, with low and high signal intensities on T1- and T2-weighted images.

Figure 60-7 Pyogenic splenic abscess. A, Axial contrast-enhanced computed tomography scan shows a large masslike lesion in the spleen, with a center of low attenuation surrounded by a thick, irregular rim. B, Transverse abdominal sonogram depicts a large, poorly defined mass with dirty internal echo and irregular rim. Pyogenic splenic abscess was diagnosed by microscopic examination of the specimen obtained by percutaneous aspiration, and *Enterococcus faecium* was isolated.



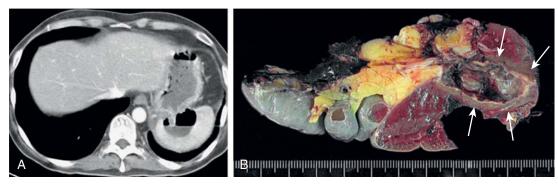


Figure 60-8 Pyogenic splenic abscess. A, Axial contrast-enhanced computed tomography scan shows a pyogenic splenic abscess, with an air/fluid level. B, The patient underwent splenectomy. The gross specimen shows a splenic abscess (*arrows*) with a thick, irregular wall.

#### **ULTRASONOGRAPHY**

Although ultrasonography is useful as a screening examination for the splenic abscesses in bedridden or dyspneic patients, it may be technically difficult because of ileus, overlying ribs, and perisplenic fluid.<sup>14</sup> Most abscesses appear as poorly defined, hypoechoic or anechoic lesions with irregular boundaries (see Figure 60-7). If gas is present, high echogenicity combined with "dirty" shadowing can be demonstrated.<sup>16</sup> Abscesses are typically avascular on color Doppler imaging.<sup>15</sup>

**Nuclear Medicine.** If an abscess is 2 cm or greater in diameter, it can be demonstrated as a nonspecific splenic filling defect on <sup>99m</sup>Tc-SC scintigraphy.<sup>14</sup>

#### Positron Emission Tomography With Computed Tomogra-

**phy.** Most splenic abscesses exhibit abnormal uptake of fluorodeoxyglucose (FDG), because activated leukocytes show increased glucose uptake.<sup>17</sup>

#### **Differential Diagnosis**

When the differentiation of splenic abscesses from other focal lesions is difficult, clinical findings of fever, chills, and leukocytosis are helpful.

The differential diagnosis of focal low-density and hypoechoic lesions is extensive and includes splenic infarction, cysts, tumors, and hematomas. Splenic infarction appears as a wedge-shaped lesion in a peripheral location, with no contrast enhancement. Splenic hematoma has a history of abdominal trauma and hemoperitoneum. Splenic tumors such as lymphoma may have findings similar to those of abscesses. If the intrasplenic low-attenuation lesion contains gas, it can be diagnostic of a splenic abscess.<sup>14,16</sup>

#### Treatment

Patients with pyogenic splenic abscesses should have proper antibiotic treatment. Splenectomy is indicated when there is persistent bacteremia and a lack of response to medical therapy. Recently, image-guided percutaneous drainage of the abscesses is becoming the standard of treatment.

#### FUNGAL INFECTION

#### Etiology

The most common fungal agents involving the spleen are *Candida, Aspergillus,* and *Cryptococcus.*<sup>14</sup>

#### Prevalence and Epidemiology

Fungal organisms are found in 26% of splenic abscesses, and they are found almost exclusively in immunocompromised patients. For example, fungal infections occur in 40% of patients with hematopoietic malignancies such as leukemia. The use of aggressive immunosuppressive agents in numerous diseases places an increasing population at risk.

#### **Clinical Presentation**

The clinical diagnosis of fungal infection is often difficult because the manifesting symptoms may be similar to those of the patient's primary disorder—fever and splenomegaly. Although the definite diagnosis requires microbiologic evidence of fungal infection, the result of blood culture may be negative in 50% of these patients. Therefore, when there is a strong clinical suspicion, a negative culture result does not rule out the diagnosis of fungal infection.<sup>18</sup> Disseminated fungal infection carries a significant morbidity and mortality. Without prompt treatment, the infection is often fatal.<sup>14</sup>

#### Pathology

Most splenic fungal infection is disseminated diffusely in the spleen. Fungal microabscesses are typically 5 to 10 mm (Figure 60-9) and seldom larger than 2 cm.

Gross examination of splenic fungal infection may show innumerable small (<5 mm in diameter) fungal deposits in the entire spleen (see Figures 60-9 and 60-10). At macroscopic examination, concentric rings can be seen with the central necrotic hyphae; these rings are surrounded by viable hyphae and a rim of peripheral inflammation.<sup>13</sup>

*Candida* is the fungal organism most frequently encountered. Splenic candidiasis may result from colonization of the gut, which locally disseminates after the onset of neutropenia and mucosal damage.<sup>14</sup> Besides the spleen, multiorgan involvement is common. The gastrointestinal tract is almost invariably involved, and esophageal candidiasis is especially common.<sup>12</sup>

#### Imaging

In immunosuppressed patients with unexplained clinical deterioration, imaging studies should be promptly performed to search for the microabscesses, because the clinical diagnosis of splenic fungal infection is often difficult.<sup>14</sup> Imaging workup should include both CT and ultrasonography to maximize sensitivity.<sup>15</sup> Use of a high-frequency transducer may be helpful to detect and monitor a small splenic lesion in a patient with

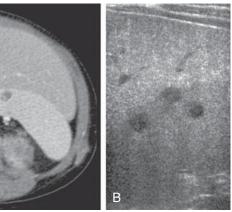


Figure 60-9 Splenic candidiasis. A, Contrast-enhanced computed tomography shows a small (usually 5 to 10 mm) low-attenuation nodule in the spleen. B, Oblique coronal ultrasonography using a linear probe with high frequency shows several bull's eye lesions, characterized by a central echogenic area surrounded by a hypoechoic band. This could not be detected on ultrasonography using a curvilinear probe with low frequency (not shown). Use of a high-frequency probe may be helpful for detection of splenic fungal infection, especially in the pediatric patient.



suggested fungal infection, especially a child (see Figures 60-9 and 60-10).

Radiography. Radiographically, acute splenic enlargement may be the sign of splenic fungal infection.<sup>1</sup>

Computed Tomography. On CT, the most common findings are multiple rounded areas of low density (see Figures 60-9 and 60-10) or calcifications. Ringlike enhancement may increase the conspicuity of some lesions on postcontrast CT.<sup>1</sup>

Magnetic Resonance Imaging. It has been proposed that MRI is superior to CT for the detection of fungal microabscesses.<sup>12</sup> These lesions are multiple, small, and of intermediate or low signal intensity on T1-weighed images and of high signal intensity on T2-weighted images.14

Ultrasonography. Four sonographic patterns of splenic fungal abscesses have been described: (1) the "wheel within a wheel" appearance, (2) "bull's-eye" appearance (see Figure 60-9), (3) hypoechoic lesions (see Figure 60-10), and (4) echogenic foci with variable posterior acoustic shadowing. The wheel within a wheel pattern is seen with early disease and consists of a central hypoechoic nidus, inner echogenic zone, and peripheral hypoechoic zone, corresponding to central necrosis, surrounding inflammation, and fibrotic ring, respectively. The most typical and specific sonographic pattern of splenic

candidiasis is the bull's-eye pattern (see Figure 60-9). The other two patterns are nonspecific.<sup>18</sup>

Nuclear Medicine. 99mTc-SC scintigraphy is often falsely negative in cases of microabscesses.<sup>1</sup>

Positron Emission Tomography With Computed Tomogra**phy.** Some cases of invasive candidiasis and cryptococcosis in the spleen have been reported that show multiple focal areas of increased activity of FDG on PET. The researchers asserted that, although not meant as a first-choice examination, FDG-PET should be considered in difficult cases for more accurate staging and treatment monitoring of infections.<sup>19,20</sup>

#### Differential Diagnosis

Clinically, it is difficult to differentiate splenic fungal infection from the aggravation or relapse of patient's primary disorder such as leukemia because the manifesting symptoms such as fever and splenomegaly may be nonspecific and similar to each other.1

Radiologically, splenic fungal microabscesses should be differentiated from metastases, lymphoma, and disseminated mycobacterial infection. However, the classic clinical findings of fever and neutropenia and a history of chemotherapy and use of broad-spectrum antibiotics suggest the diagnosis of fungal microabscesses.

#### Treatment

Although it is desirable to ascertain the microbiologic evidence of splenic fungal infection before treatment, it is not always possible. Therefore, some investigators have concluded that empirical antifungal therapy should be administered to all neutropenic patients who have positive imaging findings. Amphotericin B is a traditional antifungal agent, and fluconazole and various new azoles are becoming available for the management of systemic fungal infection.<sup>18</sup>

Splenectomy is indicated when there is no response to medical antifungal therapy.

#### MYCOBACTERIAL INFECTION

#### Etiology

Abdominal infection with *Mycobacterium tuberculosis* may develop as a result of hematogenous or lymphatic dissemination from a distant focus, usually from the lung.<sup>14</sup>

#### Prevalence and Epidemiology

Splenic tuberculous involvement is found in 80% to 100% of cases of disseminated, miliary pulmonary tuberculosis at autopsy. Immunodeficiency associated with alcoholism, intravenous drug abuse, diabetes, cancer, corticosteroid therapy, or AIDS is a risk factor. Because untreated abdominal tuberculosis carries a 50% mortality rate, early diagnosis and treatment are essential.<sup>14</sup>

#### **Clinical Presentation**

The various clinical manifestations of splenic tuberculosis include fever, hepatosplenomegaly, ascites, and, rarely, hypersplenism. Although a history or radiographic evidence of pulmonary tuberculosis may be suggestive, nearly one fifth of patients with abdominal tuberculosis have no evidence of extraabdominal disease.<sup>14</sup>

#### Pathology

Infection of the spleen with *M. tuberculosis* usually occurs in a miliary form.<sup>14</sup> The first response to tuberculous bacilli is a localized acute inflammation in the site where the largest amount of lymphoid tissue is located. After 2 to 3 weeks, a tubercle with epithelioid cells forms, surrounded by lymphatics (miliary form). Caseous necrosis of the tubercle begins after 2 to 4 weeks, and fibrous scarring may follow (tuberculoma). In patients with AIDS, however, the absence of a granuloma does not rule out tuberculosis because caseating granuloma

formation occurs infrequently. Viable mycobacteria pass into the intramural lymphatics and reach the regional lymphatics and lymph nodes, where tuberculoma formation continues.<sup>14</sup>

#### Imaging

**Radiography.** The common findings in radiographic examination include mild splenomegaly, hepatomegaly, and pleural effusion.<sup>15</sup>

**Computed Tomography.** Splenic tuberculosis appears as miliary or multiple small nodules of low density (Figure 60-11). In active infection, CT may also reveal abdominal lymphade-nopathy, often with low central attenuation (Figure 60-12). High-attenuation ascites with nodular peritoneal thickening and involvement of liver with hepatomegaly or focal lesions also may be noted. Treated splenic tuberculosis exhibits calcium deposition, representing healed, calcified granulomas (Figure 60-13) that appear as scattered, discrete, small calcifications in the normal-sized spleen.<sup>14,15</sup>

**Magnetic Resonance Imaging.** MRI findings of isolated splenic tuberculosis have not been reported in English literature.



**Figure 60-12** Splenic tuberculosis. On contrast-enhanced computed tomography, multiple scattered, small, low-attenuation nodules are seen in the slightly enlarged spleen. Also noted are hepatomegaly, hepatic nodules with ill-defined ring enhancement, and lymphadenopathy (*arrow*) in the perigastric nodal station.

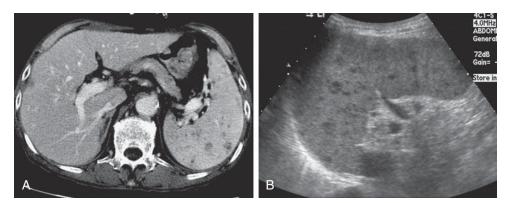


Figure 60-11 Splenic tuberculosis. A, Axial contrast-enhanced computed tomography scan demonstrates multiple small low-attenuation nodules diffusely scattered in the spleen. B, Oblique coronal ultrasound image also depicts multiple, scattered, low echoic nodules in the spleen.

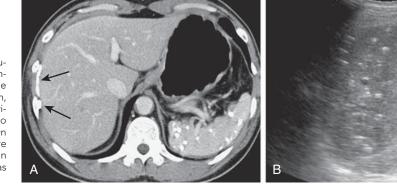


Figure 60-13 Healed splenic tuberculosis. A, Axial contrast-enhanced computed tomography scan shows multiple small nodules with calcium deposition, diffusely scattered in the spleen. Curvilinear pleural calcification (arrows) is also noted in the right hemithorax. B, On an oblique coronal sonogram there are multiple scattered echogenic foci in spleen, suggesting calcified granulomas in healed tuberculosis.

**Ultrasonography.** On ultrasonography, tuberculomas have decreased or mixed echogenicity (see Figure 60-11). Healed calcified granulomas are seen as scattered echogenic foci with acoustic shadowing<sup>14</sup> (see Figure 60-13).

**Nuclear Medicine.** Nuclear medicine has little role in the diagnosis of splenic tuberculosis.

**Positron Emission Tomography With Computed Tomography.** Most splenic granulomatous disease exhibits an abnormal uptake of FDG, because activated leukocytes show increased glucose uptake. In routine clinical practice, granulomatous disease such as tuberculosis may be suggested prospectively on whole-body imaging owing to involvement of multiple sites.<sup>17</sup>

#### **Classic Signs: Mycobacterial Infection**

- Small, focal, multiple splenic nodules of low density
- Extrasplenic lesions: Abdominal lymphadenopathy with central low attenuation, peritonitis, pulmonary tuberculosis, or pleural effusion

#### Differential Diagnosis

The differential diagnosis of splenic tuberculosis includes sarcoidosis, fungal infections, lymphoma, and metastases. Indolent fever, immunocompetence, no previous history of or current evidence of malignancy, and pulmonary abnormality are suggestive of the disease.<sup>14</sup>

The radiologic findings of splenic tuberculosis are similar to those of various diseases. In some instances, a biopsy may be needed.

#### Treatment

Patients with splenic tuberculosis should have antituberculous therapy. Although surgery may be indicated in cases of uncontrolled disease, it is seldom tried.

#### Mycobacterium Avium-Intracellulare in Acquired Immunodeficiency Syndrome

*Mycobacterium avium-intracellulare* (MAI) is a common environmental microbe found in soil, water, house dust, and dried plants. The epidemic of human immunodeficiency virus infection has increased the disease prevalence associated with MAI. The initial entry site for MAI in patients with AIDS is probably the gastrointestinal tract, from which it spreads to the mesenteric

and retroperitoneal lymph nodes and abdominal organs. MAI infection occurs late in patients with AIDS, who are debilitated and have many other opportunistic infections. Small focal lesions in the spleen occur in approximately 7% of these patients.

Pathologically, MAI is an intracellular, acid-fast bacillus residing in foamy histiocytes that produces poorly formed granulomas.<sup>14</sup>

On CT, MAI lesions appear as small focal area of decreased attenuation or inhomogeneous contrast enhancement. They should be differentiated from many entities that may appear as multiple low-attenuation lesions in the spleen in patients with AIDS, including lymphoma, disseminated Kaposi's sarcoma, tuberculosis, fungal infection, and *Pneumocystis* infection. It is especially clinically important to distinguish MAI from *M. tuberculosis*. Marked splenomegaly occurs in 20% of patients with MAI infection, whereas it is uncommon in tuberculosis. Marked hepatosplenomegaly, diffuse jejunal wall thickening, and enlarged lymph nodes are suggestive of disseminated MAI infection, whereas focal visceral lesion, lymph nodes with central low-attenuation, and segmental ileocecal wall thickening favor the diagnosis of disseminated tuberculosis.

#### PARASITIC INFECTIONS: ECHINOCOCCOSIS

#### Etiology

Echinococcal cyst is almost always caused by *Echinococcus granulosus*. Two main sources of splenic echinococcosis are systemic dissemination and intraperitoneal spread from a ruptured liver cyst. Isolated splenic involvement is very uncommon.<sup>13,14</sup>

#### Prevalence and Epidemiology

The spleen is less commonly affected than the liver, lung, brain, and musculoskeletal system. Splenic involvement of echinococcosis occurs in less than 2% of all patients with the disease. Endemic areas include the Middle East, South America, Australia, New Zealand, Central Europe, South Africa, and certain areas in the United States. Echinococcal splenic cysts are twice as common as nonparasitic cysts in endemic areas. However, they are rarely seen outside the endemic areas, unless affected patients have traveled to those areas.<sup>13,14</sup>

#### **Clinical Presentation**

Clinical findings of splenic echinococcosis are nonspecific and frequently include abdominal pain, fever, and splenomegaly. Secondary infection, cyst rupture, and anaphylactic shock may develop.<sup>13,14</sup>

#### Pathology

Echinococcal cysts are true cysts that have a cellular lining.<sup>15</sup> At gross examination, the cysts are seen to be either unilocular or multilocular. Because of invaginations in the germinal layer, loculi form in the periphery, resulting in the formation of daughter cysts. At microscopic examination, the wall of the hydatid cyst is seen to be composed of an inner germinal layer and an outer laminated membrane. These layers are surrounded by a thin band of fibrotic, compressed spleen, called a pericyst. Scolices and fragments of the germinal layer constitute the so-called hydatid sand within the cyst.<sup>13</sup>

#### Imaging

**Radiography.** Plain radiographic examination may show splenomegaly or a mass effect from the spleen.<sup>14</sup>

**Computed Tomography.** On CT, echinococcal cysts are spherical, well-defined water-attenuation lesions with a thin wall and usually no rim enhancement.<sup>15</sup> On noncontrast CT, ringlike calcifications may be seen in the periphery, within the pericyst.<sup>13</sup> These cysts also have some areas of higher attenuation caused by debris (i.e., hydatid sand) or inflammation.<sup>15</sup>

**Magnetic Resonance Imaging.** Echinococcal cysts are usually solitary, and their imaging characteristics show a well-defined rounded mass with a signal intensity equal to that of water on both T1- and T2-weighted images. However, depending on the cystic content, the signal intensity on T1- and T2-weighted images may vary. Calcification of the cyst wall may be noted as well.<sup>21</sup>

**Ultrasonography.** Echinococcal cysts show anechoic or mixed echogenic, round lesions. Separation of membranes of the cyst produces the "water lily" sign, and multiple cysts within a larger cyst are known as "daughter cysts."<sup>15</sup>

#### **Differential Diagnosis**

The presence of a splenic cyst with or without wall calcification in a patient from an endemic area and with positive serologic tests most likely indicates an echinococcal cyst.<sup>14</sup>

The differential diagnosis of a round cyst in the spleen includes a posttraumatic or postinfectious pseudocyst and a primary epithelial cyst as well as cystic tumors. The presence of daughter cysts may be helpful in confirming the diagnosis of echinococcal cyst.

#### Treatment

Surgery remains the treatment of choice for echinococcal cysts, but percutaneous drainage for echinococcosis is becoming more widespread. Various drugs such as albendazole, mebendazole, and praziquantel have cure rates of approximately 30%.

#### PNEUMOCYSTIS JIROVECI INFECTION

*Pneumocystis jiroveci* infection is one of the major causes of morbidity and mortality in patients with AIDS, affecting 80% of patients. The most commonly involved site is the lung. Extrapulmonary involvement is rare and can occur in the reticuloendothelial system of the lymph nodes, spleen, bone marrow, and liver. Histologically, splenic *P. jiroveci* infection causes necrotizing granulomas that eventually develop dystrophic calcifications.

Intrasplenic *P. jiroveci* infection is often incidentally found in patients with AIDS undergoing CT examination for fever of unknown origin. Abdominal symptoms are nonspecific and include pain, weight loss, splenomegaly, and ascites. On CT, necrotizing granulomas associated with *P. jiroveci* infection may be seen as multiple small low-attenuation lesions in an enlarged spleen. Focal lesions may become calcified in progression. On ultrasonography, they may be seen as multiple small lesions with high reflective centers.<sup>14,15</sup>

#### VIRAL INFECTION

Viral infection may result in splenomegaly. The three most common viruses to involve the spleen are Epstein-Barr virus, varicella, and cytomegalovirus.<sup>12</sup>

#### SARCOIDOSIS

#### Etiology

The cause of sarcoidosis is unknown.<sup>14-16,22</sup>

#### Prevalence and Epidemiology

Sarcoidosis is a multisystem disease, most frequently involving the lung and the mediastinal and hilar lymph nodes (Figure 60-14).

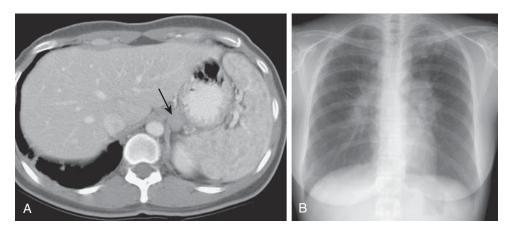


Figure 60-14 Sarcoidosis. A, Axial contrast-enhanced computed tomography image depicts splenomegaly with scattered multiple small low-attenuation nodules. Abdominal lymphadenopathy (arrow) in the left gastric nodal station is also seen. B, Chest radiograph shows mediastinal widening with bilateral hilar and right paratracheal lymph node enlargement. There was no evidence of pulmonary involvement in this patient.

Abdominal sarcoidosis is also common, and splenic involvement is microscopically reported in 29% to 59% of patients.<sup>16</sup>

#### **Clinical Presentation**

Abdominal involvement of sarcoidosis is related to clinical status and angiotensin-converting enzyme levels but not to pulmonary disease. Patients are usually asymptomatic but occasionally may present with abdominal pain. Splenomegaly is seen in 11% to 42% of patients.<sup>14,15</sup>

#### Pathology

Histologically, regardless of the affected organs or tissues, sarcoidosis is characterized by multiple noncaseating, epithelioid granulomas in the absence of organisms or particles.<sup>14,23</sup>

#### Imaging

Radiography. Plain radiographs may show splenomegaly.

**Computed Tomography.** CT most commonly shows no abnormality of the spleen or may show splenomegaly and retroperitoneal lymphadenopathy. However, multiple, focal low-attenuating lesions of 1 mm to 3 cm (see Figure 60-14) may be seen in 15% of splenic sarcoidosis cases. As the size of nodule increases, a more hypoattenuating nodular pattern is seen on CT.<sup>16</sup>

**Magnetic Resonance Imaging.** In patients with splenic sarcoidosis, the lesions are typically seen as low signal intensity on both T1- and T2-weighted images. Low signal intensity on T2-weighted images is a characteristic that differentiates it from acute infection. They enhance in a minimal and delayed pattern.<sup>12,22</sup>

**Ultrasonography.** Common ultrasonographic findings of splenic sarcoidosis are diffuse increase of splenic echogenicity with a homogeneous or heterogeneous echotexture and splenomegaly. Occasionally, focal lesions are seen as discrete hypoechoic nodules.<sup>16</sup>

**Positron Emission Tomography With Computed Tomography.** Most splenic granulomatous disease such as sarcoidosis exhibits abnormal uptake of FDG. Because sarcoidosis may involve many organs, positron emission tomography with CT (PET/CT) is useful for whole-body imaging.<sup>17</sup>

#### **Differential Diagnosis**

The clinical history of extraabdominal sarcoidosis and an elevated value of angiotensin-converting enzyme may help suggest the diagnosis of splenic sarcoidosis.<sup>14</sup>

The radiologic findings of splenic sarcoidosis are nonspecific, and it is difficult to differentiate splenic sarcoidosis from lymphoma or metastasis. It has been reported that retrocrural lymphadenopathy is less common and lymph nodes are smaller in sarcoidosis, in comparison to in lymphoma.<sup>16</sup>

#### Treatment

Most patients with sarcoidosis do not require treatment. There have been few well-controlled studies on the use of any therapeutic agents such as corticosteroids, immunosuppressants, and cytotoxic drugs in patients with sarcoidosis.<sup>23</sup>

Lung, heart, and liver transplantations have been rarely performed in patients with sarcoidosis,<sup>23</sup> but surgical treatment is generally not indicated for splenic involvement.

# Vascular and Trauma-Related Lesions VASCULAR LESIONS

#### Etiology

Splenic infarction is caused by occlusion of the splenic artery or one of its branches. The most common two causes are embolic occlusion from cardiovascular disease and local thrombosis from hematologic diseases. The other causes of splenic infarctions are pancreatic disease with vascular involvement, splenic artery aneurysm, vasculitis, arteriosclerosis, hypercoagulopathy, splenic torsion, wandering spleen, and portal hypertension.<sup>14,24</sup>

Splenic venous thrombosis also has various causes. The most common is pancreatitis, and the possible mechanisms are compression, erosion by a pseudocyst, and fibrosis. The other causes are pancreatic carcinoma, hypercoagulable state, trauma, lymphoma, liver cirrhosis, liver transplantation, splenectomy, and retroperitoneal fibrosis.<sup>22,24</sup>

Splenic artery aneurysms occur secondary to various causes, including portal hypertension, pregnancy, multiparity, pancreatitis, penetrating gastric ulcer, mycotic causes, atherosclerosis, trauma, vasculitis, fibromuscular dysplasia, and Ehlers-Danlos syndrome. Arteriovenous fistula and arteriovenous malformation are caused by congenital malformation, trauma, splenectomy, rupture of a splenic artery aneurysm, pancreatitis, and iatrogenic injury.<sup>24,25</sup>

#### Prevalence and Epidemiology

Although splenic infarction is uncommon, it is not an unusual clinical suspicion in patients with acute left upper quadrant pain. The age of the patients varies between 2 and 87 years, with a mean of 54 years, and there is no sex predilection. An embolic event is the most common cause in elderly patients, whereas hematologic disorder is the most common in patients younger than age 40 years.<sup>2,16,24</sup>

Splenic vein thrombosis is relatively frequent. It is seen in approximately 20% of patients with chronic pancreatitis.<sup>22,24</sup>

Splenic artery aneurysms are the most common among visceral artery aneurysms and are multiple in 20% of cases. They are found in 0.07% to 10% of autopsy series. Eighty-five percent of patients are female.<sup>24</sup>

Splenic arteriovenous fistula rarely occur.24,25

#### **Clinical Presentation**

Patients with splenic infarction may be asymptomatic or present with a sudden onset of left upper quadrant pain.<sup>2,14,24,26</sup> Those with embolic infarctions also may have fever. Laboratory findings include anemia, leukocytosis, and, sometimes, an elevated platelet count from splenic dysfunction. Complications such as abscess and hemorrhage may occur in 7% to 20% of patients.<sup>14,24</sup>

Common symptoms of splenic venous thrombosis are chronic abdominal pain, weight loss, and variceal bleeding from coronary, paraesophageal, esophageal, or short gastric veins.<sup>22,26</sup>

Most splenic artery aneurysms are detected incidentally in asymptomatic patients. Rupture of splenic artery aneurysm is a rare but life-threatening complication, with an overall mortality of 25%, and even increased mortality of more than 75% during pregnancy. Rupture may occur into the peritoneal cavity, gastrointestinal tract, pancreatic duct, or splenic vein, manifesting as hemoperitoneum, hematemesis or hematochezia/melena, hemoductal pancreatitis, and arteriovenous fistula, respectively.

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Patients with splenic arteriovenous fistula can present with upper gastrointestinal bleeding from esophageal varices and/or ascites secondary to portal hypertension. On physical examination, a machinery-type bruit is the most specific sign.<sup>24,25</sup>

#### Pathology

Splenic infarctions are pale and wedge-shaped. Their bases are located at the periphery, where the capsule is covered with fibrin. In the healing stage, contraction of the infarcted parenchyma occurs because of scar formation and fibrosis. When the thrombus contains bacteria, the infarction becomes soft and filled with pus.<sup>14,24</sup>

#### Imaging

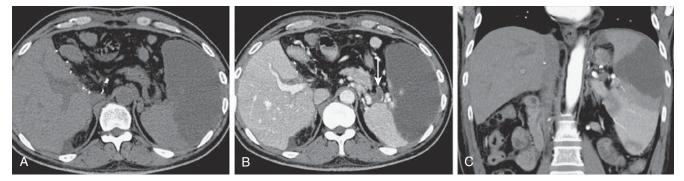
**Radiography.** In cases of acute splenic infarction, chest radiographs may demonstrate a left pleural effusion. Plain radiographs of a splenic artery aneurysm may demonstrate a ring- or arc-like calcification in the left upper quadrant.<sup>24</sup> On plain radiography, other splenic vascular lesions will not be detected because of the lack of spatial resolution.

**Computed Tomography.** On noncontrast CT, infarctions are generally seen as low attenuation or may be poorly visualized. Scattered areas of high attenuation may be seen in hemorrhagic infarctions as well. On contrast-enhanced CT, splenic infarction is

classically seen as a peripheral wedge-shaped, sharply demarcated area of low attenuation (Figure 60-15). However, this finding is seen in less than half of patients with acute splenic infarction. CT findings may vary, being round, multinodular, poorly delineated, and heterogeneous. Thromboembolus may be seen when it is lodged in sufficiently large vessels. Global infarctions show no enhancement of the spleen with or without a "cortical rim" sign, defined as a thin peripheral, enhancing linear structure, representing residual capsular flow. In the chronic stage, infarcts may shrink or disappear (Figure 60-16). In patients with hemoglobinopathies, calcifications may appear from repeated infarctions.

Splenic vein thrombosis may appear as having high attenuation on noncontrast CT and as an intraluminal, low-attenuation filling defect adjacent to the venous wall on contrast-enhanced CT (Figure 60-17). Other ancillary findings include gastric, esophageal, and colonic varices as well as splenomegaly (Figure 60-18). Also, CT reveals the direct information about the underlying cause (e.g., pseudocyst from pancreatitis, pancreatic carcinoma, or retroperitoneal mass).

Splenic artery aneurysm is seen as round to saccular or fusiform dilatation of the splenic artery, sometimes with mural thrombus. Calcification may be seen on noncontrast CT (Figure 60-19). In cases of aneurysmal rupture or pseudoaneurysm, contrast extravasation as well as surrounding acute hematoma will be seen (Figure 60-20).



**Figure 60-15** Splenic infarction. This patient underwent living-donor liver transplantation using a right-lobe graft for the treatment of liver cirrhosis. During the surgery, the splenic artery was ligated to increase blood flow to the hepatic artery. **A**, Axial noncontrast computed tomography (CT) scan shows large infarction, seen as a wedge-shaped area of low attenuation with a well-demarcated margin in the markedly enlarged spleen. **B**, On axial contrast-enhanced CT, the infarcted area is seen as perfusion defect. The splenic artery is filled with acute thrombus (*arrow*). **C**, Coronal reformatted CT image demonstrates well the typical wedge shape, corresponding to the territory of the ligated splenic artery.

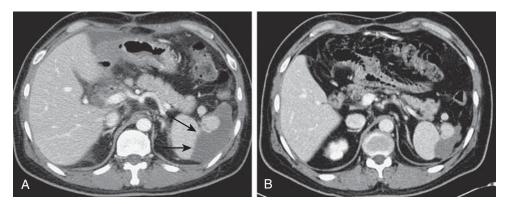
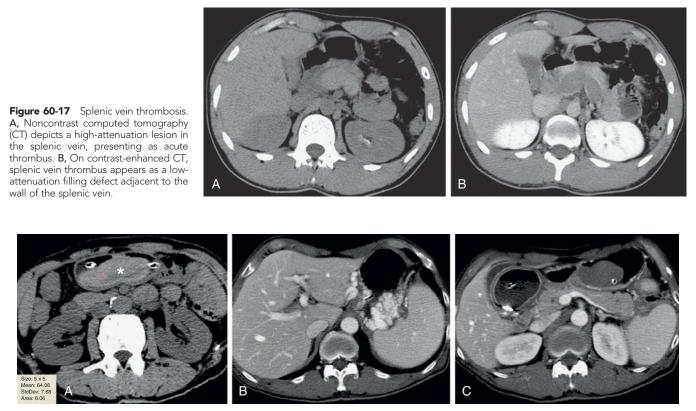


Figure 60-16 Splenic infarction. A, Axial contrast-enhanced computed tomography (CT) shows partial splenic infarction, seen as a sharply marginated lesion perfusion defect with straight border (*arrows*). B, On follow-up CT 8 months later, the infarcted area shrank without complication.



**Figure 60-18** Splenic vein thrombosis. The patient presented with hematemesis. **A**, Noncontrast computed tomography (CT) scan shows acute hematoma (*asterisk*) in the gastric lumen, seen as heterogeneous high attenuation with a mean of 64 HU. **B**, Axial contrast-enhanced CT shows variceal engorgement at the gastric fundus. There is no evidence of liver cirrhosis, but the spleen is moderately enlarged. **C**, Although no acute thrombus is seen in the lumen, the splenic vein is gradually narrowed and no longer traced around the tail of the pancreas.



Figure 60-19 Splenic artery aneurysm. A, On noncontrast computed tomography (CT), peripheral calcification is seen in the splenic arterial wall of the saccular dilatation. Note the splenomegaly and ascites. B, Thick oblique coronal CT image with maximum intensity projection depicts a saccular dilatation of the splenic artery. Also noted are liver cirrhosis and coronary varix. C, Selective splenic arteriography demonstrates a saccular aneurysm arising from the splenic artery.

Arteriovenous fistula can be diagnosed on CT when the splenic vein is dilated and opacified before the splenic parenchymal enhancement (Figure 60-21).<sup>24,25</sup>

**Magnetic Resonance Imaging.** On conventional MRI, the signal intensity of the splenic infarction depends on the age of infarctions, the degree of hemorrhagic necrosis, and the amount of different blood degradation products within the infarcted area. Recent hemorrhagic areas are hypointense on T1-weighted

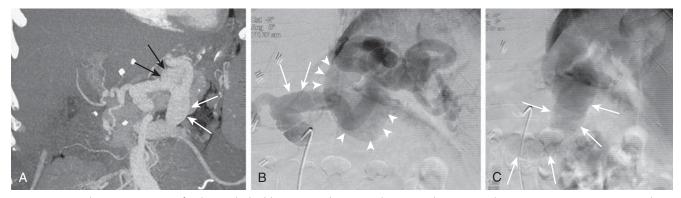
images. Chronic infarcts are seen as being of low signal intensity on all pulse sequences.

Acute thrombus in the splenic vein is hyperintense on both T1- and T2-weighted images.

The signal intensity of the splenic artery aneurysm depends on flow alteration and the extent of the mural thrombus. The patent lumen will be of low signal intensity on conventional pulse sequences, owing to the fast-flowing blood, whereas the blood clot may appear as a hyperintense lesion.



Figure 60-20 Splenic artery pseudoaneurysm. A, On noncontrast computed tomography (CT), a well-defined round hypodense lesion (arrow) is noted in the splenic hilum, surrounded by a relatively homogeneous high-attenuation lesion (arrowheads), suggesting acute hematoma. B, Axial contrast-enhanced CT image reveals an intense homogeneously enhancing lesion (arrow) arising from the distal part of the splenic artery, suggesting splenic artery pseudoaneurysm. Also noted are shrinkage of the liver secondary to cirrhosis, splenomegaly, and ascites. C, Selective splenic arteriography demonstrates a saccular pseudoaneurysm arising from the splenic artery.



**Figure 60-21** Splenic arteriovenous fistula. A, Thick oblique coronal computed tomography image with maximum intensity projection depicts dilated, tortuous splenic artery and early enhancement of part of the splenic vein (*black arrows*). Also noted is an early opacification of the splenorenal shunting vein (*white arrows*). B, Selective angiography of celiac axis shows markedly dilated splenic artery (*arrows*) and early filling of part of the splenic vein (*arrowheads*) before splenic parenchymal enhancement, suggesting arteriovenous fistula. C, Splenorenal shunting is demonstrated during the delayed phase (*arrows*).

Contrast-enhanced MRI findings of the various vascular lesions are similar to those on CT.<sup>22,24,25</sup>

**Ultrasonography.** Acute splenic infarction may appear as wedge-shaped, hypoechoic, and well-demarcated lesions on ultrasonography, and other coexistent pathologic processes such as edema, bleeding, or necrosis may lead to various findings. Color Doppler imaging may reveal the absence of blood flow in the infarcted area. In the chronic phase, infarcts may appear as a hyperechoic area with volume shrinkage.<sup>14,24</sup>

Splenic vein thrombosis is usually echogenic on ultrasonography. Color Doppler ultrasonography may reveal the absence of color flow in cases of total occlusion and retained residual flow in an incompletely obstructed splenic vein.

Splenic artery aneurysm appears as an anechoic mass with or without peripheral calcification along the course of the splenic artery on sonography. Color Doppler imaging proves the vascular lesion, often with turbulence.

Arteriovenous fistula is difficult to diagnose on ultrasonography, but diagnosis is possible when there is a high-velocity reverse flow in the splenic vein with an arterial waveform on Doppler imaging.<sup>24,25</sup> **Angiography.** In cases of splenic artery aneurysm, a splenic arteriogram shows saccular dilatation (see Figure 60-19) mostly at the convexity of the arteries. Angiography directly shows arteriovenous fistula, with findings of a tortuous, dilated splenic vein and enhancement of the vein before the parenchyma (see Figure 60-21). Although conventional angiography has been surpassed by MR and CT angiographies for diagnostic purposes, it plays a role in interventional procedures such as transarterial embolization.<sup>24,25</sup>

**Nuclear Medicine.** Splenic infarction appears as a focal area of decreased activity on splenic scintigraphy, which is nonspecific.<sup>14</sup> Otherwise, nuclear medicine has no role in the evaluation of other splenic vascular lesions.

**Positron Emission Tomography With Computed Tomography.** PET/CT has little role in evaluation of splenic vascular lesions.

#### Differential Diagnosis

In patients with splenic infarction, absence of a high fever is useful for exclusion of splenic abscess, although embolic infarctions or superimposed infection may produce fever. The absence of a previous episode of trauma is helpful to rule out splenic laceration.<sup>2</sup>

On imaging studies, splenic infarctions should be differentiated from splenic abscess, tumor, laceration, and cyst. Internal septations, air bubbles, and mass effect are useful findings to favor the diagnosis of splenic abscess rather than splenic infarction. Associated hemoperitoneum, perisplenic hematoma, and the presence of contrast agent extravasation on enhanced CT are supportive findings favorable for splenic laceration. The differentiation of splenic infarction from tumor sometimes may be difficult because of the wide spectrum of both diseases on imaging. Splenic cysts may develop secondary to the infarction.

The imaging findings of splenic artery aneurysm and arteriovenous fistula are almost always typical, pinpointing the diagnosis.

#### Treatment

Most asymptomatic patients with splenic infarction do not need any treatment.<sup>2</sup> Medical treatment of splenic vein thrombosis depends on the underlying cause, and an anticoagulant may be indicated in patients with hypercoagulable status. In cases of the other splenic vascular disorders, medical treatment is generally not indicated.

Splenectomy may be indicated in patients with upper gastrointestinal bleeding secondary to splenic vein thrombosis, because removal of the spleen eliminates venous collateral outflow and thereby decompresses surrounding varices. Additional procedures to treat underlying pancreatic pathologic processes may be performed simultaneously. Although sclerotherapy is an effective treatment for bleeding esophageal varices, it is followed by a high rate of rebleeding.<sup>27</sup>

Indications for treatment of splenic artery aneurysm or pseudoaneurysm include symptomatic lesions, a female patient of child-bearing age, portal hypertension, a candidate for liver transplantation, a pseudoaneurysm of any size, and an aneurysm with a diameter of more than 2.5 cm. Urgent surgery is indicated in patients with cardiovascular instability due to splenic aneurysmal rupture. Transarterial embolization is associated with significantly lower morbidity and mortality than the surgical procedure. Complications of endovascular intervention are uncommon and include postembolization syndrome, elevated pancreatic enzymes, splenic infarction, infection, abscess, and rupture.<sup>24</sup>

#### TRAUMA-RELATED LESIONS

#### Etiology

Various types of trauma, such as blunt trauma, penetrating injuries, and iatrogenic injuries including intraoperative accidents can injure the spleen.

#### Prevalence and Epidemiology

The frequency of splenic trauma varies, depending on the patient population surveyed. The spleen is the most commonly injured organ after blunt trauma, comprising 25% of all abdominal solid organ injuries: a motor vehicle accident is the most common cause, followed by direct blows and falls. Patients with splenomegaly are more susceptible to trauma.

Thoracoabdominal penetrating trauma can injure the spleen. Penetrating splenic injuries may occur iatrogenically during percutaneous interventional procedures on the left upper quadrant as well. Intraoperative injuries of the spleen account for 15% to 20% of all splenectomies, and most cases result from traction, application of retractors, and disruption of ligamentous attachments.<sup>28</sup>

#### **Clinical Presentation**

The diagnosis of minor splenic injury after blunt trauma may be difficult, based on symptoms and physical examination only. The clinical presentation includes left upper quadrant pain or referred pain to the left shoulder. Laboratory test results (e.g., hematocrit) do not always reflect the degree of splenic injury. However, because the spleen is the most vascular organ of the body, peritoneal bleeding from splenic injury can be potentially life-threatening. Hypotensive shock occurs in 30% to 40% of patients with splenic injuries.

#### Pathophysiology

The spleen is particularly prone to injury after blunt trauma because of its complex ligamentous attachments and spongy-like parenchymal consistency. It is firmly attached to the retroperitoneum and diaphragm by the splenorenal and the phrenicosplenic ligaments. The splenic hilum anchors the pancreatic tail. The spleen is attached to the mobile stomach and colon by the gastrosplenic and the colosplenic ligaments.<sup>28</sup>

Blunt trauma can injure the spleen by sudden compression or countercoup mechanisms during rapid deceleration. The former can occur from a direct blow or transmitted shock wave and usually results in parenchymal injuries and venous bleeding.<sup>28</sup> The degree of penetrating splenic injury depends on the wounding instrument and its course. Because penetrating trauma does not respect segmental anatomy, it can lead to a more vascular disruption.

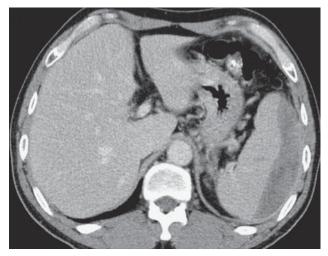
#### Imaging

**Computed Tomography.** CT is the premier imaging technique for screening of splenic injury. The accuracy of CT in the detection of splenic injuries exceeds 95%, and recent advances of scanners provide fast image acquisition, which is indispensable for trauma patients. However, attention to detail of scanning is needed to obtain these good results; for example, streak artifacts from the patient's arms should be avoided because they may obscure the splenic injury.<sup>28</sup> Although arterial phase imaging is better for the evaluation of active arterial bleeding, seen as extravasation of contrast agent, imaging in the portal venous phase is also needed to evaluate splenic parenchymal injury because normally heterogeneous enhancement during the early arterial phase may mimic injury.<sup>29</sup>

*Acute Hematoma.* Acute subcapsular and intraparenchymal hematomas are typically hyperdense on noncontrast CT and are seen as an area of low attenuation on contrast-enhanced CT between the splenic capsule and enhancing splenic parenchyma or within the parenchyma (Figure 60-22).<sup>29</sup>

*Laceration.* Acute splenic lacerations are seen as linear or branching areas of low attenuation on contrast-enhanced CT (Figure 60-23). Such lacerations decrease in size and number with time (Figure 60-24). Severe disruption of the splenic parenchyma can result in a "shattered" spleen (Figure 60-25). Vascular pedicle injuries usually result in significant hemorrhage and cardiovascular instability.

Active Bleeding. An extravasation of intravenous contrast agent indicates active bleeding from injured vessels, seen as

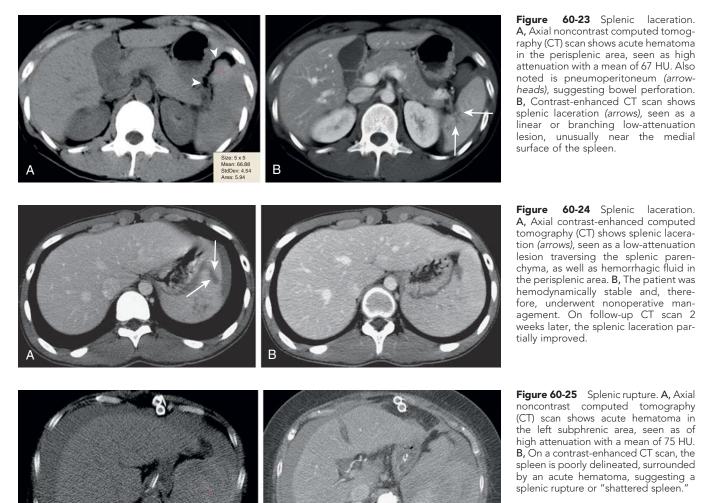


**Figure 60-22** Subcapsular hematoma. Axial contrast-enhanced computed tomography (CT) image shows subcapsular hematoma, seen as a heterogeneous low-attenuation area between the splenic capsule and enhancing splenic parenchyma. Noncontrast CT imaging was not performed in this patient.

irregular or linear areas of high attenuation (85 to 350 HU). With ongoing bleeding from the injured vessels, the area of active extravasation remains high in attenuation and increases in size on delayed-phase images. Such a finding is a valuable indicator for the need for surgical or interventional management.

*Vascular Injuries.* Posttraumatic splenic vascular injuries include pseudoaneurysms and arteriovenous fistulas. Rupture of pseudoaneurysms may be the cause of failed nonsurgical management. On contrast-enhanced CT, pseudoaneurysms appear as well-defined focal enhancing areas with attenuation as high as that of arteries and are surrounded by a low-attenuation area of hematoma. On delayed images the area becomes minimally hyperdense or isodense compared with normal spleen but does not increase in size, in contrast to an area of active bleeding.<sup>29</sup>

**Posttraumatic Infarction.** Segmental splenic infarction is a rare manifestation, seen in 1.4% of patients with blunt splenic injury. Abrupt mechanical stretching during trauma results in a focal intimal tear, leading to thrombosis. The majority of splenic infarcts heal without complication.<sup>29</sup>



**Magnetic Resonance Imaging.** MRI may produce high sensitivity in the diagnosis of splenic hematoma seen as high signal intensity on both T1- and T2-weighted images.<sup>16</sup> However, it seems that MRI plays little role in patients with splenic trauma because of the time factor; spending time for imaging is inappropriate, especially in hemodynamically unstable patients, and CT is quicker than MRI.

**Ultrasonography.** Ultrasonography can be a useful method for the screening of a splenic injury, especially in a hemodynamically unstable patient or child. However, this examination is often limited by rib fractures, chest tubes, dressings, and the insensitivity to other sites of injury. In the acute setting, lacerations and hematomas may appear echogenic but both fresh and chronic hemorrhage can appear hypoechoic. At least four areas should be evaluated to determine the presence or absence of hemoperitoneum: pericardial cavity, right upper quadrant, left upper quadrant, and pelvis.<sup>28,29</sup>

**Nuclear Medicine.** The <sup>99m</sup>Tc-SC scan has been shown to be sensitive but nonspecific. Scintigraphy cannot be used to evaluate the bowel or detect hemoperitoneum.<sup>28</sup> Currently, scintigraphy is not used in evaluation of the trauma patient because of the long time required versus the faster imaging time and high resolution of CT.

**Angiography.** Angiography is no longer appropriate as a screening modality for splenic injury but is still useful to aid in providing access for therapeutic embolization of splenic vessels.<sup>28</sup>

#### **Classic Signs: Trauma-Related Lesions**

- Acute hematoma: Hyperdense on noncontrast CT; a low-attenuation area between the splenic capsule and parenchyma on contrast-enhanced CT
- Laceration: Linear or branching areas of low attenuation
- Vascular injuries: Pseudoaneurysms and arteriovenous fistulas
- Posttraumatic infarction

#### **Differential Diagnosis**

The important clinical factor in differentiating traumatic splenic lesions from splenic clefts or other splenic lesions such as infarct and abscess is a traumatic episode. Splenic cleft may mimic splenic laceration. Typically, splenic clefts have smooth or rounded margins and are usually found along the medial surface, whereas lacerations mostly originate from the lateral surface of the spleen.<sup>1</sup> Splenic clefts appear unchanged on delayed-phase images unlike lacerations, which "fill in" from the periphery and become less visible.<sup>29</sup>

#### Treatment

Although splenectomy was considered the treatment of choice for splenic trauma in the past, nonoperative management of blunt trauma is currently the standard of care in patients who are hemodynamically stable.

To plan either nonsurgical or surgical management, a reasonable grading scale of splenic injury is needed. The splenic injury grading scale that is traditionally most often used in the United States is based on the extent of injury seen at the time of laparotomy (Table 60-3).<sup>30</sup> More recently, several CT-based classifications of splenic injury have been developed to triage the patient with blunt splenic trauma.<sup>28,29</sup> The grading system designed by Mirvis and colleagues<sup>31</sup> is commonly used (Table 60-4).

For successful nonoperative management of splenic injuries, several factors should be taken into account: grade of injury, amount of hemoperitoneum, ongoing hemorrhage, presence of vascular injury, blood pressure, and the possibility of missed injuries that require surgery.

Recently, to increase the number of patients managed nonoperatively, splenic artery embolization has been adopted as an effective adjunct when there is CT evidence of active bleeding. Compared with splenectomy, splenic artery embolization provides an advantage in that parenchymal viability is preserved by the rich network of collateral vessels. However, complications after splenic artery embolization are seen in up to 32% of

TABLE 60-3	Surgical Splenic Injury Scale	
Grade	*	Injury Description
I	Hematoma Laceration	Subcapsular, <10% surface area Capsular tear, <1 cm parenchymal depth
II	Hematoma Laceration	Subcapsular, 10%-50% surface area; intraparenchymal, <5 cm in diameter 1-3 cm parenchymal depth that does not involve a trabecular vessel
III	Hematoma	Subcapsular, >50% surface area or expanding; ruptured subcapsular or intraparenchymal hematoma Intraparenchymal hematoma >5 cm or expanding
	Laceration	>3 cm parenchymal depth or involving trabecular vessels
IV	Laceration	Laceration involving segmental or hilar vessels producing major devascularization (>25% of spleen)
V	Laceration Vascular	Completely shattered spleen Hilar vascular injury that devascularizes spleen

From Moore EE, Cogbill TH, Jurkovich GJ, et al: Organ injury scaling: spleen and liver (1994 revision). J Trauma 38:323, 1995. \*Advance one grade for multiple injuries, up to grade III.

TABLE 60-4		ted Tomography Grading System nic Injury
Grade		Description of Injury
CT gra	ade 1	Capsular avulsion, superficial laceration(s), or subcapsular hematoma <1 cm in diameter
CT gra	ade 2	Laceration(s) 1-3 cm deep, central/subcapsular hematoma(s) 1-3 cm in diameter
CT gra	ade 3	Laceration(s) >3 cm deep, central/subcapsular hematoma(s) >3 cm in diameter
CT gra	ade 4	Fragmentation of three or more sections, devascularized (nonenhanced) spleen

From Mirvis SE, Whitley NO, Gens DR: Blunt splenic trauma in adults: CT-based classification and correlation with prognosis and treatment. Radiology 171:34, 1989.

CT, Computed tomography.

patients. They include hemorrhage, infarction, abscess formation, missed injuries, iatrogenic vascular injury, and coil migration. The majority of patients will have a low-grade fever and left upper quadrant pain.<sup>28,29</sup>

Hemodynamically unstable patients or those with failed nonsurgical management require surgery. The major concern in patients after splenectomy is the loss of splenic function and the risk for postsplenectomy sepsis, in which the mortality rate is reported to be 50% to 80%. An alternative to splenectomy is the splenic salvage procedure or a simple repair.<sup>28</sup>

#### **SPLENOSIS**

Heterotopic splenic implants, so-called splenosis, may occur in the peritoneal cavity, after splenic trauma or splenectomy. Such implants can occur anywhere in the abdominal cavity. They are usually multiple and vary from some millimeters to several centimeters. They are seen as having the same echogenicity, density, and signal intensity as normal spleen on ultrasonography, CT, and MRI. On dynamic CT and MRI they also manifest a similar enhancement pattern as normal spleen.<sup>12,16</sup> However, because the most common finding of splenosis is solid, welldefined nodules in the abdominal cavity, splenosis should be differentiated from peritoneal tumor implants or lymphadenopathy. A history of splenic trauma or splenectomy is an important clue when splenosis is suggested.<sup>99m</sup>Tc-SC scintigraphy is helpful to identify the splenic functional activity of the suspected lesion (Figure 60-26).

## **Miscellaneous Conditions**

# NON-NEOPLASTIC AND NONINFECTIOUS SPLENOMEGALY

#### Etiology

The most frequent cause of non-neoplastic and noninfectious splenomegaly is portal venous hypertension (Figures 60-27 and 60-28), followed by various hematologic disorders (Figure 60-29) and storage diseases (Figures 60-30 and 60-31). A list of non-neoplastic and noninfectious causes of splenomegaly is provided in Box 60-1.<sup>2,14,16</sup>

#### Prevalence and Epidemiology

The prevalence and epidemiology of splenomegaly depend on the underlying cause. The term *splenomegaly* is somewhat subjective and often inaccurate.<sup>16</sup> Spleen size decreases with age, increases with body weight, and is slightly smaller in women. Also, spleen size varies depending on any situation (e.g., weight loss, pregnancy). Such individual and conditional variation of spleen size is problematic for deciding whether there is splenomegaly.

In 9% to 12% of patients with congestive splenomegaly secondary to portal venous hypertension, small areas of intrasplenic hemorrhage may result in foci of hemosiderin deposition, so-called Gamna-Gandy bodies. Occasionally, they can be observed in patients receiving blood transfusions.<sup>12</sup>

#### **Clinical Presentation**

The clinical presentations of splenomegaly vary from asymptomatic to hypersplenism. *Hypersplenism* is the generic term used for the syndrome in which the removal of hematopoietic elements by the spleen increases to a pathologic degree, resulting in pancytopenia. This condition can result from widening

#### BOX 60-1 CAUSES OF NON-NEOPLASTIC AND NONINFECTIOUS SPLENOMEGALY

- Congestive splenomegaly
- Portal hypertension (e.g., cirrhosis)
- Splenic vein occlusion
- Heart failure
- Hematologic diseases
- HemoglobinopathiesHereditary spherocytosis
- Idiopathic thrombocytopenic purpura
- Thrombotic thrombocytopenic purpura
- Primary neutropenia
- Myelofibrosis
- Polycythemia vera
- Storage disease
- Gaucher's disease
- Amyloidosis
- Hemochromatosis
- Histiocytosis
- Collagen vascular disease
- Felty's syndrome
- Systemic lupus erythematosus
- Juvenile rheumatoid arthritis

of the splenic cords with an increase in macrophages or connective tissue fibers and premature destruction of the normal blood cells. Therefore, hypersplenism can be seen with congestive splenomegaly, Gaucher's disease, malignant lymphoma, leukemia, angiosarcoma, and practically any condition diffusely involving the splenic parenchyma.<sup>5</sup>

#### Pathology

The enlarged spleen tends to become directed anteriorly. The splenic tip extends below the tip of the right lobe of the liver.

Gross and microscopic features of splenomegaly vary depending on the underlying cause.<sup>2</sup> In congestive splenomegaly, the spleen is large, firm, and dark. Frequently noted is fibrous thickening of the capsule. There is marked venous and sinusoidal dilatation as well as fibrosis of the red pulp.

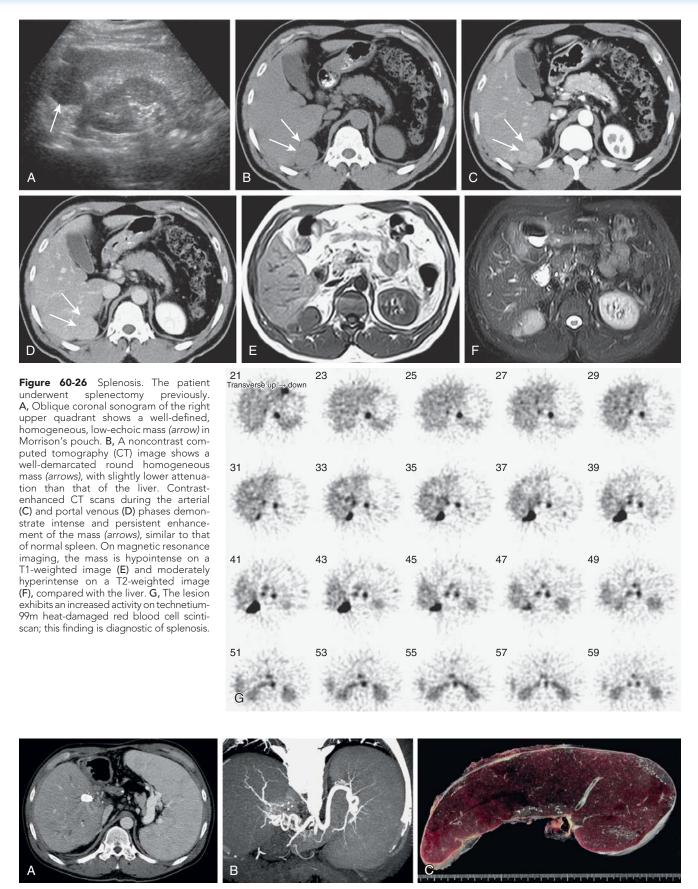
Gamna-Gandy bodies are foci of hemosiderin deposit in the spleen. They may contain a variable amount of fibrous tissue and calcium.<sup>24,26</sup> The size of the lesion varies but is usually less than 1 cm.<sup>12,24</sup>

#### Imaging

There are several methods to measure the splenic volume in vivo. Using CT, splenic volume can be measured by integrating the areas of consecutive scan slices. Using CT, MRI, or ultrasonography, it can be estimated by figuring the length, width, and thickness of the spleen (splenic index). However, these methods are time-consuming and complicated. Most radiologists apply a simpler but less accurate method using a craniocaudal measure of 13 to 14 cm.

Apart from spleen size, imaging findings can vary depending on any underlying disease.

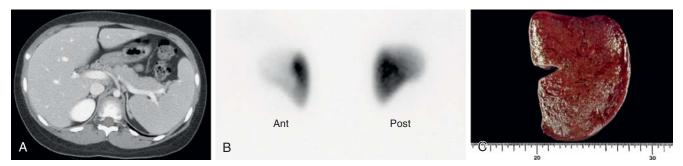
**Radiography.** Splenomegaly can be appreciated on plain radiographs in most cases; the inferior splenic contour is delineated below the 12th rib. An enlarged spleen displaces the stomach and splenic flexure of the colon medially and the left kidney inferiorly.



**Figure 60-27** Congestive splenomegaly in a patient who underwent liver transplantation for the treatment of liver cirrhosis. Splenectomy was performed to increase portal flow. Contrast-enhanced computed tomography (CT) (A) and thick oblique axial CT image with maximum intensity projection (B) show splenomegaly. C, At gross pathology, the spleen is enlarged up to 19 cm and dark red and appears congestive.



**Figure 60-28** Gamna-Gandy bodies in a patient with liver cirrhosis and portal hypertension. **A**, Oblique coronal sonogram shows marked splenomegaly and multiple tiny echogenic spots with barely perceptible acoustic shadowing. **B**, Noncontrast computed tomography (CT) scan displays splenomegaly with multiple, diffusely scattered, punctate, high-attenuation spots. **C**, On this gradient echo T1-weighted magnetic resonance image, the nodules are seen as of dark signal intensity, and the sizes of the individual lesions are obviously larger than on sonogram or CT; this phenomenon, the so-called blooming artifact, is attributed to the paramagnetic effect of hemosiderin and is nearly pathognomonic for Gamna-Gandy bodies.



**Figure 60-29** Idiopathic thrombocytopenic purpura. A, A contrast-enhanced computed tomography image shows mildly enlarged spleen in an 8-year-old boy. B, Technetium-99m-sulfur colloid scan depicts only the main spleen and proves there is no accessory spleen. The presence of accessory spleens should be thoroughly evaluated because a remnant accessory spleen after the surgery may evoke relapse of the disorder. C, Gross pathologic specimen shows mild splenomegaly with congestion. *Ant,* Anterior; *Post,* posterior.

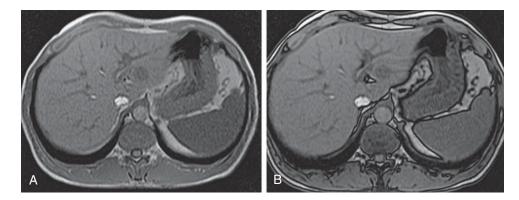


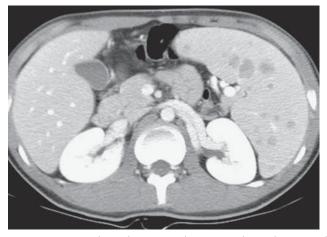
Figure 60-30 Hemosiderosis usually is seen as reduced signal intensity of the spleen on an in-phase T1-weighted gradient echo image (A) compared with signal intensity of the spleen on opposed-phase image (B), owing to the presence of iron.

**Computed Tomography.** Splenomegaly can be more confidently assessed on CT than on plain radiograph. CT may reveal the splenic disease or the cause of splenomegaly as well (see Figure 60-27). Gamna-Gandy bodies are also more distinctively seen on CT. Calcified foci appear as high-density lesions on noncontrast CT (see Figure 60-28), whereas noncalcified foci may appear as multiple, punctate, low-attenuation areas on postcontrast CT.<sup>24</sup>

Magnetic Resonance Imaging. MRI is especially useful in demonstrating splenic iron deposition and Gamna-Gandy

bodies (see Figure 60-28), which appear as dark signal intensity on all pulse sequences. On gradient-echo sequences, blooming artifact is seen as a result of the superparamagnetic effect of hemosiderin. This artifact is pathognomonic for Gamna-Gandy bodies (see Figure 60-28).<sup>12,24</sup>

**Ultrasonography.** Ultrasonography is useful only for measurement of spleen size but is free of the hazard of radiation exposure. Gamna-Gandy bodies are seen as diffuse hyperechoic spots and occasional acoustic shadowing if the lesions contain calcium (see Figure 60-28).<sup>24</sup>



**Figure 60-31** Gaucher's disease. Axial contrast-enhanced computed tomography image demonstrates multiple, well-defined, discrete nodules in the enlarged spleen.

**Nuclear Medicine.** <sup>99m</sup>Tc-SC scan can be used to detect splenic functional activity. It is especially useful in patients with hypersplenism, by means of localization of the accessory splenic tissue, when planning the splenectomy for intractable hypersplenism (see Figure 60-29). However, poor spatial resolution limits the value of this study.

#### Positron Emission Tomography With Computed Tomogra-

**phy.** PET/CT may be useful in patients with splenomegaly in that it can suggest or rule out the possibility of hematolymphoid malignancies diffusely involving the spleen. In cases of non-neoplastic and noninfectious splenomegaly, there is little role for this examination.

#### Treatment

Treatment varies based on the underlying cause. In patients with congestive splenomegaly secondary to portal venous hypertension, medical treatment may be tried to decrease the portal venous pressure, but splenectomy is seldom performed unless there is a complication (i.e., rupture of an associated splenic artery aneurysm). On the contrary, splenectomy is often indicated in patients with splenomegaly related to hematologic disorders such as hemolytic anemia and thrombocytopenic purpuras, owing to intractable pancytopenia.

#### HEMOCHROMATOSIS

After transfusion or rhabdomyolysis, iron can be deposited in the reticuloendothelial cells of the spleen, bone marrow, and Kupffer cells of the liver. This secondary iron deposition should

#### What the Referring Physician Needs to Know

#### **Accessory Spleen**

- If splenectomy is needed in patients with hematologic and autoimmune disorders, the presence of accessory spleens should be thoroughly evaluated by various imaging studies.
- A remnant accessory spleen after surgery may evoke relapse of the disorder.

#### be differentiated from primary hemochromatosis. The latter is an uncommon inherited autosomal recessive disorder primarily involving the liver.

Intracellular iron deposits produce characteristic MRI findings. The spleen, liver, and bone marrow reveal low signal intensity on T2-weighted images.<sup>2,14</sup> Iron deposits appear as darker signal intensity on in-phase T1-weighted gradient echo images compared with findings on opposed-phase images (the opposite of fat on chemical shift images)<sup>22</sup> (see Figure 60-30). On noncontrast CT, there may be diffusely increased attenuation values of the liver and spleen in patients with iron overload as well.

#### GAUCHER'S DISEASE

Gaucher's disease is an autosomal recessive lysosomal disorder in which glucocerebroside accumulates abnormally in the reticuloendothelial system as a result of a deficit of the enzyme glucocerebrosidase. The disease is clinicopathologically characterized by hepatosplenomegaly, anemia, thrombocytopenia, and endosteal erosion of the long bones. Patients with Gaucher's disease commonly undergo splenectomy because of hypersplenism and abdominal discomfort. Ultrasonography, CT, and MRI usually show marked splenomegaly and a mass effect on adjacent organs. Multiple discrete nodules representing the accumulation of glucocerebroside in the spleen are seen as hypoechoic lesions on ultrasonography, hypoattenuation nodules on CT (see Figure 60-31), and hyperintense nodules on T1-weighted MR images. The signal intensity is intermediate on T2-weighted images.<sup>12,14,22</sup>

#### **AMYLOIDOSIS**

The two recognized patterns of splenic amyloidosis are a nodular form and a diffuse form. On CT, each pattern can be appreciated as discrete low-attenuation masses in the spleen and a diffuse low-attenuation spleen with poor contrast enhancement. Splenomegaly is uncommon, with an incidence of 4% to 13%.<sup>12</sup>

#### SICKLE CELL ANEMIA

Sickle cell anemia is common in the black population, with a prevalence of 0.2% (homozygous form) and 8% to 10% (heterozygous form). The spleen is the organ most commonly involved by sickle cell anemia. Splenomegaly develops in the first year of life, and splenic function declines as a result of microinfarction. Splenic infarcts lead to loss of function, gradual decreases in size, and, ultimately, fibrosis and calcification. An excessive iron deposition from repeated blood transfusion may render the spleen as a nearly signal void area on MRI.<sup>14,22</sup>

#### Wandering Spleen

- There is little confusion in the diagnosis of wandering spleen if a comma-shaped abdominal or pelvic mass is found in the absence of the spleen in its normal location.
- Surgery is the treatment of choice for symptomatic patients.

Continued

# What the Referring Physician Needs to Know—cont'd

# **Bacterial Infection**

- Early diagnosis of splenic abscess with identification of organisms on Gram stain and culture and drug sensitivity may improve the prognosis of splenic abscess patients.
- Imaging-guided percutaneous needle aspiration can be helpful in differentiating an abscess from other focal lesions in febrile patients.

# **Fungal Infection**

- The diagnosis of splenic candidiasis is often difficult because of a nonspecific clinical presentation.
- In immunocompromised patients, an unexplained fever that is unresponsive to antibiotic agents should suggest an invasive fungal infection.

# Mycobacterial Infection

- Common radiologic findings include mild splenomegaly and abdominal lymphadenopathy with low central attenuation, high-attenuation ascites with nodular peritoneal thickening, hepatomegaly, and pleural effusions.
- The radiologic findings of splenic tuberculosis are similar to those of other diseases, and thus the clinical data are important in the differential diagnosis.

# Parasitic Infections: Echinococcosis

• The presence of a cystic lesion with wall calcification and daughter cysts in a patient in an endemic area should be considered an echinococcal cyst.

#### Sarcoidosis

 If the patient has multiple small hepatosplenic nodules or splenomegaly, as well as pulmonary abnormalities and mediastinal/hilar lymphadenopathy, sarcoidosis should be considered.

#### Vascular Lesions

- Splenic infarction: Although most patients with splenic infarctions are asymptomatic and need no treatment, those with increasing pain or splenic rupture need surgery.
- Splenic venous thrombosis: The common causes of splenic vein thrombosis are pancreatitis and associated pseudocyst. The finding of a collateral circulation of the portoportal and portocaval system is helpful for evaluation of upper gastrointestinal bleeding in patients with a previous history of pancreatic pathology.
- Splenic artery aneurysm: Transarterial embolization of a splenic artery aneurysm is necessary for patients with symptoms, female sex, or portal hypertension.

# Trauma-Related Lesions

- CT is the premier imaging modality for screening of splenic injury in trauma patients, with fast image acquisition and high diagnostic accuracy.
- Ultrasonography can be an alternative for a hemodynamically unstable patient and a child.
- Nonoperative management of blunt trauma is currently the standard of care in patients who are hemodynamically stable.
- CT-based classifications of splenic injury may help to triage a patient with blunt splenic trauma.

# Non-Neoplastic and Noninfectious Splenomegaly

• The most common cause of splenomegaly is portal venous hypertension.

# Key Points

# Asplenia Syndrome

- Absence of splenic tissue on ultrasonography/CT/splenic scan
- Ipsilateral position of IVC/hepatic veins and aorta
- Complex congenital heart disease

## Polysplenia Syndrome

- Multiple spleens or a multilobed spleen on ultrasonography/CT/splenic scan
- Interrupted IVC with continuation to azygos vein
- Congenital heart disease

# Bacterial Infection

• Round masslike lesion with thick, irregular, surrounding tissue in the spleen of a febrile patient

#### **Fungal Infection**

• Multiple small, low-attenuation, nonenhancing splenic lesions in the patient with fever, neutropenia, and a history of broad-spectrum antibiotic therapy

#### Mycobacterial Infection

• Multiple, small, focal lesions of the spleen with abdominal lymphadenopathy with central necrosis

#### Parasitic Infections: Echinococcosis

- A cystic lesion with wall calcification and daughter cysts
- Endemic area

#### Sarcoidosis

- Multiorgan involvement
- Splenomegaly or multiple small lesions

- Retroperitoneal lymphadenopathy
- Pulmonary, mediastinal, and hilar lymph nodes or hepatic involvement
- Splenic infarction: Peripheral, wedge-shaped, perfusion defect with or without a cortical rim sign
- Splenic venous thrombosis: Most commonly associated with pancreatitis, potentially resulting in gastrointestinal varices
- Splenic artery aneurysm: Early and markedly enhanced, round lesions with or without peripheral calcification
- Splenic vein aneurysm: Saccular dilatation of splenic vein
- Arteriovenous fistula: Tortuous, dilated splenic vein with earlier enhancement than parenchyma

#### **Trauma-Related Lesions**

 Contrast extravasation and vascular injury such as pseudoaneurysm or arteriovenous fistula indicate the need for urgent surgical or interventional treatment.

## Non-neoplastic and Noninfectious Splenomegaly

- The causes of splenomegaly are numerous.
- The measurement of spleen size may be subjective.
- Splenomegaly is usually caused by a systemic disease, rather than a primary pathologic process.

# Vascular Lesions

#### 60 Diffuse Splenic Lesions 697

#### **SUGGESTED READINGS**

- Akhan O, Koroglu M: Hydatid disease of the spleen. Semin Ultrasound CT MR 28:28–34, 2007.
- De Schepper AM, Vanhoenacker F, de Beeck BO, et al: Vascular pathology of the spleen. I. *Abdom Imaging* 30:96–104, 2005.

De Schepper AM, Vanhoenacker F, de Beeck BO, et al: Vascular pathology of the spleen. II. *Abdom Imaging* 30:228–238, 2005.

Fulcher AS, Turner MA: Abdominal manifestations of situs anomalies in adults. *Radiographics* 22:1439–1456, 2002.

## REFERENCESS

- Thomas S, Dachman AH: Anomalies and anatomic variants of the spleen. In Gore RM, Levine MS, editors: *Textbook of gastrointestinal radiology*, ed 4, Philadelphia, 2015, Saunders, pp 1912–1922.
- Federle MP, Jeffrey RB, Desser TS, et al: Spleen. In Federle MP, Jeffrey RB, Desser TS, et al, editors: *Diagnostic imaging: abdomen*, Salt Lake City, NV, 2004, Amirsys.
- Gayer G, Hertz M, Strauss S, et al: Congenital anomalies of the spleen. Semin Ultrasound CT MR 27:358–369, 2006.
- 4. Gayer G, Zissin R, Apter S, et al: CT findings in congenital anomalies of the spleen. *Br J Radiol* 74:767–772, 2001.
- Rosai J: Spleen. In *Surgical pathology*, ed 9, Philadelphia, 2004, Mosby, pp 2019–2045.
- Jang KM, Kim SH, Lee SJ, et al: Differentiation of an intrapancreatic accessory spleen from a small (<3-cm) solid pancreatic tumor: value of diffusion-weighted MR imaging. *Radiology* 266:159–167, 2013.
- Raissaki M, Prassopoulos P, Daskalogiannaki M, et al: Acute abdomen due to torsion of wandering spleen: CT diagnosis. *Eur Radiol* 8:1409– 1412, 1998.
- 8. Buckley O, Ward EV, Doody O, et al: MRI of the wandering spleen. *Clin Radiol* 62:504, 2007.
- 9. Ben Ely A, Zissin R, Copel L, et al: The wandering spleen: CT findings and possible pitfalls in diagnosis. *Clin Radiol* 61:954–958, 2006.
- Bartram U, Wirbelauer J, Speer CP: Heterotaxy syndrome: asplenia and polysplenia as indicators of visceral malposition and complex congenital heart disease. *Biol Neonate* 88:278–290, 2005.

- Gayer G, Hertz M, Strauss S, et al: Congenital anomalies of the spleen. Semin Ultrasound CT MR 27:358–369, 2006.
- Marmery H, Shanmuganathan K: Multidetectorrow computed tomography imaging of splenic trauma. Semin Ultrasound CT MR 27:389–403, 2006.
- Robertson F, Leander P, Ekberg O: Radiology of the spleen. *Eur Radiol* 11:80–95, 2001.
- Urrutia M, Mergo PJ, Ros LH, et al: Cystic masses of the spleen: radiologic-pathologic correlation. *Radiographics* 16:107–129, 1996.
- Vanhoenacker FM, Op de Beeck B, De Schepper AM, et al: Vascular disease of the spleen. *Semin Ultrasound CT MR* 28:35–51, 2007.
- Warshauer DM: Splenic sarcoidosis. Semin Ultrasound CT MR 28:21–27, 2007.
- Fulcher AS, Turner MA: Abdominal manifestations of situs anomalies in adults. *Radiographics* 22:1439–1456, 2002.
- Bilaj F, Rivero H, Firat Z, et al: Spleen. In Semelka RC, editor: *Abdominal-pelvic MRI*, ed 2, Hoboken, NJ, 2006, Wiley-Liss, pp 637–675.
- Urrutia M, Mergo PJ, Ros LH, et al: Cystic masses of the spleen: radiologic-pathologic correlation. *Radiographics* 16:107–129, 1996.
- Vos PM, Barnard SA, Cooperberg PL: Benign and malignant lesions of the spleen. In Gore RM, Levine MS, editors: *Textbook of gastrointestinal radiology*, ed 4, Philadelphia, 2015, Saunders, pp 1923–1964.
- Kamaya A, Weinstein S, Desser TS: Multiple lesions of the spleen: differential diagnosis of cystic and solid lesions. *Semin Ultrasound CT* MR 27:389–403, 2006.
- Robertson F, Leander P, Ekberg O: Radiology of the spleen. *Eur Radiol* 11:80–95, 2001.
- Metser U, Even-Sapir E: The role of 18F-FDG PET/CT in the evaluation of solid splenic masses. Semin Ultrasound CT MR 27:420–425, 2006.
- Semelka RC, Kelekis NL, Sallah S, et al: Hepatosplenic fungal disease: diagnostic accuracy and spectrum of appearances on MR imaging. *AJR Am J Roentgenol* 169:1311–1316, 1997.
- Seshadri N, Kaur B, Balan K: Disseminated cryptococcosis: detection by F-18 FDG PET. *Clin Nucl Med* 32:476–478, 2007.
- Ho AY, Pagliuca A, Maisey MN, et al: Positron emission scanning with 18-FDG in the diagnosis of deep fungal infections. *Br J Haematol* 101:392–393, 1998.

- Akhan O, Koroglu M: Hydatid disease of the spleen. Semin Ultrasound CT MR 28:28–34, 2007.
- Elsayes KM, Narra VR, Mukundan G, et al: MR imaging of the spleen: spectrum of abnormalities. *Radiographics* 25:967–982, 2005.
- 23. Iannuzzi MC, Rybicki BA, Teirstein AS: Sarcoidosis. N Engl J Med 357:2153–2165, 2007.
- Vanhoenacker FM, Op de Beeck B, De Schepper AM, et al: Vascular disease of the spleen. Semin Ultrasound CT MR 28:35–51, 2007.
- De Schepper AM, Vanhoenacker F, de Beeck BO, et al: Vascular pathology of the spleen. I. *Abdom Imaging* 30:96–104, 2005.
- De Schepper AM, Vanhoenacker F, de Beeck BO, et al: Vascular pathology of the spleen. II. Abdom Imaging 30:228–238, 2005.
- Weber SM, Rikkers LF: Splenic vein thrombosis and gastrointestinal bleeding in chronic pancreatitis. World J Surg 27:1271–1274, 2003.
- Yaghmai V, Seyal AR: Splenic trauma and surgery. In Gore RM, Levine MS, editors: *Textbook of gastrointestinal radiology*, ed 4, Philadelphia, 2015, Saunders, pp 1965–1976.
- Marmery H, Shanmuganathan K: Multidetectorrow computed tomography imaging of splenic trauma. Semin Ultrasound CT MR 27:389–403, 2006.
- Moore EE, Shackford SR, Pachter HL, et al: Organ injury scaling: spleen, liver, and kidney. *J Trauma* 29:1664–1666, 1989.
- Mirvis SE, Whitley NO, Gens DR: Blunt splenic trauma in adults: CT-based classification and correlation with prognosis and treatment. *Radiology* 171:33–39, 1989.

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# Lymph Node Imaging Techniques and Clinical Role

AVINASH KAMBADAKONE | JOSEPH R. GRAJO | DUSHYANT V. SAHANI

# Lymph Node Imaging Techniques

Imaging evaluation of lymph nodes forms an integral component of staging of various malignancies, including lymphomas, and is also helpful in the evaluation of certain infective and inflammatory processes within the abdomen. This has special relevance in the abdomen because the lymph node system in this region is not readily accessible for clinical examination or tissue sampling. Therefore, accurate identification and characterization of abnormalities of the lymph nodes in the abdomen and pelvis are crucial to achieve optimal diagnosis and plan treatment strategies. A wide range of imaging techniques is available for evaluation of the lymph nodes in the abdomen and pelvis. Lymphangiography was once considered the preferred imaging modality for evaluation of nodal disease. However, with the advent of imaging techniques such as ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and PET/CT, the role of lymphangiography has now faded and has only a few valid indications.<sup>1</sup> The superior soft tissue resolution of CT and MRI has improved the detection and assessment of even small lymph nodes. However, reliance on size criteria for characterization has limited the accuracy of these modalities in nodal staging of malignancies. Fluorodeoxyglucose (FDG)-labeled PET has further revolutionized oncologic imaging by recognizing benign and malignant nodes based on their FDG uptake.<sup>2</sup> Development of investigational lymphotropic nanoparticles for the diagnosis of lymph node metastases has added a new dimension to the scope of MRI of lymph nodes as well. This chapter will discuss the various imaging modalities and describe their role in imaging of lymph nodes of the abdomen and pelvis. Additionally, various clinical manifestations of lymphadenopathy in the abdomen and pelvis will be individually discussed.

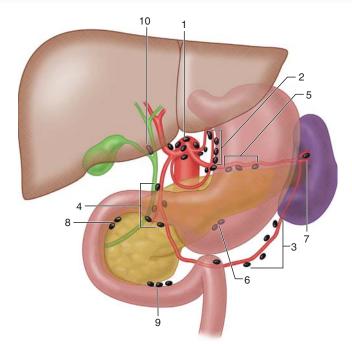
#### NORMAL ANATOMY

The lymphatic system is a complex network of lymph nodes connected by lymphatic capillaries and ducts that play an important role in the immune system.<sup>3-5</sup> It provides protection against organisms, particulate matter, and neoplastic cells by the processes of phagocytosis, cell-mediated and antibody-mediated immune complexes, production of B and T lymphocytes, and antibody-producing plasma cells.<sup>5</sup> There are approximately 230 nodes in the abdomen and pelvis and 400 to 500 lymph nodes in the entire adult body.<sup>5</sup>

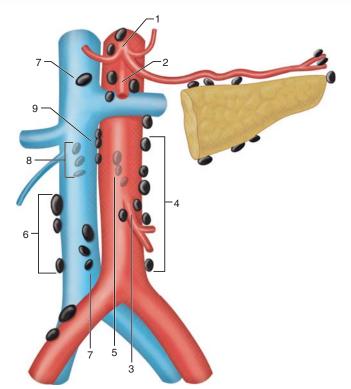
The lymphatics of the abdomen have been divided into parietal and visceral systems composed of the lymphatic channels and nodes that drain the walls and contents of the abdominal cavity.<sup>6</sup> The parietal lymphatic system has a superficial component that drains the skin and subcutaneous tissue and a deep component draining the muscles and fasciae of the abdominal wall.<sup>6</sup> The visceral lymphatics initially drain into nodes located close to the viscera, then into intermediate nodes situated along the peritoneal ligaments and mesenteries, and finally into the larger group of nodes situated along the major branches of the abdominal aorta.<sup>6</sup> The lymphatics follow the course of the parietal and visceral branches of the abdominal aorta and ultimately drain into the venous stream via the thoracic duct.<sup>6</sup> The thoracic duct is the final lymphatic pathway for the entire pelvis, retroperitoneum, and peritoneal cavity.

Lymph nodes within the abdomen can be broadly divided into those related to the abdominal viscera and retroperitoneal nodes (Figures 61-1 to 61-3).<sup>7,8</sup> The lymph nodes associated with the abdominal viscera are situated along the distribution of the celiac, superior mesenteric, and inferior mesenteric arteries.<sup>7</sup> The lymph nodes of the abdominal viscera ultimately drain into the retroperitoneum and into the cisterna chyli.<sup>7</sup> Lymph nodes within the retroperitoneum are named and grouped according to their relation to the inferior vena cava and the abdominal aorta: paracaval, precaval, retrocaval, aortocaval, preaortic, and para-aortic.7 The preaortic group comprises the celiac, superior mesenteric, and inferior mesenteric nodes that drain the lymphatics of the intestinal tract.<sup>6</sup> The para-aortic, paracaval, and aortocaval nodes form the lateral aortic group, which is the main terminal group for lymphatic drainage of all the abdominal and pelvic viscera of the urogenital system.<sup>6,7</sup> The retroperitoneal nodes finally drain into the cisterna chyli, which empties into the thoracic duct.

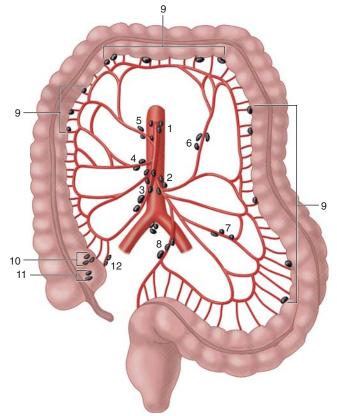
The lymphatic drainage of the pelvis has been categorized into the parietal and visceral channels as well (Figures 61-4 and 61-5).<sup>8</sup> The parietal channels drain the skin and superficial fascia, and the visceral channels drain the urinary tract, reproductive organs, rectum, perineum, and external genitalia.8 The lymphatic drainage of the pelvis occurs through nodes situated along the pelvic sidewall: common iliac, external iliac (including obturator), internal iliac or hypogastric (along the internal iliac vessels), and presacral.8 The external iliac nodes receive lymphatic drainage from the inguinal nodes and the obturator lymphatics, and the internal iliac nodes receive drainage from the visceral pelvic organs. The internal iliac and external iliac nodes drain into the common iliac nodes, which finally drain into the retroperitoneal para-aortic nodes along the aorta and inferior vena cava.8 The nodes at the junction of internal and external iliac vessels have been referred to as junctional nodes. Lymphatics from the pelvic



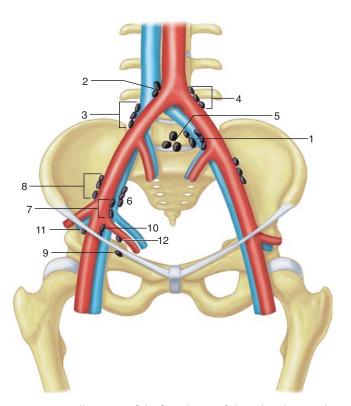
**Figure 61-1** Illustration of the upper gastrointestinal tract depicting the lymph nodes of the stomach, liver, gallbladder, pancreas, and spleen: 1, celiac; 2, gastric (right and left); 3, gastroepiploic (right and left); 4, pyloric; 5, superior pancreatic; 6, inferior pancreatic; 7, perisplenic; 8, superior pancreaticoduodenal; 9, inferior pancreaticoduodenal; 10, cystic.



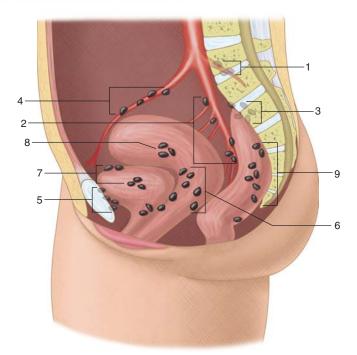
**Figure 61-2** Illustration of the retroperitoneum depicting the retroperitoneal lymph nodes: 1, celiac; 2, superior mesenteric; 3, inferior mesenteric; 4, para-aortic; 5, retroaortic; 6, paracaval; 7, precaval; 8, retrocaval; 9, aortocaval.



**Figure 61-3** Illustration of the colon with its arterial anatomy depicting the nodal system of the colon: 1, superior mesenteric; 2, inferior mesenteric; 3, ileocolic; 4, right colic; 5, middle colic; 6, left colic; 7, sigmoid; 8, superior rectal; 9, paracolic; 10, prececal; 11, retrocecal; 12, appendicular.



**Figure 61-4** Illustration of the frontal view of the pelvis showing the pelvic lymph nodes: 1, median common iliac; 2, intermediate common iliac; 3, lateral common iliac; 4, subaortic common iliac; 5, common iliac nodes of promontory; 6, medial external iliac; 7, intermediate external iliac; 8, lateral external iliac; 9, femoral (medial); 10, femoral (intermediate); 11, femoral (lateral); 12, obturator.



**Figure 61-5** Illustration of the lateral view of the pelvis showing the pelvic lymph nodes: 1, superior gluteal; 2, nodes along internal iliac branches; 3, sacral; 4, external iliac; 5, prevesical; 6, paravaginal; 7, lateral vesicular; 8, parauterine; 9, perirectal.

viscera also can have drainage into the inguinal nodes externally.<sup>7,8</sup> The pelvic nodal chains drain directly into the retroperitoneal system, and there are numerous interconnections with the celiac and mesenteric nodal systems as well.<sup>5,7,8</sup>

## **Retrocrural Nodes**

Retrocrural nodes are situated within the retrocrural space connecting the posterior mediastinum to the retroperitoneum and contain the aorta, thoracic duct, azygos vein, hemiazygos vein, and retrocrural lymph nodes (Figure 61-6, A).<sup>5</sup> The lymphatic drainage from the diaphragm, posterior mediastinum, and upper lumbar region occurs into the retrocrural nodes. The retrocrural space can act as a conduit for communication of diseases originating above or below the diaphragm. Retrocrural lymph nodes are considered to be enlarged when they exceed 6 mm.

#### **Gastric Nodes**

The gastric nodes consist of multiple groups of nodes situated along the lesser and greater curvature of the stomach (see Figure 61-6, *B*).<sup>6</sup> These include the right and left gastric nodes, which are located within the lesser omentum along the lesser curvature of stomach, and the right and left gastroepiploic nodes, which lie within the greater omentum along the lower part of the greater curvature of the stomach. Also included are the pyloric nodes, which receive drainage from the right gastroepiploic nodes and from the first part of duodenum and head of pancreas. The pyloric nodes ultimately drain into the celiac nodes.

#### Gastrohepatic Ligament Nodes

The gastrohepatic ligament (see Figure 61-6, C), which suspends the stomach from the liver, constitutes the superior

segment of the lesser omentum. This ligament contains the left gastric artery and coronary vein and merges into the fissure of ligamentum venosum, which acts as a landmark on CT. Gastrohepatic ligament nodes are considered to be enlarged when they exceed 8 mm. Potential diagnostic pitfalls, which can mimic mild lymphadenopathy in this region, include coronary varices of the upper margin of the pancreas and transverse colon.

#### Portohepatic Nodes

Portal nodes, as the name suggests, lie within the porta hepatis and extend down the hepatoduodenal ligament, thereby interconnecting with the gastrohepatic ligament nodes (see Figure 61-6, D). These nodes drain into the celiac nodes. One of these nodes around the hilum of the liver at the junction of the cystic and common bile ducts near the neck of the gallbladder has been named the Quenu's cystic node. The portal nodes lie around the portal vein and can completely surround and obliterate the portal vein when enlarged. Hence, adequate enhancement with intravenous contrast material is essential for diagnosis and to rule out portal vein involvement. Portal nodes are abnormal if greater than 7 mm in size.<sup>7</sup>

#### Pancreaticoduodenal Nodes

Pancreaticoduodenal nodes lie between the duodenal sweep and pancreatic head, anterior to the inferior vena cava (see Figure 61-6, E).<sup>5</sup> The pancreaticoduodenal nodes are often grouped with the pericaval and superior mesenteric artery nodes into a larger category termed the peripancreatic nodes. Nodes in this location exceeding 10 mm are considered enlarged.

#### Perisplenic Nodes

Perisplenic nodes are often located around the splenic hilum, and their drainage area includes the spleen, greater curvature of the stomach, and tail of the pancreas. These nodes ultimately drain into the celiac group via the pancreaticosplenic chain of nodes, which lie along the pancreas. The upper limit of normal for these nodes is 10 mm.

#### Mesenteric Nodes

The small bowel mesentery contains a large number of nodes that accompany the branches of the superior mesentery and vein (see Figure 61-6, *G*).<sup>5</sup> These are located within the mesenteric fat and are formed of three distinct groups.<sup>6</sup> The most distal group formed by the juxtaintestinal nodes is situated close to the intestinal walls between the terminal jejunal and ileal arteries.<sup>6</sup> The intermediate group is situated between the distal group, and the last group is the central mesenteric nodes and is situated near the mesenteric root.<sup>6</sup> The eventual lymphatic drainage is to the superior mesenteric artery nodes at the base of the mesentery and from there to the retroperitoneal nodes.

# Celiac, Superior Mesenteric, and Inferior Mesenteric Nodes

The celiac and superior mesenteric artery nodes, along with the nodes at the base of the inferior mesenteric artery, are the preaortic nodes (see Figures 61-6, H and I).<sup>5</sup> The celiac (at T12 vertebra) and superior mesenteric (at L1 vertebra) nodes are grouped around the origins of their respective vessels and are easily distinguished.<sup>6</sup> However, it is difficult to distinguish the inferior mesenteric nodes because the artery often is not visualized as a discrete structure on CT. The celiac and superior mesenteric groups are the terminal nodes of the gastrointestinal

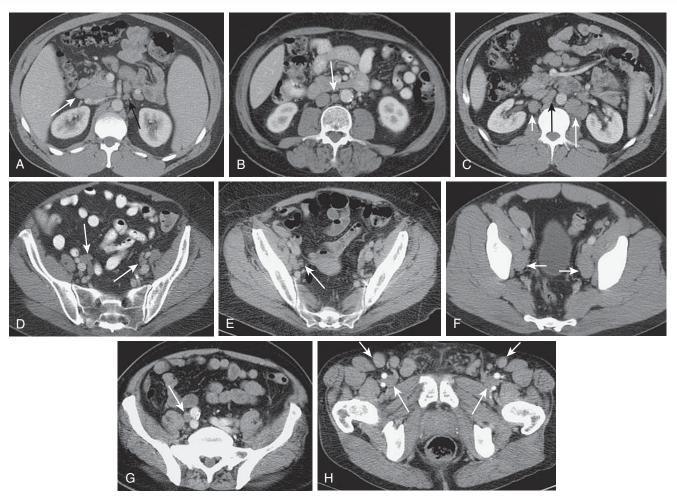


Figure 61-6 Representative axial contrast-enhanced multidetector computed tomography images of the abdomen and pelvis at various levels demonstrating the normal location of the abdominal lymph nodes. A, Portocaval (*white arrow*); SMA (*black arrow*). B, Aortocaval (*arrow*). C, Paracaval (*short white arrow*), aortocaval (*black arrow*), paraaortic (*long white arrow*). D, Right and left iliac bifurcation (*arrows*). E, Right external iliac (*arrow*). F, Right and left obturator (*arrows*). G, Right common iliac (*arrow*). H, Superficial inguinal (*short arrows*), deep inguinal (*long arrows*).

tract. The celiac nodes receive lymph from intermediate nodes such as the gastrohepatic ligament, portohepatic, pancreaticoduodenal, and perisplenic nodes draining the stomach, duodenum, and hepatobiliary system. The superior mesenteric group receives lymph from the mesenteric, ileocolic, and colic nodal chains extending from the ligament of Treitz to the splenic flexure. These nodes have interconnections with the portosplenic nodes and the retroperitoneal periaortic nodes. The inferior mesenteric nodes (at L3 vertebra) receive drainage from the nodes along the inferior mesenteric artery, sigmoid artery, and superior rectal vessels. The colic nodal chains are composed of epicolic nodes embedded in the walls of the colon, paracolic nodes along the mesenteric borders of the colon, and intermediate colic nodes located along the middle and left colic arteries.<sup>6</sup>

# Para-Aortic Nodes

The para-aortic nodes can be divided into eight subgroups on the basis of their relationship with the aorta and inferior vena cava (see Figure 61-6, J and K).<sup>8</sup> Surrounding the aorta are the bilateral lateral aortic, preaortic, and retroaortic subgroups. The

right lateral aortic subgroup is further divided into aortocaval, laterocaval, precaval, retrocaval, and paracaval subgroups to reflect the relationship with the inferior vena cava.

## **External Iliac Nodes**

The external iliac nodal group is composed of three chains: the lateral, middle, and medial. The nodes distributed along and lateral to the external iliac artery form the lateral chain (see Figure 61-6, L), and the middle nodal chain is composed of nodes located between the external iliac artery and vein. The medial chain is formed of the nodes lying medial and posterior to the external iliac vein, and they are often named obturator nodes because they accompany the obturator vessels (see Figure 61-6, N).

#### Internal Iliac Nodes

The internal iliac (hypogastric) nodes encompass several groups of lymph nodes that are located along the visceral branches of the internal iliac artery. Differentiation of these lymph nodes is difficult on imaging because they are often clustered close to each other. The lymph nodes are identified

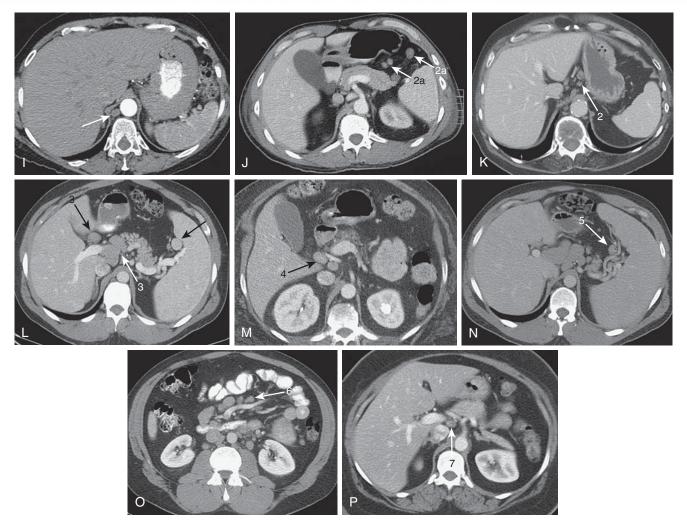


Figure 61-6, cont'd I: 8, Superior mesenteric; 4, pancreaticoduodenal. J: 9, Aortocaval. K: 10, Para-aortic; 11, retrocaval; 12, paracaval. L: 13, External iliac. M: 14, Internal iliac. N: 15, Obturator. O: 16, Common iliac. P: 17, Superficial inguinal; 18, deep inguinal.

based on the branches of the internal iliac vessels they accompany, for example, the uterine artery, the inferior vesical artery, the middle hemorrhoidal arteries, the superior and inferior gluteal arteries, and the internal pudendal artery (see Figure 61-6, M). Two specific groups of lymph nodes that can often be identified include the anterior nodes, located anterior to the internal iliac vessels at the origin of the umbilical and obturator arteries, and the lateral sacral nodes, which lie anterior to the first two sacral foramina along the lateral sacral arteries.

# Common Iliac Nodes

The common iliac nodal group consists of three groups: the medial, the middle, and the lateral groups (Figure 61-6, *O*). The medial group of lymph nodes is located in a central triangular area between the common iliac arteries, extending from the aortic bifurcation to the origin of the external and internal iliac arteries. The nodes at the sacral promontory are grouped with the medial chain. The middle group of lymph nodes occupies the region of the lumbosacral fossa, bordered by the sacral ala posteriorly, the common iliac vessels anteriorly, the psoas muscle laterally, and the lumbosacral vertebrae medially. The

lateral groups of lymph nodes lie lateral to the common iliac artery and extend lower as the lateral external lymph nodal chain. The common iliac nodes ultimately drain into the paraaortic nodes.

#### Inguinal Lymph Nodes

The inguinal nodal group his subdivided into two categories: superficial and deep. The superficial group of nodes (see Figure 61-6, P) lies anterior to the inguinal ligament in the subcutaneous tissue and can be identified as they accompany the superficial femoral and saphenous veins. The nodes at the saphenofemoral junction form an important group in the superficial inguinal nodal chain. The deep group of inguinal nodes (see Figure 61-6, *P*) is located deeper within the femoral sheath along the common femoral vessels medial to the femoral vein. The fascial planes that separate the superficial from the deep group of lymph nodes are not clearly identified on CT. The deep group of nodes drains into the medial chain of the external iliac nodes. A useful landmark to separate the deep inguinal nodes from the medial chain of the external iliac nodes is the inguinal ligament and the origins of the inferior epigastric and iliac circumflex vessels.

#### COMPUTED TOMOGRAPHY

CT is considered the initial examination of choice for the evaluation of abdominal and pelvic lymph nodes.<sup>9-11</sup> It is also the most commonly performed examination for the evaluation of abdominal lymph nodes, owing to its capability to concurrently characterize solid organ and hollow visceral abnormalities. The advent of multidetector CT (MDCT) scanners that acquire isotropic volume data and the advances in imaging workstations that allow multiplanar and three-dimensional (3D) evaluation of these isotropic data sets have broadened the function of MDCT in the evaluation of abdominal and pelvic lymph nodes. Thin collimation and higher spatial resolution of MDCT now allow detection of small lymph nodes and enhanced characterization of lymph node morphology.

#### Technique

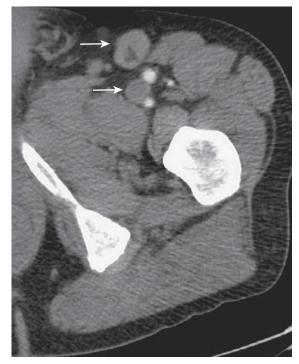
No particular technique is recommended for lymph node evaluation because their evaluation forms a part of the routine abdominal and pelvic CT examination. However, it is important to adhere to certain essential practices to maintain diagnostic accuracy. Chief among these is the administration of positive oral contrast material (1% to 2% dilute barium/Gastrografin) in particular to avoid misinterpretation of unopacified bowel loops as enlarged lymph nodes, especially in the retroperitoneum and mesentery.<sup>2,12</sup> Intravenous administration of a contrast agent is routinely recommended because it is an integral component of lymph node evaluation on CT. Its benefits are threefold, as follows:

- 1. It permits differentiation of small lymph nodes from tortuous vessels, particularly in the perigastric region and pelvis.<sup>2</sup>
- Contrast-enhanced scans are invaluable in the assessment of associated pathologic processes affecting the abdominal organs.
- 3. Lymph node enhancement patterns give important clues pertaining to the pathologic process involved.

A routine abdomen and pelvis scan obtained 60 to 75 seconds after the intravenous injection of a contrast agent is sufficient and is ideal with a volumetric acquisition with a slice thickness of at least 5 mm. This technique will provide good vascular opacification throughout the examination, allowing differentiation of enlarged nodes from adjacent vascular structures.<sup>5</sup> A dedicated examination for pelvic lymph nodes requires more intense venous enhancement compared with abdominal and retroperitoneal lymph nodes. Optimal enhancement of the pelvic veins occurs at 3 minutes after initiation of the bolus injection of contrast material.<sup>5</sup> Use of N-butyl scopolamine (Buscopan) is optional because it helps reduce artifacts from bowel peristalsis. However, it is also important to tailor the CT examination according to the clinical scenario in question, because of concerns about the dose of radiation particularly in those patients whose disease is being observed after treatment.

#### Normal Anatomy

On CT, normal nodes are ovoid and are of soft tissue density (Figure 61-7). Normal lymph nodes show mild to moderate enhancement after contrast agent administration. The excellent contrast and spatial resolution of MDCT and the presence of surrounding fat allows routine visualization of normal retroperitoneal and mesenteric lymph nodes.<sup>5</sup> Routine visualization of pelvic and perivisceral lymph nodes is less often possible



**Figure 61-7** Axial contrast-enhanced multidetector computed tomography image at the level of the pelvis highlighting the CT appearance of normal lymph nodes (*arrows*). The inguinal lymph nodes seen in the image are well marginated and oval, with homogeneous soft tissue attenuation. The presence of a fatty hilum, a distinguishing feature of benign lymph nodes, is well depicted in the superficial inguinal node.

owing to multiple adjacent vessels.<sup>5</sup> Asymmetry of pelvic vessels in healthy subjects is a pitfall in the diagnosis of lymph nodes with unenhanced CT.<sup>13</sup>

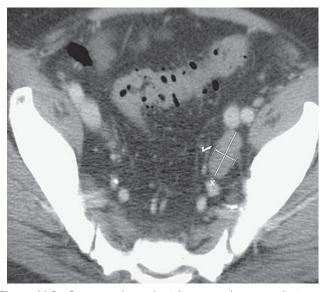
**Measurement of Nodal Size.** Lymph node size is obtained by measuring the maximum short-axis diameter, which helps minimize the errors resulting from node orientation (Figure 61-8). The size of normal nodes varies depending on the anatomic location in the body. In the abdomen, the upper limit of the maximum short-axis diameter of normal nodes varies between 6 and 10 mm and increases in size caudally.<sup>14</sup>

#### Mimics of Abnormal Lymph Nodes on Computed Tomogra-

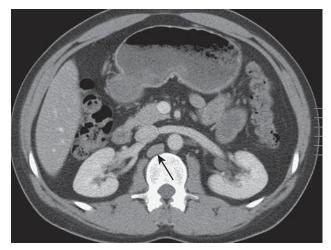
**phy.** Unopacified bowel loops and prominent normal vascular structures such as gonadal veins and iliac vessels can mimic lymphadenopathy.<sup>5</sup> Vascular anomalies including a left-sided or duplicated inferior vena cava and varices resulting from portal hypertension can mimic lymph nodes. The papillary process of the caudate lobe or bulbous scalloped diaphragmatic crus may simulate lymphadenopathy in the portocaval space or retrocrural region (Figure 61-9). An accessory spleen or normal ovarian tissue also can mimic lymph nodes (see Figure 61-6, *D*).

#### Pathophysiology and Pathology

The only widely accepted criterion for the diagnosis of abnormal lymph nodes on CT is nodal size because CT cannot display abnormal architecture in a normal-sized node.<sup>5,15</sup> CT is also unable to differentiate between reactive hyperplasia and metastases in enlarged lymph nodes. This drawback is the reason for the majority of false-negative and false-positive results from CT



**Figure 61-8** Contrast-enhanced axial computed tomography image showing the correct method of estimating nodal size. The nodal size is obtained by measuring the maximum short-axis diameter (shown here with a *check mark*).

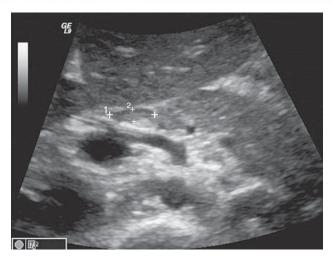


**Figure 61-9** Axial post-contrast computed tomography image at the level of the mid-abdomen shows a prominent right diaphragmatic crus (*arrow*) mimicking a retrocaval lymph node.

examinations. The secondary criteria used for characterization of nodal pathologic processes on CT are shape, margin, attenuation, and enhancement.

#### **ULTRASONOGRAPHY**

Ultrasonography is widely used for diagnosing lymph node disorders of the abdomen.<sup>4</sup> In contrast to other imaging modalities, such as CT, which primarily rely on size criteria to diagnose malignant invasion, ultrasonography also permits analysis of various echo features of the visualized lymph nodes to predict malignant invasion.<sup>4,16</sup> The detection and characterization of abdominal and pelvic lymph nodes can be done by either the transabdominal approach or the endoluminal route. Transabdominal ultrasonography is performed by using a standard 3.5- to 5-MHz convex array transducer, whereas endoscopic



**Figure 61-10** Transverse sonographic image of the abdomen in the midline shows a benign lymph node in the peripancreatic region (*cursors*). The lymph node is oval and elongated with an echogenic eccentric area representing the fatty hilum.

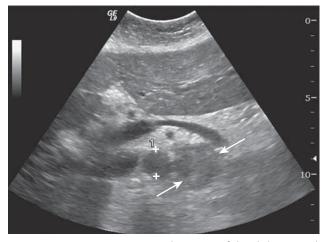
ultrasonography is performed with a radial scanning echoendo-scope at 7.5 and 12  $\rm MHz.^{16,17}$  Conventional transabdominal ultrasonography has a limited role in the evaluation of abdominopelvic lymphadenopathy owing to several factors. Endoscopic ultrasonography permits closer evaluation of the intra-abdominal lymph nodes and allows more reliable assessment of their echo structure, margin, and shape than conventional ultrasonography.<sup>16</sup> As a result, endoscopic ultrasonography is being increasingly used for detecting lymph nodes in the vicinity of the gastrointestinal tract as part of the staging evaluation of gastrointestinal and pancreaticobiliary malignancies.<sup>16</sup> Endoscopic ultrasonographic elastography is a promising method that allows characterization and differentiation of benign and malignant lymph nodes with a high sensitivity, specificity, and accuracy, offering complementary information to conventional endoscopic ultrasound imaging.<sup>18</sup> Contrast-enhanced ultrasound examination has been found to be useful in the differentiation of benign and malignant lymph nodes. On contrast-enhanced ultrasonography, benign lymph nodes have been shown to display uniform enhancement, whereas malignant lymph nodes demonstrate a defect in their enhancement.<sup>1</sup>

#### Normal Anatomy

Normal lymph nodes can be either isoechoic or hyperechoic in echotexture.<sup>4,20,21</sup> They are usually oval or polygonal (Figure 61-10).<sup>4,20,21</sup> A characteristic feature of a benign lymph node is the presence of a distinctive fatty echogenic hilum, called the "visible hilus sign." Ultrasonography has a lower sensitivity in the detection of para-aortic lymph nodes owing to interference by mesenteric fat and abdominal gas.<sup>22</sup>

#### Pathophysiology and Pathology

Features that suggest abnormality include enlargement, rounded shape, loss of central hilum, intense hypoechogenicity, and presence of altered nodal contours (Figure 61-11).<sup>4,20-24</sup> The features considered to be predictive of malignant lymph node invasion include hypoechoic structure, sharply demarcated borders, rounded contour, and a size greater than 10 mm.<sup>4,20-24</sup> If the lymph node is less than 10 mm, is not round, is



**Figure 61-11** Transverse sonographic image of the abdomen in the midline shows a malignant lymph node (*arrows*) in the left para-aortic region (aorta shown within *cursors*). The lymph node is rounded and hypoechoic, with absence of a fatty hilum, features that are indicative of metastatic involvement.

hyperechoic, and has indistinct or fuzzy margins, it is considered benign.

# MAGNETIC RESONANCE IMAGING

MRI is fast emerging as a mainstay in the evaluation of abdominal and pelvic lymph nodes, particularly as a part of staging for abdominopelvic malignancies. The inherent high soft tissue contrast resolution of MRI improves the detection of lymph nodes, particularly in malignancies of the rectum, urinary bladder, prostate, uterine cervix, and endometrium. The introduction of high field strength MR scanners (3.0 tesla) with increased signal-to-noise ratio (SNR) and improved spatial and temporal resolution have amplified the role of MRI in lymph node detection and characterization. The sequences particularly useful for MRI of lymph nodes include axial T1-weighted spin echo/gradient echo and axial T2-weighted fast spin echo and gadolinium-enhanced dynamic gradient echo sequences.<sup>25</sup> Use of breath-hold sequences has been recommended for T2-weighted sequences because it causes minimum respiratory misregistration owing to respiratory motion during data acquisition.<sup>25</sup> T1-weighted images are generally obtained for detection of enlarged retroperitoneal lymph nodes because the lymph nodes in the upper abdomen can be clearly distinguished against a background of retroperitoneal fat.<sup>26</sup>Use of T2-weighted images is preferred in the lower abdomen and pelvis because lymph nodes can be distinguished from adjacent muscles such as the iliopsoas as lymph nodes have a higher signal intensity.<sup>2</sup> MR oral contrast agents are advocated at times to distinguish between enlarged lymph nodes and adjacent bowel. Administration of gadolinium improves the conspicuity of lymph nodes, and the pattern of enhancement seen after gadolinium injection gives important clues to the type of lymph node pathology.

#### Diffusion Weighted Imaging

Diffusion weighted imaging has been advocated to improve the detection of nodal metastases in abdominal malignancies.<sup>27</sup> This technique uses pulse sequences and techniques that are sensitive to microscopic motion of water protons. Single-shot

echoplanar diffusion weighted imaging provides very rapid imaging sensitive to Brownian motion of water molecules, and areas with restricted water diffusion are displayed as areas of high signal intensity.<sup>27</sup> Diffusion weighted imaging helps in detection of lymph nodes missed on conventional MR images and depicts more sites of nodal metastases in lymphoma and other abdominal malignancies (e.g., ovarian, pancreatic, colorectal, and hepatocellular cancer).<sup>27</sup>

#### Magnetic Resonance Lymphangiography

MR lymphangiography helps in the differentiation of benign and malignant lymph nodes.<sup>28-30</sup> This technique has been found to be very accurate in detecting microscopic malignant deposits within normal-sized nodes (i.e., micrometastases, which refers to malignant foci within lymph nodes <2 mm).<sup>28</sup> MR lymphangiography is performed with ultrasmall superparamagnetic iron oxide particles (USPIOs; ferumoxtran-10), a reticuloendothelial system-specific contrast agent. Ferumoxtran-10 consists of a monocrystalline, superparamagnetic iron oxide core (2 to 3 nm or 4.3 to 6.0 nm) coated with a low molecular weight dextran.<sup>28-30</sup> The lymphotropic nanoparticles first enter the interstitial space after intravenous administration and then reach the lymph nodes through the lymphatics.<sup>31</sup> These nanoparticles are phagocytized by the intranodal macrophages. The nanoparticles accumulate in benign lymph nodes owing to abundance of macrophages, whereas malignant lymph nodes are unable to take up these particles because of neoplastic destruction of the macrophages.<sup>28,31</sup>

This technique involves a baseline MR examination that is performed before the injection of the contrast agent for identification and localization of lymph nodes.<sup>31,32</sup> After the intravenous injection of the contrast agent (2.6 mg of iron per kg of body weight reconstituted in 100 mL saline and given over a period of 20 to 25 minutes) a postcontrast scan is performed after 24 to 36 hours.<sup>31,32</sup> Thin-section MRI with high resolution is performed for accurate characterization and detection of small metastatic foci within the nodes. The changes in signal intensity are best demonstrated on T2\*-weighted gradient echo sequences.<sup>31,32</sup> Malignant lymph nodes appear bright on these sequences owing to destroyed macrophages, whereas normal and benign lymph nodes show a drop in signal intensity as a result of susceptibility effects of the iron oxide particles within the intact macrophages.<sup>28</sup> It is absolutely essential to time the postcontrast scan optimally because early scanning may result in inadequate lymph nodal localization of nanoparticles and falsepositive diagnosis of benign lymph nodes as malignant.<sup>28,</sup>

#### Normal Anatomy

Lymph nodes on MRI appear round to ovoid and have an intermediate signal intensity compared with the very low signal intensity of the flowing blood in the aorta and inferior vena cava and the high-intensity MR signal of the retroperitoneal fat.<sup>33</sup> Because of the high contrast between the lymphadenopathy and the surrounding fat, enlarged nodes are visualized on both T1- and T2-weighted images.<sup>33</sup> Although the T1-weighted images provide optimum contrast for lymph node identification, T2-weighted images are valuable as an adjunct. Increased signal of the lymph nodes on T2 weighting compared to T1 weighting helps confirm their identity.<sup>13</sup> The signal intensity of lymph nodes is lower than that of fat but higher than muscle on T1-weighted images (Figure 61-12, *A*).<sup>26,34,35</sup> On T2-weighted images, the signal intensity of lymph nodes is closer to that of



Figure 61-13 A 54-year-old woman with metastatic cervical carcinoma. T1-weighted (A), T2-weighted (B), and diffusion weighted (C) images show two enlarged metastatic left pelvic sidewall lymph nodes (arrows). The metastatic nodes are bright and are more conspicuous on the diffusion-weighted image.

fat and higher than that of muscle (see Figure 61-12, *B*).<sup>26</sup> The presence of many venous tributaries particularly in the hypogastric region makes it difficult to detect the nodes in the pelvis owing to close apposition of the lymph nodes to the pelvic neurovascular bundle.<sup>13</sup> Differentiation of lymph nodes from a vessel is made on the basis that vascular structures have low signal intensity on T1-weighted spin echo sequences and appear as tubular structures on adjacent images. After gadolinium administration, normal lymph nodes demonstrate homogeneous enhancement.<sup>34</sup>

On MR lymphangiography, normal lymph nodes show a homogeneous decrease in signal intensity after the administration of USPIOs, which is suggestive of normal contrast delivery and normal macrophage activity within the nodes.<sup>32</sup>

# Pathophysiology and Pathology

Like CT, the diagnosis of abnormal lymph nodes on MRI is based on widely accepted size criteria. Signal intensity changes within lymph nodes also have been suggested as signs of abnormality on MRI. Malignant infiltration of lymph nodes can lead to heterogeneity of signal on T2-weighted MR images.<sup>36</sup> The presence of necrosis secondary to either metastasis or infection leads to a low signal intensity on T1-weighted images and a high signal intensity on T2-weighted images.<sup>34</sup> After treatment of malignancy, T2-weighted images can help in the detection of residual tumor within lymph nodes.<sup>26</sup> Residual tumors usually show high signal on T2-weighted images, whereas successfully treated tumors show reduced signal intensity because of the presence of fibrosis.<sup>26</sup> However, caution is required because successfully treated lymph nodes may be hyperintense for up to 1 year and because increased signal on T2-weighted images sometimes can be seen with inflammatory involvement of lymph nodes.<sup>26</sup>

After gadolinium administration, the pattern of enhancement gives clues to the etiologic factor. Although homogeneous enhancement cannot substantially differentiate between normal and abnormal lymph nodes, the presence of heterogeneous or peripheral rim enhancement with central necrosis should raise suspicion. Gadolinium-enhanced MRI may be useful in differentiating between normal lymph nodes and normal-sized lymph nodes with metastatic involvement.<sup>26</sup> Lymph nodes with malignant infiltration show rapid enhancement compared with uninvolved lymph nodes, and the pattern of enhancement may be similar to the primary tumor.<sup>26</sup>

On diffusion weighted imaging, lymph nodes with malignant infiltration will appear hyperintense owing to restricted water diffusion (Figure 61-13).<sup>27</sup> Although this sign is quite specific for metastases, some overlap does occur when there is inflammatory involvement of the lymph nodes.<sup>27</sup>

On MR lymphangiography, malignant lymph nodes appear hyperintense and do not show a reduction in signal intensity on T2-weighted spin echo or gradient echo sequences.<sup>28</sup> The absence of signal loss could be either homogeneous or heterogeneous. In the latter situation, the malignant lymph nodes could either have a mottled appearance (suggesting the presence of partial infiltration of lymph node by malignant cells and areas of preserved architecture) or have an area of central hyperintensity with a peripheral rim of reduced signal.<sup>28</sup>

#### POSITRON EMISSION TOMOGRAPHY

PET is a rapidly emerging innovative imaging technique that provides a 3D image or map of the functional processes in the body. This nuclear medicine imaging technique has found great application in oncology, especially in staging and posttreatment follow-up of malignancies.<sup>37-39</sup> PET involves intravenous injection of a short-lived radioactive tracer isotope such as fluorine coupled with a metabolically active molecule such as glucose.<sup>38-40</sup> The radioactive tracer decays by the emission of positrons, which is quantified by the imaging scanner.

The molecule for oncologic imaging is FDG, which is a combination of 18-fluorine and deoxyglucose. FDG as a glucose analog competes with glucose for transport sites on the cell membrane and within the cell for various enzymatic activities. Once inside the cell, it gets trapped by getting phosphorylated by the enzyme hexokinase to FDG phosphate because it cannot be metabolized further by metabolic pathways. This trapped FDG becomes the source for positrons and lights up tumors when imaged by the PET scanner. Malignant tissues, because of their increased glycolytic activity, accumulate FDG at a higher rate than normal tissues, making FDG a very suitable analog for oncologic purposes.<sup>37</sup> The differential uptake between tumoral and nontumoral tissues also creates a good target-to-background ratio.<sup>37</sup> FDG-PET thus provides metabolic information on glucose uptake of tumors and is found to be useful in management of patients with malignancies.<sup>41</sup> PET has the potential to enhance the accuracy of lymph node detection by depicting metastatic deposits within lymph nodes and ruling out malignant infiltration in benign enlarged lymph nodes. It has been reported to be very sensitive and specific for the detection of lymph node metastases.<sup>31</sup>

Because metabolic changes precede structural changes associated with any disease process, PET has the advantage of depicting changes in tumor function before conventional imaging modalities such as CT and MRI can demonstrate change in tumor size. This ability of PET can be used to monitor tumor response to therapy (chemotherapy/irradiation) and in the detection of recurrence. A major limitation in imaging with PET is the low anatomic resolution of the images obtained that hampers accurate localization of the area of increased glucose metabolism.<sup>38,41</sup> However, this has largely been addressed by the implementation of PET/ CT fusion, which combines the anatomic data of CT with the functional information provided by PET.<sup>38,41</sup> The combination of PET/CT has several benefits because it combines the high spatial resolution of CT images with the functional information provided by PET.

#### Normal Anatomy

Areas that show normal physiologic uptake and thus interfere with interpretation include the kidney, urinary tract, liver, spleen, stomach, small intestine, and colon, which shows the highest uptake, particularly in the region of the cecum and rectosigmoid region.

#### Pathophysiology and Pathology

Malignant lymph nodes that have higher than normal levels of glucose uptake show as bright spots on PET images (Figure 61-14). The degree of brightness on PET images depends on the different levels of tissue or organ metabolic activity. A quantitative estimate of the metabolic activity of cells is made using a standardized uptake value (SUV).<sup>37</sup> Tracking the SUV values within a lesion over time offers a standardized approach for measuring the response of tumors to therapy. Increased FDG uptake indicates increased glucose uptake. Thus, FDG is not a cancer-specific agent and increased uptake can occur in several inflammatory lesions, including sarcoidosis, tuberculosis, fungal infection, and abscesses.

# **Clinical Role of Lymph Node Imaging**

A wide variety of disease processes, both benign and malignant, can result in abdominal and pelvic lymphadenopathy.<sup>5</sup> The technical advancements in cross-sectional imaging such as MDCT and MRI have brought about profound changes in the detection and characterization of lymph nodes.<sup>4</sup> The emergence of functional imaging techniques such as PET and the development of lymphotropic MR contrast agents have allowed detection of malignant lymph nodes with higher accuracy even in small lymph nodes. It is important for radiologists to

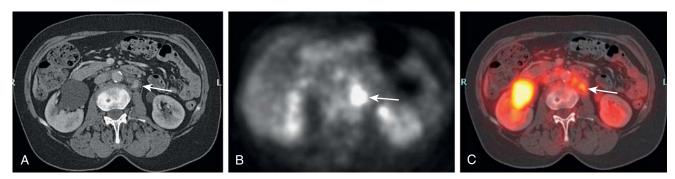


Figure 61-14 A 21-year-old man with para-aortic lymph node involvement in a T-cell–rich, B-cell lymphoma (non-Hodgkin's). A, Axial contrastenhanced computed tomography (CT) image shows a mildly enhancing left para-aortic lymph node (*arrow*) with perinodal fatty stranding. However, the CT features do not allow reliable differentiation between a reactive inactive node and active lymphomatous involvement. B, Axial fluorodeoxyglucose–positron emission positron emission tomography (FDG-PET) image shows an area of intense FDG uptake (*arrow*) in the retroperitoneum. Because of the absence of appropriate anatomic landmarks on this image, the area of high FDG uptake cannot be confidently attributed to lymphomatous spread. C, Axial PET/CT image demonstrates that the abnormal FDG uptake (*arrow*) corresponds to the left para-aortic lymph node in A, confirming the presence of nodal metastases.

#### **BENIGN DISEASES OF LYMPH NODES**

#### Infective and Noninfective Lymphadenitis

#### Infective Lymphadenitis

**Suppurative Lymphadenitis.** Suppurative lymphadenitis is a rare occurrence in the abdomen. It commonly results from *Yersinia enterocolitica* infection involving the mesenteric nodes in the right iliac fossa.<sup>42</sup> Suppurative iliac lymphadenitis can develop secondary to infection in the lower extremities, and the organism most commonly implicated is *Staphylococcus aureus*.<sup>43</sup> Metastatic *S. aureus* suppurative lymphadenitis also has been reported in the retroperitoneal nodes with spread from acute bacterial endocarditis.<sup>44</sup> Retroperitoneal abscesses usually complicate untreated suppurative lymphadenitis and can lead to various intra-abdominal complications.<sup>43,44</sup>

*Tuberculosis.* The abdomen is involved in 11% to 16% of patients with extrapulmonary tuberculosis, and lymphadenopathy is the most common manifestation.<sup>45,46</sup> Primary nodal involvement without extranodal diseases occurs in 55% of patients with abdominal tuberculosis. Tuberculous involvement of abdominal lymph nodes can occur either through infection of the gastrointestinal tract, which is the most common route, through hematogenous spread, or through direct spread from adjacent organs.<sup>45</sup>

Human Immunodeficiency Virus Infection. Lymphadenopathy is the most common abnormal CT finding in the abdomen in patients with acquired immunodeficiency syndrome (AIDS), occurring in both infective and neoplastic conditions.<sup>47</sup> Imaging, particularly CT, plays a valuable role in the evaluation of suspected opportunistic infection or neoplasia in patients with AIDS. Infection accounts for 64% of cases of abdominal adenopathy in the population positive for human immunodeficiency virus (HIV) infection and is more common than HIV-related neoplasia. 47,48 Mycobacterium tuberculosis (Mtb) infection is the most common infectious cause of adenopathy and accounts for 50% of cases.<sup>47,48</sup> Overall, infection with Mtb or Mycobacterium avium-intracellulare complex (MAC) accounts for up to 85% of infectious causes of adenopathy in AIDS.<sup>47,48</sup> Viral and protozoal infections do not cause significant lymphadenopathy in patients with AIDS.<sup>49</sup> Fungal infections such as histoplasmosis can manifest as retroperitoneal and mesenteric adenopathy, and these nodes either have soft tissue attenuation or are hypoattenuating.47,49 Kaposi's sarcoma and non-Hodgkin's lymphoma are the common malignant conditions causing adenopathy in patients with AIDS.<sup>47,4</sup>

*Whipple's Disease.* Whipple's disease is a chronic systemic illness characterized by infiltration of the small bowel mucosa and submucosa with foamy macrophages that contain glycoprotein granules that are positive for periodic acid–Schiff. It is caused by *Tropheryma whippelii*, and patients usually present with malabsorption.<sup>50</sup> Lymph node involvement is a common occurrence in Whipple's disease. Lymphadenopathy commonly responds to antibiotic therapy.<sup>50</sup>

#### Noninfective Lymphadenitis

*Inflammatory Bowel Disease.* Ulcerative colitis and Crohn's disease, collectively known as inflammatory bowel diseases, can

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involve regional lymph nodes in the abdomen, and these lymph nodes are frequently well depicted on cross-sectional imaging.

**Diffuse Liver Disease.** Chronic diffuse liver diseases, particularly cirrhosis, and viral hepatitis–related disorders lead to involvement of lymph nodes in the hepatoduodenal ligament (39%).<sup>51</sup> The highest frequency of lymph nodes is seen in primary biliary cirrhosis (85%), followed by hepatitis C (HCV)associated liver disease (42%), HCV/hepatitis B (HBV)-associated liver disease (41%), and alcoholic and idiopathic liver disease (9.5%).<sup>51</sup> HBV infection alone is less likely to cause lymph node involvement compared with HCV infection. In HCV-associated liver diseases, nodal frequency is related to the severity of liver involvement.<sup>51</sup> In HBV and HCV infections, the identification of enlarged nodes usually suggests a chronic active stage of disease.<sup>52</sup> Nonalcoholic steatohepatitis and hemochromatosis do not frequently have lymph node involvement.

*Castleman's Disease.* Castleman's disease, also known as angiofollicular lymph node hyperplasia or giant lymph node hyperplasia, is a rare benign process of unknown cause characterized pathologically by hyperplasia of both lymphatic tissue and small blood vessels.<sup>53</sup> It is very rare in the abdomen and pelvis, with its description in the literature limited to only a few case reports. Castleman's disease has been divided into two clinical types, localized and diffuse, according to the extent and spread of the disease.<sup>54,55</sup> Pathologically, Castleman's disease is categorized into three types: plasma cell type, vascular, and mixed type.

*Cavitating Mesenteric Lymph Node Syndrome.* Cavitating mesenteric lymph node syndrome is an uncommon and poorly understood complication of celiac disease and is characterized by cavitary changes confined to the mesenteric nodal chain, without evidence of malignancy or mycobacterial infection.<sup>50</sup> The involved lymph nodes have a low CT attenuation value owing to cavitation of the involved nodes.<sup>50</sup> These nodes regress on treatment of the celiac disease with a gluten-free diet. This finding helps in the management because celiac disease is associated with a high incidence of lymphoma, and the presence of cavitation within lymph nodes is reassuring.<sup>50</sup>

*Lymphangioleiomyomatosis.* Lymphangioleiomyomatosis is a rare disease of unknown cause affecting women in the reproductive age group and is characterized by progressive dyspnea, chylothorax, and chylous ascites.<sup>56</sup> It is characterized by proliferation of immature-appearing smooth muscle cells in the axial lymphatics of the thorax and abdomen.<sup>56</sup> The four major abdominopelvic abnormalities in patients with lymphangioleiomyomatosis include renal angiomyolipomas, retroperitoneal and pelvic lymphadenopathy, lymphangioma, and chylous ascites.<sup>56,57</sup> The severity of lung disease is correlated with the presence of abdominal adenopathy.<sup>57</sup>

*Sarcoidosis.* Sarcoidosis is a multiorgan chronic granulomatous disease characterized by the presence of noncaseating granulomas in the affected organs. This disease most commonly affects the lung, and occasional abdominal involvement is noted. Abdominal lymphadenopathy is a common feature, and it mimics other systemic diseases such as lymphoma, diffuse metastatic disease, and granulomatous or mycobacterial infection.<sup>58</sup>

#### **Pathophysiology and Pathology**

*Suppurative Lymphadenitis.* CT is the modality of choice for the detection and characterization of suppurative lymph nodes.

The affected lymph nodes typically show a low-density center with thin or irregular peripheral rim enhancement. Because of acute inflammatory changes, the involved lymph nodes show significant surrounding perinodal soft tissue fat stranding.

*Tuberculosis.* The mechanism of involvement of abdominal lymph nodes by tuberculosis determines the site of involvement. Extensive involvement of the lower para-aortic region usually favors a hematogenous dissemination, whereas nonhematogeneous spread seldom involves the lower para-aortic region.<sup>45,59,60</sup> The other sites of involvement such as the hepato-duodenal ligament, the portocaval space, the root of mesentery, the peripancreatic region, the periceliac region, the gastrohepatic ligament, the greater omentum, and the upper para-aortic region can occur with both hematogenous and nonhematogeneous routes.<sup>45,59,60</sup> Enlarged tuberculous lymph nodes, although reaching large sizes, are usually not responsible for invasion or obstruction of the common bile duct, blood vessels, and the urinary or gastrointestinal tract.<sup>59,60</sup>

The most characteristic features of tubercular lymph nodes on contrast-enhanced CT are circular or ovoid lesions showing peripheral rim enhancement with central hypodensity.<sup>45</sup> The peripheral enhancing portion corresponds to perinodal vascular inflammatory response or granulation tissue, whereas the central nonenhancing portion corresponds to caseation or liquefactive necrosis within the nodes (Figure 61-15, *A* and *B*).<sup>61</sup> Heterogeneous and homogeneous enhancement also have been described within the involved nodes.<sup>62,63</sup> Another specific finding is the multilocular appearance that results from the conglomeration of more than three adjacent enlarged lymph nodes.<sup>45</sup> The involved tubercular lymph nodes usually measure more than 1 cm but are rarely larger than 4 cm in diameter, keeping with the self-limiting growth pattern of tuberculosis.<sup>45</sup> Calcification of the involved lymph nodes can occasionally occur. However, calcification within lymph nodes is a nonspecific feature and can occur in a wide variety of other conditions.

On T1-weighted MR images, the lymph nodes are isointense to hypointense and show increased signal intensity on T2weighted images.<sup>61</sup> The T2 hyperintensity corresponds to liquefactive necrosis. However, the central areas can occasionally be hypointense on T2-weighted images owing to release of paramagnetic free radicals from the active phagocytic cells.<sup>61</sup> Obliteration of perinodal fat, which shows increased signal intensity on T2-weighted images, is also common.<sup>61</sup> The contrast enhancement is predominantly peripheral, which can be uniform, thin or thick, and complete or incomplete. The affected lymph nodes when conglomerated often manifest as central and peripheral areas of heterogeneous enhancement (see Figure 61-15, *C* and *E*).<sup>61</sup>

*Tuberculosis Versus Lymphoma.* Tuberculous lymphadenopathy can be easily confused with lymphoma affecting abdominal lymph nodes, and the differentiation is crucial owing to obvious difference in therapeutic management.<sup>45</sup> The different characteristics of anatomic distribution, size, attenuation, and enhancement patterns displayed on contrast-enhanced CT are helpful in distinguishing tuberculosis from lymphoma.<sup>45,60</sup> Whereas tubercular lymph nodes show a multilocular appearance with rim enhancement, lymphomatous nodes enhance homogeneously.<sup>45,60</sup> Tuberculous nodes mostly measure less than 4 cm, whereas in lymphoma the nodes often exceed 4 cm. Distinction also can be made based on involvement of the para-aortic region, but this is relevant only when the tubercular involvement is secondary to nonhematogeneous spread.<sup>45,60</sup> Nonhematogeneous disseminated tuberculosis predominantly

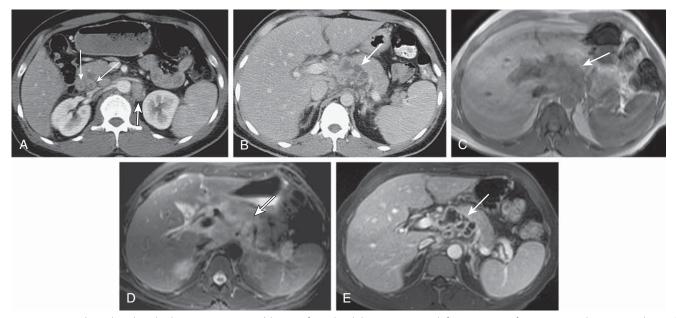


Figure 61-15 Tuberculous lymphadenitis in a 42-year-old man infected with human immunodeficiency virus infection. A, Axial contrast-enhanced computed tomography (CT) scan of the abdomen shows multiple lymph nodes in the peripancreatic and para-aortic region. These nodes have a variable enhancement pattern with some showing homogeneous enhancement (*thick arrow*) and some showing areas of necrosis (*thin arrows*). B, Axial contrast-enhanced CT scan shows conglomeration of a group of lymph nodes in the peripancreatic region (*arrow*) with peripheral enhancement and central low density. On T1-weighted magnetic resonance imaging (MRI) (C), the lymph node conglomeration is hypointense and shows high signal intensity on T2-weighted MRI (D) (*arrows*). E, On fat-suppressed contrast-enhanced T1-weighted imaging, the conglomerated lymph nodes show peripheral enhancement (*arrow*).

affects the upper para-aortic region, whereas lymphoma involves both the upper and lower para-aortic nodes.<sup>45,60</sup> Hema-togenously disseminated tuberculosis, however, involves both the upper and lower para-aortic region, making its distinction from lymphoma more difficult. Disseminated tuberculosis has other differentiating features, such as the presence of miliary nodules in the lungs, hepatomegaly, and splenomegaly with inhomogeneous densities.<sup>45</sup>

#### HUMAN IMMUNODEFICIENCY VIRUS INFECTION

Lymphadenopathy resulting from Mtb and MAC in HIV infection can be distinguished on CT depending on the presence of central low density or necrosis within the nodes. Central hypodensity within nodes is more common in Mtb (93%) than MAC (14%) infections, with most nodes in MAC showing homogeneous soft tissue attenuation because the immune system is not capable of granuloma formation.<sup>47-49,64,65</sup> Nodes in MAC infection are smaller than in MTB, and clusters of normalsized nodes are more frequently present.<sup>65</sup> In Mtb, the lymph nodes are larger and frequently seen in the mesentery, retroperitoneum, and splenic hilum.<sup>65</sup> An important distinction is the involvement of peritoneum and omentum, with resultant peritonitis and peritoneal implants in Mtb infection that do not occur in MAC infection. The retroperitoneal and mesenteric adenopathy in fungal infections such as histoplasmosis are often either of soft tissue attenuation or low attenuation.<sup>47,49</sup> Other features include large hypoattenuating hepatosplenic lesions and severe immunocompromised status.45

In nodal involvement secondary to Kaposi's sarcoma, the characteristic finding on contrast-enhanced CT is the presence of hyperattenuating lymph nodes. The lymph nodes are primarily seen in the retroperitoneum, mesentery, and groin.45 These nodes are greater in attenuation than muscle and enhance similar to adjacent vessels.<sup>66</sup> Isoattenuating and hypoattenuating lymph nodes also can be seen; however, central hypodensity is rare. Kaposi's sarcoma accounts for 85% of cases of hyperattenuating lymph nodes in patients with AIDS. Less frequent causes of hyperattenuating nodes on CT in HIV include mycobacterial infection (9%), AIDS lymphoma (3%), angioimmunoblastic lymphoma (3%), and bacillary angiomatosis. Patients with AIDS-related lymphoma present with extensive retroperitoneal, mesenteric, and pelvic adenopathy that accounts for 56% of cases.8 The lymph nodes are large and bulky, with the majority of them showing soft tissue attenuation. Massive adenopathy, with nodes larger than 3 cm, is due to AIDS-related lymphoma in up to 90% of cases.49

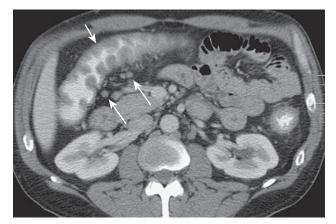
**Whipple's Disease.** The most common imaging finding in Whipple's disease is thickening of small bowel folds with no dilatation. But the characteristic feature on CT is the presence of low-density nodes in the mesentery and retroperitoneum with hepatosplenomegaly and ascites. The lymph nodes have a high fat content, giving a low CT attenuation value of 10 to 20 Hounsfield units (Figure 61-16).<sup>50</sup>

#### Inflammatory Lymphadenitis

**Inflammatory Bowel Disease.** Mesenteric lymphadenopathy is commonly seen in patients with inflammatory bowel diseases, particularly in Crohn's disease.<sup>50,67</sup> The nodes are found at the mesenteric root, mesenteric periphery, the right lower quadrant, or in the pericolic region (Figure 61-17). The nodes range



**Figure 61-16** Axial contrast-enhanced computed tomography scan of the abdomen in a 36-year-old man with Whipple's disease. Multiple discrete nonenhancing low-density nodes (*arrows*) are seen in the mesentery.



**Figure 61-17** Axial contrast-enhanced computed tomography scan of the abdomen in a 26-year-old man with ulcerative colitis. Multiple small pericolic lymph nodes *(long arrows)* are seen along the mesocolic border of the transverse colon, which shows diffuse bowel wall thickening *(short arrow)*.

in size from 3 to 8 mm, are of soft tissue attenuation, and demonstrate homogeneous enhancement. Associated changes in the small or large bowel are usually, but not always, present.<sup>50</sup> If the lymph nodes are larger than 10 mm, lymphoma and carcinoma must be excluded.<sup>67</sup>

**Diffuse Hepatic Diseases.** Normal nodes in the hepatoduodenal ligament are routinely seen clustered around the common hepatic artery and have been referred to as "daisy chain" nodes.<sup>68</sup> The normal nodes are usually isoechoic or slightly hyperechoic with respect to liver on ultrasonography.<sup>68</sup> Small hepatoduodenal ligament nodes (<5 mm) are not uncommon in patients without hepatobiliary disease. However, larger and more prominent nodes (>5 mm) in the hepatoduodenal ligament (porta hepatis) should prompt a careful evaluation of the liver for the possibility of chronic liver diseases (Figure 61-18).<sup>52</sup>

#### **Castleman's Disease**

Localized Type. The most characteristic feature of localized Castleman's disease on CT is a well-defined, homogeneous,

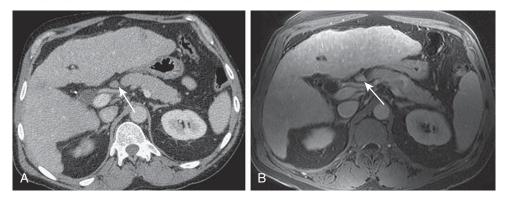


Figure 61-18 Cirrhosis with enlarged porta hepatis lymph node in a 56-year-old man. A, Axial contrast-enhanced computed tomography scan of the abdomen shows a lymph node (arrow) at the porta hepatis in a patient with cirrhosis. B, Axial contrast-enhanced T1-weighted image shows the cirrhotic changes within the liver and the homogeneously enhancing lymph node at the porta hepatis (arrow).

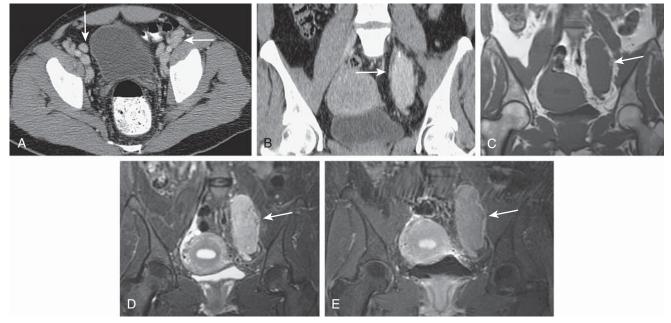


Figure 61-19 Castleman's disease in two different patients. A, Axial contrast-enhanced computed tomography (CT) examination of the pelvis in a 43-year-old asymptomatic woman shows well-defined, intensely enhancing lymph node masses along the external iliac chain (arrows). B, Coronal contrast-enhanced CT image in another patient demonstrates a well-circumscribed large mass in the left iliac region (arrow) with a small focus of calcification along the superior margin. Coronal T1-weighted (C) and T2-weighted (D) magnetic resonance (MR) images show the mass (arrows) having a hypointense signal on T1-weighted imaging and a hyperintense signal on T2-weighted imaging. E, Coronal fat-suppressed contrast-enhanced T1-weighted MR image (arrow) shows the lesion demonstrating intense homogeneous enhancement.

single intra-abdominal mass of soft tissue attenuation with typical early strong homogeneous enhancement and delayed washout on dynamic scanning (Figure 61-19).<sup>53,69</sup> These masses are circular, oval, or fusiform and range from 3.5 to 8 cm. On MRI, the lesions are either hypointense or isointense on T1-weighted images and hyperintense on T2-weighted images.<sup>53</sup> Intense enhancement occurs after gadolinium administration. Large masses can show central areas of low density with distinct nonenhancing radial or fissured bands. These areas usually show low signal intensity on T1- and T2-weighted images. The low-density areas are seen mainly in the early phase of contrast enhancement and correspond to the parallel fibrous tissues seen on histopathologic examination.<sup>53</sup> Another distinguishing feature seen in Castleman's disease is the lack of cystic necrotic

degeneration within the tumor. Calcifications have been reported in this disease and can be either coarse or punctate. Several daughter foci or satellite nodules can be seen around the primary lesion in the abdomen.<sup>53,69</sup> The differential diagnosis for localized Castleman's disease includes ectopic pheochromocytoma, accessory spleen, tuberculosis of the mesentery, and hypervascular metastatic lymph nodes.

**Diffuse Type.** The diffuse type of Castleman's disease manifests as multiple lymph node enlargement with mild to moderate and occasionally intense enhancement. Nonspecific signs such as organomegaly can be seen in certain cases.<sup>53,69</sup> The diffuse and plasma cell variants have atypical imaging manifestations, and preoperative diagnosis is difficult. The common differential diagnosis is lymphoma, which also shows as

multiple enlarged nodes with clear margins, uniform density, and mild to moderate enhancement.

**Cavitating Mesenteric Lymph Node Syndrome.** In cavitating mesenteric lymph node syndrome, multiple cystic mesenteric masses are identified on CT that have central low attenuation, indicating fluid and occasionally fatty material.<sup>70</sup> Masses range from 2 to 7 cm in diameter.<sup>70</sup> Splenic atrophy is a common and characteristic feature. On ultrasonography, the mesenteric masses appear cystic. Imaging is remarkable for the absence of mediastinal, retroperitoneal, or inguinal lymphadenopathy.<sup>70</sup> On MRI, a fat-fluid layer is seen within the lesions on both T1- and T2-weighted images, with signal loss at the fat-fluid interface occurring owing to the chemical shift artifact on out-of-phase steady-state spoiled gradient recalled echo acquisitions.<sup>71</sup>

**Lymphangioleiomyomatosis.** The affected retroperitoneal and pelvic lymph nodes in lymphangioleiomyomatosis typically show fat attenuation.<sup>56</sup> The low Hounsfield unit values within the nodes are presumed to be due to chylous lymph collections or fat within the nodes.<sup>57</sup> The adenopathy may be extensive, with nodes measuring up to 4 cm.<sup>57</sup>

Mesenteric Lymphadenopathy. The frequent use of MDCT scanners with thin collimation that allows improved spatial resolution has led to more frequent visualization of mesenteric lymph nodes in healthy adults.<sup>50,72</sup> Normal mesenteric lymph nodes measuring up to 4 to 5 mm in short-axis diameter frequently can be seen in up to 39% of healthy adults.<sup>50,72</sup> When detected, these nodes are usually multiple, with nearly half of these patients having five or more nodes.<sup>72</sup> The nodes are routinely identified at the mesenteric root or throughout the mesentery.<sup>50,72</sup> The current definition of mesenteric adenitis is the presence of a cluster of three or more lymph nodes with shortaxis diameter of 5 mm or greater (Figure 61-20).73 This definition has been described for adult patients but has limited value in children because mesenteric lymph nodes with a short-axis diameter of 5 to 10 mm are frequently found in the CT examination of children with low likelihood of mesenteric lymphadenopathy.7

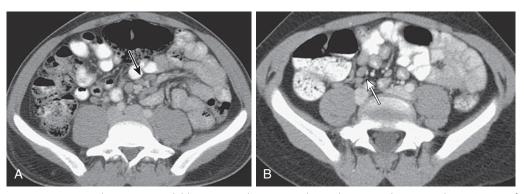
Mesenteric adenitis is divided into two distinct groups: primary and secondary. It is important to differentiate between the two entities because the diagnosis influences the treatment options.<sup>73</sup> Primary mesenteric adenitis is defined as right-sided mesenteric lymphadenopathy without an identifiable acute inflammatory process or with only mild (<5 mm) wall thickening of the terminal ileum.<sup>73</sup> Secondary mesenteric adenitis is defined as lymphadenopathy associated with a detectable intra-abdominal inflammatory process.73 The secondary causes include appendicitis, Crohn's disease, infectious colitis, ulcerative colitis, systemic lupus erythematosus, and diverticulitis.73 The incidence of primary mesenteric adenitis varies among children and adults. Mesenteric adenopathy does not occur in general, asymptomatic, immunocompetent adult populations. When it does occur, a specific focal inflammatory process can usually be determined.<sup>73</sup> In children, primary mesenteric adenitis is the second most common cause of right lower quadrant pain after appendicitis.

**Sarcoidosis.** Lymphadenopathy is seen in around 30% of patients with abdominal involvement in sarcoidosis. The most common sites of involvement are the porta hepatic, paraaortic, and celiac axis regions, whereas retrocrural regions are least commonly involved.<sup>75</sup> Diagnostic confusion with lymphoma frequently can arise, because both diseases can manifest as widespread adenopathy and splenomegaly.<sup>75</sup> The presence of larger nodes, tendency for confluence, and greater involvement of retrocrural nodes in lymphoma helps in the differentiation.<sup>76</sup>

#### LYMPHOMA

Once the diagnosis of lymphoma has been established by biopsy, determination of disease extent is important for appropriate treatment planning and determining prognosis. Because of continued improvement in chemotherapy and radiation therapy, there have been improved overall survival rates in patients with Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL). Therefore, knowing the sites of involvement at the time of diagnosis makes it possible to accurately restage at the end of therapy to document treatment response. This necessitates the need for accurate diagnosis, staging, and restaging of lymphoma.<sup>77</sup>

Imaging serves as an important tool in the monitoring of treatment response in patients with malignant lymphoma and



**Figure 61-20** Primary mesenteric adenitis in two children. A, Axial contrast-enhanced computed tomography (CT) scan of the abdomen in a 12-year-old child presenting with abdominal pain. Multiple discrete small homogeneous lymph nodes are seen within the mesentery (*arrow*). B, Axial contrast-enhanced CT scan of the abdomen in a 6-year-old child showing few lymph nodes (*arrow*) within the mesentery in the right iliac region. No concurrent pathologic process was seen in the adjacent bowel loops.

helps identify patients eligible for more aggressive protocols, such as high-dose chemotherapy. Lymphangiography, which was once the modality of choice for evaluation of the extent of lymphoma, now finds little clinical relevance. CT is the most commonly used means for staging patients with malignant lymphoma because of its widespread availability and relatively low cost. In addition to staging nodal disease, it helps in evaluation of extranodal disease and also highlights clinically important findings such as vascular occlusion or hydronephrosis. Conventional MRI, however, has better soft tissue resolution; its utility in evaluation of lymphoma has been limited because even this modality detects disease activity based on morphologic criteria. Functional and metabolic activity within the involved lymph nodes can be reliably detected by gallium scintigraphy and FDG-labeled PET.77,78 FDG-PET has proved to be reliable and useful in patients with malignant lymphoma for evaluation of definitive response to therapy and during follow-up. Careful evaluation of PET findings with consideration of clinical and investigational data together limits the false-positive rate to less than 5%.

#### Normal Anatomy

Retroperitoneal nodal disease is present in 25% to 35% of patients with HD and in 55% of patients with NHL.<sup>79-81</sup> The nodal groups commonly involved in NHL include the mesentery, portohepatic, and splenic hilum nodes, whereas HD involves the celiac axis, splenic hilar, and portocaval nodes.<sup>75</sup> Splenic hilar lymph node enlargement indicates splenic involvement in NHL and HD. Mesenteric involvement is more common in NHL (45%) compared with HD (8%).79-81 Of patients with nodal lymphoma in the abdomen, 54% have gastrointestinal tract involvement.<sup>79-81</sup> The nodal involvement in the pelvis for both HD and NHL is the same. There is a distinctive difference in the nodal spread between HD and NHL. Although it is contiguous in HD, the spread is noncontiguous and hematogeneous in NHL. Because HD spreads from one nodal group to the next via lymphatics, the presence of retrocrural disease should prompt close evaluation of the celiac axis.79-81 Also, because the involvement in HD is contiguous, in the absence of evidence of disease in the abdomen, a scan of the pelvis would not be required.80

# Pathophysiology and Pathology

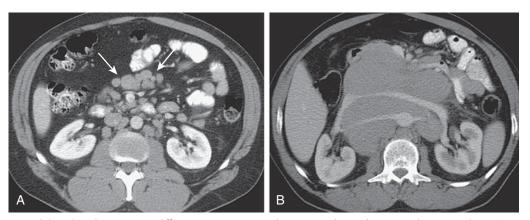
In HD, therapy is influenced by the extent of disease, whereas in NHL it is influenced by the pathologic subtype of tumor, bulk of disease, and symptomatology. In both HD and NHL, important prognostic indicators are provided by the disease bulk and presence of extranodal disease. Initial staging provides a baseline assessment against which future imaging studies can be compared. Retroperitoneal disease is more accurately depicted on CT compared with lymphangiography, which underestimates the volume and extent of retroperitoneal disease, whereas CT demonstrates extranodal and visceral involvement.<sup>79,81</sup> However, lymphangiography can detect small tumor deposits in lymph nodes that are not enlarged at CT.<sup>79,81</sup>

#### Imaging

Computed Tomography. CT has a sensitivity and specificity of 87.5% and 85.6%, respectively, for initial staging and sensitivity and specificity of 85.7% and 75.6%, respectively, in restaging of lymphoma. The key feature of lymphoma is lymph node enlargement, which is more marked in NHL than HD. The nodes in NHL are markedly enlarged with formation of conglomerate masses, whereas in HD the involvement of nodes is minimal.<sup>82</sup> Lymph nodes may be normal in size in certain pathologic subtypes of HD such as the nodular sclerosing and lymphocytedepleted subtypes.<sup>79</sup> Clustering of multiple normal-sized but prominent lymph nodes in the mesentery is also suggestive.<sup>79</sup> The most common imaging feature on CT is the moderate homogeneous contrast enhancement of the nodes.<sup>83</sup> High-grade tumors in NHL tend to be more heterogeneous on unenhanced and contrast-enhanced scans than low-grade tumors of comparable size.<sup>84</sup> Nodal involvement in abdominal lymphoma can be either as a solitary mass, multinodular, or diffuse.8

*Solitary Mass.* A solitary enlarged lymph node or a conglomeration of multiple enlarged lymph nodes can manifest in the form of a solitary mass. It is seen as a large round mass or a lobular homogeneous density with uniform enhancement and clear margins.

*Multiple Nodular Type.* Multiple nodes are seen in different regions, each of them showing uniform density and mild homogeneous enhancement with clear margins (Figure 61-21, *A*). A



**Figure 61-21** Non-Hodgkin's lymphoma in two different patients. **A**, Axial contrast-enhanced computed tomography (CT) scan in a 32-year-old man shows multiple discrete homogeneously enhancing lymph nodes (*arrows*) in the mesentery. **B**, Axial contrast-enhanced CT scan in a 45-year-old man with mesenteric disease shows a large homogeneously enhancing mass enveloping the mesenteric fat and enhanced vessels and depicting the classic "sandwich" sign.

combination of homogeneous enhancement and rim enhancement is occasionally observed. These lymph node masses encase vessels such as mesenteric vessels, renal vessels, abdominal aorta, and inferior vena cava. In the multiple nodular variety, this encasement can produce a unique imaging appearance displaying the "vascular embedded" signs. The masses also can encase and compress the duodenum, giving the "duodenal embedded" sign.

**Diffuse Type.** The diffuse type is usually seen in the mesenteric and retroperitoneal region with uniform-density masses encasing the vessels (see Figure 61-21, *B*). HD most commonly has the multinodular distribution (60%) compared with other types. NHL shows conglomeration and large masses more commonly (60%).

**"Sandwich" Sign.** The "sandwich" sign is a specific sign caused by bulky mesenteric lymphadenopathy enveloping fat and tubular vascular structures at cross-sectional imaging.<sup>87</sup> NHL almost always causes this lymphadenopathy in patients who have not undergone transplantation (see Figure 61-21, *B*). In patients who have undergone transplantation, posttransplantation lymphoproliferative disease can cause this problem. It has also been reported in cases of metastatic carcinoma, *M. avium* complex, and Mtb.<sup>88</sup>

**Magnetic Resonance Imaging.** The role of MRI in initial staging of lymphoma is limited. Active untreated lymphomatous nodes show increased signal intensity on T2-weighted images. After successful treatment, the signal intensity of the residual mass falls as a result of reduction in water content. The sensitivity of MR in the detection of relapse in the residual mass is 45% to 90%, and specificity ranges from 80% to 90%.<sup>4</sup> Low sensitivity is due to necrosis and immature fibrotic tissue, edema, and inflammation, which can simulate the high T2

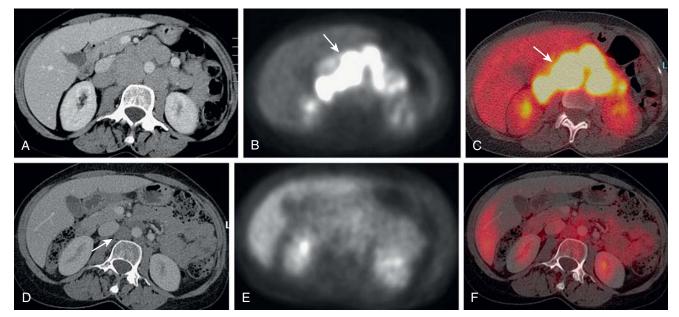
signal intensity of a viable tumor.<sup>4</sup> After gadolinium injection, residual masses with no active tumor show a lesser degree of enhancement than active tumor.

**Ultrasound.** Ultrasonography does not confer any real advantage in the assessment of nodal disease. Lymphomatous nodal masses tend to be uniformly hypoechoic and often lobulated. Although the porta hepatic and splenic hilar lymph nodes are well seen on ultrasound images, the modality is less sensitive in the detection of lower para-aortic and pelvic nodes, precluding its use in staging.<sup>61</sup>

Positron Emission Tomography. FDG-PET has been established to have a role in staging, in the evaluation of early response to chemotherapy, in the assessment of end response to therapy, in radiation therapy planning, and during follow-up.63,78 FDG-PET detects more disease sites and involved organs than conventional staging procedures such as CT. FDG-PET has the ability to diagnose active disease, and thus after completion of therapy, FDG-PET can differentiate patients with residual lymphoma (nonresponders or partial responders) from those without viable tumors (complete responders) (Figure 61-22).77,78 It also helps in the early identification of disease recurrence, thus allowing early institution of treatment. Active lymphoma shows as increased uptake of FDG owing to its metabolic activity and appears as hot spots on PET. FDG-PET has a very high positive predictive value in the detection of recurrent or residual malignant lymphoma (95%). False-positive findings sometimes can be seen in inflammatory conditions.

#### Posttreatment Appearance

After successful treatment, there is reduction in the size and extent of lesions. Although after treatment the lymph nodes



**Figure 61-22** Imaging in a 42-year-old man with non-Hodgkin's lymphoma on chemotherapy. Pretreatment imaging: A, Axial contrast-enhanced computed tomography (CT) scan demonstrates extensive retroperitoneal lymphadenopathy (*arrows*, **B** and **C**), which shows as increased uptake on the corresponding positron emission tomography (PET) (**B**) and PET/CT fusion (**C**) images. Posttreatment imaging: **D**, Axial contrast-enhanced CT scan shows residual enlarged lymph nodes in the retroperitoneum (*arrow*). However, there is no uptake seen on the corresponding PET (**E**) and PET/CT fusion (**F**) images. The absence of uptake on the PET image indicates absence of activity within the residual mass and highlights the superiority of PET over CT in follow-up of patients with lymphoma.

remain homogeneous, heterogeneous or rim enhancement or intranodal necrosis or calcification can be seen. Lymphomatous nodes treated by irradiation or chemotherapy may calcify in 2% to 8% of cases typically at least 8 months after treatment.<sup>89,90</sup> Calcifications can be in the form of small punctate foci within nodes, tiny calcifications around necrotic areas, or amorphous or linear calcifications in the periphery of the enlarged nodes or masses. Calcification, although rare before treatment, can occur with large masses of NHL and HD.<sup>89</sup>

PET and PET/CT are superior to CT in the evaluation of disease-free interval, overall survival, and monitoring of response to treatment.

#### METASTATIC LYMPHADENOPATHY

The presence of lymph node metastases in patients with abdominal and pelvic malignancies has considerable impact on management decisions, including the choice of surgery, chemotherapy, and radiation therapy, and suggests a more advanced stage of disease.<sup>2,7</sup> The presence of nodal metastases is an adverse prognostic factor in patients with cancers of the stomach, kidney, colon, rectum, prostate, urinary bladder, uterus, uterine cervix, and ovary.<sup>7,91</sup> The presence of nodal disease independently indicates poor patient outcome, and the recurrence rate of cancers is high in the presence of nodal spread.<sup>7</sup> There is wide variation in the sensitivity and accuracy in the detection rate of nodal metastases in various malignancies, particularly owing to the different size criteria used by various groups for diagnosing nodal metastases.<sup>92-107</sup>

#### Definitions

Lymph node metastases have been separated according to size by the recent sixth tumor, node, metastasis (TNM) classification as metastasis (>2 mm), micrometastasis (0.2 to 2 mm), and isolated tumor cells (<0.2 mm).<sup>107</sup> The sentinel node is the first lymph node to receive lymphatic flow from the primary tumor and is therefore the initial site of lymph node metastasis.<sup>108</sup>

#### Criteria for Assessing Metastatic Nodes on Computed Tomography and Magnetic Resonance Imaging

A variety of criteria have been proposed to assess the presence of metastatic disease in abdominopelvic lymph nodes and to differentiate them from reactive nodes on CT and MRI, but these are quite nonspecific.\* The most widely accepted and frequently used criterion for determination of nodal involvement is size. However, a major limitation of this criterion is the inability to detect metastatic involvement in normal-sized nodes.<sup>†</sup> In addition, size cannot reliably differentiate between enlarged nodes resulting from reactive hyperplasia and other diseases from malignant nodes.<sup>‡</sup> A brief overview of the various CT and MRI criteria for the evaluation of nodal metastatic disease is discussed here. The various parameters have to be used in conjunction with each other to enhance the ability of detecting and characterizing malignant nodes.

**Primary Criteria.** Size criterion is most widely used and easy to reproduce.<sup>2</sup> Nodal size is measured on cross-sectional imaging by using the maximum short-axis diameter (MSAD). The

short-axis diameter is considered more reliable than the longaxis diameter because the dimensions are less dependent on the alignment of the lymph node along the scan plane.<sup>2</sup> There is no agreement on the definition of the threshold of nodal enlargement.<sup>13</sup> However, because normal nodal size varies according to anatomic location in the body, an upper limit has been proposed according to the region of involvement. A consensus, however, is to use 10 mm in the MSAD as the threshold for abnormality.<sup>2,7</sup> Some authors propose 10 mm as the upper limit for abdominal nodes and 8 mm as the threshold for pelvic nodes.<sup>7</sup> Size criteria based on the shape of the lymph nodes is also proposed, with an upper limit of 8 mm for round nodes and 10 mm for oval nodes in MSAD.<sup>110</sup> To improve sensitivity of MRI in detection of malignant infiltration of normal-sized lymph nodes, Grubnic and colleagues<sup>13</sup> suggested that lymph nodes with MSAD greater than 6 mm in the pelvis and greater than 5 mm in the retroperitoneum should be considered pathologic. Depending on the threshold used to define nodal enlargement, the sensitivity and specificity of detecting malignant nodes vary. Generally, a reduction in the size criterion leads to increased sensitivity and reduced false-negative rate of nodal detection, but this occurs at the expense of diminished specificity.7

#### **Secondary Criteria**

*Lymph Node Location.* Nodes that are positioned along the pathway of spread of a primary tumor are more likely to be involved by metastatic dissemination.<sup>7</sup> Thus, the location of nodal involvement gives likely clues to the probable site of primary malignancy (Figure 61-23). It is also a sound practice to closely look for the likely sites of lymph node metastases while evaluating abdominal and pelvic malignancies. However, skip and distant metastases can occur in certain situations in which the rule of contiguous spread may not apply. Routine occurrence of normal-sized and enlarged reactive nodes is common in certain locations within the abdomen and pelvis. These sites include the hepatoduodenal ligament, mesentery, and inguinal region. On the contrary, lymph node detection at certain sites such as the perirectal region assumes significance even in the absence of obvious enlargement.

*Lymph Node Number.* A cluster of otherwise normalappearing nodes has been suggested to indicate malignancy.<sup>7</sup> However, this criterion is nonspecific and can give false-positive results.<sup>7</sup>

#### Lymph Node Morphology

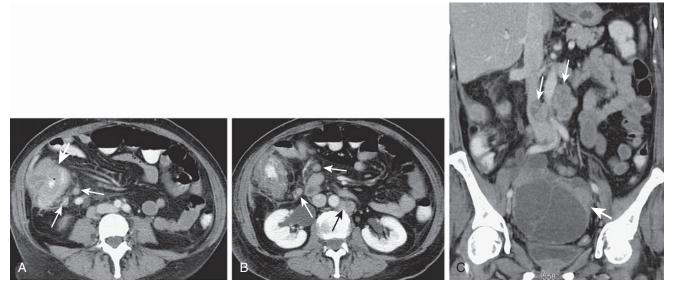
*Shape.* Volumetric data acquisition by MDCT has allowed multiplanar reconstructions of imaging data, thus enabling assessment of the shape and contour of lymph nodes.<sup>7</sup> Lymph nodes that are round or spherical are more likely to be malignant compared to ovoid or elongated nodes (Figure 61-24).<sup>7,111</sup> The roundness of the lymph node is calculated by measuring the short-axis to long-axis ratio. A higher ratio (>0.7) is considered suggestive of malignant involvement, with a ratio greater than 1 considered highly suggestive.<sup>112</sup> However, there are conflicting reports regarding the utility of this criterion in predicting malignant involvement.<sup>113,114</sup>

*Margin.* Lobulated and spiculated margins are reliable indicators of malignant infiltration, and they are caused by desmoplastic reaction or tumor infiltration into the perinodal fat.<sup>96</sup> Malignant lymph nodes also have irregular borders and show perinodal fatty infiltration, which is related to extracapsular spread of disease, and this sign is reported to be more accurate than nodal size criteria (Figure 61-25).<sup>7,115</sup> Extension of tumor

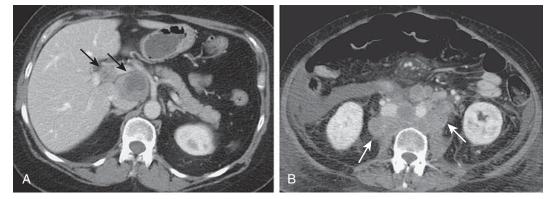
<sup>\*</sup>References 2, 4, 73, 81, 83, 85, 86, 91, 109.

<sup>&</sup>lt;sup>†</sup>References 2, 4, 81, 83, 85, 86, 91.

<sup>&</sup>lt;sup>‡</sup>References 2, 4, 81, 83, 85, 86, 91.



**Figure 61-23** Metastatic lymphadenopathy in a 56-year-old woman with colon and ovarian carcinoma. **A**, Contrast-enhanced axial computed tomography (CT) scan of the abdomen shows irregular nodular thickening of the wall of the ascending colon (*thick arrow*) with infiltration into pericolonic fat and metastatic pericolic lymph nodes (*thin arrows*). **B**, Axial contrast-enhanced CT image at a higher level shows a heterogeneously enhancing left para-aortic lymph node (*black arrow*) and enlarged right lower quadrant mesenteric nodes (*white arrows*). **C**, Coronal contrast-enhanced CT image in the same patient shows a cystic ovarian mucinous adenocarcinoma (*thick arrow*) in the pelvis with solid components. Also seen in the same image are the enlarged left para-aortic and aortocaval lymph nodes (*thin arrows*). The above series of images emphasizes the pattern of tumor spread in lymph nodes. The preaortic group of nodes (superior mesenteric/inferior mesenteric) is predominantly involved in gastrointestinal malignancies, whereas the involvement of para-aortic nodes usually occurs in genitourinary malignancies.



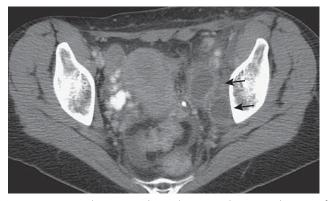
**Figure 61-24** Metastatic lymphadenopathy in a 67-year-old-man with cecal cancer. **A**, Contrast-enhanced axial computed tomography (CT) scan of the abdomen shows rounded, necrotic metastatic nodes in the celiac axis and the porta hepatis (*arrows*). **B**, CT image at a lower level in the same patient shows multiple necrotic nodes in the retroperitoneum with a conglomeration of a few of the nodes (*arrows*) and arterial encasement. Although some of these nodes are less than 1 cm, they show central necrosis, rounded shape, and perinodal fatty infiltration, which are features indicative of malignancy.

beyond nodal margins also contributes to various other manifestations of malignant adenopathy such as vascular encasement, ureteral encasement, and infiltration into biliary ducts (see Figure 61-24).

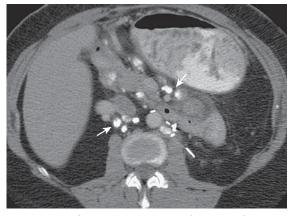
*Attenuation.* Certain neoplasms such as ovarian, colorectal, breast, and bladder cancers are known to cause calcifications within metastatic nodes (Figure 61-26). Calcifications are also common after successful treatment of lymphoma and seminoma.<sup>7</sup> However, the presence of calcifications within lymph nodes is a very nonspecific sign for the diagnosis of metastatic nodes because they can be encountered in infective conditions, particularly in tubercular lymphadenitis.

Heterogeneous density within nodes on CT is frequently seen in large nodes owing to necrosis. In the absence of nodal enlargement, the presence of heterogeneity within nodes can be indicative of malignant infiltration. On MRI, although it is not possible to differentiate between malignant and benign lymph nodes based on the T1 and T2 relaxation times, the presence of heterogeneity of signal within the nodes on T2-weighted MR images has been found to be fairly specific for metastatic involvement (Figure 61-27).<sup>7,116</sup>

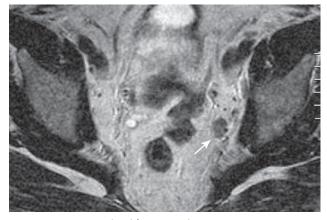
*Enhancement Patterns.* Normal lymph nodes frequently show homogeneous enhancement. Inhomogeneous (heterogeneous) enhancement within lymph nodes is more likely to indicate malignant infiltration.<sup>7,117,118</sup> Heterogeneous enhancement of lymph nodes on contrast-enhanced MRI is suggested to be an important indicator of nodal metastases.<sup>96</sup> The heterogeneous enhancement pattern has been suggested to



**Figure 61-25** Axial contrast-enhanced computed tomography scan of the pelvis in a 56-year-old woman with cervical carcinoma. Left pelvic side-wall metastatic nodes are seen with central necrosis and extensive perinodal infiltration (*arrows*), which represent extracapsular spread of tumor.



**Figure 61-26** Axial noncontrast computed tomography image in a 45-year-old woman with mucinous cystadenocarcinoma of the ovary. Multiple calcified lymph nodes (*arrows*) are seen in the retroperitoneum and the mesentery.



**Figure 61-27** T2-weighted fast spin echo magnetic resonance image in a 56-year-old man with prostatic carcinoma. The left internal iliac node demonstrates heterogeneous signal intensity (*arrow*), indicative of malignant infiltration.

be due to tumor infiltration of lymph nodes, presence of necrosis, or a mucin pool.<sup>96</sup> Metastatic nodes can show contrast enhancement patterns similar to that of the primary tumor, which reflects on the grade and aggressiveness of that primary.<sup>7</sup>

The presence of central necrosis within nodes is a very characteristic feature of metastases (see Figures 61-24 and 61-25). The necrotic nodes have a low-density center on CT and exhibit a very high signal intensity on T2-weighted MR images.<sup>115</sup> Central necrosis has been found to have a positive predictive value of 100% for nodal metastases in cervical cancer and is more common in nodes with an MSAD greater than 2 cm.<sup>118</sup> Although highly suggestive, this feature is also seen in benign conditions such as tuberculosis, fungal infections, and cavitating mesenteric lymph node syndrome.

**Patterns of Lymph Node Involvement.** Lymphatic vessels within the ligaments and mesenteries of the abdomen and pelvis allow communication between various regional lymph nodes and act as conduits for spread of malignancies.<sup>91,119</sup> This explains the extensive intra-abdominal nodal dissemination of malignancy once the regional nodes of organs are involved.<sup>91</sup> A comprehensive evaluation of nodal status during staging of malignancies requires a sound understanding of the various pathways involved in tumor spread to lymph nodes.<sup>7</sup> Assessment of lymph node enlargement at specific sites and their sequence of involvement aids in the determination of lymphatic spread, which is vital for staging, treatment, and prognosis of tumors.<sup>91</sup>

**Upper Abdominal Malignancies.** Nodal dissemination of primary malignancies of the organs of the upper abdomen (gastric, duodenum, liver, gallbladder, bile ducts, and pancreas) frequently involves the hepatoduodenal, peripancreatic, and aortocaval nodes, which act as intermediate nodes in the spread of disease from these organs to the cisterna chyli (Figures 61-28 and 61-29).<sup>91</sup> This represents the flow of lymphatics from the regional nodes of these organs to the cisterna chyli via lymph vessels in the lesser omentum. The enlargement of these groups of lymph nodes, either singly or in combination, should always raise suspicion for tumor extension from an occult malignancy of these organs.<sup>91</sup> Nonetheless, selective involvement of the peripancreatic and aortocaval lymph nodes can occur with pancreatic carcinoma and retroperitoneal lymphoma.<sup>91</sup>

Colorectal Cancer. Lymphatic drainage of colorectal cancers occurs to four groups of lymph nodes: the epicolic nodes, paracolic nodes, intermediate nodes, and principal nodes.<sup>6,120</sup> Tumor spread to the nodes occurs in a sequential fashion, initially involving the nodes close to the primary tumor followed by spread into more distal nodes (see Figure 61-23).<sup>6,120</sup> Isolated involvement of distal nodes such as the principal nodes suggests an advanced stage of disease and is usually associated with hepatic metastases or peritoneal dissemination.<sup>121</sup> Carcinomas involving the right colon disseminate to lymph nodes along the ileocolic vessels and the superior mesenteric vessels.<sup>7</sup> Left-sided colorectal tumors spread to the lymph nodes along the inferior mesenteric vessels.7 Rectal cancers disseminate first into the perirectal nodes (mesorectal nodes) and then into the nodes along the superior rectal vessels.<sup>7</sup> Rectal cancer also can have nodal spread into the internal iliac and obturator nodes before terminating into the para-aortic nodes.<sup>7</sup> Anal cancers spread into the superficial inguinal, deep inguinal, external iliac, common iliac, and finally into the para-aortic nodes.

*Urinary Tract Tumors.* The regional nodes involved in renal cell carcinoma are those in the renal hilum and the nearby paraaortic region.<sup>101</sup> Tumors of the renal pelvis and the upper portion of the ureter involve the para-aortic nodes or the nodes in the renal hilum, whereas tumors of the lower abdominal part of the ureter extend into the common iliac nodes.<sup>7,101</sup> Lymphatic

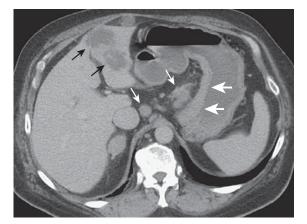
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spread from the pelvic portion of the ureter occurs into the external or internal iliac nodes.<sup>7,101</sup>

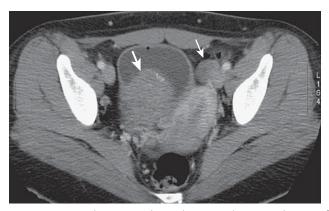
**Bladder Cancer.** Bladder cancers initially spread to the paravesicular nodes before involving the obturator and external iliac nodes (Figure 61-30).<sup>7</sup> The final drainage occurs into the common iliac and para-aortic nodal chains.<sup>7</sup> Occasional involvement of the hypogastric and presacral nodes also can occur.<sup>7</sup>

**Prostate Cancer.** Nodal metastases from prostate cancer involve the pelvic nodes from below the level of bifurcation of the common iliac artery.<sup>101</sup> Prostatic carcinoma follows a pattern similar to that of bladder cancer and spreads to the obturator, presacral, hypogastric, and external iliac nodes before eventually draining into the common iliac and para-aortic nodes.<sup>7</sup> A portion of the lymphatic flow from the prostate also drains into the lymphatic plexus anterior to the urinary bladder or the presacral nodes. Involvement of periprostatic and periseminal vesicle lymph nodes is very rare.

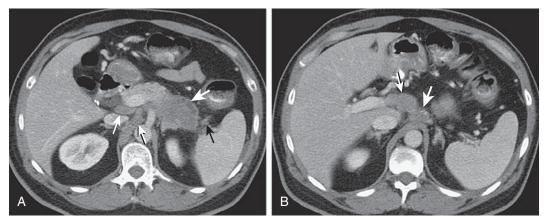
Testicular Cancer. Nodal dissemination from testicular cancer occurs along the lymphatic channels within the spermatic cord into the retroperitoneal nodes.7 The regional nodes of testicular cancer include all the para-aortic nodes located along the route of the testicular vein (Figure 61-31). The tumors most commonly involve the para-aortic nodes between the ipsilateral renal and inferior mesenteric artery. Right-sided testicular tumors spread to the right-sided retroperitoneal nodes, namely, the precaval, paracaval, aortocaval, and retrocaval nodes.<sup>7</sup> Left-sided testicular tumors disseminate to the leftsided retroperitoneal nodes, which include the preaortic and para-aortic nodes.<sup>7</sup> However, the presence of abundant lymphatic intercommunications may lead to involvement of contralateral para-aortic and aortocaval nodes. Nodes between the inferior mesenteric artery and the aortic bifurcation are less commonly involved. Pelvic and inguinal nodes, although not initially involved, can become affected later owing to altered lymphatic pathways resulting from surgery. Lymph node spread also can occur to retrocrural, mediastinal, and supraclavicular regions (see Figure 61-31).



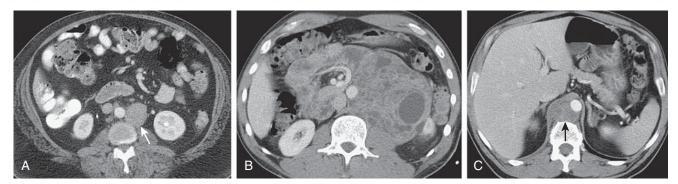
**Figure 61-28** Metastatic lymphadenopathy in a 64-year-old man with gastric cancer. Axial contrast-enhanced computed tomography scan of the abdomen shows malignant gastric wall thickening (*thick white arrows*) with enlarged gastrohepatic and celiac axis lymph nodes (*thin white arrows*) and hepatic metastases (*thin black arrows*).



**Figure 61-30** Axial contrast-enhanced computed tomography scan of the pelvis in a 43-year-old man with transitional cell carcinoma of the bladder (*thick arrow*) shows a solitary left external iliac metastatic lymph node (*thin arrow*).



**Figure 61-29** Pancreatic ductal adenocarcinoma in a 67-year-old man. **A**, Axial contrast-enhanced computed tomography (CT) scan of the abdomen shows a hypoattenuating mass (*thick white arrow*) in the pancreatic body and tail with invasion of the celiac artery. Enlarged lymph nodes are seen in the celiac region (*white thin arrows*) and at the splenic hilum (*black arrow*). **B**, Axial contrast-enhanced CT scan shows enlarged lymph nodes at the celiac axis (*thick arrow*) and at the porta hepatis (*thin arrow*).



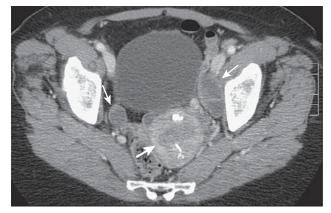
**Figure 61-31** Metastatic lymphadenopathy from testicular carcinoma in different patients. **A**, Axial contrast-enhanced computed tomography (CT) scan in 52-year-old man shows a solitary left para-aortic metastatic node (*arrow*). **B**, Axial contrast-enhanced CT scan in a 47-year-old man 1 year after left orchiectomy for mixed germ cell tumor of the testes shows large necrotic lymph nodes in the para-aortic and paracaval regions with solid and cystic areas. The enlarged contralateral para-aortic node highlights the presence of lymphatic intercommunications. **C**, Axial contrast-enhanced CT scan in a 51-year-old man with left testicular seminoma shows a necrotic enlarged retrocrural lymph node (*arrow*) partially encasing and elevating the aorta.

*Gynecologic Malignancies.* Gynecologic malignancies (cervical, uterine, and ovarian) frequently disseminate initially into the obturator nodes, followed by further spread into the common iliac nodes.<sup>7</sup> Hypogastric nodes along the internal iliac vessels also can be involved.<sup>7</sup>

*Cervical Cancer.* The obturator lymph node is the most frequently involved lymph node group in cervical carcinoma, followed by internal iliac, common iliac, and parametrial lymph nodes.<sup>122</sup> Lymphatic spread in cervical carcinoma occurs through three routes.<sup>93,122,123</sup> The most important route is laterally through the obturator, hypogastric, external iliac, and common iliac nodes. The second is the anterior channel, which terminates in the external iliac nodes. The third route passes posteriorly and drains into the common iliac, sacral, and paraaortic lymph nodes.<sup>123</sup>

**Endometrial Cancer.** The lymphatic spread of endometrial cancer corresponds to the primary tumor location and its drainage site. The upper corpus and fundus drain into the common iliac and para-aortic nodes, whereas the middle and lower portions of the uterus drain into the parametrium, paracervical, and obturator lymph nodes (Figure 61-32).<sup>124</sup> Involvement of inguinal nodes may occur secondary to spread from the round ligaments.<sup>124</sup>

**Ovarian Cancer.** Nodal metastases from ovarian cancer occur along the ovarian vessels to the upper common iliac and para-aortic lymph nodes (see Figure 61-23).<sup>100,125</sup> Dissemination along the broad ligament results in internal iliac, obturator, and external iliac adenopathy.<sup>100</sup> Involvement of the superficial and deep inguinal nodes can occur via the round ligaments.<sup>100</sup>



**Figure 61-32** Axial contrast-enhanced computed tomography of the abdomen in a 65-year-old woman with endometrial carcinoma. There is a hypoattenuating mass in the uterine corpus (*thick arrow*) with enlarged necrotic left obturator and right internal iliac nodes (*arrows*).

# **Key Points**

- CT and MRI use morphologic criteria for determination of lymph node abnormalities.
- PET determines lymph node abnormalities based on functional activity.
- The normal dimensions of lymph nodes vary from region to region, gradually increasing in the caudal direction.
- Knowledge of nodal drainage pathways is critical for accurately staging abdominal and pelvic cancers.

#### SUGGESTED READINGS

- Delorme S, van Kaick G: Imaging of abdominal nodal spread in malignant disease. *Eur Radiol* 6:262–274, 1996.
- Einstein DM, Singer AA, Chilcote WA, et al: Abdominal lymphadenopathy: spectrum of CT findings. *Radiographics* 11:457–472, 1991.
- Goldberg MA, Lee MJ, Fischman AJ, et al: Fluorodeoxyglucose PET of abdominal and pelvic neoplasms: potential role in oncologic imaging. *Radiographics* 13:1047–1062, 1993.
- Harisinghani MG, Dixon WT, Saksena MA, et al: MR lymphangiography: imaging strategies to

optimize the imaging of lymph nodes with ferumoxtran-10. *Radiographics* 24:867–878, 2004. Park JM, Charnsangavej C, Yoshimitsu K, et al: Pathways of nodal metastasis from pelvic tumors: CT demonstration. *Radiographics* 14:1309–1321, 1994.

#### REFERENCES

- Guermazi A, Brice P, Hannequin C, et al: Lymphography: an old technique retains its usefulness. *Radiographics* 23:1541–1558, discussion 1559–1560, 2003.
- 2. Delorme S, van Kaick G: Imaging of abdominal nodal spread in malignant disease. *Eur Radiol* 6:262–274, 1996.
- 3. Clement O, Luciani A: Imaging the lymphatic system: possibilities and clinical applications. *Eur Radiol* 14:1498–1507, 2004.
- 4. Luciani A, Itti E, Rahmouni A, et al: Lymph node imaging: basic principles. *Eur J Radiol* 58:338–344, 2006.
- Einstein DM, Singer AA, Chilcote WA, et al: Abdominal lymphadenopathy: spectrum of CT findings. *Radiographics* 11:457–472, 1991.
- Lengele B, Nyssen-Behets C, Scalliet P: Anatomical bases for the radiological delineation of lymph node areas: upper limbs, chest and abdomen. *Radiother Oncol* 84:335–347, 2007.
- Koh DM, Hughes M, Husband JE: Crosssectional imaging of nodal metastases in the bdomen and pelvis. *Abdom Imaging* 31:632– 643, 2006.
- Park JM, Charnsanavej C, Yoshimitsu K, et al: Pathways of nodal metastasis from pelvic tumors: CT demonstration. *Radiographics* 14:1309–1321, 1994.
- Dorfman RE, Alpern MB, Gross BH, et al: Upper abdominal lymph nodes: criteria for normal size determined with CT. *Radiology* 180:319–322, 1991.
- Einstein DM, Singer AA, Chilcote WA, et al: Abdominal lymphadenopathy: spectrum of CT findings. *Radiographics* 11:457–472, 1991.
- Williams AD, Cousins C, Soutter WP, et al: Detection of pelvic lymph node metastases in gynecologic malignancy: a comparison of CT, MR imaging, and positron emission tomography. AJR Am J Roentgenol 177:343–348, 2001.
- Korobkin M: Computed tomography of the retroperitoneal vasculature and lymph nodes. *Semin Roentgenol* 16:251–267, 1981.
- Grubnic S, Vinnicombe SJ, Norman AR, et al: MR evaluation of normal retroperitoneal and pelvic lymph nodes. *Clin Radiol* 57:193–200, discussion 201–204, 2002.
- Lee BJ: Lymphangiography in Hodgkin's disease: indications and contraindications. *Cancer Res* 26:1084–1089, 1966.
- Jing B, Wallace S, Zornoza J: Metastases to retroperitoneal and pelvic lymph nodes: computed tomography and lymphangiography. *Radiol Clin North Am* 20:511–530, 1982.
- Faige DO: EUS in patients with benign and malignant lymphadenopathy. *Gastrointest Endosc* 53:593–598, 2001.
- Okada Y, Yao YK, Yunoki M, et al: Lymph nodes in the hepatoduodenal ligament: US appearances with CT and MR correlation. *Clin Radiol* 51:160–166, 1996.
- Saftoiu A, Vilmann P, Hassan H, et al: Analysis of endoscopic ultrasound elastography used for characterisation and differentiation of benign and malignant lymph nodes. *Ultra*schall Med 27:535–542, 2006.
- Kanamori A, Hirooka Y, Itoh A, et al: Usefulness of contrast-enhanced endoscopic ultrasonography in the differentiation between malignant and benign lymphadenopathy. *Am J Gastroenterol* 101:45–51, 2006.
- 20. Hocke M, Menges M, Topalidis T, et al: Contrast-enhanced endoscopic ultrasound in

discrimination between benign and malignant mediastinal and abdominal lymph nodes. *J Cancer Res Clin Oncol* 134:473–480, 2008.

- Liao SR, Dai Y, Huo L, et al: Transabdominal ultrasonography in preoperative staging of gastric cancer. World J Gastroenterol 10:3399– 3404, 2004.
- 22. Munker R, Stengel A, Stabler A, et al: Diagnostic accuracy of ultrasound and computed tomography in the staging of Hodgkin's disease: verification by laparotomy in 100 cases. *Cancer* 76:1460–1466, 1995.
- Tregnaghi A, De Candia A, Calderone M, et al: Ultrasonographic evaluation of superficial lymph node metastases in melanoma. *Eur J Radiol* 24:216–221, 1997.
- Bhutani MS, Hawes RH, Hoffman BJ: A comparison of the accuracy of echo features during endoscopic ultrasound (EUS) and EUS-guided fine-needle aspiration for diagnosis of malignant lymph node invasion. *Gastrointest Endosc* 45:474–479, 1997.
- 25. Kato M, Saji S, Kanematsu M, et al: Detection of lymph-node metastases in patients with gastric carcinoma: comparison of three MR imaging pulse sequences. *Abdom Imaging* 25:25–29, 2000.
- 26. Gupta AK, et al: The retroperitoneum. In Haaga LC, Jr, Lanzieri CF, Gilkeson RC, editors: *CT and MR imaging of the whole body* (vol 2), ed 4, St. Louis, 2003, Elsevier, p 1685.
- Low RN, Gurney J: Diffusion-weighted MRI (DWI) in the oncology patient: value of breathhold DWI compared to unenhanced and gadolinium-enhanced MRI. J Magn Reson Imaging 25:848–858, 2007.
- Harisinghani MG, Barentsz J, Hahn PF, et al: Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. *N Engl J Med* 348:2491–2499, 2003.
- Harisinghani MG, Saini S, Weissleder R, et al: MR lymphangiography using ultrasmall superparamagnetic iron oxide in patients with primary abdominal and pelvic malignancies: radiographic-pathologic correlation. *AJR Am J Roentgenol* 172:1347–1351, 1999.
- Harisinghani MG, Sakesena MA, Hahn PF, et al: Ferumoxtran-10–enhanced MR lymphangiography: does contrast-enhanced imaging alone suffice for accurate lymph node characterization? AJR Am J Roentgenol 186:144–148, 2006.
- Saokar A, Braschi M, Harisinghani MG: Lymphotrophic nanoparticle enhanced MR imaging (LNMRI) for lymph node imaging. *Abdom Imaging* 31:660–667, 2006.
- Harisinghani MG, Dixon WT, Saksena MA, et al: MR lymphangiography: imaging strategies to optimize the imaging of lymph nodes with ferumoxtran-10. *Radiographics* 24:867– 878, 2004.
- Lawson TL, Foley WD, Thorsen MK, et al: Magnetic resonance imaging of discrete and conglomerate retroperitoneal lymph node masses. *Radiographics* 5:971–984, 1985.
- Roy C, Le Bras Y, Mangold L, et al: Small pelvic lymph node metastases: evaluation with MR imaging. *Clin Radiol* 52:437–440, 1997.
- Lee JK, Heiken JP, Ling D, et al: Magnetic resonance imaging of abdominal and pelvic lymphadenopathy. *Radiology* 153:181–188, 1984.
- van den Brekel MW, Castelijns JA, Stel HV, et al: Detection and characterization of metastatic cervical adenopathy by MR imaging:

comparison of different MR techniques. J Comput Assist Tomogr 14:581–589, 1990.

- Sanchez Salmon A, Barandela Salgado J, Ruibal Morell A: PET in abdominal pathology: advantages and limitations. *Abdom Imaging* 31:174– 181, 2006.
- Veit P, Ruehm S, Kuehl H, et al: Lymph node staging with dual-modality PET/CT: enhancing the diagnostic accuracy in oncology. *Eur J Radiol* 58:383–389, 2006.
- 39. Zinzani PL, Chierichetti F, Zompatori M, et al: Advantages of positron emission tomography (PET) with respect to computed tomography in the follow-up of lymphoma patients with abdominal presentation. *Leuk Lymphoma* 43:1239–1243, 2002.
- Goldberg MA, Lee MJ, Fischman AJ, et al: Fluorodeoxyglucose PET of abdominal and pelvic neoplasms: potential role in oncologic imaging. *Radiographics* 13:1047–1062, 1993.
- Nogami M, Nakamoto Y, Sakamoto S, et al: Diagnostic performance of CT, PET, side-byside, and fused image interpretations for restaging of non-Hodgkin lymphoma. *Ann Nucl Med* 21:189–196, 2007.
- Toshniwal R, Kocka FE, Kallick CA: Suppurative lymphadenitis with *Yersinia enterocolitica*. *Eur J Clin Microbiol* 4:587–588, 1985.
- Maull KI, Sachatello CR: Retroperitoneal iliac fossa abscess: a complication of suppurative iliac lymphadenitis. *Am J Surg* 127:270–274, 1974.
- Go CH, Cunha BA, Zhang C, et al: Retroperitoneal suppurative lymphadenitis complicating *Staphylococcus aureus* acute bacterial endocarditis. *Infection* 29:348–350, 2001.
- Li Y, Yang ZG, Guo YK, et al: Distribution and characteristics of hematogenous disseminated tuberculosis within the abdomen on contrastenhanced CT. *Abdom Imaging* 32:484–488, 2007.
   Kapoor VK: Abdominal tuberculosis. *Postgrad*
- Med J 74:459–467, 1998.
- Radin R: HIV infection: analysis in 259 consecutive patients with abnormal abdominal CT findings. *Radiology* 197:712–722, 1995.
- Halvorsen RA: AIDS and adenopathy: a computed tomographic pattern approach to diagnosis of acute abdominal complications in AIDS. *Emerg Radiol* 5:1–6, 1998.
- 49. Carucci LR, Halvorsen RA: Abdominal and pelvic CT in the HIV-positive population. *Abdom Imaging* 29:631–642, 2004.
- Lucey BC, Stuhlfaut JW, Soto JA: Mesenteric lymph nodes seen at imaging: causes and significance. *Radiographics* 25:351–365, 2005.
- Soresi M, Bonfissuto G, Magliarisi C, et al: Ultrasound detection of abdominal lymph nodes in chronic liver diseases: a retrospective analysis. *Clin Radiol* 58:372–377, 2003.
- Kuo HT, Lin CY, Chen JJ, et al: Enlarged lymph nodes in porta hepatis: sonographic sign of chronic hepatitis B and C infections. J Clin Ultrasound 34:211–216, 2006.
- Zhou LP, Zhang B, Peng WJ, et al: Imaging findings of Castleman disease of the abdomen and pelvis. *Abdom Imaging* 33:482–488, 2008.
- Weisenburger DD, Nathwani BN, Winberg CD, et al: Multicentric angiofollicular lymph node hyperplasia: a clinicopathologic study of 16 cases. *Hum Pathol* 16:162–172, 1985.
- McCarty MJ, Vukelja SJ, Banks PM, et al: Angiofollicular lymph node hyperplasia (Castleman's disease). *Cancer Treat Rev* 21:291–310, 1995.

#### 724 PART 7 Abdominal and Pelvic Lymph Nodes

- Chu SC, Horiba K, Usuki J, et al: Comprehensive evaluation of 35 patients with lymphangioleiomyomatosis. *Chest* 115:1041–1052, 1999.
- Avila NA, Kelly JA, Chu SC, et al: Lymphangioleiomyomatosis: abdominopelvic CT and US findings. *Radiology* 216:147–153, 2000.
- Prabhakar HB, Rabinowitz CB, Gibbons FK, et al: Imaging features of sarcoidosis on MDCT, FDG PET, and PET/CT. AJR Am J Roentgenol 190(3 Suppl):S1–S6, 2008.
- 59. Yang Z, Sone S, Min P, et al: Distribution and contrast enhanced CT appearance of abdominal tuberculous lymphadenopathy. *Nippon Igaku Hoshasen Gakkai Zasshi* 57:567–571, 1997.
- Yang ZG, Min PQ, Sone S, et al: Tuberculosis versus lymphomas in the abdominal lymph nodes: evaluation with contrast-enhanced CT. *AJR Am J Roentgenol* 172:619–623, 1999.
- De Backer AI, Mortele KJ, Deeren D, et al: Abdominal tuberculous lymphadenopathy: MRI features. *Eur Radiol* 15:2104–2109, 2005.
- 62. Pombo F, Rodriguez E, Mato J, et al: Patterns of contrast enhancement of tuberculous lymph nodes demonstrated by computed tomography. *Clin Radiol* 46:13–17, 1992.
- Suri S, Gupta S, Suri R: Computed tomography in abdominal tuberculosis. *Br J Radiol* 72:92– 98, 1999.
- Radin DR: Intraabdominal Mycobacterium tuberculosis vs Mycobacterium aviumintracellulare infections in patients with AIDS: distinction based on CT findings. AJR Am J Roentgenol 156:487–491, 1991.
- Koh DM, Burn PR, Mathews G, et al: Abdominal computed tomographic findings of Mycobacterium tuberculosis and Mycobacterium avium intracellulare infection in HIV-seropositive patients. Can Assoc Radiol J 54:45–50, 2003.
- Herts BR, Megibow AJ, Birnbaum BA, et al: High-attenuation lymphadenopathy in AIDS patients: significance of findings at CT. *Radiol*ogy 185:777–781, 1992.
- 67. Furukawa A, Saotome T, Yamasaki M, et al: Cross-sectional imaging in Crohn disease. *Radiographics* 24:689–702, 2004.
- 68. Metreweli C, Ward SC: Ultrasound demonstration of lymph nodes in the hepatoduodenal ligament ('daisy chain nodes') in normal subjects. *Clin Radiol* 50:99–101, 1995.
- 69. Kim TJ, Han JK, Kim YH, et al: Castleman disease of the abdomen: imaging spectrum and clinicopathologic correlations. *J Comput Assist Tomogr* 25:207–214, 2001.
- Huppert BJ, Farrell MA: Case 60: cavitating mesenteric lymph node syndrome. *Radiology* 228:180–184, 2003.
- Huppert BJ, Farrell MA, Kawashima A, et al: Diagnosis of cavitating mesenteric lymph node syndrome in celiac disease using MRI. *AJR Am J Roentgenol* 183:1375–1377, 2004.
- Lucey BC, Stuhlfaut JW, Soto JA: Mesenteric lymph nodes: detection and significance on MDCT. AJR Am J Roentgenol 184:41–44, 2005.
- Macari M, Hines J, Balthazar E, et al: Mesenteric adenitis: CT diagnosis of primary versus secondary causes, incidence, and clinical significance in pediatric and adult patients. *AJR Am J Roentgenol* 178:853–858, 2002.
- 74. Karmazyn B, Werner EA, Rejaie B, et al: Mesenteric lymph nodes in children: what is normal? *Pediatr Radiol* 35:774–777, 2005.
- 75. Warshauer DM, Dumbleton SA, Molina PI, et al: Abdominal CT findings in sarcoidosis: radiologic and clinical correlation. *Radiology* 192:93–98, 1994.

- Britt AR, Francis IR, Glazer GM, et al: Sarcoidosis: abdominal manifestations at CT. *Radiol*ogy 178:91–94, 1991.
- 77. Zinzani PL, Chierichetti F, Zompatori M, et al: Advantages of positron emission tomography (PET) with respect to computed tomography in the follow-up of lymphoma patients with abdominal presentation. *Leuk Lymphoma* 43:1239–1243, 2002.
- Castellucci P, Zinzani P, Pourdehnad M, et al: 18F-FDG-PET in malignant lymphoma: significance of positive findings. *Eur J Nucl Med Mol Imaging* 32:749–756, 2005.
- Vinnicombe SJ, Reznek RH: Computerised tomography in the staging of Hodgkin's disease and non-Hodgkin's lymphoma. *Eur J Nucl Med Mol Imaging* 30(Suppl 1):S42–S55, 2003.
- Aisen AM, Gross BH, Glazer GM, et al: Distribution of abdominal and pelvic Hodgkin disease: implications for CT scanning. J Comput Assist Tomogr 9:463–465, 1985.
- Schaner EG, Head GL, Doppman JL, et al: Computed tomography in the diagnosis, staging, and management of abdominal lymphoma. *J Comput Assist Tomogr* 1:176–180, 1977.
- Stomper PC, Cholewinski SP, Park J, et al: Abdominal staging of thoracic Hodgkin disease: CT-lymphangiography-Ga-67 scanning correlation. *Radiology* 187:381–386, 1993.
- Pombo F, Rodriguez E, Caruncho MV, et al: CT attenuation values and enhancing characteristics of thoracoabdominal lymphomatous adenopathies. J Comput Assist Tomogr 18:59–62, 1994.
- Podriguez M, Rehn SM, Nyman RS, et al: CT in malignancy grading and prognostic prediction of non-Hodgkin's lymphoma. *Acta Radiol* 40:191–197, 1999.
- Yu RS, Zhang SZ, Wu JX, et al: CT evaluation of lymphoma in the abdominal lymph nodes. *Zhejiang Da Xue Xue Bao Yi Xue Ban* 33:269– 271, 276, 2004.
- Yu RS, Zhang WM, Liu YQ: CT diagnosis of 52 patients with lymphoma in abdominal lymph nodes. World J Gastroenterol 12:7869–7873, 2006.
- Hardy SM: The sandwich sign. *Radiology* 226:651–652, 2003.
- Lien WC, Huang SP, Liu KL, et al: The sandwich sign of non-lymphomatous origin. J Clin Ultrasound 37:212–214, 2009.
- Apter S, Avigdor A, Gayer G, et al: Calcification in lymphoma occurring before therapy: CT features and clinical correlation. *AJR Am J Roentgenol* 178:935–938, 2002.
- Eisenkraft BL, Som PM: The spectrum of benign and malignant etiologies of cervical node calcification. *AJR Am J Roentgenol* 172:1433–1437, 1999.
- Efremidis SC, Vougioukilis N, Zafiriadou E, et al: Pathways of lymph node involvement in upper abdominal malignancies: evaluation with high-resolution CT. *Eur Radiol* 9:868– 874, 1999.
- Bellomi M, Bonomo G, Landoni F, et al: Accuracy of computed tomography and magnetic resonance imaging in the detection of lymph node involvement in cervix carcinoma. *Eur Radiol* 15:2469–2474, 2005.
- Buchsbaum HJ: Extrapelvic lymph node metastases in cervical carcinoma. Am J Obstet Gynecol 133:814–824, 1979.
- 94. Chen BB, Liang PC, Liu KL, et al: Preoperative diagnosis of gastric tumors by three-dimensional multidetector row CT and double contrast barium meal study: correlation with surgical

and histologic results. J Formos Med Assoc 106: 943–952, 2007.

- Chen CY, Hsu JS, Wu DC, et al: Gastric cancer: preoperative local staging with 3D multidetector row CT—correlation with surgical and histopathologic results. *Radiology* 242:472–482, 2007.
- Choi HJ, Kim SH, Seo SS, et al: MRI for pretreatment lymph node staging in uterine cervical cancer. *AJR Am J Roentgenol* 187:W538– W543, 2006.
- de Jong JJ, Pruim J, Elsinga PH, et al: Preoperative staging of pelvic lymph nodes in prostate cancer by 11C-choline PET. J Nucl Med 44:331–335, 2003.
- Delbeke D, Pinson CW: Pancreatic tumors: role of imaging in the diagnosis, staging, and treatment. J Hepatobiliary Pancreat Surg 11:4– 10, 2004.
- Filippone A, Ambrosini R, Fuschi M, et al: Preoperative T and N staging of colorectal cancer: accuracy of contrast-enhanced multi-detector row CT colonography—initial experience. *Radiology* 231:83–90, 2004.
- Mironov S, Akin O, Pandit-Taskar N, et al: Ovarian cancer. *Radiol Clin North Am* 45:149– 166, 2007.
- Morisawa N, Koyama T, Togashi K: Metastatic lymph nodes in urogenital cancers: contribution of imaging findings. *Abdom Imaging* 31:620–629, 2006.
- 102. Selman TJ, Mann CH, Zamora J, et al: A systematic review of tests for lymph node status in primary endometrial cancer. BMC Womens Health 8:8, 2008.
- Tsunoda Y, Ito M, Fujii H, et al: Preoperative diagnosis of lymph node metastases of colorectal cancer by FDG-PET/CT. *Jpn J Clin Oncol* 38:347–353, 2008.
- 104. Uenishi T, Hirohashi K, Shuto T, et al: The clinical significance of lymph node metastases in patients undergoing surgery for hepatocellular carcinoma. *Surg Today* 30:892–895, 2000.
- Wang HS, Liang WY, Lin TC, et al: Curative resection of T1 colorectal carcinoma: risk of lymph node metastasis and long-term prognosis. *Dis Colon Rectum* 48:1182–1192, 2005.
- 106. Yokota T, Ishiyama S, Saito T, et al: Lymph node metastasis as a significant prognostic factor in gastric cancer: a multiple logistic regression analysis. *Scand J Gastroenterol* 39:380–384, 2004.
- 107. Sobin LH, Wittekind CH: TNM classification of malignant tumors, ed 6, International Union Against Cancer, New York, 2002, John Wiley & Sons.
- Yanagita S, Natsugoe S, Uenosono Y, et al: Morphological distribution of metastatic foci in sentinel lymph nodes with gastric cancer. *Ann Surg Oncol* 15:770–776, 2008.
- 109. Shinohara T, Ohyama S, Yamaguchi T, et al: Clinical value of multidetector row computed tomography in detecting lymph node metastasis of early gastric cancer. *Eur J Surg Oncol* 31:743–748, 2005.
- 110. Jager GJ, Barentsz JO, Oosterhof GO, et al: Pelvic adenopathy in prostatic and urinary bladder carcinoma: MR imaging with a threedimensional T1-weighted magnetizationprepared-rapid gradient-echo sequence. AJR Am J Roentgenol 167:1503–1507, 1996.
- 111. Som PM: Detection of metastasis in cervical lymph nodes: CT and MR criteria and differential diagnosis. *AJR Am J Roentgenol* 158:961– 969, 1992.

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- 112. Fukuya T, Honda H, Hayashi T, et al: Lymphnode metastases: efficacy for detection with helical CT in patients with gastric cancer. *Radiology* 197:705–711, 1995.
- 113. Lien HH, Lindskold L, Stenwig AE, et al: Shape of retroperitoneal lymph nodes at computed tomography does not correlate to metastatic disease in early stage non-seminomatous testicular tumors. Acta Radiol 28:271–273, 1987.
- 114. Roche CJ, Hughes ML, Garvey CJ, et al: CT and pathologic assessment of prospective nodal staging in patients with ductal adenocarcinoma of the head of the pancreas. *AJR Am J Roentgenol* 180:475–480, 2003.
- 115. Kim YC, Park MS, Cha SW, et al: Comparison of CT and MRI for presurgical characterization of paraaortic lymph nodes in patients with pancreaticobiliary carcinoma. *World J Gastroenterol* 14:2208–2212, 2008.
- Dooms GC, Hricak H, Moseley ME, et al: Characterization of lymphadenopathy by magnetic resonance relaxation times: preliminary results. *Radiology* 155:691–697, 1985.

- 117. Magnusson A, Andersson T, Larsson B, et al: Contrast enhancement of pathologic lymph nodes demonstrated by computed tomography. *Acta Radiol* 30:307–310, 1989.
- 118. Yang WT, Lam WW, Yu MY, et al: Comparison of dynamic helical CT and dynamic MR imaging in the evaluation of pelvic lymph nodes in cervical carcinoma. *AJR Am J Roentgenol* 175:759–766, 2000.
- 119. Meyers MA, Oliphant M, Berne AS, et al: The peritoneal ligaments and mesenteries: pathways of intraabdominal spread of disease. *Radiology* 163:593–604, 1987.
- 120. McDaniel KP, Charnsangavej C, DuBrow RA, et al: Pathways of nodal metastasis in carcinomas of the cecum, ascending colon, and transverse colon: CT demonstration. *AJR Am J Roentgenol* 161:61–64, 1993.
- 121. Granfield CA, Charnsangavej C, Dubrow RA, et al: Regional lymph node metastases in carcinoma of the left side of the colon and rectum: CT demonstration. *AJR Am J Roentgenol* 159:757–761, 1992.

- 122. Sakuragi N, Satoh C, Takeda N, et al: Incidence and distribution pattern of pelvic and paraaortic lymph node metastasis in patients with stages IB, IIA, and IIB cervical carcinoma treated with radical hysterectomy. *Cancer* 85:1547–1554, 1999.
- 123. Sakuragi N: Up-to-date management of lymph node metastasis and the role of tailored lymphadenectomy in cervical cancer. *Int J Clin Oncol* 12:165–175, 2007.
- 124. Barwick TD, Rockall AG, Barton DP, et al: Imaging of endometrial adenocarcinoma. *Clin Radiol* 61:545–555, 2006.
- 125. Forstner R: Radiological staging of ovarian cancer: imaging findings and contribution of CT and MRI. Eur Radiol 17:3223–3235, 2007.



# Imaging of the Kidneys and Urinary Tract

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# **Anatomy Overview**

#### THE KIDNEY

The kidneys are paired retroperitoneal organs that primarily function in the excretion of metabolic waste. They are bean shaped with a convex lateral border and a concave medial surface known as the renal hilum.<sup>1</sup>

On intravenous contrast-enhanced studies, sequential enhancement of the renal vasculature, cortex, medulla, and collecting system occurs. In the early nephrographic phase, also called the corticomedullary phase, there is marked differentiation between the markedly enhancing renal cortex and relatively unenhanced renal medulla is prominent. As the nephrogram progresses, the entire kidney shows more uniform enhancement. After approximately 2 minutes, the collecting system starts to become dense with opacified urine, which progresses into the ureters and bladder (Figure 62-1).

Most kidneys are supplied by a single renal artery arising from the abdominal aorta. Near the renal hilum the main renal artery divides into a posterior and four anterior segmental renal arteries (upper, apical, middle, and lower) that course through the renal sinus.<sup>2</sup> The segmental arteries give rise to the lobar arteries that branch to form the interlobar, arcuate, and interlobular arteries. Accessory renal arteries can occur and are unilateral in 30% and bilateral in 10%.<sup>2</sup>

The kidney is usually drained by a single renal vein that forms from the sequential fusion of the arcuate, interlobar, and lobar veins.<sup>2</sup> Similar to arterial supply, there can be variant venous anatomy, including multiple right renal veins (30%), a circumaortic left renal vein (17%), and a retroaortic left renal vein (3%).<sup>2</sup>

The kidneys are situated on either side of the lumbar spine within the perirenal space of the retroperitoneum. The perirenal spaces are cone shaped and are confined by the anterior (Gerota) and posterior (Zuckerkandl) renal fascia.<sup>1,3</sup> Each collecting system consists of the minor calyces, infundibula or major calyces, and renal pelvis. There are 10 to 25 minor calyces in each kidney, each of which has a cuplike shape formed by the impression of a renal papilla.<sup>4</sup>

# Introduction to Renal Imaging Modalities

Radiographic studies to evaluate the kidneys and urinary tract include plain abdominal radiography as well as excretory

urography, also known as intravenous pyelography (IVP). Abdominal radiographs do not show most pathologic processes but may demonstrate large renal masses or urinary tract calculi. IVP was previously the gold standard for evaluation of the upper urinary tract but has been replaced by computed tomography (CT) urography at many institutions.

Ultrasonography is an important tool in the initial evaluation of the kidneys. It detects the majority of masses greater than approximately 1 cm. Doppler ultrasound imaging is an important tool in evaluating the renal vasculature.

Magnetic resonance imaging (MRI) of the kidneys and urinary tract has had an expanding role in the past decade and is typically performed to further characterize abnormalities discovered using other imaging modalities. Its multiplanar imaging capabilities, superior soft tissue contrast, and ability to demonstrate contrast enhancement with non-nephrotoxic gadolinium compounds have made MRI an attractive tool for evaluating pathologic processes affecting the urinary system. Positron emission tomography (PET) is an emerging imaging modality for the kidneys and urinary tract. Its usefulness is limited by the urinary excretion of fluorodeoxyglucose (FDG), which creates high background uptake of FDG in the kidneys, ureters, and bladder.

Nuclear medicine examinations of the kidneys and urinary tract have the advantage of demonstrating functional information and include radiolabeled mercaptoacetyl triglycine (MAG3), diethylenetriaminepentaacetic acid (DTPA), and dimercaptosuccinic acid (DMSA) scans.

# Radiography

The abdominal plain film or kidney/ureter/bladder (KUB) view plays a small role in the evaluation of the urinary tract. Ultrasonography, CT, and MRI have largely supplanted plain radiography in the evaluation of the urinary tract. Unenhanced CT is now the modality of choice for the diagnosis of renal stones, with sensitivity and specificity reported from 95% to 98% and 96% to 100%, respectively.<sup>5</sup> Plain radiography is significantly less accurate, with a reported sensitivity of 70% to 90% for the detection of urinary tract calculi and a sensitivity of 59% for the detection of ureteral calculi.<sup>6</sup> Once diagnosed with calculi, many patients are managed conservatively with the expectation that the stone(s) will pass spontaneously. The expense and relatively high radiation dose of CT make plain film radiography a more practical modality to follow the progress of calculi. This is particularly true for stones larger than 5 mm or for stones

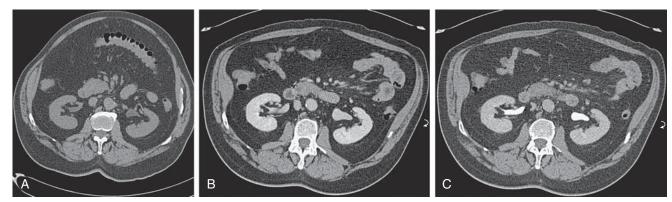
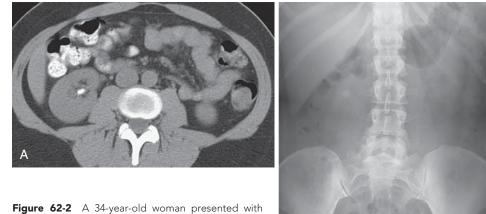


Figure 62-1 Normal computed tomography (CT) appearance of the kidneys. Unenhanced CT (A) shows uniform attenuation of the renal parenchyma in a background of renal sinus and perinephric fat. Contrast-enhanced CT images of the kidneys in nephrographic (B) and excretory or delayed-phase  $(\breve{C})$  images.



right-sided flank pain. A, Axial unenhanced computed tomography scan shows a nonobstructing right renal stone. B, Plain film radiograph also demonstrates the right renal stone and could be used for follow-up imaging.



that measure greater than 300 Hounsfield units (HU) on the diagnostic CT scan (Figure 62-2).<sup>7</sup> Plain radiography can be used to determine which urinary tract calculi can be visualized fluoroscopically for lithotripsy.7

# **Intravenous Urography**

For decades, intravenous urography was the principal imaging study for the evaluation of the upper urinary tract, particularly in the evaluation of flank pain and hematuria. Briefly, the technique generally involves a preliminary radiograph, after which contrast is administered and images are obtained in the nephrographic phase (1 to 3 minutes), followed by a 5-minute film, just as the contrast is beginning to enter the collecting system (Figure 62-3). In some centers, compression may be applied to compress the ureters against the pelvic brim. Images of the collecting system are obtained 10 minutes after contrast (Figure 62-4). The ureters are imaged after compression is released (if applicable), and a number of films or projections may be necessary to image both ureters (Figure 62-5). Radiographs should include the bladder both before and after voiding.



Figure 62-3 Radiograph obtained 5 minutes after administration of a contrast agent as the nephrographic phase is ending and the contrast agent begins to fill the collecting system.



Figure 62-4 Radiographs obtained 5 minutes after compression. The collecting systems are now well distended.



**Figure 62-5** Radiograph obtained immediately after the release of compression as contrast agent fills the ureters.

However, unenhanced CT is now the predominant modality used for the evaluation of flank pain. Smith and colleagues<sup>8</sup> showed that unenhanced CT is more sensitive than intravenous urography in the detection of stones and has the added benefit of showing nonurinary causes of flank pain. Similarly, CT urography has become the definitive imaging study in the evaluation of hematuria. Unlike intravenous urography, CT urography allows the evaluation of both the renal parenchyma and the urothelium in a single examination.<sup>9</sup>

# Ultrasonography

The kidney is well defined at ultrasonography, surrounded by an echogenic fibrous capsule and perirenal fat. The echogenic perirenal fat continues into the renal sinus medially at the renal hilum.<sup>10</sup> The renal cortex is normally equal or slightly less echogenic than the adjacent liver and spleen.<sup>1</sup> The calyces and pelvis are occasionally seen in hydrated patients and in the case of an extrarenal pelvis.<sup>10</sup> These normal variants should not be confused with hydronephrosis.

#### TECHNIQUE

Renal ultrasonography is performed with a sector or curved array transducer with a frequency of 3 to 5 MHz. A lower frequency transducer (2.25 MHz) can be used for larger patients, and a higher frequency transducer (7.0 MHz) can be used for smaller patients.<sup>4</sup> Longitudinal and transverse images are obtained sequentially through the upper pole, interpolar region, and lower pole of each kidney. Maximum renal length should be measured for both kidneys. Ideally, images that provide comparison of renal cortical echogenicity with that of the liver and spleen should be provided.<sup>11</sup> The complete ultrasound evaluation of the urinary tract also includes images of the perirenal areas, the retroperitoneum, and bladder.<sup>10</sup> Transverse and longitudinal images of the bladder are obtained.<sup>11</sup> Color Doppler and spectral waveform analysis may be performed to evaluate the renal vasculature.

#### INDICATIONS

#### Stones

Renal calculi are common, occurring at least once in a lifetime in 12% of men and 5% of women.<sup>10</sup> In fact, stone disease is one of the major indications for imaging of the urinary tract. As discussed, unenhanced CT is the imaging modality of choice in the evaluation of suspected renal colic. Ultrasonography plays a limited role, owing to suboptimal sensitivity for stone detection that ranges from 60% to 96%.<sup>12,13</sup> Despite these limitations, ultrasonography is the initial imaging modality in the evaluation of suspected renal calculi during pregnancy given the lack of ionizing radiation.<sup>14</sup>

The ultrasound criterion for the diagnosis of a renal stone is an echogenic focus with posterior acoustic shadowing (Figure 62-6). It is important to be aware of potential pitfalls in the evaluation for renal stones. Intrarenal gas, renal artery calcifications, calcified masses, and calcified papilla are some of the disease processes that can be confused with renal stones.<sup>1</sup>

#### Obstruction

Ultrasonography is a useful screening test in the evaluation of urinary tract obstruction with sensitivity greater than 90%.<sup>15</sup> With the development of obstruction, there is dilation of the calyces, pelvis, and/or ureter, which appears as anechoic regions within the echogenic renal sinus (Figure 62-7). Obstruction can be categorized depending on severity: grade 1 (minimal separation of collecting system), grade 2 (moderate separation of collecting system), and grade 3 (marked separation of the collecting system).<sup>15,16</sup> However, dilation of the collecting system (hydronephrosis) does not always indicate obstruction and can also be seen in reflux, scarring, pregnancy, high urine output states, and congenitally dilated collecting system.<sup>10</sup> In addition,

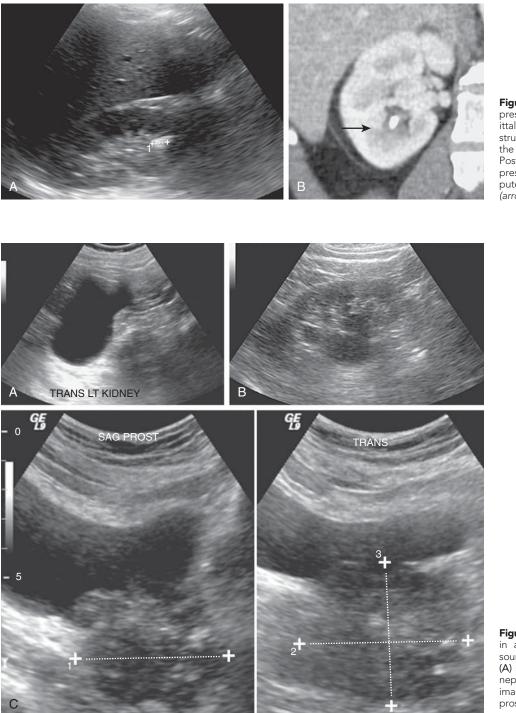


Figure 62-6 A 51-year-old woman presented with abdominal pain. A, Sagittal ultrasound image shows a nonobstructing stone (1) in the lower pole of the right kidney as an echogenic focus. Posterior acoustic shadowing was also present (not shown). B, Coronal computed tomography shows the stone (arrow).

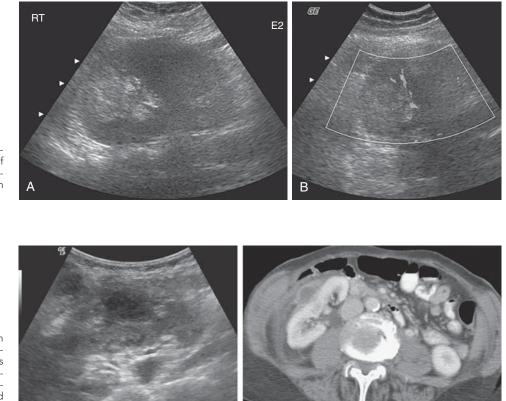
Figure 62-7 Metastatic prostate cancer in an 88-year-old man. Sagittal ultrasound images of the kidneys show (A) severe left and (B) mild right hydronephrosis. C, Sagittal and transverse images of the bladder show the enlarged prostate (measured with calipers) with mass effect on the bladder.

normal patients may show mild dilation of the renal pelvis and calyces when the bladder is full. Postvoid images can be helpful to show resolution of this normal finding.<sup>10</sup>

# Infection

Traditionally, imaging does not play a role in the evaluation of uncomplicated renal infections. However, imaging does play an important role in the detection and follow-up of the complications of renal infections. Pyelonephritis represents bacterial infection of the renal parenchyma. Ultrasonography is less sensitive than both CT and scintigraphy for the detection of acute pyelonephritis. Findings that can be seen include renal enlargement, focal regions of hypoechoic (edema) or hyperechoic (hemorrhage) echotexture, loss of corticomedullary differentiation, and a segment of decreased or absent perfusion (Figure 62-8).<sup>1,10</sup>

Pyonephrosis represents suppurative material in an obstructed collecting system.<sup>17</sup> Prompt relief of the obstruction



В

**Figure 62-8** Pyelonephritis in a 23year-old woman. Sagittal images of the right kidney show a focal hyperechoic region in the upper pole with decreased perfusion.

Figure 62-9 Perirenal abscess in an 87-year-old woman. A, Sagittal ultrasound image of the right kidney shows a hypoechoic perirenal mass with posterior acoustic enhancement and internal debris. B, Axial contrast-enhanced computed tomography confirms the right perirenal abscess.

and treatment of the infection are important to avoid bacteremia and sepsis.

A renal abscess represents progression of acute pyelonephritis to cortical necrosis. A perirenal abscess develops from rupture of either a renal abscess or pyonephrosis into the perirenal space. Both can be detected on ultrasonography as a hypoechoic mass, often with a thick wall, debris, and posterior acoustic enhancement (Figure 62-9).<sup>1,10,17</sup>

#### Tumors

Ultrasonography is less sensitive than CT and MRI in the detection of renal neoplasms. Despite this fact, renal masses are commonly encountered at routine renal ultrasound evaluation. On ultrasonography, most renal masses are solid with variable echogenicity. Doppler evaluation should be included and may reveal venous invasion and tumor vascularity.<sup>1</sup> A full discussion of specific renal neoplasms is presented in Chapter 63.

## **Renal Cystic Disease**

The renal cyst is the most common focal renal lesion. When strict criteria are used, ultrasonography is extremely accurate in the characterization of simple and minimally complex renal cysts. Ultrasonography also plays a role in the evaluation of the complex renal mass. A full discussion of cystic lesions is presented in Chapter 63.

#### Renal Parenchymal Disease

In the setting of renal failure, imaging evaluation usually begins with ultrasonography. Ultrasonography will identify potentially reversible obstructive causes of renal failure<sup>18</sup> and can demonstrate small echogenic kidneys (<9 cm) in patients with irreversible end-stage disease.<sup>10</sup> The normal renal cortex is as echogenic or slightly less echogenic than the adjacent liver and spleen. An increase in the renal cortical echogenicity greater than that of the liver suggests parenchymal disease (Figure 62-10).<sup>1</sup> However, ultrasonography can be normal in cases of early parenchymal disease.

#### Vascular Abnormalities

Duplex and color Doppler ultrasound imaging can be used to image the renal arterial tree from the main renal artery to the arcuate branches and can demonstrate both normal and abnormal renal vasculature. The normal renal artery has a low resistance pattern with forward flow throughout systole and diastole.<sup>1</sup> Normal intrarenal vessels have a rapid systolic upstroke with an acceleration time (from the start of systole to peak) of 0.07 second or less and an acceleration index (slope of initial systolic peak) of 3 m/s<sup>2</sup> or greater.<sup>19</sup> The resistive index can be calculated as a measure of arterial resistance.

The use of ultrasonography in the screening evaluation of renal artery stenosis remains controversial. Ultrasonography is universally available, inexpensive, and noninvasive. However, the examination is time consuming, operator dependent, and technically difficult. Complete examinations of the renal arteries are achieved in 50% to 90% of patients, with sensitivity for the detection of renal artery stenosis varying from 0 to 93%.<sup>20</sup> Criteria for significant renal artery stenosis include peak systolic velocity greater than a threshold value (100 to 200 cm/s), a renal

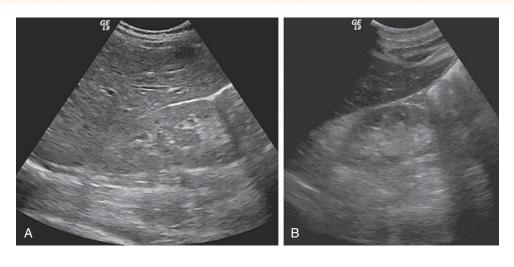
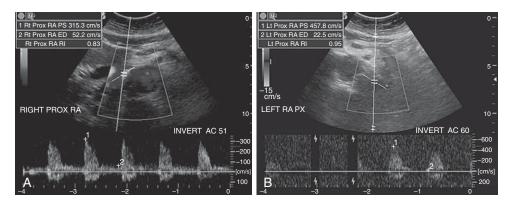


Figure 62-10 Sagittal ultrasound images in (A) a 39-year-old woman with chronic renal insufficiency of unclear cause and (B) a 56-year-old woman with diabetic nephropathy. Both images show increased renal cortical echogenicity greater than the liver, consistent with medical renal disease.



**Figure 62-11** Bilateral renal artery stenosis in a patient with refractory hypertension and advanced atherosclerotic disease. Color Doppler imaging and spectral waveform analysis of both proximal renal arteries (*RA*) show elevated peak systolic velocities of 315.3 cm/s on the right and 457.8 cm/s on the left.

artery to aortic peak systolic velocity ratio greater than 3.5, and turbulent flow with spectral broadening distal to the stenosis (Figure 62-11).<sup>20</sup> Quantitatively, an acceleration time exceeding 0.07 second or an acceleration index of less than 3 m/s<sup>2</sup> in the intrarenal arteries suggests significant renal artery stenosis.<sup>20</sup>

Renal vein thrombosis can be related to a primary renal process such as membranous glomerulonephritis or can be secondary to an extrarenal process such as dehydration, coagulopathy, extrinsic compression, or tumor thrombus.<sup>1,10</sup> On ultrasonography, the kidney is typically enlarged and hypoechoic with loss of corticomedullary differentiation. Echogenic clot may be seen in the renal vein, but clot may be isoechoic and not visualized.

#### Transplants

Renal transplantation has become an important treatment option in patients with end-stage renal disease. These transplants are typically placed extraperitoneally in the right or left lower quadrant with end-to-side anastomoses with the external iliac vasculature and a ureteral neocystostomy to the bladder dome. The superficial location in the right or left lower quadrant often makes ultrasonography the imaging procedure of choice in the evaluation of these complications and in directing interventions.<sup>21,22</sup>

Approximately 90% of obstructions will occur in the distal third of the ureter, with 50% occurring at the site of ureteral implantation to the bladder.<sup>21</sup> The most common causes of obstruction include postoperative edema at the anastomosis,

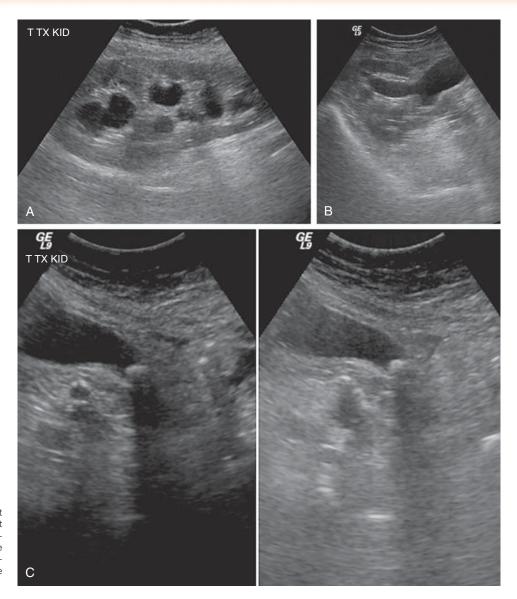
scarring, technical errors, and ureteral kinking. Stones, clots, fungus balls, papillary necrosis, and extrinsic compression are seen less often (Figure 62-12).<sup>1,21,22</sup> It is important to remember that mild hydronephrosis normally can be seen in the denervated transplant from decreased ureteral tone and with a distended bladder.<sup>22</sup> In this instance, postvoid images should be obtained.<sup>21</sup>

Peritransplant fluid collections are common, occurring in approximately 50% of transplant patients (Figure 62-13).<sup>21</sup> These fluid collections include hematomas, urinomas, lymphoceles, and abscesses.

Vascular complications are seen in 1% to 2% of transplants and include renal artery stenosis, renal vein thrombosis, renal artery thrombosis, and postbiopsy arteriovenous fistula or pseudoaneurysm. Color and duplex Doppler ultrasound imaging are excellent to evaluate these complications.<sup>21,22</sup>

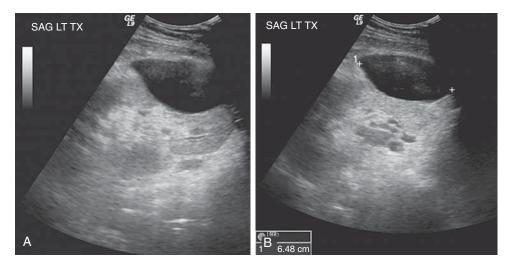
# **Key Points**

- Variant venous anatomy includes multiple right renal veins (30%), a circumaortic left renal vein (17%), and a retroaortic left renal vein (3%).
- The renal cortex is normally equally or slightly less echogenic than the adjacent liver and spleen. An increase in echogenicity greater than that of the liver suggests parenchymal disease.



**Figure 62-12** A 64-year-old patient presented with a right lower quadrant transplant. A and B, Sagittal and transverse ultrasound images show moderate hydronephrosis. C, Transverse ultrasound images show an obstructing stone in the right ureteropelvic junction.

**Figure 62-13** A 48-year-old patient presented with a left lower quadrant transplant. Sagittal ultrasound images show a nonspecific peritransplant fluid collection.



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# **Computed Tomography**

CT is the imaging study of choice for the majority of pathologic processes of the kidneys and urinary tract. Modern CT scans are typically performed using multidetector CT (MDCT) scanners. Isotropic imaging allowing for multiplanar reconstructions should be routinely employed, and dynamic imaging can be performed at multiple time points, when necessary.

Common indications for renal or urinary tract CT include suspected renal colic; abdominal trauma; detection and characterization of renal masses; staging of renal, ureteral, or bladder malignancy; and preoperative planning before renal donation or nephron-sparing surgery.

# **TECHNICAL ASPECTS**

CT of the kidneys and urinary tract may be performed without and with iodinated intravenous contrast media. Protocols are customized to the diagnostic question by varying kilovoltage peaks, milliamperes, pitch, and timing of imaging after contrast agent administration. Each examination should be tailored to match the clinical scenario while adhering to ALARA (as low as reasonably achievable) radiation dosing principles.

A complete CT evaluation of the kidneys and urinary tract includes assessment of the renal vasculature, the renal parenchyma, and the urinary collecting system. Images are obtained in the angiographic phase (15 to 25 seconds), corticomedullary phase (30 to 60 seconds), nephrographic phase (80 to 120 seconds), and delayed/excretory phase (3 to 10 minutes).

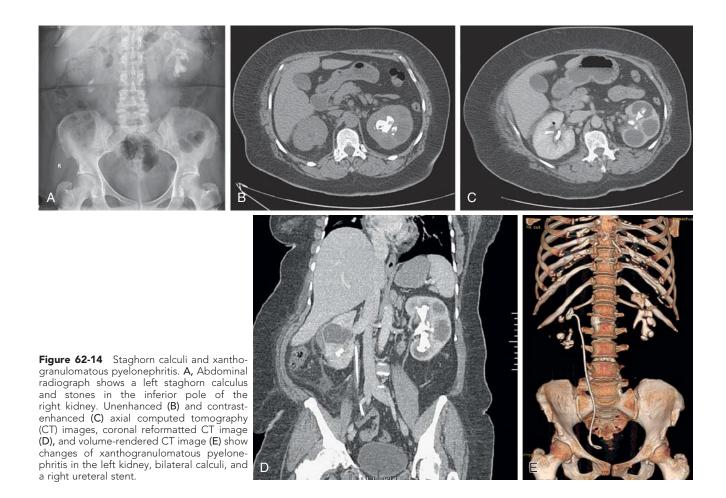
As a general rule, detection of urolithiasis in patients with suspected renal colic should be performed without contrast media.

Multiphasic multidetector volumetric CT evaluation of the kidneys and urinary tract has been termed CT urography. This technique is attractive as a single dynamic comprehensive investigation of the renal parenchyma and urothelium in multiple phases of contrast enhancement.<sup>23-27</sup> CT urography is most often indicated for the evaluation of hematuria or in patients with known urothelial malignancy.

# SPECIFIC INDICATIONS AND TECHNIQUES

# Urolithiasis and Suspected Renal Colic

Acute flank pain is a common clinical problem and an indication for CT in the emergency setting. CT has been shown to be more sensitive than abdominal radiography and/or IVP for the detection of ureteral calculi, including stones that are small or radiolucent on plain film (e.g., uric acid stones) (Figures 62-14 and 62-15).<sup>28-32</sup> CT also obviates the need for intravenous administration of contrast media in most cases and may provide an alternative diagnosis in examinations that are negative for urolithiasis.<sup>32</sup> CT has a sensitivity of 100% in detection of ureterolithiasis compared with 67% for IVP and 62% with plain abdominal radiography.<sup>28-32</sup>



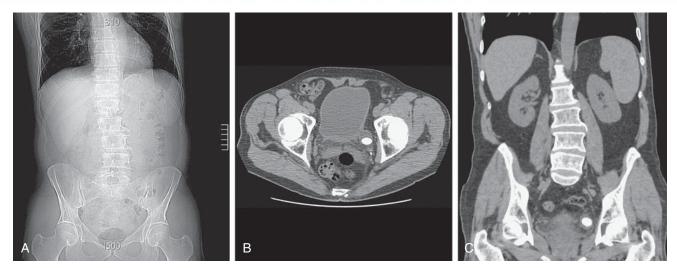


Figure 62-15 A, Scout image shows a uric acid bladder stone as minimally opaque. Unenhanced axial (B) and reformatted coronal (C) CT images show the 17- by 12-mm stone, measuring 400 Hounsfield units, in a left posterolateral bladder diverticulum.

Prone CT imaging of the bladder is sometimes helpful in determining whether a stone in the region of the ureterovesical junction is in the ureter or lying dependently in the bladder. If the ureter is difficult to visualize, intravenous iodinated contrast medium may be administered to determine whether a high-density focus is inside or outside the collecting system. Density measurements of urinary calculi have been used in character-ization of the composition of the stones, although results have been less successful in vivo than in vitro.<sup>33-35</sup> Advances in dual-energy CT have improved the in-vivo detection of renal stone composition.<sup>36</sup>

## **Renal Mass Characterization**

Thin-section unenhanced and dynamic contrast-enhanced CT of the kidneys is the study of choice for renal mass characterization (Figure 62-16). Precontrast images detect calcification and provide a baseline density measurement to evaluate the degree and pattern of lesion enhancement. Corticomedullary phase images best depict lesion vascularity, vascular invasion, and vascular anatomic variants. Some lesions, especially smaller masses or the papillary subtype of renal cell carcinoma (RCC) may be difficult to differentiate from normal renal medulla on corticomedullary phase images, necessitating a later phase of enhancement. Nephrographic phase images are the most sensitive for the detection of small lesions. Excretory phase images show whether tumor involves the renal collecting system.<sup>23,37</sup>

Density measurements of a region of interest within a renal mass on CT may definitively characterize some lesions; for example, a circumscribed mass of water density (HU~0) without enhancement is a simple cyst. CT can detect whether lesions are multiple, as well as ancillary findings such as lymphadenopathy or venous thrombosis.

In brief, RCCs, most of which are of the clear cell type, are often heterogeneous, with contrast enhancement in some regions and other regions of nonenhancing necrosis. Papillary RCC typically appears hypovascular and homogeneous. Chromophobe RCC may show the spokewheel pattern of contrast enhancement classically associated with oncocytoma. Collecting duct carcinoma and renal medullary carcinoma appear



**Figure 62-16** Sagittal reformatted image of a contrast-enhanced computed tomography image shows a circumscribed, round renal mass, which proved to be renal cell carcinoma.

infiltrative, heterogeneous because of intratumoral hemorrhage and necrosis, and hypovascular.<sup>38</sup> Renal tumors are more completely discussed in Chapter 63). CT has an accuracy of more than 95% in the detection of RCC.<sup>23</sup>

CT urography is the imaging modality of choice for detection and staging of renal urothelial malignancy, most commonly transitional cell carcinoma (TCC). In the kidney, TCC typically appears as a central soft tissue mass in the renal sinus, which obliterates or displaces the normal hilar structures and renal sinus fat. The mass may be difficult to appreciate or differentiate from normal renal parenchyma, producing the so-called faceless kidney (Figure 62-17). TCC in a calyx or the renal pelvis may appear as a sessile or polypoid filling defect or as diffuse thickening of the urothelial lining.<sup>23,37</sup> It may cause narrowing or obstruction of the collecting system. Lesions infiltrating the renal parenchyma are best identified on

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nephrographic phase images, whereas lesions confined to the intrarenal collecting system or renal pelvis are better appreciated on excretory phase images. CT may demonstrate extramural extension and regional nodal metastases.

### Hematuria and Evaluation for Urothelial Neoplasm

CT urography with MDCT allows for thin-section images, which have better sensitivity to the detection of urothelial



**Figure 62-17** Axial contrast-enhanced computed tomography image shows a central, infiltrating left renal mass with obliteration of the normal renal sinus fat. The mass proved to be transitional cell carcinoma.

lesions than conventional CT. Consequently, CT urography has largely replaced IVP in the evaluation of hematuria. The kidneys and urinary tract are best evaluated in multiple planes.<sup>25</sup>

#### Preoperative Planning (Nephron-Sparing Surgery and Renal Donor Surgery)

In addition to nephron-sparing surgery for resection of a suspicious or frankly malignant renal mass, renal donor nephrectomy has become common in major medical centers. Since first described in 1995,<sup>39</sup> laparoscopic donor nephrectomy has become instrumental in lowering the barrier to renal donation for the growing number of patients with end-stage renal failure awaiting renal transplantation.<sup>40</sup> The field of view at laparoscopic nephrectomy is limited, requiring accurate preoperative radiologic assessment of the donor's anatomy for success.<sup>40</sup>

MDCT enables precise evaluation of the donor renal arteries, veins, collecting system, and parenchyma (Figure 62-18). Single bilateral renal arteries are present in 70% to 75% of individuals, and variant anatomy, including multiple accessory vessels, is seen in the remaining 25% to 30% of cases.<sup>41</sup>

Renal venous anatomy may be demonstrated on arterial phase images; however, smaller retroperitoneal venous structures are well seen on venous or nephrographic phase images. The left renal vein is typically longer than the right, which is one reason why the left kidney is preferred by transplant surgeons. Circumaortic, retroaortic, or accessory renal veins do not exclude a kidney from consideration for donation but should be reported to facilitate comprehensive preoperative planning.

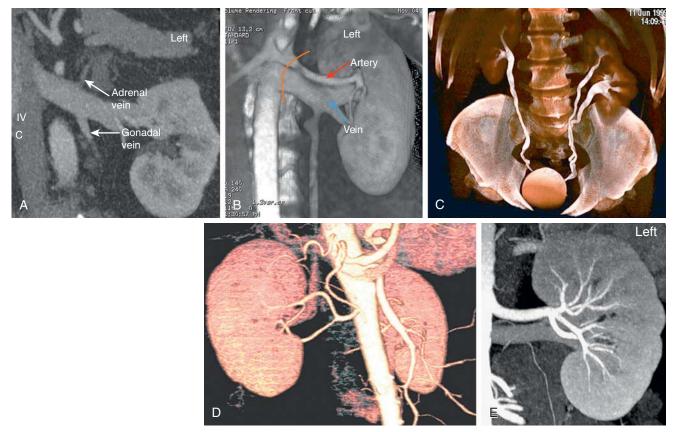


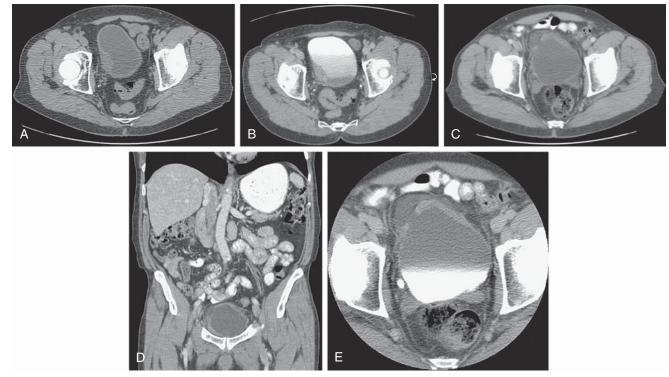
Figure 62-18 Computed tomography images from multiple preoperative renal donor protocol scans. Coronal reformatted image (A) and multiple volume-rendered images (B to E) showing renal anatomy before renal donor surgery.

# Computed Tomography Cystography

CT cystography involves CT scanning of the urinary bladder after retrograde bladder filling with iodinated contrast media. This technique is used in the setting of blunt or penetrating abdominopelvic trauma with suspected bladder rupture, typically in patients with hematuria, pelvic fluid, and/or pelvic fractures (Figures 62-19 and 62-20). Conventional fluoroscopic cystography has been the gold standard in evaluation of bladder injury; however, the technique is time consuming, may require transfer of an acutely injured patient from the CT suite to the fluoroscopy table and may be limited by overlying fracture fragments or fixation devices.<sup>42</sup> Several studies have shown equivalence of CT cystography and conventional fluoroscopic cystography in the detection of bladder rupture with diagnostic accuracy at or near 100%.<sup>42-44</sup>



Figure 62-19 Computed tomography cystogram shows a right posterolateral bladder rupture with extravasation of contrast material into the extraperitoneal space on axial (A), coronal reformatted (B), and sagittal reformatted (C) images.



**Figure 62-20** Unenhanced supine (A) and delayed contrast-enhanced prone (B) computed tomography (CT) images of the bladder show a 4.0 × 1.8 × 3.5-cm transitional cell carcinoma arising from the superolateral bladder wall on the right. Note the layering of unopacified and opacified urine in the bladder. After transurethral resection of the tumor and instillation of intravesical chemotherapy, the patient developed cystitis and a bladder rupture along the anterolateral wall on the right. Contrast-enhanced axial (C) and coronal reformatted (D) CT images and small field-of-view delayed phase (E) CT image show thickening of the bladder wall with a discrete disruption of the bladder wall. Owing to layering of contrast material in the bladder, contrast extravasation is not demonstrated. CT cystography or prone imaging may have better demonstrated extraperitoneal leak of opacified urine.

As with conventional cystography, accurate detection of bladder injury requires adequate distention of the bladder with 300 to 400 mL of dilute contrast media (typically 2% to 4% weight per volume).

If urethral injury is suspected that precludes placement of a Foley catheter, evaluation with retrograde urethrography followed by conventional cystography would likely be most efficient.<sup>44</sup>

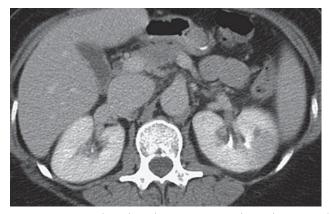
In cases of bladder rupture, CT cystography shows leakage of contrast material into the intraperitoneal space (surrounding pelvic bowel loops, between mesenteric folds, or within paracolic gutters), and/or into the extraperitoneal space (in the perivesical space or dissecting along fascial planes into the abdominal wall, pelvic sidewalls, or into the scrotum), or both.<sup>45</sup>

#### Trauma

CT is the imaging modality of choice in the setting of blunt or penetrating renal trauma because it is more sensitive and specific than IVP or ultrasonography.46-48 Renal injuries demonstrated on CT may be categorized according to radiologic classification or trauma surgical classification systems. Most renal injuries are minor and include renal contusions, minor lacerations (involve cortex alone), subcapsular hematomas, and small subsegmental renal infarctions. More significant injuries include major lacerations that extend into the medulla or collecting system, with or without urinary extravasation, and segmental renal infarcts. Catastrophic renal injuries include shattered kidney (multiple deep lacerations) or renal pedicle injury leading to renal devascularization (i.e., main renal artery avulsion or intimal injury leading to distal thrombosis). Finally, CT can demonstrate avulsion or laceration of the ureteropelvic junction with urinary extravasation.<sup>46</sup>

#### Infection

Urinary tract infection is the most common urologic problem. Infections are typically uncomplicated and confined to the urinary bladder, most commonly secondary to *Escherichia coli*. Routine clinical imaging is not necessary for uncomplicated infections. However, in cases of suspected bacterial pyelone-phritis that is refractory to an initial antibiotic course, CT may be warranted to exclude serious complications. In suspected pyelonephritis, a standard nephrographic phase CT scan is sufficient to make the diagnosis (Figure 62-21). CT findings of



**Figure 62-21** Focal pyelonephritis. Contrast-enhanced computed tomography image shows an ill-defined focal hypodensity in the interpolar region of the left kidney. Occasionally, focal pyelonephritis may be mistaken for an infiltrative renal mass.

pyelonephritis include enlarged kidney(s), striated or delayed nephrogram, delayed excretion into the collecting system, and dilation and effacement of the collecting system.<sup>49</sup>

# **Key Points**

- In renal mass characterization, unenhanced CT is used to detect calcification. Dynamic contrast-enhanced scanning is necessary to evaluate tumor vascularity as well as complications of renal tumors, such as renal vein thrombosis or invasion of the collecting system.
- CT cystography is nearly 100% accurate in detection of bladder injury but requires adequate bladder distention with instillation of 300 to 400 mL of 2% to 4% iodinated contrast material.

# Magnetic Resonance Imaging

# **TECHNICAL ASPECTS**

MRI of the kidneys and urinary tract can be arbitrarily divided into morphologic MRI of the upper urinary tract, ureters, and bladder and MR urography, which consists of MR techniques designed to optimize assessment of the collecting systems and urothelium.

MRI is better than CT for several aspects of the staging of RCC, including evaluating the renal vein and inferior vena cava for tumor involvement and differentiating between tumor and perinephric fat, renal sinus, or collecting system.

Patients with von Hippel-Lindau disease or tuberous sclerosis can be followed with yearly MRI instead of CT, reducing their exposure to ionizing radiation.<sup>50</sup>

Potential problems with MRI include imaging of patients who are unable to breath-hold (e.g., patients in intensive care units) are not ideal candidates for MRI because motion artifact from breathing limits image interpretation. Modern MDCT scanners with subsecond x-ray tube rotation times are less prone to motion artifacts.<sup>50</sup>

The presence of certain ferromagnetic implants or foreign bodies or pacemakers is a contraindication to MRI but not CT.<sup>50</sup> Finally, the discovery of nephrogenic systemic fibrosis, also known as nephrogenic fibrosing dermopathy, and its relationship to administration of gadolinium in patients with renal insufficiency makes the relative advantages of MRI over CT in patients with renal failure less clear.

# Morphologic Magnetic Resonance Imagine of the Upper Urinary Tract, Ureters, and Bladder

Complete MRI evaluation of the kidneys and upper urinary tract includes assessment of the renal vasculature, renal parenchyma, and urinary collecting system. A torso phased-array coil is used to maximize signal-to-noise ratio. Unenhanced breathhold axial gradient echo T1-weighted sequences are typically performed with in-phase and opposed-phase images. Axial and/ or coronal breath-hold fat-suppressed T2-weighted sequences are performed using the fast spin echo technique. Fat-suppressed gradient echo T1-weighted images are performed before and dynamically after gadolinium administration. Images are obtained in the angiographic phase (15 to 25 seconds), corticomedullary phase (30 to 50 seconds), nephrographic phase (80 to 120 seconds), and delayed/excretory phase (3 to 5 minutes).

# Magnetic Resonance Urography

The two most common techniques described are static fluid MR urography and excretory MR urography.

Static fluid MR urography uses T2-weighted sequences, in which fluid shows as high signal intensity. This technique is therefore ideal for patients with dilated collecting systems. Breath-hold T2-weighted MR urograms can be obtained with thick-slab single-shot fast spin echo techniques or thin-section techniques. Thin-section data sets that subsequently can be used to create maximum intensity projection images of the urinary tract in its entirety can be acquired by three-dimensional (3D) respiratory-triggered sequences. This technique also can be used to obtain cine loops, which are helpful in depicting stenoses of the urinary tract. A disadvantage of this technique is that any fluid-filled structure can interfere with the images because the T2 weighting is not specific for urine. Intravenous rather than oral hydration before imaging may help avoid this potential pitfall. Postprocessing techniques can be used to exclude other fluid-containing structures.5

Excretory MR urography uses an intravenously administered gadolinium-based contrast agent, with imaging of the collecting systems during the contrast excretory phase. Diuretics improve ureteral distention as well as dilution and distribution of the contrast agent. The 3D T1-weighted gradient echo sequences are the primary means of imaging. Fat suppression better outlines the ureters.<sup>51</sup>

# PATHOPHYSIOLOGY AND PATHOLOGY

Renal MRI has significant roles in the characterization of solid renal masses, the staging of RCC, and the evaluation of cystic renal masses.

# SOLID MASS CHARACTERIZATION

Two key features to assess when evaluating solid renal lesions are the presence or absence of fat and the presence or absence of contrast enhancement.

Macroscopic fat is hyperintense on T1-weighted images and demonstrates loss of signal on fat-suppressed images. In-phase and out-of-phase imaging is another way to identify macroscopic fat. On out-of-phase images there is an India ink artifact at the interface of fat with fluid or soft tissue. Loss of signal on out-of-phase images does not support the presence of macroscopic fat. Rather, it indicates the presence of intracellular or intravoxel fat. Macroscopic fat within a renal lesion is virtually pathognomonic for angiomyolipoma.<sup>50</sup>

Subtraction techniques are helpful in identifying enhancement in lesions that are inherently T1 hyperintense by subtracting out or removing the preexisting T1 hyperintense signal. In such lesions, the presence of any signal on subtraction images indicates enhancement (Figure 62-22).<sup>52</sup>

RCC has a variable appearance on MRI, given its multiple histologic features and variable presence of necrosis, hemorrhage, or intratumoral lipid. These carcinomas most commonly are hypointense or isointense to renal parenchyma on T1-weighted images, are heterogeneously hyperintense on T2-weighted images, and enhance with intravenous contrast administration, although variability in appearance is not uncommon.<sup>50</sup>

#### Staging of Renal Cell Carcinoma

The main advantages of MRI in staging of RCC over CT are better detection of tumor thrombus because of flow sensitivity and better tissue contrast, which allows for better detection of adjacent organ invasion or involvement of perinephric fat (Figure 62-23). Nodal disease is characterized equally well with MRI and CT (Figure 62-24). Adenopathy is best seen on T1-weighted imaging because lymph nodes stand out on a background of fat, which is bright on these images.<sup>50</sup>

#### Cystic Mass Evaluation

**Simple Cysts.** Renal cysts are the most common renal mass in the adult patient. MRI is not indicated for evaluation of a simple cyst diagnosed on ultrasonography or CT. Simple cysts are homogeneously T2 hyperintense and T1 hypointense on unenhanced images. The cyst wall is thin and imperceptible.

**Complex Cysts.** Often, a complicated cyst can be difficult to distinguish from a cystic or necrotic RCC on ultrasonography or noncontrast CT. Careful assessment for the presence of enhancing tissue in the mass is essential, because it may indicate a malignant lesion. Enhancement may be obscured on CT if there is calcification within a renal mass. In contrast, MRI is not sensitive for detecting calcification, which can be advantageous because enhancement is not obscured by the dense calcification and associated streak artifact seen on CT.<sup>50</sup>

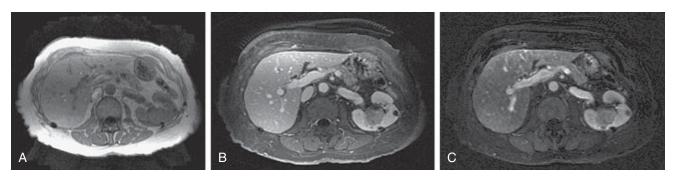
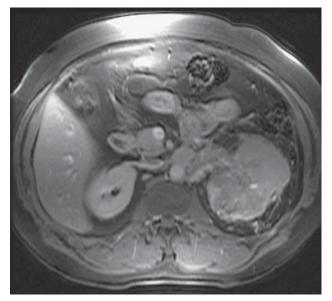


Figure 62-22 A, T1-weighted magnetic resonance image demonstrates an isointense to slightly hyperintense mass in the left kidney. B, After administration of gadolinium, this mass is hypointense to renal parenchyma and the presence of enhancement is not clear. C, Subtraction image demonstrates the presence of signal within the mass, consistent with enhancement.



**Figure 62-23** Large heterogeneous mass in the left kidney (renal cell carcinoma) with tumor thrombus extending into the left renal vein.

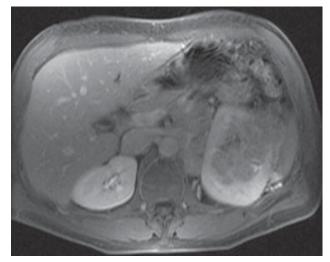


Figure 62-24 Large heterogeneous mass (renal cell carcinoma) with extensive left retroperitoneal adenopathy.

Signal characteristics of a cyst vary with the presence of protein or hemorrhage, which cause T1 shortening and variable degrees of T1 hyperintensity. On T2-weighted images, hemorrhagic cysts may appear more hyperintense than solid RCCs. RCCs may contain hemorrhagic areas.<sup>50</sup>

# Evaluation of the Urinary Tract and Urothelium With Magnetic Resonance Imaging Urography

**Stone Detection.** Urinary tract calculi typically appear as signal voids on T1- and T2-weighted sequences. On MR urography, they appear as filling defects, although this is not specific because tumor and blood clots may have a similar appearance. Blood clot may show high signal components on unenhanced T1-weighted images, which may allow differentiation from calculi. Tumors typically show contrast enhancement as opposed

to calculi, which do not. Secondary findings of urolithiasis include signs of urinary obstruction: the presence of perinephric fluid on T2-weighted images and dilation of the collecting system proximal to the stone.<sup>51</sup>

**Noncalculous Causes of Urinary Tract Obstruction.** MR urography is more sensitive and specific than CT for causes of urinary tract obstruction not related to stones. Benign causes include inflammatory strictures, infection, postradiation or postsurgical changes, and extrinsic compression. Benign strictures are smoothly tapering and do not have an associated soft tissue mass.

Neoplastic causes of urinary tract obstruction may be benign or malignant. When assessing for neoplastic obstruction, it is important to include sequences to evaluate the soft tissues as well as urographic sequences. Most neoplasms enhance after contrast agent administration.

Most urothelial malignancies are TCCs. Proximal ureteral dilatation with a goblet sign (cup-shaped collection of contrast agent just distal to an intraluminal ureteral lesion) may be present with ureteral TCC. TCC is often multifocal; therefore, thorough evaluation of the entire urinary tract is imperative. Bladder, cervical, and prostate cancer are also common causes of malignant ureteral obstruction.<sup>51</sup>

**Congenital Anomalies.** MR urography can be used to evaluate patients with congenital urologic anomalies such as renal duplication, absent or abnormally positioned kidney, ureteropelvic junction obstruction, or ureteral anomalies. The lack of ionizing radiation with MR urography makes the technique useful in the pediatric population.<sup>51</sup>

# Evaluation of the Bladder

**Magnetic Resonance Imaging of Bladder Cancer.** TCC of the bladder is the most common genitourinary malignancy and accounts for more than 90% of bladder cancers in the United States (Figure 62-25). Other histologic types of bladder cancer include squamous cell carcinoma (more common in areas with endemic schistosomiasis), adenocarcinoma, and rare sarcomas. Metastatic disease and lymphoma of the bladder are uncommon.

Bladder TCC is staged using the tumor, node, metastasis (TNM) classification. Bladder biopsy specimens may not be accurate in staging the lesion because samples may not include lamina propria to assess bladder muscle invasion. The crucial distinction to determine for staging purposes is the depth of tumor invasion. Carcinoma in situ (Tis), superficial papillary tumors (Ta), and tumors with submucosal invasion (T1) are considered superficial and treated with transurethral resection. Tumors with superficial (T2a) or deep (T2b) muscle invasion or tumors invading perivesical fat (T3) are most often treated with radical cystectomy with or without neoadjuvant chemotherapy.<sup>53</sup> Patients with adenopathy or metastatic disease are treated with palliative irradiation and chemotherapy. Superficial tumors account for 60% to 80% of bladder cancers, whereas 20% to 40% of cases are muscle invasive (Figure 62-26).<sup>54</sup>

Bladder muscle invasion is the most important finding in staging bladder TCC. The detrusor muscle has low to moderate signal intensity on T1-weighted imaging and low signal intensity on T2-weighted imaging. When compared with detrusor disease, TCC of the bladder is typically isointense on T1-weighted imaging and hyperintense on T2-weighted imaging. Detecting

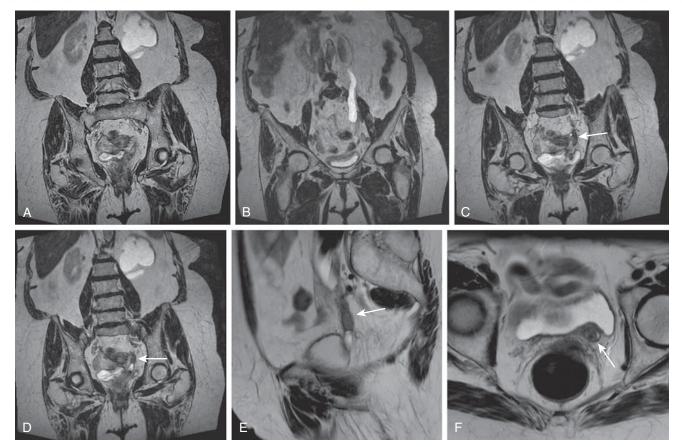
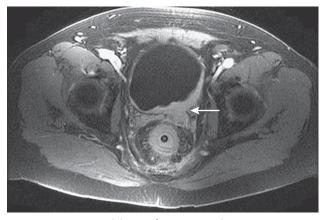


Figure 62-25 Transitional cell carcinoma. Coronal and axial T2-weighted magnetic resonance images demonstrating left hydronephrosis (A) and left hydroureter (B) to the level of the distal ureter, where there is a T2-hypointense mass (C to F, *arrows*).



**Figure 62-26** Postgadolinium fat-suppressed magnetic resonance image demonstrating thickening of the left posterolateral bladder wall with extension of tumor into the left seminal vesicle (*arrow*).

an intact band of detrusor muscle that shows low signal intensity suggests a superficial tumor, whereas a tumor with high signal intensity deep to the low signal intensity of the detrusor muscle is diagnostic of muscle invasion. Papillary configuration of a bladder tumor with a fibrous stalk that shows as low signal intensity on T2-weighted imaging implies a benign course and the absence of muscle invasion in 95% of cases.<sup>55</sup> Dynamic contrast-enhanced MR images show bladder cancer enhancing earlier than normal detrusor muscle or postbiopsy inflammation and granulation tissue.<sup>54</sup> Delayed-phase images should show a continuous enhancing layer of submucosa in superficial tumors.

Seven percent of bladder cancers occur within diverticula. These tumors are particularly challenging for the urologist to identify on cystoscopy. Bladder diverticula are at increased risk for developing carcinoma owing to prolonged exposure of the urothelium to stagnant urine.

Urachal adenocarcinomas may develop in urachal remnants along the course of the bladder dome to the umbilicus. These carcinomas are rare and when they occur are often mucinproducing adenocarcinomas. They appear as T2-hyperintense tumors with contrast enhancement. Dystrophic calcifications may be present, which are better depicted on CT.

**Renal Magnetic Resonance Angiography.** Renal MR angiography is significantly less invasive than conventional angiography for the evaluation of renovascular hypertension and ischemic nephropathy. Renal artery stenosis is the cause of hypertension in 1% to 5% of patients. Approximately 16% of patients with end-stage renal disease have ischemic nephropathy. Renal artery stenosis is caused by atherosclerosis in 75% of cases and affects older patients, whereas fibromuscular dysplasia accounts for 25% of cases and affects younger patients.<sup>56</sup>

#### 744 PART 8 Urogenital Imaging

In renal MR angiography, an intravenous bolus of gadolinium is administered and images are acquired in a series of four to six breath-holds as the contrast agent flows through the arteries and kidneys and is finally excreted. Sensitivity and specificity for detection of renal artery stenosis are 94% and 92%, respectively. Limitations include the diagnosis of fibromuscular dysplasia, susceptibility effects of renal artery stents (associated artifactual signal loss can be misinterpreted as stenosis), overestimation of stenoses with MRI, and difficulty in distinguishing significant renal artery stenosis (which causes renovascular disease) from incidental renal artery atherosclerosis. Evaluation for subtle fibromuscular dysplasia or small artery vascular changes (i.e., in polyarteritis nodosa) is suboptimal with MR angiography owing to limited resolution. Similarly, evaluation of small accessory vessels is limited because the resolution of most MR angiographic techniques is 1.5 to 2.5 mm.<sup>56</sup>

# **Nuclear Imaging**

# **TECHNICAL ASPECTS**

The basis of nuclear medicine imaging is the administration of radioactive materials in tracer concentrations, enabling the depiction of physiologic processes without altering the internal milieu. Several radiotracers and different imaging techniques are used to evaluate the kidneys and urinary tract, providing unique pathophysiologic information. Radionuclide imaging of the urinary tract has become an invaluable asset to measure of renal function, assess collecting system patency and function, monitor the function of renal transplants, and evaluate renovascular hypertension.

# Dynamic Renal Scintigraphy

Multiple radiotracers have been used for dynamic renal scintigraphy, and they are classified in two broad categories—glomerular and tubular—based on their primary mechanism of excretion.

Technetium-99m (<sup>99m</sup>Tc)-labeled diethylenetriaminepentaacetic acid (<sup>99m</sup>Tc-DTPA) is the most commonly available glomerular agent. It can be used to evaluate perfusion and glomerular filtration. <sup>99m</sup>Tc-DTPA assessment of the glomerular filtration rate has been found to closely correlate with inulin clearance. This test can be performed using imaging or by measuring radioactivity in serial blood specimens and calculating the glomerular filtration rate without images of individual renal function. A limitation of <sup>99m</sup>Tc-DTPA imaging stems from its relatively low renal extraction efficiency (only ~20%), which is further decreased in patients with impaired renal function. This results in images with lower contrast compared with tubular agents.

<sup>99m</sup>Tc-mercaptoacetyltriglycine (<sup>99m</sup>Tc-MAG3) is almost exclusively excreted by tubular secretion and currently the radiotracer of choice in dynamic renal scintigraphy. It has a higher extraction fraction (40% to 50%) compared with glomerular agents such as <sup>99m</sup>Tc-DTPA and is less affected by poor renal function. Therefore, it results in images with higher target-tobackground ratios and more reliable quantitative information.

A typical dose of <sup>99m</sup>Tc-MAG3 or <sup>99m</sup>Tc-DTPA in adults is 10 millicuries (mCi) (370 megabecquerels [MBq]), administered intravenously. During and after the bolus administration of the radiotracer, serial images are acquired in the posterior view with the gamma camera's field of view covering both kidneys and the urinary bladder. In the evaluation of a pelvic renal transplant, anterior images are acquired.

During the initial part of the study, the blood flow phase, rapid (dynamic) images are acquired at 1 to 3 s/frame for 1 minute. This is followed by the functional and drainage phases that comprise 10- to 30-second images for at least 20 minutes. Regions of interest are drawn over each kidney, and timeactivity curves are generated, reflecting the arrival of the radiotracer into and its excretion from the kidney. This allows estimates of blood flow, differential kidney function, and excretion. There are different approaches regarding timing of furosemide administration relative to radiotracer injection, with variation between different centers based on local protocols.

## Renal Cortical Scintigraphy

Renal cortical scintigraphy is commonly performed in infants and children to evaluate for acute pyelonephritis and renal scarring. Although tubular agents, such as <sup>99m</sup>Tc-MAG3, can provide information about the renal cortex, <sup>99m</sup>Tc-dimercaptosuccinic acid (<sup>99m</sup>Tc-DMSA) is the preferred tracer for renal cortical scintigraphy. The activity administered is 1 to 5 mCi (37 to 85 MBq). Approximately half of the tracer administered binds to the proximal renal tubules, and the remainder is excreted in the urine. Renal tubular acidosis decreases binding of the radiotracer to the cortex and results in increased excretion.

At 2 to 3 hours after the radiotracer administration, static images are acquired in posterior and posterior oblique views using parallel hole or pinhole (preferred) collimators. Regions of interest are drawn around each kidney, and differential renal cortical uptake is estimated. Patients should be able to remain still during that period; sedation is occasionally required in younger patients. Delayed or post-furosemide images may be helpful in cases of hydronephrosis, because increased radiotracer accumulation in a dilated pelvis may falsely shift the differential function toward the hydronephrotic kidney.

#### Radionuclide Cystography

Radionuclide cystography is indicated to diagnose and observe patients with vesicoureteral reflux (VUR). Two different techniques are described: direct (or retrograde) and indirect (or antegrade).

Indirect radionuclide cystography has the advantage of not requiring bladder catheterization. In this study, <sup>99m</sup>Tc-MAG3 (or <sup>99m</sup>Tc-DTPA) is administered intravenously, and when the patient is ready to void, dynamic images are acquired in the posterior position, starting before urination and continuing until micturition is complete. Standard dynamic renal scintigraphy can be obtained at the same time, giving information about renal perfusion and differential function. However, indirect radionuclide cystography requires the patient to be toilet trained and can only identify reflux in the voiding phase, factors that have limited the use of this technique.

In direct radionuclide cystography, the patient is catheterized and a technetium-based radiotracer (<sup>99m</sup>Tc-pertechnetate, <sup>99m</sup>Tc-DTPA or <sup>99m</sup>Tc-sulfur colloid) is instilled into the bladder until maximum distention. Dynamic images are acquired posteriorly during filling, voiding, and postmicturition phases. Residual urine and reflux volumes can be determined.

# **CLINICAL APPLICATIONS**

#### Dynamic Renal Scintigraphy

Diuretic renal scintigraphy is performed when further evaluating patients found incidentally to have a dilated collecting system and evaluate the clinical significance of a known partial obstruction (in patients with stenosis of the ureteropelvic junction or pelvic tumor). Because obstruction is a functional disturbance, diuretic renal scintigraphy is uniquely suited to provide this information.

**Renal Obstruction.** In normal dynamic renal scintigraphy, activity reaches the kidneys within 1 to 3 seconds after the bolus in the abdominal aorta passes the renal arteries. The radiotracer is then extracted from the circulation, with normal kidney parenchymal activity peaking at 3 to 5 minutes and then rapidly declining. The differential kidney function is calculated during this period. Split renal function of  $50\% \pm 5\%$  is considered normal (Figure 62-27). Estimates using the geometric mean of anterior and posterior images are more accurate than measurements using counts from just posterior images. Time-activity curves from each kidney should be symmetric with regard to shape and slope. Slight differences can be seen in normal variation in renal size or depth, patient positioning, or differences in region of interest placement.

**Renal Vascular Hypertension.** Angiotensin-converting enzyme inhibitor (ACEI) renography is indicated for excluding renovascular hypertension as a secondary cause of hypertension. A normal study in the presence of an ACEI has a high negative predictive value. It provides physiologic information, based on captopril-mediated fall in filtration pressure, amplifying differences in renal perfusion. ACEI renography is useful in predicting which patients with renovascular hypertension will respond to revascularization.<sup>57</sup>

Renal insufficiency and bilateral renal artery stenosis may cause nondiagnostic ACEI renograms.<sup>58</sup>

**Post–Renal Transplant Evaluation.** Medical and surgical complications of renal transplants can be evaluated with dynamic renal scintigraphy. Anterior images are obtained with the patient supine, because the transplanted kidney is typically

implanted in the iliac fossa. In a normal dynamic renal transplant scintigram, the radiotracer bolus should be visualized in the kidney at the same time as in the iliac vessels. Radiotracer excretion in the bladder in 4 to 8 minutes indicates normal excretion.

Hyperacute rejection manifests in the immediate postoperative period, with essentially absent perfusion to the donor kidney and absence of any appreciable extraction. The transplanted kidney during the functional and excretion phases is seen as a photopenic defect. Acute and chronic rejection will manifest in a relatively similar pattern, with decreases in both perfusion and function, although in a milder and more gradual manner.

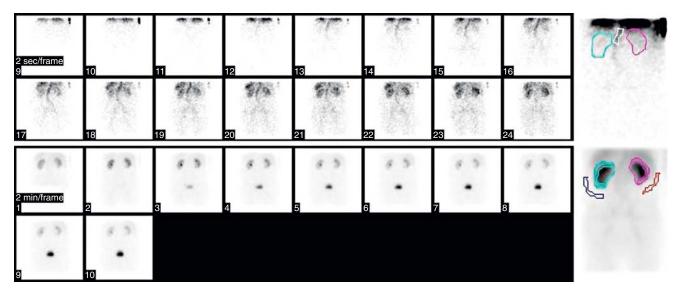
Acute tubular necrosis results from a prolonged graft ischemic time between harvesting and implantation and occurs frequently (Figure 62-28). It manifests in the first 3 to 4 days after surgery, gradually resolving in the following weeks. Scintigraphic findings of acute tubular necrosis reveal normal or mildly decreased perfusion, relatively preserved parenchymal extraction of the radiotracer, and significantly decreased or absent excretion.

Dynamic renal scintigraphy also can detect postsurgical complications such as urinomas, hematomas, and ureteral obstruction. Urinomas occur early in the postoperative period and result from leakage in the vesicoureteral anastomosis. Scintigraphic images reveal free radioactivity present in the peritoneal space.

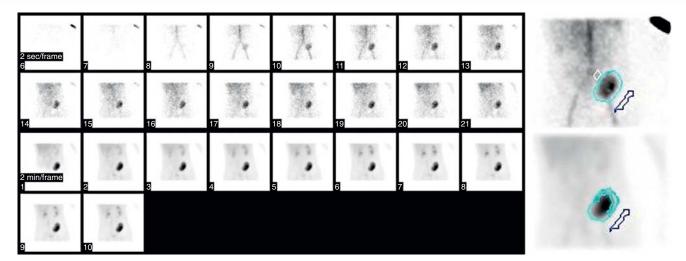
Ureteral obstruction in the transplanted kidney is evaluated in a fashion similar to that in the native kidneys, with the use of diuretics. It will manifest as accumulation of the radioactivity in the collecting system not responding to diuretic administration.

# Renal Cortical Scintigraphy

Renal cortical scintigraphy is a highly sensitive and reproducible method to detect focal parenchymal lesions. The defects seen on <sup>99m</sup>Tc-DMSA scans in patients with chronic renal scars and acute



**Figure 62-27** Dynamic renal scintigraphy with mercaptoacetyl triglycine (MAG3) in a patient with normal renal function. Upper row of images shows prompt and symmetric flow of the radiotracer to both kidneys. Lower row reveals normal extraction and excretion of the radiotracer. The split function is 50%/50%.



**Figure 62-28** Mercaptoacetyl triglycine (MAG3) diuretic renal scintigraphy in a patient with high-grade right-sided obstruction. **A**, Initial images demonstrate decreased flow to the right kidney. Functional images reveal residual extraction, but no excretion is appreciated in the right kidney. **B**, Post-furosemide images demonstrate continued extraction and no excretion. The right renal pelvis, filled with nonradioactive urine, is seen as a photopenic defect.

pyelonephritis are typically described as having sharper edges in the former and more diffuse margins in the latter. Persistent defects on <sup>99m</sup>Tc-DMSA scans 6 months after treatment of a urinary tract infection are consistent with renal scarring.

The addition of single-photon emission computed tomography (SPECT) increases sensitivity, at the expense of decreasing specificity and interobserver reproducibility, and is not proved to have incremental clinical benefit over planar images.<sup>59,60</sup> A normal <sup>99m</sup>Tc-DMSA scan demonstrates uniform radiotracer activity throughout the renal cortex. <sup>99m</sup>Tc-DMSA should not be seen in the medulla and the collecting system.

**Pediatric Urinary Tract Infections.** The current guidelines of the American Academy of Pediatrics for the evaluation of children younger than 2 years of age with a first urinary tract infection include, in addition to antibiotic prophylaxis, further evaluation with imaging studies, renal ultrasonography, and either voiding urethrocystogram (VCUG) or radionuclide cystography.<sup>61</sup>

**Acute Pyelonephritis and Renal Scarring.** In patients with clinically suspected acute pyelonephritis, 65% to 92% may have an abnormal <sup>99m</sup>Tc-DMSA scan,<sup>62-64</sup> with known reflux being a major risk factor.

Renal scarring, also termed reflux nephropathy, is associated with the development of hypertension. In otherwise healthy children with newly diagnosed hypertension, abnormal <sup>99m</sup>Tc-DMSA scans were found in 21% of the cases. The North American Pediatric Renal Transplant Cooperative Group found that reflux nephropathy was involved in 5.7% of the cases of end-stage renal disease.<sup>65</sup>

#### Radionuclide Cystography

Radionuclide cystography is indicated to detect or exclude VUR. It has greater sensitivity because images are acquired for a longer period and a lower volume of reflux is required for detection, compared with VCUG. It has a much lower radiation burden to the pelvic organs and gonads, on the order of onetwentieth the radiation exposure of VCUG. However, in boys, VCUG is required as an initial study to exclude posterior urethral valves as the cause of reflux. Direct radionuclide cystography requires bladder catheterization and therefore carries a risk for infection.

VUR is well described in the pediatric population and less commonly found in adults. It occurs in approximately 5% of children and up to 10% of adults with end-stage renal disease.<sup>66,67</sup> Radionuclide cystography and VCUG are the two most commonly used tests for the diagnosis of VUR. VCUG provides a greater anatomic detail than radionuclide cystography and has a standardized international grading system, grades I to V.

In grade I, reflux is confined to the ureter. In grade II, urine backs up into the ureter, renal pelvis, and calyces, which appear morphologically normal. In grade III, in addition to reflux there is mild dilatation of the ureter and renal pelvis, with mild blunting of the calyces. In grade IV, there is moderate dilatation of ureter and pelvis and moderate blunting of the calyces. In grade V, there is severe dilatation of the collecting system, along with tortuosity of the ureter and severe blunting of calyces.<sup>68</sup> Figure 62-29 shows grade IV reflux on VCUG. Because of the anatomic detail of radionuclide cystography, reflux can be graded only in three levels that correspond to VCUG grade I, II to III, and IV to V, respectively.

Direct radionuclide cystography has a lower anatomic resolution compared with VCUG. On radionuclide cystography, VUR is classified as grade I, grades II to III (Figure 62-30), and grades IV to V. It is a more sensitive method than VCUG.

The major advantages of radionuclide cystography include its higher sensitivity, because of continuous imaging during bladder filling and voiding with less reflux required for visualization, and significantly lower radiation dose, particularly gonadal dose.

## **Key Points**

- <sup>99m</sup>Tc-DMSA scan: Used to confirm diagnosis of acute pyelonephritis and evaluate for renal scarring
- Furosemide renal scintigraphy: Used to search for urinary obstruction

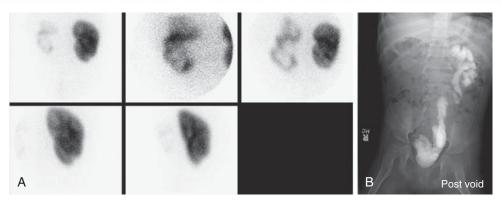


Figure 62-29 A, Dimercaptosuccinic acid scan showing multiple renal cortical defects in an enlarged left kidney. B, The voiding urethrocystogram in the same patient demonstrates high-grade vesicoureteral reflux.

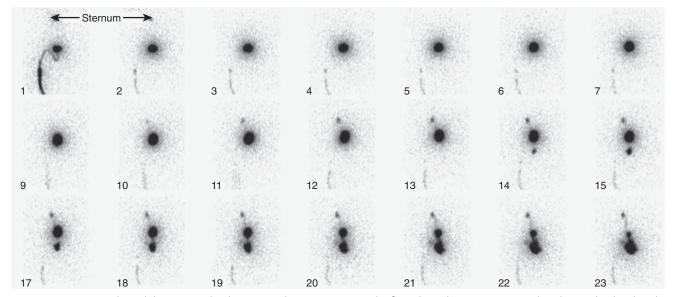


Figure 62-30 Direct radionuclide cystography showing moderate vesicoureteral reflux. The radioactive tracer reaches the renal pelvis, but there is no evidence of pelvicalyceal dilatation. These findings correspond to grades II to III vesicoureteral reflux in the International Reflux Grading System.

## **SUGGESTED READINGS**

- Akbar SA, Jafri ZH, Amendola MA, et al: Complications of renal transplantation. *Radiographics* 25:1335–1356, 2005.
- He W, Fischman AJ: Nuclear imaging in the genitourinary tract: recent advances and future directions. *Radiol Clin North Am* 46:25–43, 2008.

#### REFERENCES

- Rumack CM, Wilson SR, Charboneau JW: *Diagnostic ultrasound*, ed 2, St. Louis, 1998, Mosby, pp 329–392.
- Urban BA, Ratner LE, Fishman EK: Threedimensional volume- rendered CT angiography of the renal arteries and veins: normal anatomy, variants, and clinical applications. *Radiographics* 21:373–386, 2001.
- Bechtold RE, Dyer RB, Zagoria RJ, et al: The perirenal space: relationship of pathologic processes to normal retroperitoneal anatomy. *Radiographics* 16:841–854, 1996.

- Israel GM, Bosniak MA: MR imaging of cystic renal masses. *MRI Clin North Am* 12:403–412, 2004.
- Vaccaro JP, Brody JM: CT cystography in the evaluation of major bladder trauma. *Radiographics* 20:1373, 2000.
- Davidson AJ, Hartman DS: Radiology of the kidney and urinary tract, ed 2, Philadelphia, 1994, WB Saunders, pp 3–20, 64–78, 751–775.
- Assi Z, Platt JF, Francis IR, et al: Sensitivity of CT scout radiography and abdominal radiography for revealing ureteral calculi on helical CT: implications for radiologic follow-up. *AJR Am J Roentgenol* 204:333–337, 2000.
- Levine JA, Neitlich J, Verga M, et al: Ureteral calculi in patients with flank pain: correlation of plain radiography with unenhanced helical CT. *Radiology* 204:27–31, 1997.
- Zagoria RJ, Khatod EG, Chen MYM: Abdominal radiography after CT reveals urinary calculi: a method to predict usefulness of abdominal radiography on the basis of size and CT attenuation. *AJR Am J Roentgenol* 176:1117–1122, 2001.
- Smith RC, Rosenfield AT, Choe KA, et al: Acute flank pain: comparison of non-contrast enhanced CT and intravenous urography. *Radiology* 194:789–794, 1995.
- Kawashima A, Vrtiska TJ, LeRoy AJ, et al: CT urography. *Radiographics* 24:S35–S58, 2004.

#### 748 PART 8 Urogenital Imaging

- Brant WE: *The core curriculum ultrasound*, Philadelphia, 2001, Lippincott Williams & Wilkins, pp 103–151.
- 11. American Institute of Ultrasound in Medicine: AIUM practice guideline for the performance of an ultrasound examination of the abdomen and/ or retroperitoneum, Laurel, MD, 2007, AIUM.
- 12. Middleton WD, Dodds WJ, Lawson TL, et al: Renal calculi: sensitivity for detection with US. *Radiology* 167:239–244, 1988.
- Smith CK, Perrella RR, Kaveggia LP, et al: Detection of renal stones with real-time sonography: effect of transducers and scanning parameters. *AJR Am J Roentgenol* 157:975–980, 1991.
- Boridy IC, Maklad N, Sandler CM: Suspected urolithiasis in pregnant women: imaging algorithm and literature review. *AJR Am J Roent*genol 167:869–875, 1996.
- Malave SR, Neiman HL, Spies SM, et al: Diagnosis of hydronephrosis: comparison of radionuclide scanning and sonography. *AJR Am J Roentgenol* 135:1179–1185, 1980.
- Ellenbogen PH, Scheible FN, Talner LB, et al: Sensitivity of gray scale ultrasound in detecting urinary tract obstruction. *AJR Am J Roentgenol* 130:731–733, 1978.
- 17. Lowe LH, Zagoria RJ, Baumgartner BR, et al: Role of imaging and intervention in complex infections of the urinary tract. *AJR Am J Roentgenol* 163:363–367, 1994.
- 18. Zagoria RJ: *Genitourinary radiology: the requisites*, ed 2, Philadelphia, 2004, Mosby, pp 1–79.
- Helenon O, Rody RE, Correas JM, et al: Color Doppler US of renovascular disease in the native kidneys. *Radiographics* 15:833–854, 1995.
- Soulez G, Oliva VL, Turpin S, et al: Imaging of renovascular hypertension: respective values of renal scintigraphy, renal Doppler US, and MR angiography. *Radiographics* 20:1355–1368, 2000.
- Akbar SA, Jafri ZH, Amendola MA, et al: Complications of renal transplantation. *Radiographics* 25:1335–1356, 2005.
- 22. Brown ED, Chen MY, Wolfman NT, et al: Complications of renal transplant: evaluation with US and radionuclide imaging. *Radiographics* 20:607–622, 2000.
- 23. Albani JM, Ciaschini MW, Streem SB, et al: The role of computerized tomographic urography in the initial evaluation of hematuria. *J Urol* 177:644–648, 2007.
- Chow LC, Kwan SW, Olcott EW, et al: Splitbolus MDCT urography with synchronous nephrographic and excretory phase enhancement. AJR Am J Roentgenol 189:314–322, 2007.
- 25. Dillman JR, Caoili EM, Cohan RH, et al: Detection of upper tract urothelial neoplasms: sensitivity of axial, coronal reformatted, and curved-planar reformatted image-types utilizing 16-row multi-detector CT urography. *Abdom Imaging* 33:707–716, 2008.
- 26. Kawashima A, Vrtiska TJ, LeRoy AJ, et al: CT urography. *Radiographics* 24(Suppl 1):S35–S54, 2004.
- Perlman ES, Rosenfield AT, Wexler JS, et al: CT urography in the evaluation of urinary tract disease. J Comput Assist Tomogr 20:620–626, 1996.
- Fielding JR, Silverman SG, Rubin GD: Helical CT of the urinary tract. AJR Am J Roentgenol 172:1199–1206, 1999.
- Roth CS, Bowyer BA, Berquist TH: Utility of the plain abdominal radiograph for diagnosing ureteral calculi. Ann Emerg Med 14:311–315, 1985.
- Smith RC, Verga M, McCarthy S, et al: Diagnosis of acute flank pain: value of unenhanced helical CT. AJR Am J Roentgenol 166:97–101, 1996.
- 31. Sourtzis S, Thibeau JF, Damry N, et al: Radiologic investigation of renal colic: unenhanced

helical CT compared with excretory urography. *AJR Am J Roentgenol* 172:1491–1494, 1999.

- 32. Tack D, Sourtzis S, Delpierre I, et al: Low-dose unenhanced multidetector CT of patients with suspected renal colic. *AJR Am J Roentgenol* 180:305–311, 2003.
- Bellin MF, Renard-Penna R, Conort P, et al: Helical CT evaluation of the chemical composition of urinary tract calculi with a discriminant analysis of CT-attenuation values and density. *Eur Radiol* 14:2134–2140, 2004.
- Ketelslegers E, Van Beers BE: Urinary calculi: improved detection and characterization with thin-slice multidetector CT. *Eur Radiol* 16:161– 165, 2006.
- Newhouse JH, Prien EL, Amis ES, Jr, et al: Computed tomographic analysis of urinary calculi. *AJR Am J Roentgenol* 142:545–549, 1984.
- Kulkarni NM, Eisner BH, Pinho DF, et al: Determination of renal stone composition in phantom and patients using single-source dualenergy computed tomography. J Comput Assist Tomogr 37:37–45, 2013.
- Jamis-Dow CA, Choyke PL, Jennings SB, et al: Small (< or = 3-cm) renal masses: detection with CT versus US and pathologic correlation. *Radiology* 198:785–788, 1996.
- Prasad SR, Humphrey PA, Catena JR, et al: Common and uncommon histologic subtypes of renal cell carcinoma: imaging spectrum with pathologic correlation. *Radiographics* 26:1795– 1806, 2006.
- Ratner LE, Ciseck LJ, Moore RG, et al: Laparoscopic live donor nephrectomy. *Transplantation* 60:1047–1049, 1995.
- Kawamoto S, Montgomery RA, Lawler LP, et al: Multi-detector row CT evaluation of living renal donors prior to laparoscopic nephrectomy. *Radiographics* 24:453–466, 2004.
- Pollak R, Prusak BF, Mozes MF: Anatomic abnormalities of cadaver kidneys procured for purposes of transplantation. *Am Surg* 52:233– 235, 1986.
- Chan DP, Abujudeh HH, Cushing GL, Jr, et al: CT cystography with multiplanar reformation for suspected bladder rupture: experience in 234 cases. AJR Am J Roentgenol 187:1296–1302, 2006.
- Lis LE, Cohen AJ: CT cystography in the evaluation of bladder trauma. J Comput Assist Tomogr 14:386–389, 1990.
- Peng MY, Parisky YR, Cornwell EE, 3rd, et al: CT cystography versus conventional cystography in evaluation of bladder injury. *AJR Am J Roent*genol 173:1269–1272, 1999.
- Vaccaro JP, Brody JM: CT cystography in the evaluation of major bladder trauma. *Radiographics* 20:1373–1381, 2000.
- Kawashima A, Sandler CM, Corl FM, et al: Imaging of renal trauma: a comprehensive review. *Radiographics* 21:557–574, 2001.
- McAndrew JD, Corriere JN, Jr: Radiographic evaluation of renal trauma: evaluation of 1103 consecutive patients. *Br J Urol* 73:352–354, 1994.
- Morgan DE, Nallamala LK, Kenney PJ, et al: CT cystography: radiographic and clinical predictors of bladder rupture. *AJR Am J Roentgenol* 174:89–95, 2000.
- 49. Craig WD, Wagner BJ, Travis MD: Pyelonephritis: radiologic-pathologic review. *Radiographics* 28:255–277, 2008.
- Bassignani MJ: Understanding and interpreting MRI of the genitourinary tract. Urol Clin North Am 33:301–317, 2006.
- Leyendecker JR, Barnes CE, Zagoria RJ: MR Urography: techniques and clinical applications. *Radiographics* 28:23–48, 2008.

- 52. Hecht EM, Israel GM, Krinsky GA: Renal masses: quantitative analysis of enhancement with signal intensity measurements versus qualitative analysis of enhancement with image subtraction for diagnosing malignancy at MR imaging. *Radiology* 232:373–378, 2004.
- Grossman HB, Natale RB, Tangren CM, et al: Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. N Engl J Med 349:859– 866, 2003.
- Barentsz J: Bladder cancer. In Pollack HM, McClennan BL, Dyer R, et al, editors: *Clinical urography*, ed 2, Philadelphia, 2000, Saunders, pp 1642–1668.
- Lawler LP: MR imaging of the bladder. Radiol Clin North Am 41:161–177, 2003.
- 56. Earls JP: MRI of the abdominal aorta and renal arteries. Advanced MRI From Head to Toe 2002: 1-5. Available at http://www.amdscan .com/education/MRI\_of\_the\_Abdominal \_Aorta\_and\_Renal\_Arteries.pdf. Accessed March 3, 2016.
- Safian RD, Textor SC: Renal-artery stenosis. N Engl J Med 344:431–442, 2001.
- Blaufox MD, Fine EJ, Heller S, et al: Prospective study of simultaneous orthoiodohippurate and diethylenetriaminepentaacetic acid captopril renography. The Einstein/Cornell Collaborative Hypertension Group. J Nucl Med 39:522–528, 1998.
- Craig JC, Irwig L, Ford M, et al: Reliability of DMSA for the diagnosis of renal parenchymal abnormality in children. *Eur J Nucl Med* 27:1610–1616, 2000.
- De Sadeleer C, Bossuyt A, Goes E, et al: Renal technetium-99m-DMSA SPECT in normal volunteers. J Nucl Med 37:1346–1349, 1996.
- 61. Roberts KB: Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management. *Pediatrics* 128:595–610, 2011.
- 52. Jakobsson B, Nolstedt L, Svensson L, et al: 99mTechnetium-dimercaptosuccinic acid scan in the diagnosis of acute pyelonephritis in children: relation to clinical and radiological findings. *Pediatr Nephrol* 6:328–334, 1992.
- Levtchenko EN, Lahy C, Lévy J, et al: Role of Tc-99m DMSA scintigraphy in the diagnosis of culture negative pyelonephritis. *Pediatr Nephrol* 16:503–506, 2001.
- Benador D, Benador N, Slosman DO, et al: Cortical scintigraphy in the evaluation of renal parenchymal changes in children with pyelonephritis. *J Pediatr* 124:17–20, 1994.
- Kohaut EC, Tejani A: The 1994 annual report of the North American Pediatric Renal Transplant Cooperative Study. *Pediatr Nephrol* 10:422–434, 1996.
- 66. Smith J, Stablein D, Munoz R, et al: Contributions of the Transplant Registry: the 2006 annual report of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS). *Pediatr Transpl* 11:366–373, 2007.
- Buckley O, Geoghegan T, O'Brien J, et al: Vesicoureteric reflux in the adult. Br J Radiol 80: 392–400, 2007.
- Lebowitz RL, Olbing H, Parkkulainen KV, et al: International system of radiographic grading of vesicoureteric reflux. International Reflux Study in Children. *Pediatr Radiol* 15:105–109, 1985.



# Benign, Malignant, and Cystic Focal **Renal Lesions**

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This chapter discusses benign and malignant renal lesions (Box 63-1) with a separate note on cystic lesions based on the Bosniak classification.

# **Benign Lesions**

# THE SIMPLE RENAL CYST

# Etiology, Prevalence, and Epidemiology

The incidental detection of cystic renal lesions has dramatically increased with the widespread use of ultrasonography and cross-sectional imaging. As many as 27% of patients older than 50 years have a benign renal cyst on computed tomography (CT) examination.<sup>1,2</sup> Using strict criteria and proper technique, a simple renal cyst can be diagnosed using ultrasonography, CT, and magnetic resonance imaging (MRI).

#### Imaging

Ultrasonography. The sonographic criteria for a simple cyst are well established and include (1) anechoic contents, (2) sharp smooth walls, (3) posterior acoustic enhancement, and (4) lack of internal blood flow.<sup>3</sup>

Computed Tomography. Findings characteristic of a simple renal cyst on CT are (1) water density (-20 to 20 Hounsfield units [HU]) on precontrast images, (2) smooth thin borders with a sharp interface with the adjacent renal parenchyma, and (3) does not enhance with contrast.<sup>3,</sup>

Magnetic Resonance Imaging. A lesion can be categorized as a simple renal cyst on MRI, if the lesion (1) has a signal intensity that follows simple fluid, (2) has smooth thin borders with a sharp interface with the adjacent renal parenchyma, and (3) does not enhance on postcontrast images.<sup>5</sup>

Clinical Implications. A renal cyst that meets each of the criteria for any given imaging modality can be confidently diagnosed as a benign simple cyst and requires no additional evaluation (Figure 63-1).

# ANGIOMYOLIPOMA

# Etiology, Prevalence, and Epidemiology

Angiomyolipoma is a benign renal tumor composed of varying amounts of blood vessels, fat, and smooth muscle. The majority of angiomyolipomas are sporadic (80%) and are typically identified in adults, with a strong female predilection as compared

to men with a ratio as high as 4:1. A smaller percentage of approximately 20% are associated with tuberous sclerosis complex, and it can occur in as many as 55% 75% of patients with it.17

# **Clinical Presentation**

Angiomyolipomas are often an incidental finding on imaging. In a minority of cases, symptoms such as flank pain, nausea, vomiting, and fever are produced by mass effect and intratumoral or perirenal hemorrhage.<sup>6</sup> The risk for bleeding has been reported to be proportional to the size of the lesion once it is larger than 4 cm in diameter.

# Pathophysiology

Isolated angiomyolipomas are usually solitary, whereas angiomyolipomas associated with tuberous sclerosis are often multiple, larger, and bilateral. The majority of these tumors are intraparenchymal, but 25% are exophytic.7

# Pathology

Angiomyolipomas belong to the PEComa family. PEComas are considered a family of perivascular epithelioid cell (PEC) tumors (PEComa) and are essentially mesenchymal neoplasms.<sup>8,9</sup> Abnormalities of the blood vessels associated with angiomyolipomas explain the propensity for these lesions to hemorrhage.

On gross examination, angiomyolipomas are composed predominantly of fat and have a homogeneous yellow appearance. Tumors with more varied proportions of fat, smooth muscle, and blood vessels have a heterogeneous gross pathologic appearance. Angiomyolipomas are often well circumscribed but lack a true capsule.<sup>1</sup>

# Imaging

The imaging appearance of angiomyolipomas varies significantly because of its variable composition and can cause a diverse radiographic appearance of these lesions. However, when a large fat component is present, the imaging characteristics are usually pathognomonic and vice versa.

**Radiography.** Intravenous urography and plain radiography are generally not sensitive techniques for identifying these tumors.

**Computed Tomography.** The value of CT is in identifying any fat content present in these lesions because the presence of intratumoral fat is nearly pathognomonic of angiomyolipoma (Figure 63-2). Lesions with a component demonstrating an

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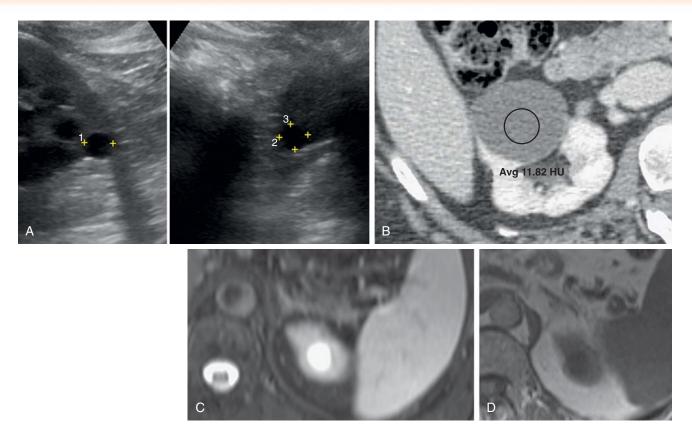


Figure 63-1 Three simple renal cysts are shown on ultrasonography (A), unenhanced computed tomography (B), and T2-weighted (C) and T1-weighted (D) magnetic resonance imaging.

# BOX 63-1 BENIGN AND MALIGNANT FOCAL RENAL LESIONS

#### **BENIGN LESIONS**

- Simple renal cyst
- Oncocytoma
- Angiomyolipoma
- Leiomyoma
- Mesoblastic nephroma
- Adenoma

#### MALIGNANT LESIONS

- Renal parenchymal tumors, including renal cell carcinoma subtypes
- Urothelial carcinoma
- Secondary renal tumors
  Lymphoma and leukemia
- Metastatic lesions
- Pediatric malignant tumors
  - Wilms' tumor
- Nephroblastomatosis
- Clear cell sarcoma
- Rhabdoid tumor



**Figure 63-2** The solid lesion in the left kidney contains a small focus of fat centrally that represents an angiomyolipoma.

Approximately 5% of angiomyolipomas have insufficient fat to be recognized on CT and cannot be distinguished from renal cell carcinoma (RCC).<sup>11</sup> Angiomyolipomas without visible fat appear homogeneous and demonstrate higher attenuation than adjacent normal renal parenchyma (Figure 63-3). These lesions also can demonstrate contrast enhancement because of the relatively larger smooth muscle and vascular components.<sup>11</sup>

Calcification is rarely seen but may be present after hemorrhage. In the presence of significant calcification, the diagnosis of angiomyolipoma should be reconsidered.<sup>11</sup>

attenuation value of less than 20 Hounsfield units (HU) are typical of angiomyolipoma on unenhanced CT. Typically, the lesion is a well-defined, cortical, heterogeneous mass with a fat component. The presence of hemorrhage may cause the lesion to appear poorly defined. Soft tissue attenuation of the lesion may be due to hemorrhage, smooth muscle, or fibrosis.

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CT is useful to evaluate for retroperitoneal hemorrhage that may be associated with angiomyolipomas (Figure 63-4). Blood products may obscure the fat content of the lesion, and in these cases carcinoma cannot be excluded.<sup>10</sup>

**Magnetic Resonance Imaging.** MRI can be used to depict intratumoral fat. Variable areas of high signal are seen on T1- and T2-weighted images owing to the fat content. However, high signal intensity on T1-weighted images also can be seen with high protein content or hemorrhage. In these cases, fat suppression techniques are useful.<sup>3</sup> Israel and coworkers<sup>12</sup> showed that angiomyolipomas also can be diagnosed using opposed-phase chemical shift MRI in which an India ink artifact at the mass/kidney interface or within a renal mass is suggestive of the tumor (Figure 63-5).<sup>12</sup> Clear cell RCC also may demonstrate signal loss on opposed-phase imaging; therefore, this is not a specific finding for angiomyolipoma.<sup>13</sup>

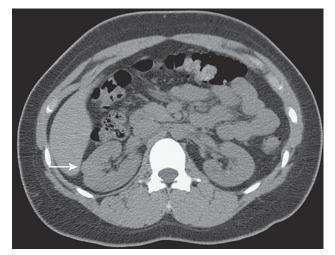
**Ultrasonography.** The typical ultrasound appearance of an angiomyolipoma is a well-defined hyperechoic mass without acoustic shadowing (Figure 63-6). This echogenicity is not necessarily due to the fat component because some lesions that contain little or no fat also can be echogenic.<sup>7</sup> Although RCC

can appear echogenic, angiomyolipomas are more likely to show posterior shadowing.<sup>10</sup> These differences, however, cannot distinguish between angiomyolipomas and carcinoma with the same degree of confidence as CT.

**Nuclear Medicine.** Nuclear medicine has a limited role in the assessment of angiomyolipoma. When surgical management is indicated, it can be used to assess differential renal function.

**Angiography.** Angiography characteristically demonstrates clusters of saccular microaneurysms or macroaneurysms. Other findings on angiography include hypervascularity, venous pooling with a whorled appearance, and lack of arteriovenous shunting (Figure 63-7).<sup>7</sup>

**Imaging Algorithm.** Thin-section noncontrast CT is the preferred and most widely available method for detection of angiomyolipoma because demonstration of fat is pathognomonic. Although MRI can detect fat within an angiomyolipoma, it is not as sensitive as CT for detecting fat in small lesions. Opposedphase chemical shift MRI has been investigated and found to be useful as a method for detecting angiomyolipomas (Table 63-1).



**Figure 63-3** The lesion in the right kidney (*arrow*) is slightly hyperdense to renal parenchyma and at biopsy was proved to be a lipid-poor angiomvolipoma.



**Figure 63-4** Angiomyolipoma is evident in the posterior left kidney. Note associated hemorrhage.

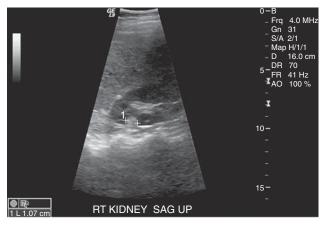


Figure 63-5 Angiomyolipoma. A, T1-weighted magnetic resonance image shows a hyperintense lesion arising from the posterior left kidney. B, Out-of-phase image shows an India ink artifact around the lesion. C, Fat-suppressed image demonstrates loss of signal intensity in the lesion.

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#### Classic Signs: Angiomyolipoma

- Fat-containing lesion on CT and MRI
- Well-circumscribed echogenic mass with posterior shadowing evident on ultrasonography
- Retroperitoneal hemorrhage associated with a renal lesion (usually >4 cm)



**Figure 63-6** Angiomyolipoma. Ultrasound image shows a round echogenic structure in the upper pole of the kidney. *RT*, Right; *SAG*, sagittal.

# Differential Diagnosis

Rare lesions that can contain fat include perirenal fat entrapment or fat necrosis, which can occur in RCC. Other rare entities include myolipoma, liposarcoma, lipoma, oncocytoma, and Wilms' tumor. In the absence of intratumoral fat, the differential diagnosis includes RCC, leiomyosarcoma, and malignant epithelioid angiomyolipoma.

# Treatment

When lesions are small, asymptomatic, and discovered incidentally, no treatment is necessary. Larger lesions if considered at risk for hemorrhage can be prophylactically embolized. In severe acute presentation, total nephrectomy may be required if conservative measures fail.<sup>7</sup>

# What the Referring Physician Needs to Know: Angiomyolipoma

- Most commonly this is an incidental diagnosis in asymptomatic patients.
- Lesions greater than 4 cm have increased risk for hemorrhage.
- These tumors are often multiple and bilateral in patients with tuberous sclerosis.

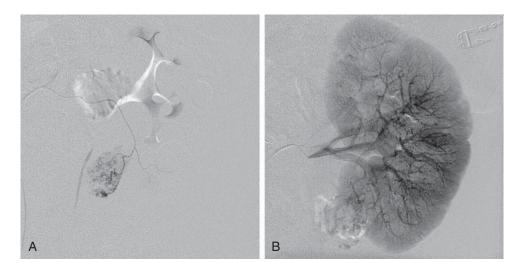


Figure 63-7 Exophytic hypervascular mass in the lower pole with multiple abnormal vessels containing microaneurysms.

Table <b>63-1</b>	Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Angiomyolipoma			
Moda	lity	Accuracy	Limitations	Pitfalls
Radiog	graphy	Poor	Limited sensitivity unless tumor is large and is predominantly fat, which may be seen as radiolucency	Exophytic mass (25%) may not be seen as a space-occupying lesion in the renal sinus
СТ		High	Minimal fat angiomyolipomas Hemorrhage may mask intratumoral fat	Minimal fat angiomyolipomas Rarely, other benign and malignant lesions may contain fat
MRI		High	Failure to detect small lesions or small amount of intratumoral fat because of volume-averaging artifacts and limitations of spatial resolution	Same as for CT Clear cell renal cell carcinoma may demonstrate signal loss on opposed-phase imaging
Ultraso	onography		Cannot assess for actual presence of fat because hyperechogenicity is not necessarily caused by fat	Echogenic renal cell carcinomas

CT, Computed tomography; MRI, magnetic resonance imaging.

# ONCOCYTOMA

# Etiology, Prevalence, and Epidemiology

Oncocytomas arise from the distal tubule or collecting ducts of the kidney. An oncocyte is a large transformed epithelial cell with a finely granular eosinophilic cytoplasm. These cells increase in number with age and are seen in many organs.<sup>14</sup>

Oncocytomas comprise 3% to 7% of all renal neoplasms.<sup>15</sup> Patients typically present in their sixth to seventh decades. The tumors are more common in males than females in a ratio of 2:1.<sup>16</sup>

# **Clinical Presentation**

As many as 75% of oncocytomas are asymptomatic and incidentally diagnosed, but patients may uncommonly present with a flank mass, pain, or hematuria.<sup>14,17</sup>

# Pathophysiology

Most oncocytomas are solitary. Approximately 3% are bilateral and 5% are multicentric within the same kidney. They average 7 cm in diameter and are most often symptomatic when larger than 5 cm.<sup>16</sup>

# Pathology

These tumors are well encapsulated and classically have a central scar. On gross inspection, they are tan-brown similar to the renal cortex and well defined. Necrosis, hemorrhage, and calcification are rare.<sup>16</sup>

#### Imaging

**Radiography.** Plain radiographic findings are nonspecific and include a soft tissue mass distorting the renal silhouette with displacement of the fat planes. Calcification is an uncommon feature.<sup>14</sup>

**Angiography.** The classic findings are a spokewheel arrangement of vessels, homogeneous dense tumor blush during the capillary phase, and sharp demarcation from the kidney. Bizarre neoplastic vessels are absent, in contrast to RCC.<sup>14</sup>

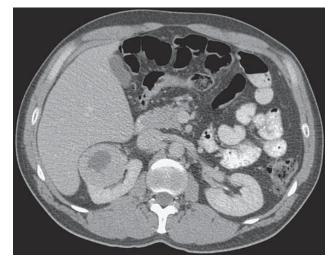
**Computed Tomography.** An oncocytoma typically appears as a well-defined solid renal mass with smooth margins. A central stellate scar is seen in one third of cases, but this is a nonspecific finding that cannot be differentiated from central necrosis in RCC.<sup>18</sup>

On noncontrast CT, oncocytoma is isodense or hyperdense relative to normal renal parenchyma. On the nephrographic phase of contrast-enhanced CT, this tumor is most commonly hypodense to renal parenchyma (Figure 63-8).<sup>14</sup>

**Magnetic Resonance Imaging.** Typically, oncocytoma demonstrates low signal on T1-weighted images and high signal on T2-weighted images. The central scar, if present, shows as a low T1 and a low T2 signal, in contrast to necrosis in RCC, which usually has a low T1 and a high T2 signal.

After administration of a contrast agent, oncocytoma typically demonstrates homogeneous enhancement. The central scar generally does not enhance (Figure 63-9).<sup>14</sup>

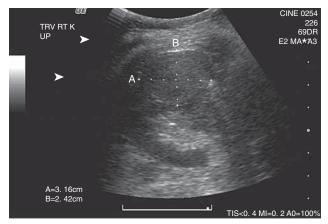
**Ultrasonography.** On ultrasonography, an oncocytoma shows as a well-defined hypoechoic to isoechoic mass (Figure 63-10). If visualized, the central scar may appear echogenic. Doppler



**Figure 63-8** Postcontrast axial computed tomography shows a solid enhancing lesion in the upper right kidney with central hypodense scar.



**Figure 63-9** T1-weighted postcontrast magnetic resonance image shows an enhancing lesion with nonenhancing central scar.



**Figure 63-10** Ultrasound image shows a well-defined solid isoechoic mass. *K*, Kidney; *RT*, right; *TRV*, transverse.

TABLE 63-2Accuracy,	Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Oncocytoma		
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor sensitivity	Cannot distinguish from other space- occupying renal masses	
СТ	Sensitive but not specific	Cannot distinguish from renal cell carcinoma	Central necrosis of renal cell carcinoma can mimic central scar of oncocytoma.
MRI	Sensitive but not specific	Cannot distinguish from renal cell carcinoma	Central scar is not specific for oncocytoma.
Ultrasonography	Poor sensitivity	Small isoechoic lesions may be missed. Larger lesions cannot be distinguished from other renal masses.	
Nuclear medicine	Poor sensitivity		
PET/CT	Poor sensitivity		

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

imaging may show central radiating vessels in a spokewheel distribution.<sup>14</sup>

**Nuclear Medicine.** Nuclear medicine is not routinely used in the evaluation of renal tumors.

**Positron Emission Tomography With Computed Tomography.** PET/CT is not routinely performed for evaluation of oncocytoma. It may show equal to slightly higher uptake of fluorodeoxyglucose (FDG) than normal renal parenchyma.<sup>14</sup>

**Imaging Algorithm.** Contrast-enhanced CT is the examination of choice for evaluating solid renal masses. Evaluation for vascular involvement, lymphadenopathy, and extent of the lesion is possible (Table 63-2).

#### **Classic Signs: Oncocytoma**

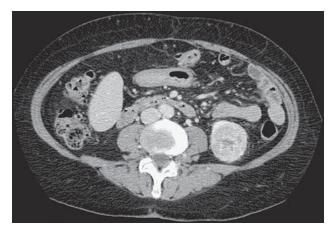
- Central scar on CT and MRI
- Spokewheel pattern of vessels on angiography and Doppler imaging

## Differential Diagnosis

The main differential diagnostic consideration is RCC. Although central scar on CT/MRI and central radiating vessels on angiography and Doppler imaging are suggestive of oncocytoma, RCC cannot be excluded and histopathologic diagnosis is necessary (Figure 63-11).<sup>18</sup>

#### Treatment

If radiographic findings suggest the possibility of oncocytoma, percutaneous biopsy may be considered. It is controversial whether oncocytoma can be reliably differentiated from oncocytic RCC on biopsy. Consequently, many clinicians choose pathologic sampling with partial or total nephrectomy. Many oncocytic RCCs are of low metastatic potential and include granular cell carcinoma, chromophobe RCC, and the eosinophilic variant of papillary RCC. Notably, oncocytoma cannot always be reliably distinguished from oncocytic RCC on pathologic examination.<sup>11</sup>



**Figure 63-11** Contrast enhanced computed tomography shows a well-defined left renal mass with a hypodense scar, found on biopsy to be renal cell carcinoma.

# What the Referring Physician Needs to Know: Oncocytoma

- Statistically, RCC is more common than oncocytoma.
- Because of overlap in imaging and pathologic findings between oncocytoma and RCC, preoperative diagnosis remains difficult.
- Whether oncocytoma can be reliably diagnosed on biopsy is controversial.

# MESOBLASTIC NEPHROMA

# Etiology, Prevalence, and Epidemiology

Mesoblastic nephroma is usually present at birth. It also has been called congenital Wilms' tumor or fetal mesenchymal hamartoma.<sup>18</sup>

This mesenchymal renal tumor is typically benign but may demonstrate aggressive features such as local invasion or recurrence. There is a male predominance with a peak age at presentation of 3 months. Mesoblastic nephroma is the most common benign fetal renal neoplasm.<sup>19</sup>

# **Clinical Presentation**

The most common manifestation is a large, palpable abdominal mass in a neonate. Less common signs and symptoms include hematuria, hypertension, vomiting, and hypercalcemia. Prenatal hydrops and polyhydramnios also may be seen.<sup>19</sup>

# Pathology

On gross examination this tumor has a homogeneous rubbery appearance. The cut surface has a whorled appearance similar to that of uterine leiomyoma. Hemorrhage and necrosis are uncommon. Histologically, there are sheets of fibromatous cells. There is an aggressive variant that is highly cellular with immature mesenchymal cells and a high number of active mitotic figures. This variant has a poorer prognosis and is usually seen in infants and children older than 3 months of age.<sup>19</sup>

# Imaging

**Radiography.** A large mass may be seen involving the entire kidney. Calcification is uncommon, and radiography is not a reliable modality for evaluating for the presence of renal tumors.<sup>19</sup>

**Computed Tomography.** A solid, homogeneous mass arising from the kidney that may replace all or part of the involved kidney. There can be areas of necrosis, although this is uncommon. The tumor does not enhance after contrast agent administration. However, entrapment of nephrons within the mass may cause excretion of contrast agent within the mass. No calcification is evident.<sup>19</sup>

**Magnetic Resonance Imaging.** There is low signal intensity on T1-weighted imaging, and the tumor is typically nonenhancing.<sup>19</sup>

**Ultrasonography.** A well-circumscribed, homogeneous and hyperechoic mass is evident. Concentric hypoechoic and hyperechoic rings are a helpful imaging feature.<sup>19</sup>

**Imaging Algorithm.** Prenatal or pediatric ultrasonography is usually the first imaging study performed when the abdominal mass is palpated. Ultrasonography is easily and widely available; it is inexpensive and involves no ionizing radiation. CT has an important role in evaluating recurrent or metastatic disease.<sup>19</sup>

### **Classic Signs: Mesoblastic Nephroma**

- This homogeneous solid renal mass affects neonates.
- The cut surface resembles that of uterine leiomyoma.

# **Differential Diagnosis**

The differential diagnosis includes hydronephrosis and multicystic dysplastic kidney, the most common causes of unilateral renal enlargement in a neonate, and also Wilms' tumor (different peak age).

# Treatment

Patients with the aggressive variant may benefit from adjunctive chemotherapy or irradiation. Surgical resection is the treatment of choice and is curative.

# JUXTAGLOMERULAR TUMORS

# Etiology

Juxtaglomerular tumors are renin-producing tumors of juxtaglomerular cells.<sup>20</sup>

# Prevalence and Epidemiology

First described by Robertson in 1967, these tumors are also called reninomas. There is a female predominance, and patients are younger than those with essential hypertension.<sup>20</sup>

# **Clinical Presentation**

Patients can present with hypertension with headache, polydipsia, and polyuria. Hypokalemia is due to secondary aldosteronism. Occasionally, acute flank pain, hypotension, and anemia secondary to tumor hemorrhage are noted.<sup>20</sup>

# Pathophysiology

These tumors are solitary and 3 to 7 cm in diameter. Most are located beneath the renal capsule, although they may arise near the renal pelvis. Rarely, they may arise from perinephric tissue, possibly from embryonic rests.<sup>20</sup>

# Pathology

On gross examination they appear tan or gray. They are sharply defined with a pseudocapsule and commonly contain foci of hemorrhage within them. There is an abundance of small vascular channels.<sup>20</sup>

# Imaging

**Radiography.** Lack of calcification makes these tumors difficult to identify on plain radiographs.<sup>20</sup>

**Computed Tomography.** Juxtaglomerular tumors are small and isodense to renal parenchyma on unenhanced CT. Therefore, contrast-enhanced CT should be performed. Despite numerous small vascular channels, these are hypovascular tumors.<sup>20</sup>

**Ultrasonography.** On ultrasonography, an echogenic mass is evident.<sup>20</sup>

# **Differential Diagnosis**

The differential diagnosis includes renal artery stenosis, essential hypertension, and other renin-secreting tumors. One should also consider tumors compressing the renal artery or renal parenchyma (as a cause of hypertension)<sup>1</sup> and RCC and Wilms' tumor.<sup>20</sup>

# Treatment

Surgical excision is curative with subsequent relief of hypertension. $^{20}$ 

### What the Referring Physician Needs to Know: Juxtaglomerular Tumor

• This tumor is a rare, curable cause of hypertension in females.

# ADENOMA

# Etiology

Renal adenomas develop in the proximal convoluted tubule. The cause is unknown.<sup>21</sup>

# Prevalence and Epidemiology

At autopsy, 7% to 22% of patients are found to have renal a denoma. They occur in the same age group as RCC, and there is a male predominance.<sup>21</sup>

#### Clinical Presentation

An adenoma is usually asymptomatic.

### Pathophysiology

Adenomas are small, well-differentiated tumors of the renal cortex.<sup>21</sup>

#### Pathology

Histologically, an adenoma appears similar to low-grade RCC.  $^{\rm 21}$ 

#### Imaging

Adenoma is indistinguishable from RCC on imaging. Most of these lesions are identified at autopsy and are therefore of little clinical significance.<sup>21</sup>

## **Differential Diagnosis**

Adenoma should be differentiated from RCC.

# Treatment

Because many authors think that adenoma is an early RCC that has not yet metastasized, these should be treated as such.<sup>21</sup>

# **Malignant Tumors**

## MALIGNANT RENAL PARENCHYMAL TUMORS, INCLUDING RENAL CELL CARCINOMA AND ITS SUBTYPES

RCC accounts for approximately 3% of all malignancies and about 3% of cancer deaths in the United States.<sup>22</sup> It is by far the most common renal malignancy, accounting for 85% to 90% of cases.<sup>23</sup>

# Etiology

The vast majority of RCCs are sporadic. Environmental risk factors include smoking; unopposed estrogen exposure; obesity (particularly in women); occupational exposure to petroleum products, heavy metals, and asbestos; and hypertension and its treatment.<sup>24</sup>

Patients with acquired cystic kidney disease from chronic hemodialysis are also at increased risk. Hereditary risk factors include von Hippel-Lindau disease, tuberous sclerosis, uterine leiomyosarcoma/RCC syndrome, Birt-Hogg-Dubé syndrome, and familial clear cell carcinoma.<sup>25</sup>

# Prevalence and Epidemiology

RCC typically occurs in people older than the age of 40 with a median age at diagnosis in the mid-60s. It is nearly twice as common in men as in women.

Bilateral or multifocal tumors are seen in approximately 5% of sporadic cases, typically with identical histologic subtype in the multiple tumors.<sup>24</sup>

Renal medullary carcinoma is a rare aggressive subtype of RCC, occurring between 10 and 40 years of age (mean age, 22 years) in patients with sickle cell trait.<sup>26</sup>

#### **Clinical Presentation**

The classic presenting symptoms include hematuria, flank pain, and flank mass.<sup>27</sup> Many tumors are detected incidentally on imaging. Less commonly, patients present with symptoms of metastatic disease, such as bone pain. Patients also may present with systemic symptoms of malignancy such as fatigue, weight loss, and fever. A well-described presentation in men is new unilateral (usually left) varicocele secondary to compression or obstruction of the ipsilateral renal vein by tumor or thrombus. RCCs can secrete a variety of hormones, including renin, erythropoietin, parathyroid hormone, prolactin, gonadotropin, or adrenocorticotropic hormone, resulting in a paraneoplastic syndrome. Because of the increased use of cross-sectional imaging, up to 60% of RCCs are now detected incidentally.<sup>28</sup>

#### Pathophysiology

RCCs arise from the renal tubular epithelium of the renal cortex.

#### Pathology

Grossly, RCCs are expansile, spherical masses. They are usually well marginated and distort the normal renal contour. Rarely, RCC may show an infiltrative growth pattern more typical of urothelial neoplasms.

RCCs are classified by the Heidelberg system, which describes common, conventional, or clear cell RCC (75%), papillary or chromophilic RCC (10%), chromophobe RCC (5%), collecting duct (Bellini duct) carcinoma (1%), and rare unclassified tumors.<sup>29</sup> Medullary carcinoma of the kidney is a rare aggressive subtype of collecting duct carcinoma with an infiltrative growth pattern originally described in young patients with sickle cell trait.

These subtypes carry important prognostic implications. Clear cell RCC accounts for 90% of cases with metastatic disease. Papillary RCC has less metastatic potential, and the chromophobe subtype has the least metastatic potential and best prognosis. The 5-year survival of papillary and chromophobe subtypes (80% to 90%) is significantly higher than for clear cell subtype (50% to 60%).<sup>24</sup> Papillary carcinomas are often multifocal and bilateral, typically presenting at a small size (~3 cm).

Renal medullary carcinoma is extremely aggressive, and metastases, especially to regional lymph nodes, are commonly present at diagnosis. The mean survival after surgery in these patients is only 15 weeks.<sup>30,31</sup>

RCC is staged using the tumor, node, metastasis (TNM) classification of the American Joint Committee on Cancer or the Robson staging criteria (Table 63-3).<sup>32</sup> Survival is highly correlated with stage. RCC most commonly metastasizes to lung, bone, liver, and brain.<sup>27</sup>

## Imaging

**Radiography.** Conventional abdominal radiography and excretory urography play little role in the modern imaging of RCC. A large renal tumor, particularly one containing calcification, may be detected incidentally on abdominal radiography as an expansile mass (Figure 63-12). Peripheral rim calcification is due to benign cysts in 80% of cases and to RCCs in 20% of cases.<sup>33</sup>

Skeletal plain film imaging may show RCC metastases, which are typically lytic, expansile "bubbly" lesions.

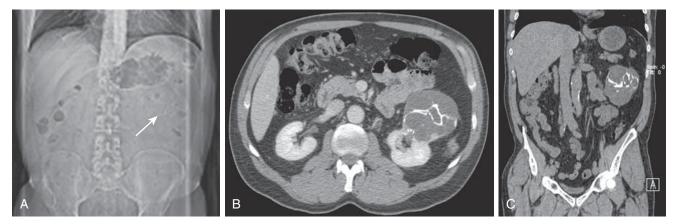


Figure 63-12 Calcified, cystic renal cell carcinoma. A, Scout tomogram from a computed tomography scan shows calcification in the left upper quadrant (*arrow*). Axial contrast-enhanced (B) and coronal unenhanced (C) images show the irregular pattern of calcification associated with this tumor arising from the anterior aspect of the lower pole of the left kidney.

TABLE 63-3	Modified Robson Staging Criteria for Renal Cell Carcinoma	
Stage	Extent of Disease	
1	Confined to renal capsule	
Ш	Extending through renal capsule but confined to Gerota's fascia	
Illa	Regional lymph node involvement	
IIIb	Renal vein or inferior vena cava extension	
IIIc	Regional lymph node involvement and extension into renal vein or inferior vena cava	
IVa	Direct extension beyond Gerota's fascia	
IVb	Distant metastases	

From Motzer RJ, Bander NH, Nanus DM: Renal-cell carcinoma. N Engl J Med 335:865, 1996.

A chest radiograph is usually sufficient in the initial staging of RCC if the primary tumor is small (<3 cm); however, a chest CT should be performed to exclude metastases if the primary tumor is large. In many cases, dedicated CT of the thorax is performed to complete the staging.

**Computed Tomography.** Unenhanced and dynamic contrastenhanced CT scanning of the kidneys with thin-section images are the studies of choice for evaluation of hematuria or suspected renal mass (Table 63-4).

Precontrast images are required to detect renal mass calcification and provide a baseline density measurement to evaluate the degree and pattern of lesion enhancement. Corticomedullary phase images are best for evaluation of lesion vascularity, assessment of vascular invasion, and depiction of renal vascular anatomy for surgical planning. Some lesions, especially smaller lesions or papillary subtype, may be difficult to differentiate from normal renal medulla on corticomedullary phase images. Nephrographic phase images are most sensitive in detection of small lesions. Excretory phase images provide information regarding involvement of the renal collecting system.

On CT, malignant renal parenchymal tumors have a variable appearance. RCC is typically ball shaped and distorts the normal renal shape and contour (Figure 63-13). The majority of lesions

are solid (attenuation value >20 HU) and show significant enhancement ( $\sim$ 15 HU), with 20% of RCCs appearing at least partially cystic (Figure 63-14).

The CT appearance of RCC varies with lesion size and histologic subtype. Large RCCs, most of which are clear cell type, are often heterogeneous. Papillary RCC is typically hypovascular and homogeneous. Chromophobe RCC may show the spokewheel pattern of contrast enhancement classically associated with oncocytoma. Collecting duct carcinoma and renal medullary carcinoma appear infiltrative and heterogeneous because intratumoral hemorrhage and necrosis.<sup>5</sup>

RCC may invade the renal vein, with tumor thrombus sometimes extending into the inferior vena cava. Thrombus in the renal vein in a patient with RCC may represent direct tumor extension or bland thrombus. These entities can sometimes be differentiated by the presence of thrombus enhancement, which denotes tumor thrombus (Figure 63-15).

CT is more than 95% accurate in the detection of RCC. Preoperative CT is more than 90% accurate in staging RCC, with most errors made in the identification of perinephric tumor spread, which distinguishes T2 from T3a lesions and is difficult to detect on CT because perinephric stranding is non-specific.<sup>34,35</sup> The presence of a hypodense, T2-hyperintense pseudocapsule of compressed normal renal parenchyma and fibrous tissue, seen in 66% of cases, is helpful in determining whether the tumor is confined by the renal capsule.<sup>36</sup>

**Magnetic Resonance Imaging.** Although CT is the most commonly used imaging modality in the initial evaluation of the upper urinary tract for hematuria or the characterization of a renal mass, MRI is at least as sensitive for the detection and characterization of renal masses owing to its excellent intrinsic soft tissue contrast. MRI accuracy in the staging of RCC is comparable or superior to that of CT.<sup>37</sup>

RCCs typically are isointense or hypointense to renal parenchyma on T1-weighted images, although they may show some T1 hyperintensity because of proteinaceous material or hemorrhage. RCCs usually demonstrate T2 hyperintensity of variable degree, again depending on the size of a cystic or necrotic component. Papillary RCC and collecting duct carcinoma commonly show T2 hypointensity, and chromophobe RCC may show T2 hypointensity.<sup>26</sup>

TABLE         Accuracy           63-4         Accuracy	, Limitations, and Pitfalls of Modalitie	s Used in Imaging of Renal Cel	Carcinoma
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor (calcification present in 20% of cases)	Insensitive, nonspecific Requires ionizing radiation	Only detects large renal masses that distort the renal contour
Excretory urography	Poor (detects 50% of masses between 2 and 3 cm)	Insensitive, nonspecific Requires ionizing radiation and intravenous contrast	Only detects large renal masses that distort the renal contour
Angiography	Specific data are not available to specify accuracy	Invasive, nonspecific Requires ionizing radiation and intravenous contrast	Only detects large renal masses that have visible neovascularity
СТ	>95% sensitive detection, >90% accurate staging	Requires ionizing radiation and intravenous contrast	Difficult to determine perinephric tumor spread Pseudoenhancement of renal cysts may mimic solid masses Cannot differentiate renal cell carcinoma from benign oncocytoma or "minimal fat" angiomyolipoma
MRI	>95% sensitive, 90% accurate staging Often best at depicting stage accurately	Expensive Lack of availability Requires intravenous gadolinium	Calcification not well seen
Ultrasonography	Useful to diagnose simple cysts and to differentiate cystic versus solid lesions 79% sensitive for masses <3 cm	Limited detection in obese patients Operator dependent	Small lesions may not be detected
Nuclear medicine	Specific data are not available to specify accuracy.	Poor spatial resolution Requires ionizing radiation	
PET/CT	Variable (60% to 94% sensitive)	Requires ionizing radiation Expensive Lack of availability	Urinary excretion of fluorodeoxyglucose may obscure a primary renal tumor

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

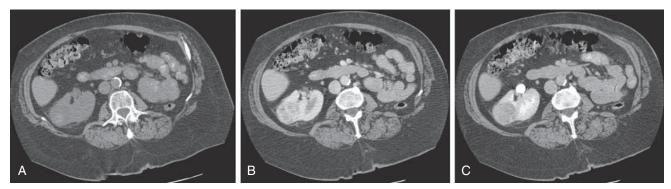


Figure 63-13 Typical computed tomography appearance of a renal cell carcinoma. Axial unenhanced (A), corticomedullary phase (B), and nephrographic phase (C) images show a ball-shaped mass arising from the right kidney. Note the high-attenuation intratumoral hemorrhage on the unenhanced image.

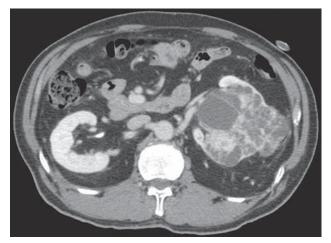
Dynamic gadolinium-enhanced images typically show a hypervascular tumor (Figure 63-16). The presence of enhancement is required to confidently diagnose a solid renal tumor. Both quantitative and qualitative assessments of enhancement on subtraction images have been shown to be accurate.<sup>38</sup>

**Ultrasonography.** Most RCCs are solid, with variable echogenicity. Small RCCs (<3 cm) are more likely to be hyperechoic, which can lead to misdiagnosis as angiomyolipoma. Despite their large size, chromophobe RCCs are homogeneously hyperechoic on ultrasonography (Figure 63-17).<sup>26</sup>

**Nuclear Medicine.** Nuclear scintigraphy is not typically used in the initial evaluation of a renal mass. Because 85% of skeletal

metastases from RCC are symptomatic, bone scintigraphy is not routinely performed in the initial staging.<sup>24</sup> Moreover, because most RCC metastases have little osteoblastic activity, many do not demonstrate radiotracer uptake on bone scintigraphy.

**Positron Emission Tomography With Computed Tomography.** The role of FDG-labeled PET in the detection and evaluation of renal masses has not been fully defined. Normal urinary excretion of FDG may decrease the contrast between FDG-avid tumor and adjacent normal kidney and collecting system, limiting the usefulness of PET in primary tumor detection. Benign renal lesions, such as oncocytoma and inflammation, have been reported to show FDG uptake. In addition, it has been reported that patients with markedly FDG-avid metastases often do not



**Figure 63-14** Contrast-enhanced computed tomography image of a large, partially cystic renal cell carcinoma.

demonstrate FDG avidity of the primary lesion. Thus, FDG-PET may play a role in evaluating distant metastases, in differentiating local tumor recurrence from posttreatment changes, and when conventional imaging of the primary tumor is equivocal.

#### **Differential Diagnosis**

The differential diagnosis of RCC depends on its manifestation. A solid renal mass may represent RCC, oncocytoma, lipid-poor angiomyolipoma, hyperdense renal cyst, focal pyelonephritis, metastasis, or lymphoma. A cystic renal lesion may be an RCC, multilocular cystic nephroma, metastasis, cyst complicated by hemorrhage, or focal infectious or inflammatory lesion (including focal pyelonephritis, abscess, or xanthogranulomatous pyelonephritis). The differential diagnosis of an infiltrative renal lesion includes urothelial neoplasm (transitional cell carcinoma [TCC] or squamous cell carcinoma [SCC]), lymphoma, leukemia, pyelonephritis, infarction, or, rarely, infiltrative RCC.

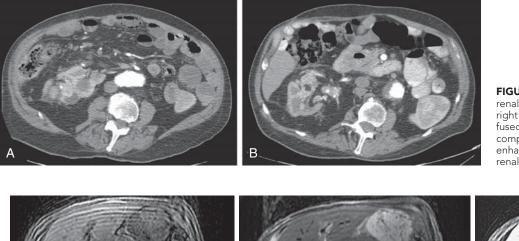


FIGURE 63-15 Tumor thrombus of a renal cell carcinoma arising within the right kidney in a patient with crossed-fused renal ectopia. Arterial phase computed tomography images show enhancement of thrombus in the right renal vein (A) and inferior vena cava (B).

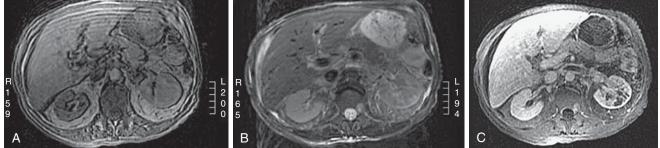
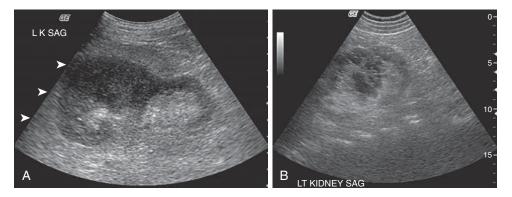


Figure 63-16 Axial T1-weighted (A), T2-weighted (B), and postgadolinium (C) magnetic resonance images of a left renal cell carcinoma. Note the tumor thrombus in the left renal vein on the postgadolinium image.



**Figure 63-17** Sagittal ultrasound images of a solid (A) and partially cystic (B) renal cell carcinoma in the upper poles of the left kidneys in two different patients. *L*, Left; *LT*, left; *K*, kidney; *SAG*, sagittal.

If imaging suggests renal neoplasm, surgery is usually recommended, although the role of percutaneous renal mass biopsy is evolving.<sup>39</sup> Specifically, biopsy may be indicated when secondary renal tumor is a consideration, when RCC subtype influences the choice of systemic therapy, or when ablative techniques are used as definitive therapy for RCC.

# Treatment

**Medical Treatment.** RCC is relatively resistant to radiation therapy and chemotherapy. The key to long-term survival in RCC is prompt tumor detection at an early stage. Advanced RCC carries a poor prognosis, which has changed little in the past few decades.

First-line medical therapy for metastatic RCC consists of the administration of cytokines, specifically interferon-alfa or interleukin-2. These treatments result in a median overall survival of approximately 12 months.<sup>40</sup> There are documented cases of spontaneous regression of RCC in the absence of therapy, but these cases are rare and poorly understood.

**Surgical Treatment.** Surgery remains the definitive therapy for early-stage RCC. Classically, the treatment of choice for RCC has been nephrectomy. Nephron-sparing surgery was reserved for patients with bilateral renal tumors, solitary kidney, or renal insufficiency. However, partial nephrectomy is being performed with increasing frequency to preserve renal function. In patients with small, solitary tumors the local recurrence rate is 2% or less, similar to the percentage of patients developing contralateral RCC after radical nephrectomy.<sup>41</sup> In patients with contraindications to surgery, local ablative techniques are indicated.

#### What the Referring Physician Needs to Know: Malignant Renal Parenchymal Tumors, Including Renal Cell Carcinoma and Its Subtypes

- A chest radiograph is usually sufficient in the initial staging of RCC if the primary tumor is small. If the chest radiograph is abnormal or the primary tumor is large, a chest CT should be performed to exclude metastases.
- Renal biopsy may be performed safely and has an evolving role in the evaluation of indeterminate renal masses.
- Image-guided tumor ablation has become an important alternative treatment for RCC in poor surgical candidates.

# UROTHELIAL CARCINOMAS

Urothelial neoplasms arise from the urothelial lining of the collecting system. Ninety percent of urothelial neoplasms are TCC. Most of the remaining 10% are SCC. TCC accounts for up to 10% of the neoplasms of the upper urinary tract. Of these, approximately 25% directly invade renal parenchyma.

Over 90% of TCCs develop in the urinary bladder and only 5% of urothelial tumors develop in the upper tract.<sup>42</sup> Most upper tract cases occur in the renal pelvis and, less commonly, the infundibulocalyceal portion of the collecting system. In patients with TCC of the renal pelvis, 30% have multicentric disease.<sup>43</sup>

Similarly, SCC of the urothelium is much more common in the bladder than in the upper tract.

# Etiology

Risk factors for TCC include advanced age, male gender, and smoking. Multiple chemical carcinogens are also associated with TCC, including aniline, benzidine, aromatic amine, azo dyes, cyclophosphamide and its metabolites, and heavy caffeine intake.<sup>43</sup> Analgesic abuse predisposes to TCC, as does urinary stasis. Other risk factors include Balkan nephropathy, ureteral pseudodiverticulosis, and the hereditary nonpolyposis colon cancer syndromes.<sup>42</sup> SCC of the urothelium occurs in patients with chronic urothelial irritation, which may be secondary to chronic indwelling Foley catheter, chronic urinary calculi, or schistosomiasis.

#### Prevalence and Epidemiology

TCC is rarely seen in persons younger than age 50, usually occurring in the sixth and seventh decades of life, with a male-to-female ratio of 3:1. Bilateral lesions are seen in 2% to 4% of cases.<sup>43</sup>

#### Clinical Presentation

Gross or microscopic hematuria (75%) is commonly seen in patients with upper tract TCC, and flank pain or acute renal colic is the presenting symptom in approximately 30%.<sup>44</sup> Weight loss and urinary frequency are less common. Of the cases, 10% to 15% are asymptomatic.

Of patients with upper tract TCC, 50% have synchronous or metachronous bladder tumors.<sup>42</sup> Conversely, patients with bladder TCC show upper tract TCC only 0.7% to 4% of the time. In these patients, higher-grade, incompletely excised, or multifocal tumors increase the risk for development of upper tract lesions. Upper tract lesions that develop after cystectomy tend to be more aggressive with worse prognosis; thus, routine postoperative surveillance is performed.

### Pathology

TCC manifests in two morphologic patterns: superficial papillary lesions and invasive tumors. In the kidney, TCC appears as a soft tissue mass centered in the renal sinus. It may invade the renal parenchyma, obliterating the renal sinus fat. Renal TCC and SCC are indistinguishable on imaging.

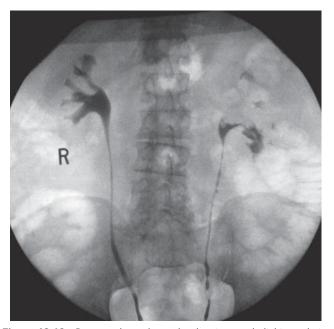
#### Imaging

Radiography. Excretory urography has classically been used for the detection and characterization of upper urinary tract anomalies, although sensitivity is limited, ranging from 43% to 64%.45 TCC appears as a single or multiple filling defects. A classic sign of upper tract TCC is a markedly distended, tumorfilled calyx referred to as an oncocalyx. The surface of the filling defect may be irregular, stippled, or frondlike, depending on the shape of the tumor. Alternatively, TCC may cause obstruction or stenosis of a calvx or infundibulum, resulting in the "phantom calyx" or "amputated calyx," mimicking renal tuberculosis. The characteristic findings of TCC on excretory urography may also be demonstrated with retrograde pyelography (Figure 63-18). In addition, the goblet sign or champagne glass sign of ureteral TCC, first described on retrograde pyelography, may be demonstrated—this is a cup-shaped dilated segment of ureter distal to a polypoid intraluminal filling defect.

**Computed Tomography.** CT urography is the imaging modality of choice for the detection and staging of renal TCC (Table 63-5).

## 762 PART 8 Urogenital Imaging

Renal TCC and SCC appear as central soft tissue masses located in the renal sinus. Although the mass may be difficult to appreciate, it can obscure the normal renal hilar and pyramidal anatomy, displacing normal renal sinus fat to produce the so-called "faceless kidney" (Figure 63-19). TCC in a calyx or



**Figure 63-18** Retrograde pyelography showing urothelial irregularity in the left ureter and a large filling defect in the left renal pelvis, which proved to be transitional cell carcinoma.

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TABLE

renal pelvis appears as a sessile or polypoid filling defect or as diffuse thickening of the urothelial lining (Figure 63-20).

Renal TCC is isodense to slightly hyperdense relative to renal parenchyma on unenhanced CT. It enhances less than normal renal parenchyma. Calcification is uncommon, occurring in less than 2% of cases.

CT is superior to excretory urography in staging renal TCC because extramural extension and regional nodal metastases may be seen.

**Magnetic Resonance Imaging.** Renal TCC shows decreased enhancement compared with renal parenchyma. The lesions are isointense to slightly hypointense on T1-weighted images and isointense to slightly hyperintense on T2-weighted images. Heavily T2-weighted images often show hydronephrosis secondary to obstruction and may demonstrate the tumor as a filling defect (Figure 63-21). The accuracy of MRI in detection of TCC (74% to 88%) is slightly less than CT urography (89% to 100%), and MR urography should be reserved for cases in which CT is contraindicated.<sup>46</sup>

**Ultrasonography.** Ultrasonography is generally insensitive to renal TCC. Infiltrating central tumors show obliteration of the normal echogenic renal sinus fat. Diffuse hydronephrosis or focal caliectasis may be seen secondary to urinary obstruction (Figure 63-22). Generally, TCC is hyperechoic relative to renal parenchyma.

**Positron Emission Tomography With Computed Tomography.** FDG-PET is not well suited to the evaluation of urothelial malignancy owing to the urinary excretion of FDG, which obscures FDG uptake by the primary tumor.

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63-5 Accuracy, Limitations, and Pitfalls of Modalities Used in Imaging of Urothelial Carcinoma			
Modality	Accuracy	Limitations	Pitfalls
Radiography	Poor	Insensitive, nonspecific Requires ionizing radiation	Only detects large renal masses that distort the renal contour Misses anterior, posterior, infiltrative lesions
Excretory urography	Poor	Insensitive, nonspecific Requires ionizing radiation and intravenous contrast	Only detects large renal masses that distort the renal contour
Angiography	Poor	Invasive Nonspecific Requires ionizing radiation and intravenous contrast	Only detects large renal masses that distort the renal contour Transitional and squamous cell carcinoma not typically hypervascular
СТ	91%-94% sensitive	Requires ionizing radiation and intravenous contrast Small mass characterization difficult	Requires good opacification of the collecting system and therefore adequate excretory function
MRI	74%-88% sensitive	Expensive Lack of availability Ideally, requires intravenous gadolinium	Calcifications not well visualized
Ultrasonography	Specific data are not available to specify accuracy	Limited detection in obese Operator dependent	Small lesions may be undetected May only detect tumor that obstructs collecting system
Nuclear medicine	Specific data are not available to specify accuracy	Poor spatial resolution Requires ionizing radiation	
PET/CT	Specific data are not available to specify accuracy	Requires ionizing radiation Expensive Lack of availability	Urinary excretion of fluorodeoxyglucose may obscure a primary urothelial tumor

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

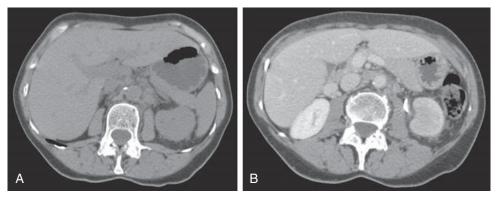


Figure 63-19 Faceless kidney. On computed tomography, transitional cell carcinoma and other infiltrating renal neoplasms may replace the normal low-attenuation renal sinus fat with soft tissue attenuation, as seen in the left kidney on these unenhanced (A) and contrast-enhanced (B) images.

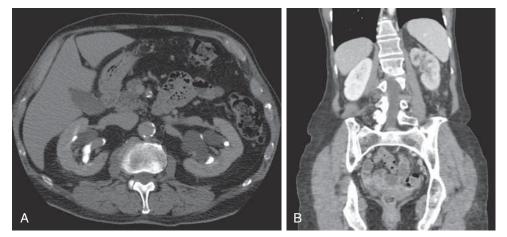
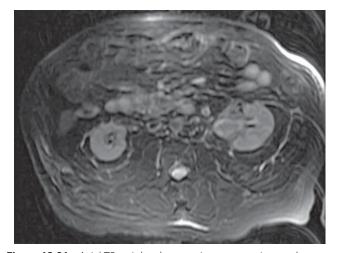


Figure 63-20 Transitional cell carcinoma may manifest as a filling defect in the collecting system, seen in the right renal pelvis on an excretory phase computed tomography (CT) image (A) or as diffuse soft tissue thickening of the urothelium, seen in the left intrarenal collecting system in a coronal reformatted CT image of a different patient (B).



**Figure 63-21** Axial T2-weighted magnetic resonance image shows an isointense mass in the left renal pelvis, which proved to be transitional cell carcinoma.



**Figure 63-22** Sagittal ultrasound image shows a solid, heterogeneous mass in the inferior pole of the left kidney with associated pelvicaliectasis.

# **Differential Diagnosis**

The differential diagnosis of an intraluminal filling defect in the renal pelvis includes urothelial tumor, calculus, blood clot, sloughed papilla, fungus ball, air bubble, and debris. The differential diagnosis of an infiltrative renal mass with preservation of the normal reniform shape of the kidney includes TCC, SCC, renal lymphoma, infiltrative RCC, metastases, and inflammatory conditions, such as pyelonephritis, renal tuberculosis, and retroperitoneal fibrosis. An infiltrative renal mass is most likely to represent TCC.

TCC is typically hypodense relative to other collecting system filling defects, including clot (40 to 80 HU) or calculus (>100 HU).  $^{44}$ 

Attenuation values of a collecting system filling defect may differentiate neoplasm from other causes. Urine bacteriologic studies may help differentiate urinary tuberculosis from TCC. Urine cytology is often used to help diagnose TCC but shows only 25% to 59% sensitivity.<sup>42</sup> Additional noninvasive laboratory urinalyses for tumor markers may be combined with urine cytology to increase detection rates.

In any case with suspicion for TCC, tissue diagnosis is necessary. Biopsy may be performed percutaneously with image guidance or ureteroscopically.

## Treatment

**Medical Treatment.** The role of adjuvant topical chemotherapeutic or immunotherapeutic agents in upper tract TCC after conservative tumor excision is unclear but gaining popularity given positive results with bladder TCC. Current treatment regimens include use of bacille Calmette-Guérin, mitomycin-C, thiotepa, or doxorubicin instilled via the bladder with a ureteral stent in place.

Chemotherapy in advanced TCC uses the MVAC regimen (methotrexate, vincristine, doxorubicin [Adriamycin], and cisplatin). The overall response rate is reported to be 54% with durable response rates as low as 5% to 10%.<sup>47</sup>

**Surgical Treatment.** Standard surgical treatment for a unilateral upper tract TCC is nephroureterectomy, including resection of the bladder cuff surrounding the ipsilateral ureterovesical junction. The rationale for this treatment is the high frequency of multifocal tumor and ipsilateral recurrence and the low incidence of contralateral disease.

#### What the Referring Physician Needs to Know: Urothelial Carcinomas

• Patients with upper tract TCC are at increased risk for synchronous or metachronous bladder TCC and require close surveillance.

### SECONDARY RENAL NEOPLASMS (RENAL LYMPHOMA AND LEUKEMIA AND METASTASES)

Renal metastases are uncommon. Because the kidneys do not contain lymphoid tissue, primary renal lymphoma is rare.

# Etiology

The most common primary tumors to metastasize to the kidneys are lung carcinoma, breast carcinoma, stomach carcinoma, and melanoma.<sup>48</sup>

Renal lymphoma is typically part of diffuse disease involving multiple nodal sites and/or other solid organs. Typically, the kidneys become secondarily involved with lymphoma via hematogeneous spread or direct extension of retroperitoneal adenopathy. Non-Hodgkin's lymphoma much more commonly involves the kidneys than does Hodgkin's disease. Certain subgroups of lymphoma have a predilection for renal involvement, specifically, poorly differentiated Burkitt's lymphoma (affects the kidneys in 10%) and lymphoma related to acquired immunodeficiency syndrome (11%).<sup>48</sup> Iatrogenic immunocompromise increases the incidence of renal lymphoma, particularly in patients with renal transplants.

#### Prevalence and Epidemiology

Several large autopsy series show metastases to the kidneys in 1.5% to 1.8% of all deaths in patients with lymphoma. In autopsy series there is secondary involvement of the kidneys in up to 60% of lymphoma cases. However, the prevalence of renal lymphoma on staging CT is estimated to be 5% to 8%.<sup>49</sup>

#### **Clinical Presentation**

Most patients with renal metastases have overwhelming metastatic burden, and their renal metastases are not clinically significant. Renal hemorrhage with gross or microscopic hematuria may occur with either metastases or lymphoma.

#### Pathology

The pathologic processes of secondary renal malignancy reflect those of the primary tumor. Lymphoma involving the kidneys is usually the diffuse large cell type.<sup>48</sup>

#### Imaging

Renal lymphoma has four patterns on imaging: solitary renal mass, multifocal or bilateral renal masses, diffuse renal enlargement, and perirenal soft tissue mass or thickening. In addition, the kidneys may be involved by extension of adjacent paraaortic lymphadenopathy. The finding of multiple renal masses is the most common manifestation, occurring in more than half of cases.<sup>50</sup>

Renal leukemia typically appears as bilateral renal enlargement, with discrete renal masses less common.

Renal metastases usually appear as solitary or bilateral renal masses. As with renal lymphoma, nodal extension into the kidneys is another potential appearance. Perirenal masses have been described in patients with lung cancer and melanoma.

**Radiography.** Abdominal radiographs and excretory urography may show diffuse nephromegaly or one or more focal renal masses. These findings are nonspecific.

Bulky lymphadenopathy may cause lateral displacement of the ureters in the para-aortic region and medial ureteral displacement in the pelvis.

**Computed Tomography.** Contrast-enhanced CT is the imaging modality of choice. Renal metastases usually appear as multiple, small, hypoattenuating masses (Figures 63-23 and 63-24). Perinephric metastases (particularly with melanoma or lung carcinoma primary) or infiltrating renal metastases have also been reported.<sup>51</sup> Renal metastases are typically isodense to hypodense on unenhanced CT (10 to 40 HU) with minimal enhancement (5 to 15 HU).<sup>48</sup>

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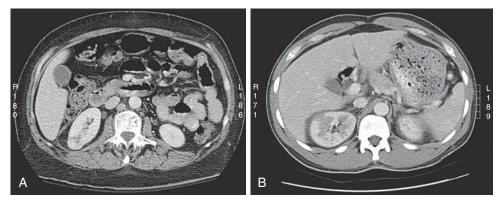


Figure 63-23 Axial contrast-enhanced computed tomography images of different patients with renal lymphoma show a solitary solid mass in the posterior aspect of the right kidney (A) and multiple, small, bilateral, hypodense renal masses, which mimic the striated kidney appearance (B).



Figure 63-24 A, Axial contrast-enhanced computed tomography (CT) image shows a solitary hypodense right renal mass, which proved to be a breast carcinoma metastasis. B, Coronal reformatted contrast-enhanced CT image shows multiple bilateral hypodense lung carcinoma metastases.

Perirenal lymphoma is well demonstrated on CT as a rind of enhancing soft tissue surrounding the kidneys in the perirenal or pararenal spaces.

**Magnetic Resonance Imaging.** Renal lymphoma shows T1 isointensity and T2 hyperintensity on MRI. With diffuse infiltration of the renal parenchyma, MRI may show loss of corticomedullary differentiation.

Renal metastases have a variable appearance, although most are multiple and T2 hyperintense (Figure 63-25).

**Ultrasonography.** Lymphoma usually appears hypoechoic and uniform. A lymphomatous mass may be mistaken for a cyst.

Metastases may be hyperechoic, isoechoic, or hypoechoic to renal parenchyma. Hydronephrosis resulting from adenopathy may be seen in secondary malignancy. Ultrasonography showed sensitivity for detection of renal metastasis of 67% in one study and 80% in another.<sup>48</sup>

**Positron Emission Tomography With Computed Tomography.** PET is not well suited to the detection of secondary renal neoplasms because of urinary excretion of FDG.

#### **Differential Diagnosis**

The differential diagnosis for a solid renal mass has been discussed previously in the section on RCC.

When renal lymphoma is suspected, pathologic sampling is imperative. Primary renal malignancy generally requires surgery, whereas surgery is not indicated for renal lymphoma or metastases (Table 63-6). Core biopsy should be performed to assist in the diagnosis and classification of the disease.<sup>49</sup>

# Treatment

**Medical Treatment.** Renal lymphoma, leukemia, and metastases are all treated medically with chemotherapy and radiation therapy.

**Surgical Treatment.** Secondary tumors of the kidney are not treated surgically, unless for palliation or in rare circumstances such as severe renal hemorrhage.

### What the Referring Physician Needs to Know: Secondary Renal Neoplasms (Renal Lymphoma or Leukemia and Metastases)

- Secondary tumors of the kidneys are difficult to differentiate from primary renal malignancy.
- Contrast-enhanced CT and MRI are accurate techniques for the evaluation of renal metastases, lymphoma, or leukemia.
- Suspected renal metastases or lymphoma may be an indication for renal mass biopsy.

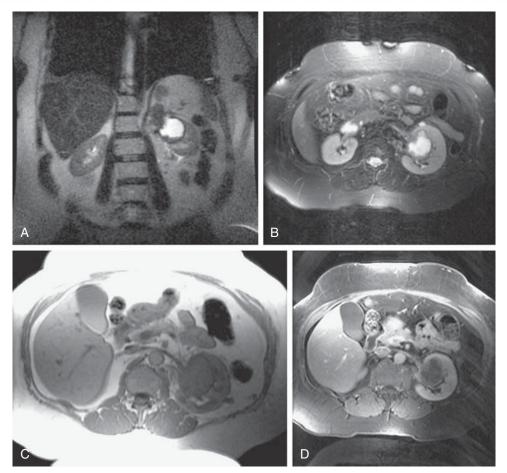


Figure 63-25 Coronal (A) and axial (B) T2-weighted magnetic resonance (MR) images, axial T1-weighted MR image (C), and postgadolinium MR image (D) of a solitary left renal metastasis from lung carcinoma.

TABLE         Comparison of Rel	nal Metastases, Lymphoma, and	Leukemia	
Comparison Factors	Metastases	Lymphoma	Leukemia
Incidence/prevalence	1.5%-1.8% autopsy series	Up to 60% in autopsy series; 5%-8% on staging CT scans	
Туре	Lung, breast, gastric, melanoma, colon	NHL ≫ HD; especially Burkitt's and AIDS-related	Lymphocytic > granulocytic
Clinical setting	Large metastatic burden	Late in course of disease Immunocompromised patients	
General manifestations	Multiple small renal masses most commonly; hemorrhage common; occasionally large, solitary lesion	Four patterns: Multiple renal masses (>50%), solitary renal mass, diffuse renal enlargement (10%), perirenal soft tissue	Bilateral diffuse renal enlargement most commonly; hemorrhage common
Imaging modality of choice	Contrast-enhanced CT or MRI	Contrast-enhanced CT or MRI	Contrast-enhanced CT or MRI
CT appearance	Hypodense	Homogeneous hypodense mass; rind of perirenal soft tissue	Diffuse renal enlargement
MRI appearance	Variable; most commonly multiple T1 isointense and T2 hyperintense masses	T1 isointensity, T2 hyperintensity, obscured corticomedullary distinction	Similar to lymphoma
Ultrasound appearance	Variable	Usually hypoechoic; can mimic renal cyst but typically less acoustic enhancement	Similar to lymphoma
Additional diagnostic steps	Other sites of involvement apparent on imaging, serum tumor markers	Core needle biopsy	Core needle biopsy Complete blood cell count

AIDS, Acquired immunodeficiency; CT, computed tomography; HD, Hodgkin's disease; MRI, magnetic resonance imaging; NHL, non-Hodgkin's lymphoma.

# PEDIATRIC SOLID RENAL MALIGNANCIES (WILMS' TUMOR, NEPHROBLASTOMATOSIS, CLEAR CELL SARCOMA, RHABDOID TUMOR OF THE KIDNEY)

Many types of pediatric renal malignancies previously have been combined and categorized as Wilms' tumor.

## Etiology

Most pediatric renal malignancies are congenital, and a variety of chromosomal mutations are associated with each tumor. Inactivation of *WT1*, a tumor suppressor gene, is found in most Wilms' tumors as well as in association with intralobar nephrogenic rests, 1% of which give rise to Wilms' tumor. Mutations of this gene are also associated in WAGR syndrome (Wilms' tumor, aniridia, genitourinary anomalies, and mental retardation), Denys-Drash syndrome (male pseudohermaphroditism, glomerulonephritis, and Wilms' tumor), and Beckwith-Wiedemann syndrome (macroglossia, omphalocele, adrenal cytomegaly, and visceromegaly). Nephrogenic rests, which are precursors to Wilms' tumor, are found in 1% of neonates and undergo malignant transformation 1% of the time.<sup>52</sup>

#### Prevalence and Epidemiology

Wilms' tumor accounts for 6% of childhood malignancies and nearly 90% of pediatric renal masses.<sup>53</sup> Peak incidence is at 3 to 4 years, with 80% of cases presenting before age 5 and occurs equally in males and females.

Wilms' tumor is associated with other congenital genitourinary anomalies, including horseshoe kidney, müllerian duct anomalies, septated or unicornuate uteri, cryptorchidism, and hypospadias. Other associations are hemihypertrophy (2.5%) and sporadic aniridia.

Nephroblastomatosis is persistent nephrogenic blastema resulting from arrested nephrogenesis. It is not malignant but is associated with Wilms' tumor.

Rhabdoid tumor of the kidney is a rare childhood neoplasm, occurring in children with a median age of 11 months. It is strongly associated with central nervous system neoplasms, including astrocytoma, ependymoma, and primitive neuroectodermal tumor.

Pediatric RCC is relatively rare, accounting for 2% to 6% of solid renal malignancies in children. It occurs at an older age than Wilms' tumor, typically between 9 and 15 years, and is extremely rare in children younger than 4 years of age.<sup>54</sup>

Clear cell sarcoma of the kidney occurs with peak incidence of 1 to 4 years and has a male predominance.

Mesoblastic nephroma is the most common tumor in infants younger than the age of 3 months. Ninety percent of cases occur in the first year of life. The tumor shows a male predominance, and its most common presentations include an abdominal mass and, less commonly, hematuria.<sup>55</sup> Imaging shows a solid renal mass, frequently involving the renal sinus, with variable degrees of cystic change or hemorrhage and local infiltration.

#### **Clinical Presentation**

A palpable abdominal mass is the most common manifesting symptom in children with Wilms' tumor. Abdominal pain and hematuria are less common manifesting symptoms.<sup>31</sup>

Pediatric RCC manifests as gross hematuria, abdominal pain, palpable mass, and polycythemia.<sup>56</sup>

# Pathophysiology

Wilms' tumor may arise from the renal medulla or cortex. The tumor typically has a fibrous pseudocapsule causing sharp demarcation from normal renal parenchyma, which is often compressed by the large mass.

# Pathology

The tumor arises from the metanephric blastema and is composed of a combination of blastemal, stromal, and epithelial cells, which may or may not show anaplasia.<sup>52</sup> It is often large at the time of diagnosis, typically 5 to 10 cm. Wilms' tumor is bilateral in 5% to 10% of cases. Metachronous lesions are seen in 1.5% of cases within 5 years of initial diagnosis.<sup>53</sup>

Wilms' tumor extends into the inferior vena cava in 4% to 10% of cases and the most common sites of metastasis are the lung, lymph nodes, and liver. Rarely, Wilms' tumor metastasizes to bone or to the brain.<sup>52</sup>

The stage of Wilms' tumor is less important than the histologic grade for prognosis (Table 63-7).

#### Imaging

Wilms' tumor is usually large, expansile, and well circumscribed. The tumor commonly distorts the kidney and renal collecting system, but direct invasion of the renal pelvis is uncommon. It may be difficult to differentiate Wilms' tumor from adrenal neuroblastoma with renal involvement.

**Radiography.** Conventional radiography plays no role in the evaluation of pediatric abdominal masses.

**Computed Tomography.** Wilms' tumor is typically a large, solid renal mass with variable heterogeneity related to the degree of intratumoral necrosis and hemorrhage. It enhances to a lesser degree than normal renal parenchyma and often compresses normal kidney. Portal venous imaging is typically sufficient (Figure 63-26). A small amount of free peritoneal fluid may commonly be seen at initial imaging and does not imply tumor rupture; the fluid may be related to compression of the inferior vena cava, thrombosis, or peritoneal reaction.<sup>57</sup> Tumor rupture may be presumed in cases of hemoperitoneum or solid peritoneal nodules. Nephroblastomatosis may be diffuse or multinodular. In the diffuse form, the kidneys are enlarged with distortion of the collecting system by hypoenhancing subcapsular parenchymal nodules.

Magnetic Resonance Imaging. MRI does not appear to have significant advantage over CT in evaluating Wilms' tumor.

TABLE 63-7	Wilms' Tumor Staging	
Stage	Disease Extent	
1	Limited to kidney	
II	Extends beyond kidney but completely resected	
III	Residual nonhematogeneous tumor confined to the abdomen	
IV	Hematogenous metastases to lung, liver, bone, or brain	
V	Bilateral renal involvement	

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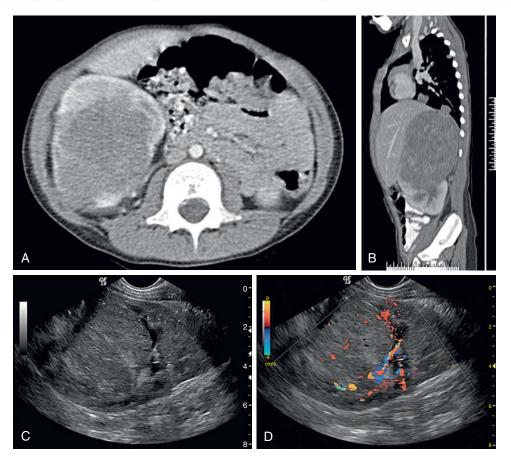


Figure 63-26 Wilms' tumor. Contrastenhanced axial (A) and sagittal reformatted (B) computed tomography images of a well-demarcated, hypodense mass in the upper pole of the right kidney in this pediatric patient. Ultrasound image (C) and color Doppler image (D) of the same mass.

Although it spares the patient ionizing radiation and iodinated contrast material, MRI typically requires sedation and monitoring.

Wilms' tumor typically appears hypointense on T1-weighted images and hypointense to isointense on T2-weighted images. Intratumoral hemorrhage, fat, necrosis, and cystic change are common, causing heterogeneous appearance.<sup>57</sup>

**Ultrasonography.** Ultrasonography, including color Doppler imaging, is the preferred method of evaluation of a child who presents with an abdominal mass. Wilms' tumor appears as a solid, well-defined, heterogeneous mass arising from the kidney. Dystrophic calcifications (9%) appear as echogenic, shadowing foci within the tumor. Color flow Doppler evaluation may demonstrate thrombus in the renal vein and inferior vena cava.

#### **Positron Emission Tomography With Computed Tomography.** PET is infrequently used in the imaging of Wilms' tumor.

#### Differential Diagnosis

The differential diagnosis of a solid renal mass in a pediatric patient includes Wilms' tumor, pediatric RCC, rhabdoid tumor of the kidney, renal lymphoma, and metastasis. Uncommonly, focal infection may have a masslike appearance.

#### Treatment

Prognosis of Wilms' tumor has dramatically improved over the past 3 decades, with the 5-year disease-free survival now approximately 90% and overall 20-year survival greater than 80%.  $^{\rm 53}$ 

**Medical Treatment.** The role of neoadjuvant chemotherapy in Wilms' tumor is controversial. Preoperative therapy allows assessment of tumor responsiveness to chemotherapeutic agents, decreases tumor stage (which is performed at time of surgery), potentially allows minimally invasive surgery, decreases the risk for tumor rupture at surgery, and may eliminate the need for surgical bed irradiation.<sup>52</sup> Tumors with favorable histology show benefit from flank radiation therapy, whereas unfavorable histology Wilms' tumor shows no benefit.

Patients with nephroblastomatosis are treated with chemotherapy and require continued imaging surveillance.

Most (90%) relapses occur in the first 4 years after diagnosis.<sup>57</sup> Because patients with relapse have reasonable cure rates with salvage therapy, routine imaging follow-up is recommended of the chest, abdomen, and pelvis.

**Surgical Treatment.** Surgical excision is the mainstay of treatment for Wilms' tumor. Low-stage tumors in selected patients may benefit from nephron-sparing surgery; however, its use is controversial because there is an increased rate of positive surgical margins and tumor recurrence and potential risk for understaging by limited lymph node dissection.<sup>52,58</sup> Metastasectomy with wedge resection is an option with pulmonary or hepatic metastases and can lead to cure.

#### What the Referring Physician Needs to Know: Pediatric Solid Renal Malignancies (Wilms' Tumor, Nephroblastomatosis, Clear Cell Sarcoma, Rhabdoid Tumor of the Kidney)

- Wilms' tumor formal staging is performed surgically.
- Preoperative tumor biopsy is a contraindication to partial nephrectomy so percutaneous biopsy of a pediatric renal mass should only be undertaken with caution.

# **Complex Cystic Renal Mass**

A simple renal cyst may be complicated by hemorrhage, inflammation, or infection, which may lead to the formation of septations, calcification, hemorrhage, wall thickening, and nodularit.<sup>59</sup> Approximately 10% of RCCs will manifest as complex cystic lesions. These two groups of lesions—complex benign renal cysts and neoplastic renal cysts—may therefore have similar pathologic and imaging appearances.<sup>60</sup> This often creates a difficult diagnostic dilemma. When a cystic renal lesion does not meet the imaging criteria of a simple renal cyst, it should be considered a cystic renal mass.<sup>59</sup> For practical purposes, the differential diagnosis for such includes a complicated renal cyst and cystic RCC.

# IMAGING

# Ultrasonography

Ultrasonography is often the first imaging modality used to detect a cystic renal lesion. However, more complex cystic masses have traditionally required additional imaging with contrast-enhanced CT or MRI to evaluate for enhancement.<sup>60</sup>

# Computed Tomography

CT is the primary imaging modality used in evaluation of the cystic renal mass. The ability to accurately demonstrate morphology and enhancement make it an excellent modality for this purpose. Typically, a three-phase examination is performed using a multidetector row CT scanner. Unenhanced images are obtained before the administration of 150 mL of iodinated contrast medium. Corticomedullary and nephrographic phases are obtained using delays of 40 and 100 seconds, respectively. A section thickness of 2.5 to 5 mm is typically adequate, but thinner reconstructions can be obtained when necessary and may help reduce partial volume averaging. Finally, it is important to remember that scan parameters should be held constant between series to allow accurate evaluation of enhancement.<sup>59,61</sup>

#### Magnetic Resonance Imaging

MRI is being used with increasing frequency in cases in which CT and/or ultrasonography is not definitive. In fact, MRI has been shown to be of accuracy similar to that of CT in the evaluation of cystic renal masses, with the additional capacity to show more septa, wall thickening, and enhancement.<sup>62</sup>

MRI protocols can vary but usually consist of at least a twodimensional (2D) gradient recalled echo T1-weighted sequence, a 2D T2-weighted sequence, and 3D fat-suppressed T1-weighted spoiled gradient recalled echo sequences obtained before and after the administration of a gadolinium chelate contrast agent.<sup>62-64</sup> The T1-weighted sequences are often helpful to depict hemorrhage and protein, whereas the T2-weighted sequences often demonstrate septa and nodules.<sup>5</sup> Postgadolinium images are used to identify enhancement, particularly in cases with indeterminate enhancement on CT.

Enhancement can be more difficult to evaluate with MRI than CT, given the variability and nonlinear gray-scale display of signal intensity.<sup>63,64</sup> A second limitation is the relative insensitivity of MRI to detect calcification. Fortunately, calcification now plays a less important role in the imaging evaluation and management of cystic renal masses.<sup>62</sup>

# THE BOSNIAK CLASSIFICATION

In 1986, Bosniak proposed an approach for the diagnosis and management of cysts of the kidney based on CT findings.<sup>3</sup> They have since modified the classification.<sup>65-67</sup> The Bosniak classification is useful, is widely used, and gives the radiologist and referring clinician a strategy to manage the complex renal cyst.

Based on morphology and enhancement, a cystic lesion is placed into one of five categories (Table 63-8), each with implications for management. Category I cysts are simple benign renal cysts (discussed earlier), which can be accurately diagnosed using ultrasonography, CT, or MRI and require no additional imaging or intervention. Category II lesions are minimally complicated cysts, which are not simple cysts but can be confidently diagnosed as benign and also require no additional imaging or intervention. Category IIF (F for follow-up) cysts are thought to be benign but are slightly more complicated than category II lesions and thus require follow-up to document stability. Category III lesions are more complicated, indeterminate cystic lesions with findings that can be seen in malignancy. Surgery is recommended for these lesions. Finally, category IV cysts are clearly malignant lesions.<sup>3,65,67</sup> Israel and Bosniak<sup>67</sup> have shown the risk for malignancy in a Bosniak IIF lesion to be approximately 5%. They suggest performing a repeat CT scan at 6 months with additional examinations yearly for 5 years. On the other hand, the risk for malignancy for indeterminate category III and category IV lesions has been shown to vary from 31% to 100% and from 67% to 100%, respectively.<sup>68</sup> Accordingly, category III and category IV lesions are managed with surgery or ablative therapy.

The Bosniak classification is an approach to renal cysts that attempts to categorize each cyst as benign/nonsurgical (category I and II), probably benign but requires follow-up (category IIF), and suspicious and surgical (category III and IV, respectively). Overall, studies have found the Bosniak classification scheme to be clinically useful, but some critics point to interobserver variation in categorizing category II and category III lesions as a potential drawback.<sup>69</sup> Although originally based on CT findings, the Bosniak classification has recently been successfully applied to both contrast-enhanced MRI and ultrasonography.<sup>60,62,70</sup> When findings differ between examinations, the most worrisome findings should guide lesion classification and management.<sup>59</sup>

#### **Clinical Implications**

**Calcifications.** It has long been accepted that calcifications can occur in both benign and malignant cysts. However, the role that calcifications play in the characterization and management of renal cysts has evolved considerably. Calcification is now considered to be less important in the evaluation of the cystic

TABLE 63-8	Bosniak Renal Cyst	Classification System
Categ	ory	Description
I		A benign simple cyst with a hairline thin wall that does not contain septa, calcifications, or solid components. It measures water density and does not enhance.
II		A benign cyst that may contain a few hairline thin septa in which "perceived" enhancement may be present. Fine calcification or a short segment of slightly thickened calcification may be present in the wall or septa. Uniformly high-attenuation lesions <3 cm (so-called high-density cysts) that are well marginated and do not enhance are included in this group. Cysts in this category do not require further evaluation.
IIF (F f	or follow-up)	Cysts that may contain multiple hairline thin septa or minimal smooth thickening of their wall or septa. Perceived enhancement of their septa or wall may be present. Their wall or septa may contain calcification that may be thick and nodular, but no measurable contrast enhancement is present. These lesions are generally well marginated. Totally intrarenal nonenhancing high-attenuation renal lesions >3 cm are also included in this category. These lesions require follow-up studies to prove benignity.
111		"Indeterminate" cystic masses that have thickened irregular or smooth walls or septa in which measurable enhancement is present. These are surgical lesions; although some will prove to be benign (e.g., hemorrhagic cysts, chronic infected cysts, and multiloculated cystic nephroma), some will be malignant (e.g., cystic renal cell carcinoma and multiloculated cystic renal cell carcinoma).
IV		These are clearly malignant cystic masses that can have all the criteria of category III but also contain enhancing soft tissue components adjacent to, but independent of, the wall or septum. These lesions include cystic carcinomas and require surgical removal.

From Israel GM, Bosniak MA: An update of the bosniak renal cyst classification system. Urology 66:484-488, 2005.

Figure 63-27 Axial unenhanced (A) and coronal contrast-enhanced (B) computed tomography scans show incidentally detected benign calcifications in a right renal cyst. The calcifications are thin without thickening, nodularity, or associated enhancement.

renal mass.<sup>66</sup> CT is better than both ultrasonography and MRI in the detection and characterization of calcification in a renal cyst, with the caveat that MRI can be superior to CT for the detection of enhancement in heavily calcified lesions.<sup>59,62</sup>

A calcified cyst with only a thin calcification or a short, slightly thickened calcification can be considered benign (category II) (Figure 63-27).<sup>1,66,71</sup>

A calcified cyst with thick and nodular calcifications without tissue enhancement can be safely followed (category IIF) (Figure 63-28).<sup>66,71</sup> There can be a change in the amount of the calcification on follow-up examinations without changing classification. However, an increase in the soft tissue component or the development of associated enhancement would prompt reclassification to a surgical lesion (category III or IV).<sup>66</sup>

A calcified cyst with enhancing soft tissue components is a surgical lesion (category III or IV) (Figure 63-29).<sup>66</sup>

**Septa.** Simple cysts complicated by hemorrhage, infection, or inflammation may develop septations.<sup>59</sup> At the same time, cystic RCC can manifest as a septated mass. Ultrasonography and CT are similar in their ability to define internal septations.<sup>72</sup> On the other hand, MRI can show more septa than CT and ultrasonography, which can alter the lesion classification.<sup>62</sup>

To be classified as benign (category II), a septation must be hairline thin ( $\leq 1$  mm) without thickening, nodularity, or measurable enhancement (Figure 63-30).<sup>1,59,72</sup> When there is more than one septation, benign septations should be few in number.

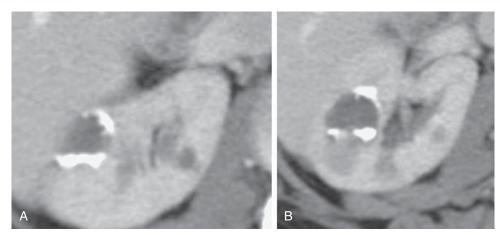


Figure 63-28 Follow-up calcifications in a 56-year-old woman. A and B, Axial contrast-enhanced computed tomography scans show thickened and nodular calcifications without associated enhancement. These calcifications have remained stable over 3 years of follow-up.

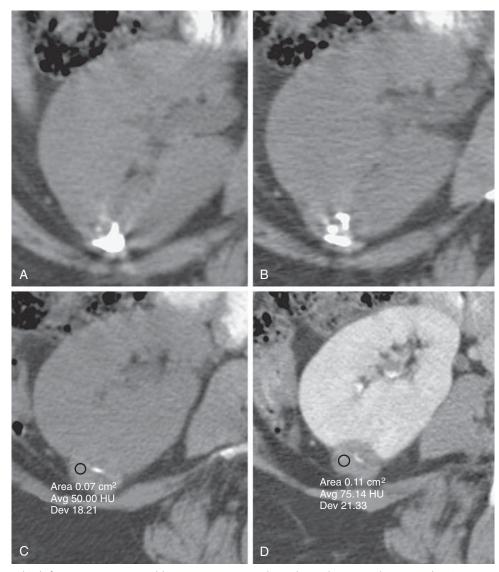
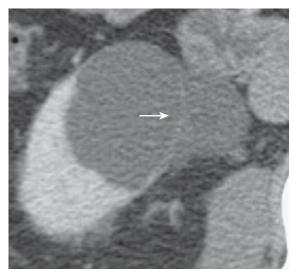


Figure 63-29 Surgical calcifications in a 59-year-old woman. A to C, Axial unenhanced computed tomography (CT) scans show thickened and nodular calcifications. D, Axial contrast-enhanced CT scan shows an area of enhancement adjacent to the calcifications. Clear cell renal cell carcinoma was found at nephrectomy.

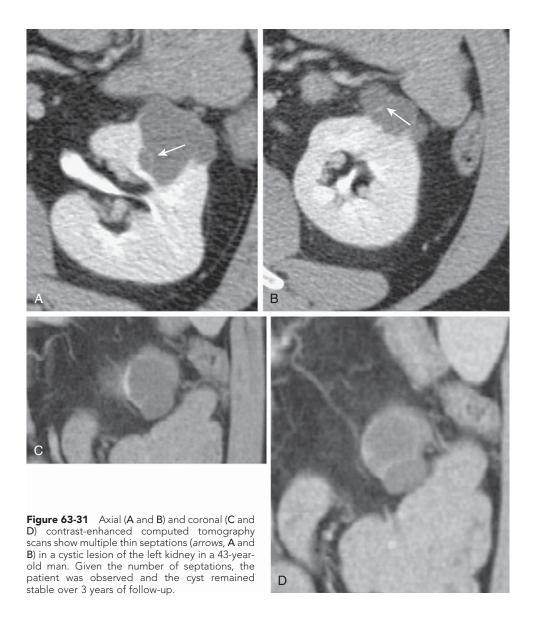


**Figure 63-30** Benign septation in a 65-year-old man. Axial contrastenhanced computed tomography scan shows a hairline thin septation (*arrow*) without thickening, nodularity, or measurable enhancement.

A cyst with minimal septal thickening or multiple septations should be followed (category IIF) for signs of increasing thickening or irregularity or for the development of measurable enhancement (Figure 63-31).<sup>59,71</sup> Unfortunately, the differentiation of a few and minimally thickened from thick or irregular is subjective.<sup>1</sup>

Cysts with thickened or irregular septations or measurable enhancement within the septation are considered surgical (category III) and should be treated as RCC (Figure 63-32).<sup>1,59,71,72</sup>

**High Attenuation.** A renal mass with attenuation greater than that of simple fluid (–20 to 20 HU) on unenhanced CT is considered of high attenuation or hyperdense. The MRI correlate is a mass with T1 signal intensity higher than that of water. The majority of these lesions are benign cysts with the increased attenuation attributed to blood or its breakdown products, high protein content, elevated iron, colloid formation, infection, or transient iodine accumulation.<sup>73</sup> However, densely packed cells in a solid renal mass such as RCC or lymphoma can have a similar appearance.<sup>73</sup> On unenhanced CT, it is not possible to differentiate these lesions from one another.<sup>59</sup>



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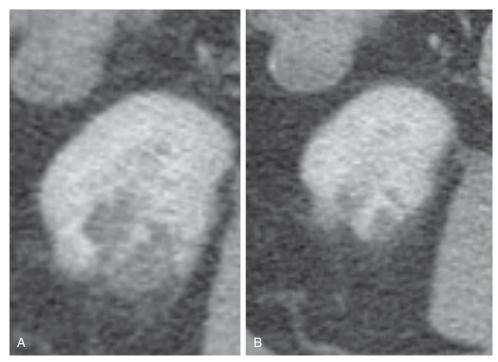
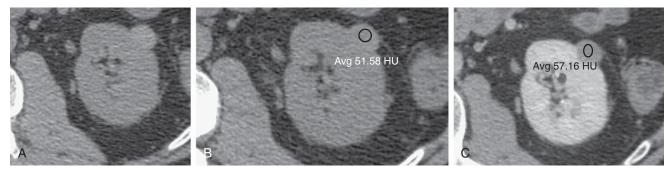


Figure 63-32 Surgical septations in a 73-year-old man. A and B, Axial contrast-enhanced CT scans show thickened and nodular septations with enhancement when compared with unenhanced CT scan (not shown). Renal cell carcinoma was found at surgery.



**Figure 63-33** Benign hyperattenuating renal cyst in a 51-year-old asymptomatic man. Unenhanced (A and B) and contrast-enhanced (C) computed tomography scans show a partially exophytic hyperattenuating lesion that is homogeneous, is sharply marginated, measures less than 3 cm, and does not enhance.

Fortunately, additional imaging with ultrasonography or contrast-enhanced CT or MRI can be performed for more definitive characterization.

To be considered benign (category II), Israel and Bosniak have proposed the following criteria for a high-attenuation lesion, it must (1) be homogeneous, smooth, and sharply marginated; (2) measure less than 3 cm; (3) extend outside the kidney by at least one fourth of its diameter; and (4) demonstrate no enhancement (Figure 63-33).<sup>59,60,73</sup> A recent study found that a homogeneous hyperdense mass that measures 70 HU or more on an unenhanced examination has a greater than 99.9% chance of being a cyst.<sup>74</sup> The authors suggest that ultrasonography could be the next appropriate test for these lesions, with contrast-enhanced examinations reserved for masses that measure less than 70 HU or are heterogeneous.<sup>74</sup> Approximately 50% of hyperattenuating renal cysts will meet the criteria for a simple cyst at ultrasonography. The remainder often have internal echoes and decreased through-transmission.<sup>73</sup>

Israel and Bosniak<sup>71</sup> recommend following any highattenuation lesion (category IIF) that measures more than 3 cm or is totally intrarenal.

A hyperattenuating lesion is considered surgical (category III and IV) when it fails to meet the previously mentioned criteria. Specifically, a lesion that has an irregular margin and heterogeneous density and demonstrates enhancement or appears solid on ultrasound evaluation should be considered surgical (Figure 63-34).<sup>59</sup>

**Wall Thickening and Nodularity.** Wall thickening is best assessed in partially exophytic cysts. A simple cyst has thin walls. Wall thickening can be seen in complicated benign cysts and cystic RCC. The presence of smooth or irregular wall thickening excludes a radiologic diagnosis of benignity and makes a cyst a surgical lesion (category III).<sup>1,68,71</sup> Similarly, the presence of nodularity precludes a benign diagnosis (category III or IV) (Figures 63-35 and 63-36).

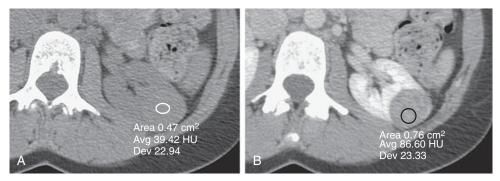


Figure 63-34 A 41-year-old woman presented with a surgical high attenuation lesion in the left kidney. A, Unenhanced computed tomography (CT) scan shows a partially exophytic high-attenuation mass that measures 39 Hounsfield units (HU). B, Contrast-enhanced CT scan shows enhancement within the mass by 47 HU.

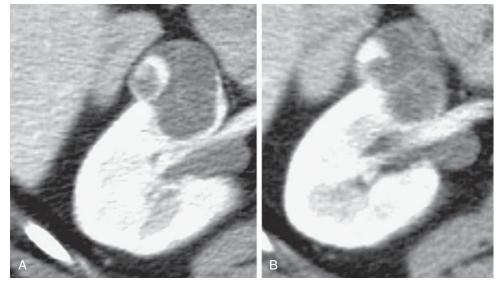


Figure 63-35 Cystic renal cell carcinoma in a 55-year-old man. A and B, Contrast-enhanced computed tomography scans show an enhancing nodule and wall thickening.

A potential pitfall in the evaluation of the cystic lesion is mistaking normal renal parenchyma that can surround renal lesions (parenchymal beak) for wall thickening or nodularity. Familiarity with the concept and the use of multiple planes will help avoid this error (Figure 63-37).<sup>4,59</sup>

**Enhancement.** Of the imaging criteria, enhancement is the most important. The likelihood of malignancy significantly increases in the presence of enhancement.<sup>59,61,71,75</sup> A mass without enhancing components is nonvascular and benign. On the other hand, the presence of measurable enhancement implies vascularity, which can be seen in both neoplastic and non-neoplastic lesions. Because it is not possible to reliably differentiate causes of enhancement, all enhancing lesions are considered potentially malignant.

A high-quality CT scan is essential. Enhancement not only reflects vascularity but also is influenced by the administration of a contrast agent (amount and rate) and imaging delay.<sup>61</sup> Technical factors should be held identical between scans. Measurements must include the nephrographic phase, which is superior for the detection of enhancement.<sup>76</sup> The size and level of the region of interest measurement should be held constant

when comparing unenhanced and enhanced series. The largest possible region of interest should be used with homogeneous lesions. On the other hand, a smaller region of interest is appropriate for heterogeneous lesions to detect small areas of enhancement.<sup>77,78</sup>

In the past, a difference of 10 HU was accepted as proof of enhancement.<sup>61</sup> However, the transition to helical CT has brought this value into question. Several reports have shown that simple cysts may change by more than 10 HU between unenhanced and enhanced series.79-81 This phenomenon has been called *pseudoenhancement* and refers to an artifactual increase in attenuation after contrast agent administration.<sup>79</sup> Beam hardening and inappropriate reconstruction algorithms are believed to be the major factors behind pseudoenhancement. This occurs primarily in small (<1.5 cm) intrarenal lesions measured during the nephrographic phase of renal enhancement.<sup>81</sup> Pseudoenhancement can lead to the mischaracterization of a simple cyst as an enhancing (surgical) lesion. Currently, there is no universally accepted Hounsfield unit increase that defines enhancement. Some authors advocate threshold values of 15 or 20 HU.<sup>79,81</sup> The use of fluid-containing structures (gallbladder or simple cyst) may be helpful as an internal reference. Israel

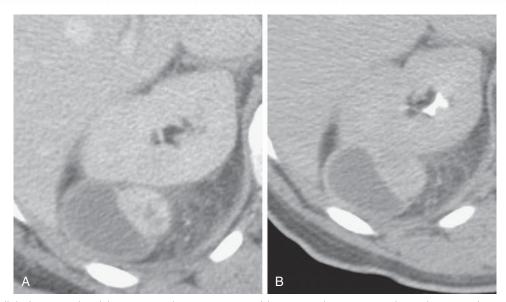


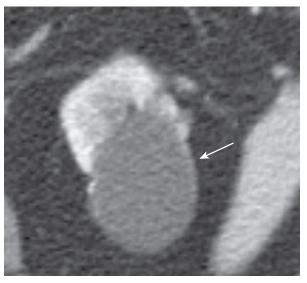
Figure 63-36 Wall thickening and nodularity in a renal cyst in a 69-year-old man. A and B, Contrast-enhanced computed tomography scans show an enhancing nodule and wall thickening. Clear cell renal cell carcinoma was found at surgery.



**Figure 63-37** Simple renal cyst in a 67-year-old man who presented with right upper quadrant pain. The normal renal parenchyma (parenchymal beak) should not be mistaken for wall thickening or nodularity.

and Bosniak<sup>61</sup> consider a change of 10 to 20 HU as "indeterminate" and recommend further evaluation of these lesions with optimized CT scan, ultrasonography, or MRI.<sup>61</sup>

De-enhancement is an additional method that can be used to determine vascularity. It is not unusual to encounter a renal mass that measures approximately 30 HU on a contrastenhanced examination. This mass could represent an enhancing renal neoplasm or a high-attenuation cyst. Further characterization could be performed with ultrasonography or a multiphase CT examination. Alternatively, Macari and Bosniak<sup>82</sup> have shown that delayed images at 15 minutes can be used to



**Figure 63-38** Complicated cyst in an 81-year-old woman. Axial contrast-enhanced computed tomography scan shows perceived enhancement (*arrow*) in the wall of the cyst. No measurable enhancement was present. Follow-up was recommended given the presence of thickened calcifications (not shown).

demonstrate de-enhancement (decrease in attenuation as contrast medium leaves a lesion) in vascular neoplasms, differentiating these lesions from avascular high-attenuation cysts that do not diminish in attenuation on delayed scans.<sup>82</sup>

Renal lesions classified as benign (category I or II) or probably benign (category IIF) cannot demonstrate measurable enhancement. However, Israel and Bosniak<sup>71</sup> do describe "perceived" enhancement within the septa and walls of these lesions. They describe this phenomenon as the subjective appearance of enhancement in thin walls or septa related to contrast media within tiny capillaries (Figure 63-38).<sup>71</sup>

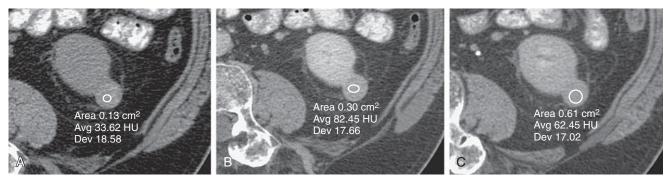
The presence of unequivocal and measurable enhancement within a cystic renal lesion implies vascularity. These lesions are classified as surgical (category III or IV) (Figure 63-39).<sup>71</sup>

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**Multilocular Lesion.** The multiloculated renal mass is a subgroup of cystic renal lesion. It should be considered when a cystic mass has more than three or four septations.<sup>59</sup> Many disease processes may result in a multiloculated renal mass, including neoplastic, cystic, inflammatory, and vascular lesions.<sup>83</sup> Excluding infection, some cystic diseases, and vascular lesions, the majority of multiloculated renal masses are treated with excision.<sup>59</sup>

In adults, the two most common multiloculated renal masses are RCC and multilocular cystic nephroma.<sup>83</sup> Both masses are

typically well encapsulated with multiple cysts separated by septations. There is sufficient overlap in the imaging appearance that definitive radiologic diagnosis is not possible.<sup>59</sup> Factors that favor RCC include distant metastatic disease, intravascular extension, large solid areas, extensive calcification, hemorrhage, and male gender (Figure 63-40).<sup>83</sup> Factors that favor multilocular cystic nephroma include female gender, absence of hemorrhage, and herniation into the renal pelvis (Figure 63-41).<sup>83</sup> Ultimately, definitive diagnosis is made after surgical excision.



**Figure 63-39** Enhancing and de-enhancing mass in a 66-year-old man. A, Axial unenhanced computed tomography (CT) scan shows a hyperattenuating mass in the lower pole of the left kidney. B, Axial contrast-enhanced CT scan shows unequivocal enhancement by approximately 50 Hounsfield units (HU). C, Axial delayed contrast-enhanced CT scan 7 minutes after contrast agent administration shows de-enhancement by 20 HU. Papillary renal cell carcinoma was found at histologic analysis.





Figure 63-40 Multiloculated renal cell carcinoma in a 62-year-old man. A and B, Axial contrast-enhanced computed tomography images show a multiloculated cystic lesion in the interpolar region of the left kidney. The large solid areas and male gender favor a diagnosis of multiloculated renal cell carcinoma.

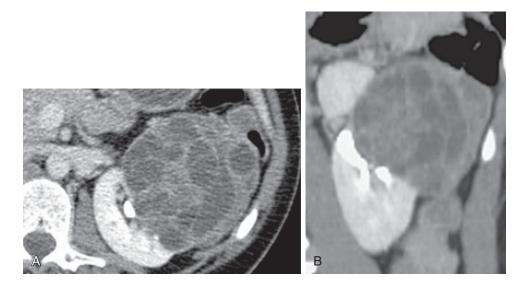
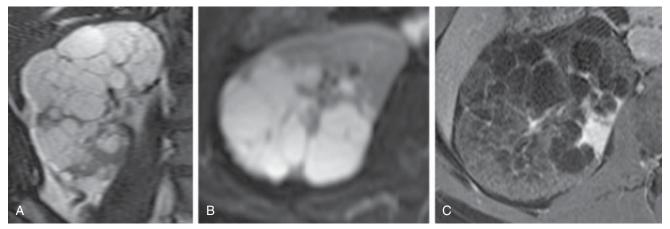


Figure 63-41 A 46-year-old woman presented with a multiloculated mass in the left kidney. Axial (A) and coronal (B) contrast-enhanced images show a well-encapsulated multiloculated cystic lesion with herniation into the renal pelvis. The herniation into the renal pelvis and female gender favored a diagnosis of multilocular cystic nephroma, which was confirmed at laparoscopic nephrectomy.



**Figure 63-42** Localized cystic disease of the kidney in a 51-year-old man. Coronal FIESTA (A), axial T2-weighed (B), and axial gradient recalled echo T1-weighted postcontrast (C) images show multiple renal cysts replacing the renal parenchyma. The lack of encapsulation, normal renal parenchyma in between some of the cysts, and several satellite cysts clearly separate from the main cluster all favor localized cystic disease of the kidney.

Localized cystic disease is an uncommon renal cystic disease of unknown pathogenesis that can imitate a multiloculated renal mass. It consists of multiple renal cysts focally or diffusely involving the kidney.<sup>84</sup> Findings that suggest localized cystic disease includes lack of encapsulation, normal renal parenchyma separating the cysts, and additional satellite cysts adjacent to but separate from the main group.<sup>59,84</sup> When recognized, localized cystic disease can be safely observed to document stability and establish benignity (Figure 63-42). metastatic disease. However, there have been recent reports of renal biopsies of indeterminate cystic renal masses to avoid surgery in benign category III lesions.<sup>68</sup> Arguments against biopsy of indeterminate cystic renal masses include procedural complications, needle track seeding, and the fact that negative biopsy results may not be definitive.<sup>85</sup> At this time, more studies are needed to further define the role of biopsy in the evaluation of cystic renal lesions.

#### **ROLE OF BIOPSY**

Traditionally, biopsy or aspiration of a cystic renal lesion has been limited to cases of clinically suspected abscess or

#### What the Referring Physician Needs to Know: Cystic Renal Diseases

- A renal cyst that meets each of the criteria for a given imaging modality can be confidently diagnosed as a benign simple cyst and requires no additional evaluation.
- When a cystic renal lesion does not meet the imaging criteria for a simple renal cyst, it should be considered a cystic renal mass. For practical purposes, the differential diagnosis for such includes a complicated renal cyst and cystic RCC.
- Últrasonography can accurately characterize most simple and minimally complex renal cysts without need for further imaging follow-up.

#### **Key Points**

#### **Benign Lesions**

Angiomyolipoma

- Fat-containing lesion on CT is nearly pathognomonic for angiomyolipoma.
- Minimal fat angiomyolipoma cannot be differentiated from RCC on imaging alone.

Oncocytoma

- A well-defined, solid renal mass with central stellate scar is evident on imaging.
- It cannot reliably be distinguished from RCC on imaging alone.

- CT is the primary imaging modality used in the evaluation of the cystic renal mass.
- MRI is being used with increasing frequency in cases in which the findings on CT and/or ultrasonography are not definitive.
- The Bosniak classification is an approach to renal cysts that attempts to categorize each cyst as benign/ nonsurgical (categories 1 and 2), probably benign but requires follow-up (category 2F), and suspicious/surgical (categories 3 and 4).
- Biopsy may suggest the diagnosis. Leiomyoma
- This is a well-circumscribed, peripheral lesion.
- It is rare and cannot be differentiated from other solid renal tumors on imaging.

Mesoblastic Nephroma

- This is the most common benign renal mass in a neonate.
- It is congenital and usually large.

Continued

#### Key Points-cont'd

#### Adenoma

 Adenoma is indistinguishable from RCC on imaging and can be indistinguishable from it on histology.

#### **Malignant Lesions**

- Malignant Renal Parenchymal Tumors, Including Renal Cell Carcinoma and Its Subtypes
- RCC is the most common malignant renal tumor and represents the majority of solid renal masses. Classification of RCC subtypes is difficult on imaging.
- Multiphase CT and MRI with dynamic contrast enhancement are both acceptable techniques for the characterization of renal masses and staging of RCC.
- Urothelial Carcinomas
- CT urography is the examination of choice for accurate staging of urothelial malignancy.
- Urothelial carcinoma may appear as a sessile or polypoid filling defect in the collecting system, as diffuse urothelial thickening, or as an infiltrative renal lesion, producing a "faceless" kidney.
- False-negative results in detecting urothelial malignancy may arise with inadequate contrast opacification of the collecting system, which can be minimized with repeat delayed and/or prone imaging.

Wilms' Tumor

• Wilms' tumor accounts for nearly 90% of pediatric renal masses and is bilateral in 5% to 10% of cases.

• Screening is typically performed with ultrasonography. Either contrast-enhanced CT or MRI is a suitable method for radiologic staging.

#### **Cystic Lesions**

Simple Cysts and Complex Cystic Renal Masses

- A simple cyst may change by more than 10 HU on helical CT because of pseudoenhancement.
- De-enhancement in vascular neoplasms differs from avascular high attenuation cysts that do not decrease in attenuation on delayed scans.
- Multiloculated renal masses are in a subgroup of cystic renal lesions that should be considered when a cystic mass has more than three or four septations. The two most common multiloculated renal masses are RCC and multilocular cystic nephroma.
- When findings differ between examinations, the most worrisome finding should guide lesion classification and management.
- Calcification is now considered less important in the evaluation of the cystic renal mass.
- A renal mass with attenuation greater than simple fluid on unenhanced CT is considered of high attenuation or hyperdense.
- The presence of wall thickening or nodularity precludes a benign diagnosis and the likelihood of malignancy increases significantly in the presence of enhancement.
- There is no universally accepted Hounsfield unit increase that defines enhancement.

#### SUGGESTED READING

- Allen BC, Tirman P, Jennings Clingan M, et al: Characterizing solid renal neoplasms with MRI in adults. *Abdom Imaging* 39:358–387, 2014.
- Browne RF, Meehan ČP, Colville J, et al: Transitional cell carcinoma of the upper urinary tract: spectrum of imaging findings. *Radiographics* 25:1609– 1627, 2005.
- Jinzaki M, Silverman SG, Akita H, et al: Renal angiomyolipoma: a radiological classification and update on recent developments in diagnosis and management. *Abdom Imaging* 39:588–604, 2014. Kang SK, Huang WC, Pandharipande PV, et al: Solid
- renal masses: what the numbers tell us. *AJR Am J Roentgenol* 202:1196–1206, 2014.
- Sahni VA, Silverman SG: Imaging management of incidentally detected small renal masses. Semin Intervent Radiol 31:9–19, 2014.

#### REFERENCES

- Siegel CL, McFarland EG, Brink JA, et al: CT of cystic renal masses: analysis of diagnostic performance and interobserver variation. *AJR Am J Roentgenol* 169:813–818, 1997.
- 2. Kissane JM: The morphology of renal cystic disease. *Perspect Nephrol Hypertens* 4:31–63, 1976.
- 3. Bosniak MA: The current radiological approach to renal cysts. *Radiology* 158:1–10, 1986.
- Davidson AJ, Hartman DS, Choyke PL, et al: Radiologic assessment of renal masses: implications for patient care. *Radiology* 202:297–305, 1997.
- Nascimento AB, Mitchell DG, Zhang XM, et al: Rapid MR imaging detection of renal cysts: agebased standards. *Radiology* 221:628–632, 2001.
- Logue LG, Acker RE, Sienko AE: Angiomyolipoma in tuberous sclerosis: best cases from the AFIP. *Radiographics* 23:241–246, 2003.
- Khan AN, Boylan C, Macdonald S, et al: Angiomyolipoma, kidney. <a href="http://emedicine.medscape.com/">http://emedicine.medscape.com/</a> article/376848-overview>. (Accessed 31.08.09.)
- 8. Zamboni G, Pea M, Martignoni G, et al: Clear cell "sugar" tumor of the pancreas: a novel member of the family of lesions characterized

by the presence of perivascular epithelioid cells. *Am J Surg Pathol* 20:722–730, 1996.

- Hornick JL, Fletcher CD: PEComa: what do we know so far? *Histopathology* 48:75–82, 2006.
- 0. Wagner BJ, Wong-You-Cheong JJ, Davis CJ: Adult renal hamartomas: archives of the AFIP. *Radiographics* 17:155–169, 1997.
- Silverman SG, Mortele KJ, Tuncali K, et al: Hyperattenuating renal masses: etiologies, pathogenesis, and imaging evaulation. *Radiographics* 27:1131–1143, 2007.
- Israel G, Hindman N, Hecht E, et al: The use of opposed-phase chemical shift MRI in the diagnosis of renal angiomyolipomas. *AJR Am J Roentgenol* 184:1868–1872, 2005.
- Outwater EK, Bhatia M, Siegelman ES, et al: Lipid in renal clear cell carcinoma: detection on opposed-phase gradient-echo MR images. *Radiology* 205:103–107, 1997.
- 14. Kalva SP, Sahani D *Oncocytoma, kidney.* <a href="http://emedicine.medscape.com/article/379653-media">http://emedicine.medscape.com/article/379653-media</a>. (Accessed 15.03.10.)
- 15. Choudhary S, Rajesh A, Mayer NJ, et al: Renal oncocytoma: CT features cannot reliably

distinguish oncocytoma from other renal neoplasms. *Clin Radiol* 64:517–522, 2009.

- Laperriere J, Lafortune M: Case of the day: general: oncocytoma of the right kidney. *Radio-graphics* 10:1105–1107, 1990.
- Crino PB, Nathanson KL, Henske EP: The tuberous sclerosis complex. N Engl J Med 355:1345–1356, 2006.
- Dunnick NR, Sandler CM, Newhouse JH, et al: Textbook of uroradiology, ed 3, Philadelphia, 2001, Lippincott Williams & Wilkins.
- Wootton SL, Rowen SJ, Griscom NT: Pediatric case of the day: congenital mesoblastic nephroma. *Radiographics* 11:719–721, 1991.
- Dunnick NR, Hartman DS, Ford KK: The radiology of juxtaglomerular tumors. *Radiographics* 20:260–261, 2000.
- 21. Licht MR: Renal adenoma and oncocytoma. Semin Urol Oncol 13:262–266, 1995.
- 22. Jemal A, Siegel R, Ward E, et al: Cancer statistics, 2006. *CA Cancer J Clin* 56:106, 2006.
- Ries LAG, Melbert D, Krapcho M, et al, editors: SEER cancer statistics review, 1975–2004, Bethesda, MD, 2007, National Cancer Institute.

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<a href="http://seer.cancer.gov/csr/1975\_2004/">http://seer.cancer.gov/csr/1975\_2004/</a>>. Based on November 2006 SEER data submission, posted to the SEER website.

- Zhang J, Lefkowitz RA, Bach A: Imaging of kidney cancer. *Radiol Clin North Am* 45:119– 147, 2007.
- Choyke PL, Glenn GM, Walther MM, et al: Hereditary renal cancers. *Radiology* 226:33–46, 2003.
- 26. Prasad SR, Humphrey PA, Catena JR, et al: Common and uncommon histologic subtypes of renal cell carcinoma: imaging spectrum with pathologic correlation. *Radiographics* 26:1795– 1806, 2006.
- Ritchie AW, Chisholm GD: The natural history of renal carcinoma. *Semin Oncol* 10:390–400, 1983.
- Coll DM, Smith RC: Update on radiological imaging of renal cell carcinoma. *BJU Int* 99:1217–1222, 2007.
- 29. Kovacs G, Akhtar M, Beckwith BJ, et al: The Heidelberg classification of renal cell tumours. *J Pathol* 183:131–133, 1997.
- Davidson AJ, Choyke PL, Hartman DS, et al: Renal medullary carcinoma associated with sickle cell trait: radiologic findings. *Radiology* 195:83–85, 1995.
- Davis CJ, Jr, Mostofi FK, Sesterhenn IA: Renal medullary carcinoma: the seventh sickle cell nephropathy. Am J Surg Pathol 19:1–11, 1995.
- Robson CJ, Churchill BM, Anderson W: The results of radical nephrectomy for renal cell carcinoma. J Urol 101:297–301, 1969.
- Daniel WW, Jr, Hartman GW, Witten DM, et al: Calcified renal masses: a review of ten years' experience at the Mayo Clinic. *Radiology* 103:503–508, 1972.
- 34. Catalano C, Fraioli F, Laghi A, et al: Highresolution multidetector CT in the preoperative evaluation of patients with renal cell carcinoma. *AJR Am J Roentgenol* 180:1271–1277, 2003.
- Johnson CD, Dunnick NR, Cohan RH, et al: Renal adenocarcinoma: CT staging of 100 tumors. AJR Am J Roentgenol 148:59–63, 1987.
- Yamashita Y, Honda S, Nishiharu T, et al: Detection of pseudocapsule of renal cell carcinoma with MR imaging and CT. AJR Am J Roentgenol 166:1151–1155, 1996.
- Semelka RC, Shoenut JP, Magro CM, et al: Renal cancer staging: comparison of contrast-enhanced CT and gadolinium-enhanced fat-suppressed spin-echo and gradient-echo MR imaging. *J Magn Reson Imaging* 3:597–602, 1993.
- 38. Hecht EM, Israel GM, Krinsky GA, et al: Renal masses: quantitative analysis of enhancement with signal intensity measurements versus qualitative analysis of enhancement with image subtraction for diagnosing malignancy at MR imaging. *Radiology* 232:373–378, 2004.
- Maturen KE, Nghiem HV, Caoili EM, et al: Renal mass core biopsy: accuracy and impact on clinical management. *AJR Am J Roentgenol* 188: 563–570, 2007.
- Motzer RJ, Michaelson MD, Rosenberg J, et al: Sunitinib efficacy against advanced renal cell carcinoma. J Urol 178:1883–1887, 2007.
- 41. Motzer RJ, Bander NH, Nanus DM: Renal-cell carcinoma. N Engl J Med 335:865–870, 1996.
- Kirkali Z, Tuzel E: Transitional cell carcinoma of the ureter and renal pelvis. *Crit Rev Oncol Hematol* 47:155–169, 2003.
- Wong-You-Cheong JJ, Wagner BJ, Davis CJ, Jr: Transitional cell carcinoma of the urinary tract: radiologic-pathologic correlation. *Radiographics* 18:123–142, 1998.
- 44. Browne RF, Meehan CP, Colville J, et al: Transitional cell carcinoma of the upper urinary tract:

spectrum of imaging findings. *Radiographics* 25:1609–1627, 2005.

- Caoili EM, Cohan RH, Korobkin M, et al: Urinary tract abnormalities: initial experience with multi-detector row CT urography. *Radiol*ogy 222:353–360, 2002.
- Takahashi N, Kawashima A, Glockner JF, et al: MR urography for suspected upper tract urothelial carcinoma. *Eur Radiol* 19:912–923, 2009.
- Lerner SE, Blute ML, Richardson RL, et al: Platinum-based chemotherapy for advanced transitional cell carcinoma of the upper urinary tract. *Mayo Clin Proc* 71:945–950, 1996.
- Bailey JE, Roubidoux MA, Dunnick NR: Secondary renal neoplasms. *Abdom Imaging* 23:266–274, 1998.
- Hunter S, Samir A, Eisner B, et al: Diagnosis of renal lymphoma by percutaneous image guided biopsy: experience with 11 cases. J Urol 176:1952–1956, 2006.
- Urban BA, Fishman EK: Renal lymphoma: CT patterns with emphasis on helical CT. *Radiographics* 20:197–212, 2000.
- Choyke PL, White EM, Zeman RK, et al: Renal metastases: clinicopathologic and radiologic correlation. *Radiology* 162:359–363, 1987.
- Kaste SC, Dome JS, Babyn PS, et al: Wilms tumour: prognostic factors, staging, therapy and late effects. *Pediatr Radiol* 38:217, 2008.
- Slovis TL: Wilms tumour minisymposium. Pediatr Radiol 38:1, 2008.
- Otgun I, Arda IS, Haberal N, et al: Renal cell carcinoma: case report and literature review. *J Pediatr Surg* 40:e13–e16, 2005.
- Ahmed HU, Arya M, Levitt G, et al: Part I. Primary malignant non-Wilms' renal tumours in children. *Lancet Oncol* 8:730–737, 2007.
- Cook A, Lorenzo AJ, Salle JL, et al: Pediatric renal cell carcinoma: single institution 25-year case series and initial experience with partial nephrectomy. *J Urol* 175:1456–1460, 2006.
- Brisse HJ, Smets AM, Kaste SC, et al: Imaging in unilateral Wilms tumour. *Pediatr Radiol* 38:18– 29, 2008.
- 58. Ritchey ML: Renal sparing surgery for Wilms tumor. J Urol 174:1172–1173, 2005.
- Hartman DS, Choyke PL, Hartman MS: A practical approach to the cystic renal mass. *Radiographics* 24:S101–S115, 2004.
- Ascenti G, Silvio M, Zimbaro G, et al: Complex cystic renal masses: characterization with contrastenhanced US. *Radiology* 243:158–165, 2007.
- 61. Israel GM, Bosniak MA: How I do it: evaluating renal masses. *Radiology* 236:441–450, 2005.
- Israel GM, Hindman N, Bosniak MA: Evaluation of cystic renal masses: comparison of CT and MR imaging by using the Bosniak classification system. *Radiology* 231:365–371, 2004.
- 63. Hecht EM, Israel GM, Krinsky GA, et al: Renal masses: quantitative analysis of enhancement with signal intensity measurements versus qualitative analysis of enhancement with image subtraction for diagnosing malignancy at MR imaging. *Radiology* 232:373–378, 2004.
- Ho VB, Allen SF, Hood MN, et al: Renal masses: quantitative assessment of enhancement with dynamic MR imaging. *Radiology* 224:695–700, 2002.
- Bosniak MA: Problems in the radiologic diagnosis of renal parenchymal tumors. Urol Clin North Am 20:217–230, 1993.
- Israel GM, Bosniak MA: Calcification in cystic renal masses: is it important in diagnosis? *Radiology* 226:47–52, 2002.
- 67. Israel GM, Bosniak MA: Follow up CT of moderately complex cystic lesions of the kidney:

(Bosniak IIF). AJR Am J Roentgenol 181:627–633, 2003.

- Harisinghani MG, Maher MM, Gervais DA, et al: Incidence of malignancy in complex cystic renal masses. *AJR Am J Roentgenol* 180:755–758, 2003.
- Siegel CL, McFarland EG, Brink JA, et al: CT of cystic renal masses: analysis of diagnostic performance and interobserver variation. *AJR Am J Roentgenol* 169:813–818, 1997.
- Park KB, Kim B, Kim SH, et al: Assessment of cystic renal masses based on Bosniak classification: comparison of CT and contrast-enhanced US. *Eur J Radiol* 61:310–314, 2007.
- Israel GM, Bosniak MA: An update of the Bosniak Renal Cyst Classification System. Urology 66:484–488, 2005.
- Rosenberg ER, Korobkin M, Foster W, et al: The significance of septations in a renal cyst. *AJR Am J Roentgenol* 144:593–595, 1985.
- 73. Hartman DS, Weatherby E, Laskin WB, et al: Cystic renal cell carcinoma: CT findings simulating a benign hyperdense cyst. *AJR Am J Roentgenol* 159:1235–1237, 1992.
- 74. Jonisch AI, Rubinowitz AN, Mutalik PG, et al: Can high-attenuation renal cysts be differentiated from renal cell carcinoma at unenhanced CT? *Radiology* 243:445–450, 2007.
- Benjaminov O, Atri M, O'Malley M, et al: Enhancing component on CT to predict malignancy in cystic renal masses and interobserver agreement of different CT features. *AJR Am J Roentgenol* 186:665–672, 2006.
- Birnbaum BA, Jacobs JE, Ramchandani P: Multiphasic renal CT: comparison of renal mass enhancement during the corticomedullary and nephrographic phases. *Radiology* 200:753–758, 1996.
- Bosniak MA: The small renal parenchymal tumor: detection, diagnosis and controversies. *Radiology* 179:307–317, 1991.
- Siegel CL, Fisher AJ, Bennet HF: Interobserver variability in determining enhancement of renal masses on helical CT. AJR Am J Roentgenol 172:1207–1212, 1999.
- Birnbaum BA, Maki DD, Chakraborty DP, et al: Renal cyst pseudoenhancement: evaluation with an anthropomorphic body CT phantom. *Radiology* 225:83–90, 2002.
- Coulam CH, Sheafor DH, Leder RA, et al: Evaluation of pseudoenhancement of renal cysts during contrast-enhanced CT. *AJR Am J Roentgenol* 174:493–498, 2000.
- Maki DD, Birnbaum BA, Chakraborty DP, et al: Renal cyst pseudoenhancement: beamhardening effects on CT numbers. *Radiology* 213:468–472, 1999.
- Macari M, Bosniak M: Delayed CT to evaluate renal masses incidentally discovered at contrastenhanced CT: demonstration of vascularity with de-enhancement. *Radiology* 213:674–680, 1999.
- Hartman DS, Davis CJ, Johns TT, et al: The multiloculated renal mass: considerations and differential features. *Radiographics* 7:29–52, 1987.
- Slywotzky CM, Bosniak MA: Localized cystic disease of the kidney. AJR Am J Roentgenol 176:843–849, 2001.
- Bosniak MA: Should we biopsy complex cystic renal masses (Bosniak Category III)? AJR Am J Roentgenol 181:1425–1426, 2003.

# **Diffuse Renal Parenchymal Diseases**

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Renal failure may be classified as prerenal when secondary to a reduction in the renal perfusion pressure gradient, renal when the result of intrinsic disease of the renal parenchyma, and postrenal when secondary to an abnormality of urine outflow.

Prerenal renal failure may arise from alterations in renal artery perfusion or venous drainage. Renal artery stenosis results in decreased perfusion. Renal vein thrombosis results in increased backpressure and edema. Postrenal causes of abnormal renal function are typically those causing obstruction to the urine outflow from calculi, ureteropelvic dysfunction, or masses.

Renal parenchymal abnormalities may be divided into those that involve the entire kidney, such as rejection, glomerulonephritides, amyloidosis, and drugs, and those that are either primarily cortical or primarily medullary, such as nephrocalcinosis. These conditions are discussed in this section.

### **Imaging Overview**

Glomerulonephritis (GN) has no specific imaging findings. Pathologic and immunologic assessment of biopsy samples continues to be the mainstay in diagnosis. Ultrasound evaluation of the kidneys is useful to exclude other causes of renal function impairment. Ultrasonography also may demonstrate calculi and nephrocalcinosis. The kidneys may be enlarged in acute GN or may be small in chronic GN. Morphologically the kidneys show a smooth contour.<sup>1,2</sup> Excretory or intravenous pyelography (IVP) (requires the administration of potentially nephrotoxic iodinated contrast and is therefore generally not performed in patients with diffuse renal parenchymal disease. Noncontrast computed tomography (CT) is useful for visualizing stones and the distribution of nephrocalcinosis. Contrastenhanced CT, as with IVP, requires nephrotoxic iodinated contrast and therefore is typically not used if renal function is abnormal. Magnetic resonance imaging (MRI) is insensitive to urinary stones and nephrocalcinosis, but it is useful in the imaging of renovascular abnormalities. Newer techniques such as diffusion- and perfusion-weighted imaging and ultrasmall superparamagnetic iron oxide (USPIO)-enhanced imaging may have advantages when evaluating diffuse renal diseases by not requiring a biopsy.<sup>3</sup>

#### RADIOGRAPHY

Intravenous urography may show bilaterally smooth, enlarged or small kidneys. The kidneys may show poor contrast excretion, depending on the stage of renal failure. Apparent expansion of the renal sinus fat is a commonly seen secondary sign of diffuse atrophy due to chronic renal diseases (Figure 64-1).

#### ULTRASONOGRAPHY

Renal echogenicity is typically equal to or less than that of the adjacent liver or spleen, respectively. Corticomedullary differentiation is normally better visualized on the right than the left. Abnormal ultrasonographic findings include increased renal echogenicity and bilateral enlarged kidneys (Figure 64-2). The utility of ultrasonography is to evaluate for hydronephrosis and vascular abnormalities (inflow or outflow) as causes for renal failure. The absence of both suggests intrinsic renal parenchymal disease. In chronic GN, the kidneys may show increased echogenicity and are usually small or show cortical loss with smooth margins. There may be proliferation of sinus fat.

Doppler ultrasonography, although nonspecific, can assist in the differential diagnosis of acute renal failure.<sup>4</sup> The normal renal resistive index is between 0.6 and 0.7. The RI is elevated in a large number of conditions, including prerenal, parenchymal, and postrenal causes. These include hepatorenal syndrome, renal vasculitis, acute crescentic and proliferative GN, and tubulointerstitial disease. Thus, without prior knowledge of the diagnosis, an elevation is useful only to suggest that renal parenchyma is indeed abnormal. The RI is normal in acute primary or secondary GN. Renal Doppler imaging has been used to follow treatment response.

#### COMPUTED TOMOGRAPHY

Noncontrast CT may show cortical calcification in chronic GN. The kidneys appear small and have a smooth contour in chronic GN but may show scarring in chronic pyelonephritis (Figure 64-3). CT scan may show normal or bilateral renal enlargement in acute GN (Figure 64-4).

#### MAGNETIC RESONANCE IMAGING

Nonspecific changes in renal size (Figure 64-5) and enhancement are seen in diffuse renal disease. Recent literature suggests that USPIO-enhanced MRI may be useful. USPIO-enhanced imaging shows the distribution of macrophages. Diffuse macrophage infiltration in rejection versus focal medullary in acute tubular necrosis (ATN), monitoring of drug reactions in immunosuppressed patients, and differentiating between reversible and chronic abnormalities are potential future uses of this modality.<sup>3</sup>

#### NUCLEAR MEDICINE

Renal function can be assessed using technetium-99m (<sup>99m</sup>Tc)labeled mercaptoacetyl triglycine (<sup>99m</sup>Tc-MAG3) or diethylenetetraminepentaacetic acid (<sup>99m</sup>Tc-DTPA). Cortical agents such

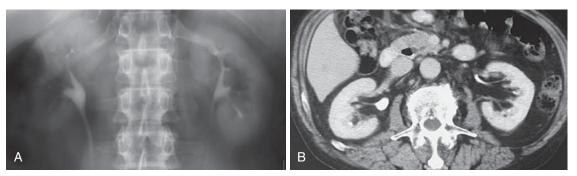
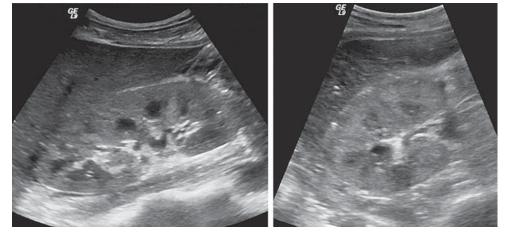


Figure 64-1 Renal sinus lipomatosis in a case with mild bilateral renal parenchymal disease. A, Intravenous pyelogram shows low-density prominent renal sinus fat. B, Computed tomography scan in the same patient confirms sinus lipomatosis.



**Figure 64-2** Longitudinal and transverse ultrasound images of the right kidney show an enlarged echogenic kidney with mild prominence of the relatively hypoechoic medullary pyramids. This is a nonspecific finding seen in patients with diffuse renal parenchymal disease. (*Courtesy Dr. Srinivas Prasad.*)



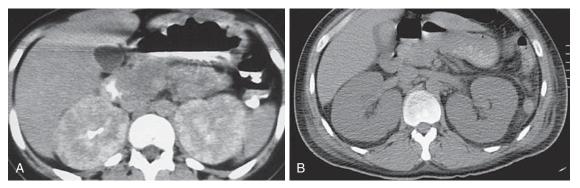
**Figure 64-3** Delayed image from contrast-enhanced computed tomography shows a unilateral small scarred kidney in a case of chronic pyelonephritis. Note the polar scar and the corresponding clubbed calyx in the left kidney.

as dimercaptosuccinic acid (DMSA) are used for evaluation of scars, such as in patients with pyelonephritis. Captopril renography is useful in evaluation of renal vascular diseases.

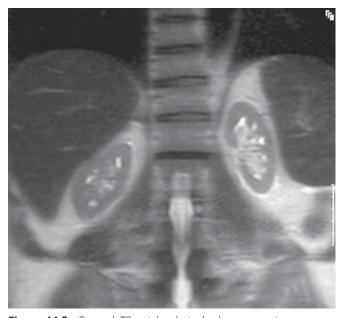
#### IMAGING ALGORITHM

The first step is to assess for dilation of the pelvicalyceal system and ureter with ultrasonography to determine if renal failure is renal or postrenal (Figure 64-6). If there is no hydronephrosis, Doppler imaging may be performed to assess for renovascular disease.

Renal size should be assessed in all patients. Renal size varies considerably within populations and by gender from 10 to 14 cm in males and 9 to 13 cm in females. Disease processes may initially cause an increase in renal size as a result of acute-phase edema and then cause a chronic decrease in renal size as a result of fibrosis. Thus, prior or serial ultrasound evaluation may be of greater benefit than a single measurement.<sup>1,2</sup> The



**Figure 64-4** Bilateral enlarged kidneys. Two different cases. **A**, A patient presented with a known history of lymphoma. Delayed image from contrast-enhanced computed tomography (CT) through the kidneys shows bilateral enlarged kidneys. The extremely heterogeneous appearance is consistent with diffuse parenchymal infiltration by lymphoma. **B**, Noncontrast CT in a patient with human immunodeficiency virus infection shows diffusely enlarged kidneys, a nonspecific finding seen in renal parenchymal diseases. (*Courtesy Dr. Hemendra Shah.*)



**Figure 64-5** Coronal T2-weighted single-shot magnetic resonance image shows bilateral, small, smooth kidneys in a patient with end-stage renal disease secondary to multiple myeloma.

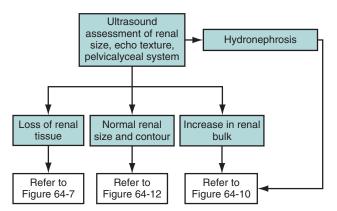


Figure 64-6 Radiologic approach to renal parenchymal diseases.

finding of small kidneys therefore implies that chronic diffuse renal disease is present.

Diseases that manifest as small kidneys are further categorized into those with smooth or irregular contour (Figure 64-7). Contour irregularity is seen with renal infarction, reflux nephropathy, and advanced analgesic nephropathy. Of these, only renal infarction will not cause any underlying calyceal abnormality (Figure 64-8). Smoothly marginated, small kidneys are seen in diseases that cause tubular atrophy and fine interstitial fibrosis. No focal scars or calyceal papillary distortions are noted. Further differentiation is limited in this subgroup except determination if the process is unilateral or bilateral (see Figure 64-7). Diseases that cause renal cortical atrophy also may result in compensatory renal sinus lipomatosis with little alteration in bipolar renal length (Figure 64-9).

The conditions that cause nephromegaly may do so in a focal or diffuse manner (Figure 64-10). Focal renal masses are most commonly secondary to cysts or neoplasms and rarely may be a focal manifestation of a disease that is usually diffuse (e.g., focal nephritis).

Unilateral diffuse nephromegaly may be secondary to renal edema from renal vein thrombosis or urinary obstruction. Diffuse unilateral nephromegaly also may be seen when physiologic compensatory hypertrophy occurs in the setting of contralateral renal failure. The causes of bilateral renal enlargement include infiltrative processes and infectious and immune disorders, most of which consist of glomerular diseases (see Figure 64-10). The spectrum of changes in renal size, contour, and pelvicalyceal system is summarized in (Figure 64-11).

Several diffuse parenchymal diseases do not cause any change in renal size (Figure 64-12). This group consists of diseases causing nephrocalcinosis and those that present primarily with calyceal or papillary abnormalities. Included in this latter subset are essentially all causes of renal papillary necrosis as well as granulomatous infections such as tuberculosis (TB) and brucellosis (see Figure 64-12).

### **Differential Diagnosis**

The differential diagnosis of diffuse renal parenchymal diseases includes the following:

• Immunoglobulin A (IgA) disease (Berger's nephropathy) is the most common type of GN in adults worldwide.<sup>5</sup>

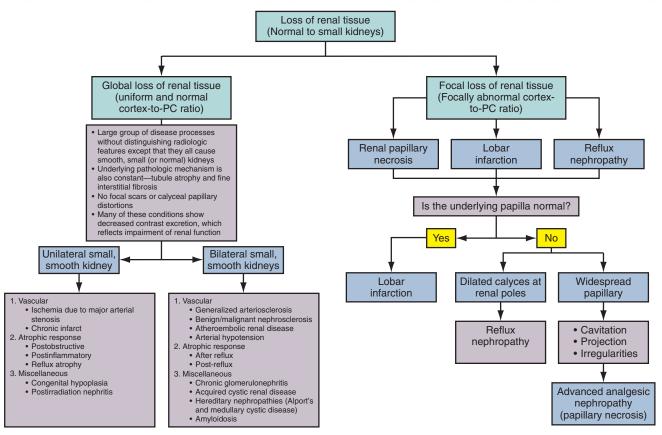


Figure 64-7 Algorithm showing approach to diffuse renal parenchymal diseases with loss of renal tissue.

- Henoch-Schönlein purpura is a systemic variant of IgA nephropathy that causes vasculitis of small vessels of which GN is a feature.
- Postinfectious GN occurs after streptococcal infection (usually of the skin), after a latency of 10 to 14 days. It manifests as nephritic syndrome, with a positive antistreptolysin O titer as diagnostic, and recovery is the rule in 2 to 3 weeks.<sup>6</sup>
- Mesangiocapillary GN can be primary or secondary to systemic lupus erythematosus, viral hepatitis, or hypocomplementemia; it usually manifests as a nephrotic syndrome but can be nephritic, with inevitable progression to end-stage renal failure.
- Rapidly progressive GN (crescentic GN) has a poor prognosis, with rapid progression to kidney failure over weeks. Vasculitic disorders such as Wegener's granulomatosis, polyarteritis, and Goodpasture's syndrome are diseases manifesting solely as rapidly progressive GN.<sup>7</sup> Patients with Wegener's granulomatosis and Goodpasture's syndrome may have hemoptysis in addition to renal failure.
- Minimal change GN causes 80% of nephrotic syndrome in children but only 20% in adults.
- Focal segmental glomerulosclerosis (FSGS) may be primary or secondary to reflux nephropathy, Alport's syndrome, heroin use, or human immunodeficiency virus (HIV) infection. FSGS presents as a nephrotic syndrome with varying degrees of renal impairment; 50% of people with FSGS progress to renal failure.

 Membranous GN is the leading cause of nephrotic syndrome in adults (35%). It is usually idiopathic but may be associated with cancers (lung, bowel), infection (hepatitis, malaria), drugs (penicillamine), and systemic lupus erythematosus.<sup>8</sup> A third of patients have stable disease, and a third progress to end-stage kidney failure.

## Glomerulonephritis

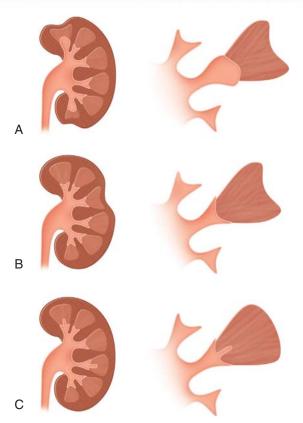
#### ETIOLOGY

GN is a complex spectrum of immune-mediated renal disease characterized by inflammation of the glomeruli that may be divided into primary and secondary types.<sup>4,9,10</sup> Primary GN is intrinsic to the kidney without additional systemic manifestations. Most cases are immune mediated. The most common type is poststreptococcal GN (PSGN). Secondary GN is associated with systemic disease, including certain infections (bacterial, viral, or parasitic pathogens), drugs, systemic disorders (systemic lupus erythematosus, vasculitis), or cancers.

#### PREVALENCE AND EPIDEMIOLOGY

#### Acute Glomerulonephritis

Acute GN comprises 25% to 30% of all cases of end-stage renal disease (ESRD) in the United States. Approximately one fourth of affected patients present with acute nephritis. Internationally, PSGN is associated with pharyngeal infection rather than



**Figure 64-9** Renal response to diseases causing global loss of renal bulk. The kidney usually responds by showing a decrease in renal size (*thick arrow*). Also note that the renal contour is smooth and the normal pelvicalyceal relationships are preserved. Uncommonly, there may be replacement of the wasted renal tissue with fatty proliferation in the renal sinus (renal sinus lipomatosis). The reduction in renal length is less in this case (*thin arrow*). (*Redrawn from Davidson AJ*, *Hartman DS*, *Choyke PL*, *Wagner BJ*, *editors*: Davidson's radiology of the kidney and genitourinary tract, ed 3, *Philadelphia*, 1999, WB Saunders, pp 76–79.)

**Figure 64-8** Focal loss of renal tissue. Diagrammatic representation of the pyelocalyceal and corresponding renal contour abnormalities. A, Reflux nephropathy, which shows papillary abnormality with overlying scar commonly seen at the renal poles. B, Lobar infarction showing scar with no underlying papillary abnormality. C, Papillary necrosis showing random papillary abnormalities without cortical involvement. (*Redrawn from Davidson AJ, Hartman DS, Choyke PL, Wagner BJ, editors: Davidson's* radiology of the kidney and genitourinary tract, *ed 3, Philadelphia, 1999, WB Saunders, pp 76–79.*)

cutaneous infection.<sup>11</sup> Acute GN has no predilection for any racial or ethnic group. Poor socioeconomic status is associated with an increased risk for PSGN. There is a 2:1 male-to-female ratio. Acute GN can occur at any age. Acute postinfectious GN usually develops in children 6 to 10 years of age but can affect any age group.

#### Chronic Glomerulonephritis

In the United States, chronic GN is the third leading cause of ESRD and accounts for 10% of patients on dialysis.<sup>12</sup> A recent decline in chronic GN in these countries has been noted, with an increase in diabetic nephropathy in patients on dialysis.<sup>13</sup> ESRD and death are common outcomes unless renal replacement therapy is instituted.

#### **CLINICAL PRESENTATION**

Patients may present with isolated hematuria, may be asymptomatic, may have nephrotic and nephritic syndromes, or may have either acute or chronic renal failure.<sup>14</sup> Acute GN develops over days and manifests as proteinuria, hematuria, hypertension, edema, and oliguria. Rapidly progressive GN develops over weeks to months, and chronic GN develops over months to years.

#### PATHOLOGY

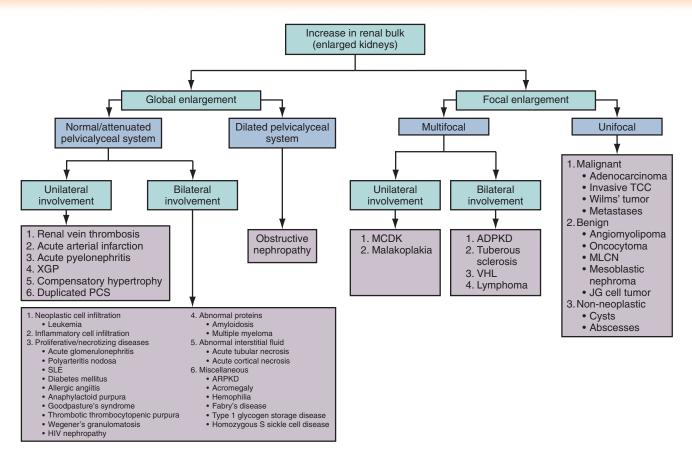
Kidneys are grossly normal or enlarged in diseases that manifest acutely and those without significant fibrosis and small and scarred in chronic disease and those with renal fibrosis. There may be hypercellularity with thickening of the glomerular basement membrane, hyalinization with deposition of amorphous proteinaceous material, and sclerosis that leads to obliteration of the glomerular tuft.<sup>10,15</sup>

#### **Pyelonephritis**

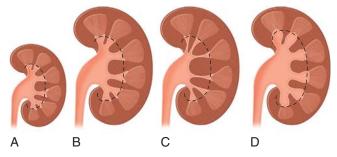
#### **ETIOLOGY**

Acute pyelonephritis is an infection of the renal parenchyma and renal pelvis inclusive of the tubules and interstitium commonly with a gram-negative organism such as *Escherichia coli* (>80%), *Proteus, Klebsiella, or Enterobacter*. Fungi or mycobacteria also may be causative. Inflammatory changes in the glomerulus (GN) are often excluded.<sup>16</sup> Most cases are ascending infections from the lower urinary tract (Figure 64-13), and a few are hematogeneous.

Emphysematous pyelonephritis is a necrotizing infection of the renal parenchyma seen primarily in diabetic patients. Xanthogranulomatous pyelonephritis (XGP) is usually secondary to chronic renal obstruction, as may be seen with ureteropelvic junction syndrome, congenital abnormalities, tumor, stricture, or stones in the calyces or renal pelvis. These patients often have comorbid conditions such as diabetes, pregnancy, systemic disease, or chronic liver disease.



**Figure 64-10** Algorithm showing approach to diffuse renal parenchymal diseases with increase in renal bulk. *ADPKD*, Autosomal dominant polycystic kidney disease; *ARPKD*, autosomal recessive polycystic kidney disease; *HIV*, human immunodeficiency virus; *JG*, juxtaglomerular; *MCDK*, multicystic dysplastic kidney disease; *MLCN*, multilocular cystic nephroma; *PCS*, pelvicalyceal system; *SLE*, systemic lupus erythematosus; *TCC*, transitional cell carcinoma; *VHL*, von Hippel-Lindau syndrome; *XGP*, xanthogranulomatous pyelonephritis.



**Figure 64-11** Diagrammatic representation of a spectrum of renal abnormalities in diseases causing generalized increase in renal bulk. A, Normal kidney. B, Enlarged kidney with normal pelvicalyceal system. C, Renal enlargement with constriction of pelvicalyceal system. D, Renal enlargement secondary to obstructive nephropathy. (*Redrawn from Davidson AJ, Hartman DS, Choyke PL, Wagner BJ, editors: Davidson's radiology of the kidney and genitourinary tract, ed 3, Philadelphia, 1999, WB Saunders, pp 76–79.)* 

#### PREVALENCE AND EPIDEMIOLOGY

Pyelonephritis may be divided into uncomplicated and complicated subgroups. Uncomplicated pyelonephritis refers to cases in which there are no permanent sequelae. Complicated pyelonephritis is associated with recurrent disease, structural abnormalities, diabetes, pregnancy, immunosuppression, and prolonged symptoms (>2 weeks in duration).

Predisposing factors for pyelonephritis include urinary tract obstruction, vesicoureteral reflux, pregnancy, urinary tract instrumentation, preexisting renal disease or systemic predisposition such as diabetes mellitus, and immunosuppression.<sup>17-21</sup>

Acute pyelonephritis implies an acute infection of the renal parenchyma, commonly infectious in cause. It is more common in adults than in children, in females younger than the 40 years of age, and in males older than the age of 65 years. A subtype of uncomplicated acute pyelonephritis affects young women.

Chronic pyelonephritis is renal injury induced by recurrent or persistent renal infections characterized by progressive renal scarring that may lead to ESRD. It is most commonly seen in children owing to the much higher incidence of vesicoureteral reflux in this population.<sup>22</sup> It is more common in females.

Emphysematous pyelonephritis is a life-threatening, fulminant, necrotizing upper urinary tract infection (UTI) associated with gas in the kidney. A rare infection, it affects adults of any age (mean, age 54 years). It is two to six times more common in females than in males<sup>23</sup> and is often seen in diabetic patients.

XGP is an unusual form of chronic pyelonephritis in which there is a chronic suppurative granulomatous infection of the kidney and surrounding tissues. An abnormal host response leads to destruction and replacement of the renal parenchyma by lipid-laden macrophages. XGP is typically a diffuse

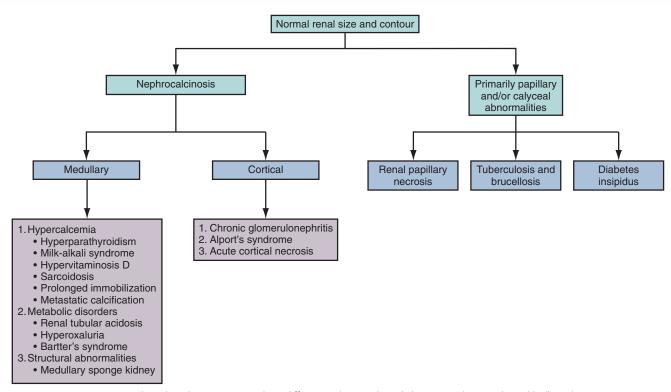


Figure 64-12 Algorithm showing approach to diffuse renal parenchymal diseases with normal renal bulk and contour.

condition; however, a rare focal form may be seen in children.<sup>24,26</sup> It can occur at any age but is more common between ages 45 and 65 years. Women are three times more commonly affected than men. *Proteus* and *E. coli* are the most common causative organisms.

The presentation of pyelonephritis in the pediatric age group is different from that in the adult and may be challenging to the clinician. There is less easy differentiation between upper and lower UTI on physical examination and by laboratory methods. Imaging is therefore of greater consideration even in the presence of uncomplicated disease or single episodes. The American Academy of Pediatrics recommends that children with confirmed UTI should undergo ultrasound of the kidneys and bladder. However, voiding urethrocystogram should not be performed routinely after the first febrile UTI.<sup>27</sup>

#### **CLINICAL PRESENTATION**

Patients present with fever, malaise, dysuria, flank pain, and tenderness. Laboratory data may show an elevated erythrocyte sedimentation rate, increased white blood cell count, and proteinuria. Children may show failure to thrive.<sup>28,29</sup>

XGP may mimic a neoplasm, with patients presenting with anorexia, a palpable mass, or weight loss. A fistulous tract to the skin may be noticed if there is involvement of surrounding tissues. Emphysematous pyelonephritis may manifest as a crepitant mass, a very suggestive finding. The laboratory studies may show hyperglycemia, acidosis, electrolyte imbalance, and thrombocytopenia. Blood, urine, or aspirate may be positive on culture.

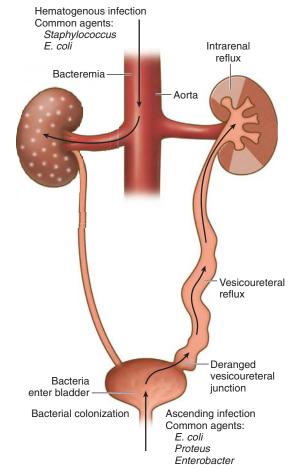
#### PATHOLOGY

In acute pyelonephritis, microabscesses are seen on the renal surfaces, mostly on the poles. These are often referred to as polar abscesses. Microscopic examination shows interstitial or tubular necrosis and mononuclear cell infiltrate with fibrosis. Chronic pyelonephritis appears as a small shrunken kidney with scars and blunted calyces. Emphysematous pyelonephritis is evident as a suppurative necrotizing infection of the renal parenchyma and perirenal tissues with multiple cortical abscesses. The gross appearance of XGP is a mass of yellow tissue with regional necrosis and hemorrhage, superficially resembling that of a renal cell carcinoma. The pathognomonic microscopic feature is the lipid-laden "foamy" macrophage accompanied by both chronic- and acute-phase inflammatory cells. Focal abscesses may be observed.

#### IMAGING

#### Acute Pyelonephritis

Acute pyelonephritis is usually multifocal. The diagnosis is commonly a clinical one based on increased renal size. American College of Radiology appropriateness criteria state that "imaging adds little to management if the patient responds to therapy within 72 hours" for uncomplicated pyelonephritis. As a result, imaging studies are rarely indicated for the diagnosis of acute uncomplicated pyelonephritis in the adult who presents with typical signs and symptoms. Imaging may be warranted if the presentation is atypical or confusing or if the patient's condition deteriorates or does not respond to therapy.



**Figure 64-13** Pathoanatomy of pyelonephritis. Ascending infection via the ureter is the most important cause and results from vesicoureteral reflux from the lower urinary tract. Hematogenous infection is less common and results from septicemia or bacterial endocarditis. (From Kumar V, Coltran R, Robbins SL, editor: The kidney and its collecting system. In Basic pathology, ed 6, Philadelphia, 1997, WB Saunders, pp 455–458.)

The imaging modality of choice is contrast-enhanced helical and/or spiral CT when there is suspicion of the development of a complication of acute pyelonephritis, in both adults and children. The algorithmic approach for the imaging diagnosis of acute pyelonephritis is summarized in Figure 64-14.<sup>30</sup>

Contrast-enhanced CT is the imaging study of choice in adults. It is more sensitive than ultrasonography or excretory urography and can more readily identify alterations in renal parenchymal perfusion, alterations in contrast excretion, presence of perinephric fluid, and nonrenal disease. Classically, a striated nephrogram may be seen (Figure 64-15).

Ultrasonography can sometimes detect acute pyelonephritis, but a negative study does not exclude the possibility.

Imaging may be required to make the diagnosis in infants and children in whom pyelonephritis manifests insidiously. The American Academy of Pediatrics recommends ultrasonography and either voiding cystourethrography or radionuclide cystography in the 2-month to 2-year age group after a single episode of pyelonephritis. Renal cortical scintigraphy with <sup>99m</sup>Tc-DMSA or glucoheptonate is primarily used to identify the presence of scars rather than acute infection, because both may manifest as photopenic areas. Scintigraphy is more sensitive for scarring than ultrasonography. Both scar and acute pyelonephritis show focal areas of diminished uptake in approximately 90% of patients (Figure 64-16). Vesicoureteral reflux is an important cause of pyelonephritis in children and can be detected and quantified with radionuclide cystography.

Imaging studies in conjunction with urologic procedures, including cystoscopy and excretory urography, may be used during follow-up examination to evaluate for urinary tract abnormalities that can predispose the patient to infection.

#### Chronic Pyelonephritis

Chronic pyelonephritis is associated with major anatomic abnormalities, urinary tract obstruction, renal calculi, renal dysplasia, or vesicoureteral reflux in young children. Recurrent or chronic infections are often present historically. The disease may be focal, segmental, or diffuse and unilateral or bilateral. Typically there is a scarred contracted kidney. There also may be focal atrophy (usually upper pole). A patient may present with a unilateral small contracted kidney and contralateral compensatory hypertrophy.

CT is the imaging modality of choice to help diagnose chronic pyelonephritis. It can show cortical scarring with distribution that could be focal, multifocal, and diffuse and involve one or both kidneys (Figure 64-17) and also compensatory contralateral renal hypertrophy. Radioisotopic scanning with <sup>99m</sup>Tc-DMSA is more sensitive than excretory urography for detecting renal scars. This is the preferred test in patients in the pediatric age group because it is sensitive and easy to perform and requires less radiation (Figures 64-18 and 64-19).

#### Emphysematous Pyelonephritis

Emphysematous pyelonephritis is unilateral more often than bilateral, and the left side is more often involved than the right side. On radiography, air can sometimes be seen overlying the renal fossa (Figure 64-20). Findings of excretory urography include increased renal size and delayed or absent excretion. CT helps differentiate between air in parenchyma and air and fluid collections (Figure 64-21). On ultrasound, there may be shadowing, ring-down artifacts, and nonvisualization of the kidney (Figure 64-22).

#### Xanthogranulomatous Pyelonephritis

XGP is unilateral more often than bilateral. The two forms are diffuse (>80%) and segmental. The kidney is enlarged with poor or no function. When extension occurs outside the kidney, it may involve the psoas and there may be fistulas to the abdominal wall. On excretory urography the disease may be diffusely or focally absent on the nephrogenic phase. A central stone may be seen in XGP. There may be fracture of the central stone secondary to rapid enlargement of the kidney in some cases of XGP. Findings on CT include an enlarged kidney, with decreased or absent function and possible central stone. The abscess cavity walls may enhance (Figure 64-23) and extension into the perinephric soft tissues may be seen. On MRI, lipid content results in increased signal on T1- and T2-weighted images (because of fat content in macrophages). Short tau inversion recovery and fat suppression can be used to confirm presence of XGP.

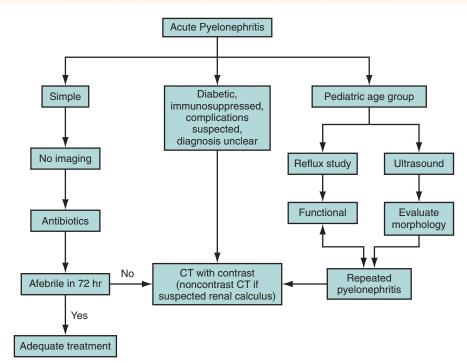


Figure 64-14 Algorithm for evaluation of acute pyelonephritis. CT, Computed tomography.

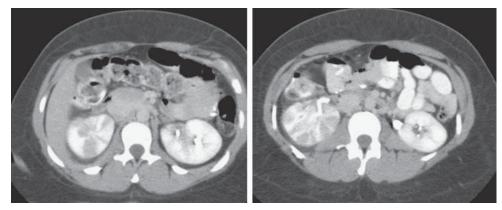


Figure 64-15 Contrast-enhanced computed tomography study in a young woman with suspected appendicitis. An enlarged right kidney is seen with multiple wedge-shaped nonenhancing areas and perinephric stranding, findings consistent with acute pyelonephritis.

# **Renal Tuberculosis**

#### ETIOLOGY

The genitourinary system is one of the most common sites of extrapulmonary tuberculous involvement. TB of the kidney is caused by hematogenous seeding of the kidney by *Mycobacterium tuberculosis* from the lungs, which serve as the primary site of infection. A long latent period (5 to 40 years) between primary infection and genitourinary disease is often noted. Of patients with pulmonary TB, 4% to 8% develop clinically significant genitourinary disease.<sup>31</sup>

#### PREVALENCE AND EPIDEMIOLOGY

TB is the most common worldwide cause of mortality from infectious disease. More than 90% of cases are seen in developing countries.

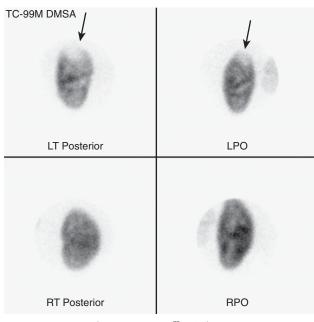
#### **CLINICAL PRESENTATION**

The most common presentation is frequent voiding and dysuria. Other symptoms include back, flank, and abdominal pain and hematuria. Constitutional symptoms such as weight loss, fever, and fatigue are also sometimes noted. Although the disease occurs secondary to hematogenous spread, clinically significant disease is usually limited to one side.

#### PATHOLOGY

A high rate of perfusion and high oxygen tension in the glomerular and peritubular capillary bed increases the likelihood of bacilli proliferating in this location and the formation of granulomas.

With impaired host immunity there is enlargement and coalescence of the granulomas. Communication with the



**Figure 64-16** Technetium-99m (<sup>99m</sup>Tc)-dimercaptosuccinic acid (DMSA) scan showing a focal photopenic defect (*arrows*) in the upper pole of the left kidney (*top row*) that was confirmed to be an area of focal acute pyelonephritis on computed tomography scan. Notice the normal parenchymal tracer uptake in the right kidney (*bottom row*).



**Figure 64-17** Contrast-enhanced computed tomography study showing bilateral renal cortical scarring (*arrows*) consistent with chronic pyelonephritis.

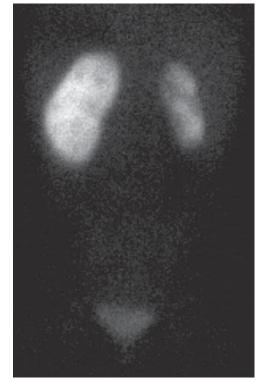
collecting system can lead to spread into the renal pelvis, ureters, urinary bladder, and accessory genital organs.

Granuloma formation, caseous necrosis, and cavitation occur as the infection progresses, eventually destroying the entire kidney.<sup>31</sup>

Caseating granulomas are the pathologic hallmark of tuberculous infection. Mycobacteria are visualized at microscopy or cultured from a morning urine sample. Repeated collection may be required to make the diagnosis.

#### IMAGING

Of patients with renal TB, 25% to 50% patients will have prior radiographic evidence of TB.



**Figure 64-18** Technetium-99m (<sup>99m</sup>Tc)-labeled mercaptoacetyl triglycine (<sup>99m</sup>Tc-MAG3) scan showing small poorly functioning right kidney with split renal function of 12%.

#### Radiography

Renal calcifications are a common manifestation, seen in up to 45% of patients. These may be granular, amorphous, curvilinear, and triangular or ringlike.<sup>32</sup>

End-stage TB is characterized by extensive parenchymal calcification in a nonfunctioning, "autonephrectomized" kidney, also termed a "putty kidney."<sup>32</sup>

- Findings of excretory urography include the following:
- Normal examination in 10% to 15%
- Parenchymal scars
- Papillary necrosis
- Infundibular strictures that lead to localized caliectasis or incomplete calyceal opacification (phantom calyx)<sup>32</sup>
- Kerr kink: Sharp angulation of the renal pelvis secondary to scarring

#### Computed Tomography

CT is done to determine the extent of renal and extrarenal disease spread (Figure 64-24).<sup>33</sup> Unenhanced CT is highly sensitive for detection of renal calcification, and contrast-enhanced CT shows a focal area of hypoperfusion, cortical thinning, parenchymal scarring, and fibrotic strictures of the infundibula, renal pelvis, and ureters.

#### Magnetic Resonance Imaging

On T2-weighted imaging there is a focal area of high signal intensity in areas of focal pyelonephritis. MR urography can show infundibular strictures with calyceal dilatation and also ureteral strictures. On postcontrast T1-weighted imaging there can be a focal area of hypoperfusion.

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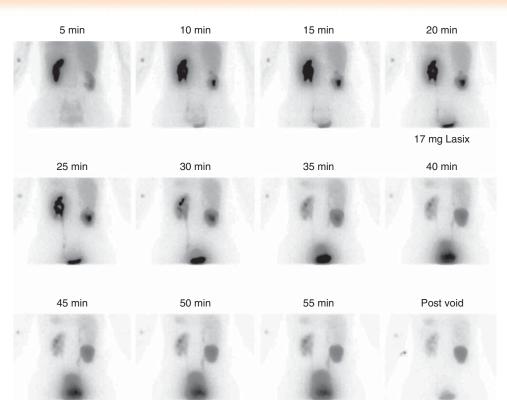
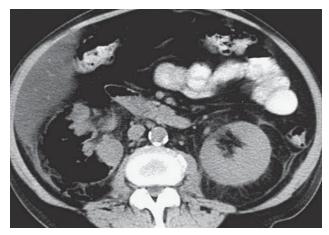


Figure 64-19 Dimercaptosuccinic acid (DMSA) scan (posterior projection) in a patient with chronic pyelonephritis showing small right kidney with focal photopenic areas consistent with cortical scars.



**Figure 64-20** Kidney, ureter, and bladder radiograph showing mottled air bubbles in the expected location of the left ureter consistent with emphysematous pyelitis. Note also the presence of ill-defined air bubbles in the left renal parenchyma also consistent with emphysematous pyelonephritis.



**Figure 64-21** Axial computed tomography images through the kidneys in a patient with diabetes, demonstrating the presence of air within the renal parenchyma consistent with emphysematous pyelonephritis.

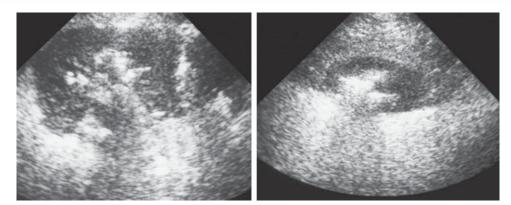


Figure 64-22 Ultrasound images through the kidney showing the presence of echogenic material with "dirty" shadowing consistent with parenchymal air secondary to emphysematous pyelonephritis.

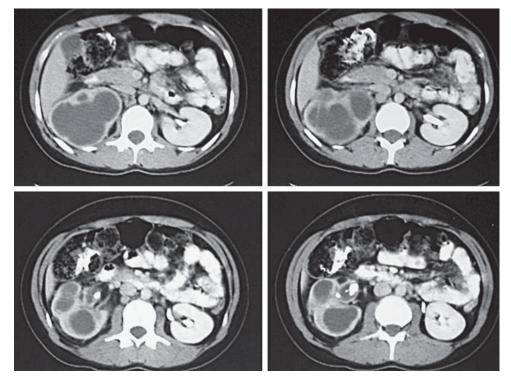


Figure 64-23 Contrast-enhanced computed tomography scan through the abdomen demonstrates multiple calculi in the renal pelvis and replacement of the normal right renal parenchyma with multiple cystic areas. These findings are consistent with xanthogranulomatous pyelonephritis.

#### Ultrasonography

A focal hypoechoic area is evident at the site of focal pyelonephritis. Hydronephrosis is focal and diffuse secondary to ureteral strictures. In the late state of the disease, ultrasound imaging will show a small calcified kidney with dense shadowing.

#### Nuclear Medicine

Scintigraphy will show a focal cold defect at the site of a renal abscess. A nonfunctioning kidney is seen in end-stage disease.

#### **Classic Signs: Renal Tuberculosis**

- Papillary necrosis
- Infundibular strictures with localized caliectasis or incomplete calyceal opacification
- End-stage renal parenchymal disease manifesting as a calcified putty kidney

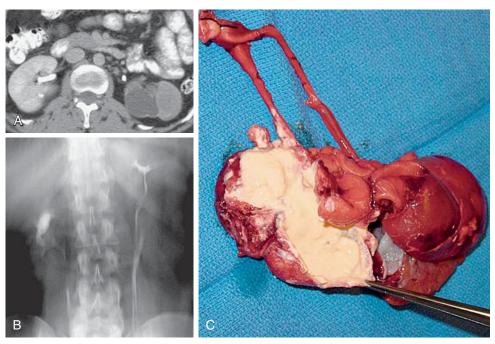


Figure 64-24 Renal tuberculosis. A, Contrast-enhanced computed tomography scan during excretory phase shows cystic degeneration involving predominantly the lower moiety of the left kidney. B, Intravenous pyelogram shows the duplicated left kidney and ureter with poor excretion from the left lower moiety. C, Gross specimen from the same case shows typical caseous material in the lower moiety of the kidney.

#### DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes chronic pyelonephritis, other causes of papillary necrosis, medullary sponge kidney, calyceal diverticulum, renal carcinoma, and XGP.

#### TREATMENT

A multidrug therapy regimen includes isoniazid, rifampicin, pyrazinamide, and ethambutol.<sup>33</sup> Surgery is done for treatment of complications, including ureteral strictures. Nephrectomy as a treatment for end-stage disease is controversial.

# Nephropathy Associated With Human Deficiency Virus

Human immunodeficiency virus (HIV)-associated renal disease may be secondary to renal parenchymal infection by HIV, opportunistic renal infection, or a side effect of antiviral drug therapy. The most common signs and symptoms include nephrotic-range proteinuria, hematuria, and sometimes pyuria. The clinical profile is HIV-positive African-American males, with early and rapidly progressive renal failure and near 100% mortality within 6 months.

On noncontrast CT, there is medullary hyperattenuation. After administration of a contrast agent, striations can be seen on the nephrographic phase. Complications related to HIV can be seen, such as fungal abscesses, which are well visualized as low-density lesions in the liver, spleen, and kidneys. With MRI, on T2-weighted imaging there is loss of corticomedullary differentiation.

#### **Key Points**

#### Pyelonephritis

- Pyelonephritis is infection of the renal pelvis, tubules, and interstitium.
- CT is the best overall diagnostic modality for diagnosis of all forms of pyelonephritis and their complications.
- The major differential diagnosis of acute pyelonephritis includes vasculitis and renal infarction and, less commonly, multifocal tumors and renal trauma.
- An assessment should be made for underlying anatomic abnormalities such as benign prostatic hypertrophy, vesicoureteral reflux, or urinary tract obstruction.

# Human Immunodeficiency Virus—Associated Nephropathy

- HIV infection is associated with FSGS.
- Enlarged echogenic kidneys are seen on ultrasonography.
- Differential diagnosis includes medical renal disease, ATN, and renal Pneumocystis jiroveci infection.

#### **Renal Tuberculosis**

- Infection starts as pyelonephritis or papillary necrosis and progresses to destruction of the entire kidney.
- Differential diagnosis includes chronic pyelonephritis, papillary necrosis, medullary sponge kidney, renal carcinoma, and XGP.

# Nephrocalcinosis

#### ETIOLOGY

Nephrocalcinosis is the pathologic deposition of calcium in the renal parenchyma. It affects the kidney diffusely as opposed to the localized calcification that may be observed in renal infarcts or caseating renal tuberculosis.<sup>34</sup> The three primary mechanisms for calcium deposition are as follows:

- 1. Metastatic calcification, in which a metabolic abnormality leads to deposition of calcium in the medulla of morphologically normal kidneys. The common causes are renal tubular acidosis type 1 (distal), hyperparathyroidism, hypercalciuria, and hyperoxaluria.
- 2. Urinary stasis, in which calcium salts precipitate in dilated collecting ducts containing static urine, as in medullary sponge kidney.
- 3. Dystrophic calcification, in which calcium deposition occurs in damaged renal tissue (e.g., acute cortical necrosis secondary to shock, placental abruption, or nephrotoxins).

Nephrocalcinosis can be divided into three categories: macroscopic, chemical, and microscopic. Macroscopic nephrocalcinosis is relevant in a discussion of imaging techniques and can be further divided into medullary and cortical types (Table 64-1).<sup>34-36</sup>

Medullary nephrocalcinosis (95%) is characterized by nodular calcification clustered in each medullary pyramid. The common causes are hyperparathyroidism (40%), renal tubular acidosis type 1 (20%), and medullary sponge kidney (20%). The pathogenesis includes hypercalcemia and hypercalciuria. Foci of calcification develop in renal tubular cells or the interstitium with hypercalcemia and in the tubular lumen with hypercalciuria.

Cortical nephrocalcinosis (5%) is rare. It is characterized by patchy calcification of the renal cortex. Causes include chronic

GN, familial infantile nephrotic syndrome, Alport's syndrome, and acute cortical necrosis. Chronic pyelonephritis and vesicoureteral reflux are also implicated. Other rare causes of cortical nephrocalcinosis include renal transplantation, primary hyperoxaluria, methoxyflurane abuse, autosomal recessive polycystic kidney disease, benign nodular cortical nephrocalcinosis, and chronic rejection in a transplant kidney.

#### PREVALENCE AND EPIDEMIOLOGY

Nephrocalcinosis may occur at any age. Males are affected more often than females.

#### **CLINICAL PRESENTATION**

Most patients are asymptomatic. Possible signs and symptoms include nephrolithiasis, polyuria and polydipsia, hypertension, proteinuria, microscopic pyuria, distal tubular dysfunction, secondary distal tubular acidosis, and renal failure (see Table 64-1).<sup>37-43</sup>

#### PATHOLOGY

The gross features of the disease depend on the underlying cause. Histologic findings include interstitial crystal deposition, within or between the tubules. These deposits consist of calcium phosphate or calcium oxalate. Special stains (e.g., von Kossa's and Pizzolato's) may be required for optimal visualization.

#### IMAGING

In medullary nephrocalcinosis the kidneys often are of normal size and contour. In cortical disease they are scarred. The distribution and density of calcification vary.<sup>44</sup> Cortical nephrocalcinosis is within the cortex or within 2 cm of the periphery of

TABLE 64-1	Nephrocalcinosis: Clinical Profiles and Mechanisms	
Туре	Clinical Profile	Mechanism
Cortica	Acute cortical necrosis	Nephrotoxic drugs (ethylene glycol, methoxyflurane anesthesia, amphotericin B) Acute vascular insult (shock, placental abruption)
	Chronic glomerulonephritis	End-stage renal disease with dystrophic calcification
	Alport's syndrome: Hereditary nephritis and nerve deafness	Dystrophic calcification
Medull	ary Primary and secondary hyperparathyroidism Bony metastases Prolonged immobilization	Skeletal deossification
	Sarcoidosis Milk-alkali syndrome	Increased intestinal absorption of calcium
	Medullary sponge kidney	ldiopathic Usually asymptomatic unless complicated Calcification secondary to urinary stasis in ectatic tubules
	Renal tubular acidosis (RTA) type 1 (distal RTA)	May be primary or secondary to other systemic disease (Sjögren's, lupus, others) Distal tubule unable to secrete hydrogen ions Metabolic acidosis with urinary pH >5.5 Type 2 (proximal) RTA does not cause nephrocalcinosis.
	Hyperoxaluria	Hereditary type Acquired: Secondary to small bowel disease or bariatric surgery



**Figure 64-25** Axial noncontrast computed tomography through the kidneys demonstrates diffuse bilateral cortical calcification consistent with cortical nephrocalcinosis in a patient with chronic glomerulonephritis.

the kidney (Figure 64-25). Medullary nephrocalcinosis does not involve the cortex.

#### Radiography

On plain radiography, medullary nephrocalcinosis appears as fine, stippled calcification or coarse calcification in the renal pyramids (Figure 64-26). Cortical nephrocalcinosis is evident as punctate or linear cortical calcification. On IVP there may be a "paintbrush" appearance or linear striations in patients with underlying medullary sponge kidney.

#### Computed Tomography

CT findings include stippled or confluent calcifications in the renal parenchyma (Figure 64-27). A ringlike pattern may be evident owing to relatively increased calcification at the corticomedullary junction.<sup>45,46</sup>

#### Magnetic Resonance Imaging

Calcification is not well seen on MRI compared with other modalities. Thus, MRI is not recommended in the evaluation of nephrocalcinosis.

#### Ultrasonography

Calcification manifests as hyperechoic foci, typically with posterior shadowing.<sup>46,47</sup> In medullary nephrocalcinosis there are echogenic renal pyramids (Figure 64-28) or increased echogenicity along the periphery of the pyramids. In cortical disease there is peripheral cortical hyperechogenicity. The kidney is typically scarred and may be shrunken. Acoustic shadowing may be absent.

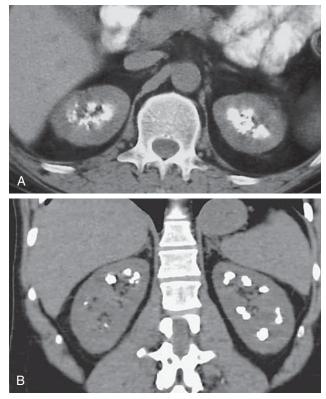
#### **Differential Diagnosis**

The differential diagnosis includes the following:

- Papillary necrosis is a common finding in analgesic nephropathy; curvilinear, ring-shaped, or triangular calcification in sloughed papillae; has irregular contour of pyramids; and may be indistinguishable from medullary nephrocalcinosis.
- Renal tuberculosis has focal amorphous calcification within kidney at sites of caseating infection or diffuse



**Figure 64-26** Kidney, ureter, and bladder radiograph in a known case of medullary sponge kidney shows clustered calcifications in the renal medulla bilaterally, consistent with medullary nephrocalcinosis.



**Figure 64-27** Axial (A) and coronal (B) computed tomography images demonstrating bilateral renal medullary calcifications consistent with medullary nephrocalcinosis in two different patients.

dense calcification throughout an entirely necrotic kidney ("putty" kidney)

• Extrapulmonary *Pneumocystis jiroveci* or *Mycobacterium avium-intracellulare* infection are seen in acquired immunodeficiency syndrome; may have both cortical and medullary punctate calcification.



Figure 64-28 Longitudinal ultrasound image shows well-defined echogenic pyramids secondary to calcifications consistent with medullary nephrocalcinosis.

# **Renal Papillary Necrosis**

#### **ETIOLOGY**

Renal papillary necrosis is an end point of various diseases that induce chronic tubulointerstitial nephropathy. The inner medulla is affected predominantly. These diseases have a common underlying mechanism that involves impairment of the vascular supply to the distal segments of the renal pyramids, leading to focal or diffuse ischemic necrosis of the pyramids.<sup>4</sup>

The diverse causes of renal papillary necrosis are easy to remember using the mnemonic POSTCARDS, which stands for Pyelonephritis, Obstruction, Sickle cell disease, Tuberculosis, Cirrhosis, Analgesics, Renal vein thrombosis, Diabetes, and Systemic vasculitis.

The most common cause in adults is diabetes. In this case there is often an association with UTI and impaired renal function, but the disorder also may be present in patients without any apparent diabetic nephropathy.<sup>4</sup>

#### PREVALENCE AND EPIDEMIOLOGY

Age group and gender prevalence depend on the cause. Renal papillary necrosis secondary to analgesic nephropathy typically affects middle-aged women. Diabetic renal papillary necrosis affects adults of both sexes. Obstructive renal papillary necrosis is more common in adult males.

#### **CLINICAL PRESENTATION**

The most common signs and symptoms include flank pain, dysuria, fever, ureteral colic, hypertension, pyuria, hematuria, and acute oliguric renal failure.

Laboratory findings include increased white or red blood cell counts, proteinuria, and impaired renal function.

#### PATHOPHYSIOLOGY

The renal medulla and papillae are particularly vulnerable to ischemic necrosis because they are in a constant state of relative hypoxia owing to slow blood flow in their supplying vasa recta



Figure 64-29 Intravenous urographic compression radiograph shows changes consistent with bilateral papillary necrosis. Note the pooling of the contrast agent in the necrotic papillae and tracking of the agent along the fornices.

and the hypertonic environment. Conditions that further reduce blood flow may produce frank ischemic necrosis.<sup>56</sup>

#### PATHOLOGY

In early-stage disease, medullary ischemia results in necrosis of the papillary tip. In the intermediate stage, patchy necrosis may progress to involve all elements of the papillae with clear demarcation between necrotic and viable papillary tissue. When the disease is advanced, diffuse fibrosis and chronic inflammatory cell infiltration extend into the renal interstitium.<sup>57</sup>

In the early stages of the disease the kidneys may be of normal size or mildly enlarged. In advanced disease the kidneys are reduced in size and may be smooth or scarred.

#### IMAGING

Bilateral disease occurs in patients who chronically use analgesics and in those with diabetes. In unilateral disease obstruction, infection or renal vein thrombosis should be suspected. There may be papillary swelling, irregular papillae, tract formation, cavitation, and sloughing.4

#### Radiography

Plain radiographs may show curvilinear or triangular small calcifications within the kidneys that represent calcified papillae.

The findings on an intravenous pyelogram depend on the stage of the disease (Figure 64-29).<sup>58</sup> In the early stages it is important to know that the study may be normal because there is only papillary swelling. In later states the classic findings are seen, which include the following:

• Contrast streaking from the fornix along the long axis of the papilla, which indicates that there is a breach in the urothelium. The "lobster claw" sign is a manifestation of this process with streaking that occurs on both sides of the

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fornix. The "ring" sign is an extreme manifestation of this phenomenon in which the circumferential contrast streaking occurs around a completely detached papilla.

- Varying degrees of necrosis within the papillae, which manifests as contrast puddles within the necrosed papillae. These contrast pools may be of different shapes and sizes, depending on the extent of necrosis.
- Both of these changes can coexist, and the necrotic papilla can be seen as a "signet ring" sign.

In the chronic stage, necrotic shrinkage of the papilla occurs along the continuum of the disease process, resulting in forniceal widening or sloughing of the papilla, which appears as a club-shaped calyx and may be associated with triangular filling defect(s) within the pelvis or ureter.

#### Computer Tomography

The classic signs of renal papillary necrosis also may be seen on CT.<sup>59</sup> Recently, multidetector-row CT has been shown to be helpful in identifying renal papillary necrosis at an early stage, when effective treatment of the underlying cause may reverse the ischemic process.<sup>60,61</sup> CT with or without CT urography also has been shown to be similar if not superior to intravenous urography for the demonstration of the abnormalities of renal papillary necrosis.<sup>61</sup> The various findings, which can be seen on CT, include the following (Figure 64-30):

• *Early stage:* CT can show a poorly marginated area of decreased enhancement at the tip(s) of the medullary



**Figure 64-30** Excretory phase computed tomography urogram of a patient with bilateral papillary necrosis secondary to phenacetin overdose, showing contrast agent pooling within sloughed papillae.

pyramid. These are thought to represent the early ischemic changes and are potentially reversible if the underlying cause is removed. Unlike areas of pyelonephritis, these do not demonstrate delayed marginal hyperemia.

- *Subacute stage:* The forniceal contrast penetration can be well visualized on CT. Also, necrosis of papillae results in contrast-filled cavities of various sizes. The sloughed papilla may be seen as a filling defect with or without associated hydronephrosis.
- *Chronic stage:* Similar to IVP, CT also demonstrates clubshaped calyces after necrosis and sloughing of the papillae. These can sometimes lead to diagnostic confusion with entities such as hydronephrosis, megacalyces, parapelvic cysts, or calyceal diverticula.

#### Magnetic Resonance Imaging

This modality generally is not used for the diagnosis of renal papillary necrosis.

#### Ultrasonography

Early-stage renal papillary necrosis can be diagnosed using ultrasonography.<sup>62</sup> However, the ultrasound findings at this stage may be nonspecific. Necrotic renal papillae may appear echogenic with a lucent rim produced by fluid surrounding the necrotic papilla.

Advanced disease may result in cystic cavities in the pyramids that communicate with the collecting system. Medullary calcification also may occur.<sup>63</sup>

#### **Classic Signs: Renal Papillary Necrosis**

- Lobster claw sign, ring sign, and signet ring sign
- Excavation of papillae with different patterns of contrast puddling
- Clubbing of calyces and triangular pelvic or ureteric filling defects secondary to papillary sloughing

# **Renal Transplant Complications** ETIOLOGY

Renal transplantation is a well-established treatment for patients with ESRD, conferring longer survival and a better quality of life than dialysis.<sup>64</sup> Currently, the average normal life expectancy of a transplanted cadaveric kidney is 7 to 10 years and it is 15 to 20 years when a live donor organ is used.<sup>65</sup> Complications of renal transplantation may be vascular, renal, urologic, or systemic.<sup>66</sup>

#### PREVALENCE AND EPIDEMIOLOGY

Postoperative complications occur in 12% to 20% of patients with renal transplants (Boxes 64-1 and 64-2).<sup>67</sup> Vascular complications account for 3% to 15% of complications and include transplant renal artery stenosis, arteriovenous fistulas and intrarenal pseudoaneurysms after transplant biopsy, extrarenal pseudoaneurysms, and graft thrombosis. Urologic complications include ureteral obstruction, urine leak, and perigraft fluid collections (lymphocele, abscess, urinoma, and hematoma). Parenchymal insults in the postoperative period include ATN, acute rejection, cyclosporine toxicity, and infection. A delay in

#### BOX 64-1 RENAL TRANSPLANT COMPLICATIONS

- Vascular
- Renal artery or venous thrombosis and occlusion
- Pseudoaneurysm
- Arteriovenous fistula
- RenalRejection
- Infection
- Acute tubular necrosis
- Drug toxicity (particularly cyclosporine)
- Urologic
- Ureteral obstruction
- Ureteral necrosis
- Calculi
- Leak
- Perinephric collection
- Systemic
- Infection
- Posttransplant lymphoproliferative disorder or other malignancy
- Hypertension

#### BOX 64-2 RENAL TRANSPLANT COMPLICATIONS ACCORDING TO TIME FROM TRANSPLANT SURGERY

#### **DURING SURGERY**

Hyperacute rejection

#### FIRST WEEK

- Acute rejection
- Acute tubular necrosis
- Arterial thrombosis
- Hematoma

#### 1 WEEK TO 1 MONTH

- Acute rejection
- Urinoma
- Transplant rupture

#### LONGER THAN 1 MONTH

- Chronic rejection
- Cyclosporine toxicity
- Lymphocele
- Ureteral stricture

treating any of these complications may lead to the loss of renal graft function or even to the patient's death.

#### **CLINICAL PRESENTATION**

Vascular complications may be asymptomatic or manifest as impaired renal function or hematuria. Acute rejection is typically asymptomatic. It may be accompanied by fever, graft tenderness, oliguria, or proteinuria. Fluid collections can manifest as pain or fever as well as worsening renal function.

#### PATHOPHYSIOLOGY

Generally, the transplanted kidney is placed heterotopically in the extraperitoneal space in the pelvis—that is, a right kidney is placed in the left iliac fossa and vice versa. The right iliac fossa is usually preferred, because the right iliac vein runs a more superficial and horizontal course, which makes creation of vascular anastomoses easier (Figure 64-31). For urinary tract reconstruction, the most common method is creation of a ureteroneocystostomy, although some institutions prefer ureteroureterostomy or ureteropyelostomy that connects the recipient native ureter to the donor pelvis.

#### PATHOLOGY

#### Vascular Complications

Vascular compromise may be due to surgical technique and anatomic factors (e.g., kinking of the vessels, anastomotic stricture) or to thrombosis.

#### Renal Complications

Hyperacute rejection results from circulating antibodies with immediate lack of perfusion. Acute rejection is caused by interstitial cell-mediated inflammation with or without hemorrhage, tubulitis, and arterial or arteriolar endotheliitis. Chronic rejection occurs from sclerosing vasculitis and extensive interstitial fibrosis.

#### Urologic Complications

Edema from surgery is often the cause of urologic problems in the immediate postoperative period. Later, anatomic and surgical factors (e.g., kinking of ureter, anastomotic leak, edema, or stricture) may play a role.

#### Systemic Complications

Infection and malignancy are increased as a result of immunosuppression.

#### IMAGING

#### Vascular Complications: Renal Artery Stenosis

Transplant renal artery stenosis is a potentially curable cause of treatment-refractory hypertension that accounts for 1% to 5% of cases of posttransplant hypertension. It typically manifests as accelerated hypertension of either sudden or insidious onset that is refractory to multiple drug regimens and is associated with progressive renal insufficiency in the presence of excessive diuretic use or treatment with angiotensin-converting enzyme inhibitors.

The cause of transplant renal artery stenosis appears to be multifactorial. Suture technique, trauma during the procedure, twisting of the artery, rejection, atherosclerosis, and cytomega-lovirus infection have been implicated.<sup>68</sup>

Ultrasound evaluation of the renal arteries is the best first test, particularly because transplant kidneys are located superficially and are thus easy to image. However, the test is useful only if the entire renal artery is evaluated. Elevated peak systolic velocities (>250 cm/s) and spectral broadening are associated with transplant artery stenosis. If vascular tortuosity prevents evaluation with ultrasound, MR angiography may be useful.<sup>66</sup> Formal angiography is sometimes required.

**Treatment.** Percutaneous transluminal angioplasty (PTA) is the treatment of choice for significant transplant renal artery stenosis. The success rate of PTA, as shown by serum creatinine levels, ranges from 85% to 93%, with levels usually returning to baseline values within 3 to 5 days. Blood pressure is normalized in 63% to 83% of patients with transplant renal artery stenosis.<sup>69</sup> Restenosis occurs in 5% to 30% and can be treated with



Figure 64-31 Axial noncontrast computed tomography (A) and longitudinal ultrasound image (B) showing the normal appearance of a transplant kidney. C, Three-dimensional volume-rendered angiogram in a different patient showing the normal renal transplant arterial anatomy with end-to-side arterial anastomosis. Note the small bilateral native kidneys.

repeat PTA or endovascular stent placement. Occasionally, surgery is required to treat an anastomotic stenosis.

#### Vascular Complications: Biopsy-Induced Vascular Injury

Arteriovenous fistulas and pseudoaneurysms are the two most common types of vascular injury resulting from percutaneous needle biopsy, occurring in 1% to 18% of renal allograft biopsies.<sup>70</sup> An arteriovenous fistula occurs when an adjacent artery and vein are lacerated simultaneously; a pseudoaneurysm occurs when only an artery is lacerated.

Arteriovenous fistulas can result in persistent hematuria or transplant dysfunction as a result of intrarenal steal phenomena. If large, pseudoaneurysms may rupture. On CT there may be abnormal enhancement of a pseudoaneurysm and/or early filling of the renal vein with contrast agent. On ultrasound, an arteriovenous fistula may manifest as focal areas of disorganized color flow outside the borders of normal renal vasculature. Spectral analysis may show increased arterial and venous flow, with high velocities and low impedance in both artery and vein. The vein may show a pulsed-wave Doppler trace resembling that of the artery.

Pseudoaneurysm is shown by a simple or complex hypoechoic structure on gray-scale ultrasonography that demonstrates blood flow, possibly with flow jets that alternate direction at the pseudoaneurysm neck on color flow Doppler images.

**Treatment.** Transcatheter embolization with coaxial catheter and coils is the treatment of choice for symptomatic arteriovenous fistulas and enlarging pseudoaneurysms.<sup>71</sup>

#### Vascular Complications: Graft Thrombosis

Graft thrombosis is an unusual complication seen in 0.5% to 3% of renal transplants.<sup>72</sup> It is a major cause of graft loss in the early (<1 week) posttransplant period. Arterial or venous thrombosis may occur from torsion, kinking, or angulation of the vessels. Other causes include hypercoagulable state and acute rejection.

In renal artery thrombosis, flow in both main and intrarenal arteries is completely absent on color Doppler imaging. In renal vein thrombosis, color Doppler flow shows complete absence of venous flow and abnormal arterial signal with a plateau-like reversed diastolic flow.<sup>37</sup>

CT angiography may be helpful in evaluating the transplant renal arterial and venous anatomy and patency, if renal function is good enough to allow the use of iodinated contrast.

**Treatment.** Surgical thrombectomy with arterial or venous repair is usually performed. However, nephrectomy is necessary in many cases. Catheter-directed thrombolysis is not recommended during the first 10 to 14 days after transplantation because of the risk for vascular suture line leakage of an immature anastomosis.<sup>73</sup>

#### **Renal Complications**

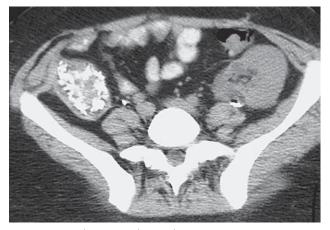
Parenchymal insults, including ATN, acute rejection, cyclosporine toxicity, and infection, are common in the postoperative period. Often the main differential diagnosis is between ATN and acute rejection. Because these entities are treated differently, early and accurate diagnosis is essential. ATN occurs in the immediate posttransplant period as a result of ischemia before revascularization and is seen more commonly in cadaveric transplants. ATN is common in the postoperative period, with 10% to 30% of transplant patients requiring temporary dialysis. It is generally self-limiting, with renal function recovering in days or weeks.

Acute rejection is the most common type of allograft rejection, affecting up to 40% of renal transplant patients, and occurs 1 to 3 weeks after transplant. Chronic rejection produces a slow deterioration in renal function that progresses over months or years, eventually leading to azotemia and hypertension.

**Computed Tomography.** Chronic rejection may result in cortical calcification (Figure 64-32).

**Magnetic Resonance Imaging.** Loss of corticomedullary differentiation on MR renography in the early cortical phase of enhancement has been suggested by some investigators as a sign of rejection, the degree correlating with severity of rejection.<sup>74</sup> However, this finding has not been substantiated in subsequent studies that have found loss of corticomedullary differentiation a nonspecific finding.<sup>75</sup> It has been shown that ATN and graft rejection exhibit distinct patterns of cortical and medullary enhancement<sup>76</sup>; however, differentiation is not possible when both conditions coexist.

**Ultrasonography.** Ultrasonography is not useful in differentiating between acute rejection and ATN. In acute rejection, increased graft size, increased size and decreased echogenicity of renal pyramids, decreased cortical echogenicity, and loss of corticomedullary differentiation are nonspecific findings that may be caused by vascular or parenchymal dysfunction.<sup>77</sup> In



**Figure 64-32** Chronic renal transplant rejection. Noncontrast computed tomography of the pelvis shows a normal-appearing transplant kidney in the left lower quadrant with a completely calcified chronically rejected kidney visible in the right lower quadrant.

severe rejection, scattered heterogeneous areas of increased echogenicity seen in the cortex reflect multifocal hemorrhage.

With chronic rejection there may be a small kidney with cortical thinning, increased graft echogenicity, and decreased intrarenal vascularity.

An increased intrarenal resistive index (>0.80) is indicative of graft dysfunction and may be seen with acute and chronic rejection, ATN, or cyclosporine toxicity. Cyclosporine toxicity may manifest as nephromegaly, increased cortical echogenicity, and prominent medullary pyramids.

**Nuclear Medicine.** Although in both acute rejection and ATN there is a decrease in renal function, perfusion is relatively preserved in ATN, allowing the difference in diagnosis to be made in the majority of cases. ATN typically resolves within 2 weeks. Persistent poor function and worsening graft blood flow after 2 weeks is suggestive of superimposed rejection (Figures 64-33 and 64-34).

Chronic rejection will typically manifest as prompt radiotracer uptake but overall decreased uptake and slightly prolonged retention.

#### Urologic Complications

These include ureteral obstruction, urine leak (3% to 9%), and perigraft fluid collections (50%). Perigraft collections include urinoma, lymphocele, abscess, and hematoma.

Ureteral obstruction occurs in 2% to 10% of all transplant recipients. The most common cause is ischemia occurring at the ureterovesical junction. Other causes include kinking, perigraft fibrosis, extrinsic compression from fluid collections, and intrinsic obstruction from edema, stricture, clots, calculi, or tumors. Antegrade nephrostography depicts the site and nature of the obstruction. It also provides an access route for urinary drainage. Retrograde pyelography is ideal in patients with ureteroureterostomy or ureteropyelostomy but can be difficult to perform in patients with ureteroneocystostomy owing to difficulty with cannulating the ureteral orifice.

Of renal transplant patients, 1% to 5% have leakage of urine (Figure 64-35). This complication is potentially serious owing to the risk for infection in the immunocompromised state. Most leaks occur at the distal ureter (possibly secondary to ischemia or rejection) or at the ureteroneocystostomy site.

A lymphocele is caused by lymphatic leakage from the allograft bed or allograft itself; the incidence is 0.6% to 18%. These leaks are usually slow and typically manifest more than 4 weeks after surgery (Figure 64-36). Hematoma, urinoma, and seroma typically occur in the acute postoperative period.

**Computed Tomography.** CT findings include the following:

- Ureteral obstruction: Fluid collections causing extrinsic compression with obstruction
- Urine leak and urinoma: Usually appears as a perigraft fluid collection without septa
- *Lymphocele:* Well-defined low-density collection with thin septa
- *Pyelonephritis and abscess:* Low-density areas with/without rim enhancement; abscess may also contain air locules (Figures 64-37 and 64-38).
- *Hematoma:* Acute hematoma appearing as a hyperattenuating nonenhancing area; older hematomas appear as heterogeneous fluid collections.

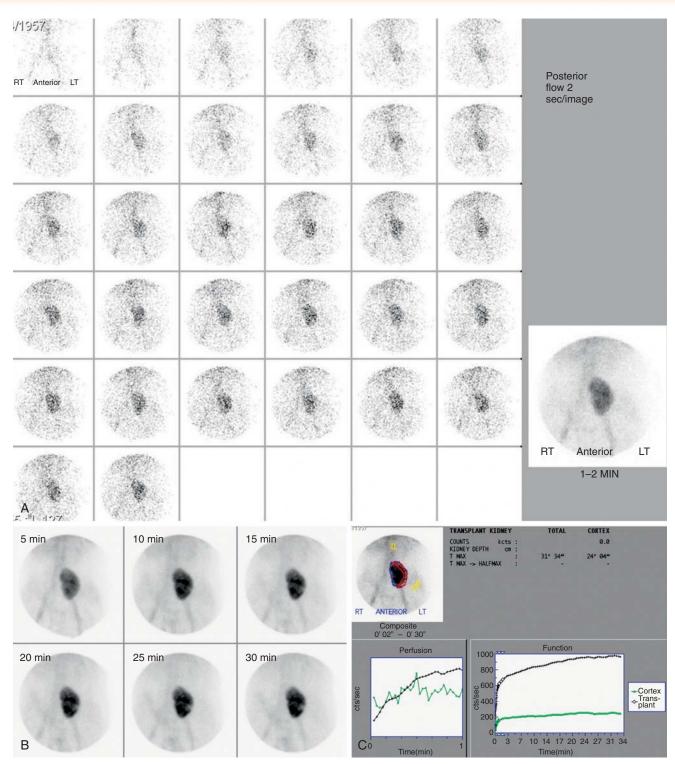


Figure 64-33 A, Technetium-99m (<sup>99m</sup>Tc)-labeled mercaptoacetyl triglycine (<sup>99m</sup>Tc-MAG3) study demonstrating normal flow to a transplant kidney in the left iliac fossa. B, Serial static images demonstrate normal uptake in the transplant kidney at 5 minutes with progressive accumulation of activity, without excretion, probably secondary to acute tubular necrosis. C, The upsloping renogram activity curve correlates with the flow and static images.

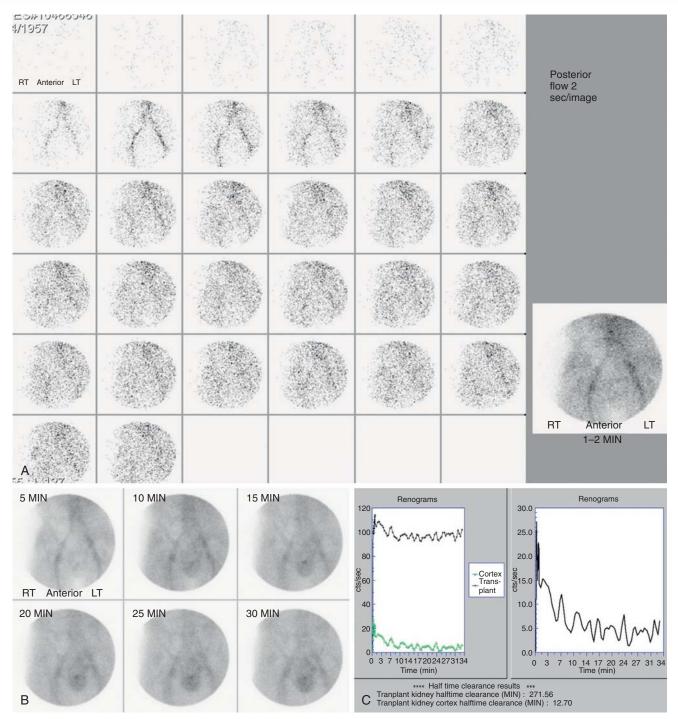
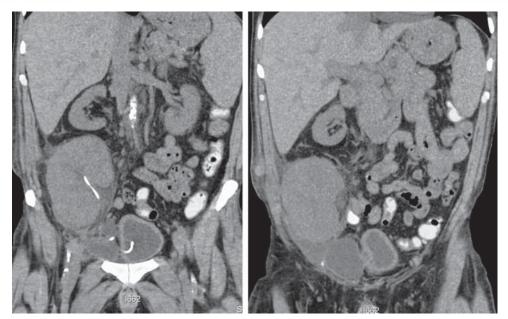


Figure 64-34 A, Technetium-99m (<sup>99m</sup>Tc)-labeled mercaptoacetyl triglycine (<sup>99m</sup>Tc-MAG3) study demonstrating absent flow to a transplant kidney in the left iliac fossa, probably as a result of rejection. B, Serial static images demonstrate no uptake in the transplant kidney over a period of 30 minutes, consistent with transplant rejection. C, The flat renogram activity curve correlates with the flow and static images.



**Figure 64-35** Renal transplant complication: urinoma. Coronal computed tomography images showing a low-density collection inferior to the transplant kidney, consistent with urinoma. Note the ureteral stent extending from the right renal pelvis to the bladder.

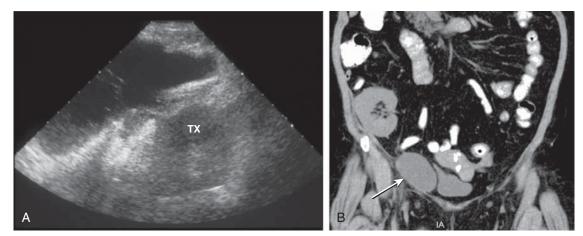


Figure 64-36 Renal transplant complication: lymphocele. A, Ultrasound image shows an anechoic collection adjacent to the transplant kidney. B, Computed tomography image in another patient shows a well-defined low-density collection (*arrow*) adjacent to the bladder.

**Magnetic Resonance Imaging.** MRI findings includes the following:

- Ureteral obstruction: Fluid collections causing obstruction by extrinsic compression
- Urine leak: Perigraft fluid collection
- *Lymphocele:* Well-defined fluid signal intensity collection with thin septa
- *Abscess*: Nonspecific findings; fluid collection with peripheral rim enhancement
- *Hematoma:* Signal changes, depending on the stage of the blood breakdown products

**Ultrasonography.** On ultrasonography the following may be seen:

- Ureteral obstruction: Hydronephrosis
- Urine leak: Perigraft fluid collection
- Lymphocele: Round anechoic collection; thin septa
- Abscess: Nonspecific finding of perigraft fluid

• *Hematoma:* Acute hematoma typically highly echogenic; resolving hematomas hypoechoic or anechoic

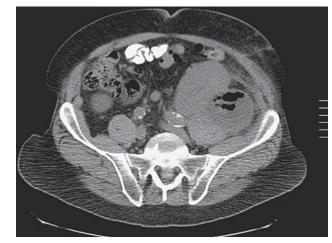
#### Nuclear Medicine. The following findings may be noted:

- *Ureteral obstruction:* May demonstrate hydronephrosis (however, scintigraphy is much less sensitive than ultrasonography)
- Urine leak: Abnormal distribution of radiotracer around the transplant
- *Lymphocele, abscess, hematoma:* Photopenic area adjacent to the transplant

**Differential Diagnosis.** For urine leak and urinoma, definitive diagnosis can be made on the basis of creatinine level in the fluid obtained under ultrasound or CT guidance. A lymphocele will have the same chemical composition as serum; thus, chemical analysis can help differentiate it from urinoma, seroma, and abscess.



**Figure 64-37** Focal low-density cortical lesion in a transplant kidney on a coronal CT image (*arrow*) consistent with, but not specific for, focal pyelonephritis.



**Figure 64-38** Axial computed tomography image showing a fluid collection containing air bubbles adjacent to a left iliac fossa renal transplant, consistent with an abscess.

#### REFERENCES

- Davidson AJ, Hartman DS, Choyke PL, et al: Radiology of the kidney and genitourinary tract, ed 3, Philadelphia, 1999, WB Saunders, pp 143–183.
- Zagoria RJ: The kidney: diffuse parenchymal abnormalities. In Zagoria RJ, editor: *The requisites: genitourinary radiology*, ed 2, Philadelphia, 2004, Mosby, pp 126–158.
- Hauger O, Grenier N, Deminère C, et al: USPIOenhanced MR imaging of macrophage infiltration in native and transplanted kidneys: initial results in humans. *Eur Radiol* 17:2898–2907, 2007.
- Madaio MP, Harrington JT: Current concepts: the diagnosis of acute glomerulonephritis. *N Engl J Med* 309:1299–1302, 1983.
- Levy M, Berger J: Worldwide perspective of IgA nephropathy. Am J Kidney Dis 12:340–347, 1988.
- Dodge WF, Spargo BH, Travis LB, et al: Poststreptococcal glomerulonephritis: a prospective study in children. N Engl J Med 286:273–278, 1972.
- Cameron JS: The long-term outcome of glomerular diseases. In Schrier RW, Gottschalk CW, editors: *Diseases of the kidney*, ed 6, Boston, 1997, Little, Brown, p 1919.
- Troyanov S, Wall CA, Miller JA, et al: Idiopathic membranous nephropathy: definition and relevance of a partial remission. *Kidney Int* 66: 1199–1205, 2004.
- Glassock RJ, Cohen AH, Adler SG: Primary glomerular disease. In Brenner BM, editor: *The kidney*, ed 5, Philadelphia, 1996, WB Saunders, pp 1392–1479.

- Kumar V, Cotran RS, Robbins SL, editors: The kidney and its collecting system. In *Basic pathology*, Philadelphia, 1997, WB Saunders, pp 439–469.
- Brouhard BH, Travis LB: Acute postinfectious glomerulonephritis. In Edelmann CM, editor: *Pediatric kidney disease*, Boston, 1992, Little Brown, pp 1199–1221.
- Boulware LE, Troll MU, Jaar BG, et al: Identification and referral of patients with progressive CKD: a national study. *Am J Kidney Dis* 48:192– 204, 2006.
- Research Group on Progressive Chronic Renal Disease: Nationwide and long-term survey of primary glomerulonephritis in Japan as observed in 1,850 biopsied cases. *Nephron* 82: 205–213, 1999.
- National Kidney Foundation: K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 39(2 Suppl 1):S1–S266, 2002.
- Remuzzi G, Bertani T: Pathophysiology of progressive nephropathies. N Engl J Med 339:1448– 1456, 1998.
- Miller O, Hemphill RR: Urinary tract infection and pyelonephritis. *Emerg Med Clin North Am* 19:655–674, 2001.
- Sobel JD: Pathogenesis of urinary tract infection: role of host defenses. *Infect Dis Clin North Am* 11:531–549, 1997.
- Scholes D, Hooton TM, Roberts PL, et al: Risk factors associated with acute pyelonephritis in healthy women. *Ann Intern Med* 142:20–27, 2005.

- Smellie JM, Prescod NP, Shaw PJ, et al: Childhood reflux and urinary infection: a follow-up of 10-41 years in 226 adults. *Pediatr Nephrol* 12:727–736, 1998.
- Hill JB, Sheffield JS, McIntire DD, et al: Acute pyelonephritis in pregnancy. Obstet Gynecol 105:18–23, 2005.
- Hooton TM, Scholes D, Hughes JP, et al: A prospective study of risk factors for symptomatic urinary tract infection in young women. N Engl J Med 335:468–474, 1996.
- Dillon MJ, Goonasekera CD: Reflux nephropathy. J Am Soc Nephrol 9:2377–2383, 1998.
- Huang JJ, Tseng CC: Emphysematous pyelonephritis: clinicoradiological classification, management, prognosis, and pathogenesis. Arch Intern Med 160:797–805, 2000.
- 24. Quinn FM, Dick AC, Corbally MT, et al: Xanthogranulomatous pyelonephritis in childhood. *Arch Dis Child* 81:483–486, 1999.
- Loffroy R, Guiu B, Watfa J, et al: Xanthogranulomatous pyelonephritis in adults: clinical and radiological findings in diffuse and focal forms. *Clin Radiol* 62:884–890, 2007.
- Chuang CK, Lai MK, Chang PL, et al: Xanthogranulomatous pyelonephritis: experience in 36 cases. J Urol 147:333–336, 1992.
- 27. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management, Roberts KB: Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. *Pediatrics* 128:595–610, 2011.

- Hooton TM, Stamm W: Diagnosis and treatment of uncomplicated urinary tract infection. *Infect Dis Clin North Am* 11:551–581, 1997.
- Hooton TM: The current management strategies for community-acquired tract infection. *Infect Dis Clin North Am* 17:303–332, 2003.
- Goldman SM, Fishman EK: Upper urinary tract infection: the current role of CT, ultrasound and MRI. Semin Ultrasound CT MR 12:335–360, 1991.
- Leder RA, Low VH: Tuberculosis of the abdomen. *Radiol Clin North Am* 33:691–705, 1995.
- Engin G, Acunas B, Tunaci M: Imaging of extrapulmonary tuberculosis. *Radiographics* 20:449– 470, 2000.
- 33. Gibson M, Puckett M, Shelly M: Renal tuberculosis. *Radiographics* 24:251–256, 2004.
- Monk RD, Bushinsky DA: Nephrolithiasis and nephrocalcinosis. In Johnson RJ, Feehally J, editors: *Comprehensive clinical nephrology*, ed 2, St. Louis, 2003, Mosby, pp 731–734.
- 35. Epstein FH: Calcium and the kidney. *Am J Med* 45:700–714, 1968.
- Frick KK, Bushinsky DA: Molecular mechanisms of primary hypercalciuria. J Am Soc Nephrol 14:1082–1095, 2003.
- Göbel U, Kettritz R, Schneider W, et al: The protean face of renal sarcoidosis. J Am Soc Nephrol 12:616–623, 2001.
- Karet FE: Inherited distal renal tubular acidosis. J Am Soc Nephrol 13:2178–2184, 2002.
- Leumann E, Hoppe B: The primary hyperoxalurias. J Am Soc Nephrol 12:1986–1993, 2001.
- 40. Markowitz GS, Stokes MB, Radhakrishnan J, et al: Acute phosphate nephropathy following oral sodium phosphate bowel purgative: an underrecognized cause of chronic renal failure. *J Am Soc Nephrol* 16:3389–3396, 2005.
- Oguzkurt L, Karabulut N, Haliloglu M, et al: Medullary nephrocalcinosis associated with vesicoureteral reflux. *Br J Radiol* 70:850–851, 1997.
- Scarpelli DG, Tremblay G, Pearce AGE: A comparative cytochemical and cytologic study of vitamin D-induced nephrocalcinosis. *Am J Pathol* 36:331–353, 1960.
- Alon U, Lovell HB, Donaldson DL: Nephrocalcinosis, hyperparathyroidism, and renal failure in familial hypophosphatemic rickets. *Clin Pediatr (Phila)* 31:180–183, 1992.
- Schepens D, Verswijvel G, Kuypers D, et al: Images in nephrology: renal cortical nephrocalcinosis. *Nephrol Dial Transplant* 15:1080–1082, 2000.

- Forget S, Patriquin HB, Dubois J, et al: The kidney in children with tyrosinemia: sonographic, CT and biochemical findings. *Pediatr Radiol* 29:104–108, 1999.
- Curry NS, Gordon L, Gobien RP, et al: Renal medullary "rings": possible CT manifestation of hypercalcemia. Urol Radiol 6:48–50, 1984.
- Slovis TL, Bernstein J, Gruskin A: Hyperechoic kidneys in the newborn and young infant. *Pediatr Nephrol* 7:294–302, 1993.
- Kim SH: Renal papillary necrosis. In Kim SH, editor: *Radiology illustrated: uroradiology*, Philadelphia, 2003, WB Saunders, pp 273–310.
- Simon HB, Bennett WA, Emmet JL: Renal papillary necrosis: a clinicopathologic study of 42 cases. J Urol 77:557–567, 1957.
- Rao VM, Rao AK, Steiner RM, et al: The effect of ionic and nonionic contrast media on the sickling phenomenon. *Radiology* 144:291–293, 1982.
- Sekine H, Mine M, Ohya K, et al: Renal papillary necrosis caused by urinary calculus-induced obstruction alone. *Urol Int* 54:112–114, 1995.
- Hare WS, Poynter JD: The radiology of renal papillary necrosis as seen in analgesic nephropathy. *Clin Radiol* 25:423–443, 1974.
- Kaude JV, Stone M, Fuller TJ, et al: Papillary necrosis in kidney transplant patients. *Radiology* 120:69–74, 1976.
- Edmondson HA, Reynolds TB, Jacobson HG: Renal papillary necrosis with special reference to chronic alcoholism: a report of 20 cases. Arch Intern Med 118:255–264, 1966.
- Groop L, Laasonen L, Edgren J: Renal papillary necrosis in patients with IDDM. *Diabetes Care* 12:198–202, 1989.
- Kabalin JN: Anatomy of the retroperitoneum and kidney. In Walsh PC, editor: *Campbell's urology*, vol 1, ed 6, Philadelphia, 1992, WB Saunders, pp 3–40.
- Khan NA, Muthusamy C, McDonald S: Papillary necrosis. e-medicine, updated December 5, 2008.
- Lindvall N: Renal papillary necrosis: a roentgenographic study of 155 cases. Acta Radiol 192(Suppl):1–153, 1960.
- Saifuddin A, Bark M: Case report: computed tomography demonstration of renal papillary necrosis. *Clin Radiol* 44:275–276, 1991.
- 60. Lang EK, Macchia RJ, Thomas R, et al: Multiphasic helical CT diagnosis of early medullary and papillary necrosis. *J Endourol* 18:49–56, 2004.
- Jung DC, Kim SH, Jung SI, et al: Renal papillary necrosis: review and comparison of findings at multi-detector row CT and intravenous urography. *Radiographics* 26:1827–1836, 2006.

- 62. Braden GL, Kozinn DR, Hampf FE, Jr, et al: Ultrasound diagnosis of early renal papillary necrosis. *J Ultrasound Med* 10:401–403, 1991.
- Hoffman JC, Schnur MJ, Koenigsberg M: Demonstration of renal papillary necrosis by sonography. *Radiology* 145:785–787, 1982.
- Vollmer WM, Wahl PW, Blagg CR: Survival with dialysis and transplantation in patients with end-stage renal disease. N Engl J Med 308:1553– 1558, 1983.
- 65. Baxter GM: Imaging in renal transplantation. *Ultrasound Q* 19:123–138, 2003.
- Rajiah P, Lim YY, Taylor P: Renal transplant imaging and complications. *Abdom Imaging* 31:735–746, 2006.
- Orons PD, Zajko AB: Angiography and interventional aspects of renal transplantation. *Radiol Clin North Am* 33:461–471, 1995.
- Luke RG, Curtus J: Hypertension: pathophysiology, diagnosis and management. New York, 1995, Raven, pp 2471–2483.
- Beecroft JR, Rajan DK, Clark TW, et al: Transplant renal artery stenosis: outcome after percutaneous intervention. J Vasc Interv Radiol 15:1407–1413, 2004.
- Grenier N, Claudon M, Trillaud H, et al: Noninvasive radiology of vascular complications in renal transplantation. *Eur Radiol* 7:385–391, 1997.
- Nakatani T, Uchida J, Han YS, et al: Renal allograft arteriovenous fistula and large pseudoaneurysm. *Clin Transplant* 17:9–12, 2003.
- Rerolle JP, Antoine C, Raynaud A, et al: Successful endoluminal thrombo-aspiration of renal graft venous thrombosis. *Transpl Int* 13:82–86, 2000.
- Surlan M, Popovic P: The role of interventional radiology in management of patients with endstage renal disease. *Eur J Radiol* 46:96–114, 2003.
- Hricak H, Terrier F, Marotti M, et al: Posttransplant renal rejection: comparison of quantitative scintigraphy, US, and MR imaging. *Radiology* 162:685–688, 1987.
- Rholl KS, Lee JK, Ling D, et al: Acute renal rejection versus acute tubular necrosis in a canine model: MR evaluation. *Radiology* 160:113–117, 1986.
- Szolar DH, Preidler K, Ebner F, et al: Functional magnetic resonance imaging of human renal allografts during the post-transplant period: preliminary observations. *Magn Reson Imaging* 15:727–735, 1997.
- 77. Baxter GM: Ultrasound of renal transplantation. *Clin Radiol* 56:802–818, 2001.

# **Renal Vascular Diseases**

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## **Renovascular Hypertension**

#### **ETIOLOGY**

The most common cause of renovascular hypertension is renal artery stenosis, which may be caused by atherosclerosis (70% to 90%) or less commonly by fibromuscular dysplasia (10% to 30%).<sup>1,2</sup> Rare causes of renal artery stenosis include arteritis, arterial dissection, and neurofibromatosis.

#### PREVALENCE AND EPIDEMIOLOGY

Renovascular hypertension pertains to the causal relationship between renal artery stenosis and its clinical consequences, namely, hypertension and/or renal failure. Among hypertensive patients, 1% to 5% have true renovascular hypertension.<sup>3</sup> However, renovascular hypertension affects 15% to 30% of patients who have clinical criteria that suggest renal vascular disease.<sup>4</sup>

#### **CLINICAL PRESENTATION**

Clinical clues that suggest renal artery stenosis include<sup>5</sup>:

- Hypertension, early onset (<30 years of age) or severe hypertension over 55 years of age
- Accelerated, resistant, or malignant hypertension
- Sudden development or worsening of hypertension at any age
- Hypertension and unexplained renal insufficiency
- Hypertension refractory to multiple drug therapy
- Sudden unexplained pulmonary edema
- Epigastric or flank bruit
- Unexplained congestive heart failure or refractory angina
- Unexplained unilateral small kidney or size discrepancy greater than 1.5 cm between kidneys (Figure 65-1)

#### PATHOPHYSIOLOGY

The renal arteries arise from the abdominal aorta and pass in a dorsal and inferolateral direction to enter the renal hilum. One or more accessory renal arteries is present in over 30% of the population, which is clinically important because, rarely, renal artery stenosis in an accessory renal artery can cause renovascular hypertension.<sup>6,7</sup>

#### PATHOLOGY

A 50% reduction in renal artery diameter (which corresponds to a 75% reduction of the cross-sectional area of the vessel) is considered hemodynamically significant.8

Atherosclerosis typically involves the ostium and proximal one third of the main renal artery and is often associated with aortic atherosclerosis.

Fibromuscular dysplasia is a collection of vascular diseases that cause proliferation of components of the arterial wall. Subtypes are classified by the layers of the arterial wall involved. The renal arteries are the most commonly affected vessels.

Renal artery stenosis caused by fibromuscular dysplasia involves the mid to distal main renal arteries and the segmental renal arteries.

#### IMAGING

#### Digital Subtraction Angiography

For decades, digital subtraction angiography (DSA) was the method of choice for diagnosing renal artery stenosis. With DSA, pressure may be measured across renovascular stenoses, allowing quantitative assessment of the physiologic effect of the stenosis and objective assessment of the physiologic effect of endovascular therapy.

However, DSA is invasive and subject to substantial interobserver variation.9 Technologic advances in other imaging modalities (duplex ultrasonography, computed tomography [CT], magnetic resonance imaging [MRI], magnetic resonance angiography [MRA]) now permit the noninvasive diagnosis of renovascular stenosis, and the role of DSA is now limited to prerevascularization planning and therapy.

On DSA, signs of atherosclerotic renal artery stenosis include ostial or proximal renal artery narrowing and plaque in the adjacent aorta, whereas fibromuscular dysplasia causes "beading" as a result of alternating areas of fibromuscular proliferation and arterial wall thinning or aneurysm formation (Figure 65-2).

#### Computed Tomography

Multidetector CT angiography has significantly improved resolution and reduced the contrast dose for evaluation of the renal arteries in a single breath-hold. Bolus tracking methods should be used to ensure optimal arterial opacification. In addition to evaluating the abdominal aorta and renal arteries, assessment of other visceral arteries, evaluation of renal size, cortical thickness, and detection of other renal parenchymal abnormalities can be performed in the same study (Figure 65-3). CT angiography has a high sensitivity (88% to 96%) and specificity (83% to 99%) for detection of renal artery stenosis.<sup>10</sup>

However, CT angiography requires the administration of iodinated contrast media, precluding its use in the many patients with renal artery stenosis who have significantly impaired renal function.

#### Magnetic Resonance Imaging

MR angiography has moved from flow-enhanced (time of flight) sequences to breath-hold three-dimensional (3D) spoiled gradient recalled echo gadolinium-enhanced MR angiography (Gd-MRA) using bolus-tracking methods to evaluate the renal arteries. Maximum intensity projection images are routinely reconstructed, but the accurate diagnosis of stenoses requires the evaluation of source images (Figure 65-4). Gd-MRA has a sensitivity of 88% to 100% and a specificity of 71% to 99% for renal artery stenosis and a sensitivity of up to 90% for the detection of accessory renal arteries.<sup>12</sup>

Phase-contrast imaging allows evaluation for turbulence, a finding representative of flow-limiting lesions with more than 50% diameter reduction and is used in addition to Gd-MRA. Phase contrast and steady-state free precession (SSFP) noncontrast techniques are useful in patients whose renal function precludes the use of gadolinium.<sup>13</sup>

In addition, nonenhanced MR angiography allows a safely repeated examination, if required (Figure 65-5). Two recent papers compared a non-contrast-enhanced MRA technique—

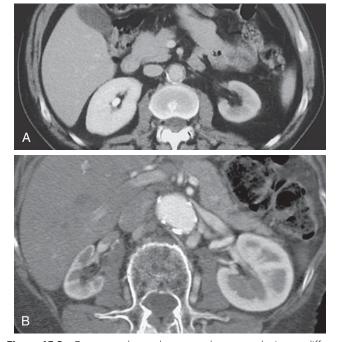


**Figure 65-1** A 10-minute delayed image from an intravenous urogram shows a unilateral atrophic kidney on the right secondary to chronic renal insufficiency related to renal artery stenosis.

time-spatial labeling inversion pulse three-dimensional MR with balanced SSFP with DSA<sup>14</sup> and CT angiography.<sup>15</sup>

In the study by Parienty and colleagues,<sup>T4</sup> the nonenhanced 3D MR technique provided sensitivity of 93%, specificity of 88%, and accuracy of 91% when compared with DSA. Similarly, in the Renal Artery Contrast Free Trial (REACT), nonenhanced MRA was compared with contrast-enhanced computed tomography angiography and showed a sensitivity of 74%, specificity of 93%, and accuracy of 90%.

Phase-contrast imaging and flow estimation also reduce interobserver variability when evaluating relatively small-caliber vessels, including the renal arteries.<sup>16</sup>



**Figure 65-3** Contrast-enhanced computed tomography in two different patients with sequelae of renal artery stenosis. **A**, Delayed enhancement in a small left kidney. **B**, Atrophic right kidney. Note the atherosclerotic changes involving the aorta in both patients.

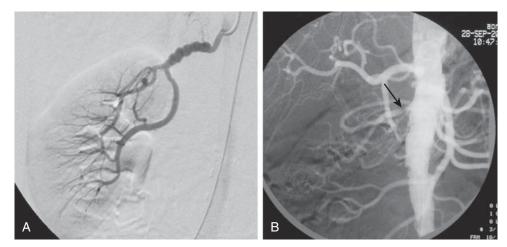


Figure 65-2 Digital subtraction angiography in two different patients. A, Beading of the renal artery consistent with fibromuscular dysplasia. B, Proximal severe right renal artery stenosis (arrow) secondary to atherosclerosis.



**Figure 65-4** Three-dimensional magnetic resonance angiography of the renal arteries showing bilateral proximal renal artery stenosis. The stenosis is greater on the right.



**Figure 65-5** Three-dimensional balanced steady-state free precession noncontrast magnetic resonance angiography demonstrating normal renal arteries, two on the right and one on the left. Incidentally seen is a dilated tortuous left ovarian vein. (From Soulez G, Olivia VL, Turpin S, et al: Imaging of renovascular hypertension: respective values of renal scintigraphy, renal Doppler US, and MR angiography. Radiographics 20:1355–1368, 2000.)

#### Ultrasonography

The main renal arteries are visualized and examined with color or power Doppler imaging, followed by renal artery velocity analysis with spectral Doppler imaging. Ultrasonography is widely available, noninvasive, and relatively inexpensive and involves no ionizing radiation. However, there are some drawbacks, as follows:

- Accessory renal artery detection is poor.
- The wide range of sensitivity of 40% to 90% reflects the intrinsic difficulty of imaging of the renal arteries, the high level of expertise needed, and interobserver variation.
- There is a high rate (10% to 20%) of nondiagnostic studies.

Criteria to diagnose significant stenosis of a renal artery include:

- 1. Peak systolic velocity (PSV) at the site of stenosis of 150 cm/s or greater (indicates 50% stenosis)<sup>17</sup> and 180 cm/s or greater (60% stenosis)<sup>18</sup>
- 2. Ratio of renal to aortic PSV greater than 3.5 (indicates >60% stenosis)<sup>19</sup>
- 3. Turbulent flow in the poststenotic area
- 4. Undetectable Doppler signal in renal artery indicates occlusion, provided that proper technique has been used
- 5. Indirect diagnosis by assessment of intrarenal arteries; severe stenoses that decrease renal artery diameter by more than 75% produce distal intrarenal vascular changes—a tardus parvus phenomenon with a slowed systolic acceleration and a decreased resistive index.<sup>20</sup> Findings include (1) acceleration of less than 370 to 470 cm/s, (2) time of acceleration greater than 0.05 to 0.08 second, and (3) a resistive index difference of greater than 5% between the right and left kidneys.

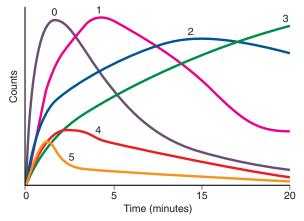
Interobserver and intraobserver variability using these criteria is high. The factors responsible for changes in the distal waveform are complex and probably more dependent on changes of compliance than on perfusion pressure. Therefore, these criteria are used only when obvious on spectral traces, when quantifying the stenosis as severe (>75%), or when identifying stenosis of a segmental or accessory artery that cannot be identified with spectral Doppler imaging.

Recently developed intravenous microbubble contrast agents may improve diagnostic accuracy and study success rates.<sup>21</sup>

#### Nuclear Medicine

Unlike cross-sectional imaging, nuclear medicine techniques assess for functional changes secondary to renal artery stenosis. Renal artery stenosis causes hyperactivity of the reninangiotensin-angiotensin-converting enzyme (ACE) feedback loop. The subsequent efferent arteriolar constriction and secondary elevation of blood pressure maintain renal perfusion and hence function. ACE inhibition removes this efferent arteriolar constriction, decreasing perfusion and function in the affected kidney.<sup>22</sup> The test is therefore useful in identifying physiologically significant renal artery stenosis, thereby facilitating the selection of patients with renal artery stenosis who will benefit from revascularization.

Technetium-99m (<sup>99m</sup>Tc)–labeled mercaptoacetyl triglycine (MAG-3) is the radiotracer of choice for renal imaging. Studies are performed before and after the administration of ACE inhibitors (ACEIs), with unilateral decrease in function or prolonged radiotracer retention after ACE inhibition representing a high probability (>90%) of renal artery stenosis. Criteria include change in the 20-minute/peak uptake ratio of 0.15 or greater, a significantly prolonged transit time, or a change in the scintigraphic grade.



**Figure 65-6** Scintigraphic grading of renal artery stenosis. 0 = Normal, 1 = minor abnormalities but with T<sub>max</sub> greater than 5 minutes and (for technetium-99m-mercaptoacetyl triglycine and iodine-131 orthoiodo-hippurate scintigrams) 20-min/peak uptake ratio greater than 0.3, <math>2 = marked delayed excretion rate with preserved washout phase, 3 = delayed excretion rate without washout phase, 4 = renal failure pattern with measurable kidney uptake, <math>5 = renal failure pattern without measurable kidney uptake. (From Soulez G, Oliva VL, Turpin S, et al: Imaging of renovascular hypertension: respective values of renal scintigraphy, renal Doppler US, and MR angiography. Radiographics 20:1355–1368, 2000.)

Grades are based on the scintigraphic curves (Figure 65-6) and are classified as follows<sup>4,23</sup>:

- $\mathbf{0} = Normal$
- 1 = Minor abnormalities but  $T_{max}$  (time to maximum activity) greater than 5 minutes and 20 min/peak uptake ratio greater than 0.3
- 2 = Marked delayed excretion with preserved washout phase
- 3 = Delayed excretion without washout phase
- 4 = Renal failure pattern with measurable kidney uptake
- 5 = Renal failure pattern without measurable kidney uptake General interpretive criteria include the following<sup>23</sup>:
- 1. Normal ACEI scintigram: Low (<10%) probability of renovascular hypertension.
- 2. Small, poorly functioning kidney (<30% uptake) with no change in time to peak when ACEI scintigram and bilateral symmetric cortical retention indicate intermediate probability of renovascular hypertension.
- 3. Worsening of scintigraphic curve, reduction in relative uptake, prolongation of renal and parenchymal transit time, increase in the 20-minute/peak uptake ratio, and prolongation of time to maximum activity ( $T_{max}$ ) are associated with high probability of renovascular hypertension.

## Imaging Algorithm

There is no single accepted algorithm for diagnosing renal artery stenosis (Box 65-1). One approach is to perform ACEI renography in patients with normal or mildly decreased renal function, followed by CT angiography or MR angiography if scintigraphy suggests an intermediate to high probability for physiologically significant renovascular hypertension. Patients with severely impaired renal function should have anatomic evaluation with MR angiography or Doppler ultrasound imaging and functional evaluation with renal scintigraphy (Table 65-1).<sup>10,11,24-28</sup>

## BOX 65-1 **DIFFERENTIAL DIAGNOSIS**

Essential hypertension is a diagnosis of exclusion, made after careful history taking, physical examination, and laboratory studies. Other causes of secondary hypertension include:

- Adrenal adenoma: shown by raised plasma cortisol levels
- Aortic dissection/coarctation: diagnosed by cross-sectional imaging
- Hyperthyroidism: indicated by suppressed thyroid-stimulating hormone
- Pheochromocytoma: evident by raised plasma metanephrine levels and 24-hour urinary catecholamine values

Some authors consider ultrasonography the best screening tool because the presence of normal kidney size and normal intrarenal waveforms makes renal artery stenosis unlikely. In patients with borderline or poor renal function, MR angiography is currently the best alternative available. MR contrast is, however, not recommended if the glomerular filtration rate (GFR) is less than 30 mg/dL for fear of nephrogenic systemic fibrosis or if the patient is on dialysis. Conventional angiography is now performed only before treatment by angioplasty or stenting.

#### TREATMENT

Percutaneous transluminal angioplasty is the most effective treatment for renal artery stenosis as a result of fibromuscular dysplasia. There is, however, considerable debate even among experts regarding the optimal treatment for renovacsular hypertension. Many recent trials, including the Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) Trial,<sup>25</sup> there was no statistically significant difference observed in the primary end point (which was a composite of cardiovascular or renal death, stroke, myocardial infarction, etc.) between optimal medical therapy and renal stenting. The CORAL trial, however did not evaluate those who failed medical therapy. Another meta-analysis,<sup>30</sup> which compared revascularization versus medical therapy for atherosclerotic renal artery stenosis, also concluded that revascularization did not improve outcomes compared to medical therapy in patients with atherosclerotic renal artery stenosis.

A recent consensus statement<sup>31</sup> for renal arterial intervention provides clinical scenarios in which treatment of hemodynamically significant renal artery stenosis may be considered. Under the clinical scenarios, the strongest evidence supporting stenting for renal artery stenosis is in patients with the presence of cardiac disturbance syndromes, including flash pulmonary edema or acute coronary syndrome with severe hypertension. Others include resistant hypertension, ischemic nephropathy with chronic kidney disease with eGFR less than 45 mL/min and global renal ischemia (unilateral significant renal artery stenosis with a solitary kidney or bilateral significant renal artery stenosis) (Figure 65-7).

#### What the Referring Physician Needs to Know: Renovascular Hypertension

 Treatment of renovascular hypertension is controversial, with many recent randomized controlled trials suggesting that there is no statistically significant difference between treatments by stenting versus optimal medical therapy.

TABLE         Accuracy           65-1         Accuracy	, Limitations, and Pitfalls of the Moda	alities Used in Imaging of Renal V	/ascular Disease
Modality	Accuracy	Limitations	Pitfalls
СТ	Sensitivity (88%-96%) Specificity (83%-99%) <sup>10,11</sup> Best with thin-section multidetector systems	No functional evaluation lodinated radiation exposure Contraindicated if elevated renal function	Extensive calcification may obscure lumen. Not as accurate in the diagnosis of fibromuscular dysplasia as digital subtraction angiography
MRI	Gd-MRA: Sensitivity >95% and specificity >90% for ± 50% renal artery stenosis <sup>25,26</sup> Noncontrast MRA using 3D SSFP techniques yield sensitivity of 73%-93%, specificity of 88%, and accuracy of 91% <sup>14,15</sup>	No functional evaluation Usual contraindications to MRI (e.g., pacemakers, metallic implants) Decreased renal function may limit the intravenous use of gadolinium.	Renal artery stenosis may be overestimated. Not sensitive in diagnosis of fibromuscular dysplasia
Ultrasonography	Sensitivity for detection of renal artery stenosis 70% or greater is 72%-90%. <sup>27</sup> Primary use is screening for renal artery stenosis.	Needs well-trained technologist Excessive bowel gas and obesity limit evaluation.	Interobserver variability
Nuclear medicine	Sensitivity for detection of renal artery stenosis 70% or greater is 51%-96%. <sup>28</sup>	Bilateral disease	Patient hydration influences results.

3D, Three-dimensional; CT, computed tomography; Gd-MRA, gadolinium-enhanced magnetic resonance imaging; MRI, magnetic resonance imaging.

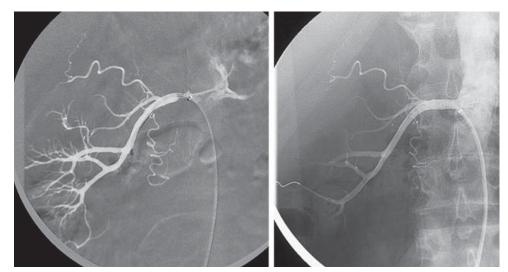


Figure 65-7 Percutaneous intervention in the same patient shown in Figure 65-4 demonstrating stent placement at the site of the proximal stenosis.

# **Renal Vein Thrombosis**

## **ETIOLOGY**

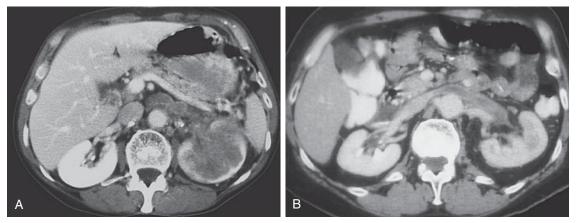
Renal vein thrombosis in adults usually is due to a hypercoagulable state, most commonly nephrotic syndrome. In children, it is usually associated with sepsis and dehydration.<sup>32,33</sup>

- Causes of renal vein thrombosis include the following:
- Hypercoagulable state
  - Nephrotic syndrome (most common cause in adults, and usually secondary to glomerulonephritis)
  - Systemic lupus erythematosus
  - Inherited hypercoagulable states (e.g., antithrombin III deficiency, protein C deficiency)
  - Pregnancy
  - Malignancy

- Hypovolemia: Dehydration, sepsis, blood loss
- Trauma
- Neoplastic invasion of the renal vein: Renal cell carcinoma, transitional cell carcinoma, Wilms' tumor; these may cause formation of bland or tumor thrombus.
- Mechanical compression of renal vein: Abscess, tumor, lymphadenopathy, aneurysm
- Extension of left ovarian vein thrombosis

## PREVALENCE AND EPIDEMIOLOGY

Renal vein thrombosis has an incidence between 5% and 62% in patients with nephrotic syndrome, especially membranous nephropathy.<sup>34</sup>



**Figure 65-8** Renal vein thrombosis. **A**, Contrast-enhanced computed tomography through the kidneys demonstrates a large infiltrating mass expanding the left kidney with a dilated left renal vein that contains nonenhancing thrombus. **B**, Renal vein thrombosis secondary to dehydration. (*Courtesy Dr. Srinivas Prasad.*)

## **CLINICAL PRESENTATION**

Classic acute presentation includes gross hematuria, flank pain, and loss of renal function. Chronic renal vein thrombosis may be asymptomatic.

## PATHOPHYSIOLOGY

Renal vein thrombosis is more common on the left side, presumably owing to the longer course of the left renal vein.

### IMAGING

### Radiography

Although historically an enlarged ipsilateral kidney may be seen on intravenous pyelography, this technique has largely been replaced with cross-sectional imaging.

## Computed Tomography

Primary signs are based on visualization of the clot. In acute renal vein thrombosis a bland thrombus is seen as a filling defect in an expanded renal vein (Figure 65-8). Tumor thrombus also causes a filling defect, which may enhance but does not always do so. Hence, in the setting of local malignancy, nonenhancing renal vein thrombosis may represent bland or tumor thrombus.

In chronic disease there is an attenuated renal vein with extensive collateral vessels along the proximal to midureter. The clot itself is usually not seen.

Secondary signs include enlargement of the ipsilateral kidney, renal sinus edema, and diminished and delayed nephrogram. The cause of thrombus may be identified (e.g., renal or retroperitoneal tumor or abscess).

#### Magnetic Resonance Imaging

MRI is the best test for evaluation of both bland and tumor thrombus. Contrast-enhanced T1-weighted 3D sequences reveal a filling defect within the renal vein. Enhancement may also show in the tumor thrombus. In patients with poor renal function, noncontrast evaluation using flow-sensitive noncontrast MRI sequences (e.g., SSFPS) can help detect thrombus as low signal intensity within the flowing venous blood of high signal intensity.

### Ultrasonography

Renal enlargement and heterogeneous echogenicity within an enlarged renal vein with no evidence of flow on Doppler interrogation is suggestive of renal vein thrombosis. Signs of the underlying pathology (e.g., renal mass) may be evident. Flow may be detected in tumor thrombus using Doppler imaging.

Renal arterial Doppler ultrasonography demonstrates a high resistance waveform in the main renal artery and increased intrarenal resistive indexes with complete renal vein occlusion.

#### Imaging Algorithm

If renal vein thrombosis is suggested, ultrasonography is typically performed first but usually is not diagnostic. CT is the imaging modality of choice at present, although MRI may be the imaging modality in the future for thrombus detection, especially if an iodinated contrast agent cannot be administered.

#### **Classic Signs: Renal Vein Thrombosis**

- Acute renal vein thrombosis: Expanded renal vein with lack of normal vascular enhancement/demonstrable flow
- Chronic renal vein thrombosis: Attenuated renal vein and presence of collateral vessels

# **Miscellaneous Vascular Diseases**

## VASCULITIS

The common vasculitides involving the kidneys include polyarteritis nodosa (PAN), systemic lupus erythematosus (SLE), and drug-induced vasculitis.

PAN is an idiopathic vasculitis of small to medium-sized muscular arteries. Renal involvement occurs in 90% of patients with PAN. Patients often present with hematuria. Renal ischemia occurs as a result of involvement of medium-sized vessels.

Renal involvement occurs in 30% to 50% of patients with SLE and involves the glomeruli, tubules, and vessels.<sup>35</sup> There is a high risk for renal vein thrombosis associated with SLE.

Vasculitis associated with intravenous drug abuse has features similar to those of PAN.<sup>36</sup> Methamphetamine is a commonly implicated drug, and other illicit drugs such as cocaine have also been reported as a cause of vasculitis.<sup>37</sup>

## ACUTE CORTICAL NECROSIS

Acute cortical necrosis is ischemic necrosis of the renal cortex with sparing of the medulla. It has been attributed to ischemia secondary to vasospasm of small vessels, toxic damage to glomerular capillary endothelium, and primary intravascular thrombosis, as occurs in disseminated intravascular coagulation.<sup>38</sup> Causes include sepsis, shock, severe dehydration, transfusion reaction, hemolytic-uremic syndrome, snakebite, and complications of pregnancy, such as placental abruption and septic abortion.

## IMAGING

#### Vasculitis

**Intravenous Pyelography and Angiography.** There is generalized increased bulk of the kidneys. With PAN, selective angiography shows small aneurysms at the bifurcation of interlobar and arcuate arteries.

**Computed Tomography.** With PAN, microaneurysms may occasionally be seen on dynamic contrast-enhanced CT. The kidneys may be lobulated with irregular thinning of the parenchyma resulting from prior cortical infarcts with preservation of the collecting system.<sup>39</sup> Multiple linear bands of low attenuation in the kidneys are attributed to renal artery occlusion. Occasional rupture of microaneuryms can lead to intrarenal, subcapsular, or perinephric hematoma. The other visceral arteries should be evaluated, because they are involved in approximately 50% of cases.

With SLE, kidneys may be large or small depending on the stage of lupus nephritis. Microaneuryms and hematomas are rare in patients with SLE. Larger lobular arteries are affected more than interlobular arteries. Renal vein thrombosis may be seen as a filling defect within the renal vein on contrastenhanced CT.

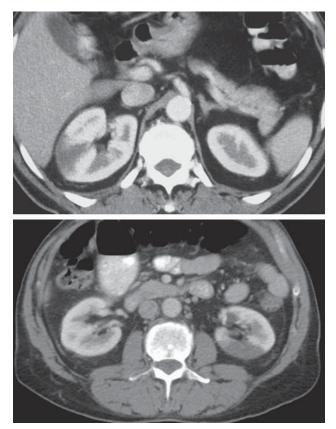
**Ultrasonography.** Ultrasonography is not definitive in cases of vasculitis. The kidneys may be enlarged or small, depending on the stage of the disease. Renal vein thrombosis may be detected as absent flow on Doppler interrogation or directly visualized on B-mode imaging.

## Renal Infarct

**Computed Tomography.** CT findings include the following:

- Enhancement is absent in affected renal tissue on contrastenhanced CT.
- Acute infarct: Wedge-shaped areas of decreased attenuation within otherwise normal-appearing kidney (Figure 65-9). A thin rim of enhancing cortex may overlie the infarct. Infarct is differentiated from scar by location. Scar from infections typically occurs in the cortical tissue that directly overlies a calyx, whereas scars from infarcts occur in the cortical tissue between calyces.
- Global infarction: The entire kidney is enlarged, and its reniform configuration is preserved.
- Chronic infarct: Infarcted tissue contracts, leaving a parenchymal scar.

**Magnetic Resonance Imaging.** Morphologic changes are similar to those of contrast-enhanced CT.



**Figure 65-9** Axial contrast-enhanced computed tomography through the kidneys shows wedge-shaped low-density nonenhancing areas in the kidneys extending from the cortex to the medulla consistent with infarcts in two different patients. Note the peripheral rim of enhancing cortex in the right kidney. (*Courtesy Dr. Srinivas Prasad.*)

**Ultrasonography.** There are no specific findings on ultrasonography.

**Nuclear Medicine.** A wedge-shaped photopenic area is seen at the site of infarction.

## Acute Cortical Necrosis

**Radiography.** In early-stage disease, kidneys are diffusely enlarged and poorly visualized. In the late stages, peripheral "tram-track" calcification can be seen.

**Computed Tomography.** In the early arterial phase there are enhancing interlobar and arcuate arteries adjacent to nonenhancing cortex.<sup>40</sup> Kidneys get progressively smaller with decreased renal function, and a single thin rim of calcification (tram-track calcification) is seen in the renal cortex. Characteristic findings include medullary enhancement with lack of cortical enhancement as well as subcapsular cortical enhancement as a result of collateral vessels.

**Magnetic Resonance Imaging.** The findings on MRI are similar to those of contrast-enhanced CT.

**Ultrasonography.** Findings on ultrasonography are nonspecific.

#### **Key Points**

- Renal artery stenosis is caused by atherosclerosis and, less commonly, fibromuscular dysplasia.
- Ultrasonography is the least expensive diagnostic examination and is suitable for screening.

#### REFERENCES

- Safian RD, Textor SC: Renal-artery stenosis. N Engl J Med 344:431–442, 2001.
- Working Group on Renovascular Hypertension: Detection, evaluation, and treatment of renovascular hypertension: final report. *Arch Intern Med* 147:820–829, 1987.
- Mann SJ, Pickering TG: Detection of renovascular hypertension: state of the art—1992. Ann Intern Med 117:845–853, 1992.
- Soulez G, Oliva VL, Turpin S, et al: Imaging of renovascular hypertension: respective values of renal scintigraphy, renal Doppler US, and MR angiography. *Radiographics* 20:1355–1368, 2000.
- 5. Hirsch AT, Haskal ZJ, Hertzer NR, et al: ACC/ AHA 2005 practice guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American association for vascular surgery/ society for vascular surgery, society for cardiovascular angiography and interventions, society for vascular medicine and biology, society of interventional radiology, and the ACC/AHA task force on practice guidelines (writing committee to develop guidelines for the management of patients with peripheral arterial disease); endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. Circulation 113:e463-e654, 2006.
- Vasbinder GB, Nelemans PJ, Kessels AG, et al: Accuracy of computed tomographic angiography and magnetic resonance angiography for diagnosing renal artery stenosis. *Ann Intern Med* 141:674–682, 2004.
- Bude RO, Forauer AR, Caoili EM, et al: Is it necessary to study accessory arteries when screening the renal arteries for renovascular hypertension? *Radiology* 226:411–416, 2003.
- Blum U, Krumme B, Flugel P, et al: Treatment of ostial renal-artery stenoses with vascular endoprostheses after unsuccessful balloon angioplasty. N Engl J Med 336:459–465, 1997.
- 9. Schreij G, de Haan MW, Oei TK, et al: Interpretation of renal angiography by radiologists. *J Hypertens* 17:1737–1741, 1999.
- Kaatee R, Beek FJ, de Lange EE, et al: Renal artery stenosis: detection and quantification with spiral CT angiography versus optimized digital subtraction angiography. *Radiology* 205: 121–127, 1997.
- 11. Wittenberg G, Kenn W, Tschammler A, et al: Spiral CT angiography of renal arteries: comparison with angiography. *Eur Radiol* 9:546– 551, 1999.
- 12. Bakker J, Beek FJ, Beutler JJ, et al: Renal artery stenosis and accessory renal arteries: accuracy of

detection and visualization with gadoliniumenhanced breath-hold MR angiography. *Radiology* 207:497–504, 1998.

- Wyttenbach R, Braghetti A, Wyss M, et al: Renal artery assessment with nonenhanced steadystate free precession versus contrast-enhanced MR angiography. *Radiology* 245:186–195, 2007.
- 14. Parienty I, Rostoker G, Jouniaux F, et al: Renal artery stenosis evaluation in chronic kidney disease patients: nonenhanced time-spatial labeling inversion-pulse three-dimensional MR angiography with regulated breathing versus DSA. *Radiology* 259:592–601, 2011.
- 15. Albert TS, Akahane M, Parienty I, et al: An international multicenter comparison of time-SLIP unenhanced MR angiography and contrastenhanced CT angiography for assessing renal artery stenosis: the renal artery contrast-free trial. *AJR Am J Roentgenol* 204(1):182–188, 2015.
- Schoenberg SO, Knopp MV, Londy F, et al: Morphologic and functional magnetic resonance imaging of renal artery stenosis: a multireader tricenter study. J Am Soc Nephrol 13:158–169, 2002.
- Hélénon O, el Rody F, Correas JM, et al: Color doppler US of renovascular disease in native kidneys. *Radiographics* 15:833–854, 1995.
- Strandness DE, Jr: Duplex imaging for the detection of renal artery stenosis. Am J Kidney Dis 24:674–678, 1994.
- Taylor DC, Kettler MD, Moneta GL, et al: Duplex ultrasound scanning in the diagnosis of renal artery stenosis: a prospective evaluation. *J Vasc Surg* 7:363–369, 1988.
- Schwerk WB, Restrepo IK, Stellwaag M, et al: Renal artery stenosis: grading with imagedirected Doppler US evaluation of renal resistive index. *Radiology* 190:785–790, 1994.
- Robbin ML, Lockhart ME, Barr RG: Renal imaging with ultrasound contrast: current status. *Radiol Clin North Am* 41:963–978, 2003.
- Taylor A, Nally J, Aurell M, et al: Consensus report on ACE inhibitor renography for detecting renovascular hypertension. Radionuclides in nephrourology group. Consensus group on ACEI renography. J Nucl Med 37:1876–1882, 1996.
- Taylor AT, Jr, Fletcher JW, Nally JV, Jr, et al: Procedure guideline for diagnosis of renovascular hypertension. Society of Nuclear Medicine. *J Nucl Med* 39:1297–1302, 1998.
- 24. Henkin R, Boya D: *Nuclear Medicine*, St. Louis, 2006, Mosby, p 1058.
- Bakker J, Beek FJ, Beutler JJ, et al: Renal artery stenosis and accessory renal arteries: accuracy of detection and visualization with gadoliniumenhanced breath-hold MR angiography. *Radiology* 207:497–504, 1998.
- Voiculescu A, Hofer M, Hetzel GR, et al: Noninvasive investigation for renal artery stenosis:

contrast-enhanced magnetic resonance angiography and color Doppler sonography as compared to digital subtraction angiography. *Clin Exp Hypertens* 23:521–531, 2001.

- Vasbinder GB, Nelemans PJ, Kessels AG, et al: Diagnostic tests for renal artery stenosis in patients suspected of having renovascular hypertension: a meta-analysis. *Ann Intern Med* 135: 401–411, 2001.
- Prigent A: The diagnosis of renovascular hypertension: the role of captopril renal scintigraphy and related issues. *Eur J Nucl Med* 20:625–644, 1993.
- Cooper CJ, Murphy TP, Cutlip DE, et al: Stenting and medical therapy for atherosclerotic renal-artery stenosis. N Engl J Med 370:13–22, 2014.
- Riaz IB, Husnain M, Riaz H, et al: Meta-analysis of revascularization versus medical therapy for atherosclerotic renal artery stenosis. *Am J Cardiol* 114:1116–1123, 2014.
- Parikh SA, Shishehbor MH, Gray BH, et al: SCAI expert consensus statement for renal artery stenting appropriate use. *Catheter Cardiovasc Interv* 84:1163–1171, 2014.
- Markowitz GS, Brignol F, Burns ER, et al: Renal vein thrombosis treated with thrombolytic therapy: case report and brief review. *Am J Kidney Dis* 25:801–806, 1995.
- Llach F, Papper S, Massry SG: The clinical spectrum of renal vein thrombosis: acute and chronic. *Am J Med* 69:819–827, 1980.
- Llach F: Hypercoagulability, renal vein thrombosis, and other thrombotic complications of nephrotic syndrome [editorial review]. *Kidney Int* 28:429–439, 1985.
- Si-Hoe CK, Thng CH, Chee SG, et al: Abdominal computed tomography in systemic lupus erythematosus. *Clin Radiol* 52:284–289, 1997.
- Halpern M, Citron BP: Necrotizing angiitis associated with drug abuse. Am J Roentgenol Radium Ther Nucl Med 111:663–671, 1971.
- Bacharach JM, Colville DS, Lie JT: Accelerated atherosclerosis, aneurysmal disease, and aortitis: possible pathogenetic association with cocaine abuse. *Int Angiol* 11:83–86, 1992.
- Davidson AJ, Hartman DS, Choyke PL, et al: Davidson's radiology of the kidney and genitourinary tract, Philadelphia, 1999, WB Saunders, pp 157–235.
- Hekali P, Kivisaari L, Standerskjold-Nordenstam CG, et al: Renal complications of polyarteritis nodosa: CT findings. J Comput Assist Tomogr 9:333–338, 1985.
- 40. Mertens PR, Duque-Reina D, Ittel TH, et al: Contrast-enhanced computed tomography for demonstration of bilateral renal cortical necrosis. *Clin Invest* 72:499–501, 1994.

Fibromuscular dysplasia is treated with angioplasty.
Patient selection is the key for successfully treating atherosclerotic renal artery stenosis.

# **Urinary Tract Obstruction**

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# **Etiology**

60

Urinary tract obstruction (UTO) is a syndrome that may be caused by a wide range of pathologic processes. It may vary in the following:

- *Degree:* May be partial or complete.
- *Site:* May be unilateral or bilateral and may occur at any level of the urinary tract from the calyces to the urethral meatus.
- *Duration:* May be acute or chronic.
- *Demographics:* Common causes vary among prenatal, neonatal, pediatric, young adult, and older adult patient groups and between males and females.
- *Physiologic response:* Can be compensated or uncompensated.
- Presence or absence of a morphologic stricture: Anatomic versus functional obstruction. Anatomic or mechanical obstruction is due to a fixed point of narrowing or an obstructing lesion. In functional obstruction, there is no demonstrable fixed narrowing, but, nonetheless, proximal pressures are raised (e.g., primary obstructive megaureter and some forms of pelviureteral junction obstruction).<sup>1</sup>

Many of the causes of UTO are presented in Table 66-1.

# Prevalence, Epidemiology, and Definitions

UTO is a common clinical and uroradiologic diagnostic problem. The incidence of hydronephrosis in one autopsy series was 3.1%,<sup>2</sup> with no difference in incidence between the sexes in patients younger than age 20 years. It is more common in women than men between 20 and 60 years of age (owing to obstetric and gynecologic causes) and more common in men older than 60 years (predominantly owing to benign prostatic hyperplasia). Hydronephrosis is the most common cause of an abdominal mass in neonates, and UTO is the most common cause of end-stage renal failure in children.<sup>1</sup>

UTO has been defined as "a narrowing such that proximal pressure must be raised to transmit usual flow."<sup>3</sup> It is important to understand that this definition does not refer to dilation of the urinary tract. UTO may occur without dilation (Box 66-1) and dilation may occur without UTO (Box 66-2), creating potential causes of false-negative and false-positive findings in radiologic investigations of UTO.

Other useful definitions include the following:

- Hydronephrosis (or pelvicaliectasis, pyelocaliectasis) refers to dilatation of the collecting system. This is often, but not always, due to UTO.
- Obstructive uropathy is synonymous with UTO. It describes the state in which there is increased resistance to urine flow.

• Obstructive nephropathy refers to renal damage caused by UTO. Over time, UTO results in medullary and cortical atrophy secondary to irreversible nephron loss.

# **Clinical Presentation**

The presentation of UTO varies with the underlying cause. Acute UTO often manifests as pain, decreased urine output, and signs and symptoms of acute renal failure. Chronic UTO is often insidious. Patients may present with hypertension, irreversible chronic renal failure, recurrent urinary tract infections, or change in micturition. Upper tract obstruction may manifest with flank, back, or groin pain and lower tract obstruction with voiding dysfunction or suprapubic pain.

# Pathophysiology

UTO may be caused by a pathologic process at any level of the urinary tract from the calyces to the urethral meatus. The resultant pathophysiology of UTO is complex. Collecting system pressure and renal blood flow (RBF) are important factors. In simple terms, UTO leads to increased collecting system pressure proximal to obstruction, which leads to the following:

- Initial transient renal vasodilation
- Increased RBF then vasoconstriction
- Increased resistance to RBF
- Decreased diastolic flow
- Ischemia
- Atrophy

In addition, UTO results in reduced urine concentration, reduced urine acidification, and abnormalities of electrolyte excretion. UTO causes urinary stasis, predisposing to infection and stones. If untreated, UTO causes progressive and eventually irreversible structural renal changes, including tubular atrophy, tubulointerstitial fibrosis, interstitial inflammation,<sup>2</sup> and glomerular loss.<sup>1</sup>

Recovery of renal function after relief of obstruction may be complete if obstruction is brief, but complete UTO lasting longer than 24 hours may cause irreversible loss of renal function. Increased age, lower baseline renal function, and highgrade and lengthy obstruction are factors associated with greater residual renal impairment.<sup>2</sup>

# Pathology

Macroscopically, the obstructed kidney may demonstrate mild to marked enlargement. There is progressive blunting of the apices of the medullary pyramids, which eventually become cupped. Variable parenchymal atrophy may be evident. In advanced obstruction, there may be complete obliteration of

TABLE (	Comm	non Causes of Urinary	/ Tract Obstruction		
Type of Obstruct		Kidney/Renal Pelvis	Ureter	Bladder	Urethra
Intralumi	inal	Staghorn calculus	Calculus Transitional cell carcinoma Sloughed papilla Blood clot	Calculus Transitional cell carcinoma	Posterior urethral valves
Intramura	al	Pelviureteral junction obstruction Infundibular stenosis	Stricture (e.g., postinfection, surgery or radiation therapy) Ureterocele Vesicoureteral reflux	Neuropathic bladder	Urethritis Stricture
Extramural Extramural Retroperitoneal lymphadenopathy Retroperitoneal abscess Retroperitoneal fibrosis Inflammatory abdominal aortic aneurysm Large abdominal aortic aneurysm or iliac artery aneurysm Endometriosis Pregnancy			Benign prostatic hypertrophy Prostate carcinoma		

#### BOX 66-1 **CAUSES OF URINARY TRACT OBSTRUCTION ASSOCIATED WITH** LITTLE OR NO DILATION OR **HYDRONEPHROSIS**

- Retroperitoneal fibrosis
- Retroperitoneal tumor encasing ureters or renal pelvis, with loss of normal distensibility of collecting system
- Obstruction with urine extravasation, resulting in decompression of pelvicalyceal system
- Hyperacute urinary tract obstruction

#### NONOBSTRUCTIVE CAUSES OF BOX 66-2 URINARY TRACT DILATION

- Vesicoureteral reflux
- Primary megaureter
- Previous obstruction
- Infection (pyelonephritis, peritonitis)
- High-flow states (diabetes insipidus, psychogenic polydipsia)
- Prune belly syndrome Congenital megacalyces
- Beckwith-Wiedemann syndrome

the pyramids, marked cortical thinning, and massive dilation of the collecting system.

Early renal microscopic changes include edema and tubular dilation. Increasing edema widens Bowman's space, followed by thickening of the tubular basement membrane, then papillary necrosis, infiltration with inflammatory cells, and interstitial fibrosis. In the end stages, there is glomerular collapse, tubular atrophy, and connective tissue proliferation.<sup>2,4</sup>

# Imaging

When interpreting radiologic studies of the urinary tract, anatomic and functional factors should be considered and modalities that depict one without the other should be interpreted with caution.

## PLAIN RADIOGRAPHY

Ninety percent of urinary calculi are radiopaque and therefore theoretically visible on plain radiographs. Factors limiting visualization include stone composition and size, patient habitus, extraurinary calcifications, and overlying bowel gas and content.<sup>1</sup> Radiolucent calculi (pure urate or xanthine calculi, matrix stones) may not be detected, nor may noncalculous causes of obstruction.

## **EXCRETORY UROGRAPHY**

Excretory urography (EUG), also referred to as intravenous pyelography (IVP), was previously the gold standard in the assessment of UTO. It provides anatomic and functional information.

## Excretory Urography Findings of Acute Urinary Tract Obstruction

The principle EUG findings in acute UTO are as follows:

- · Immediate nephrogram usually normal or mildly diminished (reflects normal RBF)
- Increasingly dense nephrogram over time
- Delayed excretion of contrast agent into the collecting system
- Variable dilation of collecting system proximal to point of obstruction

Other findings may include the following:

- Heterotopic excretion of contrast via the biliary system, leading to opacification of the gallbladder
- Urine or contrast extravasation occurs if renal pelvis pressure is sufficiently high
  - Pyelotubular extravasation: Contrast agent refluxes into the renal papillae; also referred to as "back flow." This is referred to as intrarenal reflux in the setting of severe vesicoureteral reflux. Reflux of infected urine

into the renal papillae leads to scarring and chronic pyelonephritis.

- Pyelosinus extravasation: Forniceal rupture allows contrast agent to track into the renal sinus; contrast medium may outline the proximal ureter and psoas muscle.
- Less common forms are pyelolymphatic, pyelovenous, and pyelosubcapsular extravasation.

## Excretory Urography Findings of Chronic Urinary Tract Obstruction

The principle EUG findings in chronic UTO are as follows:

- Small, normal, or large kidneys
- Nephrogram delayed (decreased RBF) and diminished in density
- Variable renal atrophy: Seen as parenchymal thinning
- Delayed excretion of contrast agent into the collecting system
- Variable dilation of collecting system to point of obstruction (Figure 66-1)

## Grading of Hydronephrosis on Excretory Urography

Hydronephrosis can be graded as follows<sup>1</sup>:

- *Grade 1:* Slight blunting of fornices
- *Grade 2*: Obvious blunting of fornices, enlargement of calyces, papillae flattened but visible



**Figure 66-1** Chronic urinary tract obstruction on excretory urography. Grade 3 hydronephrosis and mild parenchymal thinning of the left kidney are seen. The left ureter is dilated down to the level of the sacroiliac joint, where there is irregular narrowing, consistent with a malignant stricture. (*Courtesy WK, Lee, MD, MBBS, St. Vincent's Hospital, Melbourne, Australia.*)

- Grade 3: Rounded calyces, papillary silhouette obliterated
- Grade 4: Extreme ballooning of calyces

EUG has now been largely superseded by ultrasonography, noncontrast computed tomography (CT), and CT and magnetic resonance (MR) urography for assessing UTO. It may still have a limited role in monitoring stone disease.<sup>5</sup>

## **RETROGRADE PYELOGRAPHY**

Retrograde pyelography is invasive but demonstrates the collecting system anatomy well. It may be useful when allergy or renal insufficiency preclude the intravenous use of a contrast agent. If the cause of UTO is intraluminal, brushings or biopsy may be performed at the time of retrograde pyelography; ureteral calculi also may be extracted. However, it provides little information about intramural or extraluminal causes of obstruction.

## ANTEGRADE PYELOGRAPHY

Antegrade pyelography is achieved by performing a percutaneous ultrasound-guided renal puncture, followed by injection of iodinated contrast. It is performed before nephrostomy and/or antegrade stenting or, uncommonly, when other imaging methods have failed to demonstrate the cause or site of obstruction.

## DIGITAL SUBTRACTION ANGIOGRAPHY

Digital subtraction angiography has largely been superseded by multidetector CT (MDCT) angiography. Before the use of CT angiography, digital subtraction angiography was used to determine the course of vessels, especially before operative management of ureteropelvic junction obstruction.

## COMPUTED TOMOGRAPHY

### Noncontrast Computed Tomography

Noncontrast helical CT was first demonstrated to be equal to EUG in demonstrating ureteral obstruction and more sensitive in diagnosing ureteral calculi by Smith and colleagues<sup>6</sup> in 1995, and it has become the imaging modality of choice for evaluating patients with suspected ureteral colic. It has sensitivity of 95% to 97% and specificity of 96% to 98% for ureteral calculi (Figure 66-2).<sup>7,8</sup>

Secondary signs of UTO on CT include ureteral dilation, hydronephrosis, perinephric and periureteral stranding, and renal enlargement.<sup>9</sup>

Disadvantages and pitfalls of noncontrast CT include the following:

- Differentiating calculi from phleboliths. The latter are not in the path of the ureter and often have a radiolucent center.
- Calculi at the vesicoureteral junction (VUJ). Prone scanning is necessary to determine whether these are impacted at the VUJ or free in the posterolateral bladder (Figure 66-3).
- Indinavir, a protease inhibitor given to people infected with human immunodeficiency virus, may produce urinary calculi that are difficult to identify on CT because their density is similar to that of adjacent soft tissue.
- It may be difficult or impossible to differentiate parapelvic cysts from hydronephrosis (Figure 66-4).

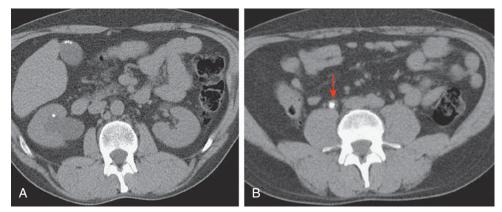
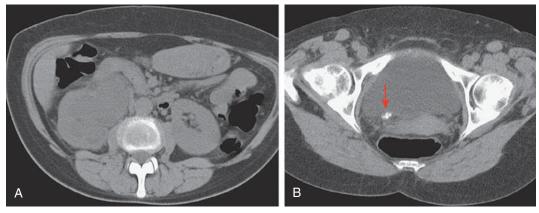
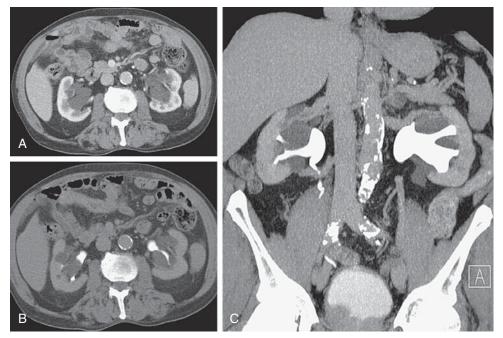


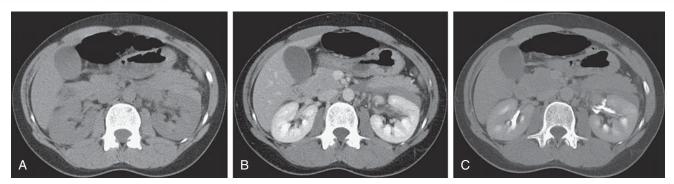
Figure 66-2 Noncontrast prone axial computed tomography images in a 60-year-old man who presented with right flank pain. A, Upper abdomen: Moderate right hydronephrosis and nonobstructing right renal calculus. B, Mid-abdomen: Mid-right ureteral calculus (arrow).



**Figure 66-3** Noncontrast prone axial computed tomography images in a 70-year-old woman who presented with a known history of right renal calculi and recurrent urinary tract infection. **A**, Moderate to severe hydronephrosis of the right kidney is evident. **B**, Small calculi impacted at the vesicoureteral junction (*arrow*). In a supine patient these may be mistaken for dependent bladder calculi, but this prone scan confirms that the calculi are in the distal ureter.



**Figure 66-4** Computed tomography urography in an 81-year-old man with hydronephrosis reported on ultrasonography. **A**, Axial image, nephrographic phase shows well-circumscribed, nonenhancing low-attenuation areas without a perceptible wall are present in the renal sinus bilaterally. Axial (**B**) and coronal (**C**) images (delayed phase) show that the collecting system is well opacified and mildly effaced by low-attenuation masses that have characteristic features of parapelvic cysts. (*Courtesy WK, Lee, MD, MBBS, St. Vincent's Hospital, Melbourne, Australia.*)



**Figure 66-5** Axial computed tomography with (A) noncontrast, (B) nephrographic-phase, and (C) delayed-phase images in a 31-year-old woman with left flank trauma. Although there is no urinary tract obstruction in this case, it is an example of extravasation from a disrupted collecting system. Contrast agent is clearly seen outside the collecting system in the region of the left renal sinus on the delayed-phase image. Note also the moderate anterior perinephric hematoma. (*Courtesy WK, Lee, MD, MBBS, St. Vincent's Hospital, Melbourne, Australia.*)

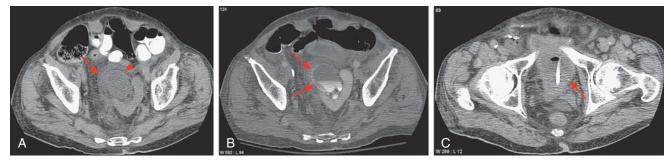


Figure 66-6 An 87-year-old man with a left pelvic kidney presented with hematuria and abdominal pain. A, Initial noncontrast axial computed tomography (CT) image demonstrates hydronephrosis of the pelvic kidney, with ill-defined heterogeneous density (*arrow*) adjacent to the dilated renal pelvis (*arrowhead*). B, Axial image of delayed phase of CT urogram demonstrates pyelosinus extravasation (*arrows*). C, Review of noncontrast CT revealed a small left vesicoureteral junction calculus (*arrow*).

• Relative contraindications exist for pregnant patients with flank pain, owing to the administration of ionizing radiation.

## Multidetector Computed Tomography

MDCT urography involves CT of the urinary tract before and after intravenous contrast administration, typically in the nephrographic and delayed phase.<sup>10</sup> It allows high spatial resolution imaging of the entire urinary tract within a breath-hold, with isotropic voxels, allowing multiplanar evaluation of urothelium and surrounding structures. Hence, MDCT urography has replaced EUG in most centers.<sup>10</sup> It should be considered in the following settings:

- Flank pain and/or urinary tract dilation on ultrasonography or unenhanced CT but no stone or other cause demonstrated on these studies
- Flank pain and/or suspicion of UTO but negative findings on ultrasonography and unenhanced CT

Specific signs of obstruction on MDCT urography are similar to those seen on EUG. In acute UTO, enhancement of renal parenchyma in the nephrographic phase remains normal or mildly diminished. Renal parenchyma becomes increasingly dense with time. Excretion of contrast agent into the collecting system is delayed, often with layering of hyperdense contrast medium and hypodense urine. There is variable dilation of the collecting system proximal to the point of obstruction.

Heterotopic excretion is usually not seen unless a very delayed study is performed or unless there has been an earlier contrast study. MDCT urography is more sensitive to contrast agent extravasation than EUG (Figures 66-5 and 66-6).

In chronic UTO, loss of renal parenchymal thickness and the delayed, diminished nephrogram are clearly demonstrated.

Some examples of causes of UTO readily identified at CT urography are as follows:

- Ureteropelvic junction obstruction (Figure 66-7), retrocaval ureter, duplicated system (Figure 66-8)
- Stricture (benign or malignant)
- Retroperitoneal or pelvic mass
- Retroperitoneal fibrosis
- Inflammatory abdominal aortic aneurysm (Figure 66-9)

The drawbacks of MDCT urography include increased dose of ionizing radiation with multiple-phase imaging, the use of iodinated contrast, and the postprocessing time required.<sup>11</sup>

#### MAGNETIC RESONANCE IMAGING

MR urography, or MRI of the collecting system (as opposed to MRI of kidneys) is performed with two main techniques: static fluid MR urography and excretory MR urography.

Static fluid MR urography uses heavily T2-weighted sequences to demonstrate fluid in the urinary tract, similar to the technique used in MR cholangiopancreatography. Breathhold thick- or thin-slab single-shot fast spin echo sequences or respiratory-triggered three-dimensional (3D) acquisition with postprocessing (e.g., maximum intensity projections) are performed, typically in the coronal plane. This technique is



**Figure 66-7** Known ureteropelvic junction (UPJ) obstruction in a 28-year-old man. Volume-rendered image from a preoperative computed tomography urogram clearly demonstrates the site and morphology of the UPJ narrowing. (*Courtesy WK, Lee, MD, MBBS, St. Vincent's Hospital, Melbourne, Australia.*)

particularly good for demonstrating a dilated system. It should be performed before administration of a contrast agent to avoid T2 shortening by excreted contrast medium in the urinary tract.<sup>12</sup>

Excretory MR urography is analogous to conventional intravenous urography and MDCT urography. An intravenous contrast medium is administered, and the collecting system is imaged during excretion of the agent, typically 5 to 8 minutes after injection.<sup>13</sup> Multiple phases are often obtained (e.g., corticomedullary, nephrographic, delayed). Low-dose gadolinium (~0.01 mmol/kg) is recommended to avoid low urine signal intensity resulting from T2\* effects. The use of intravenous hydration and a diuretic (usually furosemide) is recommended by many authors because increased urine flow better distends the collecting systems and ureters. A fat-suppressed 3D gradient echo imaging sequence is used.<sup>12,14</sup>

Although MR urography is useful to determine the site of obstruction and degree of ureteral dilation, conventional T1and T2-weighted sequences are often still necessary to demonstrate any underlying pathologic process.

MR urography is particularly useful in pediatric and pregnant patients owing to lack of ionizing radiation. In pregnant patients, static-fluid MR urography is usually sufficient and administration of a contrast agent should be avoided because of uncertain effects on the developing fetus. Similarly, contrast agent should be used with caution in patients with impaired renal function because of the risk for nephrogenic systemic fibrosis. Specifically, in patients with known renal impairment or at risk for reduced renal function, and eGFR less than 60 mL/ min/1.73 m<sup>2</sup>, use of gadolinium-containing contrast agents is relatively contraindicated.<sup>15</sup>

Patients with suspected ureteral calculi should have noncontrast helical CT rather than MRI, because MRI is relatively insensitive to calcification. However, because calculi are the most common urinary filling defect<sup>16</sup> it is important to be aware of their features on MRI. On MRI, calculi appear as a signal void surrounded by hyperintense urine. In the setting of noncalculous UTO, MR urography has been shown to be more sensitive and specific than noncontrast CT.<sup>17</sup> Conventional MR urography is more sensitive to perirenal and periureteral edema than CT.<sup>13</sup> Pitfalls of MR urography include its relative insensitivity to calculi,<sup>12</sup> relatively high cost, long acquisition time, and lower spatial resolution than CT urography.

## ULTRASONOGRAPHY

Ultrasonography is a mainstay in the assessment of UTO because it is inexpensive, quick, and widely available and requires no radiation or intravenous contrast agent.

Dilation of the calyces, renal pelvis, and upper ureter is readily demonstrated, although this is not always due to obstruction and should be assessed in the context of the clinical presentation. Hydronephrosis is recognized as dilation of the calyces, renal pelvis, or both. It can be graded at ultrasonography as minimal (well-defined anechoic band or anechoic pockets within the central renal sinus echo complex), moderate (larger anechoic collecting system), or severe (marked dilation of collecting system, often larger than remainder of kidney) (Figures 66-10 and 66-11).<sup>18,19</sup> Mild, moderate, and severe hydronephrosis on ultrasonography correlates, respectively, with grades 2, 3, and 4 hydronephrosis seen at EUG.<sup>1</sup>

Renal parenchymal thickness may be decreased in chronic UTO and so should be measured on each side and compared. The ureter should be followed as far as possible, and the bladder (and prostate in men) should be visualized because a cause of UTO may be identified (Figures 66-12 and 66-13).

Doppler techniques may add further information. The bladder should be interrogated with color Doppler imaging for the presence of jets of urine exiting the ureteral orifices. Marked asymmetry of jets or a decreased or absent jet ipsilateral to a dilated upper tract is suggestive of ureteral obstruction. Assessment should be performed for at least 1 minute, because normal peristalsis may result in the intermittent presence of ureteral jets.<sup>20</sup>

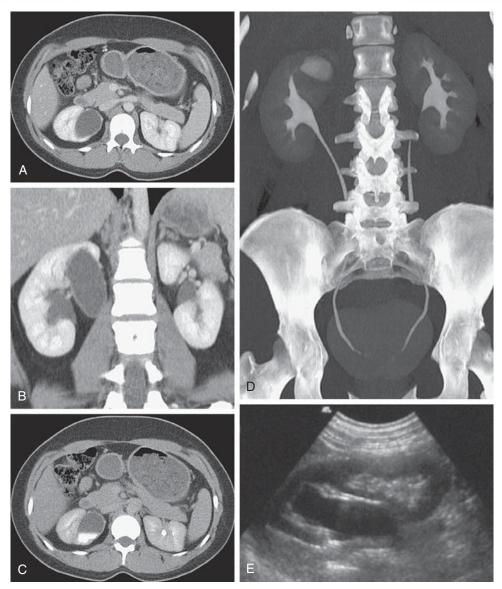
Intrarenal vascular resistance may be a useful marker of significant obstruction.<sup>21</sup> The resistive index (RI) of vessels at the corticomedullary junction is used.

$$RI = \frac{Peak systolic velocity - End-diastolic velocity}{Peak systolic velocity}$$
[66-1]

Increased vascular resistance causes relatively more reduction in diastolic than systolic flow, causing elevation of the RI. Optimal Doppler settings and a cooperative patient are required. Obstruction has been shown to cause an elevated RI. An elevated RI (>0.7), an intrarenal difference in RI (of at least 0.06 to 0.10), and an abnormal RI response to diuretic challenge have been suggested as criteria to diagnose significant obstruction.<sup>22</sup> Results should be correlated with gray-scale findings and are most reliable in cases of complete obstruction. The utility of RI measurement in partial obstruction is less clear. Certainly, a normal intrarenal RI suggests that significant physiologic obstruction is unlikely.<sup>22</sup>

Disadvantages of ultrasonography include dependence on operator technique and patient factors such as body habitus and bowel gas. Potential pitfalls include a lack of correlation between degree of hydronephrosis and grade of obstruction and falsenegative and false-positive findings.<sup>23,24</sup>

False-negative findings of UTO on ultrasonography are most commonly due to minimal dilation in early acute obstruction. Other causes are listed in Box 66-1. False-positive ultrasound diagnosis of UTO may occur in the following settings:



**Figure 66-8** Computed tomographic urography shows a dilated upper pole moiety of the right duplex collecting system in a 26-year-old woman. Nephrographic phase images in axial (A) and coronal (B) planes with delayed axial image (C) and coronal delayed-phase maximum intensity projection (D). The dilated upper pole moiety was initially thought to be a cyst on ultrasonography (E). (Courtesy WK, Lee, MD, MBBS, St. Vincent's Hospital, Melbourne, Australia.)

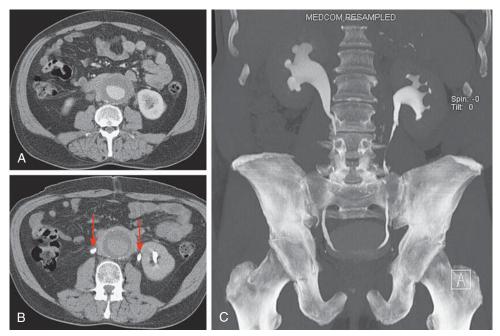
- Conditions causing dilation without obstruction (see Box 66-2)
- Presence of structures that may mimic a dilated collecting system (e.g., peripelvic and parapelvic cysts, extrarenal pelvis, prominent renal vein)
- Distended bladder with mild upper tract dilation if patient has not voided
- Renal pelvis filled by large staghorn calculus or clot

### NUCLEAR MEDICINE

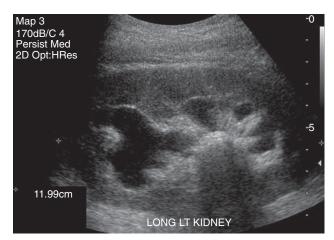
Radionuclide imaging is rarely used to diagnose acute obstruction, which is more effectively diagnosed by clinical and radiologic means, particularly ultrasonography, CT urography, and, less commonly, intravenous urography.<sup>25</sup> However, it is very useful to differentiate chronic obstruction from a nonobstructed dilated system. In addition, it has a prognostic role in chronic obstruction because uptake, transit, and excretion of radiotracer correlates with functional status of each kidney.<sup>25</sup> Calculating split renal function may help determine whether surgical treatment or nephrectomy is preferable in a chronically obstructed kidney (Figure 66-14). Nuclear renography also can be used to monitor response to treatment of chronic UTO.

Technetium-99m–labeled mercaptoacetyl triglycine (<sup>99m</sup>Tc-MAG3) is the agent of choice (rather than <sup>99m</sup>Tc-diethylenetriaminepentaacetic acid) because it is cleared by tubular secretion, producing superior images in patients with reduced GFR.

Patients should be well hydrated before the examination, because dehydration may mimic obstruction (moderate urine flow rate is required for a normal study). After administration of a radiotracer, images are collected over 30 to 40 minutes and



**Figure 66-9** Known inflammatory abdominal aortic aneurysm in a 63-year-old man. Axial nephrographic (A), delayed-phase axial (B), and maximum intensity projection (C) images from computed tomographic urography demonstrate an infrarenal aneurysm with enhancing rind of tissue around its anterolateral aspect. This is intimately associated with the ureters (arrows, B), causing grade 2 hydronephrosis on the left and grade 3 on the right. (*Courtesy WK, Lee, MD, MBBS, St. Vincent's Hospital, Melbourne, Australia.*)



**Figure 66-10** A 35-year-old woman had a clinical diagnosis of left pyelonephritis that was not responding to antibiotics. Ultrasonography demonstrates a large renal pelvis calculus with associated moderate hydronephrosis.

tracer uptake and clearance can be quantified scintigraphically. Time-activity curves for each kidney and collecting system can be constructed.

In diuretic renography, furosemide is typically administered 20 minutes after a radiotracer to enhance the urine flow rate. When a diuretic is administered, the radiotracer that has accumulated in a nonobstructed dilated system will wash out, whereas a radiotracer in an obstructed system will continue to accumulate proximal to the point of obstruction. A clearance half-time (time at which 50% of the radiotracer has been cleared) of less than 10 minutes after administration of furose-mide is considered normal; if this time is more than 20 minutes,

obstruction is denoted; a result between 10 and 20 minutes is considered equivocal.

Modified protocols may be useful in patients with equivocal results (e.g., furosemide administered 15 minutes before radio-tracer, so tracer clearance corresponds with period of maximal diuresis).<sup>26</sup>

Potential pitfalls of diuretic renography include the following:

- Equivocal response to diuretic challenge; this may be overcome by administering a diuretic 15 minutes before imaging.<sup>25,26</sup>
- Poor renal function, with inability to respond to diuretic challenge

### POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

Positron emission tomography with CT (PET/CT) has a very limited role in patients with cancer who have UTO, in differentiating recurrent malignancy or posttherapeutic scarring as a cause of ureteral obstruction.

### **IMAGING ALGORITHM**

Ultrasonography should almost always be the first imaging modality for investigation of possible UTO, unless the patient presents with a classic history of renal colic, in which case non-contrast helical CT is the investigation of choice (Table 66-2).

#### **Classic Signs: Urinary Tract Obstruction**

- Hydronephrosis, hydroureter, and enlarged bladder volume may be seen.
- Other signs are specific to the cause of the obstruction.

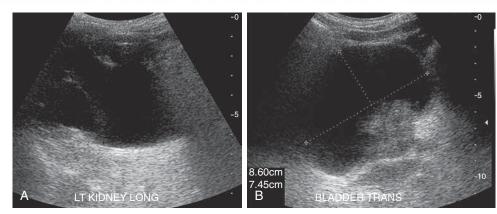
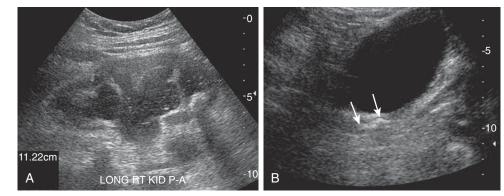


Figure 66-11 Ultrasonography in an 87-year-old woman with known bladder tumor. Note the severe left hydronephrosis (A) secondary to a bladder tumor (B) obstructing the left ureteral orifice.



**Figure 66-12** Ultrasound images of the patient in Figure 66-3 (performed before computed tomography [CT]) demonstrate hydronephrosis (A) and echogenic debris (*arrows*, **B**) in the distal right ureter, in keeping with calculus fragments that were later confirmed at CT.

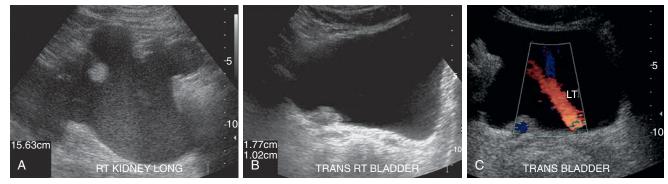


Figure 66-13 Ultrasound images in a 75-year-old man who presented with hematuria. A, Severe hydronephrosis of the right kidney is evident. B, Gray-scale ultrasonography of the bladder reveals a lobulated mass in the vicinity of the right ureteral orifice. C, Color Doppler examination shows the right ureteral jet is absent, whereas the left jet is normal.

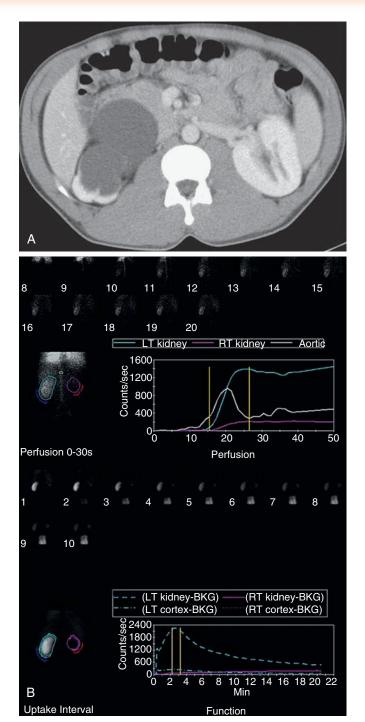
## DIFFERENTIAL DIAGNOSIS

The differential diagnosis of UTO depends on the presentation. In patients presenting with new-onset acute renal failure or chronic renal failure, imaging is often the first investigation to rule UTO out or in. If there is no evidence of UTO, other causes of renal failure are then considered (i.e., renal and prerenal causes).

Ureteral colic classically manifests as "loin to groin" pain and often can be diagnosed clinically but occasionally may manifest as pain in an atypical distribution. Once UTO is diagnosed, the cause should be elucidated. In children, congenital causes such as ureteropelvic junction obstruction, ectopic ureter, ureterocele, and posterior urethral valves should be considered.

In young adults, ureteral calculi are the most common cause of obstruction. Pregnancy may cause ureteral obstruction secondary to extrinsic compression by the gravid uterus.

In older men, benign prostatic hyperplasia is the most common cause of UTO. Urinary tract and other malignant tumors also should be considered.



**Figure 66-14** A 25-year-old man presented with known right ureteropelvic junction obstruction and ongoing pain. **A**, Contrast-enhanced axial computed tomography image of the upper abdomen demonstrates severe right hydronephrosis with marked parenchymal thinning. Because of these findings, nephrectomy was considered. **B**, Technetium 99m–labeled mercaptoacetyl triglycine (<sup>29m</sup>Tc-MAG3) renogram shows the right kidney contributed a negligible 3.65% of renal function, so nephrectomy was performed.

In older women, gynecologic malignancy is a common cause of UTO.

Determination of serum levels of urea, creatinine, and electrolytes is used to diagnose impaired renal function. Imaging is the cornerstone in diagnosing the presence and cause of UTO, and any further laboratory investigations are usually interpreted in conjunction with imaging findings.

## Treatment

## MEDICAL TREATMENT

Medical management of UTO is generally limited to management of symptoms (e.g., analgesia in renal colic) and complications (e.g., acute pulmonary edema secondary to renal failure, dialysis for uremia, electrolyte imbalances in postobstructive diuresis).

Chemotherapy and/or radiotherapy may relieve extrinsic compression of the ureter in the setting of malignant obstruction.

## SURGICAL TREATMENT

Surgical and interventional radiologic techniques are the mainstay of the management of UTO. In acute UTO, the aim of treatment is to relieve obstruction to prevent renal damage and relieve pain. In the setting of an infected obstructed kidney, drainage is emergent to prevent septicemia.

The two main drainage procedures in acute UTO are percutaneous nephrostomy and retrograde stent placement. Although several studies have shown these to be equally effective at draining the kidney in calculous obstruction, the preferred technique is controversial.<sup>27</sup> Nephrostomy tube placement is invasive and results in external drainage of urine but may be less irritative than ureteral stenting in the setting of calculous obstruction. Percutaneous nephrostomy is generally preferred over stenting in cases of extrinsic malignant obstruction of the ureter owing to the tendency of stents to fail early and require operative cystoscopic replacement.

Access to an obstructed system by percutaneous nephrostomy is successful in 99% of cases. Failure is most commonly due to decompression by forniceal rupture.<sup>27</sup> In these cases, retrograde stenting may be necessary.

The definitive management of UTO depends on the cause, and the reader is referred to the relevant chapters for specific management details of the many causes of UTO.

#### What the Referring Physician Needs to Know

- Ultrasonography is usually the modality of choice to diagnose UTO, unless there is the classic renal colic manifestation when noncontrast CT should be performed first.
- CT urography and MR urography are useful when preliminary investigations have been unrevealing.

#### **Key Points**

- UTO may cause renal impairment, with duration of obstruction proportional to degree of damage. If diagnosed and treated early, permanent renal impairment may be avoided.
- Ultrasonography and noncontrast CT are the first-line investigations.

TABLE Accuracy	y, Limitations, and Pitfalls of t	the Modalities Used in Imaging of Urina	ary Tract Obstruction
Modality	Accuracy	Limitations	Pitfalls
Radiography	Moderate to poor for calculi	Poor delineation of extraurinary tissues Nonspecific	Radiolucent stones and noncalculous causes of obstruction may be missed.
СТ	Noncontrast CT: Very sensitive, specific, accurate for calculi CT urography: Useful for identifying other causes of obstruction	Contrast agent is relatively contraindicated in the setting of renal impairment.	Evaluation of the prostate and urethra is limited.
MRI	More sensitive and specific in diagnosing noncalculous urinary tract obstruction than noncontrast CT	Expensive, time consuming, limited availability Contrast agent cannot be used in significant renal impairment because of risk for nephrogenic systemic fibrosis. Metallic artifact from abdominal surgical clips may obscure images.	Small filling defects may be missed on thick-slab T2-weighted sequences used in static-fluid MR urography. Flow artifact may occur in the ureters on static fluid MR urography.
Ultrasonography	Excellent for dilation	Operator dependent; patient-dependent (habitus, bowel gas) Poor visualization of ureters	False-positive and false-negative results are possible (see <u>Boxes 66-1</u> and <u>66-2</u> )
Nuclear medicine	Reliable in assessing for obstruction in the setting of a known dilated collecting system	Not useful in acute obstruction	Dehydration may mimic obstruction.
PET/CT		Limited application	
CT Computed tom	araphy MPI magnetic reconance	imaging: PET positron emission tomography	

CT, Computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

#### SUGGESTED READING

- Koelliker SL, Cronan JJ: Acute urinary tract obstruction: imaging update. Urol Clin North Am 24:571– 582, 1997.
- Leydendecker JR, Barnes CE, Zagoria RJ: MR urography: techniques and clinical applications. *Radiographics* 28:23–46, 2008.

#### **REFERENCES**

- Talner LB, O'Reilly PH, Roy C: Urinary obstruction. In Pollack HM, McClennan BL, editors: *Clinical urography*, ed 2, Philadelphia, 2000, WB Saunders.
- Pais VM, Strandhoy JW, Assimos DG: Pathophysiology of urinary tract obstruction. In Wein AJ, Kavoussi LR, Novick AC, et al, editors: *Campbell walsh urology*, ed 9, Philadelphia, 2007, Saunders.
- Koelliker SL, Cronan JJ: Acute urinary tract obstruction: imaging update. Urol Clin North Am 24:571–582, 1997.
- Cotran RS, Kumar V, Collins T: The kidney. In Robbins pathologic basis of disease, ed 6, Philadelphia, 1999, WB Saunders, pp 988–989.
- Dyer RB, Chen MYM, Zagoria RJ: Intravenous urography: technique and interpretation. *Radiographics* 21:799–824, 2001.
- Smith RC, Rosenfeld AT, Choe KA, et al: Acute flank pain: comparison of non-contrastenhanced CT and intravenous urography. *Radiology* 194:789–794, 1995.
- Smith RC, Verga M, McCarthy S, et al: Diagnosis of acute flank pain: value of unenhanced helical CT. AJR Am J Roentgenol 166:97–101, 1996.
- Dalrymple NC, Verga M, Anderson KR, et al: The value of unenhanced computerized tomography in the management of acute flank pain. *J Urol* 159:735–740, 1998.
- 9. Smith RC, Verga M, Dalrymple N, et al: Acute ureteral obstruction: value of secondary signs

on helical unenhanced CT. *AJR Am J Roentgenol* 167:1109–1113, 1996. 10. Silverman S, Leydendeker J, Amis E: What is the current role of CT urography and MR urogra-

- current role of CT urography and MR urography in the evaluation of the urinary tract? *Radiology* 250:309–323, 2009.
- 11. Kawashima A, Vrtiska TJ, LeRoy AJ, et al: CT urography. *Radiographics* 24:S35–S54, 2004.
- 12. Leydendecker JR, Barnes CE, Zagoria RJ: MR urography: techniques and clinical applications. *Radiographics* 28:23–46, 2008.
- O'Connor O, McLaughlin P, Maher M: MR urography. AJR Am J Roentgenol 195:W201– W206, 2010.
- 14. Kaewlai R, Abujudeh H: Nephrogenic systemic fibrosis. *AJR Am J Roentgenol* 199:W17–W23, 2012.
- Nikken JJ, Krestin GP: MRI of the kidney: state of the art. *Eur Radiol* 17:2780–2793, 2007.
- Garcia-Valtuille R, Garcia-Valtuille A, Abascal F, et al: Magnetic resonance urography: a pictorial overview. *Br J Radiol* 79:614–626, 2006.
- Shokeir AA, El-Diasty T, Eassa W, et al: Diagnosis of noncalcareous hydronephrosis: role of magnetic resonance urography and noncontrast computed tomography. *Urology* 63:225–229, 2004.
- Malave SR, Neiman HL, Spies SM, et al: Diagnosis of hydronephrosis: comparison of radionuclide scanning and sonography. *AJR Am J Roentgenol* 135:1179–1185, 1980.

- Ellenbogen PH, Scheible FW, Talner LB, et al: Sensitivity of gray scale ultrasound in detecting urinary tract obstruction. *AJR Am J Roentgenol* 130:731–733, 1978.
- Burge HJ, Middleton WD, McClennan BL, et al: Ureteral jets in healthy subjects and in patients with unilateral ureteral calculi: comparison with color Doppler US. *Radiology* 180:437–442, 1991.
- Platt JF: Duplex Doppler evaluation of native kidney dysfunction: obstructive and nonobstructive disease. *AJR Am J Roentgenol* 158:1035– 1042, 1992.
- 22. Platt JF: Advances in ultrasonography of urinary tract obstruction. *Abdom Imaging* 23:3–9, 1998.
- Mostbeck GH, Zontsich T, Turetschek K: Ultrasound of the kidney: obstruction and medical diseases. *Eur Radiol* 11:1878–1889, 2001.
- Wachsberg RH: Pitfalls in the ultrasound diagnosis of upper urinary tract obstruction. *Emerg Radiol* 98:289–296, 1998.
- Dubovsky EV, Russell CD: Advances in radionuclide evaluation of urinary tract obstruction. *Abdom Imaging* 23:17–26, 1998.
- English PJ, Testa HJ, Lawson RS: Modified method of diuresis renography for the assessment of equivocal pelviureteral junction obstruction. *Br J Urol* 59:10–14, 1987.
- 27. Gupta M, Ost MS, Shah JB, et al: Percutaneous management of the upper urinary tract. In Pollack HM, McClennan BL, editors: *Clinical urography*, ed 2, Philadelphia, 2000, WB Saunders.

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Mostbeck GH, Zontsich T, Turetschek K: Ultrasound of the kidney: obstruction and medical diseases. *Eur Radiol* 11:1878–1889, 2001.

Talner LB, O'Reilly PH, Roy C: Urinary obstruction. In Pollack HM, McClennan BL, editors: *Clinical urography*, ed 2, Philadelphia, 2000, WB Saunders.



# **Benign and Malignant Ureteral Strictures**

ALISSA SAUNDERS | COLIN J. MCCARTHY | ANTHONY E. SAMIR

A ureteral stricture is a narrowing of the ureter that results in a functional obstruction. It may be the result of a variety of benign and malignant causes, which may be classified as intrinsic or extrinsic processes. The clinical presentation of patients with ureteral strictures depends on the cause of the stricture and the severity and duration of the associated obstruction. In acute ureteral obstruction, pain is a common symptom. Chronic ureteral obstruction is most commonly asymptomatic unless urosepsis or renal failure supervenes. Both acute and chronic ureteral obstruction may manifest as hematuria.

## **Normal Anatomy**

The ureter is a muscular tube that courses in the retroperitoneum connecting the collecting system of the kidney to the bladder. In an adult, the ureteral length varies from 28 to 34 cm.<sup>1</sup> In the abdomen, the ureter is located along the medial aspect of the psoas muscles and passes anterior to the common or external iliac artery. The ureter travels in the lateral pelvic wall before coursing medially toward the bladder. In the female pelvis, the ureter travels beneath the broad ligament, lateral to the cervix and under the uterine artery. In the male, the ureter passes under the vas deferens. The ureters join the bladder and travel submucosally within the bladder wall for 2 to 3 cm before opening into the bladder at the ureteral orifices. The diagonal course of the intramural segment of the ureter helps prevent urinary reflux. This intramural segment of ureter at the ureterovesical junction is a site of normal narrowing and should not be mistaken for a pathologic narrowing. Physiologic narrowing along the course of the ureter also occurs at the ureteropelvic junction (UPJ) and where the ureter passes anterior to the iliac vessels.

The ureter is composed of two muscle layers, an inner longitudinal layer and an outer circular layer. In the wall of the distal ureter, near its insertion into the bladder, a third muscle layer is continuous with the detrusor muscle of the bladder. The mucosa of the ureter is a transitional epithelium. The ureter is surrounded by an outer fibrous layer, the adventitia, which is continuous with the renal capsule and the adventitia of the bladder.<sup>2</sup> The wall of the ureter is usually less than 1 mm thick.

The abdominal portions of the ureters receive their blood supply from a ureteral branch of the renal artery and from branches arising from the aorta, retroperitoneal vessels, gonadal vessels, and iliac vessels. In the abdomen, the arterial branches supplying the ureter are located medial to the ureter, whereas in the pelvis the ureteral arteries arise lateral to the ureter from the iliac, gluteal, obturator, rectal, and vesical arteries. The

supplying artery and draining veins travel in the connective tissue surrounding the ureter called the mesoureter. In most patients, an anastomosing plexus forms within the adventitia along the course of the ureter.<sup>2</sup>

The veins and lymphatics follow the arterial supply, also forming an anastomosing plexus along the ureter. The veins of the ureter drain into the renal vein, gonadal vein, lumbar veins, iliac veins, and vesical veins. The lymphatics of the proximal ureter drain into the renal lymphatics, and those of the midureter drain into periaortic and common iliac lymph nodes. The lymphatics of the distal ureter drain into iliac and presacral lymph nodes and join with the lymphatics of the bladder.

The innervation of the ureter consists of sympathetic nerves from the aortic plexus and superior and inferior hypogastric plexus that course with the arterial supply to the connective tissue around the ureter. Pelvic splanchnic nerves from the sacral roots provide parasympathetic innervation to pelvic viscera.

## Imaging

The appearance of strictures of the ureter depends on the cause. Intrinsic processes may obstruct the lumen, incite inflammation and edema in the wall of the ureter, or infiltrate the wall of the ureter. Extrinsic processes may cause narrowing of the ureter by compression, encasement, or infiltration. Strictures may be focal or multifocal.

Filling defects in the ureter may be intraluminal, mucosal, or submucosal. Intraluminal filling defects are often completely surrounded by contrast material. Mucosal and submucosal filling defects are intimately associated with the wall of the ureter and can be differentiated by evaluation of the relationship of the lesion to the adjacent ureteral wall, with mucosal lesions typically demonstrating acute angles and submucosal lesions demonstrating obtuse angles.

An infiltrative process usually causes an abrupt change in caliber of the ureter with an apple core-like appearance of the involved ureter. The narrowed segment of ureter demonstrates circumferential wall thickening and mucosal irregularity. This appearance is classically produced by neoplastic infiltration, but benign causes, such as irradiation, stone disease, and iatrogenic injury, can cause a similar appearance.

Encasement of the ureter often results in a gradual tapered contour and smooth mucosal surface. Alternatively, encasement of the ureter may result in a focal abrupt transition with a dilated proximal ureter and a narrow or normal-caliber ureter distally. This appearance on intravenous pyelography has been

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referred to as the "bullet and bodkin" sign, which can be seen with both benign and malignant conditions.

Many of these processes cause focal ureteral abnormalities; however, occasionally a multifocal process occurs. Multifocal involvement is more commonly seen with transitional cell carcinoma (TCC), tuberculosis (TB), metastases, and lymphadenopathy than with other causes of strictures.

Although certain features of the pattern of ureteral narrowing may indicate a benign or malignant cause, there is significant overlap in these characteristics and a definitive diagnosis is not always possible. Often, other associated imaging findings can help narrow the differential diagnosis, such as the location of the stricture, focal or multifocal involvement, deviation of the ureter, and involvement of the kidney, bladder, or other organ systems.

## RADIOGRAPHY

Conventional abdominal radiography does not have a major role in imaging ureteral pathology. Excretory urography (EUG), although now largely replaced by computed tomography (CT) urography, is still performed in some centers as part of the initial evaluation of the upper urinary tract in patients with hematuria. EUG is a noninvasive test that was once the study of choice for evaluating the renal collecting system and ureters. Changes in the course and caliber of the ureters as well as filling defects and strictures are well demonstrated on EUG. Disadvantages of this modality include limited utility in patients with impaired renal function and poor soft tissue contrast.

In patients who do not excrete intravenously administered contrast agent in the urine owing to abnormal renal function, direct injection of a contrast medium into the renal collecting system or ureter can be performed with antegrade or retrograde pyelography. This allows evaluation of the collecting system and ureters and the opportunity for interventions such as stent placement. Retrograde urography requires cystoscopy for direct visualization of the ureteral orifice.

## COMPUTED TOMOGRAPHY

CT is the major imaging modality for evaluating the ureters. CT allows identification of certain characteristics and secondary findings that help to narrow the differential diagnosis of the cause of the ureteral stricture. In addition to identifying the site of narrowing and the extent of urothelial involvement, CT allows visualization of adjacent structures, which can help differentiate whether the stricture is due to an extrinsic or intrinsic process.

#### MAGNETIC RESONANCE IMAGING

Magnetic resonance (MR) urography is not yet commonly used in the evaluation of ureteral disease and is primarily used as a problem-solving tool. The high T2 signal intensity of urine is advantageous in noncontrast images, particularly when the collecting system is dilated. Other techniques, such as intravenous hydration, diuretics, and gadolinium can enhance evaluation of the nondilated collecting system.<sup>3</sup> However, image quality depends on patient cooperation and image acquisition often requires monitoring by a radiologist. Other limitations include motion artifacts from respiration and ureteral peristalsis, small field of view because of coil size, incomplete ureteral distention, and artifacts from adjacent bowel, particularly in 3.0-tesla MRI. $^3$ 

Given the absence of ionizing radiation, MR urography is useful in the evaluation of pediatric patients, particularly in the setting of congenital anomalies, in pregnant women with dilated collecting systems, and in those who cannot receive iodinated contrast media.

However, MRI is insensitive to the presence of calcification, and the sensitivity of MR urography for the detection of urothelial neoplasms has not yet been determined.<sup>3</sup> When compared with CT, MRI offers better contrast resolution but CT has higher spatial resolution. Another consideration in patients with renal insufficiency is the risk for nephrogenic systemic fibrosis secondary to gadolinium versus contrast-induced nephropathy from iodinated contrast media.

#### **ULTRASONOGRAPHY**

Ultrasonography is not generally used to evaluate ureteral stricture but is useful to diagnose urinary obstruction. The ureters sometimes can be imaged at the site of obstruction, particularly in children. For example, a distal ureteral stone may be identified as a shadowing hyperechoic focus at the side of ureteral obstruction, or a retroperitoneal mass may be identified in the setting of retroperitoneal fibrosis. However, overlying bowel often obscures visualization of the midureter. Color Doppler imaging of the bladder may detect jets of urine originating at the ureteral orifices. If this finding is absent, high-grade or complete ureteral obstruction may be present.

### NUCLEAR MEDICINE

Radionuclide examinations are generally not used for imaging of ureteral disease. Radionuclide studies can help quantify differences in renal function. In the setting of ureteral stricture and obstruction, diuretic renograms can be used to differentiate collecting system dilation from urinary obstruction.

# POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

The role of positron emission tomography (PET) in evaluating urothelial lesions is limited because normal urinary excretion of fluorodeoxyglucose (FDG) limits the evaluation of the ureters, bladder, and adjacent structures. Occasionally, ureteral obstruction may be identified in patients undergoing PET for other processes.

#### **IMAGING ALGORITHM**

The imaging algorithm depends on the clinical presentation of the individual patient. Of primary concern is the underlying renal function. Patients with poor renal function may not be well evaluated by EUG and CT urography. If obstructive nephropathy necessitates placement of nephrostomy tubes, antegrade urography can be performed.

When an intrinsic ureteral process is suspected, initial evaluation with ureteroscopy and retrograde ureterography may be helpful because tissue sampling can be obtained at the same time as the imaging. Alternatively, when an extrinsic process is suspected, cross-sectional imaging allows evaluation of tissues adjacent to the genitourinary system.

### **Classic Signs**

- "Balloon on a string" sign: Dilation of the renal collecting system and proximal ureter classically seen in UPJ obstruction
- "Bullet and bodkin" sign: Encasement of the ureter that causes an abrupt transition at the site of encasement with focal narrowing or normal-caliber ureter and proximal dilation
- "Hiked-up" or "purse-string" appearance of the renal pelvis: Results from retraction and stricture formation in patients with TB
- "Sawtooth" appearance of the ureter: Occurs in patients with TB involvement of the ureter characterized by luminal irregularity with areas of narrowing and dilation
- "Pipe stem" ureter: Occurs later in the course of tuberculous involvement of the ureter with the ureter rigid and straight
- "Corkscrew" or "beaded" ureter: Seen after healing and fibrosis in patients with tuberculous involvement of the ureter
- "Soft tissue rim" sign: Soft tissue surrounding a ureteral stone from edema within the wall of the ureter at the site of stone impaction (Figure 67-1)
- "Goblet" or "champagne glass" sign: Dilation of the ureter below the site of slowly growing lesions. Although classically seen with TCC, this finding also can be seen with metastases and endometriosis (Figure 67-2).
- Bergman's sign: Coiling of the catheter within the dilated segment of ureter below the intraluminal lesion during retrograde catheterization
- Stipple sign: Foci of contrast agent trapped within the interstices of the projections of papillary transitional carcinoma
- Ureteral pseudodiverticulosis: Consists of small (<4 mm) outpouchings in the ureter and is associated with urothelial neoplasms

## **Treatment**

The management of strictures of the ureter depends on the cause of the stricture. Benign strictures are usually successfully managed with balloon dilation and stent placement. Endoure-terotomy also has been helpful in management of benign strictures. Stent placement is helpful for both benign and malignant strictures. In some instances, surgery may be the only option. Placement of a percutaneous nephrostomy tube is often used to relieve obstruction and preserve renal function until a definitive intervention can be performed.

# **Congenital Disorders**

## PRIMARY MEGAURETER

Primary megaureter is one of the causes of obstructive uropathy in infants and children. Boys are more commonly affected than girls, and in some patients' primary megaureter can be bilateral. Associated anomalies in the contralateral kidney include renal agenesis and dysplasia.

When the ureter of a child is dilated to a diameter greater than 7 mm, it is considered a megaureter. A megaureter can be primary or secondary. There are three types of primary megaureter<sup>4</sup>: obstructing, refluxing, and nonobstructing nonrefluxing.

In the obstructing type, an aperistaltic segment of ureter just proximal to the ureterovesical junction causes a functional obstruction with proximal dilation. Refluxing megaureter is due to an absent or short intravesical ureteral insertion or other abnormalities at the ureterovesical junction. The cause of nonobstructing nonrefluxing megaureter, which is the most



**Figure 67-1** Noncontrast axial computed tomography image in a patient with flank pain shows soft tissue thickening surrounding a ure-teral calculus (*arrow*), the soft tissue rim sign.



**Figure 67-2** Retrograde urography in a patient with transitional cell carcinoma of the ureter shows dilation of the ureter below the lesion, the goblet sign. (*Courtesy Isabel Yoder, MD.*)

common cause of primary megaureter in neonates, is unknown; it presents as ureteral dilation beginning just above the bladder.<sup>4</sup>

#### **Clinical Presentation**

Primary megaureter is often detected by fetal screening. Other children may present with abdominal pain, urinary tract infections (UTIs), or fevers. Patients may have microscopic hematuria.

## Pathophysiology

It has not been determined whether the cause is related to abnormal innervation, abnormal musculature, or abnormal connective tissue of the distal ureter.

#### Imaging

Imaging begins with ultrasonography of the kidneys and bladder to document the presence of obstruction. In primary obstructed megaureter, ultrasound imaging may demonstrate peristaltic waves in the dilated ureter and a persistently narrowed distal segment.<sup>4</sup> Recently, the use of Doppler ultrasonography has shown potential in monitoring and potentially diagnosing obstruction. In adults, a resistive index greater than 0.7 may indicate obstruction. Although children may have slightly higher values normally, an elevated resistive index is also an indicator of obstruction in children.

Secondary causes of megaureter must be excluded before a diagnosis of primary megaureter can be made. A voiding cystourethrogram is usually performed to exclude reflux as a cause of megaureter.

Once it is determined that there is no vesicoureteral reflux, diuretic renography is performed to determine whether urinary obstruction is present. In an obstructed primary megaureter, the radiotracer will not wash out of the collecting system after diuretic administration. An excretory urogram may demonstrate a tortuous and dilated ureter proximal to the aperistaltic, normal-caliber distal segment (Figure 67-3). The distal ureter is often more dilated than the proximal ureter and collecting system.

The nonrefluxing nonobstructed subtype can be distinguished from obstructed primary megaureter by evaluating the distal ureter. In the nonrefluxing nonobstructed subtype, the distal ureter is also dilated rather than normal in caliber.

## **Differential Diagnosis**

The differential diagnosis of megaureter in a child consists of the various types of primary megaureter as well as secondary causes of megaureter. The list of secondary causes of megaureter is long and includes posterior urethral valves, urethral strictures, bladder abnormalities, and other causes of vesicoureteral reflux.

### TREATMENT

Expectant management of the refluxing or nonobstructed nonrefluxing primary types of megaureter may result in improvement over time. In severe or persistent cases, surgery may be necessary.

## URETEROPELVIC JUNCTION OBSTRUCTION

UPJ obstruction is a common cause of obstruction in newborns and is more common in males. Occasionally, adults can present with UPJ obstruction.



**Figure 67-3** Excretory urography in a patient with primary megaureter shows dilatation of the ureter proximal to the normal-caliber aperistaltic segment (*arrow*). (*Courtesy Isabel Yoder*, *MD*.)

#### **Clinical Presentation**

Children with UPJ obstruction may present with intermittent abdominal pain, hematuria, or recurrent UTIs or be asymptomatic. Increasingly, patients are identified by prenatal screening. Adult patients may be asymptomatic or may experience episodes of urinary colic, particularly after ingesting large volumes of fluid or alcohol, known as Dietl's crisis.

#### Pathophysiology

There are many causes of UPJ obstruction, and the cause varies depending on patient age and clinical history. UPJ obstruction may be functional or anatomic and is most commonly the result of a congenital smooth muscle abnormality that leads to abnormal peristalsis and focal ureteral narrowing. Congenital causes include ureteral hypoplasia, ureteral valves, abnormal insertion of the ureter into the renal pelvis, and crossing vessels. The obstruction may be due to scarring or may be related to prior surgery. Secondary causes include extrinsic tumors, iatrogenic injury, or extrinsic inflammation.

## Imaging

Children with UPJ obstruction are usually evaluated with a voiding cystourethrogram and with diuretic renograms. Contrast-enhanced CT, although associated with a higher radiation dose, is helpful to evaluate structures adjacent to the ureter such as crossing vessels. A classic appearance of UPJ obstruction is the balloon on a string sign produced by dilation of the renal collecting system and proximal ureter (Figure 67-4).

After repair, patients are followed using a combination of renal ultrasonography and diuretic renography.

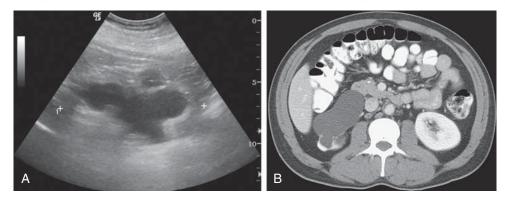


Figure 67-4 Ultrasound (A) and axial contrast-enhanced computed tomography (B) images in a patient with chronic right ureteropelvic junction obstruction show right hydronephrosis and renal parenchymal atrophy.

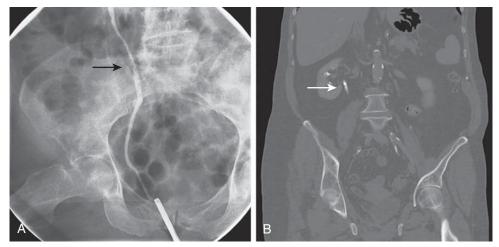


Figure 67-5 Retrograde pyelogram (A) and coronal reconstructed computed tomography image (B) in a 78-year-old man with hematuria show multiple filling defects (arrows) consistent with pyeloureteritis cystica.

## **Differential Diagnosis**

The differential diagnosis of UPJ obstruction includes congenital causes such as ureteral hypoplasia, ureteral valves, and crossing vessels, as well as other intrinsic and extrinsic causes of ureteral strictures that happen to occur at the UPJ, such as stone disease, scarring, and urothelial and extrinsic neoplasms.

### Treatment

Management of UPJ obstruction depends on the cause of the obstruction. Endoscopic intervention or surgical pyeloplasty can be performed. It is essential to identify extrinsic structures, such as crossing blood vessels that may cause UPJ obstruction and be injured during operative management.

# **Inflammatory Disorders**

## PYELOURETERITIS CYSTICA

Pyeloureteritis cystica is a rare disease, first described by Morgagni in 1761.<sup>5</sup> It occurs in the setting of chronic inflammation when degeneration of cells results in the formation of submucosal cysts. The disorder is classically found in patients 50 to 60 years of age. Some studies report that this disorder is more common in women.

### **Clinical Presentation**

Patients are often asymptomatic but may have a history of UTIs, ureterolithiasis, or hematuria. Obstruction is not usually present.

## Pathophysiology

Suburothelial cysts form as a result of chronic inflammation. The pathophysiology is unknown. Cyst rupture, chronic inflammation, or associated stone disease may result in hematuria.<sup>5</sup>

## Imaging

Pyeloureteritis cystica results in multiple round filling defects 2 to 3 mm in size that produce a scalloped appearance of the ureter. There is usually no associated obstruction. The process generally involves the proximal ureter and is more often unilateral than bilateral.<sup>5</sup> The diagnosis is often made by intravenous pyelography, retrograde pyelography, or ureteroscopy (Figure 67-5).

#### **Differential Diagnosis**

Pyeloureteritis cystica can appear similar to other submucosal or extrinsic processes such as malakoplakia, intramural hemorrhage, polyposis, urothelial tumors, and metastasis. However, the filling defects seen with intramural hemorrhage and malignant neoplasms are usually not as uniformly round as those seen with pyeloureteritis cystica.

#### Treatment

Historically, management included ureteral dilation, rupture of the cysts, and instillation of silver nitrate.<sup>5</sup> Current therapy is targeted at treating the underlying inflammatory process and associated complications, such as ureterolithiasis. With management of the underlying infection, the cysts may resolve, but they often persist for many years.<sup>5</sup> The disease has a benign course, with no malignant potential. Nonetheless, follow-up imaging is often performed to evaluate for resolution of the lesions and possible neoplasms such as papillomas.

## MALAKOPLAKIA

Malakoplakia is a rare granulomatous disease that usually occurs in immunocompromised patients, especially those with diabetes mellitus. The disease is most often seen in middle-aged women and is associated with chronic UTIs. The bladder is more commonly involved than the ureter.

#### **Clinical Presentation**

Patients often have a history of chronic UTIs and may be immunocompromised. Symptoms can mimic TCC and include hematuria, flank pain, and dysuria.

#### Pathophysiology

Chronic inflammation results in the formation of subepithelial plaques. The plaques contain basophilic inclusions called Michaelis-Gutmann bodies, which represent fragments of incompletely digested bacteria.

#### Imaging

Malakoplakia usually causes multiple filling defects in the lower ureter. Circumferential ureteral involvement may cause a ureteral stricture with proximal hydroureter. The lesions are usually multiple and may cause a cobblestone appearance. The ureter may be dilated above the lesion.

#### Differential Diagnosis

Malakoplakia can be difficult to distinguish from other lesions that produce ureteral strictures and filling defects, including pyeloureteritis cystica and TCC. The diagnosis is established by biopsy.<sup>6</sup>

#### Treatment

Therapy involves treating the underlying infection, although the disease may recur after therapy.

# **Infectious Disorders**

## TUBERCULOSIS

The genitourinary tract is the second most common site of tuberculous involvement. Patients are usually older than 40 years of age when they become symptomatic.

#### **Clinical Presentation**

Clinical symptoms include hematuria, dysuria, and suprapubic pain. Confirmation of the diagnosis can be made by urinary culture and by examination of a tissue biopsy specimen.

#### Pathophysiology

Hematogenous dissemination of *Mycobacterium tuberculosis* results in renal infection, with subsequent spread to the ureters and bladder by descent in the urine. After the initial acute inflammatory phase of infection, healing results in fibrosis that can lead to ureteral strictures.

### Imaging

Ureteral TB usually occurs in the setting of renal and bladder TB. Therefore, it is helpful to be familiar with the appearance of TB involving the kidneys and bladder. The classic appearance of tuberculous involvement of the kidneys is the "putty" kidney. Other findings include calyceal irregularity with a moth-eaten appearance that can coalesce, resulting in cavitation of the renal papilla. If the renal pelvis is involved, retraction and stricture formation may result in a hiked-up or purse-string appearance.<sup>7</sup> Bladder involvement may result in a calcified bladder with small bladder volume known as a "thimble" bladder.

Strictures caused by TB usually involve the distal ureter with long-segment strictures, but occasionally short strictures may develop. The strictures may be multifocal, with an irregular or sawtooth appearance. After healing and fibrosis, the ureter may have a corkscrew or beaded appearance (Figure 67-6). With more long-standing disease, the ureter may become rigid and straight. This appearance is often called a pipe stem ureter.<sup>7</sup> Ureteral calcifications may be seen but are less common than renal calcification. Cross-sectional imaging may show ureteral wall thickening and enhancement.<sup>8</sup>

## Differential Diagnosis

Whenever multifocal ureteral strictures are seen, TB should be the main differential diagnosis. Other considerations include metastatic disease and lymphadenopathy.

#### Treatment

Systemic antituberculous chemotherapy is the mainstay of treatment. Strictures may require stenting or surgical management.

## **SCHISTOSOMIASIS**

Schistosomiasis is endemic in many parts of the world. It is estimated that 8% of the world population is infected.<sup>9</sup> *Schistosoma hematobium* is the causative organism of urinary schistosomiasis.

#### **Clinical Presentation**

Patients may present with hematuria and dysuria and, later, with hydronephrosis, proteinuria, and renal dysfunction.<sup>10</sup> Affected individuals are predisposed to secondary bacterial UTI and squamous cell carcinoma (SCC) of the urinary tract. Finding schistosome eggs in urine or feces makes the diagnosis. Malignancy secondary to schistosomiasis occurs most commonly in the bladder and rarely in the ureter.

#### Pathophysiology

The eggs of *S. hematobium* hatch in fresh water, and the organism grows in the intermediate host, the snail. The larvae enter the skin of humans who come in contact with the water, migrate to the lungs and liver, and, subsequently, when mature, migrate to the pelvis, including the walls of the genitourinary system,

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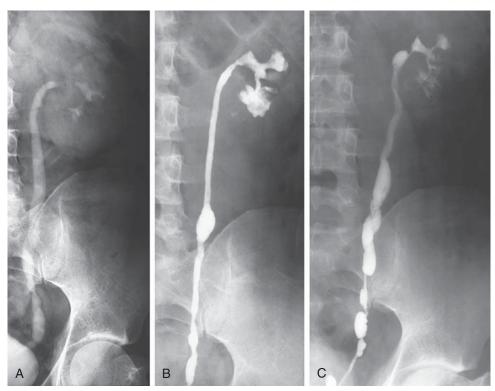


Figure 67-6 A, Excretory urogram in a patient with tuberculosis. Retrograde urograms performed 5 (B) and 7 (C) months later show progressive stenosis and beaded appearance of the ureter. (*Courtesy Isabel Yoder, MD.*)

where they then deposit eggs.<sup>10</sup> The eggs incite fibrosis and dystrophic calcification, which leads to stricture formation.

## Imaging

Schistosomiasis of the ureter is seen in the presence of bladder involvement. Conventional radiography can show calcification of the bladder and ureter (Figure 67-7). In addition to ureteral wall calcification, CT may demonstrate ureteral wall thickening. The distal ureter is most commonly involved. The ureter may be displaced cephalad and medially. Filling defects may be seen early in the course of the disease; however, as the disease progresses, multiple strictures form, resulting in a beaded appearance. If the ureterovesical junction is involved, vesicoureteral reflux can result.

## **Differential Diagnosis**

Differential considerations include other infectious causes (Figure 67-8). Both TB and schistosomiasis can result in calcification and stricture of the ureters. Schistosomiasis is preceded by bladder involvement, whereas TB usually occurs in the setting of both renal and bladder involvement.

#### Treatment

Schistosomiasis is treated with systemic antiparasitic agents.

## **URETERIC CALCULI**

## **Clinical Presentation**

Patients usually report a history of ureterolithiasis that may have required intervention. When a ureteral stricture develops, if patients are symptomatic, they often present with obstruction.

## Pathophysiology

Local edema and inflammation from an impacted stone can cause localized ureteral wall thickening. The edema usually involves a shorter segment than that found in TCC.<sup>6</sup> Follow-up evaluation may help distinguish strictures produced by edema from tumor-related strictures. A stone that is impacted for longer than 2 months has a higher incidence of stricture formation.<sup>11</sup>

Rarely, after ureteroscopic stone removal or extracorporeal shock wave lithotripsy, fragmented stone particles may become embedded in the wall of the ureter. The resulting immune response leads to fibrotic stricture formation that can be refractory to endourologic treatment.

#### Imaging

Edema and inflammation at the site of stone impaction can cause ureteral narrowing that usually involves a segment less than 1 cm in length. The location and length of the stricture as well as the presence of stones can be demonstrated with EUG or pyelography (Figures 67-9 and 67-10). Ultrasonography shows hydronephrosis and is used after therapy to confirm resolution of obstruction. On CT, ureteral edema at the site of stone impaction is seen as soft tissue surrounding the ureteral stone, termed the ureteral soft tissue rim sign on CT (see Figure 67-1). The soft tissue rim sign is usually seen with stones less than 5 mm in diameter.<sup>7</sup>

#### **Differential Diagnosis**

The history of prior stone disease or intervention helps to narrow the differential diagnosis. However, other causes of

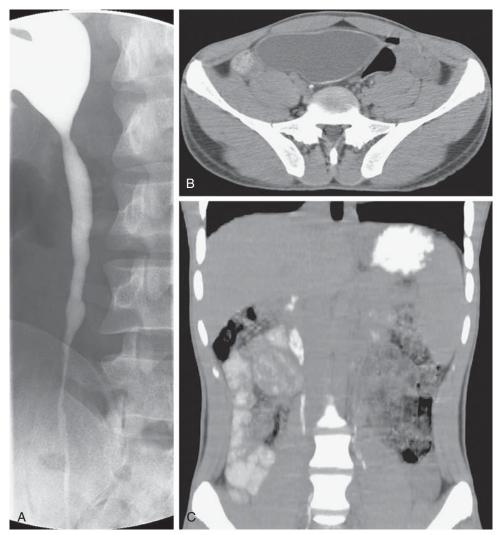


Figure 67-7 A 28-year-old man from Somalia with an 8-year history of intermittent flank pain. A, Anterograde pyelogram shows a long irregular ureteral stricture and hydronephrosis. Noncontrast axial (B) and coronal (C) reconstructed computed tomography images show ureteral and bladder calcifications consistent with the diagnosis of schistosomiasis.

stricture, such as malignancy, may precipitate local stone formation or impaction and must be excluded.

#### Treatment

Strictures secondary to edema generally resolve with expectant management. Chronic strictures may require stent placement. Ureteroscopy and laser lithotripsy also may be used. In severe cases, surgery may be necessary. Typically, ultrasonography is used to confirm resolution of hydronephrosis. CT urography may be used to directly follow the area of concern.

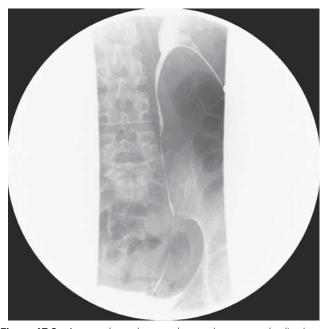
# **Malignant Conditions**

## INTRINSIC UROTHELIAL NEOPLASMS

Urothelial carcinoma includes TCC, which accounts for 90% of urothelial neoplasms, and SCC (Box 67-1). Both occur more commonly in the bladder than in the upper urinary tract. Approximately 1% of upper tract urothelial neoplasms involve the ureter.12

#### BOX 67-1 **CAUSE OF MALIGNANT URETERAL STRICTURES**

- Intrinsic
- Urothelial
- Transitional cell carcinoma Squamous cell carcinoma
- Metastases
  - Transitional cell carcinoma
  - Squamous cell carcinoma
  - Transitional cell carcinoma
  - Breast .
  - Melanoma .
  - .
  - Renal
  - Colon
  - Rectal
  - Prostate
  - Testicular
- Extrinsic
- Lymphoma
- Metastases
- Prostate cancer
- Cervical carcinoma



**Figure 67-8** Antegrade pyelogram shows a long, smooth, distal ureteral stricture in an immunosuppressed patient with viral hemorrhagic cystitis with bilateral long ureteral strictures. The strictures improved after stenting and adjustments in immunosuppressive therapy.

#### Transitional Cell Carcinoma

**Prevalence and Epidemiology.** TCC most commonly occurs in the bladder, followed by the renal pelvis and ureter, at a frequency of approximately 50:3:1.<sup>13</sup> Tumors arising in the urothelium of the ureter and renal pelvis make up approximately 5% of urothelial neoplasms.<sup>14</sup> Although primary TCC of the ureter is relatively rare, it accounts for approximately 90% of all cancers of the ureter.<sup>15</sup>

TCC is more common in men than women and usually occurs in the sixth and seventh decades of life. Other risk factors include smoking, chronic infection, exposure to analgesics and other chemical carcinogens that are excreted in the urine, Balkan nephritis, ureteral pseudodiverticulosis, and hereditary nonpolyposis colon cancer syndrome.<sup>16</sup>

Urothelial TCC is a multifocal process. Patients with a history of bladder carcinoma have a 2% risk for having synchronous disease and a 6% chance for subsequently developing TCC of the upper urinary tract. In patients with upper tract TCC, 20% to 50% have or will develop TCC of the bladder.<sup>16</sup> Patients with upper tract TCC have a higher risk for developing TCC of the ureter.<sup>17</sup> Ureteral TCC may be bilateral in 2% to 9% of cases, and 11% to 13% of patients may develop additional upper tract TCC.<sup>17</sup> Because of the high incidence of synchronous and metachronous lesions, it is important to carefully evaluate the entire urothelium both at the time of initial diagnosis and as part of routine surveillance.

**Clinical Presentation.** Patients with TCC may present with microscopic or macroscopic hematuria, urinary frequency, dysuria, or pain. Patients with ureteral TCC also may have hydronephrosis and hydroureter proximal to the lesion. Confirmation of the diagnosis is made by cytologic analysis of the urine or specimens obtained endoscopically from the ureter.

Urine cytology is frequently used in the evaluation of patients with suspected TCC but only detects 25% to 59% of upper tract TCC.<sup>16</sup> Cytology is less useful in patients with upper tract TCC or low-grade lesions or in the setting of obstruction. False-positive results may occur in the setting of inflammation and stone disease.

**Pathophysiology.** The three pathologic subtypes of TCC are the papillary, infiltrating papillary, and diffusely infiltrating types. Most upper tract TCCs are the infiltrating papillary subtype (85%).<sup>15</sup> TCC may spread through the urinary system or may directly invade the urothelial wall. Lymphatic spread involves regional lymph nodes and follows the lymphatic drainage pattern of the involved segment of the ureter.<sup>13</sup> Hematogenous spread can result in lung, liver, and bone metastases.

**Imaging.** Two thirds of cases involve the distal one third of the ureter. Imaging studies may show hydronephrosis with or without hydroureter, a ureteral mass, or fixed ureteral narrowing (Figure 67-11). Multifocal ureteral involvement is more commonly seen with the papillary subtype than with the infiltrating subtype (Figure 67-12).

*Radiography.* Calcifications may be uncommonly identified in ureteral TCC.

Excretory Urography. Findings include a nonfunctioning kidney as well as hydronephrosis with or without hydroureter. The infiltrating papillary subtype usually manifests as a smooth or irregularly marginated filling defect within the ureter. Contrast medium may be seen within the interstices of the tumor, resulting in the stipple sign on imaging. The diffusely infiltrating subtype usually involves a short segment and can cause irregular strictures that typically have nontapering margins. Infiltration of the ureteral wall may cause fixation of the ureter with a resultant lack of peristalsis, which can be identified as an unchanging appearance of the ureter on different imaging phases.<sup>15</sup> The globlet or champagne glass sign is a classic sign of ureteral TCC in which a dilated segment is seen distal to a ureteral narrowing or filling defect. This sign is not seen in other causes of acute ureteral obstruction such as ureteral stones and blood clots because these entities often cause ureteral narrowing secondary to inflammation and edema.1

**Retrograde Urography.** In the setting of a nonfunctioning kidney, retrograde ureterography may be needed to adequately opacify the ureter with contrast medium. The ureter is cannulated at cystoscopy, and water-soluble contrast is injected. As with EUG, the goblet or champagne glass sign may be seen (Figure 67-13). During the procedure, coiling of the catheter below the ureteral mass is known as the Bergman sign. If the ureter cannot be accessed through the bladder, or if severe obstruction requires placement of a nephrostomy tube, antegrade urography can be performed.

**Computed Tomography.** CT permits evaluation of the periureteral tissues and delineates the relationship of the tumor to adjacent retroperitoneal structures. In addition to demonstrating extramural extension of tumor, CT is able to demonstrate regional nodal metastases. As with excretory and retrograde ureterography, the CT appearance of TCC varies depending on the subtype of tumor. The infiltrating papillary subtype usually manifests as a smooth or irregularly marginated soft tissue density ureteral filling defect that enhances after administration

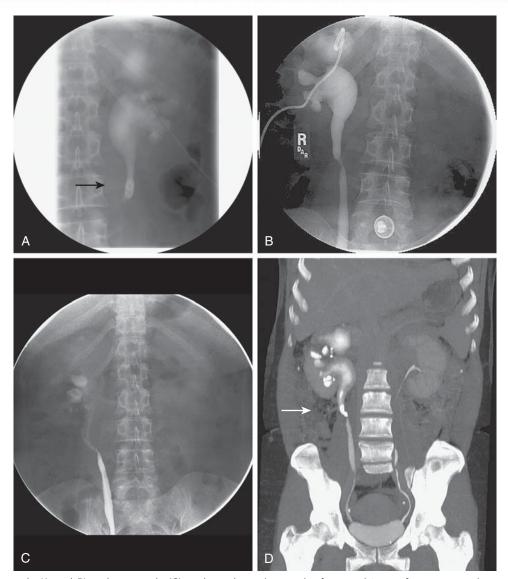


Figure 67-9 Antegrade (A and B) and retrograde (C) pyelography and coronal reformatted image from computed tomography urography (D) show a right ureteral stricture secondary to impacted stones, seen as filling defects (*arrow*, A) and hyperdensities (*arrow*, D) within the ureter proximal to the stenosis.

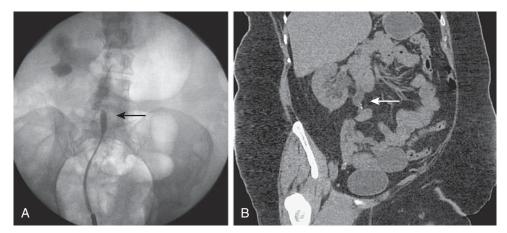


Figure 67-10 Retrograde pyelogram (A) and coronal computed tomography image (B) from a 46-year-old patient with a history of chronic ureterolithiasis show a smoothly tapered stricture of the mid-right ureter (*arrow*, A) and calcifications at the site of stricture (*arrow*, B).



Figure 67-11 Curved coronal reformatted computed tomography (A) and axial (B) images in a 78-year-old patient with hematuria show a focal right ureteral stricture (*arrows*) associated with ureteral wall thickening and enhancement and proximal hydroureteronephrosis resulting from transitional cell carcinoma of the ureter.

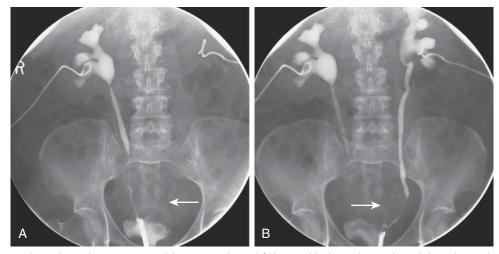


Figure 67-12 Retrograde pyelography in a 53-year-old woman with renal failure and hydronephrosis shows bilateral irregular distal ureteral strictures (arrows) secondary to invasive papillary transitional cell carcinoma of the bladder.

of a contrast agent. The tumor usually measures 8 to 30 Hounsfield units (HU) on noncontrast images and enhances to 18 to 55 HU.<sup>15</sup>

The diffusely infiltrating subtype typically causes ureteral wall thickening and fixation of the ureter. The infiltrative tumor growth usually involves a short segment of the ureter and may cause eccentric or circumferential strictures (Figure 67-14). CT may show infiltration in the periureteral fat, which can help distinguish infiltrative tumor from benign strictures (Figure 67-15).<sup>15</sup> Enhancement of the thickened ureteral wall and increased density in the periureteral fat may indicate transmural spread of tumor (Figure 67-16) but also may be seen with inflammation, infection, and fibrosis.

Pitfalls of CT urography include overlap in the appearance of benign and malignant strictures and limited detection of

small lesions. Although multidetector CT urography has shown improved accuracy in predicting tumor stage, CT cannot identify microscopic infiltration and cannot reliably distinguish tumoral infiltration from inflammation.

*Magnetic Resonance Imaging.* On MRI, the tumor appears as an irregular enhancing mass or as abnormal wall thickening. TCC is isointense to the kidney on both T1- and T2-weighted images and is hypointense relative to the T2-hyperintense urine.<sup>17</sup> After administration of a contrast agent the images show enhancement of the tumor to a lesser extent than the kidney. Ureteral TCC is isointense to muscle on T1-weighted images and hyperintense on T2-weighted images.

**Ultrasonography.** Ultrasonography can demonstrate hydronephrosis and may show lesions in the kidney and renal pelvis but is of limited utility for imaging the ureters directly.

#### **Classic Signs: Upper Tract Neoplasms**

- Goblet or champagne glass sign: Dilation of the ureter below the site of slowly growing lesions. Although classically seen with TCC, this finding also can be seen with metastases and endometriosis (see Figure 67-13).
- Bergman's sign: Coiling of the catheter within the dilated segment of ureter below the intraluminal lesion during retrograde catheterization.
- Stipple sign: Foci of contrast medium trapped within the interstices of the projections of papillary transitional carcinoma.
- Ureteral pseudodiverticulosis: Consists of small (<4 mm) outpouchings in the ureter and associated with urothelial neoplasms

Differential Diagnosis. Both benign and malignant entities can have an appearance similar to that of TCC. Fibroepithelial polyps can mimic the appearance of the papillary subtype of TCC. Some filling defects can be definitively identified as stones or other benign disorders such as blood clot, sloughed papilla, and fungal balls owing to the absence of enhancement, but, often, ureteroscopy and biopsy are necessary. The differential diagnosis of infiltrating papillary TCCs includes endometriosis, malacoplakia, nephrogenic adenomas, and inflammatory pseudopolyps, whereas ureterolithiasis, TB, malacoplakia, and UPJ obstruction with infection can mimic infiltrating TCCs.<sup>15</sup> Ureterolithiasis usually causes short-segment (1 cm) involvement, but with superimposed infection the appearance can be indistinguishable from neoplasm. Other urothelial malignancies, such as SCC and adenocarcinoma, also may mimic the appearance of TCC.

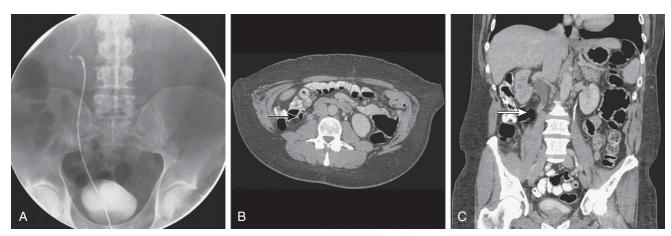
**Treatment.** The prognosis of patients with upper tract TCC depends on the grade and stage of the tumor and extent of invasion and metastatic disease (Table 67-1). Upper tract TCCs are usually treated by nephroureterectomy, including resection of a cuff of bladder tissue at the ureteral orifice. In certain circumstances, such as with low-grade ureteral neoplasms or in

patients with a solitary kidney, the tumors may be managed conservatively with percutaneous endoscopic resection or nephron-sparing surgery.<sup>16</sup> The role of topical adjuvant agents in the management of upper tract TCC has not yet been defined.<sup>16</sup>

Because of the high incidence of synchronous and metachronous lesions, ongoing follow-up cystoscopy and imaging of the upper tracts should be performed (Figures 67-15 and 67-17). Given the advantages of CT urography, this modality will likely



**Figure 67-13** Retrograde urography in a patient with transitional cell carcinoma of the ureter shows dilation of the ureter below the tumor—the goblet sign. (*Courtesy Isabel Yoder, MD.*)



**Figure 67-14** A, Retrograde pyelogram shows irregular narrowing in the proximal right ureter in a 51-year-old man who presented with hematuria. Axial (B) and coronal (C) images from computed tomography urography show urothelial thickening and enhancement *(arrows)*. Biopsy confirmed the diagnosis of transitional cell carcinoma.

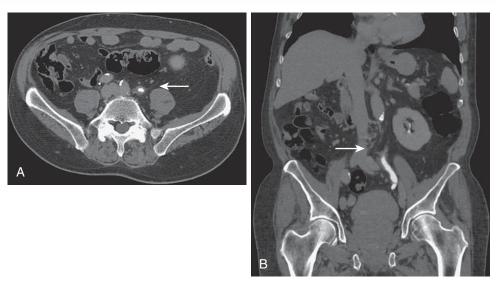
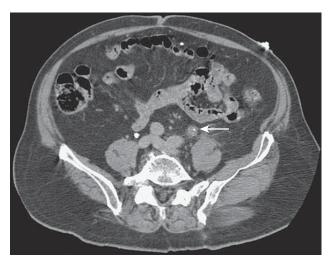


Figure 67-15 Delayed postcontrast axial (A) and coronal (B) reformatted images from a computed tomography urogram show irregular left ureteral wall thickening (arrows) in an 80-year-old patient with prior right nephrectomy for transitional cell carcinoma.



**Figure 67-16** Axial excretory phase image in a 78-year-old man with hematuria when started on anticoagulation therapy shows a left ureteral filling defect (*arrow*), luminal narrowing, and periureteral soft tissue infiltration. Ureterectomy confirmed grade 3 transitional cell carcinoma.

become the primary imaging modality used for follow-up of patients with TCC.  $^{\rm 17}$ 

#### Squamous Cell Carcinoma

**Prevalence and Epidemiology.** SCC is less common than TCC, accounting for approximately 8% of malignant neoplasms of the collecting system and 10% to 15% of malignant neoplasms of the ureter.<sup>13</sup> As with TCC, upper tract SCC is less common than SCC of the bladder.

**Pathophysiology.** SCC is associated with predisposing factors that cause urothelial irritation such as calculi, chronic indwelling Foley catheter, chronic infection, leukoplakia, and carcinogen or drug exposure.

**Imaging.** SCC often is an infiltrative process and does not typically manifest as intraluminal filling defects.

## METASTASES

## Prevalence and Epidemiology

Direct metastases to the ureter are due to hematogenous or lymphatic spread and may be caused by carcinoma of the breast, prostate carcinoma, colorectal carcinoma, renal cell carcinoma (RCC), and melanoma.

### **Clinical Presentation**

Patients may be asymptomatic or may present with symptoms of urinary obstruction, renal failure, or hematuria.

## Imaging

Submucosal metastases manifest as submucosal nodules or strictures (Figures 67-18 and 67-19). Ureteral involvement may be unilateral, bilateral, focal, or multifocal (Figure 67-20). Pseudodiverticulosis also has been reported in association with ureteral metastatic disease.

## **Differential Diagnosis**

Other causes of submucosal nodules, such as primary urothelial neoplasms and benign disorders such as malakoplakia, can mimic the appearance of intrinsic ureteral metastases.

### Treatment

Management is targeted at relief of the obstruction by nephrostomy and/or stent placement, followed by treatment of the metastasis.

## EXTRINSIC UROTHELIAL NEOPLASMS

### **Clinical Presentation**

Metastases to the ureter are often detected at autopsy in previously asymptomatic patients. Ureteral metastases may be symptomatic if there is associated obstruction or may cause hematuria, dysuria, urinary frequency, and proteinuria.

TABLE 67-1		an Joint Committee on Cancer Tumor, Metastasis Classification of Neoplasms Ureter			
Classi	Classification Description				
PRIMA	PRIMARY TUMOR (T)				
Тx		Primary tumor cannot be assessed.			
TO		No evidence of primary tumor			
Та		Noninvasive papilloma			
Tis		Carcinoma in situ			
T1		Tumor invades subepithelial connective tissue.			
T2		Tumor invades the muscularis.			
Т3		Tumor invades beyond muscularis into periureteral fat.			
Τ4		Tumor invades adjacent organs or through the kidney into periureteral fat.			
REGIC	REGIONAL LYMPH NODES (N)				
		Regional lymph nodes cannot be assessed.			
N0		No regional lymph nodes metastases			
N1		Metastasis in a single lymph node ±2 cm in greatest dimension			
N2		Metastasis in a single lymph node 2 to 5 cm in greatest dimension, or multiple lymph nodes, none >5 cm in greatest dimension			
N3		Metastasis in a lymph node >5 cm in greatest dimension			
DISTA	NT META	STASES (M)			
Mx		Distant metastasis cannot be assessed.			
MO		No distant metastasis			
M1		Distant metastases			
AJCC	AJCC STAGE GROUPINGS				
Stage	0a	Ta, N0, M0			
Stage	Ois	Tis, N0, M0			
Stage	I	T1, N0, M0			
Stage	11	T2, N0, M0			
Stage		T3, N0, M0			
Stage	IV	T4, N0, M0 or any T, N1-3, M0 or any T, any N, M1			

From Edge SB, Byrd DR, Compton CC, et al: American joint committee on cancer (AJCC) cancer staging manual, ed 7, New York, 2010, Springer, p 495.
AJCC, American Joint Committee on Cancer.

## Pathophysiology

Extrinsic tumors, including adjacent primary lesions and metastatic lesions, cause ureteral narrowing by extrinsic compression and/or direct invasion. Direct invasion of tumor from adjacent primary neoplasms is more common than invasion from adjacent metastatic disease.<sup>13</sup>

Direct extension from adjacent tumor usually involves the lower one third of the ureter and is most often caused by carcinomas of the cervix, ovary, endometrium, prostate, rectum, and sigmoid colon (Figure 67-21).

Metastases to the ureter may be due to hematogenous or lymphatic spread in patients with carcinoma of the breast, kidney, gastrointestinal tract, cervix, and prostate and less commonly from carcinoma of the skin, lung, ovaries, uterus, and testes.<sup>13</sup>

Metastases from breast, lung, stomach, pancreas, colon, and lymphoma, as well as prostate, kidney, and cervical carcinomas, may cause ureteral narrowing secondary to a prominent desmoplastic reaction.

Lymphadenopathy from metastatic disease and lymphoma can result in ureteral displacement, narrowing, and obstruction, as well as ureteral encasement.

#### Imaging

Metastases often manifest as a periureteral mass but can manifest as periureteral soft tissue infiltration, transmural ureteral wall involvement, or nodules.<sup>13</sup> Ureteral strictures caused by transmural tumor involvement or periureteral soft tissue infiltration tend to cause irregular strictures. Sometimes tumors metastasize to the periureteral lymphatics and may cause a short or long stricture that may be smooth or irregular and may result in displacement or angulation of the ureter. The desmoplastic reaction caused by some metastases can mimic the typical appearance of benign ureteral strictures. Alternatively, submucosal metastases may manifest as smooth submucosal nodules.

Lymphadenopathy from metastatic disease and lymphoma can cause ureteral narrowing and displacement (Figure 67-22). Para-aortic lymphadenopathy results in lateral deviation of the upper ureter, whereas iliac lymphadenopathy results in medial deviation of the distal ureter. Displacement of the ureter is more common than encasement of the ureter.<sup>13</sup>

Extrinsic ureteral strictures can have a variety of appearances, with significant overlap in malignant and benign causes.

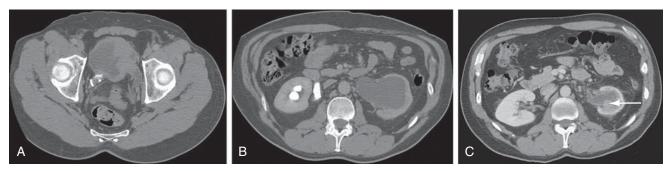
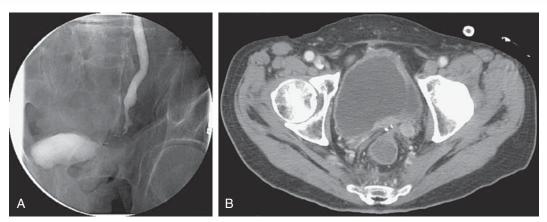


Figure 67-17 A and B, Axial delayed computed tomographic (CT) urography images in a 57-year-old man with invasive transitional cell carcinoma (TCC) of the bladder involving the ureteral insertions causing hydronephrosis. C, Axial image from a contrast-enhanced CT scan 2 years later shows a new urothelial lesion in the left renal pelvis (*arrow*) confirmed as TCC.



**Figure 67-18** A, Antegrade pyelography in a 78-year-old man with metastatic colon carcinoma shows an irregular stricture of the distal left ureter. B, Corresponding contrast-enhanced axial computed tomography image shows ureteral wall thickening and soft tissue filling defect.

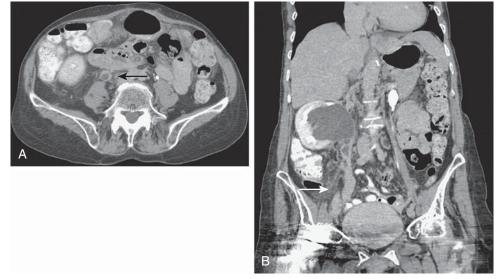


Figure 67-19 Axial (A) and coronal (B) contrast-enhanced computed tomography images in a patient with metastatic colon cancer show new right hydronephrosis, hydroureter, and delayed renal function with new right periureteral soft tissue thickening (*arrows*).

Differential considerations include other causes of irregular strictures, such as primary urothelial neoplasms, retroperitoneal fibrosis, irradiation, and other inflammatory processes.

## **Differential Diagnosis**

The desmoplastic reaction caused by some metastases is more infiltrative and mimics the appearance of benign causes of ureteral stricture, such as radiation fibrosis, endometriosis, retroperitoneal fibrosis, and inflammatory strictures.

Retroperitoneal collections and benign causes of lymphadenopathy also can cause extrinsic compression and displacement of the ureter.

#### Treatment

Therapy is targeted at treatment of the extrinsic compressing mass or relief of obstruction by stenting or nephrostomy placement.<sup>18</sup> In the setting of pelvic neoplasms, nephrostomy placement followed by antegrade stent placement is often used. Advanced or complicated cases may require surgery with urinary diversion or even ureteral embolization and nephrostomy placement.

#### What the Referring Physician Needs to Know

- TCC is the most common cause of malignant ureteral stricture.
- CT urography is able to simultaneously depict the urothelium and regional lymph nodes and is the initial test of choice for evaluating a malignant ureteral stricture.

## Trauma

# IATROGENIC AND PRIOR URETERAL INSTRUMENTATION

Iatrogenic ureteral injury may occur during abdominal or pelvic surgeries, endourologic procedures, and interventional radiology procedures. The incidence of iatrogenic ureteral injury is reported as 0.5% to 1% of abdominal or pelvic surgeries. Over 50% of iatrogenic ureteral injuries are caused

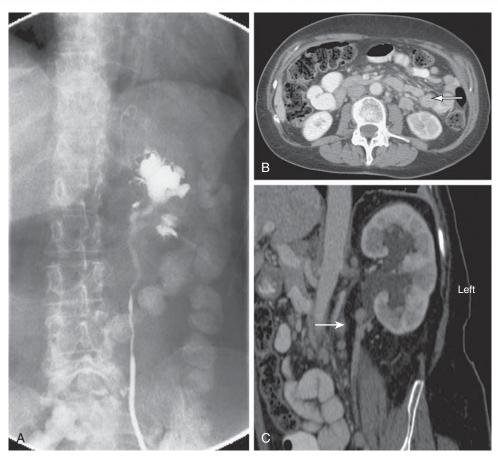


Figure 67-20 A, Retrograde pyelogram in a 62-year-old woman with lung cancer shows irregular narrowing of the proximal left ureter and hydronephrosis. Axial (B) and curved reformatted (C) images from a contrast-enhanced computed tomography show irregular enhancing nodules (arrows) along the wall of the left ureter.

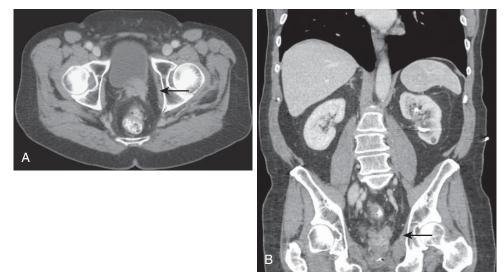


Figure 67-21 Axial (A) and coronal (B) images from split-bolus technique computed tomography in a 68-year-old patient who underwent nephrostomy placement for declining renal function resulting from left hydronephrosis show locally invasive prostate carcinoma involving the left ureteral insertion (arrows).

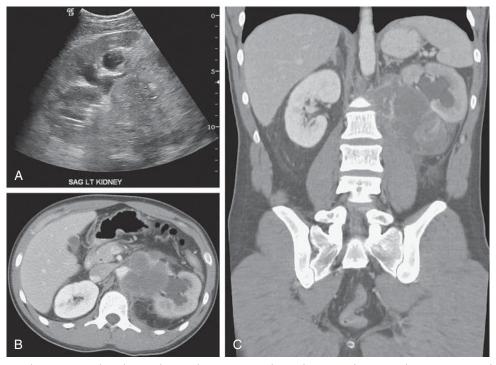


Figure 67-22 Ultrasound image (A) and axial (B) and coronal (C) contrast-enhanced computed tomography images in a male patient with metastatic testicular carcinoma show hydronephrosis secondary to extrinsic compression of the ureter by retroperitoneal lymphadenopathy.

by gynecologic surgery, in particular, radical abdominal hysterectomy, whereas approximately 30% are due to ureteral intervention. An additional 5% to 15% of iatrogenic injuries occur during colorectal and abdominal aortic surgery.<sup>19</sup> With the increased use of endourologic interventions, the incidence of ureteral injury also has increased. Radiofrequency ablation of RCC may result in thermal injury to the ureter with stricture formation.<sup>20</sup>

Most iatrogenic ureteral injuries involve the lower one third of the ureter (Figure 67-23), except those resulting from renal radiofrequency ablation, which usually involve the upper ureter.

## **Clinical Presentation**

The presentation of patients with ureteral injury depends on the type of injury and the delay to the time of diagnosis. Symptoms include abdominal or flank pain, hematuria, fever, or, in the setting of a ureterovaginal fistula, vaginal drainage. Most injuries are detected during surgery, and when treated promptly the outcome is favorable. However, the more delayed the diagnosis, the higher risk for complications.

## Pathophysiology

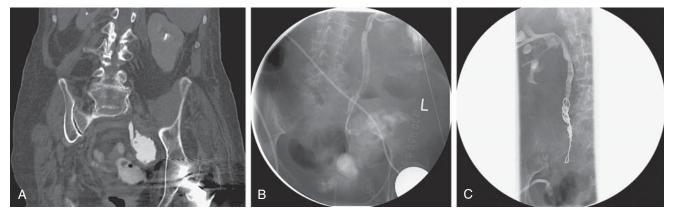
During urologic interventions, the ureter may be perforated, transected, or avulsed.<sup>19</sup> The ureter is particularly at risk for injury during gynecologic procedures owing to its intimate relationship with the uterine artery. Ureteral injuries detected post-operatively for both nonurologic and urologic procedures include strictures, ligations, fistulas, and perforations. Strictures may develop after ureteral catheterization, stone removal, lithotripsy, and ureteral anastomosis. Factors that increase the risk for stricture formation after urologic procedures include larger



Figure 67-23 Computed tomographic urography in a woman who developed a smooth stricture (*arrow*) after cesarean section.

endoscope size, longer procedures, stone impaction, and perforation of the ureter.

Radiofrequency thermal ablation is increasingly used to treat tumors of the kidney, liver, and adrenal gland. Image guidance is used to place electrodes in the tumor, after which radiofrequency energy is used to achieve thermal necrosis of the tumor and a margin of surrounding tissue. Inadvertent thermal injury of the ureter may occur, particularly when treating kidney lesions located near the ureter or collecting system.<sup>20</sup> Retrograde ureteral perfusion with cooled 5% dextrose in water has been described as a technique to reduce the risk for thermal injury to the ureter.<sup>20</sup>



**Figure 67-24** Coronal reformatted images from computed tomographic urography (A) and antegrade pyelography (B) in an 88-year-old woman after ureteral injury during sigmoidectomy for complicated diverticular disease show contrast extravasation consistent with left ureteral disruption. The ureter could not be repaired, and the leak was treated with ureteral coil embolization (C).

## Imaging

Ureteral injuries are usually detected in the operative or immediate postoperative setting and may manifest as signs and symptoms of urinary obstruction or urinoma formation (Figure 67-24). With prompt intervention, morbidity is typically limited.

#### Treatment

The management of iatrogenic injury depends on the type and severity of the injury. Patients often can be managed with ureteral stenting alone, but surgical repair may be necessary when the injury is more severe. In the setting of obstruction, nephrostomy tube placement can preserve renal function until stenting or definitive surgical repair.

## ANASTOMOTIC STRICTURE

Invasive TCC of the bladder is often treated by cystectomy and creation of an ileal conduit. One of the potential complications of this procedure is development of a stricture at the ureteroileal anastomosis, which occurs in 2% to 10% of patients after cystectomy and urinary diversion.<sup>21</sup>

#### **Clinical Presentation**

Ureteroileal anastomotic strictures are often clinically occult, resulting in chronic urinary obstruction and loss of renal function. In these patients, imaging reveals new or progressive dilation of the renal collecting system. When symptomatic, anastomotic strictures may manifest as symptoms of UTI, renal failure, or flank pain.

## Pathophysiology

Anastomotic urothelial strictures often are a late complication of cystectomy, occurring at least 6 months after surgery.<sup>21</sup> The strictures are likely a result of ischemia and fibrosis. During surgery, the blood supply to the distal ureter may be compromised.<sup>21</sup>

#### Imaging

Anastomotic strictures manifest as new hydronephrosis or progressive renal collecting system dilation. The diagnosis can be confirmed with dynamic imaging such as CT urography, radionuclide renography, and antegrade nephrostography.<sup>21</sup> The obstructed kidney may show delayed or absent secretion of contrast agent or radionuclide. In the case of a nonfunctioning kidney, a percutaneous nephrostomy is placed and the collecting system can be evaluated after antegrade injection of a contrast agent.

#### Differential Diagnosis

In patients with a history of cystectomy and urinary diversion for TCC, differential considerations for anastomotic strictures include benign fibrosis and irradiation-induced strictures. The possibility of tumor recurrence and extrinsic compression secondary to metastatic disease must be excluded.

#### Treatment

Traditionally, surgical excision of the stenotic segment and reanastomosis was the only available treatment option. Currently, endourologic procedures offer less invasive management options, such as nephrostomy placement to preserve renal function, followed by balloon dilation or stent placement with or without incisional endoureterotomy. Surgery, however, remains the preferred definitive treatment because it provides the best long-term success.<sup>21</sup>

## **RADIATION THERAPY**

Radiation therapy is commonly used to treat pelvic neoplasms, particularly carcinoma of the bladder, prostate, and cervix, with unavoidable irradiation of the ureters.<sup>22</sup> Radiation injury typically results in stricture formation. Ureteral strictures are reported to occur in 1% to 3% of patients receiving external-beam irradiation or brachytherapy.<sup>23</sup> Changes can occur from 6 months to 10 years after therapy.

#### **Clinical Presentation**

Although bladder symptoms are more common in patients with radiation therapy, ureteral strictures may develop as a late complication.

#### Pathophysiology

Information on the pathophysiology of radiation injury to the urothelium is based mostly on studies on the bladder.<sup>22</sup>



**Figure 67-25** Retrograde pyelography in a 35-year-old woman with a history of chemotherapy and pelvic irradiation for cervical carcinoma shows a long smooth stricture. Biopsy finding was negative for malignancy, and the stricture is likely due to radiation injury.

Radiation injures smooth muscle and small blood vessels, resulting in ischemia and fibrosis.

#### Imaging

Radiation-induced ureteral strictures are usually smooth, as are most benign strictures. However, in patients with invasive neoplasms, it can be difficult to distinguish radiation changes from residual or recurrent carcinoma. Usually, the distal ureter is involved, near the ureterovesical junction, and the strictures may be long (Figure 67-25).<sup>23</sup>

EUG, as well as antegrade and retrograde pyelography, will demonstrate the ureteral stricture. These studies may also show fistulas, which can develop as a late complication of radiation. CT and MRI, in addition to demonstrating the ureteral stricture and associated obstruction, have the advantage of visualizing adjacent structures and therefore may show residual or recurrent tumor. PET is increasingly being used in evaluation of patients with metastatic disease and to follow therapy response. As previously described, FDG-PET is generally not helpful for imaging urothelial lesions owing to urinary excretion of FDG.

### **Differential Diagnosis**

Given the setting of radiation therapy for malignancy, the most important differential consideration is recurrent or metastatic disease, which may require histologic sampling for definitive diagnosis.

## Treatment

As with other strictures, management includes relief of obstruction to preserve renal function as well as stent placement and possible surgical intervention.

# Other Conditions Affecting the Ureter

### IDIOPATHIC DISORDERS

Idiopathic benign strictures of the ureter are very rare. In children, congenital idiopathic strictures often occur at sites of normal physiologic narrowing. In adults, the stricture often involves the midureter.<sup>24</sup>

#### **Differential Diagnosis**

Idiopathic benign stricture is a diagnosis of exclusion, with differential considerations including ureterolithiasis, infection, malignancy, endometriosis, retroperitoneal fibrosis, irradiation, prior trauma, and instrumentation of the ureter.

#### Treatment

As with other strictures, idiopathic benign strictures can be managed by stent placement and possible surgical excision with ureteroureterostomy.

## VASCULAR DISEASE

Ureteral narrowing may be caused by various vascular impressions. A circumcaval (retrocaval) ureter occurs in approximately 1 in 1000 individuals, is almost always on the right, and is more common in males than females.<sup>25</sup>

## **Clinical Presentation**

Vascular impressions may be incidental findings, or patients can present with flank pain, obstruction, and associated complications such as infection. Crossing vessels are an important differential consideration in the diagnosis of UPJ obstruction.

### Pathophysiology

Vascular impression on the ureters by arteries or veins may be secondary to anatomic anomalies or acquired stenosis with enlargement of periureteral collateral vessels. These include accessory renal arteries, enlargement of the ureteral artery in the setting of renal artery stenosis, gonadal veins, and ureteral varices (Figure 67-26).

Another vascular anomaly that can cause obstruction and focal ureteral narrowing is the circumcaval ureter, which is due to abnormal development of the vena cava with persistence of the right subcardinal vein.<sup>25</sup> This condition predominantly occurs on the right and predisposes to obstruction, infection, and ureterolithiasis.

## Imaging

A crossing vessel, such as an accessory renal artery, may cause a focal compression and kinking of the ureter. This usually involves the proximal ureter near the UPJ. A focal impression may be caused by a gonadal vein, which can cross the ureter proximally, inferior to the UPJ, or inferiorly at the level of S1. A more diffuse, serpiginous appearance may be caused by dilation of the ureteral artery, which can occur in the setting of renal artery stenosis or iliac artery occlusion.<sup>26</sup>

In the setting of a circumcaval ureter, the ureter is deviated medially at the L3-4 level and courses behind the inferior vena cava (Figure 67-27). Obstruction may or may not be present. In the more common subtype, the ureter is narrowed lateral to



Figure 67-26 Coronal computed tomographic (CT) urogram (A) and maximum intensity projection (B) in a 53-year-old man who presented with an elevated creatinine level as a result of right hydronephrosis and hydroureter. Surgery confirmed the CT finding of extrinsic compression by crossing vessels (*arrows*).



**Figure 67-27** Excretory urography and venocavogram show ureteral narrowing and medial deviation secondary to a retrocaval ureter. (*Courtesy Isabel Yoder, MD.*)

the psoas muscle. When obstructed, the proximal ureter is dilated and tortuous with a reverse-J configuration on EUG. If not obstructed, the ureter has a "7" configuration. In the second, rare, subtype, also called the high loop variant, the ureter is narrowed lateral to the inferior vena cava, has less medial deviation, and may have a sickle shape.<sup>15</sup> The course of the ureter

relative to the vena cava is better demonstrated on CT, which also can show the relative lateral position of the inferior vena cava. Similarly, MRI can show the same anatomic position and course of the ureter as CT, with the advantage of no radiation.

### Differential Diagnosis

Other retroperitoneal processes, such as retroperitoneal fibrosis or metastatic disease, can cause vascular occlusions, which then lead to the development of collateral vessels that cause extrinsic compression, including focal narrowing or more diffuse, serpiginous ureteral narrowing. In differentiating retroperitoneal fibrosis from circumcaval ureter, involvement of both sides and a long segment of the ureter may indicate retroperitoneal fibrosis.

#### Treatment

The management of vascular lesions depends on the degree of obstruction and associated symptoms. Asymptomatic patients can be observed. However, symptomatic patients with obstruction from a circumcaval ureter or other crossing vessel often require surgery.<sup>25</sup>

## INFLAMMATORY DISORDERS

#### **Retroperitoneal Fibrosis**

Retroperitoneal fibrosis is a rare entity, occurring in approximately 1 in 200,000 people. It usually affects patients 40 to 60 years of age, and men are more commonly affected than women.<sup>27</sup> It may be associated with other systemic diseases such as mediastinal fibrosis, sclerosing cholangitis, ankylosing spondylosis, mesenteric fibrosis, and other immune disorders.

**Clinical Presentation.** The clinical presentation is variable and usually related to compression of retroperitoneal structures. The ureters are frequently involved, and the gradual onset of fibrosis may result in patients being relatively asymptomatic. Symptoms such as flank pain, renal colic, and declining renal function secondary to chronic obstruction may occur. Patients

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also may present with symptoms related to vascular or lymphatic obstruction, such as lower extremity edema, deep venous thrombosis, or even mesenteric ischemia.

**Pathophysiology.** Retroperitoneal fibrosis is a fibrotic process that usually involves the retroperitoneum around the lower aorta. Two thirds of cases are idiopathic and may be due to a hypersensitivity reaction to antigen from atheromatous plaque leaking into the retroperitoneal space.

The remaining one third of cases can be attributed to a specific cause, such as retroperitoneal hemorrhage; urine extravasation; drug reactions; desmoplastic reaction to metastases; or postsurgical, postirradiation, or fibrosing infection (e.g., TB, syphilis, actinomycosis).<sup>28</sup>

In a small number of cases, the condition may be associated with immunoglobulin G (IgG 4)-related disease.<sup>29</sup>

**Imaging.** Initially, fibrosis is seen around the lower abdominal aorta and then extends into the retroperitoneum and to adjacent structures. Retroperitoneal fibrosis therefore often involves the lower abdominal ureter. Associated systemic involvement includes mediastinal fibrosis, Hashimoto's thyroiditis, sclerosing cholangitis, ankylosing spondylitis, sclerosing mesenteritis, and systemic lupus erythematosus.<sup>27</sup>

**Radiography.** Abdominal radiography is usually of limited use in the evaluation of retroperitoneal fibrosis, except in the rare cases of advanced disease, when a central soft tissue mass may distort the psoas shadow. Intravenous pyelography may demonstrate a delayed nephrogram, hydronephrosis, and hydroureter, which may be unilateral or bilateral, fusiform ure-teral tapering at the L4 and L5 level, and medial deviation and angulation of the ureter (Figure 67-28).<sup>28</sup>

*Ultrasonography.* Ultrasonography may show a hypoechoic retroperitoneal mass as well as hydronephrosis.<sup>27</sup>

*Computed Tomography.* CT is generally the best imaging modality and can demonstrate the location and extent of the retroperitoneal mass. Retroperitoneal fibrosis may manifest as a well-defined or infiltrative mass that may be midline or eccentric or as a small amount of soft tissue surrounding the aorta and retroperitoneal structures. Usually the mass begins at a level above the aortic bifurcation, encases the aorta, and can extend inferiorly, superiorly, and laterally. Retroperitoneal fibrosis usually does not displace the aorta away from the adjacent vertebral body, a feature that can help distinguish retroperitoneal fibrosis from lymphoma or other causes of retroperitoneal lymphadenopathy. In the early stages, immature fibrosis can show enhancement after intravenous contrast agent administration. As the fibrosis matures, it becomes hypovascular and enhances less. Although CT is excellent at demonstrating the extent of involvement, CT cannot distinguish benign from malignant causes of retroperitoneal fibrosis, and surgical biopsy is often necessary for definitive diagnosis.

*Magnetic Resonance Imaging.* MRI, like CT, demonstrates the location of the retroperitoneal mass and the extent of involvement of other retroperitoneal structures. Benign retroperitoneal fibrosis usually has low signal on both T1- and T2-weighted images. Although high T2 signal and heterogeneity can be seen with malignant retroperitoneal fibrosis, high T2 signal may reflect edema or inflammation and is not a reliable indicator of malignant disease.<sup>27</sup>

Positron Emission Tomography With Computed Tomography. Metabolically active retroperitoneal fibrosis of both benign



Figure 67-28 Antegrade pyelography in a patient with retroperitoneal fibrosis. (Courtesy Isabel Yoder, MD.)

and malignant causes can show increased uptake of FDG as well as increased uptake on gallium-67 imaging. The degree of radiotracer uptake has been shown to correlate with disease activity, with more uptake in the inflammatory stage and mild uptake later in the fibrotic stage of the disease.<sup>27</sup>

**Differential Diagnosis.** The main differential diagnoses include lymphoma and retroperitoneal lymphadenopathy. In general, retroperitoneal lymphadenopathy is a more lobular process that causes anterior displacement of the aorta and lateral displacement of the ureters. Uncommonly, retroperitoneal infection and amyloidosis may have an appearance similar to that of retroperitoneal fibrosis.

Treatment. The management of retroperitoneal fibrosis is targeted at relieving renal obstruction. Specific therapies vary depending on the cause of the retroperitoneal fibrosis. In cases resulting from methysergide therapy, cessation of the medication usually results in disease regression. For idiopathic retroperitoneal fibrosis, treatment may include surgical intervention and corticosteroid therapy. Surgical therapy includes ureterolysis and/or moving the ureter laterally and wrapping it with omentum to prevent recurrent stricture formation. For malignant causes of retroperitoneal fibrosis, treatment is usually targeted at the primary neoplasm. In some cases of malignant retroperitoneal fibrosis or for patients who are not surgical candidates, percutaneous nephrostomy or ureteral stenting can be used to relieve ureteral obstruction.<sup>27</sup> Benign causes of retroperitoneal fibrosis generally have good outcomes, whereas malignant retroperitoneal fibrosis has a poor prognosis.

# Inflammatory Bowel Process

Extraintestinal extension of both acute and chronic inflammatory bowel processes can cause ureteral strictures. Such processes include inflammatory bowel disease, enteritis, appendicitis, and diverticulitis. Inflammatory bowel disease may cause ureteral complications as a result of urolithiasis secondary to metabolic abnormalities as well as direct extension of bowel inflammation into the ureters. Genitourinary involvement in patients with inflammatory bowel disease usually develops in the setting of long-standing disease.

**Clinical Presentation.** When the ureter is directly involved from adjacent bowel inflammation or fistula, patients often present with fever and abdominal pain secondary to the underlying inflammatory process. The ureteral stricture may be asymptomatic or cause obstructive nephropathy.

**Pathophysiology.** Inflammation from the involved segment of bowel spreads and extends into the adjacent ureter, usually in the region of the pelvic brim.

**Imaging.** Imaging demonstrates a smooth segment of ureteral narrowing with or without associated obstruction. In patients with Crohn's disease, the right ureter is usually involved. Cross-sectional imaging is the most helpful imaging modality because it shows bowel inflammation and the extent of the inflammatory process with a soft tissue mass or fistula involving the ureter. In the setting of diverticulitis, which commonly involves the sigmoid colon, the left ureter is usually involved. The ureter may be displaced or compressed by an adjacent abscess or encased by inflammation. Rarely, complications from appendicitis, such as abscess formation and inflammation, can extend to involve the right ureter.

**Differential Diagnosis.** The smooth segmental ureteral narrowing seen with inflammatory bowel processes that involve the ureter are similar to that in other benign ureteral strictures. Other pelvic processes, such as neoplasm and hemorrhage, also can cause extrinsic compression and displacement of the distal ureters (Figure 67-29).

**Treatment.** Depending on the cause and severity of ureteral involvement, management may involve stent placement or surgical intervention.

#### Endometriosis

Involvement of the ureter by endometriosis is usually seen in the setting of extensive pelvic disease and occurs in 0.01% to 1% of all women with endometriosis.<sup>30</sup>

**Clinical Presentation.** Patients with endometriosis usually present with pelvic pain associated with menses and infertility. When the ureters are involved, patients may present with hematuria and flank pain that may occur at the time of menstruation as well as obstruction.

**Pathophysiology.** In endometriosis, ectopic endometrial tissue implants on the peritoneal surfaces of the pelvis. Hormonal changes of the menstrual cycle result in repeated episodes of hemorrhage from the endometriotic implants with resultant inflammation and fibrosis. Common sites include the ovaries and fallopian tubes, uterine ligaments, peritoneal reflections, sigmoid colon, and bladder. Endometriosis may cause ureteral narrowing by extrinsic compression by transmural invasion from adjacent endometrial implants or can incite surrounding fibrosis and smooth muscle proliferation. Rarely, endometrial tissue may primarily implant in the ureteral wall.

**Imaging.** Imaging findings depend on the size of the endometrial implants and the extent of ureteral involvement. Strictures secondary to endometriosis have smooth margins. The stricture typically ranges from 0.5 to 2.2 cm in length and usually involves the pelvic ureter near the attachment of the uterosacral ligaments, 2 to 5 cm from the ureterovesical junction.<sup>31</sup> This location is slightly more proximal than ureteral strictures caused by direct extension of pelvic tumors, such as cervical carcinoma. Distal to the involved segment, the ureter is usually normal. One or both ureters may be affected.

**Radiography.** EUG and retrograde urography may show a filling defect, medial deviation of the ureter, ureteral narrowing, and varying degrees of associated obstruction (Figures 67-30 and 67-31).

*Ultrasonography.* Ultrasonography is frequently used to image women with endometriosis. Although it often shows adnexal involvement, ureteral implants are not well demonstrated.

*Computed Tomography.* CT is not the primary imaging modality for patients with endometriosis, because the findings are nonspecific. However, when large enough, soft tissue pelvic

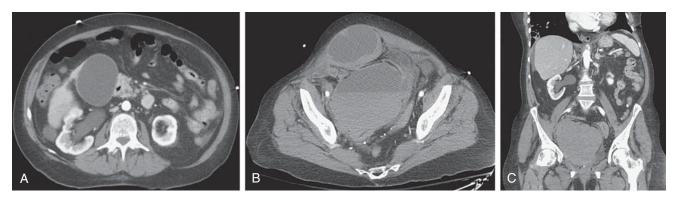


Figure 67-29 Axial (A and B) and coronal (C) contrast-enhanced computed tomography images in a 77-year-old man on Coumadin show left hydronephrosis and hydroureter secondary to extrinsic compression by a pelvic hematoma.

endometriosis can be detected on CT, and CT urography can demonstrate ureteral filling defects, stricture, and associated obstruction (see Figure 67-31).

*Magnetic Resonance Imaging.* MRI plays an important role in imaging the pelvis of patients with endometriosis by identifying T1-hyperintense endometrial implants on fat-suppressed images. However, the signal intensity of implants is variable owing to the different age and stages of blood products and the different types of implants. Some implants consist mostly of glandular tissue, are T2 hyperintense, and enhance after administration of a contrast agent. Solid endometriosis has hyperintense foci of hemorrhage as well as surrounding fibrosis, which



**Figure 67-30** Ureteral stricture in a young woman with endometriosis. (*Courtesy Isabel Yoder, MD.*)

is hypointense on T2-weighted images and enhances. In the setting of deep pelvic endometriosis, endometrial implants and fibrosis can involve the ureter, resulting in ureteral stricture and obstruction.

By demonstrating the extent and location of pelvic involvement, MRI is useful in the preoperative evaluation of patients with endometriosis.

**Differential Diagnosis.** The imaging appearance of ureteral endometriosis cannot be differentiated from malignant urothelial lesions. Other differential considerations include TB, radiation fibrosis, retroperitoneal fibrosis, surgical injury, metastases, and primary urothelial neoplasms. Identification of endometriosis in the absence of other pelvic disease or manifestations associated with other entities assists in making the diagnosis.

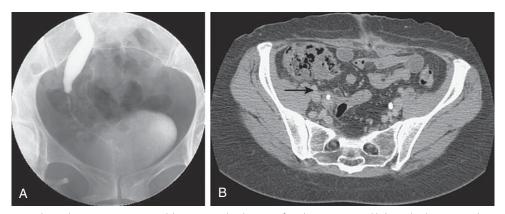
**Treatment.** Laparoscopy remains the gold standard for diagnosing the extent of disease and allows for resection of implants and associated adhesions. Ureteral strictures from endometriosis usually require surgery, including laparoscopic resection of the implant with preoperative or perioperative placement of a ureteral stent. Occasionally, laparotomy with segmental ureteral resection and reimplantation is necessary.

#### What the Referring Physician Needs to Know

- Benign ureteral strictures have a broad differential diagnosis.
- Imaging can narrow this differential diagnosis by depicting the site of the stricture and potentially the cause.

## **Key Points**

- CT is very useful for assessment of benign ureteral strictures, because it is highly accurate in the detection of urinary calculi and is able to precisely depict the level of the stricture in the majority of cases.
- Retrograde pyelography or antegrade nephrostography may be necessary to evaluate the urothelium, especially when renal function is impaired.



**Figure 67-31** A, Antegrade pyelogram in a 45-year-old woman with a history of endometriosis and bilateral salpingo-oophorectomy shows a long, smooth, right ureteral stricture with an abrupt transition and proximal hydroureter. B, Axial computed tomography image shows periureteral soft tissue thickening (*arrow*).

# **SUGGESTED READINGS**

- Bosniak M, Megibow A, Ambos M, et al: Computed tomography of ureteral obstruction. *AJR Am J Roentgenol* 138:1107–1113, 1982.
- Caoili EM, Cohan RH, Inampudi P, et al: MDCT urography of upper tract urothelial neoplasms. AJR Am J Roentgenol 184:1873–1881, 2005.

# REFERENCES

- El-Galley RES, Keane TE: Embryology, anatomy, and surgical applications of the kidney and ureter. *Surg Clin North Am* 80:381–401, 2000.
- Winalski Č, Lipman J, Tumeh S: Ureteral neoplasms. *Radiographics* 10:271–283, 1990.
   Silverman SG, Leyendecker JR, Amis ES, Jr: What is the guarant rale of CT uncertable and
- What is the current role of CT urography and MR urography in the evaluation of the urinary tract? *Radiology* 250:309–323, 2009.
  4. Berrocal T, Lopez-Pereira P, Arjonilla A, et al:
- Anomalies of the distal ureter, bladder, and urethra in children: embryologic, radiologic, and pathologic features. *Radiographics* 22:1139– 1164, 2002.
- Menéndez V, Sala X, Alvarez-Vijande R, et al: Cystic pyeloureteritis: review of 34 cases radiologic aspects and differential diagnosis. Urology 50:31–37, 1997.
- Wang J, Wang H, Tang G, et al: Transitional cell carcinoma of upper urinary tract vs. benign lesions: distinctive MSCT features. *Abdom Imaging* 34:94–106, 2009.
- Dyer RB, Chen MY, Zagoria RJ: Classic signs in uroradiology. *Radiographics* 24(Suppl 1):S247– S280, 2004.
- Jung YY, Kim JK, Cho K: Genitourinary tuberculosis: comprehensive cross-sectional imaging. *AJR Am J Roentgenol* 184:143–150, 2005.
- 9. Jorulf H, Lindstedt E: Urogenital schistosomiasis: CT evaluation. *Radiology* 157:745, 1985.
- Ross AGP, Bartley PB, Sleigh AC, et al: Schistosomiasis. N Engl J Med 346:1212–1220, 2002.
- Roberts WW, Cadeddu JA, Micali S, et al: Ureteral stricture formation after removal of impacted calculi. J Urol 159:723–726, 1998.

- Grossfeld GD, Litwin MS, Wolf JS, et al: Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy. II. Patient evaluation, cytology, voided markers, imaging, cystoscopy, nephrology evaluation, and follow-up. *Urology* 57:604–610, 2001.
- Wang J, Wang H, Tang G, et al: Transitional cell carcinoma of upper urinary tract vs. benign lesions: distinctive MSCT features. *Abdom Imaging* 34:94– 106, 2009.
- Caoili EM, Cohan RH, Inampudi P, et al: MDCT urography of upper tract urothelial neoplasms. *AJR Am J Roentgenol* 184:1873–1881, 2005.
- Winalski C, Lipman J, Tumeh S: Ureteral neoplasms. *Radiographics* 10:271–283, 1990.
- Wong-You-Cheong J, Wagner B, Davis C, Jr: Transitional cell carcinoma of the urinary tract: radiologic-pathologic correlation. *Radiographics* 18:123–142, 1998.
- Wang J, Wang H, Tang G, et al: Transitional cell carcinoma of upper urinary tract vs. benign lesions: distinctive MSCT features. *Abdom Imaging* 34:94–106, 2009.
- Kirkali Z, Tuzel E: Transitional cell carcinoma of the ureter and renal pelvis. *Crit Rev Oncol Hematol* 47:155–169, 2003.
- Browne RFJ, Meehan CP, Colville J, et al: Transitional cell carcinoma of the upper urinary tract: spectrum of imaging findings. *Radiographics* 25:1609–1627, 2005.
- Patel RC, Newman RC: Ureteroscopic management of ureteral and ureteroenteral strictures. Urol Clin North Am 31:107–113, 2004.
- Selzman AA, Spirnak JP: Iatrogenic ureteral injuries: a 20-year experience in treating 165 injuries. J Urol 155:878–881, 1996.
- Cantwell CP, Wah TM, Gervais DA, et al: Protecting the ureter during radiofrequency ablation of renal cell cancer: a pilot study of retrograde pyeloperfusion with cooled dextrose 5% in water. J Vasc Interv Radiol 19:1034–1040, 2008.
- 21. Tal R, Sivan B, Kedar D, et al: Management of benign ureteral strictures following radical cystectomy and urinary diversion for bladder cancer. *J Urol* 178:538–542, 2007.

- Marks LB, Carroll PR, Dugan TC, et al: The response of the urinary bladder, urethra, and ureter to radiation and chemotherapy. *Int J Radiat Oncol Biol Phys* 31:1257–1280, 1995.
- Capps G, Fulcher A, Szucs R, et al: Imaging features of radiation-induced changes in the abdomen. *Radiographics* 17:1455–1473, 1997.
- Bhatta Dhar N, Angermeier KW, Streem SB, et al: Idiopathic ureteral strictures without evidence of malignancy. *Urology* 64:377–378, 2004.
- Salonia A, Maccagnano C, Lesma A, et al: Diagnosis and treatment of the circumcaval ureter. *Eur Urol Suppl* 5:449–462, 2006.
- Chait A, Matasar KW, Fabian CE, et al: Vascular impressions on the ureters. *AJR Am J Roentgenol* 111:729–749, 1971.
- Cronin CG, Lohan DG, Blake MA, et al: Retroperitoneal fibrosis: a review of clinical features and imaging findings. *AJR Am J Roentgenol* 191: 423–431, 2008.
- Buyl L, Oosterlinck W, Verstraete K, et al: An unusual case of unilateral periureteral retroperitoneal fibrosis. *Clin Radiol* 58:492–494, 2003.
- Stone JR: Aortitis, periaortitis, and retroperitoneal fibrosis, as manifestations of IgG4-related systemic disease. *Curr Opin Rheumatol* 23:88– 94, 2011.
- Del Frate C, Girometti R, Pittino M, et al: Deep retroperitoneal pelvic endometriosis: MR imaging appearance with laparoscopic correlation. *Radiographics* 26:1705–1718, 2006.
- Pollack H, Wills J: Radiographic features of ureteral endometriosis. AJR Am J Roentgenol 131: 627–631, 1978.



# Benign and Malignant Bladder Lesions

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The urinary bladder is composed of the following four layers:

- Urothelium: Transitional epithelium
   Lamina propria: Vascular layer of connective tissue deep
- to the urothelium
- 3. Muscularis propria: Detrusor muscle
- 4. Adventitia: Connective tissue

The bladder is an extraperitoneal organ with a serosal (peritoneal) covering present only over the dome. The remainder of the bladder is surrounded by perivesical fat.

This chapter reviews the benign and malignant processes that can affect the urinary bladder. With a nonspecific clinical presentation, most bladder tumors have a broad differential diagnosis that includes both benign and malignant entities. Definitive diagnosis is usually established by histologic examination. Paraganglioma is the only bladder lesion with symptoms and biochemical findings that permit a specific clinical diagnosis.

The differential diagnosis is broad when imaging findings are nonspecific and includes both benign and malignant entities. Other benign lesions to consider that also may manifest as single or multiple focal masses include blood clot, endometriosis, nephrogenic adenoma, eosinophilic cystitis, malakoplakia, and infections such as tuberculosis, schistosomiasis, and fungal infections. Primary bladder carcinomas, lymphoma, and metastatic disease from adjacent or distant organs should be considered among the differential diagnoses for malignant bladder tumors. Clinical presentation, accompanying secondary imaging findings, and histologic analysis allow for more accurate differentiation from the primary benign tumors of the bladder.

# **Benign Bladder Lesions**

# ETIOLOGY

Primary tumors of the urinary bladder may arise from any of the four layers of the bladder wall, with the majority (95%) arising from the epithelial layer.<sup>1</sup> By contrast, primary benign tumors of the urinary bladder arise from the submucosa, accounting for a minority (~1%) of bladder tumors. These tumors are typically mesenchymal with differentiation toward vasculature, nerve, cartilage, fat, muscle, or fibrous tissue. Mesenchymal bladder tumors include leiomyoma, hemangioma, paraganglioma, neurofibroma, inflammatory pseudosarcoma, solitary fibrous tumor, lipoma, and fibroma.<sup>2-4</sup>

# PREVALENCE AND EPIDEMIOLOGY

#### Leiomyoma

Leiomyoma is the most common benign mesenchymal tumor of the bladder, accounting for 0.4% of all bladder tumors.<sup>5</sup> Most leiomyomas occur in middle-aged women, with 76% of patients with leiomyoma being female.<sup>6</sup>

# Hemangioma

Bladder hemangioma, accounting for 0.3% of all bladder tumors, is typically a congenital tumor that is usually noted during childhood or adolescence but may be diagnosed at a later age as well. There may be a slight male predominance.<sup>7</sup> It is most commonly observed as a single lesion, although additional hemangiomas may be observed elsewhere in the body up to 30% of the time, for example, in the skin.<sup>8</sup> These tumors may occur in association with Klippel-Trenaunay-Weber and Sturge-Weber syndromes.

# Paraganglioma

Paraganglioma, a pheochromocytoma occurring outside the adrenal gland, is uncommon, accounting for 0.1% of all bladder tumors.<sup>2-4</sup> Although it may occur at any age, paraganglioma is more common among adults. There is a slight female predilection. Whereas most paragangliomas are isolated, they also may occur in conjunction with phakomatoses such as neurofibromatosis, Sturge-Weber syndrome, and tuberous sclerosis or other syndromes, including von Hippel-Lindau syndrome or multiple endocrine neoplasia types 2a and 2b. Rare observations of familial extra-adrenal pheochromocytomas also have been reported.<sup>9</sup> In 5% to 15% of cases, paraganglioma of the bladder may be malignant.<sup>1,10</sup>

# Neurofibroma

Neurofibroma is a rare bladder tumor, although the urinary bladder is the most common site of involvement within the genitourinary system. These tumors occur in isolation or in association with neurofibromatosis type 1 (NF1) in 55% of cases. Neurofibromas are more common in men 20 to 40 years of age. A younger age at onset suggests association with NF1. Neurofibromas associated with NF1 are usually multiple or are of the pathognomonic plexiform type. Malignant degeneration of neurofibromas, more common in cases associated with NF1, should be suspected in tumors that rapidly increase in size or are heterogeneous in appearance.<sup>11,12</sup>

# Inflammatory Pseudotumor

Inflammatory pseudotumor is also known by its more descriptive name, pseudosarcomatous fibromyxoid tumor, which better reflects its histologic composition.<sup>1</sup> This is a rare tumor that occurs at any age from childhood to late adulthood and may have a slight male predilection. First described in the lung, inflammatory pseudotumor may involve any organ. The tumor behaves aggressively and mimics malignancy on imaging. Distinction is made only by histologic examination.

#### Solitary Fibrous Tumor

Solitary fibrous tumor is an exceedingly rare tumor in the urinary bladder with only seven reported cases in the literature.<sup>13</sup> It is most commonly seen in the thoracic cavity, where it involves the visceral pleura. Reports of extrapleural involvement in multiple other organ systems also exist. It preferentially affects men 42 to 67 years of age.<sup>13</sup>

#### Lipoma and Fibroma

Lipoma and fibroma occur only rarely in the urinary bladder and demonstrate features in the urinary bladder similar to those seen in other more commonly involved sites in the body.

# CLINICAL PRESENTATION

Most patients with bladder tumors present with nonspecific urinary symptoms, such as hematuria, frequency, urgency, dribbling, or urinary obstruction, that vary depending on the size and location of the tumor. Some may be asymptomatic. Painless hematuria is a common manifestation of hemangiomas.

Patients with paragangliomas may present with episodic headaches, anxiety, sweating, tremors, and hypertension occurring with each catecholamine surge with urination—so-called micturition attacks. Hematuria is also common with paragangliomas. Twenty-four-hour urine collection analysis reveals elevated levels of metanephrines or vanillylmandelic acid. Most (83%) but not all paragangliomas are hormonally active.

#### PATHOLOGY

#### Leiomyoma

Leiomyoma is usually a solitary tumor that exhibits growth intraluminally (63%), intramurally (7%), or outside the confines of the bladder (30%).<sup>14,15</sup> The lesion typically occurs at the bladder base near the trigone, although it also may be found on the lateral or posterior walls.

## Hemangioma

Hemangioma manifests as a small, lobulated, broad-based, sessile mass in the bladder dome or posterolateral wall. Although most hemangiomas extend into the muscular layer of the bladder wall, approximately one third are located in the submucosa and a minority may also extend beyond the bladder wall. Hemangiomas also may manifest as diffuse bladder wall thickening.<sup>8,16</sup>

The three distinct types of hemangiomas described include cavernous, capillary, and arteriovenous. The cavernous type accounts for most (78%) bladder hemangiomas, whereas capillary and arteriovenous types each represent 10% of cases.<sup>8</sup>

#### Paraganglioma

Paragangliomas arise from the chromaffin cells of the sympathetic plexus in the bladder wall. Most are found near the trigone, although they may occur anywhere in the bladder.

## Neurofibroma

Neurofibromas originate from the sheath of nerve plexuses entering near the bladder trigone. The tumor manifests as a smooth, well-defined focal intraluminal or intramural mass anywhere in the bladder. The plexiform variety manifests as a focal, nodular mass resulting in bladder wall thickening or as diffuse bladder wall thickening that involves only the inner wall, sparing the outer bladder wall. Plexiform neurofibromas also may involve surrounding structures such as the rectum, urethra, prostate, seminal vesicles, uterus, vagina, and the pelvic sidewalls.<sup>11,12</sup>

#### Inflammatory Pseudotumor

The pathogenesis of this tumor is uncertain, although it is postulated to develop as a result of recurrent cystitis, inflammation, or prior surgery. However, many patients give no such prior history.<sup>17</sup> This tumor usually occurs as a solitary mass ranging from 2 to 8 cm anywhere in the bladder with a tendency to spare the trigone.<sup>18</sup> The solitary mass may project into the lumen, may be intramural, or may demonstrate extension into the surrounding extravesical tissues.<sup>19</sup>

#### Solitary Fibrous Tumor

Solitary fibrous tumor may be an incidental finding or it may produce symptoms owing to its large size, which ranges from 3 to 17 cm. It may occur anywhere in the bladder.

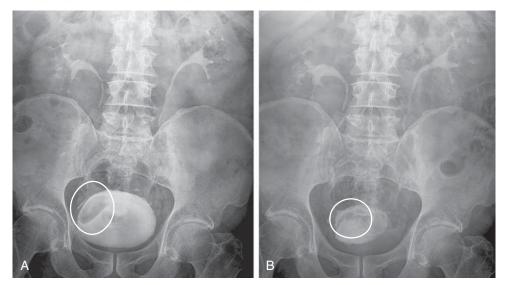
The histopathologic features of solitary fibrous tumor may be confused with those of other tumors such as hemangiopericytoma, leiomyoma, leiomyosarcoma, and schwannoma.<sup>13</sup> However, immunohistochemical analysis specifies the diagnosis because a solitary fibrous tumor strongly expresses CD34 on its surface that is not expressed as exuberantly by other tumors. Recently, this tumor has also shown positivity to BCL2, insulinlike growth factor type 2, and CD99.<sup>20,21</sup>

# IMAGING

The imaging features of most benign bladder tumors are not specific. The tumor generally appears as a solid enhancing mass that is well circumscribed with smooth margins on crosssectional imaging. However, differing histologic composition may give rise to characteristic imaging findings in certain tumors that allow greater specificity. Magnetic resonance imaging (MRI) is superior to other modalities given its ability to better characterize soft tissue as well as demonstrate the submucosal location of these tumors. Enhancing mucosa overlying the mass is seen on postgadolinium images. Because the imaging features of most primary benign bladder tumors are not specific, only those tumors with distinct imaging characteristics are discussed in the following sections.

#### Radiography

Intravenous urography and cystography demonstrate a filling defect or defects in the case of multiple lesions (Figure 68-1). A specific diagnosis or even differentiation between benign or malignant tumors cannot be made with these techniques, and



**Figure 68-1** A 67-year-old man with gross hematuria. **A**, Intravenous pyelogram in excretory phase demonstrates a nonspecific filling defect (*oval*) in the right side of the bladder. **B**, The filling defect (*circle*) persists on the postvoid image. A stone was found on cystoscopy. (*Case courtesy Alton B, Farris III, MD, Department of Pathology, Massachusetts General Hospital.*)

additional imaging or evaluation is required for more definitive diagnosis.

# Computed Tomography

Computed tomography (CT) typically demonstrates an enhancing mass in the background of a urine-filled bladder on contrastenhanced images and a filling defect of variable morphology in the background of a contrast-filled urinary bladder in the excretory phase of imaging.

Calcifications have not been reported in bladder leiomyomas (Figure 68-2, A). Although rarely observed, ring calcification around the periphery of a bladder mass is highly suggestive of a paraganglioma (Figure 68-3, A and B).<sup>22</sup> Hemangiomas also may be associated with calcifications, which in the case of cavernous hemangiomas represent phleboliths.<sup>16</sup>

**Neurofibroma.** Neurofibroma appears as a homogeneous, well-defined mass of low attenuation on unenhanced images with homogeneous enhancement on postcontrast images. Scattered areas of low attenuation, reflecting myxoid degeneration, also may be seen after administration of a contrast agent. A target-like enhancement pattern, characteristic of plexiform neurofibromas, also may be observed (Figure 68-4). In this pattern there are areas of high attenuation centrally, which corresponds histologically to nerve tissue, as well as areas of low attenuation peripherally, corresponding to myxoid degeneration.<sup>23,24</sup>

**Inflammatory Pseudotumor.** Inflammatory pseudotumor appears as an enhancing, solitary, polypoid mass with a central area of low-density corresponding histologically to necrosis (Figure 68-5). This appearance results in peripheral enhancement surrounding a central nonenhancing area.<sup>25</sup> Extravesical spread may also be noted.<sup>19</sup>

#### Magnetic Resonance Imaging

Many tumors demonstrate low to intermediate signal intensity on T1-weighted sequences and high signal intensity on T2weighted sequences. Only those tumors with distinct MRI features are discussed here.

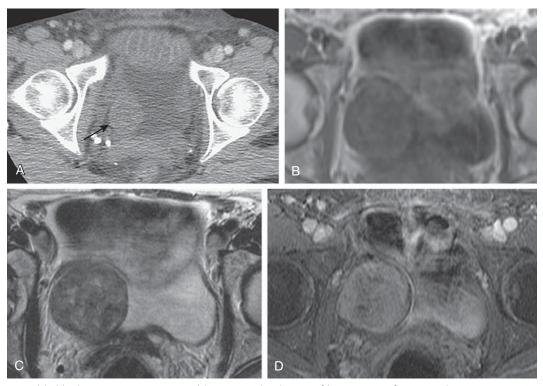
**Leiomyoma.** Because of the smooth muscle composition of leiomyomas, MRI allows for more specific characterization than other modalities. Imaging characteristics are similar to those seen with the more commonly encountered uterine leiomyomas. MRI usually demonstrates a homogeneous, well-defined mass of decreased to intermediate T1 signal and decreased T2 signal that enhances after administration of gado-linium (see Figure 68-2, *B* to *D*). Enlarging leiomyomas may demonstrate heterogeneity and degeneration, which may be cystic in the case of bladder leiomyomas. Cystic degeneration manifests as increased T2 signal and a corresponding area of nonenhancement.<sup>15,26</sup>

**Hemangioma.** Hemangiomas give low to intermediate signal on T1-weighted images, with marked hyperintensity on T2-weighted images.<sup>27</sup>

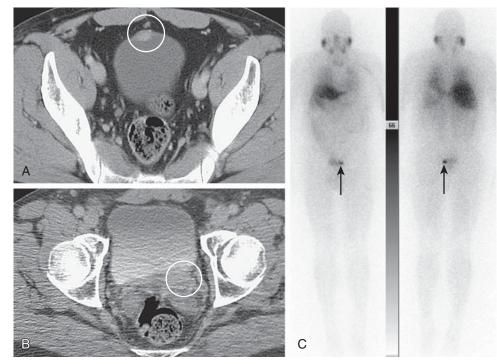
**Paraganglioma.** Paragangliomas are usually hypointense on T1-weighted images. Classically, and as also observed with their adrenal counterparts, paragangliomas are hyperintense ("light bulb") on T2-weighted images. However, only mild hyperintensity on T2-weighted images is seen in 20% of cases. There is marked enhancement after contrast agent administration.<sup>9,28</sup>

**Neurofibroma.** The highly characteristic target pattern of enhancement also may be seen with MRI. On T1-weighted images, the central portion demonstrates increased signal compared with the periphery. On T2-weighted images, the peripheral portion, corresponding histologically to myxoid degeneration, demonstrates increased signal compared with the central portion, which corresponds histologically to nerve tissue.<sup>23,24</sup>

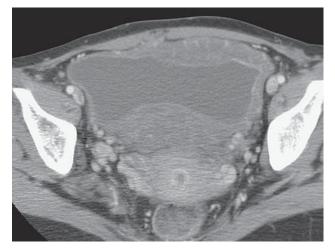
**Inflammatory Pseudotumor.** Inflammatory pseudotumor exhibits low signal on T1-weighted images and heterogeneously



**Figure 68-2** Urinary bladder leiomyoma in a 52-year-old woman with a history of hysterectomy for uterine leiomyomas. A, Contrast-enhanced computed tomography image in portal venous phase demonstrates a well-defined, solid mass arising from the medial wall of urinary bladder (*arrow*). T1-weighted (**B**) and T2-weighted (**C**) magnetic resonance images in the same patient demonstrate a well-defined T1-hypointense mass arising from the medial wall of the urinary bladder. The mass is heterogeneously hypointense on the T2-weighted image and demonstrates slightly heterogeneous enhancement on a postgadolinium fat-saturated image (**D**).



**Figure 68-3** Paraganglioma of urinary bladder in two different 52-year-old men with elevated levels of urine metanephrines and normetanephrines. Contrast-enhanced computed tomography (CT) images in the portal venous phase demonstrate nonspecific finding of a solid enhancing mass (*oval*) in patient 1 (A) and patient 2 (B). Ring calcifications were not observed in these cases. Both patients were treated with partial cystectomy. C, Wholebody meta-iodobenzylguanidine images in anterior (*left*) and posterior (*right*) projections of patient 2 demonstrate focal area of radiotracer uptake (*arrows*) near the left ureterovesical junction, corresponding to the mass seen on CT (B).



**Figure 68-4** Neurofibroma, diffuse type, in a 36-year-old woman with neurofibromatosis type 1. This patient also had plexiform neurofibroma of right thigh (not shown). Contrast-enhanced computed tomography image in arterial phase demonstrates nonspecific diffuse bladder wall thickening. The findings were limited to the bladder without involvement of adjacent organs. The target-like pattern sometimes seen with neurofibromas is not evident in this case. (*Case courtesy Alton B, Farris III, MD, Department of Pathology, Massachusetts General Hospital.*)

high signal on T2-weighted images. Enhancement characteristics are similar to those seen on CT.<sup>19,25</sup>

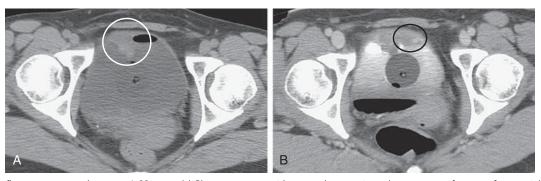
**Solitary Fibrous Tumor.** Solitary fibrous tumor is a solid enhancing mass that exhibits T2 hypointensity (Figure 68-6).

## Ultrasonography

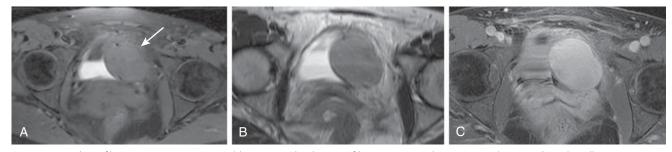
Ultrasonography shows an isoechoic to hypoechoic intramural mass with a variable degree of vascularity on color Doppler evaluation (Figure 68-7). Of note, hemangiomas<sup>16</sup> and paragangliomas<sup>9</sup> manifest as hyperechoic masses with marked vascularity. Color Doppler evaluation of hemangiomas and paragangliomas demonstrates a high-velocity, low-resistance arterial waveform.

#### Nuclear Medicine

Except for paragangliomas, in which iodine-131–labeled metaiodobenzylguanidine (<sup>131</sup>I-MIBG) scan may demonstrate increased uptake in the bladder mass with a specificity of 96%, nuclear medicine plays no role in the evaluation of primary benign bladder tumors (see Figure 68-3, *C*). However, sensitivity of this scan is much lower, at approximately 65%.<sup>29</sup> The <sup>131</sup>I-MIBG scan also may be useful for evaluating the whole body for metastatic paraganglioma.



**Figure 68-5** Inflammatory pseudotumor. A 33-year-old Chinese woman with severe hematuria and recurrence of tumor after partial resection. She subsequently had a partial cystectomy and has been tumor free for 7 years. A, Contrast-enhanced computed tomography (CT) scan in portal venous phase demonstrates a hyperdense, polypoid mass (*circle*) arising from the bladder dome. B, CT image in delayed phase demonstrates the same mass as heterogeneously hypodense. A small amount of blood clot (*oval*) from hematuria is also seen adherent to the bladder wall. Extension through the bladder wall was not present.



**Figure 68-6** Solitary fibrous tumor in a 52-year-old woman with a history of breast cancer. The mass was discovered incidentally on imaging performed for routine follow-up for breast cancer. **A**, T1-weighted precontrast fat-saturated magnetic resonance image demonstrates a wellcircumscribed, isointense to hypointense mass arising from left bladder wall (*arrow*). The mass is hypointense on the T2-weighted image (**B**) and demonstrates homogeneous enhancement on the postgadolinium fat-saturated image (**C**).

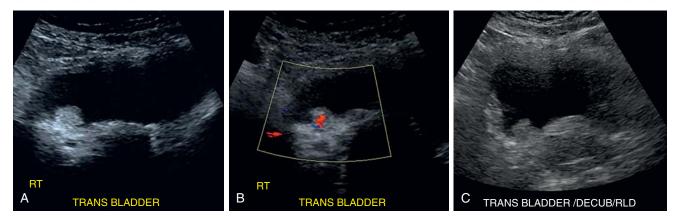


Figure 68-7 A 53-year-old woman with right flank pain. A, Ultrasound findings demonstrate a nonspecific, well-defined, isoechoic to hyperechoic mass attached to the right wall of the urinary bladder. B, On color Doppler evaluation there is flow at the base of the mass. C, Decubitus view demonstrates immobility of the mass. Histologic evaluation was consistent with an epithelial neoplasm of the bladder.

# TREATMENT

Treatment of most benign bladder tumors is surgical, often using a cystoscopic approach. However, in the case of paraganglioma, partial cystectomy is usually performed after adrenergic blockade to prevent hypertensive crisis. Adjacent lymph node dissection is also performed if there is evidence of involvement. Some patients will undergo cystoscopic surveillance, because some tumors have a tendency to recur, such as solitary fibrous tumors, in which long-term follow-up is required because 10% to 15% of these tumors can be malignant.<sup>13</sup>

#### Key Points: Benign Bladder Lesions

- Benign mesenchymal tumors of the bladder are uncommon.
- Imaging findings, although generally nonspecific, may suggest the correct diagnosis in certain cases and further guide management.

# **Malignant Bladder Lesions**

# **ETIOLOGY**

Bladder cancer accounts for 2% to 6% of all new cancers in the United States. Most bladder cancers occur in men older than 65 years of age and are associated with smoking and occupational exposure to carcinogens.<sup>30</sup> Bladder calculi, chronic infection, urinary stasis (e.g., within diverticula), arsenic in drinking water, and drugs such as phenacetin and cyclophosphamide have been linked with development of bladder cancer.<sup>31</sup>

Urothelial cancer pathogenesis is related to prolonged urothelial contact with excreted carcinogens in the urine. Tobacco smoking is considered the biggest risk factor for developing bladder carcinoma and confers a relative risk of 4 times that of the nonsmoking population. It is estimated that 50% of bladder cancers in men are related to smoking.<sup>32</sup> In addition, occupational exposure to aromatic amines in the dye industry has been proved to induce bladder cancer. Because the bladder has a proportionately higher surface area and remains in contact longer with excreted carcinogens, it is 40 times more likely to develop urothelial malignancy than the upper urinary tracts. Prolonged irritation from bladder stones and chronic infection (especially schistosomiasis) also increases risk but is more strongly associated with squamous cell bladder cancer. Drugs that have been linked with bladder cancer include phenacetin and cyclophosphamide. Although occupational exposure to aniline dyes in hair products confers increased risk, personal use of hair dye products has not been implicated.<sup>31</sup> Arsenic content in drinking water and pelvic radiation therapy for cervical carcinoma also have been linked to increased risk. Familial risk is poorly understood but likely plays a limited role, as demonstrated by twin studies and family-based population analyses.<sup>30</sup> Positive family history results in as much as a twofold risk for developing bladder cancer.<sup>33</sup>

# PREVALENCE AND EPIDEMIOLOGY

In the United States, bladder cancer is the fourth most common malignancy in males and ninth most common malignancy in females.<sup>30</sup> Approximately 77,000 new cases of bladder cancer are diagnosed each year, with a male predominance of 4:1. An estimated 16,400 deaths will be due to bladder cancer in 2016. At diagnosis, 74% of bladder cancers are localized, 19% demonstrate regional spread, and 4% present as distant metastases.<sup>34</sup>

The majority of bladder cancers occur in patients older than 65 years of age, with the peak incidence between 75 and 84 years of age. Overall, 1 in 42 (2.4%) individuals will be diagnosed with cancer of the urinary bladder during their lifetime.<sup>34</sup>

Bladder malignancies are broadly classified as primary or secondary, with primary lesions further divided by their histologic layer of origin. The overwhelming majority (95%) of malignant bladder lesions are primary malignancies that arise from the epithelium. These include urothelial carcinoma (90%), squamous cell carcinoma (2% to 15%), and adenocarcinoma (<2%).<sup>31</sup> Nonepithelial tumors comprise only 5% of bladder cancer cases and include rhabdomyosarcoma (more common in children) and leiomyosarcoma (more common in adults). Rare bladder tumors include metastases, lymphoma, pheochromocytoma, carcinosarcoma, and malignant fibrous histiocytoma.

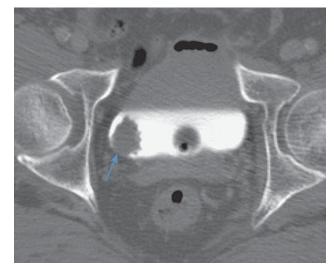
The Tumor, Node, Metastasis (TNM) staging system is widely used and based on the modified Jewett-Strong system (Table 68-1).

TABLE 68-1	American Joint Committee on Cancer Tumor, Node, Metastasis Classification of Neoplasms of the Bladder
Stage	Description
PRIMARY TUMOR (T)	
Тx	Primary tumor cannot be assessed.
TO	No evidence of primary tumor.
Та	Noninvasive papillary carcinoma.
Tis	Carcinoma in situ (i.e., flat tumor).
T1	Tumor invades subepithelial connective tissue.
T2	Tumor invades muscle.
pT2a	Tumor invades superficial muscle (inner half).
pT2b	Tumor invades deep muscle (outer half).
Т3	Tumor invades perivesical tissue.
рТЗа	Microscopically
pT3b	Macroscopically (extravesical mass)
Τ4	Tumor invades any of the following: Prostate, uterus, vagina, pelvic wall, or abdominal wall.
T4a	Tumor invades the prostate, uterus, or vagina.
T4b	Tumor invades the pelvic wall, or abdominal wall.
REGIONAL LYMPH NODES (N)	
Nx	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis.
N1	Metastasis in a single lymph node ≤2 cm in largest dimension.
N2	Metastasis in a single lymph node >2 cm but ≤5 cm in largest dimension; or multiple lymph nodes ≤5 cm in largest dimension.
N3	Metastasis in a lymph node >5 cm in largest dimension.
DISTANT METASTASIS (M)	
Mx	Distant metastasis cannot be assessed.
MO	No distant metastasis.
M1	Distant metastasis.
AJCC STAGE GROUPINGS	
Stage	0a Ta, N0, M0
Stage	Ois Tis, NO, MO
Stage	I T1, N0, M0
Stage	II T2a, N0, M0 T2b, N0, M0
Stage	III T3a, N0, M0 T3b, N0, M0 T4a, N0, M0
Stage	IV T4b, N0, M0 Any T, N1, M0 Any T, N2, M0 Any T, N3, M0 Any T, any N, M1

From Edge SB, et al: American Joint Committee on Cancer (AJCC) Cancer Staging Manual, ed 7, New York, 2010, Springer. AJCC, American Joint Committee on Cancer.

# **CLINICAL PRESENTATION**

Hematuria, either gross or microscopic, is the presenting symptom in more than 80% of cases.<sup>30</sup> Other symptoms include dysuria, increased frequency, and/or pelvic pain and pressure. Obstructive uropathy related to bladder cancer usually occurs



**Figure 68-8** Delayed-phase contrast-enhanced computed tomography image showing papillary urothelial carcinoma (*arrow*) arising from the right wall of the bladder.

in the setting of muscularis propria invasion. Typical symptoms of bladder outlet obstruction are often absent, owing to the slowly progressive nature of the tumor.

# PATHOLOGY

Urothelial carcinoma, a term now preferred over the previously used transitional cell carcinoma, accounts for over 90% of epithelial bladder malignancies.<sup>31</sup> Substantial overlap exists in the imaging characteristics of different subtypes of malignant bladder lesions. Lesions originating from the urothelium typically have a papillary or nodular appearance (Figure 68-8). They also can manifest as flat or plaque-like lesions such as squamous cell carcinoma, which tends to be more sessile rather than the typical papillary appearance of urothelial carcinoma. Alternatively, lesions that originate from the muscularis propria, such as rhabdomyosarcoma, can have a lobulated appearance sometimes referred to as "sarcoma botryoides," akin to a cluster of grapes. Urachal adenocarcinoma typically manifests as a large (mean diameter, 6 cm), often partially calcified, infraumbilical soft tissue mass with disproportionate extravesical component (Figure 68-9) compared with other bladder neoplasms.

Bladder cancer most commonly arises in the lateral bladder walls and less commonly along the trigone. The bladder dome is the least common site, except in cases of urachal carcinoma (see Figure 68-9). Bladder diverticula, when present, have a higher incidence of cancer than the remainder of the bladder, presumably owing to urinary stasis (Figure 68-10).

Pelvic lymph nodes and regional invasion are the most common manifestations of local metastatic disease, whereas the most common distant metastatic sites are lung, liver, and bone.

# IMAGING

# Urothelial Carcinoma

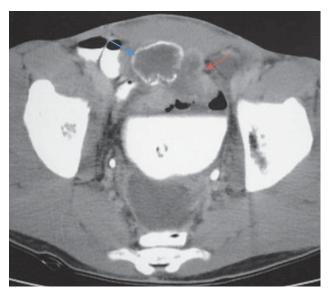
The presentation and natural course of bladder cancer is variable, ranging from superficial well-differentiated tumors with a high 5-year survival rate to aggressive lesions with transmural

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**Radiography.** Plain radiographs are nonspecific and play little role in the diagnosis of bladder cancer. Only 1% of plain radiographs demonstrate abnormal calcifications when bladder cancer is present (Figure 68-12). Although intravenous urography is sometimes used in evaluating hematuria and assessing the upper tracts for synchronous lesions in cases of diagnosed bladder cancer, multidetector CT (MDCT) urography has become the primary diagnostic modality for evaluation of the upper tracts.<sup>35</sup>

**Computed Tomography.** Urothelial carcinoma manifests as an intraluminal mass that is usually papillary or nodular (Figure 68-13). However, some tumors manifest only with wall thicken-



**Figure 68-9** Urachal carcinoma with large peripherally calcified mass (blue arrow) and disproportionate extravesical soft tissue component (red arrow) involving the bladder dome, arising from a urachal remnant. (Courtesy H. Shah, MD.)

ing that is either focal or diffuse. For adequate evaluation, the bladder must be well distended; otherwise, small, flat tumors can be easily missed. Typically, urothelial carcinoma shows enhancement approximately 60 seconds after injection of a contrast agent. As many as 5% of lesions show calcifications, usually along the surface of the lesion (Figure 68-14).<sup>31</sup> CT is widely used as a primary diagnostic and staging modality. Invasion of the perivesical fat (stage T3) can be seen as increased attenuation or haziness of the perivesical fat (Figure 68-15). It is important to note that perivesical inflammation, often related to recent transurethral biopsy, can mimic perivesical invasion and result in incorrect staging. Therefore, MDCT staging should optimally be performed at least 7 days after biopsy to improve sensitivity and specificity.<sup>36</sup>

CT virtual cystoscopy after insufflation of the bladder with carbon dioxide has been shown to be a promising technique for detecting lesions greater than 5 mm. However, the clinical utility of this technique has not yet been established.<sup>37</sup>



**Figure 68-10** Urothelial carcinoma (*M*) within a right posterolateral bladder diverticulum on unenhanced computed tomography image. Bladder malignancies are more likely to develop within diverticula owing to stasis.

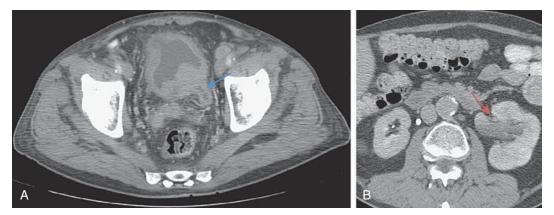


Figure 68-11 Concentric thickening of the bladder wall with focal mass involving the left bladder wall and trigone, with retrograde concentric extension along the left distal ureter (*blue arrow*, A) and resulting left hydronephrosis (*red arrow*, B).

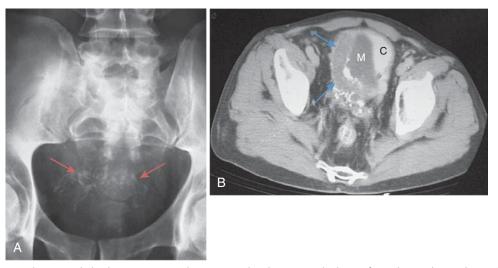


Figure 68-12 Patient with nonurachal adenocarcinoma who presented with mucous discharge from the urethra. Pelvic radiograph (A) shows stippled soft tissue calcifications (red arrows). B, Contrast-enhanced computed tomography shows a partially calcified right bladder wall mass (blue arrows) with low-attenuation mucus (M) interfaced with excreted contrast medium (C). (Courtesy H. Shah, MD.)



**Figure 68-13** Coronal reconstructed images from nonenhanced computed tomography showing multiple papillary masses within the urinary bladder. Urothelial carcinoma often manifests as multifocal lesions.

**Magnetic Resonance Imaging.** MRI also can be used for primary diagnosis or staging. It is superior to CT in detecting deep muscle layer invasion because it has superior soft tissue contrast resolution (Figures 68-16 and 68-17). Similar to CT, perivesical inflammation can be misinterpreted as tumor invasion and result in incorrect tumor staging. Detection of nodal metastases in normal-sized lymph nodes is a limitation of both CT and MRI. MRI with ferumoxtran-10, an investigational ultra-small superparamagnetic iron oxide (USPIO) imaging agent, may improve the sensitivity and specificity of MRI for



**Figure 68-14** Unenhanced computed tomography (CT) shows punctate peripheral calcifications (*arrow*) (detectable by CT in 5% of urothelial cancers) along the periphery of a papillary urothelial carcinoma arising from the right lateral wall of the bladder.

lymph node metastases.<sup>38</sup> New noninvasive imaging techniques such as virtual MRI cystography show promise in noninvasive diagnosis and follow-up of bladder tumors.<sup>39</sup> These methods, however, have not yet been adopted into everyday practice.

**Ultrasonography.** Ultrasonography is not a first-line diagnostic modality for bladder cancer. The primary utility of ultrasonography is to exclude coexisting hydronephrosis. Bladder cancer usually appears as a hypoechoic to isoechoic mass that projects into the bladder lumen. Color or power Doppler imaging can help distinguish a soft tissue mass from an intravesical blood clot (Figure 68-18).

**Nuclear Medicine.** A bone scan can be performed if osseous metastases are clinically suspected. However, in patients with normal calcium and alkaline phosphatase levels, it is not part of the routine workup.<sup>33</sup>



Figure 68-15 Irregular concentric bladder wall thickening of a known urothelial carcinoma with perivesical haziness (blue arrows) consistent with T3 disease. Also note the left hydroureter (red arrow), typically indicative of muscularis propria invasion.

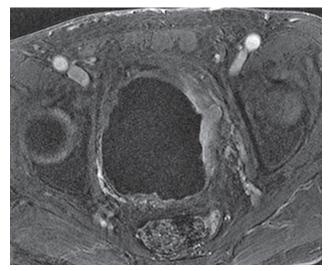


Figure 68-16 T1-weighted postgadolinium magnetic resonance image showing early enhancement of a muscle-invasive urothelial carcinoma in the left lateral wall of the bladder.

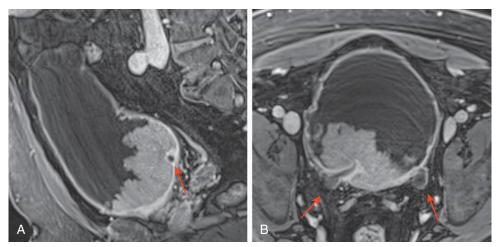


Figure 68-17 Sagittal (A) and axial (B) T1-weighted postgadolinium magnetic resonance images showing an enhancing papillary mass in the bladder neck and trigone resulting in bilateral hydroureter (arrows). Obstruction typically indicates invasion of the muscularis propria.

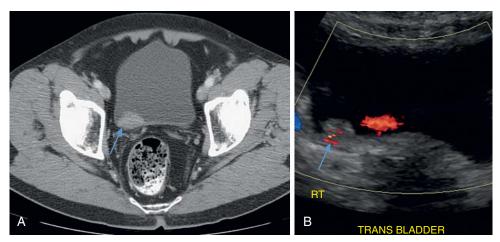


Figure 68-18 A, Contrast-enhanced computed tomography image shows an enhancing papillary mass (arrow) arising from the right base of the bladder. B, Corresponding ultrasound image of the lesion demonstrates color Doppler flow within the lesion (*arrow*). Document téléchargé de ClinicalKey.fr par Faculte de Medecine de Tunis août 30, 2016. Pour un usage personnel seulement. Aucune autre utilisation n'est autorisée. Copyright ©2016. Elsevier Inc. Tous droits réservés.

**Positron Emission Tomography With Computed Tomography.** Fluorodeoxyglucose (FDG) excreted in the urine usually obscures the primary bladder tumor, limiting the role of positron emission tomography (PET)/CT in the detection of primary lesions. However, PET/CT is useful for the detection of metastases and local recurrence. The sensitivity of fused PET/ CT for the detection of metastases is 77% in patients who had not received systemic chemotherapy but decreases to 50% in those who have received systemic chemotherapy.<sup>40</sup>

**Imaging Algorithm.** CT urography is the most appropriate initial imaging modality for the assessment of painless hematuria. Because of its limited sensitivity for the detection of flat lesions, it is typically combined with cystoscopy. Evaluation of both upper and lower urinary tracts is necessary because multicentric disease is present in up to 40% of cases.<sup>31</sup> When poor renal function precludes the intravenous use of a contrast agent, noncontrast pelvic MRI may yield useful diagnostic and staging information. CT and MRI remain the primary modalities used for staging. PET/CT and emerging techniques such as USPIO MR nodal imaging, three-dimensional ultrasonography, and virtual CT or MR cystography may improve diagnostic accuracy and could become incorporated into imaging algorithms. However, further clinical investigation is needed to establish the clinical effectiveness of these modalities.<sup>41</sup>

# OTHER TYPES OF BLADDER CANCER

#### Squamous Cell Carcinoma

Squamous cell carcinoma accounts for less than 5% of bladder cancers in the United States but occurs more frequently (up to 15%) in regions of the world where schistosomiasis is prevalent.

Mechanical irritation of the bladder urothelium plays a role, with increased risk for squamous cell bladder cancer in those with bladder stones, chronic infection, and indwelling catheters. Squamous cell carcinoma has a propensity to occur at the trigone and lateral walls and in bladder diverticula.

Squamous cell carcinoma invades the muscularis propria more readily than urothelial carcinoma (80%).<sup>31</sup> Extravesical spread is also more common in squamous cell carcinoma. Given its aggressive local behavior, radical cystectomy is typically performed.

#### Adenocarcinoma

Adenocarcinoma accounts for 2% of bladder neoplasms. Bladder adenocarcinomas can be classified as urachal or nonurachal. Both types can manifest with hematuria and/or mucus in the urine. Urachal adenocarcinoma arises from an existing urachal remnant. Umbilical discharge may be present in cases in which the urachal remnant communicates with the umbilicus. Urachal carcinomas typically manifest as a mass in the infraumbilical region. They are partially calcified in 50% to 70% of cases (see Figure 68-9).<sup>42</sup>

Nonurachal adenocarcinoma, which is more common than urachal carcinoma (2:1), manifests as diffuse (75%) or focal (25%) bladder wall thickening (see Figure 68-12). In a series of eight cases of nonurachal carcinoma described by Hughes and associates,<sup>43</sup> the mean bladder wall thickness was 1.8 cm.

#### Leiomyosarcoma

Leiomyosarcoma is the most common nonepithelial malignant bladder tumor in adults but is still rare, accounting for less than 1% of all bladder malignancies. Leiomyosarcoma has a 3:1 male predominance and occurs at a mean age of 64.<sup>44</sup> It typically manifests as hematuria, which may lead to bladder outlet obstruction. Leiomyosarcoma is usually large (mean diameter, 7 cm), high grade, and often invasive at manifestation.

MRI evaluation may demonstrate heterogeneity on both T2-weighted and postgadolinium T1-weighted imaging secondary to tumor necrosis.

#### Rhabdomyosarcoma

Rhabdomyosarcoma is more common in children, with a peak incidence at 2 to 6 years of age. As with other bladder malignancies, males are more commonly affected than females (3:1) Rhabdomyosarcoma can have a "grape-like" (sarcoma botryoides) or an infiltrative appearance (Figure 68-19). It is usually hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging with a heterogeneous enhancement.<sup>31</sup>

Local invasion may be present, and regional lymph nodes are involved in 20% of cases.<sup>45</sup> Its typical manifestation within the bladder trigone makes combined irradiation and chemotherapy a preferred treatment option over surgery. Overall prognosis is favorable, with 5-year survival rates of over 80%.<sup>46</sup>

#### Lymphoma

Primary lymphoma of the urinary bladder is exceedingly rare, with approximately 100 cases reported worldwide.<sup>47</sup> Secondary involvement of the urinary bladder is more common and seen in up to 25% of patients with lymphoma or leukemia.<sup>31</sup> Unlike the diffuse circumferential involvement of lymphoma in the gastrointestinal tract, bladder lymphoma tends to manifest as well-defined masses in the lateral walls or bladder dome (Figure 68-20). These are usually low-grade tumors with a good prognosis after chemotherapy and/or irradiation.<sup>31</sup>

#### Metastases

Metastases to the bladder are usually secondary to local invasion from cancers arising in the prostate, colon, rectum, and uterus. Other cancers that rarely metastasize to the urinary bladder include those of the breast, lung, and stomach.

# DIFFERENTIAL DIAGNOSIS

The workup of hematuria yields no identifiable cause in 60% of cases.<sup>48</sup> Although malignancy must be excluded, especially in patients older than 50 years, there are many other causes of hematuria, including urolithiasis, infection and inflammation, benign prostatic hypertrophy, trauma, medical renal disease, iatrogenic causes, coagulopathy, radiation injury, and cyclophosphamide-induced cystitis. Although multiple biomarkers are under investigation to aid in the detection of bladder cancer, gross or microscopic hematuria remains the most reliable marker and is present in more than 85% of cases.<sup>30</sup> However, because hematuria may be intermittent, it is important to note that its absence does not entirely exclude bladder cancer.

MDCT urography also can aid in detecting malignancy or another cause of hematuria elsewhere in the urinary tract.

#### TREATMENT

#### Medical Treatment

Medical treatment options consist primarily of chemotherapy for advanced disease (Figure 68-21) or intravesical

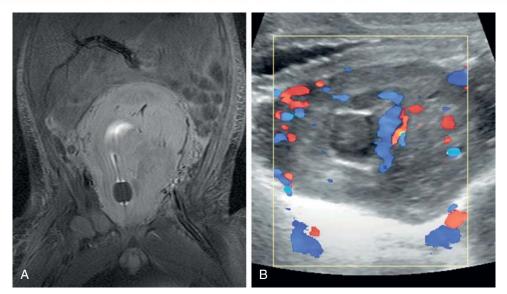


Figure 68-19 A, Rhabdomyosarcoma on delayed postgadolinium T1-weighted magnetic resonance image manifesting as a large infiltrative bladder mass with obliteration of the bladder lumen. B, Transabdominal color Doppler image shows marked vascularity of the same lesion.

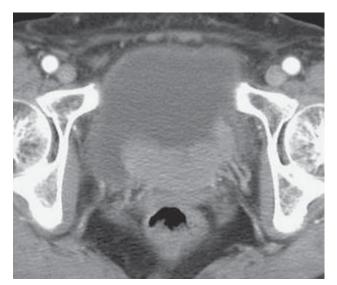
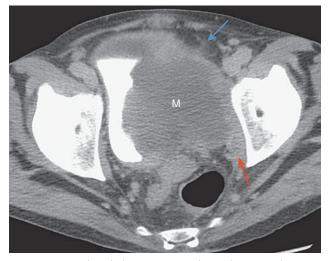


Figure 68-20 Lymphoma presenting as a well-defined mass arising from the posterolateral wall of the bladder. (Courtesy A. Garg, MD.)



**Figure 68-21** Delayed-phase contrast-enhanced computed tomography image shows a large heterogeneous mass (*M*) arising from the left wall of the bladder. This advanced urothelial carcinoma (stage T4b) shows perivesical stranding (*blue arrow*) and involvement of the left pelvic side wall (*red arrow*).

immunotherapy for superficial tumors. The mainstay of intravesical treatment is bacillus Calmette-Guérin (BCG), which is instilled into the bladder to induce a local immune response aimed at low-stage bladder carcinoma. Other intravesical immunotherapy agents include mitomycin C, doxorubicin, and interferon-alfa. Intravesical immunotherapy can be used alone or in combination with transurethral resection of the bladder tumor. Radiation therapy is employed in conjunction with chemotherapy for palliation in advanced or recurrent disease. It is also used as adjuvant therapy after surgery.<sup>49</sup>

# Surgical Treatment

Surgery remains the primary means of bladder cancer treatment. Superficial tumors are often treated with transurethral resection of the bladder tumor and followed with surveillance cystoscopy. Partial cystectomy can be performed for nonmuscle-invasive tumors confined to a single resectable area. Radical cystectomy and urinary diversion is reserved for muscleinvasive tumors. In males with muscle-invasive tumors, the prostate is usually resected along with the bladder. In females with muscle-invasive tumors, pelvic exenteration is usually performed unless the bladder base is free of disease, in which case the anterior vaginal wall and urethra are spared. After radical cystectomy, urinary reconstruction options include an ileal conduit, neobladder, or urostomy. Bilateral pelvic lymphadenectomy is usually performed with radical cystectomy, because nodal metastases are present in 25% of patients undergoing this procedure.<sup>49</sup>

#### What the Referring Physician Needs to Know

- Painless hematuria workup should include MDCT urography.
- Sixty percent of investigations of hematuria yield no identifiable cause.
- Cystoscopy with tissue biopsy is the diagnostic gold standard.
- Imaging within 1 week of transurethral resection of a bladder tumor can result in false-positive findings.

# **SUGGESTED READINGS**

Kirkali Z, Chan T, Manoharan M, et al: Bladder cancer: epidemiology, staging and grading, and diagnosis. *Urology* 66(Suppl 1):4–34, 2005. Manunta A, Vincendeau S, Kiriakou G, et al: Nontransitional cell bladder carcinomas. *BJU Int* 95:497–502, 2005.

#### REFERENCES

- 1. Murphy WM, Grignon DJ, Perlman EJ: *Tumors* of the kidney, bladder, and related urinary structures, Washington, DC, 2004, American Registry of Pathology, p 394.
- Heiken JP, McClennan BL, DiSantis DJ: Nontransitional cell tumors of the bladder. In Taveras JM, editor: *Radiology*, Philadelphia, 1993, JB Lippincott, pp 1–7.
- 3. Walker AN, Mills SE, Young RH: Mesenchymal and miscellaneous other primary tumors of the urinary bladder. In Young RH, editor: *Pathology of the urinary bladder*, New York, 1989, Churchill Livingstone, pp 139–178.
- Hahn D: Neoplasms of the urinary bladder. In Pollack HM, editor: *Clinical urology*, Philadelphia, 1990, WB Saunders, pp 1358–1380.
- Binsaleh S, Corcos J, Elhilali MM, et al: Bladder leiomyoma: report of two cases and literature review. *Can J Urol* 11:2411–2413, 2004.
- Cornella JL, Larson TR, Lee RA, et al: Leiomyoma of the female urethra and bladder: report of twenty-three patients and review of the literature. *Am J Obstet Gynecol* 176:1278– 1285, 1997.
- Melicow MM: Tumors of the urinary bladder: a clinicopathologic analysis of over 2,500 specimens and biopsies. J Urol 74:498–521, 1955.
- Hendry WF, Vinnicombe J: Hemangioma of the bladder in children and young adults. *Br J Urol* 43:309–316, 1971.
- Crecelius SA, Bellah R: Pheochromocytoma of the bladder in an adolescent: sonographic and MR imaging findings. *AJR Am J Roentgenol* 165:101–103, 1995.
- Doran F, Varinli S, Bayazit Y, et al: Pheochromocytoma of the urinary bladder. *APMIS* 110:733– 736, 2002.
- 11. Shonnard KM, Jelinek JS, Benedikt RA, et al: CT and MR of neurofibromatosis of the bladder. *J Comput Assist Tomogr* 16:433–438, 1992.
- Levy AD, Patel N, Dow N, et al: Abdominal neoplasms in patients with neurofibromatosis type 1: radiologic-pathologic correlation. *Radiographics* 25:455–480, 2005.
- Leite KR, Srougi M, Miotto A, et al: Solitary fibrous tumor in bladder wall. *Int Braz J Urol* 30:406–409, 2004.
- Knoll LD, Segura JW, Scheithauer BW: Leiomyoma of the bladder. J Urol 136:906–908, 1986.
- Maya MM, Slywotzky C: Urinary bladder leiomyoma: magnetic resonance imaging findings. Urol Radiol 14:197–199, 1992.

- Pakter R, Nussbaum A, Fishman EK: Hemangioma of the bladder: sonographic and computerized tomographic findings. *J Urol* 140:601–602, 1988.
- Roth JA: Reactive pseudosarcomatous response in the urinary bladder. *Urology* 16:635–637, 1980.
- Stark GL, Fedderson R, Lowe BA, et al: Inflammatory pseudotumor (pseudosarcoma) of the bladder. J Urol 141:610–612, 1989.
- Angulo JC, Lopez JI, Flores N: Pseudosarcomatous myofibroblastic proliferation of the bladder: report of 2 cases and literature review. *J Urol* 151:1008–1012, 1994.
- Mentzel T, Bainbridge TC, Katenkamp D: Solitary fibrous tumour: clinicopathological, immunohistochemical, and ultrastructural analysis of 12 cases arising in soft tissues, nasal cavity, and nasopharynx, urinary bladder, and prostate. *Virchows Arch* 430:445–453, 1997.
- Corti B, Carella R, Gabusi E, et al: Solitary fibrous tumour of the urinary bladder with expression of bcl-2, CD34, and insulin-like growth factor type II. *Eur Urol* 39:484–488, 2001.
- Asbury WL, Jr, Hatcher PA, Gould HR, et al: Bladder pheochromocytoma with ring calcification. *Abdom Imaging* 21:275–277, 1996.
- Sakai F, Sone S, Kiyono K, et al: Intrathoracic neurogenic tumors: MR-pathologic correlation. *AJR Am J Roentgenol* 159:279–283, 1992.
- Wilkinson LM, Manson D, Smith CR: Plexiform neurofibroma of the bladder. *Radiographics* 24(Spec issue):S237–S242, 2004.
- Sugita R, Saito M, Miura M, et al: Inflammatory pseudotumour of the bladder: CT and MRI findings. *Br J Radiol* 72:809–811, 1999.
- Sundaram CP, Rawal A, Saltzman B: Characteristics of bladder leiomyoma as noted on magnetic resonance imaging. *Urology* 52:1142–1143, 1998.
- Amano T, Kunimi K, Hisazumi H, et al: Magnetic resonance imaging of bladder hemangioma. *Abdom Imaging* 18:97–99, 1993.
- Francis IR, Korobkin M: Pheochromocytoma. Radiol Clin North Am 34:1101–1112, 1996.
- 29. Jalil ND, Pattou FN, Combemale F, et al: Effectiveness and limits of preoperative imaging studies for the localization of pheochromocytomas and paragangliomas: a review of 282 cases. French Association of Surgery (AFC), and The French Association of Endocrine Surgeons (AFCE). *Eur J Surg* 164:23–28, 1998.

# **Key Points**

- Urothelial carcinoma accounts for more than 90% of bladder malignancies.
- Smoking is the leading risk factor for bladder cancer.
- Intravenous pyelography has largely been replaced with MDCT urography.

26:553-580, 2006.

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Wong-You-Cheong JJ, Woodward PJ, Manning

MA, et al: Neoplasms of the urinary bladder:

radiologic-pathologic correlation. Radiographics

- Crawford JM: The origins of bladder cancer. Lab Invest 88:686–693, 2007.
- Wong-You-Cheong JJ, Woodward PJ, Manning MA, et al: From the archives of the AFIP: Neoplasms of the urinary bladder: Radiologicpathologic correlation. *Radiographics* 26:553– 580, 2006.
- 32. Marcus PM, Hayes RB, Vineis P, et al: Cigarette smoking, N-acetyltransferase-2 acetylation status, and bladder cancer risk: a case-series meta-analysis of a gene-environment interaction. *Cancer Epidemiol Biomarkers Prev* 9:461– 467, 2000.
- Kirkali Z, Chan T, Manoharan M, et al: Bladder cancer: epidemiology, staging and grading, and diagnosis. Urology 66(Suppl 1):4–34, 2005.
- Ries L, et al: SEER stat fact sheets: cancer of the urinary bladder. Available at <<u>http://</u> seer.cancer.gov/statfacts/html/urinb.html>, (Accessed 09.09.08.)
- Anderson EM, Murphy R, Rennie AT, et al: Multidetector computed tomography urography (MDCTU) for diagnosing urothelial malignancy. *Clin Radiol* 62:324–332, 2007.
- 36. Kim JK, Park SY, Ahn HJ, et al: Bladder cancer: analysis of multi-detector row helical CT enhancement pattern and accuracy in tumor detection and perivesical staging. *Radiology* 231:725–731, 2004.
- Song JH, Francis IR, Platt JF, et al: Bladder tumor detection at virtual cystoscopy. *Radiology* 218:95–100, 2001.
- Deserno WM, Harisinghani MG, Taupitz M, et al: Urinary bladder cancer: preoperative nodal staging with ferumoxtran-10-enhanced MR imaging. *Radiology* 233:449–456, 2004.
- Beer A, Saar B, Zantl N, et al: MR cystography for bladder tumor detection. *Eur Radiol* 14:2311–2319, 2004.
- Bouchelouche K, Oehr P: Positron emission tomography and positron emission tomography/ computerized tomography of urological malignancies: an update review. J Urol 179:34–45, 2008.
- Saksena MA, Dahl DM, Harisinghani MG: New imaging modalities in bladder cancer. World J Urol 24:473–480, 2006.
- 42. Yu J, Kim KW, Lee H, et al: Urachal remnant diseases: spectrum of CT and US findings. *Radiographics* 21:451–461, 2001.
- 43. Hughes MJ, Fisher C, Sohaib SAA: Imaging features of primary nonurachal adenocarcinoma

- 44. Martin SA, Sears DL, Sebo TJ, et al: Smooth muscle neoplasms of the urinary bladder: a clinicopathologic comparison of leiomyoma and leiomyosarcoma. *Am J Surg Pathol* 26:292– 300, 2002.
- Castellino SM, McLean TW: Pediatric genitourinary tumors. *Curr Opin Oncol* 19:248–253, 2007.
   Lott S, Lopez-Beltran A, Montironi R, et al: Soft
- tissue tumors of the urinary bladder. II. Malignant neoplasms. *Hum Pathol* 38:963–977, 2007.
- 47. Tasu JP, Geffroy D, Rocher L, et al: Primary malignant lymphoma of the urinary bladder:

report of three cases and review of the literature. *Eur Radiol* 10:1261–1264, 2000.

- 48. Bryant RJ, Catto JWF: Haematuria. Surgery 26:150–153, 2008.
- 49. Legg JS: Bladder cancer imaging. *Radiol Technol* 79:333–346, 2008.

# **Urinary Tract Anomalies and Variants**

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# Etiology

Urinary tract anomalies encompass a wide range of abnormalities from the multiple varied components of the urinary tract the renal parenchyma, the collecting system, the bladder, the urethra, and the vasculature. Anomalies result from alterations in the normal embryologic development of the urinary system. Detecting these anomalies requires an understanding of the embryologic development of the urinary system.

# **Prevalence and Epidemiology**

Overall, it is estimated that congenital anomalies of the kidney and urinary tract occur in approximately 1 in every 500 newborns and account for 20% to 30% of all anomalies in the prenatal period.<sup>1</sup> Many of these anomalies manifest during fetal development, carrying risks to the fetus, and are detected at routine ultrasound screening during pregnancy. However, some are detected decades later as physical ailments related to the urinary system or incidentally during imaging performed for other purposes. Congenital anomalies of the urinary tract are a major cause of renal failure in infants<sup>2</sup> and a cause of hypertension and cardiovascular disease in adults.

# Normal Anatomy

Urinary tract development begins at the 4th gestational week when the intermediate mesoderm separates into three parts: pronephros, mesonephros, and metanephros. In the cervical region these nephrotomes form the pronephros, a rudimentary urinary system that regresses before birth. The second segmented portion becomes the mesonephros, which gives rise to the ureteral bud that becomes the renal collecting system. The third segmented portion is the metanephros, which becomes the permanent kidney.

At the 5th week of gestation, the ureteral bud, arising from the mesonephros, penetrates the adjacent metanephros and dilates, forming the renal pelvis. Subsequently, it divides into cranial and caudal portions, becoming the major calyces. These calyces continue to subdivide, forming the minor calyces, the renal pyramids, and the 1 to 3 million collecting tubules.

The metanephros, stimulated by the penetration of the ureteral bud, develops into nephrons. Portions of these nephrons lengthen and become the proximal convoluted tubules, the loop of Henle, and the distal convoluted tubules. The metanephric tissue eventually migrates craniad and is positioned in the retroperitoneal space in the upper lumbar native position of the kidneys.

The distal portion of the mesodermal tissue becomes the posterior wall of the bladder, including the trigone and bladder

neck. The ventral cloaca develops into the urogenital sinus, which eventually becomes the remaining portions of the bladder and urethra.

During embryologic development, multiple renal arteries are created as lateral intersegmental arteries arising from the mesonephros. As the kidneys migrate craniad, the lower arteries regress. The final, definitive renal artery comes from the artery originally supplying the adrenal glands.

# **Specific Lesions**

To organize the numerous and varied congenital anomalies of the urinary tract, the entities have been organized under subcomponents of the urinary tract system: the renal parenchyma, collecting system, bladder, urethra, and renal vasculature.

# **RENAL PARENCHYMA**

Anomalies of the renal parenchyma are organized into the following major categories: renal agenesis, renal hypoplasia, renal dysmorphisms, anomalies of renal ascent, and renal fusion anomalies.

#### Renal Agenesis

Unilateral regional agenesis occurs in approximately 1 in 5000 newborns. Bilateral renal agenesis occurs in 1 in 30,000 newborns.<sup>1</sup>

**Pathophysiology.** On a molecular scale, renal agenesis has been linked to the failure of glial-derived neurotropic factor. Embryologically, renal agenesis occurs because of early degeneration of the ureteral bud, which fails to reach the metanephric tissue cap. Bilateral regional agenesis appears to have a genetic cause and is twice as common in males as in females.

**Clinical Presentation.** Bilateral renal agenesis is rare. Bilateral renal agenesis was described by Edith Potter in 1946 and is a component of Potter's syndrome, in which there is oligohy-dramnios or anhydramnios (absent amniotic fluid) owing to a renal developmental abnormality. It is suspected clinically with oligohydramnios as a result of inability for the fetus to excrete the swallowed amniotic fluid. Although the fetus will survive gestation because the kidneys are not necessary for exchange of waste products, bilateral renal agenesis is incompatible with life after birth and typically the neonate will die within a few days. Unilateral renal agenesis may remain undetected if there is normal renal function.

**Imaging.** Bilateral renal agenesis is detected on screening pregnancy ultrasonography as oligohydramnios and nonvisualization of the kidneys. Unilateral renal agenesis is visualized as absence of one kidney in either the native retroperitoneal location or in the pelvis.

Unilateral renal agenesis typically is incidentally visualized on computed tomography (CT) or magnetic resonance imaging (MRI) as absence of one kidney (Figure 69-1). Often there is compensatory enlargement of the solitary kidney.

**Treatment.** Bilateral renal agenesis is incompatible with life. Unilateral renal agenesis requires no treatment owing to compensatory hypertrophy of the solitary kidney. In patients who have poor renal function, dialysis may be necessary.

#### Renal Hypoplasia

In the U.S. Renal Data System all hypoplasias and dysplasias, reported in a single category, account for 8.9% of pediatric patients presenting with end-stage renal disease. The size of the kidneys depends on the number of nephrons created during embryologic development. The average number of nephrons ranges from 300,000 to 1 million in each kidney.<sup>3</sup>

**Pathophysiology.** The most common cause of renal hypoplasia is defective ureteral branching in embryologic life. Other factors implicated include nutrition during pregnancy and genetic factors.

**Clinical Presentation.** There may be no clinical manifestations of the disease, and renal hypoplasia may be detected incidentally as a decrease in the size of one or both kidneys. However, patients with renal hypoplasia are at risk for developing primary hypertension. These patients are reported to have 46% fewer



**Figure 69-1** Coronal reformatted computed tomography image shows left renal agenesis and compensatory hypertrophy of the right kidney.

glomeruli than normal individuals<sup>4</sup> and are at risk for chronic renal failure. Patients can present with anorexia, vomiting, and failure to thrive and also with short stature, polyuria, polydipsia, and proteinuria.

**Imaging.** On ultrasonography, CT, or MRI, renal hypoplasia is visualized as a decrease in the size of kidneys.

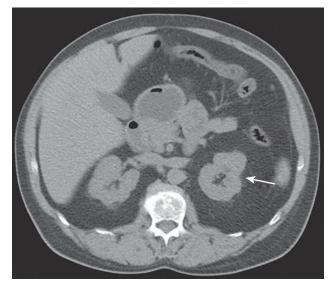
**Treatment.** There is no specific treatment. Patients with renal failure may consider dialysis. Primary hypertension is treated with medication.

#### Renal Dysmorphisms

Renal dysmorphisms include a wide variation of anomalies of the renal cortical contour. Documented dysmorphisms include persistent fetal lobulation, junctional parenchymal defect, dromedary hump, septum of Bertin, aberrant papilla, and sinus lipomatosis. Renal dysmorphisms occur secondary to embryologic developmental anomalies of the metanephros. Many of these dysmorphisms are seen as variants in the appearance of the kidney.

**Persistent Fetal Lobulation.** Persistent fetal lobulation is the result of fetal lobulation that persists into adulthood. Typically, the fetal kidneys are subdivided into lobes by grooves that disappear by the end of the fetal period. This anomaly is discovered incidentally and carries no clinical significance. It is important in imaging to distinguish between lobulation and scarring, which can occur from reflux or chronic infection. Lobulation can be seen on CT or ultrasonography as indentations that occur between the medullary pyramids (Figure 69-2).

**Junctional Parenchymal Defect.** Junctional parenchymal defect is a fusion defect in the upper pole of the kidney. It is the result of partial fusion of the embryonic renal parenchyma. The incomplete fusion occurs at the junction of the fusing parenchyma.<sup>5</sup> This disorder has no clinical significance. It can be confused with a renal scar or laceration. It typically appears as



**Figure 69-2** Noncontrast axial computed tomography image shows soft tissue prominence from the left lateral renal cortex (*arrow*). Findings are consistent with those of fetal lobulation.

an echogenic linear defect on ultrasound that extends from the renal sinuses to the cortex (Figure 69-3, A). On CT it is seen as a defect extending to the renal sinus (see Figure 69-3, B).

**Dromedary Hump.** Dromedary hump represents prominence of the cortical parenchyma, typically of the left kidney, owing to the compression from the adjacent spleen. It has no clinical significance and should not be confused with a solid renal tumor. On ultrasonography, CT, and MRI, dromedary hump is seen as a focal bulge arising from the lateral cortex of the left kidney (Figure 69-4).

**Septum of Bertin.** The septum of Bertin is a normal variant that represents hypertrophied cortical tissue between the medullary pyramids that projects into the renal sinus. It carries no clinical significance. However, it can occasionally be confused with a solid renal tumor.

Septum of Bertin often occurs in the middle third of the kidney and more commonly on the left. On ultrasonography it is seen as cortical tissue indenting the renal sinuses. Although typically similar to the renal cortex in echogenicity, it is also reported to be more echogenic than the renal cortex.<sup>6</sup> On CT and MRI, it is seen as a portion of the cortex indenting into the renal sinuses and enhancing similar to the cortex.

**Lobar Dysmorphism.** Lobar dysmorphism represents a pseudotumor in the central kidney resulting from anomalous embryologic development. It is distinguished from the septum of Bertin by the finding of calyx in the central portion of the mass, reflecting a complete renal lobe rather than cortical tissue positioned in the central kidney.<sup>7</sup> This anomaly has no clinical significance and should not be confused with a renal tumor.

On ultrasonography, lobar dysmorphism is seen as a central mass that can be difficult to distinguish from a renal tumor or septum of Bertin. Cortical and nephrographic contrastenhanced CT can distinguish this central mass from septum of Bertin by the finding of a small central collecting calyx in the mass.

**Aberrant Papilla.** An aberrant papilla is an otherwise normal papilla that projects into the lumen of the renal infundibulum or renal pelvis. It results during embryologic development from a shortened minor calyx.<sup>8</sup> This anomaly has no clinical significance and should not be confused with a collecting system tumor.

On excretory phase CT, an aberrant papilla is seen as a small filling defect that projects into the renal calyx (Figure 69-5). It typically has a broad base, and the tip is smooth and conical. It has a similar appearance on intravenous pyelography (IVP).

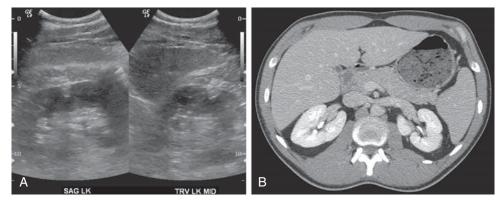
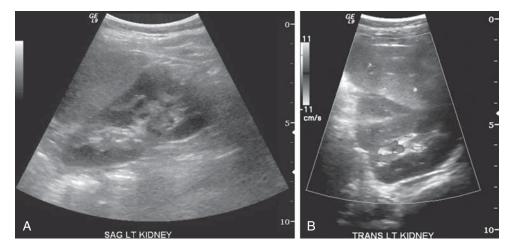
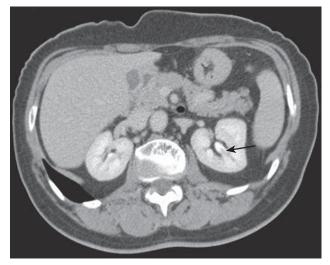


Figure 69-3 A, Sagittal and transverse ultrasound images showed an echogenic band in the renal cortex that does not appear to extend to the renal sinus. B, Axial computed tomography image confirmed extension to the renal sinus consistent with a junctional parenchymal defect.



**Figure 69-4** A, Sagittal ultrasound image shows classic bulge arising from the lateral cortex of the left kidney consistent with a dromedary hump. B, Transverse ultrasound image of the left kidney shows a dromedary hump and its relation to the adjacent spleen.



**Figure 69-5** Delayed-phase contrast-enhanced computed tomography scan shows aberrant papilla with small oval defect with broad base (*arrow*) arising from the base of an upper pole minor calyx in the left kidney.

**Sinus Lipomatosis.** Sinus lipomatosis represents an abundance of fat in the renal sinuses. It is typically associated with parenchymal atrophy from severe renal infection or vascular ischemia. It also can be seen in patients who have increased endogenous steroids or who take exogenous steroids. It has no clinical significance and typically does not cause calyceal obstruction. It should be distinguished from fat-containing neoplasms in the renal sinuses.

On imaging, sinus lipomatosis is visualized as increased central renal fat. On ultrasonography it is seen as increased echogenicity, and on CT it is visualized as increased fat density adjacent to the central renal collecting system (Figure 69-6).

#### Anomalies of Ascent

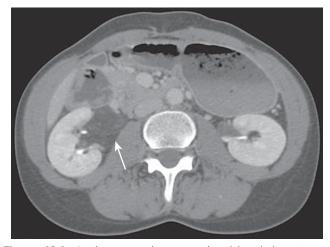
**Pelvic Kidney.** One or both kidneys can be positioned in the pelvis remote from their expected anatomic location in the upper retroperitoneum. The incidence of pelvic kidney is 1 in 725 births.<sup>9</sup>

**Pathophysiology.** After the kidney forms in the pelvis from the metanephric tissue, it ascends to a more cranial position in the abdomen because of a decrease in the body curvature as well as growth of the lumbar and sacral regions.<sup>3</sup> Interruptions in this ascent may occur at the level of the arterial fork formed by the umbilical arteries. Failure to pass this area can result in a kidney close to the common iliac artery and consistent with a pelvic kidney. Pelvic kidney is associated with vesicoureteral reflux, hydronephrosis, hypospadias, and contralateral renal agenesis.

*Imaging.* On ultrasonography, CT, and MRI there is absence of the kidney in its native upper retroperitoneal location. The kidney can be found in the pelvis and its vascular supply identified arising from the iliac vessels (Figure 69-7). Pelvic kidneys may occasionally be mistaken for pelvic adenopathy.

#### **Renal Fusion Anomalies**

**Crossed-Fused Ectopia.** Kidneys are positioned both on the same side with crossing of the ureters. Usually they are fused,



**Figure 69-6** Axial computed tomography delayed-phase image shows fat density near the right renal hilum (*arrow*) consistent with sinus lipomatosis.

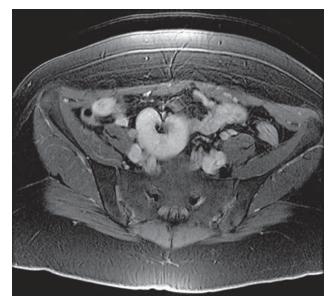


Figure 69-7 T1-weighted, fat-saturated, contrast-enhanced axial magnetic resonance image of the pelvis confirms a pelvic right kidney.

but they can occasionally be separate. This anomaly occurs more often on the left than on the right. Renal fusion, ectopia, and rotation anomalies occur in 1 in 500 births.

# PATHOPHYSIOLOGY

Crossed ectopia or crossed-fused ectopia is believed to occur because of abnormal growth of the ureteral bud, resulting in failure of the nephrogenic cell masses to separate.

# CLINICAL PRESENTATION

This disorder may be asymptomatic. Associated clinical findings may not be detected until later in life and include obstructive uropathy, infection, and reflux.



**Figure 69-8** Axial computed tomography image shows fused kidney to the right of midline (*arrow*) consistent with crossed-fused ectopia.

# IMAGING

Imaging will show both kidneys in the same side of the abdomen (Figure 69-8). They can be fused. Typically, the abnormally placed kidney will have a ureter that crosses to the correct side.

**Pancake Kidney.** A pancake kidney is a fusion anomaly in which the upper and lower poles fuse and the resulting fusion is ring-like. It is also known as a disc kidney or doughnut kidney.

# PATHOPHYSIOLOGY

Pancake kidney is caused by failure of the metanephric tissues to separate.

# **CLINICAL PRESENTATION**

Most patients have no symptoms. When present, symptoms may be secondary to hydronephrosis, infection, stone formation, or hematuria.

# IMAGING

CT and MRI can show the fused disc-shaped kidney (Figure 69-9).

# Horseshoe Kidney

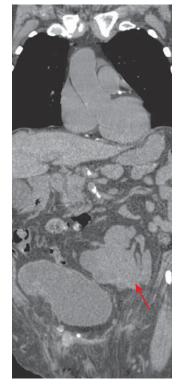
A horseshoe kidney is fusion of the lower pole of both kidneys. It occurs in 1 in 600 individuals and is slightly more common in females.

# PATHOPHYSIOLOGY

The kidneys cease embryologic ascent at the root of the inferior mesenteric artery, and the lower poles are pushed together, causing them to fuse.

# **CLINICAL PRESENTATION**

Clinically, patients may have other congenital anomalies, including cardiac and skeletal disorders and trisomy 18 and Turner's



**Figure 69-9** Coronal reformatted computed tomography image shows disc-shaped fused kidneys (*arrow*) consistent with a pancake kidney.

syndrome. Individuals with horseshoe kidney are at increased risk for developing ureteropelvic junction (UPJ) obstruction and urinary tract stones. There is also a slight increased risk for Wilms' tumor and carcinoid.<sup>10</sup> The incidence of renal cell carcinoma is the same as for individuals with normal kidneys.

## IMAGING

On imaging the kidney can be seen to have medially oriented lower poles fused underneath the inferior mesenteric artery (Figure 69-10). The renal pelvis and ureters of both kidneys are positioned anteriorly.

#### TREATMENT

Treatment is based on the management of complications of the horseshoe kidney, including surgical management of UPJ obstruction with pyeloureteroplasty and management of stone disease with lithotripsy or surgery.<sup>11</sup>

# Multicystic Dysplastic Kidneys

Cystic dilation of the collecting tubules can occur in the renal cortex. It is the most common cause of cystic disease in infants and the second most common cause of an abdominal mass in a neonate. It occurs in 1 in 2400 live births and is slightly more common in males. The condition may be unilateral or bilateral and is detected prenatally in almost 90% of cases. When unilateral, the rate of associated malformation or syndrome is 16%. If bilateral multicystic dysplastic kidneys are present, there is a higher rate of associated syndrome or malformation, and only one third of those affected are liveborn.<sup>12</sup>

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**Figure 69-10** Axial contrast-enhanced computed tomography scan shows classic horseshoe kidney with fusion of both lower poles across midline.

### PATHOPHYSIOLOGY

Collecting tubules of the kidneys enlarge into cysts secondary to obstruction or atresia of the ureteral bud before 8 to 10 weeks of fetal life. The anomaly is most commonly unilateral but can be segmental or bilateral. The following two types have been described:

- *Potter IIa:* Multicystic kidney seen as a large kidney with multiple large cysts
- Potter IIb: Small kidneys

# **CLINICAL PRESENTATION**

Clinically, infants can present with a large abdominal mass. If the disorder is bilateral, infants can die of pulmonary hypoplasia. Occasionally, if unilateral, the kidneys can remain undetected until adulthood, at which time they can manifest with intermittent abdominal pain, hematuria, or recurrent urinary tract infections (UTIs).

# IMAGING

On ultrasonography multiple cysts of various shapes and sizes are seen (Figure 69-11) in Potter IIa disease. The largest cysts are peripherally oriented with replacement of the normal renal architecture. In Potter IIB disease the kidneys are small and echogenic.

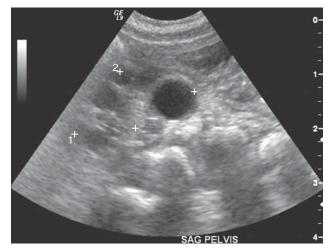
#### TREATMENT

There is no specific treatment. Surgery is indicated in patients who have symptomatic disease with hypertension, mass effect, pain, or infection.

# COLLECTING SYSTEM

#### Ureteropelvic Junction Obstruction

UPJ obstruction is the most common cause of a palpable abdominal mass in a neonate.  $^{\rm 13,14}$ 



**Figure 69-11** Sagittal ultrasound image shows a small echogenic kidney with a peripherally oriented cyst in an infant with proven multi-cystic dysplastic kidney.

**Pathophysiology.** There are many potential causes for UPJ obstruction, including ureteral hypoplasia, abnormal insertion of the ureter into the renal pelvis, anomalous crossing vessels, and renal ectopy. UPJ obstruction also may develop later in life secondary to stenosis or scarring from stones, infection, or instrumentation.

**Clinical Presentation.** Neonates will present with hydronephrosis. Children also can present with recurrent UTIs and flank pain.

**Imaging.** Ultrasonography can identify the dilated renal pelvis. IVP and retrograde ureteral pyelography can show the anatomic relationship of the renal pelvis and ureter. CT with reformatted imaging also can accurately depict the anatomy of the renal collecting system and the surrounding structures (Figure 69-12).

**Treatment.** If obstruction is incomplete, children and adults can be monitored with serial imaging. In patients with symptoms and/or complete obstruction, surgical intervention is required, including antegrade or retrograde endopyelotomy or pyeloplasty.

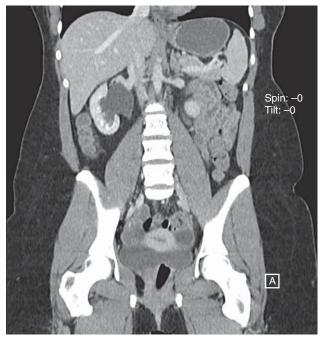
#### Primary Vesicoureteral Reflux

Vesicoureteral reflux is abnormal flow from a urine-filled bladder into the upper urinary tract.

**Pathophysiology.** Vesicoureteral reflux is a result of a primary maturation abnormality of the vesicoureteral junction (VUJ) or a very short distal ureteral submucosal tunnel that alters the normal valve mechanism.<sup>15</sup>

**Clinical Presentation.** Vesicoureteral reflux can result in pyelonephritis and resultant renal parenchymal scarring. The reflux carries bacteria from the bladder to the upper urinary tract.

**Imaging.** Voiding cystourethrography (VCUG) is the primary diagnostic study for vesicoureteral reflux (Figure 69-13). It is typically performed after the first documented UTI in a neonate.



**Figure 69-12** Coronal reformatted computed tomography image shows a dilated right renal pelvis with abrupt narrowing at the ureteropelvic junction consistent with ureteropelvic junction obstruction.

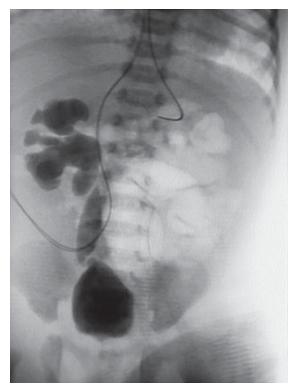


Figure 69-13 Voiding cystourethrography study shows severe reflux into the right renal collecting system.

Alternatively, nuclear cystography may be used to assess the degree of reflux. The degree of reflux as measured on nuclear cystography is less precise and can only determine whether there is mild, moderate, or severe reflux. The advantage of nuclear cystography is a low radiation dose. The disadvantage is the poor spatial resolution and the inability to assess associated bladder disease such as bladder diverticula and the inability to visualize the male urethra.

Although postnatal ultrasonography may not directly visualize vesicoureteral reflux, secondary findings may be seen, including hydronephrosis and thickening of the wall of the renal collecting system.

**Treatment.** Treatment is initially medical and includes the administration of antibiotics, vigorous hydration, and frequent bladder emptying to decrease the risk for UTIs. If these methods fail and there is persistent, severe reflux, surgical intervention may be necessary, including ureteral reimplantation and endoscopic treatments.

#### Megaureter

Megaureter in children is defined as a distal ureter measuring greater than 7 mm in diameter. It may be primary or secondary. There are three major categories of primary megaureter: obstructed primary megaureter, refluxing primary megaureter, and nonrefluxing unobstructed primary megaureter. Secondary megaureter is a result of a bladder or urethral abnormality, including urethral valves, idiopathic bladder dysfunction, urethral stricture, or ureterocele. Primary megaureter more often occurs in males and is more common on the left.

**Pathophysiology.** In obstructed primary megaureter there is aperistalsis, possibly the result of either a paucity of ganglion cells in the connective tissue that surrounds the ureter or muscular derangements and increased interstitial connective tissue in the nondilated terminal ureteral segment.<sup>16</sup>

In refluxing primary megaureter there is an abnormality of the VUJ, including a short or absent intravesical ureter or a paraureteral diverticulum.

In nonrefluxing unobstructed primary megaureter there is dilation of the ureter just above the bladder with no evidence of reflux or VUJ stenosis. This is the most common cause of primary megaureter in neonates.

**Clinical Presentation.** Most megaureters are asymptomatic and are found incidentally on imaging. When present, symptoms are those of urinary obstruction and its complications and include abdominal pain, abdominal mass, hematuria, and signs of infection.

**Imaging.** On prenatal screening ultrasonography, megaureter may be detected as hydroureteronephrosis with dilation of the urinary collecting system. Ultrasonography can show peristaltic waves in the dilated ureter down to the narrowed segment. Once this finding is confirmed, megaureter is classified into primary or secondary with VCUG (Figure 69-14). In secondary megaureter, vesicoureteral reflux will be visualized. In primary megaureter, VCUG will demonstrate no evidence of a vesicoureteral reflux.

Diuresis renography is a radioisotope study that is used to determine whether there is a functionally obstructive megaureter that requires surgical treatment versus a variant in



**Figure 69-14** Voiding cystourethrography study shows a dilated left ureter with normal calyx, findings consistent with secondary megaureter as a result of reflux.



Figure 69-15 Intravenous pyelogram shows enlarged dilated calyces in the right kidney, a finding consistent with congenital megacalyces.

normal ureteral anatomy that initially can be treated conservatively.

**Treatment.** Treatment includes antibiotics and close imaging surveillance. In patients with severe reflux or obstruction, ure-teral reimplantation is the treatment of choice.

# **Congenital Megacalyces**

Enlarged calyces are due to hypoplasia of the medullary pyramids.

**Pathophysiology.** Embryologic hypoplasia of the medullary pyramids leads to enlargement of the renal calyces.

**Clinical Presentation.** The enlarged calyces can lead to infections and stone formation. This anomaly has also been associated with primary megaureter.<sup>17</sup>

**Imaging.** IVP, ultrasonography, and CT show enlarged calyces with normal renal pelvis and ureters. The calyces have a convex, blunted juxtapapillary border (Figure 69-15).

**Treatment.** There is no specific treatment except for management of the infection and stone disease.

#### Infundibulopelvic Dysgenesis

Infundibulopelvic dysgenesis is an obstructive process of the pyelocalyceal system that can lead to other congenital disorders,

including hydrocalycosis, calyceal diverticula, UPJ stenosis, and multicystic kidney.

### **Bifid Renal Pelvis**

Duplication of the renal pelvis is part of a spectrum of congenital anomalies extending from bifid renal pelvis to complete ureteral duplication.

**Pathophysiology.** Premature branching of the ureteral buds may occur in embryologic life.

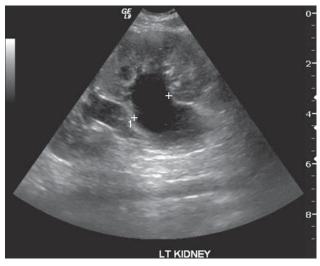
**Clinical Presentation.** Patients may be asymptomatic or present with recurrent UTIs.

**Imaging.** On ultrasonography and CT the separate collecting systems can be visualized (Figure 69-16).

## Ureteral Duplication

Partial or complete duplication of the ureter can occur. Typically, the duplication occurs in the proximal collecting system. In partial duplication the ureters unite before entering the bladder. In complete duplication the ureters remain separate and follow the Weigert-Meyer rule: the upper pole moiety inserts into the bladder medially and inferiorly to the insertion of the lower pole moiety. Ureteral duplication occurs in 0.2% of live births.

**Pathophysiology.** Partial or complete ureteral duplication is due to early splitting of the ureteral bud. Depending on the age and degree of splitting, it also can result in division of the



**Figure 69-16** Sagittal ultrasound image shows two separate renal collecting systems consistent with a bifid renal pelvis. The diameter of the larger moiety is measured here with calipers.

metanephric tissue with creation of two completely separate renal pelves and ureters.

**Clinical Presentation.** The patient may be asymptomatic or may present with reflux, UTIs, or stone disease.

**Imaging.** IVP and delayed-phase contrast-enhanced CT can identify the location and extent of duplication (Figure 69-17). MRI, particularly MR urography, is useful in children.

# Pyelocalyceal Diverticulum

A small outpouching of the renal collecting system that typically arises from a minor calyx but also can arise from a major calyx or the renal pelvis is called a pyelocalyceal diverticulum.

**Clinical Presentation.** Most of these lesions are asymptomatic. Occasionally, stasis may result in infection, stone formation, flank pain, or hematuria.

**Imaging.** On ultrasonography a pyelocalyceal diverticulum may be seen as a cystlike structure in the renal cortex.<sup>18</sup> Echogenic material in the cyst can represent layering milk of calcium. Contrast-enhanced CT can confirm communication with the calyx.

**Treatment.** Treatment is indicated only in patients who have symptoms secondary to stones that have formed in the diverticulum.

#### **Ectopic Ureter**

Ectopic insertion of the ureter can occur either in association with a complete ureteral duplication (70%) or in isolation. In females, the ectopic ureter can insert into the lower bladder, urethra, vestibule, or vagina. In males, the ectopic ureter can insert into the posterior urethra, seminal vesicle, vas deferens, or ejaculatory duct. In very rare cases the ectopic ureter can insert into the rectum. When there is complete ureteral duplication with an ectopic ureter, the Weigert-Meyer rule applies: the upper pole moiety inserts into the bladder medially and inferiorly to the lower pole moiety.



**Figure 69-17** Coronal volume-rendered computed tomography image of the renal collecting system shows left ureteral duplication. The lower pelvis is dilated, likely secondary to reflux.

**Pathophysiology.** Ectopic ureter results from abnormal ureteral bud migration. Often this occurs because the ureteral bud fails to separate the wolffian duct and is carried caudad.

**Clinical Presentation.** The classic history is a continuous dribbling incontinence despite a normal voiding pattern.<sup>19</sup>

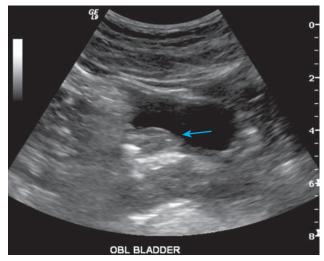
**Imaging.** Screening ultrasonography may detect a duplex kidney with obstruction of the upper pole moiety. Occasionally, the dilated ureter may be traced into the pelvis and its abnormal insertion identified. If there is no duplication, the involved kidney may be small and dysplastic and may not be visible on ultrasonography.

Intravenous urography occasionally may be used to trace the ectopic insertion of the ureter. Renal scintigraphy can be used to assess the renal function in a patient with an ectopic ureter. CT may be used to locate the small dysplastic kidney and also can identify a duplicate collecting system with abnormal insertion of the ectopic ureter. MR urography can demonstrate ectopic ureters, dilated collecting systems, and ureteroceles and can better identify cases of extravesical ureteral insertion than ultrasonography and intravenous urography.

#### Ureterocele

Ureteroceles are cystic dilations of the distal ureter extending into the bladder. Of patients with a ureterocele, 75% have ureteral duplication.<sup>20</sup>

**Pathophysiology.** Obstruction of the ureteral meatus can result in dilation of the distal ureter, causing a ureterocele. The



**Figure 69-18** Transverse ultrasound image of the bladder shows a filling defect (*arrow*) in the region of the right ureteral orifice consistent with a right ureterocele.

obstruction may be congenital or secondary to inflammation. Congenital obstruction is secondary to persistence of a membrane (i.e., the Chwalla membrane) between the mesonephric duct and the urogenital bud.

**Imaging.** On ultrasonography, a ureterocele is identified as a cystic intravesical mass contiguous with the distal ureter. The wall of the ureterocele may be visualized as a rounded echogenic structure near the trigone (Figure 69-18).

On VCUG, a ureterocele is identified as a rounded filling defect in the bladder.

On intravenous urography, contrast material in the ureterocele can demonstrate the classic "cobra head" appearance produced by contrast agent in the distal ureter surrounded by the radiolucent halo of the wall of the ureterocele.

#### **Retrocaval Ureter**

Retrocaval ureter is a rare anomaly in which the ureter is S-shaped and courses behind the inferior vena cava.<sup>21</sup>

**Pathophysiology.** Retrocaval ureter arises from persistence of the posterior cardinal veins during embryologic development.

**Clinical Presentation.** Typically, patients are asymptomatic, but retrocaval ureter has been reported to be a cause of urinary tract obstruction.<sup>22</sup>

**Imaging.** On IVP and retrograde pyelography, the ureter takes an S-shaped course. CT can trace the course of the ureter behind the inferior vena cava (Figure 69-19).

**Treatment.** Retrocaval ureter generally does not require treatment. If obstruction is present, pyeloplasty or ureteroureterostomy can be performed.

# Ureteral Diverticulum

Ureteral diverticulum is a rare anomaly in which there is outpouching of the ureter. Most ureteral diverticula occur at the ureterovesical junction.



**Figure 69-19** Axial computed tomography image shows the classic S-shaped configuration of a retrocaval ureter extending behind the inferior vena cava.

**Pathophysiology.** Potential causes include chronic infection, reflux, or stones<sup>23</sup> and an overextended bifid renal pelvis.<sup>24</sup>

**Clinical Presentation.** Patients may present with recurrent UTIs.

**Imaging.** On IVP or delayed-phase contrast-enhanced CT, diverticula can fill with contrast or can be seen as a small outpouching.

#### Ureteral Pseudodiverticulosis

In this anomaly, multiple outpouchings less than 4 mm are typically found in the upper and middle two thirds of the ureter.

**Pathophysiology.** The cause is not known. Pseudodiverticula are mucosal outpouchings that originate through weak spots in the ureteral wall where the arteries pierce the muscle layer.<sup>25</sup>

**Clinical Presentation.** No specific clinical symptoms are noted, although patients are at increased risk for developing transitional cell carcinoma.

**Imaging.** On IVP and retrograde pyelography, multiple small outpouchings (1 to 3 mm) can be seen.

**Treatment.** Urine cytologic examination and imaging surveillance for transitional cell carcinoma are performed.

# Medullary Sponge Kidney (Benign Renal Tubular Ectasia)

Medullary sponge kidney is a developmental anomaly with cystic dilation of the collecting tubules in the renal pyramids.<sup>26</sup> It is noted in 0.5% of individuals examined with intravenous urography.

**Pathophysiology.** Medullary sponge kidney is believed to be secondary to hyperplasia of the renal collecting tubules.<sup>25</sup>

**Clinical Presentation.** Most patients are asymptomatic. About 10% present with infection, hematuria, or stones.

**Imaging.** On plain radiographs, medullary sponge kidney may be seen as nephrocalcinosis with clusters of calcifications in the renal medulla.

On ultrasonography it is seen as echogenic medullary pyramids (Figure 69-20). Unenhanced CT also can show the medullary nephrocalcinosis (Figure 69-21).

**Treatment.** There is no special treatment except for that of stone disease or infections.



**Figure 69-20** Sagittal ultrasound image shows echogenic renal pyramids, a finding consistent with medullary nephrocalcinosis, in a patient with medullary sponge kidney.



**Figure 69-21** Coronal noncontrast computed tomography scan in bone windows shows medullary nephrocalcinosis in a patient with medullary sponge kidney.

# BLADDER

## Bladder Agenesis

Bladder agenesis is congenital absence of the bladder. It is extremely rare, with only 45 cases reported in the literature.

**Pathophysiology.** Bladder development occurs in the 5th to 7th weeks of gestation. Derangements in mesenchymal differentiation, growth, and urine production are postulated to be the cause of this anomaly.

**Clinical Presentation.** Bladder agenesis is incompatible with life.

**Imaging.** On prenatal ultrasonography there will be absence of the bladder.

**Treatment.** Treatment is surgical creation of a urinary diversion.

#### **Bladder Duplication**

Bladder duplication is an extremely rare condition with approximately 50 reported cases. Each ureter drains into the ipsilateral bladder. With complete duplication there are two urethras. With incomplete duplication, the bladders join to drain into one urethra. Bladder duplication may be associated with other congenital anomalies.

#### **Congenital Urachal Anomalies**

Congenital urachal anomalies include a wide range of abnormalities, including a patent urachus, urachal cyst, umbilicalurachal sinus, and vesicourachal diverticulum.<sup>27</sup>

**Pathophysiology.** Abnormalities of the urachus are due to persistence of the allantois. If the entire allantois persists, there will be a communication between the bladder and the umbilicus resulting in a patent urachus. If only a localized area of the allantois remains, a urachal cyst forms as a result of secretory activity in the lining of the allantois. If there is persistent communication with the umbilicus, a urachal sinus forms. If there is persistent communication with the bladder, a vesicourachal diverticulum forms.

## Patent Urachus

A persistent communication exists between the bladder lumen and the umbilicus. Patients present in the neonatal period with urine leakage from the umbilicus. CT and ultrasonography may show the tubular connection between the bladder and umbilicus. Definitive confirmation can be made with injection into the umbilicus showing communication with the bladder or cystography.

# Urachal Cyst

A small cyst may develop when the urachus closes at both ends with a segment of patent urachus between.

**Clinical Presentation.** Patients are typically asymptomatic. There is a small risk for these cysts becoming infected.

**Imaging.** On CT and ultrasonography there is a small cyst in the midline lower abdominal wall.

# Umbilical-Urachal Sinus

An umbilical-urachal sinus occurs from communication of the urachus with the umbilicus.

**Clinical Presentation.** There may be periodic discharge of fluid from the umbilicus.

**Imaging.** On CT and ultrasonography this anomaly may be seen as a blind-ending tubular structure connected to the umbilicus. Injection of a contrast agent through the umbilicus can confirm the finding.

## Vesicourachal Diverticulum

A vesicourachal diverticulum can arise from the dome of the bladder and represents persistent communication of the urachal remnant with the bladder.

**Clinical Presentation.** Patients are typically asymptomatic, and cases are usually discovered incidentally.

**Imaging.** On ultrasonography and CT a vesicourachal diverticulum is seen as a small cyst near the dome of the bladder (Figure 69-22).

# Bladder Diverticulum

A bladder diverticulum is a small outpouching from the bladder.

**Pathophysiology.** Bladder diverticula may be congenital or acquired. Congenital diverticula most often occur lateral and superior to the ureteral entrance. They are reported to result from a deficiency or weakness in the Waldeyer fascial sheath. The incidence of this disorder is 1.7%.

**Clinical Presentation.** Typically, bladder diverticula cause no symptoms. Occasionally they can cause infections or bladder outlet obstruction.

**Imaging.** Ultrasonography, CT, IVP, and VCUG will show outpouching of the bladder wall in the classic location—lateral and superior to the ureteral orifice (Figure 69-23).

**Treatment.** There is no specific treatment except for management of complications including infections and bladder outlet obstruction.

#### Prune Belly Syndrome

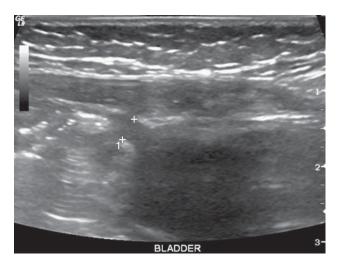
Prune belly syndrome, also known as Eagle-Barrett syndrome or triad syndrome, is characterized by a wrinkled appearance of the distended and lax abdominal wall; bilateral impalpable undescended testes; and abnormalities of the urinary tract, including tortuous dilated ureters, dilated prostatic urethra, and renal dysmorphism. The syndrome is estimated to occur in 1 in 30,000 births and occurs almost exclusively in males, with only a few cases described in females.<sup>28</sup>

**Pathophysiology.** Although the cause is unknown, it is thought that there is either a mesenchymal insult to the fetus at 6 weeks of gestation that results in deficient abdominal muscular development or chronic intrauterine abdominal distention resulting in pressure atrophy of the abdominal muscles.<sup>29</sup> In patients with prune belly syndrome there are multiple other skeletal, gastrointestinal, cardiac, and pulmonary anomalies.

**Clinical Presentation.** Clinically, patients can present with varying degrees of the following: partial or complete lack of abdominal muscles, resulting in wrinkly folds covering the skin; undescended testes in males; distended bladder, reflux, and larger ureters; and frequent UTIs.

**Imaging.** Prune belly syndrome can be detected with screening ultrasonography during pregnancy. Findings include bilateral hydronephrosis, dilated and tortuous ureters, and varying degrees of renal dysplasia.

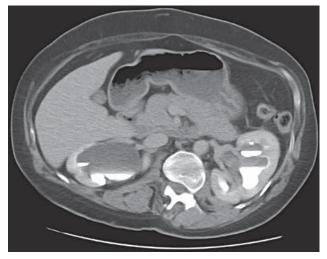
On a VCUG there is a large, elongated bladder with irregular contour and bilateral ureteral reflux. Dilated, tortuous ureters also may be seen. During voiding there is dilation of the prostatic urethra, which tapers to the membranous urethra.



**Figure 69-22** Sagittal ultrasound image of the bladder shows a tubular structure (measured with calipers) arising from the anterosuperior dome of the bladder and consistent with a vesicourachal diverticulum. It was blind ending and did not communicate with the umbilicus.



Figure 69-23 Axial computed tomography scan shows a small diverticulum arising from the left lateral wall of the bladder.



**Figure 69-24** Delayed-phase axial computed tomography image shows massively dilated bilateral renal collecting systems in an older patient with a history of prune belly syndrome.

On CT there is bilateral dilation of the renal collecting systems (Figure 69-24).

**Treatment.** Treatment depends on the severity of the symptoms. A vesicostomy can be performed to allow the bladder to drain through a small hole in the abdomen. In severe cases, surgical reconstruction of the bladder and abdominal wall may be necessary.

#### URETHRA

#### Posterior Urethral Valves

Posterior urethral valves are the most common congenital obstructive lesions in the male urethra.

**Pathophysiology.** A thick valve-like membrane forms from the wolffian ducts and extends from the verumontanum to the distal prostatic urethra. Centrally there is often a small opening allowing minimal passage of urine, but progressive distention during voiding causes the valve to become sail-like.

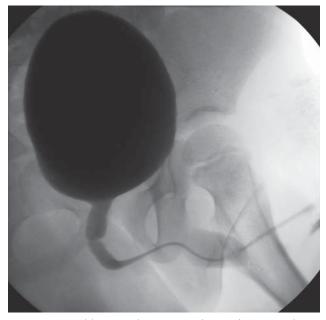
**Imaging.** Abdominal ultrasonography can only suggest the diagnosis based on the findings of bilateral hydronephrosis, a thickened bladder wall, and bladder diverticula.

VCUG is the best imaging technique for the diagnosis of posterior urethral valves. Findings include dilation and elongation of the posterior urethra. Occasionally, the linear radiolucent band corresponding to the valve can be visualized (Figure 69-25).

**Treatment.** Standard treatment is transurethral ablation of the valves.<sup>30</sup>

# Anterior Urethral Valves

Anterior urethral valves are more rare than posterior urethral valves. As their name implies, they represent persistent anomalous valves along the anterior urethra. Typically, 40% are in the bulbar urethra, 30% are at the penoscrotal junction, and 30% are in the pendulous urethra.



**Figure 69-25** Oblique voiding cystourethrography image shows a small linear band in the posterior urethra consistent with posterior urethral valves.

**Pathophysiology.** The embryologic development of anterior urethral valves is unclear. Proposed mechanisms include aborted attempt of urethral duplication, failure of alignment between the anterior and posterior urethra, excessive tissue growth in the developing urethra, and congenital cystic dilation of the periurethral glands.<sup>31</sup>

**Clinical Presentation.** Clinically, the presentation varies with the patient's age and the degree of obstruction. Symptoms can range from minimal obstruction to severe hydronephrosis, end-stage renal disease, and bladder rupture.

**Imaging.** VCUG is the diagnostic study of choice to evaluate for anterior urethral valves. Findings include dilation of the urethra proximal to the valve. The valve may be seen as a linear filling defect along the ventral wall. Reflux into the ureters has been reported in one third of cases, and atrophy of the upper urinary tract occurs in half of cases.

# What the Treating Physician Needs to Know

- Screening ultrasound examination of the fetus is important in identifying many of the congenital anomalies of the urinary tract. Early detection and treatment offer the potential to reduce later renal damage.<sup>32</sup>
- Items to look for in a screening ultrasound examination include oligohydramnios; number, location, and shape of the kidneys; presence of hydronephrosis or hydroureter; and presence and size and shape of the bladder.
- Many urinary tract anomalies may manifest later as symptoms of recurrent UTIs, stone disease, flank pain, or obstruction.

#### SUGGESTED READINGS

Berrocal T, Lopez-Pereira P, Arjonilla A, et al: Anomalies of the distal ureter, bladder, and urethra in children: embryologic, radiologic, and pathologic features. *Radiographics* 22:1139–1164, 2002.

#### REFERENCES

- Schedl A: Renal abnormalities and their developmental origin. Nat Rev Genet 8:791–802, 2007.
- Seikaly MG, Ho PL, Emmett L, et al: Chronic renal insufficiency in children: the 2001 Annual Report of the NAPRTCS. *Pediatr Nephrol* 18: 796–804, 2003.
- 3. Nyengaard JR, Bendtsen TF: Glomerular number and size in relation to age, kidney weight, and body surface in normal man. *Anat Rec* 232:194–201, 1992.
- Keller G, Zimmer G, Mall G, et al: Nephron number in patients with primary hypertension. *N Engl J Med* 348:101–108, 2003.
- Carter AR, Horgan JG, Jennings TA, et al: The junctional parenchymal defect: a sonographic variant of renal anatomy. *Radiology* 154:499– 502, 1985.
- Yeh HC, Halton KP, Shapiro RS, et al: Junctional parenchyma: revised definition of hypertrophic column of Bertin. *Radiology* 185:725–732, 1992.
- Zwirewich CV, Rowley VA: Lobar dysmorphism of the kidney: report of two cases and review of the literature. J Comput Assist Tomogr 21:742– 744, 1997.
- Binder R, Korobkin M, Clark RE, et al: Aberrant papillae and other filling defects of the renal pelvis. *AJR Am J Roentgenol* 114:746–752, 1972.
- Tolson HL: Ectopic (pelvic) kidney. Ann Surg 93:880–885, 1931.
- Krishnan B, Truong LD, Saleh G, et al: Horseshoe kidney is associated with an increased relative risk of primary renal carcinoid tumor. *J Urol* 157:2059–2066, 1997.

- Spence HM: Congenital unilateral multicystic kidney: an entity to be distinguished from polycystic kidney disease and other cystic disorders. *J Urol* 74:693–706, 1955.
- Viola D, Anagnostou T, Thompson TJ, et al: Sixteen years of experience with stone management in horseshoe kidneys. *Urol Int* 78:214–218, 2007.
- Winding L1, Loane M, Wellesley D, et al: Prenatal diagnosis and epidemiology of multicystic kidney dysplasia in Europe. *Prenat Diagn* 34:1093–1098, 2014.
- Brown T, Mandell J, Lebowitz RL: Neonatal hydronephrosis in the era of sonography. AJR Am J Roentgenol 148:959–963, 1987.
- Johnston JH, Evans JP, Glassberg KI: Pelvic hydronephrosis in children: a review of 219 personal cases. J Urol 117:97–101, 1977.
- Gross GW, Lebowitz RL: Infection does not cause reflux. AJR Am J Roentgenol 137:929–932, 1981.
- Tokunaka S, Gotoh T, Koyanagi T, et al: Muscle dysplasia in megaureters. J Urol 131:383–390, 1984.
- Vargas B, Lebowitz RL: The coexistence of megacalyces and primary megaureter. AJR Am J Roentgenol 147:313–316, 1986.
- Rathaus V, Konen O, Werner M, et al: Pyelocalyceal diverticulum: the imaging spectrum with emphasis on the ultrasound features. *Br J Radiol* 74:595–601, 2001.
- Fernbach SK, Feinstein KA, Spencer K, et al: Ureteral duplication and its complications. *Radiographics* 17:109–117, 1997.
- Brock WA, Kaplan WG: Ectopic ureteroceles in children. J Urol 119:800–804, 1878.
- Considine J: Retrocaval ureter. Br J Urol 38:412– 423, 1966.

- Mahmood M, Tandon V, Dwivedi US, et al: Retrocaval ureter: a rare entity in the spectrum of upper tract obstruction. *JK Practitioner* 12:24–25, 2005.
- 23. Barrett DM, Malek RS: Ureteral diverticulum. *J Urol* 114:33–35, 1975.
- Rank WB, Mellinger GT, Spiro E: Ureteral diverticula: etiologic considerations. J Urol 83:566– 568, 1960.
- 25. Khonsari H, Oliver JA: Multiple ureteral diverticula. J Urol 96:152, 1966.
- 26. Lalli AF: Medullary sponge kidney disease. *Radiology* 92:92–96, 1969.
- Yu JS, Kim KW, Lee HJ, et al: Urachal remnant diseases: spectrum of CT and US findings. *Radiographics* 21:451–461, 2001.
- Aaronson IA, Cremin BJ: Prune belly syndrome in young females. Urol Radiol 1:151–155, 1980.
- Nakayama DK, Harrison MR, Chinn DH, et al: The pathogenesis of prune belly. *Am J Dis Child* 138:834–836, 1984.
- Warren J, Pike JG, Leonard MP: Posterior urethral valves in Eastern Ontario: a 30 year perspective. *Can J Urol* 11:2210–2215, 2004.
- Kaplan GW, Scherz HC: Anterior urethral valves. In Kelalis PP, King LR, Belman AB, editors: *Clinical pediatric urology*, ed 3, Philadelphia, 1993, WB Saunders, pp 851–853.
- Gunn TR, Mora JD, Pease P: Antenatal diagnosis of urinary tract abnormalities by ultrasonography after 28 weeks' gestation: incidence and outcome. Am J Obstet Gynecol 172(2 Pt 1):479– 486, 1995.

# **Enlarged Adrenal Glands**

NAGARAJ-SETTY HOLALKERE | NAVEEN M. KULKARNI | MICHAEL BLAKE

Recent technical advances in computed tomography (CT) and magnetic resonance imaging (MRI) have resulted in improved detection of subtle changes in adrenal gland morphology. The different morphologic patterns of adrenal gland enlargement on imaging can be classified as follows (Figure 70-1):

- Diffuse enlargement
- Focal nodule or mass in a limb
- Multiple nodules in the gland
- Nodule with a smaller nodule within the nodule, the so-called nodule within a nodule appearance

The various causes and imaging manifestations of diffuse enlargement, multiple nodules in a single gland, and nodule within a nodule are discussed here.

# **Diffuse Enlargement**

The adrenal gland is diffusely enlarged and usually maintains the normal adrenal shape. The limbs of the adrenal glands are longer than 5 cm and exceed 10 mm in thickness. The causes of diffuse enlargement include adrenal hyperplasia, lymphoma, metastatic disease, tuberculosis, and histoplasmosis.

# ADRENAL HYPERPLASIA

Adrenal cortical hyperplasia may be primary or secondary to a pituitary or hypothalamic lesion or ectopic production of adrenocorticotropic hormone (ACTH). Clinically, adrenal hyperplasia often manifests as Cushing's disease. It also may be associated with Conn's syndrome or adrenogenital syndrome.

On CT and MRI, hyperplasia of the adrenals is commonly present as enlarged glands bilaterally but maintains an adreniform shape with a smooth surface (Figure 70-2). Rarely, adrenal hyperplasia may have a normal appearance or nodular enlargement.<sup>1</sup> The maximum diffuse enlargement of the adrenals in hyperplasia is associated with ectopic ACTH production secondary to various tumors, such as bronchial carcinoid.<sup>2</sup> In a patient with hyperaldosteronism, differentiation of adrenal hyperplasia versus hyperfunctioning adenoma is critical because adrenal hyperplasia is treated medically, whereas a hyperfunctioning adenoma requires surgery. Renal venous sampling is usually indicated in patients with hyperaldosteronism, particularly when a focal nodule on cross-sectional imaging is not identified. Most often, hyperaldosteronism is associated with micronodules that are not usually detected on CT or MRI; hence, even if hyperplasia is identified on CT or MRI, renal vein sampling is still performed to exclude unilateral hypersecretion of aldosterone.

If a focal nodule is not identified on imaging in patients with hyperaldosteronism, further evaluation is usually performed with renal vein sampling.

#### LYMPHOMA

Adrenal involvement occurs in nearly 25% of patients with non-Hodgkin's lymphoma (NHL) at autopsy. Adrenal involvement in NHL is usually associated with diffuse enlargement similar to hyperplasia.<sup>3</sup> However, here the enlargement is either asymmetric or unilateral. On CT, adrenal lymphoma appears as unilateral or bilateral homogeneous solid involvement without calcifications. The shape of the adrenals may be maintained, and mild enhancement may be noted after intravenous administration of a contrast agent. In NHL, the adrenal gland involvement may be due to a primary or metastatic lymphoma. Primary adrenal NHL involves only the adrenal gland and is very rare. It tends to be cystic and heterogeneous, which makes it difficult to differentiate from adrenal cortical carcinoma, pheochromocytomas, and metastasis. It is bilateral in 50% to 68% of cases.<sup>4</sup> The common presentation of adrenal primary NHL is adrenal insufficiency, and it is known to be the most common cause of adrenal insufficiency secondary to malignancy. The diagnosis is suggested by the presence of lymphadenopathy elsewhere; however, lymphadenopathy is not required to make a diagnosis.4,5 MRI features of lymphoma are nonspecific and may resemble metastases. Typically, the enlargement is hypointense on a T1-weighted image and has variable or heterogeneous hyperintensity on T2-weighted images.<sup>5</sup> Positron emission tomography with CT (PET/CT) is helpful in identification of adrenal as well as extra-adrenal involvement. The 18F-fluorodeoxyglucose (FDG) uptake will be greater than the liver uptake in adrenals with lymphomatous involvement.

#### **GRANULOMATOUS DISEASE**

Granulomatous infections are usually due to tuberculosis or histoplasmosis and are the second most common cause of chronic adrenal insufficiency in the United States, after idiopathic Addison's disease.<sup>1</sup>

In adrenal tuberculosis on CT, the glands are often asymmetrically enlarged. Acute bilateral involvement results in adrenal insufficiency. In the subacute phase, adrenal enlargement with peripheral enhancement and with cystic low-density or necrotic changes may be present. In the late phase, either diffuse or focal calcifications are present (Figure 70-3). Nearly 50% of adrenal calcifications are secondary to tuberculosis.<sup>6</sup> In diffuse involvement with histoplasmosis, the adrenals are also enlarged, with peripheral enhancement and central low density (Figure 70-4). The adrenal enlargement may be more symmetric than in tuberculous involvement. Calcifications also may be present.<sup>7</sup>

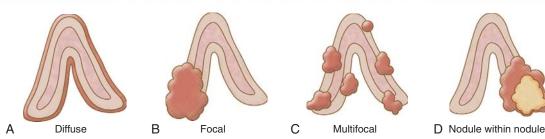
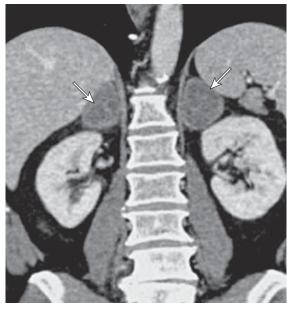


Figure 70-1 The different morphologic patterns of adrenal gland enlargement.



**Figure 70-2** Axial computed tomography of the abdomen of a 42-year-old man with Cushing's disease at the level of the adrenal glands depicts enlarged bilateral adrenal glands (>10 mm) (*arrows*) that maintain an adreniform shape with a smooth surface without any discrete nodules, a finding consistent with adrenal hyperplasia.



**Figure 70-4** Coronal reformatted image of contrast-enhanced abdominal computed tomography scan demonstrates diffusely enlarged bilateral adrenal glands (*arrows*) with peripheral enhancement and cystic low density in the center. The appearance was confirmed on biopsy examination to be due to histoplasmosis.

# **METASTASIS**

Diffuse enlargement of adrenal gland from metastases is rare. Local extension from renal cancer or retroperitoneal sarcomas into the adrenal gland can be associated with unilateral diffuse enlargement. In these cases, the gland will be enlarged, with ill-defined margins and imaging features similar to those of a focal mass or nodular metastasis.

# **Focal Nodule or Mass**

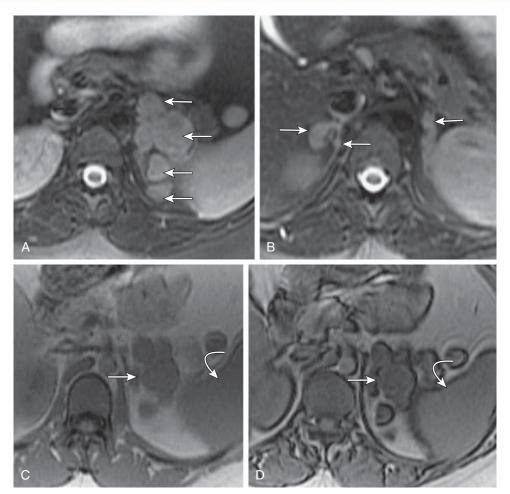
Imaging manifestations of a focal adrenal nodule or mass are discussed in Chapter 71.

# **Multiple Nodules in the Gland**

Here more than one nodule are in a single gland. Multiple nodules can be present either unilaterally or bilaterally. Unilateral multiple nodules are most often due to metastatic disease. On the other hand, bilateral multiple nodules may be due to metastatic disease, multiple bilateral adenomas, or benign multinodular hyperplasia. Multiple nodular metastatic disease and nodular bilateral adenomas are relatively uncommon. Typically,



**Figure 70-3** Axial computed tomography section demonstrating diffuse bilateral adrenal calcification (*arrows*) in a patient with tuberculosis.



**Figure 70-5** A 28-year-old woman presented with an adrenocorticotropin hormone–producing pituitary microadenoma. A to D, Note bilateral, large multiple adrenal nodules on the upper abdominal T2-weighted axial magnetic resonance images (*arrows*). There is minimal drop in signal intensity on the out-of-phase image (D) compared with the spleen (*curved arrow*) and in-phase image (C). The patient subsequently underwent bilateral adrenalectomy, and the histopathologic findings were consistent with multinodular adrenal hyperplasia.

each of the individual nodules demonstrates similar findings, as seen with single nodular metastasis or adenoma, respectively. The imaging features of nodular metastasis and adenoma are discussed in Chapter 71.

#### BENIGN MULTINODULAR HYPERPLASIA

Benign multinodular hyperplasia typically manifests as enlarged multinodular adrenal glands in older patients who often have clinical features of mild Cushing's syndrome. Benign multinodular hyperplasia can be due to either ACTH-dependent or ACTH-independent processes.<sup>8,9</sup> In patients with ACTHdependent multinodular hyperplasia, ACTH levels are elevated and hypersecretion is either from a pituitary tumor or an ectopic ACTH production, such as lung cancer. In patients with ACTH-independent multinodular hyperplasia, popularly called ACTH-independent macronodular adrenocortical hyperplasia (AIMAH), the ACTH levels are often either suppressed or undetectable. In both conditions, the adrenal glands are enlarged with multiple bilateral nodules. Hence in patients with Cushing's syndrome with abnormal ACTH levels, the imaging finding of multiple bilateral adrenal nodules should prompt a diagnosis of benign multinodular hyperplasia.<sup>5</sup>

On imaging, ACTH-independent nodular hyperplasia is typically associated with multiple tiny adrenal gland nodules that do not demonstrate microscopic lipid on in-phase and out-of-phase chemical-shift MRI (Figure 70-5). In contrast, the nodules of ACTH-dependent nodular hyperplasia are typically larger; each nodule may measure up to 5 cm and demonstrate microscopic lipid on in-phase and out-of-phase chemical-shift MRI.<sup>9</sup> Bilateral metastases or multiple bilateral adenomas can have similar morphologic and imaging appearances. Consequently, in absence of biochemical evidence, it is difficult to make an accurate diagnosis of multinodular hyperplasia on imaging findings alone (see Figure 70-5). In one series, 25% (5 of 24) of patients with this appearance had a subsequent diagnosis of adrenal adenoma.<sup>10</sup>

The internodular cortex is always hyperplastic in ACTHdependent hyperplasia as a result of ACTH effects, whereas the internodular cortex is usually atrophic in ACTH-independent hyperplasia owing to lack of ACTH.<sup>9,11</sup>

#### **COLLISION TUMORS**

Collision tumors refer to coexistence of two adjacent but histologically distinct tumors with no significant tissue

also can be used to identify adrenal collision tumors. For

example, one case report described the ability of PET/CT to

distinguish adrenal metastasis from adenoma.<sup>14</sup> Adenomas typically show little or no significant FDG uptake, whereas metas-

tases show uptake greater than that of the liver.

to both benign and malignant causes.

What the Referring Physician Needs to Know

• Accurate characterization of adrenal enlargement is

with and without a known primary malignancy.

critical for appropriate management of patients both

• Enlarged adrenal glands are common and may be due

• Imaging plays an important role in both the detection of

adrenal enlargement and its characterization in concert

with appropriate endocrine/oncologic/infectious history

• Image-guided biopsy is less commonly required for

characterization of adrenal enlargement that has

diagnosis but can sometimes be helpful for

remained indeterminate by imaging.



**Figure 70-6** A 65-year-old man presented with a known history of lung cancer and adrenal adenoma in the left adrenal gland. Note typical features of metastasis (*arrow*) and adrenal adenoma (*arrowhead*) in a collision tumor on (A) coronal T2-weighted magnetic resonance image, where the metastasis in the upper portion of the adenoma is slightly more hyperintense than the adenoma, and on (B) in-phase and (C) out-of-phase imaging, suggesting microscopic lipid, whereas there is no loss of signal from the metastasis.

**Key Points** 

and testing.

admixture.<sup>12,13</sup> Both tumors may be malignant, both may be benign, or one may be benign and the other malignant. Adrenal collision tumors are rare, and their prevalence is unknown. The most common cause for adrenal collision tumors is metastasis at the margin of a preexisting adrenal adenoma. Adenoma/ metastasis collision tumors should be suspected on chemicalshift MRI when there is only focal decrease in the signal intensity of the mass on opposed-phase images or significant interval change in the morphology of the preexisting adrenal lesion compared with prior imaging studies. However, hemorrhage or necrosis in a preexisting lesion also may mimic a collision tumor. Many adrenal collision tumors are not diagnosed by biopsy because of sampling error or a significant difference in the size of the two components, making it more likely that only the larger component will be examined at pathologic analysis. One should consider a collision tumor if findings suggestive of metastatic disease are present, including an increase in size or the development of an additional soft tissue component. Radiologists should understand and consider the existence of collision tumors during biopsy so that appropriate tissue samples can be obtained to help guide treatment.

Chemical shift MRI can differentiate between benign lipidrich adenomas and malignant tumors, because the latter do not show a decrease in signal intensity on opposed-phase imaging relative to that on in-phase imaging (Figure 70-6).<sup>13</sup> PET/CT

#### SUGGESTED READINGS

Kawashima A, Sandler CM, Fishman EK, et al: Spectrum of CT findings in nonmalignant disease of the adrenal gland. *Radiographics* 18:393–412, 1998.

Rockall AG, Babar SA, Sohaib SAA, et al: CT and MR imaging of the adrenal glands in ACTHindependent Cushing syndrome. *Radiographics* 24:435–445, 2004.

#### REFERENCES

- 1. Cirillo RL, Jr, Bennett WF, Vitellas KM, et al: Pathology of the adrenal gland: imaging features. *AJR Am J Roentgenol* 170:429–435, 1998.
- 2. Sohaib SA, Hanson JA, Newell-Price JD, et al: CT appearance of the adrenal glands in adreno-

corticotrophic hormone-dependent Cushing's syndrome. *AJR Am J Roentgenol* 172:997–1002, 1999.

- Paling MR, Williamson BR: Adrenal involvement in non-Hodgkin lymphoma. AJR Am J Roentgenol 141:303–305, 1983.
- Kato H, Itami J, Shiina T, et al: MR imaging of primary adrenal lymphoma. *Clin Imaging* 20: 126–128, 1996.
- Lee FT, Jr, Thornbury JR, Grist TM, et al: MR imaging of adrenal lymphoma. *Abdom Imaging* 18:95–96, 1993.

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- Patnaik MM, Deshpande AK: Diagnosis: Addison's disease secondary to tuberculosis of the adrenal glands. *Clin Med Res* 6:29, 2008.
- Kawashima A, Sandler CM, Fishman EK, et al: Spectrum of CT findings in nonmalignant disease of the adrenal gland. *Radiographics* 18: 393–412, 1998.
- Westra SJ, Zaninovic AC, Hall TR, et al: Imaging of the adrenal gland in children. *Radiographics* 14:1323–1340, 1994.
- 9. Doppman JL, Chrousos GP, Papanicolaou DA, et al: Adrenocorticotropin-independent macronodular adrenal hyperplasia: an uncommon

cause of primary adrenal hypercortisolism. *Radiology* 216:797–802, 2000.

- Doppman JL, Gill JR, Jr, Miller DL, et al: Distinction between hyperaldosteronism due to bilateral hyperplasia and unilateral aldosteronoma: reliability of CT. *Radiology* 184:677– 682, 1992.
- Lack EE, Travis WD, Oertel JE: Adrenal cortical nodules, hyperplasia, and hyperfunction. In Lack EE, editor: *Pathology of the adrenal* gland, New York, 1990, Churchill Livingstone, pp 75–114.
- Banik S, Hasleton PS, Lyon RL: An unusual variant of multiple endocrine neoplasia syndrome: a case report. *Histopathology* 8:135–144, 1984.
- Khati NJ, Javitt MC, Schwartz AM: Adrenal adenoma and hematoma mimicking a collision tumor at MR imaging. *Radiographics* 19:235– 239, 1999.
- Blake MA, Sweeney AT, Kalra MK, et al: Collision adrenal tumors on PET/CT. AJR Am J Roentgenol 183:864–865, 2004.

# 71 Adrenal Masses

NAGARAJ-SETTY HOLALKERE | NAVEEN M. KULKARNI | MICHAEL BLAKE

## Etiology

Adrenal masses may be neoplastic, infectious, or hemorrhagic (Box 71-1). Neoplasia is the most common cause for an adrenal mass seen on imaging. An incidentally detected adrenal mass as well as an adrenal mass in a patient with known malignancy elsewhere is most commonly due to a benign adenoma.<sup>1</sup>

## **Prevalence and Epidemiology**

In one large autopsy series of more than 1000 patients, an incidence was reported of 1.4% to 5.7% with an adrenal mass.<sup>2,3</sup> However, adrenal masses are increasingly being encountered on cross-sectional imaging done for evaluation of both abdominal symptoms and cancer staging. The overall prevalence of adrenal masses on computed tomography (CT) approaches 3% in middle age and increases to as much as 10% in the elderly.<sup>4</sup>

## Imaging

The imaging features of adrenal masses are listed in Table 71-1.

## ADRENAL ADENOMA

Adrenal cortical adenomas are common benign tumors arising from the cortex of the adrenal gland. The majority of adrenal adenomas are nonfunctional incidentalomas. A small percentage of adenomas that produce excessive steroid hormones will cause symptoms manifesting as Cushing's syndrome or Conn's syndrome or with excess acne and hair growth. Therefore, all incidentally detected adenomas or adrenal masses on imaging should be correlated with the clinical presentation and, if necessary, serum and urine biochemical analysis for the presence of a functional adenoma. The overall prevalence of adrenal adenomas increases with advancing age.<sup>5</sup>

## Computed Tomography

Computed tomography (CT) is the primary imaging modality used in establishing a diagnosis of adenoma. Histologically, two types of adrenal cortical adenomas are identified: those that contain a high percentage of intracytoplasmic lipid (lipid rich), which represent approximately 70% of all adrenal cortical adenomas, and those that are lipid poor, which represent the remaining approximately 30%. Calcifications, necrosis, and hemorrhage are atypical but can occur, especially in larger lesions. The vast majority of lipid-rich adenomas can be accurately identified by CT density. Typically, adenomas demonstrate a density of less than 10 Hounsfield units (HU) on unenhanced images (Figure 71-1, *A*). Approximately 10% to 40% of all adenomas demonstrate CT density greater than 10 HU and are considered lipid-poor adenomas. Some of the lipid-poor adenomas can be characterized on washout characteristics on delayed-phase contrast-enhanced images. On analysis of washout characteristics, adenomas have relative percentage washout (RPW) and absolute percentage washout (APW) values of more than 38% and 52%, respectively, after a 10-minute delay or 40% and 60%, respectively, after a 15-minute delay. These washout patterns are diagnostic for adenoma. Both lipidrich and lipid-poor adenomas have a similar washout pattern.<sup>6-11</sup>

## Magnetic Resonance Imaging

Adenomas on T1-weighted, T2-weighted, and post–gadoliniumenhanced T1-weighted imaging have varied signal intensity and, consequently, these sequences are generally not used for characterization. The most important and specific finding of lipid-rich adenoma on magnetic resonance imaging (MRI) is signal "drop out" on out-of-phase (opposed-phase) imaging compared with in-phase imaging on chemical-shift T1-weighted images (see Figure 71-1, *B* and *C*). A signal drop of more than 20% has a sensitivity of 71% and a specificity of 100%. Again, lipid-poor adenomas may not be accurately characterized on MRI.<sup>12</sup>

## Ultrasonography

Ultrasonography has very limited role.

## Nuclear Medicine

Malignant adrenal lesions typically display intense accumulation of fluorodeoxyglucose (FDG), reflected in activity that exceeds that of the liver on FDG-labeled positron emission tomography (PET). Nonfunctional adenomas, on the other hand, being metabolically inactive, are not typically FDG avid. However, adenomas do occasionally demonstrate FDG uptake that is higher than background activity and lower, equal to, or slightly higher than liver activity. Adrenocortical scintigraphy using NP-59 and iodine-131 (<sup>131</sup>I)-labeled 1,6 $\beta$ -iodomethyl-19norcholesterol is currently not widely available but is known to accurately identify adenomas.

## Positron Emission Tomography With Computed Tomography

FDG-PET and CT information can be complementary to each other on combined PET/CT and may increase the accuracy of adenoma identification. If PET demonstrates FDG uptake in an adenoma, CT can be useful if it demonstrates a density of less than 10 HU or washout characteristics typical of an adenoma.<sup>13</sup>

## ADRENAL MYELOLIPOMA

Myelolipomas are usually nonfunctional benign neoplasms of the adrenal cortex composed of mature fat and hematopoietic

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tissue in varying proportions. There are isolated reports of endocrine abnormalities associated with myelolipomas, including Cushing's and Conn's syndromes and disorders associated with excess androgens or estrogens. Large tumors may cause pain or may manifest as a retroperitoneal hemorrhage. There have been case reports of malignant tumors, including teratoma or liposarcoma, containing gross fat, but they are rare.<sup>14</sup> Although there is almost always detectable fat on CT or MRI, a myelolipoma may occasionally have predominantly myeloid components.

## Computed Tomography

The diagnosis of myelolipoma is made by demonstrating the presence of fat within an adrenal mass. This can be accomplished with either CT or MRI, although the presence of hem-

## BOX 71-1 CAUSES OF ADRENAL MASSES

#### **BENIGN LESIONS**

#### Common

- Adenoma (lipid-rich)
- Adenoma (lipid-poor)
- Myelolipoma
- Adrenal hemorrhage
- Pheochromocytoma

#### Uncommon

- Adrenal cysts
- Ganglioneuroma

#### MALIGNANT LESIONS

#### Common

- Metastasis
- Uncommon
- Adrenal carcinoma
- Neuroblastoma
- Pheochromocytoma

orrhage or infarction can complicate the diagnosis. The proportion of fat detected on CT is variable; in some patients, most of the tumor consists of fatty tissue, and in others the use of thin slices on CT will usually confirm discrete regions of fat attenuation (-30 to -100 HU). Focal calcifications may be present in myelolipomas in up to 24% of cases (Figure 71-2, A).<sup>15</sup> A pseudocapsule often can be identified between the mass and the adjacent retroperitoneal fat, which represents a thin rim of residual adrenal cortex around the lesion. In cases of myelo-lipoma complicated by hemorrhage, CT is the most accurate modality for diagnosis. Rarely, extra-adrenal myelolipomas have been described in the pelvis or retroperitoneal fat.<sup>15</sup> These lesions resemble adrenal myelolipomas but may be indistinguishable from liposarcoma on imaging studies.

### Magnetic Resonance Imaging

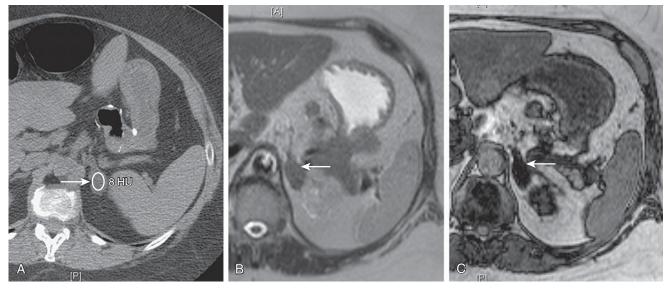
Unlike adrenal adenoma, the fat in myelolipoma is macroscopic. Hence, on MRI, the presence of fat is best demonstrated on T1-weighted images with and without fat suppression (see Figure 71-2, *B* and *C*).<sup>16</sup> Again, moderate T2 signal should resemble that of other fat within the abdomen. The myeloid portion of the myelolipoma is vascular and may demonstrate enhancement after gadolinium administration.

## Ultrasonography

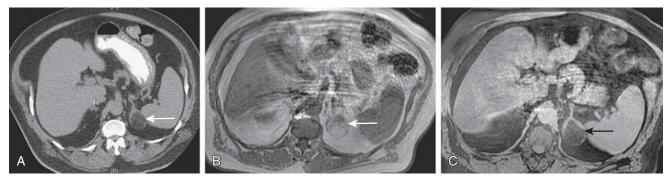
Myelolipomas may demonstrate flow on Doppler ultrasonography. However, this is a nonspecific finding that does not assist with characterization.

## PHEOCHROMOCYTOMA

Pheochromocytoma is a rare lesion most commonly found in the adrenal medulla, but it may arise anywhere along the sympathetic chain (e.g., the retroperitoneal ganglia, organ of Zuckerkandl, or urinary bladder). Cases may occur in the chest, skull base, vagina, anus, or spermatic cord. Clinical signs and



**Figure 71-1** Unenhanced axial computed tomography (CT) (A) and axial magnetic resonance (B) in-phase and out-of-phase (C) images in a 42-year-old woman demonstrate a small low-density (8 Hounsfield units) left adrenal lesion (*arrow*) on CT that is isointense to hypointense as compared with spleen on in-phase imaging with significant drop out of signal on out-of-phase imaging, suggestive of microscopic fat within the lesion. These features are consistent with an adenoma.



**Figure 71-2** Unenhanced axial computed tomography (CT) image (A) and axial T1-weighted magnetic resonance images with (B) and without (C) fat saturation in a 35-year-old woman demonstrating macroscopic fat in the left adrenal lesion (*arrow*) on CT that is hyperintense on axial T1-weighted imaging without fat saturation with signal drop on a fat-suppressed image. This appearance is consistent with a myelolipoma.

symptoms, such as uncontrolled hypertension and palpitations, may direct a search for the lesion. Most pheochromocytomas are sporadic. However, approximately 10% are associated with syndromes, including von Hippel-Lindau disease, multiple endocrine neoplasia, neurofibromatosis, and tuberous sclerosis.<sup>17,18</sup> Pheochromocytomas in the setting of multiple endocrine neoplasia tend to be smaller than in sporadic cases. Multiplicity is more commonly associated with syndromes.<sup>18</sup>

Pheochromocytomas are often described according to the "rule of 10s," as follows:

- 10% are extra-adrenal (i.e., 10% would, by common usage, be described as paragangliomas) (Figure 71-3, *A*)
- 10% are malignant (15% to 30% of paragangliomas are malignant) (see Figure 71-3, *B*)
- 10% are bilateral (see Figure 71-3, *C*)
- 10% are not associated with hypertension. Although hypertension is a common symptom, it is important to note that pheochromocytomas (and paragangliomas) cause only approximately 0.1% of all hypertension cases.

Imaging is used for localization of tumors to guide therapy rather than for diagnosis. The diagnosis is generally based on history, symptoms, and catecholamine testing. Imaging may, however, be used to search for recurrent or metastatic disease.

## Computed Tomography

On CT, small pheochromocytomas are usually discrete, round or oval masses of similar density to liver on nonenhanced scans. When small, they are typically homogeneous and exceed 10 HU in density on unenhanced CT. More commonly, they are large, with central necrosis.<sup>17-19</sup> Calcifications occur in approximately 12%. Typically, pheochromocytomas enhance very intensely (Figure 71-4, A). Some case reports suggest that hypertensive crises have been induced by anesthesia, surgical intervention, trauma, and selective angiography with iodinated contrast media.<sup>19</sup> Recently, studies have demonstrated that there is no association of acute catecholamine elevation with nonionic, low osmolar contrast agents. On contrast-enhanced CT, one should be careful and not misguided by the falsely positive washout sign and term a pheochromocytoma as an adrenal adenoma. The false-positive washout sign is due to a high degree of enhancement seen with pheochromocytoma. This can be resolved by high index of suspicion when an incidental adrenal lesion demonstrated enhancement of more than 100 to 120 HU.

#### Magnetic Resonance Imaging

On MRI, most pheochromocytomas are typically hypointense on T1-weighted images and markedly hyperintense on T2-weighted images, but can be variable in appearance. Up to 35% of pheochromocytomas may not have high signal intensity on T2-weighted images.<sup>20</sup> The use of intravenous gadolinium is rarely necessary, because on CT, pheochromocytomas enhance markedly after injection (see Figure 71-4, *B* and *C*). MRI and CT are equivalent for detection of primary adrenal pheochromocytoma, but MRI is significantly more accurate than CT for extra-adrenal disease. In one study, MRI was 100% sensitive, including detection of an intracardiac lesion. This compared favorably with other imaging modalities.<sup>21</sup> The specificity was less than that with <sup>131</sup>I-labeled meta-iodobenzylguanidine (MIBG) imaging in this series.<sup>21</sup>

## Nuclear Medicine and Positron Emission Tomography With Computed Tomography

Whole-body scintigraphy with MIBG compounds can detect functional lesions and is superior to other modalities in the detection of extra-adrenal lesions. MIBG can be particularly useful in evaluation of metastases in patients with malignant pheochromocytoma or rare tumors in the chest. For patients with suspected pheochromocytoma and negative findings on MIBG imaging, FDG-PET or PET/CT may be useful.<sup>22</sup>

## ADRENAL METASTASIS

Adrenal metastases account for up to 21% of incidentally discovered adrenal masses in patients without a known primary malignancy; conversely, even in patients with a known malignancy many masses are benign.<sup>1</sup> Adrenal metastases commonly arise from lung, breast, lymphoma, gastrointestinal tract, thyroid, kidney, and melanoma primary lesions. In the setting of extra-adrenal primary malignancy, diagnosis of a solitary metastasis in the adrenal may change the treatment from surgical resection to systemic therapy.

## Computed Tomography

Metastases tend to be larger than adenomas, less well defined, and inhomogeneous and occasionally have a thick enhancing rim after intravenous administration of a contrast agent. When TABLE

71-1 Imaging Fe	eatures of Adrenal I	Vlasses			
Adrenal Masses	Adenoma (Lipid-Rich)	Adenoma (Lipid-Poor)	Myelolipoma	Pheochromocytoma	Metastasis
Size	Small, usually <3 cm	Small, usually <3 cm	Usually <3 cm	Large, >3 cm	Variable
Shape	Round or oval	Round or oval	Round or oval	Round or oval	Oval or irregular
Margins	Smooth	Smooth	Smooth	Well defined	III defined
Consistency	Homogeneous	Homogeneous	Heterogeneous	Heterogeneous	Heterogeneous
Computed tomography Unenhanced Enhanced	<10 HU Mild enhancement	>10 HU Mild enhancement	<–50 HU No to mild enhancement	>10 HU Intense enhancement	>10 HU Moderate to intense enhancement
Washout	RPW ≥40% APW ≥60%	RPW ≥40% APW ≥60%	Variable	RPW ≤40% APW ≤60%	$\begin{array}{l} RPW \leq \!$
Magnetic resonance imaging T1 T2 Chemical shift	lso to hypo Iso to mild hyper >20% drop in SI	lso to hypo Iso to mild hyper <20% drop in SI	Hyper Iso to hypo India ink artifact around the macroscopic fat	lso to hypo Intense hyper in 70% No drop in Sl	lso to hypo Hyper No drop in Sl
Post Gd-T1	Nonspecific	Nonspecific	No or heterogeneous enhancement	Intense enhancement	Mild to moderate enhancement
Positron emission tomography	≤Liver uptake ≤4 SUV	≤Liver uptake ≤4 SUV	≤Liver uptake ≤4 SUV	≤Liver uptake ≤4 SUV	≥Liver uptake ≥4 SUV

APW, Absolute percentage washout: measured using 15-minute delayed images after contrast agent administration; HU, Hounsfield unit; RPW, relative percentage washout; SI, signal intensity; SUV, standardized uptake value.

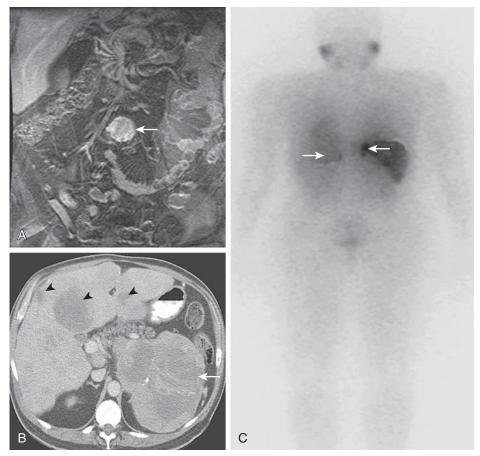
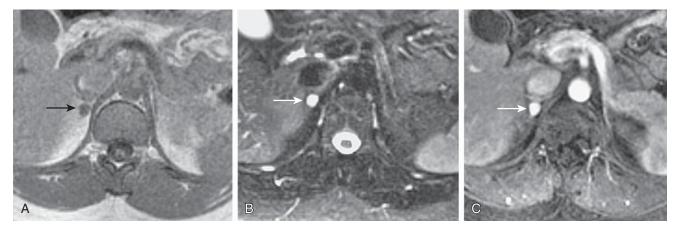


Figure 71-3 Examples of extra-adrenal (A), metastatic (B), and bilateral pheochromocytoma (C) in three different patients. A, Coronal T1-weighted postcontrast magnetic resonance image of the abdomen demonstrates an extra-adrenal pheochromocytoma (arrow) at the organ of Zuckerkandl. B, Axial contrast-enhanced computed tomography image in a 48-year-old woman with hypertension demonstrates a large heterogeneous enhancing mass (arrow) in the region of the left adrenal gland with multiple metastases (arrowheads) consistent with malignant pheochromocytoma. C, Static image of an iodine-131-labeled meta-iodobenzylguanidine (MIBG) scan in a 28-year-old woman with hypertension depicts intense foci of uptake in bilateral adrenal glands (arrows) consistent with pheochromocytoma. Document téléchargé de ClinicalKey.fr par Faculte de Medecine de Tunis août 30, 2016. Pour un usage personnel seulement. Aucune autre utilisation n'est autorisée. Copyright ©2016. Elsevier Inc. Tous droits réservés.

Carcinoma	Neuroblastoma	Ganglioneuroma	Cyst	Hematoma
Large, >4 cm	Large, >4 cm	Large, >4 cm	Large, >3 cm	Variable
Irregular	Irregular	Oval or irregular	Round or oval	Round or oval
III-defined	Ill-defined	Variable	Smooth	Variable
Heterogeneous	Heterogeneous	Heterogeneous	Homogeneous	Heterogeneous
>10 HU, ± calcification Variable enhancement and necrotic areas	>10 HU, ± calcification Variable enhancement	>10 HU, ± calcification Variable enhancement	10 to 20 HU No enhancement	Variable, acute >50 HU No enhancement
$RPW \le 40\%$	Variable	Variable	No washout	No washout
$APW \le 60\%$				
lso to hypo	lso to hypo	lso to hypo	Нуро	Hyper or hypo
Hyper	Hyper	Hyper	Hyper	Нуро
No drop in SI	No drop in SI	No drop in SI	No drop in SI	No drop in SI
Heterogeneous enhancement	Heterogeneous enhancement	Heterogeneous enhancement	No enhancement	No enhancement
≥Liver uptake ≥4 SUV	≥Liver uptake ≥4 SUV	≥Liver uptake ≥4 SUV	≤Liver uptake <4 SUV	≤Liver uptake ≤4 SUV
24 JUV	≥4 30V	∠4 3UV	≥4 3UV	≥4 30 V



**Figure 71-4** Typical features of a pheochromocytoma on axial T1-weighted (A), T2-weighted (B), and postcontrast T1-weighted (C) magnetic resonance images. The lesion (*arrow*) in the right adrenal gland demonstrates T1 hypointensity and uniform T2 hyperintensity and enhances intensely after gadolinium administration.

metastases are small, precontrast CT attenuation is typically greater than 10 HU. When they are large, central necrotic areas may be less than 10 HU but a thick or nodular periphery is usually present distinguishing these from adenomas. However, many patients, particularly when being screened for metastatic disease, are scanned only after intravenous administration of a contrast medium, and in these patients the attenuation values on enhanced scans cannot be used for characterization. CT densitometry on delayed-phase images has been described but is not useful.<sup>8,10</sup> Hence, the lesions identified on contrast-enhanced CT are further evaluated with a dedicated adrenal protocol CT. Metastases typically demonstrate slow contrast

washout or even an increase in attenuation on delayed-phase images. When delayed-phase images are obtained at 10 minutes, a relative washout and an absolute washout of less than 52% and less than 38%, respectively, indicate an indeterminate but likely malignant lesion.<sup>10</sup> For 15-minute delays, the corresponding thresholds are 40% and 60%.

## Magnetic Resonance Imaging

On MRI, adrenal metastases have nonspecific low T1/high T2 signal characteristics and do not drop signal on opposed-phase MRI.<sup>23</sup> Hemorrhage is uncommon but may occur, especially in lung carcinoma or malignant melanoma metastases. Washout

studies using MRI and gadolinium have not been proved reliable.  $^{\rm 23}$ 

## Positron Emission Tomography With Computed Tomography

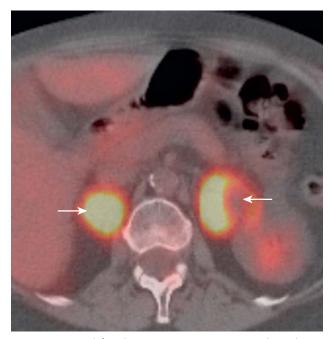
FDG-PET in conjunction with CT is now routinely used for staging the majority of cancers. This modality has been reported to be highly accurate in the detection of adrenal metastasis and allows differentiation from benign causes of adrenal enlargement. In most reported cases, malignant adrenal lesions display intense FDG accumulation higher than hepatic activity. Nonfunctional adenomas, on the other hand, being metabolically inactive, are not typically FDG avid. The degree of uptake within an adenoma, however, can be variable, occasionally being higher than background activity and lower, equal to, or slightly higher than liver activity. The cause of FDG uptake in adenomas is not well understood, and this is a limitation of FDG-PET imaging in the absolute differentiation of benign from malignant adrenal lesions (Figure 71-5).<sup>24</sup>

## ADRENOCORTICAL CARCINOMA

Primary adrenal carcinoma is a rare lesion, and 40% to 50% of cases are hyperfunctional and often associated with Cushing's syndrome. Virilization or feminization also can occur but rarely manifests as hyperaldosteronism. Nearly 76% are large ( $\sim$ 6 cm) at presentation. They occur more commonly on the left than on the right, and approximately 10% are bilateral.<sup>25</sup>

## Computed Tomography

Small lesions may be homogeneous on unenhanced CT but usually display heterogeneous peripheral enhancement with contrast CT. Large tumors commonly demonstrate necrosis or hemorrhage pathologically or on CT.<sup>26</sup> Approximately 30% have calcifications detected by CT (Figure 71-6, A). The tumor spreads by local extension, lymphatic extension, or renal vein extension or to the liver, lung, or bone. Up to 24% of tumors are less than 6 cm, and on CT some are homogeneous and



**Figure 71-5** Axial fused positron emission tomography with computed tomography image at the level of the adrenal glands in a 78-yearold man with known lung cancer depicts intense fluorodeoxyglucose activity (*arrows*) in both adrenal masses that is significantly greater than that of the liver, consistent with adrenal metastases.

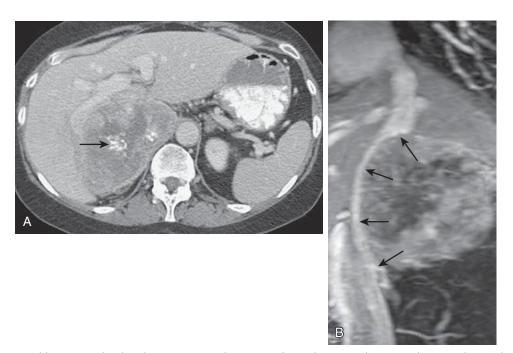


Figure 71-6 A 65-year-old woman with adrenal carcinoma. Axial contrast-enhanced computed tomography (A) and sagittal maximum intensity projection magnetic resonance angiography (B) images demonstrate a large heterogeneous enhancing mass (*arrow*, A) with necrotic areas and calcified foci in the region of the right adrenal gland invading into the liver with compression of the inferior vena cava (*arrows*, B) without thrombosis.

morphologically resemble nonhyperfunctioning adenomas. Adrenocortical carcinoma has relative contrast retention on delayed-phase contrast-enhanced CT consistent with that of other malignancies. It should be noted that biologically aggressive adrenal carcinomas can vary in their histologic appearance, so that the pathologist may not be able to accurately distinguish cortical adenoma from cortical adenocarcinoma on a histologic basis alone. False-negative results are common on samples of percutaneous biopsy of lesions that are less than 6 cm, and in view of this in many institutions all adrenal masses between 3

## Magnetic Resonance Imaging

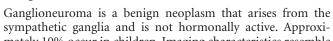
and 5 cm are surgically removed for diagnosis.<sup>25,26</sup>

MRI allows multiplanar evaluation, and it is best for defining extension of tumor particularly into the inferior vena cava (see Figure 71-6, B). Heterogeneous T1 and T2 signal intensity are due to the presence of hemorrhage and necrosis within the lesion. There is usually peripheral nodular enhancement and central hypoenhancement on contrast-enhanced MRI.14 These lesions may have focal areas of well-differentiated cortical tissue that can contain significant intracellular lipid, as in benign adenomas, so limited areas of signal drop out in a large heterogeneous adrenal mass should not deter this diagnosis.<sup>1</sup>

## **OTHER MASSES**

## Neuroblastoma

Neuroblastoma usually manifests as a palpable abdominal mass and is the most common adrenal mass in a young child. It is rare in the adult population. Nearly 66% to 80% of neuroblastomas are located in the adrenal glands, but can occur anywhere along the adrenal chain. They commonly contain calcifications, necrosis, or hemorrhage.<sup>25</sup> Ultrasonography is the preferred initial imaging modality because of its availability and lack of ionizing radiation to the child. Evaluation for local tumor extension as well as distant metastasis is usually performed by CT or MRI. The mass usually crosses midline and encases the aorta, inferior vena cava, and superior mesenteric vessels (Figure 71-7). On MRI, neuroblastoma has a typical mixed low T1/high T2 signal appearance with marked internal heterogeneity. For



mately 10% occur in children. Imaging characteristics resemble those of neuroblastoma or adrenal carcinoma within the adrenal gland.<sup>25</sup> The lesions are well-defined, homogeneously hypodense adrenal masses that may contain calcifications (Figure 71-8). Some heterogeneous enhancement may be present.<sup>28</sup> Although the appearance may resemble primary adrenal carcinoma and neuroblastoma, the lack of both clinical symptoms and local invasion may suggest the diagnosis of adrenal ganglioneuroma. The diagnosis is usually established by either biopsy or surgery.

staging of tumor, MRI is considered by some to be superior to

CT. <sup>131</sup>I-MIBG imaging is sensitive for neuroblastoma and

## Adrenal Cysts

pheochromocytoma.2

Ganglioneuroma

Adrenal cysts are rare, but imaging findings are often diagnostic. Approximately 84% represent either endothelial cysts or pseudocysts.<sup>27</sup> True cysts are characterized by thin nonenhancing walls and fluid attenuation on CT (Figure 71-9). They have fluid density, and peripheral calcifications may be seen in 15%.25 Pseudocysts are usually of low density, but they may have thick walls, internal septations, and calcifications.<sup>27</sup> On CT, approximately 54% of benign adrenal cysts can have calcifications, usually in the cyst wall. Higher density within the cyst may occur secondary to hemorrhage. Simple cysts have the characteristic homogeneous low T1/high T2 signal on MRI that is seen in cysts of other organs. An atypical signal may result from proteinaceous material or blood in the cyst. Pseudocysts can be large and complex in appearance on MRI, possibly because of hemorrhage. A complex cyst may be difficult to differentiate from metastasis or other necrotic tumor or abscess.<sup>21</sup>

## Hematoma

Adrenal hematomas generally result from trauma, sepsis, hypotension, or anticoagulation therapy. In newborns, hypoxia, septicemia, birth trauma, and coagulopathy are common causes.<sup>2</sup> Left-sided hemorrhage may result from left renal vein thrombosis. Patients with coagulopathy are prone to bilateral adrenal



adrenal gland. Axial contrast-enhanced computed tomography demonstrates an ill-defined heterogeneously enhancing mass (arrowheads) with necrotic areas within that encase the aorta (a) and superior mesenteric artery (s).

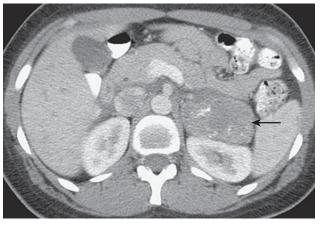


Figure 71-8 Axial contrast-enhanced computed tomography image from a 20-year-old man with ganglioneuroma in the left adrenal gland shows a heterogeneously enhancing mass (arrow) with necrotic areas and calcification in the region of the left adrenal gland.

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hemorrhage. When bilateral, adrenal hemorrhage in adults may rarely result in sudden adrenal insufficiency.<sup>25</sup> Traumatic adrenal hematomas are usually right sided or bilateral and are typically associated with other injuries but in some cases may be the only abdominal finding. The adrenal shape may be preserved despite

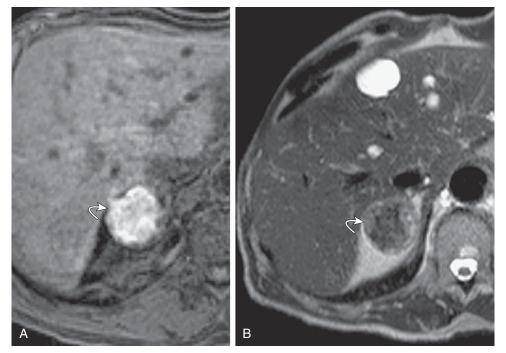


**Figure 71-9** Axial contrast-enhanced computed tomography image demonstrates a fluid density lesion (*arrow*) in the right adrenal gland, consistent with a cyst.

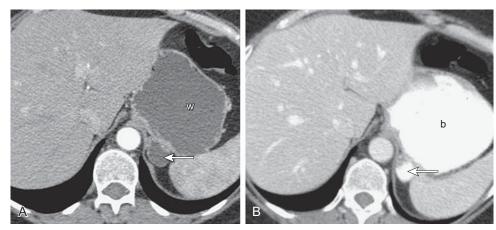
enlargement of the gland.<sup>27</sup> The gland may return to normal appearance, or it may calcify within 8 to 12 weeks. The appearance on MRI varies with the age of the blood products. Acute hemorrhage will have intermediate or high T1 signal. Chronic hematoma has nonspecific low T1/high T2 or low T1 and T2 signal intensity (Figure 71-10).<sup>27</sup> Ultrasound can be useful in children but has limited role in adults.

## EMERGING TECHNOLOGY: DUAL ENERGY COMPUTED TOMOGRAPHY

Dual-energy CT (DECT) is new technology that has ability for improved lesion detection and characterization. DECT typically acquires images at two different energies (usually combination of 80 and 140 kVp). The reconstructed data can generate virtual unenhanced, iodine and material density images. The virtual unenhanced images derived from contrasted DECT acquisitions have important implications for characterizing lipid-rich adenoma in patients who have only received a postcontrast examination. On the other hand, iodine and material density images are optimized for better detection of lesion enhancement. Studies have described the utility of DECT in adrenal lesion characterization.<sup>29</sup> Helck and colleagues<sup>30</sup> studied whether single-phase dual-source DECT-based attenuation measurements can reliably differentiate lipid-rich adrenal adenomas from malignant adrenal lesions. Adrenal adenoma was diagnosed if density on virtual noncontrast images was 10 HU or less. Based on this reference standard, 46 of 57 (80.7%) adrenal masses were characterized as adenomas or other benign lesions (9 malignant lesions were detected). Based on a cutoff value of 10 HU, virtual noncontrast images allowed for correct identification of adrenal adenomas in 33 of 46 (71%) masses, whereas 13 of 46 (28%) adrenal adenomas were lipid poor, with a density



**Figure 71-10** Magnetic resonance imaging in a 28-year-old woman with a recent history of abdominal trauma demonstrates typical features of adrenal hematoma on an axial T1-weighted image with fat saturation (A) and an axial T2-weighted image (B). The lesion in the right adrenal gland has T1 hyperintensity with corresponding T2 hypointensity (*arrows*), suggestive of the early subacute stage of hematoma.



**Figure 71-11 A**, A small diverticulum (*arrow*) arising from the posterior wall (*w*) of the fundus of the stomach can mimic a low-density adrenal lesion on axial contrast-enhanced computed tomography with negative oral contrast. **B**, However, here the adrenal lesion was excluded by giving barium (*b*) at a different time point where the diverticulum (*arrow*) was filled with contrast agent.

of 10 HU or greater. The reported sensitivity, specificity, and accuracy for detection of benign adrenal lesions were 73%, 100%, and 81%, respectively, based on threshold of 10 HU on the virtual noncontrast images.<sup>30</sup> More recently, Mileto and associates<sup>31</sup> investigated the feasibility of dual-energy spectral CT-based material density imaging in differentiation of adrenal adenoma from nonadenomatous lesions and its comparison with standard unenhanced images. They studied 38 patients who underwent multiphasic DECT for other indications. They found lipid-rich and lipid-poor adenomas with significantly different mean density values (in milligrams per cubic centimeter) than those of nonadenomas on fat-iodine (970.4  $\pm$  17.2 vs. 1012.3  $\pm$  9.3), iodine-fat (2.5  $\pm$  0.3 vs. 4.5  $\pm$  1.5), fat-water  $(-666.7 \pm 154.8 \text{ vs.} -2141.8 \pm 953.2)$ , and water-fat (1628.4  $\pm$ 177.3 vs.  $3225 \pm 986.1$ ) images, respectively. For diagnosis of adenomas, DECT material density analysis showed a sensitivity of 96% and specificity of 100%, providing significantly improved diagnostic performance compared with unenhanced multidetector CT attenuation (sensitivity of 67% at a specificity of 100%).<sup>3</sup>

In spite of current studies, many of which are promising, evaluation of adrenal lesions using DECT needs further validation before widespread clinical use. Specifically, the characterization on conventional true unenhanced CT was based on Hounsfield unit values derived at 120-kVp settings, and corresponding values on DECT have not yet been established. Additional studies are needed to determine Hounsfield unit threshold values for virtual noncontrast sequences to characterize adrenal adenomas.

## PITFALLS

Adjacent normal structures may mimic adrenal lesions. These adrenal pseudotumors may be due to tortuous splenic vessels, splenic lobulations, pancreatic projections, exophytic upper pole renal masses, portosystemic venous collateral vessels, retroperitoneal adenopathy, gastric diverticula, and portions of the stomach. Use of positive oral and intravenous contrast media with multiplanar reformatted images on CT or supplemental MRI studies often identifies the true nature of these conditions (Figure 71-11).

## **Key Points**

- Many pathologic entities can manifest in the adrenal glands.
- All incidentally detected adrenal nodules need clinical evaluation for hormonal secretion.
- Current imaging techniques can help characterize many adrenal masses.
- Adrenal protocol CT has a high sensitivity for differentiating between benign and malignant masses.

## SUGGESTED READINGS

- Blake MA, Kalra MK: Current status of imaging for adrenal malignant involvement. *Cancer Treat Res* 143:319–329, 2008.
- Blake MA, Holalkere NS, Boland GW: Imaging techniques for adrenal lesion characterization. *Radiol Clin North Am* 46:65–78, 2008.
- Blake MA, Jhaveri KS, Sweeney AT, et al: State of the art in adrenal imaging. *Curr Probl Diagn Radiol* 31:67–78, 2002.
- Blake MA, Kalra MK, Maher MM, et al: Pheochromocytoma: an imaging chameleon. *Radiographics* 24(Suppl 1):S87–S99, 2004.
- Boland GW, Blake MA, Hahn PF, et al: Incidental adrenal lesions: principles, techniques, and algorithms for imaging characterization. *Radiology* 249:756–775, 2008.
- Elsayes KM, Mukundan G, Narra VR, et al: Adrenal masses: MR imaging features with pathologic correlation. *Radiographics* 24(Suppl 1):S73–S86, 2004.

#### REFERENCES

- Oliver TW, Jr, Bernardino ME, Miller JI, et al: Isolated adrenal masses in non–small-cell bronchogenic carcinoma. *Radiology* 153:217–218, 1984.
- 2. Devenyi I: The significance of the incidence of adrenal cortex adenoma and hyperplasia based on autopsy material. *Orv Hetil* 108:2370–2373, 1967.
- Russell RP, Masi AT, Richter ED: Adrenal cortical adenomas and hypertension: a clinical pathologic analysis of 690 cases with matched controls and a review of the literature. *Medicine* 51:211–225, 1972.
- Kloos RT, Gross MD, Francis IR, et al: Incidentally discovered adrenal masses. *Endocr Rev* 16:460–484, 1995.
- Young WF, Jr: Clinical practice: the incidentally discovered adrenal mass. N Engl J Med 356:601– 610, 2007.
- Blake MA, Holalkere NS, Boland GW: Imaging techniques for adrenal lesion characterization. *Radiol Clin North Am* 46:65–78, vi, 2008.
- Boland GW, Lee MJ, Gazelle GS, et al: Characterization of adrenal masses using unenhanced CT: an analysis of the CT literature. *AJR Am J Roentgenol* 171:201–204, 1998.
- Boland GW, Hahn PF, Pena C, et al: Adrenal masses: characterization with delayed contrastenhanced CT. *Radiology* 202:693–696, 1997.
- 9. Lee MJ, Hahn PF, Papanicolaou N, et al: Benign and malignant adrenal masses: CT distinction with attenuation coefficients, size, and observer analysis. *Radiology* 179:415–418, 1991.
- Szolar DH, Kammerhuber F: Quantitative CT evaluation of adrenal gland masses: a step forward in the differentiation between adenomas and nonadenomas? *Radiology* 202:517–521, 1997.
- 11. Blake MA, Kalra MK, Sweeney AT, et al: Distinguishing benign from malignant adrenal masses:

multi-detector row CT protocol with 10-minute delay. *Radiology* 238:578–585, 2006.

- Jhaveri KS, Wong F, Ghai S, et al: Comparison of CT histogram analysis and chemical shift MRI in the characterization of indeterminate adrenal nodules. *AJR Am J Roentgenol* 187:1303– 1308, 2006.
- Chong S, Lee KS, Kim AH: Integrated PET-CT for the characterization of adrenal lesions in cancer patients: diagnostic efficacy and interpretation pitfalls. *Radiographics* 26:1811–1826, 2006.
- Krebs TL, Wagner BJ: The adrenal gland: radiologic-pathologic correlation. *Magn Reson Imaging Clin North Am* 5:127–146, 1997.
- Kenney PJ, Wagner BJ, Rao P, et al: Myelolipoma: CT and pathologic features. *Radiology* 208:87–95, 1998.
- Cyran KM, Kenney PJ, Memel DS, et al: Adrenal myelolipoma. AJR Am J Roentgenol 166:395– 400, 1996.
- Blake MA, Kalra MK, Maher MM, et al: Pheochromocytoma: an imaging chameleon. *Radiographics* 24(Suppl 1):S87–S99, 2004.
- Radin DR, Ralls PW, Boswell WD, Jr, et al: Pheochromocytoma: detection by unenhanced CT. AJR Am J Roentgenol 146:741–744, 1986.
- Mukherjee JJ, Peppercorn PD, Reznek RH, et al: Pheochromocytoma: effect of nonionic contrast medium in CT on circulating catecholamine levels. *Radiology* 202:227–231, 1997.
- Lee MJ, Hahn PF, Papanicolaou N, et al: Benign and malignant adrenal masses: CT distinction with attenuation coefficients, size, and observer analysis. *Radiology* 179:415–418, 1991.
- Lucon AM, Pereira MA, Mendonca BB, et al: Pheochromocytoma: study of 50 cases. J Urol 157:1208–1212, 1997.
- 22. Ilias I, Yu J, Carrasquillo JA, et al: Superiority of 6-[18F]-fluorodopamine positron emission

tomography versus [1311]-metaiodobenzylguanidine scintigraphy in the localization of metastatic pheochromocytoma. *J Clin Endocrinol Metab* 88:4083–4087, 2003.

- Korobkin M, Dunnick NR: Characterization of adrenal masses. AJR Am J Roentgenol 164:643– 644, 1995.
- Yun M, Kim W, Alnafisi N, et al: 18F-FDG PET in characterizing adrenal lesions detected on CT and MRI. J Nucl Med 42:1795–1799, 2001.
- Lockhart ME, Smith JK, Kenney PJ: Imaging of adrenal masses. *Eur J Radiol* 41:95–112, 2002.
- Dunnick NR, Heaston D, Halvorsen R, et al: CT appearance of adrenal cortical carcinoma. *J Comput Assist Tomogr* 6:978–982, 1982.
- Elsayes KM, Mukundan G, Narra VR, et al: Adrenal masses: MR imaging features with pathologic correlation. *Radiographics* 24(Suppl 1):S73–S86, 2004.
- Johnson GL, Hruban RH, Marshall FF, et al: Primary adrenal ganglioneuroma: CT findings in four patients. *AJR Am J Roentgenol* 169:169– 171, 1997.
- Heye T, Nelson RC, Ho LM, et al: Dual-energy CT applications in the abdomen. AJR Am J Roentgenol 199:S64–S70, 2012.
- Helck A, Hummel N, Meinel FG, et al: Can single phase dual-energy CT reliably identify adrenal adenomas? *Eur Radiol* 24:1636–1642, 2014.
- Mileto A, Nelson RC, Marin D, et al: Dual energy multidetector CT for the characterization of incidental adrenal nodules: diagnostic performance of contrast-enhanced material density analysis. *Radiology* 274:445–454, 2015.

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## **Benign Prostatic Hyperplasia**

JOSEPH R. GRAJO | CARMEL CRONIN

## Etiology

Benign prostatic hyperplasia (BPH) is characterized by the increased volume of prostatic stroma and glandular epithelial cells involving the transitional zone and periurethral region of the prostate. Hormones such as androgens (testosterone and dihydrotestosterone [DHT]) and estrogens are thought to play a central role in proliferation of glandular epithelial elements. The neural, endocrine, and immune systems are also implicated in the prostatic tissue remodeling process.

Prostate tissue remodeling in the transitional zone is characterized by (1) hypertrophic basal cells, (2) calcification and inflammation, (3) lymphocytic infiltration, (4) increased radical oxygen species production, (5) increased basic fibroblast growth factor and transforming growth factor-beta 1 production, (6) altered autonomic innervation, and (7) altered neuroendocrine cell function with release of neuroendocrine peptides.<sup>1</sup> Smooth muscle hypertrophy resulting in increased tone in the prostate, the prostate capsule, and the bladder neck leads to increased intrinsic prostatic urethral resistance, contributing to the sequelae of BPH. These factors—glandular enlargement and increased smooth muscle tone—are targeted with medical therapy.

## Prevalence and Epidemiology

The prostate gland gradually increases in size as men age.<sup>2</sup> It is estimated that nearly 80% of men will develop BPH and as many as 30% will receive treatment for this condition during their lifetime. One in four men older than the 40 years of age will develop symptoms of BPH. More than 50% of men in the United States between the ages of 60 and 70 and as many as 80% between the ages of 70 and 90 have symptoms of BPH.<sup>3</sup>

## **Clinical Presentation**

The presenting symptoms of BPH are classified as obstructive or irritative. Obstructive symptoms include hesitancy, intermittency, incomplete voiding, weak urinary stream, and straining. Irritative symptoms include frequency of urination, nocturia, and urgency. Digital rectal examination (DRE) is commonly performed in assessing BPH. DRE tends to underestimate prostate size because much of the hyperplasia may occur away from the examining finger, which primarily feels the posterior prostate.

The symptoms of BPH may be evaluated using the American Urological Association (AUA) Symptom Index (also known as

the International Prostate Symptom Score [IPSS]). This scoring system was designed to assess the severity of BPH. It consists of seven symptoms: frequency, nocturia, weak urinary stream, hesitancy, intermittence, incomplete emptying, and urgency, each of which is scored on a scale of 0 (not present) to 5 (almost always present). Symptoms are classified as mild (total score, 0 to 7), moderate (total score, 8 to 19), and severe (total score, 20 to 35).

Prostate-specific antigen (PSA) may be elevated in both BPH and prostate cancer. BPH can increase PSA levels to two to three times normal owing to increased organ volume and/or inflammation. PSA density, PSA free percentage, and, ultimately, transrectal ultrasound (TRUS)-guided biopsy may be required to differentiate between the two pathologic processes. BPH is not a premalignant lesion, and having BPH does not seem to increase the probability of developing prostate cancer.

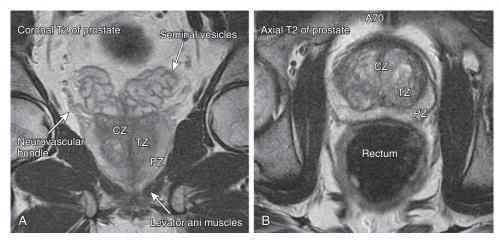
However, BPH may cause significant problems if left untreated. Patients may present with complications such as cystitis, recurrent urinary tract infections (UTIs), bladder calculi, and acute or chronic urinary retention. Some patients who have chronic urinary retention may eventually progress to renal failure. Early detection of BPH lowers the risk for bladder and renal damage caused by chronic urinary tract obstruction.

## Normal Anatomy

The prostate is a cone-shaped exocrine gland located inferior to the bladder and anterior to the rectum. It surrounds the uppermost segment of the urethra and is enveloped by an incomplete fibromuscular capsule. The gland contains a base superiorly, a mid-gland, and an apex inferiorly. It can be divided into lobes, which include the anterior lobe, posterior lobe, lateral lobes, and median lobe. The posterior lobe is palpated on DRE, and the median lobe can enlarge at the midline of the prostatic base and protrude into the base of the bladder. Important neurovascular structures lie within the pericapsular fat anterior to the apex (anterior periprostatic plexus) and posterolaterally (neurovascular bundles). The neurovascular bundles innervate the corpus cavernosum and are critical for normal erectile function.

The anatomic zonal architecture of the prostate gland is divided into three main regions: peripheral zone, central gland, and anterior fibromuscular stroma (Figures 72-1 and 72-2). The central gland is composed of the transitional zone and central zone. The peripheral zone occupies the posterolateral compartment of the prostate gland. It occupies the majority of the prostate volume in young men and is the origin of up to 70% of adenocarcinomas. The transitional zone surrounds the

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**Figure 72-1** A and B, Prostatic zonal anatomy is well seen on T2-weighted magnetic resonance imaging. The peripheral zone (*PZ*) is of intermediate to high signal intensity. This contrasts to the intermediate to low signal intensity of the transitional zone (*TZ*) and central zone (*CZ*). The capsule is seen as having an outer band of low signal intensity, and the periprostatic venous plexus has high signal intensity.

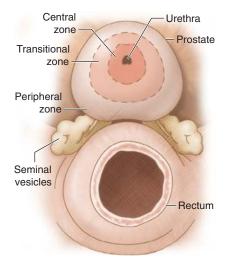


Figure 72-2 Line drawing demonstrating the zonal anatomy of the prostate along with its relationship to the seminal vesicles and rectum.

prostatic urethra proximal to the verumontanum. It accounts for only 5% to 10% of prostate volume in young men but is the zone responsible for prostatic enlargement in the setting of BPH. Up to 20% of prostate cancers occur in the transitional zone. The central zone surrounds the ejaculatory ducts and makes up approximately 25% of the prostate in young men. Only 1% to 5% of prostate cancers arise in the central zone. Carcinoma is similarly uncommon in the anterior fibromuscular stroma.

The architecture of the prostate gland changes with age. From the mid-20s, the prostate begins to gradually enlarge. The central zone atrophies, and the transitional zone enlarges secondary to BPH, with subsequent compression of the urethra. Although large prostate glands are more likely to cause symptoms of BPH, obstructive symptoms correlate poorly with gland size.

## Pathophysiology

The pathophysiologic processes of BPH are poorly understood. BPH is thought to result from both static (androgen-induced hyperplasia) and dynamic (increased smooth muscle tone) processes. Prostate gland hyperplasia and increased smooth muscle tone cause gradual compression of the urethra, interrupting the normal flow of urine (Figure 72-3). The bladder compensates by increasing micturating pressures to overcome the obstruction leading to detrusor muscle hypertrophy. This, in turn, leads to more frequent bladder contractions, more frequent micturition, and symptoms of urinary hesitancy and frequent urination. Detrusor muscle thickening also causes bladder wall trabeculation and formation of diverticula (Figure 72-4).

The bladder wall cannot maintain high micturating pressures and, in time, decompensates and weakens. It starts to accommodate high volumes of urine and fails to empty normally. This results in incomplete micturition and high residual urine volumes, which predispose to cystitis and bladder stone formation. There may be gradual development of hydroureter and hydronephrosis, which can ultimately lead to renal failure (Figure 72-5).

## Imaging

Imaging of the prostate and the urinary tract is not recommended in the routine evaluation of men with prostatism unless there are symptoms suggesting complications of BPH (e.g., recurrent UTI), findings suggesting another diagnosis (e.g., hematuria, marked prostatic asymmetry on DRE), or a history of previous urologic surgery.

TRUS and MRI provide detailed information about the internal structure of the prostate and pathologic prostate enlargement. These modalities are more accurate in estimating prostate volume than DRE and transabdominal ultrasound.

Transabdominal ultrasound is the preferred method of determining postvoid residual volume. The significance of an increased postvoid residual volume is that it indicates bladder dysfunction and is associated with a less favorable response to treatment or treatment failure.<sup>4</sup> Measuring postvoid volume is

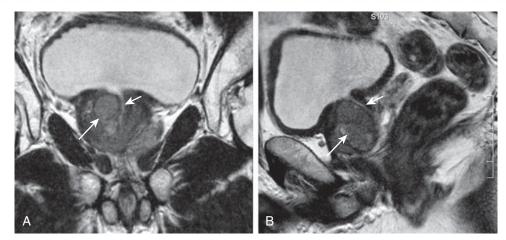


Figure 72-3 Coronal (A) and sagittal (B) T2-weighted magnetic resonance images of an enlarged prostate. A large benign prostatic hyperplasia nodule is seen on the right side anteriorly (long arrows). It is compressing and pushing the urethra posteriorly (short arrows).

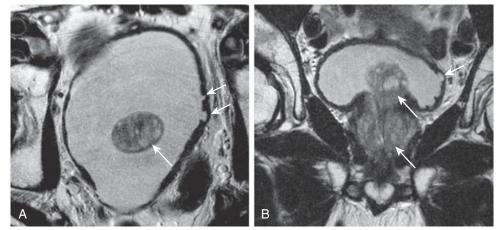
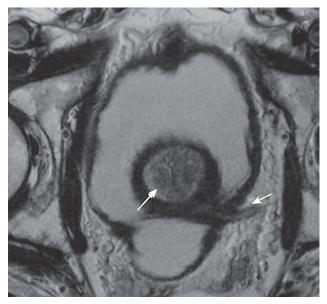


Figure 72-4 Grossly enlarged prostate (long arrows) bulging into the bladder. The bladder wall is trabeculated, and small diverticula have formed (short arrows).



**Figure 72-5** Median lobe hypertrophy (*long arrow*) in the setting of benign prostatic hyperplasia causing obstruction of the left ureter (*short arrow*).

recommended in those with symptomatic BPH by the AUA and the European Urological Association (EUA).<sup>5</sup>

## COMPUTED TOMOGRAPHY

CT can demonstrate prostate enlargement and define the gland's relationship to other pelvic organs (Figures 72-6 and 72-7). However, it requires ionizing radiation and does not accurately define prostatic zonal anatomy. Thus, the value of CT in the diagnosis and management of patients with BPH is limited.

## MAGNETIC RESONANCE IMAGING

Although not specifically performed for the evaluation of BPH, enlargement of the prostate gland related to BPH is often encountered at MRI in the evaluation of patients with elevated PSA. The presence of BPH makes identification of cancer in the central gland, particularly the transitional zone, quite challenging. In BPH, enlargement of the transitional zone will cause the prostate to increase in volume. The transitional zone will typically be heterogeneous and contain numerous nodules. This appearance is best appreciated on small field-of-view (FOV)



**Figure 72-6** Axial contrast-enhanced computed tomography image demonstrating an enlarged prostate (*arrow*) impressing on the base of the bladder.

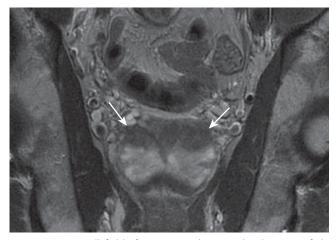


**Figure 72-7** Axial contrast-enhanced computed tomography (CT) image shows an enlarged prostate gland with parenchymal calcifications, which are commonly encountered on CT.

T2-weighted sequences, which exquisitely define the zonal anatomy of the prostate gland, especially when imaged at 3 T and/or with an endorectal coil (see Figure 72-1). The enlarged transitional zone may compress the central and peripheral zones, distorting the normal zonal architecture (Figure 72-8). There are two types of nodules that form in the transitional zone in the setting of BPH, both of which should be differentiated from tumor.

## Stromal Nodules

Stromal nodules are round BPH nodules in the transitional zone that typically demonstrate low T2 signal.<sup>6</sup> They often show restricted diffusion due their dense cellularity and smaller



**Figure 72-8** Small field-of-view coronal T2-weighted image of the prostate at 3 T demonstrating symmetric compression of the central zone bilaterally (*arrows*). Central zone compression occurs as a result of transitional zone enlargement in benign prostatic hyperplasia. Asymmetry of a compressed central zone on axial oblique images can mimic peripheral zone tumor.

volume of extracellular fluid compared to glandular tissue (Figure 72-9).<sup>7</sup> Stromal nodules also can demonstrate abnormal perfusion on dynamic contrast-enhanced sequences, specifically early arterial enhancement with rapid washout (a type 3 kinetic curve).<sup>6</sup> These characteristics make differentiation from cancer difficult.

## **Glandular Nodules**

Unlike stromal nodules, glandular nodules are typically heterogeneous and more hyperintense on T2-weighted images, allowing for easier differentiation from tumors that are usually uniformly T2 hypointense. They may show abnormal perfusion in the form of early enhancement and rapid washout, similar to both stromal nodules and tumors. However, glandular nodules typically do not show restricted diffusion because of their higher extracellular content.<sup>6</sup>

Both the stromal and glandular forms of BPH nodules classically contain a T2 hypointense rim, which creates well-defined margins on T2-weighted images (Figure 72-10). Conversely, tumors in the transitional zone typically contain more illdefined margins and lack the T2 hypointense rim seen in BPH nodules. Because of overlap in patterns of restricted diffusion and enhancement characteristics between BPH nodules and transitional zone tumors, margins are the key characteristic.

Careful examination of coronal and sagittal T2-weighted images is crucial when attempting to differentiate BPH nodules from cancer. Nodules that appear ill-defined on axial oblique images may actually be well-defined when correlated with coronal and sagittal images. Additionally, T2 hypointense nodules with restricted diffusion in the transitional zone that may appear ill-defined on tri-plane imaging may actually be a portion of a mixed BPH nodule containing a T2 hypointense rim. Although described as distinct entities, stromal and glandular elements may coexist within a single BPH nodule (Figure 72-11). BPH nodules can further confound prostate evaluation by mimicking peripheral zone tumors. Although classically located entirely within the central gland, BPH nodules can, rarely, bulge into the peripheral zone (Figure 72-12).

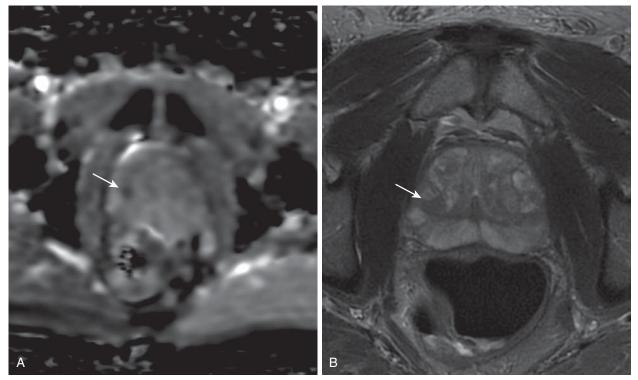
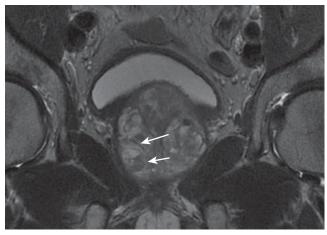


Figure 72-9 A, Apparent diffusion coefficient (ADC) map demonstrating focal restricted diffusion (*arrow*) in the transitional zone of the right midgland. B, Small field-of-view axial oblique T2-weighted image of the prostate at 3 T demonstrates a well-marginated T2 stromal nodule (*arrow*) accounting for the restricted diffusion. Restricted diffusion in stromal nodules within the transitional zone makes differentiation from tumor difficult.



**Figure 72-10** Small field-of-view coronal T2-weighted image of the prostate at 3 T demonstrating T2-hypointense rims around both a stromal nodule (*short arrow*) and glandular nodule (*long arrow*).

## ULTRASOUND

The sonographic appearance of BPH is variable, depending on histologic features and anatomic distribution. The earliest visible ultrasound finding of BPH can be seen in the fourth decade as symmetric, predominantly homogeneous hypoechoic spherical areas just superior and anterolateral to the verumontanum. As growth continues, the tissues of the anterior paraurethral transitional zone become more variable in appearance but remain hypoechoic. Additional transitional zone growth results in diffusely heterogeneous or multinodular 2 to 5 mm isoechoic foci superimposed on a hypoechoic background.<sup>8</sup> Continued enlargement produces fusion of these isoechoic nodules into 1- to 2-cm macronodules.<sup>9</sup>

BPH may be identified as a single, focal nodule or as multiple nodules within the transitional zone. Nodules may be hypoechoic or demonstrate mixed echogenicity. They may be surrounded by a thin hypoechoic rim and may distort the capsule, but they do not disrupt it. Blockage of prostatic ducts by stromal hyperplasia may produce cystic dilation of the glands of the transitional zone that can be extensive and may be easily resolved by ultrasound.<sup>10</sup> Calcifications commonly occur within the central gland or surgical capsule (Figures 72-13 to 72-16).

### Transabdominal Ultrasound

Suprapubic ultrasound has become a common first-line investigation for BPH. It is easy to perform and allows measurement of prostate size, bladder wall thickening, and postvoid residual bladder volume. Typically, there is an increase in volume of the prostate to greater than 30 mL. Approximate prostate volume is calculated by measuring the prostate in three dimensions in centimeters and multiplying the result by 0.52 ( $[A \times B \times C] \times$ 0.52). Postvoid residual should be measured and may be elevated in the setting of BPH.

### Transrectal Ultrasound

TRUS provides excellent images of internal prostatic anatomy and an accurate estimate of prostate volume.

## IMAGING ALGORITHM

See Figure 72-17 for the imaging algorithm of BPH according to the American Urological Society Symptom Index.

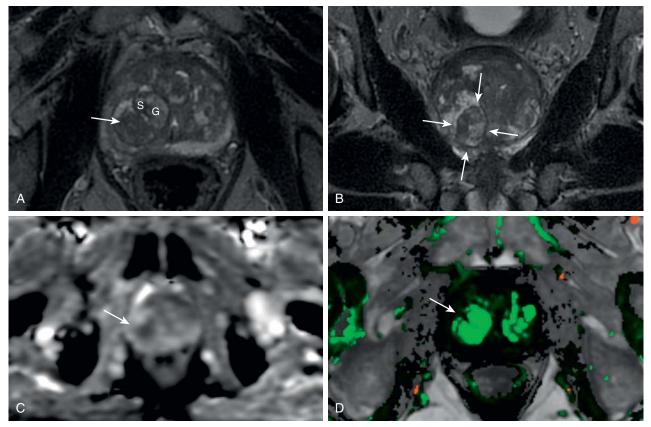


Figure 72-11 A (top left image), Small field-of-view axial oblique T2-weighted image of the prostate at 3 T demonstrates a nodule with both stromal (S) and glandular (G) elements. Note the T2 hypointense rim around the nodule, which is often better appreciated on coronal images (arrows, B). A prominent T2 hypointense stromal component of the benign prostatic hyperplasia nodule (arrow, A) shows restricted diffusion (arrow, C) and perfusion abnormality evidenced by rapid washout on a Kep color map (arrow, D).

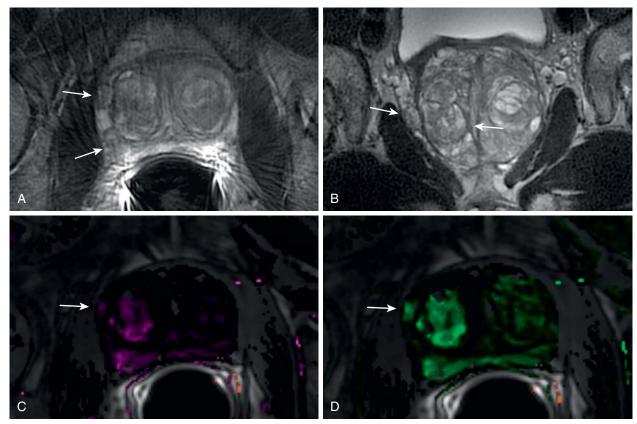
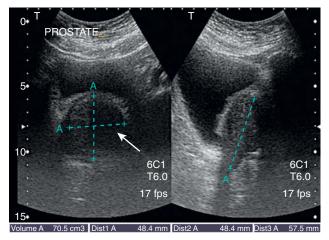


Figure 72-12 Rarely, benign prostatic hyperplasia nodules can protrude from the transitional zone into the peripheral zone, mimicking peripheral zone tumor. A, Small field-of-view axial oblique T2-weighted image of the prostate at 3 T demonstrates two heterogeneous hyperintense nodules (arrows) with hypointense rims. B, One of the nodules (short arrow) is depicted well on the coronal sequence. Note that the heterogeneous T2 (arrows) with hypointense rims. **b**, One of the hodules (snorw) is depicted well on the coronal sequence, note that the heterogeneous 12 hyperintense signal mirrors that of the larger adjacent glandular nodule in its typical transitional zone location (long arrow). Glandular nodules often show abnormal perfusion with increased wash-in (arrow, **C**; K-trans perfusion map) and rapid washout (arrow, **D**; Kep perfusion map). Targeted fusion biopsy of the nodules in this patient with elevated prostate-specific antigen confirmed benign prostate tissue. Document téléchargé de ClinicalKey.fr par Faculte de Medecine de Tunis août 30, 2016. Pour un usage personnel seulement. Aucune autre utilisation n'est autorisée. Copyright ©2016. Elsevier Inc. Tous droits réservés.

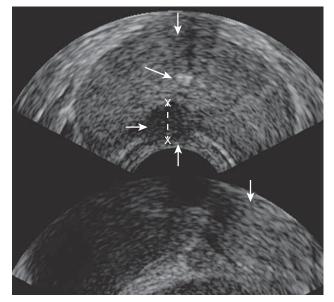


**Figure 72-13** Transabdominal ultrasound image shows an enlarged prostate gland bulging into the bladder base (*arrow*).

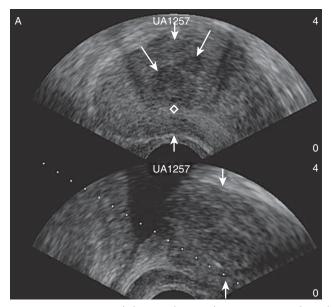
## **Differential Diagnosis**

In the setting of lower urinary tract symptoms, other causes of bladder outlet obstruction, including urethral stricture, prostate cancer, bladder neck contracture, and neurogenic disease, also should be considered.

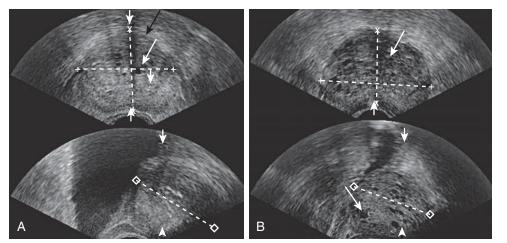
Prostate enlargement, specifically involving the transitional zone, is most commonly secondary to changes of BPH. However, up to 20% of prostate cancers will occur in the transitional zone. Identifying a transitional zone cancer in the setting of BPH can be a diagnostic challenge, even at high-quality MRI. BPH nodules, particularly stromal nodules, can mimic tumor because they often show restricted diffusion and abnormal perfusion. Recognition of well-marginated borders on small FOV T2-weighted imaging, sometimes best appreciated on coronal and sagittal sequences, is key in distinguishing stromal nodules from tumor. If tumor is not identified in the peripheral zone



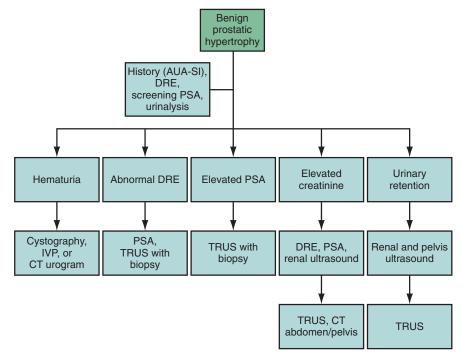
**Figure 72-14** Ultrasound image shows early calcification (arrows) in benign prostatic hyperplasia.



**Figure 72-15** Transrectal ultrasound image demonstrates an enlarged prostate gland. Focal hyperplastic nodules are seen within the enlarged transitional zone (*arrows*).



**Figure 72-16** A and B, Transrectal ultrasound images show cystic degeneration (*arrows*) within an enlarged gland—a feature of benign prostatic hyperplasia.



**Figure 72-17** Imaging algorithm for benign prostatic hyperplasia. *AUA-SI*, American Urological Society Symptom Index; *CT*, computed tomography; *DRE*, digital rectal examination; *IVP*, intravenous pyelography; *PSA*, prostate-specific antigen; *TRUS*, transrectal ultrasonography.

on MRI in the setting of an elevated PSA, indeterminate or suspicious nodules in the transitional zone can be targeted with fusion biopsy.

## Treatment

## MEDICAL TREATMENT

Available treatments include watchful waiting, lifestyle changes, medical therapies, and minimally invasive or surgical therapies. Patients with mild or moderate symptoms (AUA-SI score of  $\leq$ 7) should be managed with watchful waiting and lifestyle changes. Patients should decrease fluid intake before bedtime, reduce alcohol and caffeine intake, and follow timed voiding schedules.<sup>11</sup> Both static (androgen-induced prostate enlargement) and dynamic (increased smooth muscle tone) components are targeted with medical therapy.

Alpha-adrenergic blockers and 5-alpha reductase inhibitors may be used alone or in combination. Alpha-1 adrenergic receptor antagonists (doxazosin, terazosin, alfuzosin, and tamsulosin) reduce prostatic urethral resistance and may relieve outflow obstruction. 5-Alpha reductase inhibitors (finasteride and dutasteride) block the conversion of testosterone to its more potent counterpart, DHT. This reduces prostate size and may relieve lower urinary tract symptoms in men who have BPH while maintaining serum testosterone levels within the normal range.<sup>12</sup>

## SURGICAL TREATMENT

Indications for surgical therapy for BPH include urinary retention, intractable lower urinary tract symptoms, recurrent UTIs, azotemia, or recurrent hematuria when other causes have been excluded. In today's practice, many procedures are performed for patients who have tried medical management but continue to suffer moderate to severe lower urinary tract symptoms. Prostate size influences the operative approach. Transurethral resection of the prostate (TURP) is the preferred option and has largely replaced open surgery. Open surgery is rarely performed but may be considered in situations in which the gland is very large, when there are complicating factors, or when the bladder has been damaged and needs to be repaired.<sup>13</sup> Newer alternatives include transurethral electrovaporization of the prostate (TVP), laser TURP, visual laser ablation (VLAP), transurethral microwave thermotherapy (TUMT), transurethral needle ablation (TUNA), and ethanol injection.

#### What the Referring Physician Needs to Know

- BPH is a common process in aging men and involves enlargement of the prostate's transitional zone.
- Differentiating tumor from BPH nodules within the transitional zone can be challenging.
- Management of BPH is tailored to symptoms and AUA-SI score. A combination of watchful waiting, medications, and surgery can be used.

## **Key Point**

 Although BPH is a benign condition, it can cause serious long-term problems, such as urinary obstruction and renal failure.

#### SUGGESTED READING

Oto A, Kayhan A, Jian Y, et al: Prostate cancer: differentiation of central gland cancer from benign prostatic hyperplasia by using diffusion-weighted and dynamic contrast-enhanced MR imaging. *Radiology* 257:715–723, 2010.

#### REFERENCES

- 1. Untergasser G, Madersbacher S, Berger P: Benign prostatic hyperplasia: age-related tissueremodeling. *Exp Gerontol* 40:121–128, 2005.
- Berry SJ, Coffey DS, Walsh PC, et al: The development of human benign prostatic hyperplasia with age. J Urol 132:474–479, 1984.
- 3. O'Brien WM: Benign prostatic hypertrophy. Am Fam Physician 44:162–171, 1991.
- Wasson JH, Reda DJ, Bruskewitz RC, et al: A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate. N Engl J Med 332:75–79, 1995.
- American Urological Association: EUA guideline update 2002, AUA guidelines, 2003, Linthicum, MD, 2003, American Urological Association.
- 6. Pokharel SS, Patel NU, Garg K, et al: Multiparametric MRI findings of transitional zone prostate cancers: correlation with 3-dimensional transperineal mapping biopsy. *Abdom Imaging* 40:143–150, 2015.
- Oto A, Kayhan A, Jian Y, et al: Prostate cancer: differentiation of central gland cancer from benign prostatic hyperplasia by using diffusionweighted and dynamic contrast-enhanced MR imaging. *Radiology* 257:715–723, 2010.
- Wasserman NF: Benign prostatic hyperplasia: a review and ultrasound classification. *Radiol Clin North Am* 44:689–710, 2006.
- Hasegawa Y, Sakamoto N, Gotoh K: Relationship of ultrasonic and histologic findings in benign prostatic hyperplasia. *Prostate* 28:111– 116, 1996.

- Kawashima A, Glockner J, King B: CT urography and MR urography. *Radiol Clin North Am* 41:945–961, 2003.
- Walmsley K, Gjertsen CK, Kaplan SA: Medical management of BPH: an update. In Walsh PC, Retik AB, Vaughan ED, et al, editors: *Campbell's urology updates*, Philadelphia, 2004, Elsevier, pp 1–12.
- 12. Chapple CR: Pharmacological therapy of benign prostatic hyperplasia/lower urinary tract symptoms: an overview for the practising clinician. *BJU Int* 94:738–744, 2004.
- Yuen JS, Ngiap JT, Cheng CW, et al: Effects of bladder volume on transabdominal ultrasound measurements of intravesical prostatic protrusion and volume. *Int J Urol* 9:225–229, 2002.



## Benign and Malignant Focal Prostate Lesions

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## **Benign Focal Prostate Lesions**

## ETIOLOGY

Benign focal lesions of the prostate include benign prostatic hyperplasia (BPH) (see Chapter 72), congenital cysts, acquired cysts, prostatitis (acute bacterial, chronic bacterial, chronic pelvic pain syndrome [inflammatory and noninflammatory], and asymptomatic prostatitis), prostatic abscess, and prostatic calcification.

The National Institutes of Health classification of prostatitis syndromes provides a useful conceptual framework.<sup>1</sup> Categories I and II reflect acute and chronic bacterial prostatitis, respectively. Category III, known as chronic prostatitis/chronic pelvic pain syndrome, constitutes the vast majority (>90%) of cases and is divided into IIIA (inflammatory) and IIIB (noninflammatory). Category IV refers to asymptomatic inflammatory prostatitis, usually diagnosed incidentally.

## PREVALENCE AND EPIDEMIOLOGY

Prostatitis is perhaps the most common urologic complaint in men younger than 50 years of age and affects 11% to 16% of American men over the course of their lifetime.

## CLINICAL PRESENTATION

The presentation of benign prostate disease varies according to the particular pathologic process. For example, acquired prostate cysts and calcification are typically asymptomatic, whereas prostatitis ranges from incidentally detected asymptomatic conditions to symptomatic cases.

## PATHOLOGY

Any part of the prostate gland can be involved by prostatitis, abscess, or calcification. Acquired cysts are located in a paramedian distribution. In prostatitis, there is an increased number of inflammatory cells. Cysts and calcifications are benign processes.

## IMAGING

The most commonly used diagnostic imaging techniques for prostate evaluation are transrectal ultrasound (TRUS) and MRI. Benign findings such as cysts and calcifications are typically incidental, usually found on routine investigation for other conditions; most benign processes such as BPH and prostatitis require little investigation. TRUS can provide high-resolution images of the prostate and real-time guidance for intervention such as biopsy, aspiration, and drainage, without the use of radiation. Magnetic resonance imaging (MRI) accurately delineates the internal prostatic anatomy but is not routinely used for the investigation of benign prostate lesions owing to its high cost and relatively limited availability. Relative to these modalities, radiography and computed tomography (CT) have limited roles in the evaluation of most prostate processes.

## TREATMENT

Antibiotics are the mainstay of treatment for prostatitis. Other treatments, including both pharmacologic and nonpharmacologic approaches, have been assessed as potential treatments for chronic prostatitis and pelvic pain syndromes.<sup>2</sup> Prostatic abscess drainage is the only indication for surgical intervention in benign prostatic disease.

## SPECIFIC LESIONS

## Acute Bacterial Prostatitis

**Etiology.** Acute bacterial prostatitis is most commonly caused by aerobic gram-negative rods, in particular *Escherichia coli* and *Pseudomonas* species. Bacteria may ascend to the prostate by reflux of infected urine into the prostatic duct, by lymphatic or hematogenous dissemination, or during interventions such as prostatic biopsy.<sup>3</sup> Emphysematous prostatitis occurs secondary to infection with gas-forming organisms; while rare, it is associated with high mortality.

**Prevalence and Epidemiology.** Acute bacterial prostatitis is rare and is seen in less than 5% of patients with prostatitis.

**Clinical Presentation.** Acute bacterial prostatitis usually manifests as an acute illness with fever, chills, lower back and perineal pain, urinary frequency and urgency, and dysuria. Rectal palpation usually reveals an enlarged, exquisitely tender prostate gland. The diagnosis of acute bacterial prostatitis is based primarily on clinical findings, in association with positive results of urinalysis and urine culture.

**Pathology.** The prostate may be focally or diffusely involved. In acute infection, the prostate enlarges secondary to infection and inflammation. An increased number of inflammatory cells is seen in prostate biopsy specimens.

**Imaging.** Radiologic examinations usually are not required, unless severe infection and/or abscess is suspected. When indicated, ultrasonography and MRI are favored for their high soft tissue contrast, multiplanar capabilities, and lack of ionizing



**Figure 73-1** Axial contrast-enhanced computed tomography image of the prostate in a patient with acute bacterial prostatitis. Note the enlarged gland with areas of low attenuation (*arrows*).

radiation. However, imaging modalities may be limited in the differentiation of prostatitis from BPH and prostate cancer. Prostatic tenderness associated with acute prostatitis may preclude TRUS.

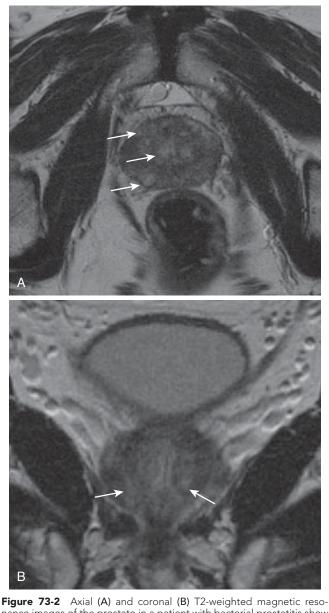
*Computed Tomography.* In acute prostatitis, the gland may appear normal or focally or diffusely enlarged. There is homogeneous attenuation with possible nonspecific stranding in the periprostatic fat (Figure 73-1).

*Magnetic Resonance Imaging.* The prostate may appear normal on MRI in the setting of acute prostatitis. It may be focally or diffusely enlarged. Single or multiple foci of high signal intensity on T2-weighted images may be seen (Figure 73-2). T1-weighted imaging is nonspecific owing to limited delineation of the internal structure of the prostate. On postcontrast T1-weighted images, the areas of inflammation enhance with gadolinium. Diffusion weighted imaging (DWI) has been reported to yield higher apparent diffusion coefficients (ADCs) in prostatitis cases than in malignancy, but with significant overlap; caution must be taken to not mistake malignancy for acute or chronic prostatitis.<sup>4</sup>

*Ultrasound.* By TRUS, the prostate gland may be of normal or enlarged size and may appear normal or demonstrate focal or diffuse areas of mixed echogenicity. Doppler vascularity may be increased. Other ultrasound features of prostatitis include dilatation of the periprostatic venous plexus, elongated seminal vesicles, and thickening of the inner septa. These features can resemble both the changes of BPH and prostatic carcinoma.

*Imaging Algorithm.* Radiologic imaging is rarely required and only in the instance when severe infection and/or abscess is suspected.

**Differential Diagnosis.** The diagnosis of acute bacterial prostatitis is based primarily on clinical findings, in association with positive results on urinalysis and urine culture. Prostatitis cannot be definitively differentiated from prostate cancer by imaging alone. Further confounding this point, in the presence of acute infection, the prostate-specific antigen (PSA) value



**Figure 73-2** Axial (A) and coronal (B) 12-weighted magnetic resonance images of the prostate in a patient with bacterial prostatitis show multifocal areas of increased signal intensity (*arrows*) consistent with prostatitis.

may be elevated. Investigation for prostate cancer should be initiated if the PSA level fails to return to normal levels after therapy.

**Treatment.** Antibiotics are the mainstay of treatment for acute bacterial prostatitis. Full response and resolution are expected. Radiologic or surgical interventions are usually not required for acute prostatitis unless complicated by abscess formation.

## What the Referring Physician Needs to Know: Acute Bacterial Prostatitis

- The diagnosis of acute bacterial prostatitis is based primarily on clinical and laboratory findings.
- Antibiotics are the mainstay of treatment.

## **Prostatic Abscess**

**Etiology.** Prostatic abscess can occur from local spread of infection, hematogeneous seeding, or instrumentation of the prostate or lower urinary tract or may be secondary to preexisting prostatitis. *E. coli* and *Staphylococcus* are the most commonly involved organisms. Early antibiotic therapy has reduced the incidence of abscess as a complication of prostatitis.

**Prevalence and Epidemiology.** Prostate abscess is rare, diagnosed only in 0.2% of patients with urologic symptoms and in 0.5% to 2.5% of patients hospitalized for prostatic symptoms.<sup>5</sup>

**Clinical Presentation.** A high degree of clinical suspicion and close monitoring of response to treatment is required to make the diagnosis, as the symptoms of prostatic abscess are similar to those of acute prostatitis and other lower urinary tract inflammatory conditions. Prostatic abscess should be suspected when there is failure to respond to treatment of acute bacterial prostatitis.

**Pathophysiology.** Prostatic abscess may involve any part of the gland. If it occurs at the apex, spontaneous bladder or proximal prostatic urethra fistula formation may occur. If the abscess is situated at the base of the gland, it may extend through perirectal tissues into the ischiorectal fossa, resulting in rectal and perineal fistulas.

**Pathology.** Inflammatory cells and bacteria are seen in abscess aspirates.

**Imaging.** The imaging features of prostate abscess are similar to those of abscess in other areas of the body. They range from focal tissue abnormality to gas-containing fluid collections.

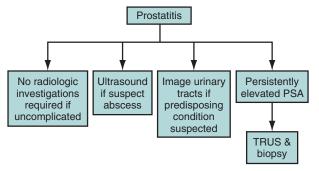
*Computed Tomography.* CT allows for rapid, comprehensive evaluation of prostatic abscess and assessment for involvement of periprostatic tissue, organs, and vascular structures.

CT features of prostatic abscess include focal or diffuse enlargement, heterogeneous attenuation, and low-density collection (Figure 73-3). Prostatic abscess may be unilocular or multilocular, may contain gas, and enhances peripherally after administration of intravenous contrast. Periprostatic fat and adjacent seminal vesicles and bladder may be secondarily infected.<sup>6</sup> *Magnetic Resonance Imaging.* MRI features closely parallel those found on CT, with the added benefit of superior soft tissue contrast (though with longer examination time). A prostatic abscess demonstrates well-defined high signal intensity on T2-weighted images but is usually not well seen on T1-weighted images without contrast enhancement. On administration of intravenous gadolinium, it shows peripheral enhancement of variable intensity. Spread of infection or complications of chronic disease such as fistula formation may be evident. In patients with prostatic abscess, T2-weighted MRI shows a fluid-containing lesion with radiating, streaky areas of low signal intensity.

*Ultrasound.* On ultrasound evaluation, prostatic abscess appears as a heterogeneous mass that may contain internal echoes, septations, and shadowing. When there is marked edema, a hypoechoic halo may be observed on gray-scale ultrasonography. When air is present, shadowing may limit full visualization of the abscess and gland. There may be increased Doppler vascularity secondary to hyperemia and inflammation.

TRUS-guided drainage may be useful in the treatment of prostate abscess. Abscesses greater than 1.5 cm are usually aspirated; aspiration of the infected fluid in combination with intravenous antibiotics has a success rate of over 80% in curing prostate abscesses.<sup>7</sup> Close follow-up is key to prevent chronic prostatitis.

*Imaging Algorithm.* Cross-sectional imaging is recommended when there is a clinical suspicion of prostate abscess, usually owing to failure of prostatitis to respond to appropriate treatment (Figure 73-4). Ultrasound and MRI are preferred to



**Figure 73-4** Imaging algorithm for prostatitis. *PSA*, prostate-specific antigen; *TRUS*, transrectal ultrasonography.



Figure 73-3 Axial (A) and coronal (B) computed tomography images demonstrate a right-sided hypodense collection that is slightly irregular in outline (*arrows*, A). The prostate gland is mildly enlarged on the right side (*arrow*, B). These findings are consistent with a prostate abscess that was subsequently successfully treated with a combination of antibiotics and percutaneous interventional radiology catheter drainage (C).

## 908 PART 8 Urogenital Imaging

CT because of superior soft tissue contrast resolution. Ultrasound can guide transrectal aspiration. CT also demonstrates prostate abscess well and can guide transperineal drainage.

**Differential Diagnosis.** Acute bacterial prostatitis has a similar presentation. A high index of suspicion is required to diagnose prostatic abscess. The presence of the abscess is confirmed with ultrasound, MRI, or CT.

**Treatment.** Medical treatment with broad-spectrum antibiotics alone is usually unsuccessful. The presence of a prostatic abscess is an indication for drainage.

## What the Referring Physician Needs to Know: Prostatic Abscess

- A high index of suspicion is required for diagnosis.
- Adequate treatment is required to prevent sepsis and long-term complications such as formation of a pelvic fistula.
- Image-guided or surgical drainage with broad-spectrum antibiotics is the treatment of choice.

## Chronic Bacterial Prostatitis

**Etiology.** The same organisms that produce acute prostatitis also have been implicated in chronic prostatitis. Chronic prostatitis may follow acute prostatitis, but some clinicians believe that noninfective venous congestion of the prostate may be the initial change that predisposes to subsequent chronic infection. Separately, granulomatous prostatitis has been reported as a rare form of chronic inflammation. A diagnosis established only by biopsy, granulomatous prostatitis can be seen in infectious (including *Mycobacterium*), postsurgical or postradiation, and idiopathic settings.<sup>8</sup>

**Prevalence and Epidemiology.** Chronic prostatitis is rare, occurring in 5% to 10% of all men with prostatitis.<sup>3</sup>

**Clinical Presentation.** Chronic bacterial prostatitis manifests as chronic pain and recurrent urinary tract infections.

**Pathology.** Any part of the prostate may be involved. There are an increased number of inflammatory cells in the parenchyma.

**Imaging.** A chronically inflamed gland is usually small, but it may be of normal size or enlarged if BPH is present concurrently. Imaging cannot confidently differentiate prostatitis from BPH and prostate cancer.

*Computed Tomography.* CT has not been widely used in the investigation of chronic prostatitis. The prostate may be small, hypoattenuating, and may contain calcifications.

*Magnetic Resonance Imaging.* Chronic prostatitis often demonstrates diffuse streaky areas of low signal intensity on T2-weighted images, known as the "watermelon" sign. T1-weighted imaging is nonspecific, and the affected prostate may not enhance after administration of gadolinium. When chronic infection involves the peripheral zone, its appearance is difficult to distinguish from that of prostate cancer; biopsy is required for definitive diagnosis.<sup>5</sup>

Ultrasound. Similar to findings on CT and MRI, chronic prostatitis can be focal or diffuse and mostly appears as an

irregular, hypoechoic area in the peripheral zone on ultrasound evaluation.

*Imaging Algorithm.* See the imaging algorithm in Figure 73-4.

**Differential Diagnosis.** Chronic bacterial prostatitis has a similar presentation to that of chronic pelvic pain. Chronic prostatitis cannot be definitively distinguished from prostate cancer by imaging alone and may require prostate biopsy.

**Treatment.** Both pharmacologic and nonpharmacologic therapies have been evaluated in the treatment of chronic prostatitis.<sup>2</sup> Surgery usually is not required.

## What the Referring Physician Needs to Know: Chronic Bacterial Prostatitis

• Antibiotics are the mainstay of treatment of chronic prostatitis.

## Prostate Cysts

**Etiology.** Prostate cysts may be congenital or acquired. Acquired cysts include retention cysts, ejaculatory duct cysts, and cystic degeneration of BPH. Cystic carcinoma of the prostate is rare.

Cystic degeneration of BPH is the most common cause of cystic lesions in the prostate. They are located in the transitional zone and are seen as small cysts within the nodules of BPH.

Retention cysts are 1- to 2-cm, smooth, thin-walled unilocular cysts that occur in the fifth to sixth decades. They occur as a result of acquired obstruction and dilation of glandular acini and may be found in all zones of the prostate.

Ejaculatory duct cysts are typically small and are located in the lateral aspects of the prostate gland. They may accompany ejaculatory duct obstruction/obliteration with azoospermia.

**Prevalence and Epidemiology.** The exact prevalence of prostate cysts is unknown. However, cystic degeneration of BPH is common.

**Clinical Presentation.** Most patients are asymptomatic, and these cysts are detected incidentally. Rarely, they become symptomatic when inflamed or infected or when they are large, causing urinary outflow obstruction or infertility secondary to ejaculatory duct obstruction.

**Pathophysiology.** Midline cysts are usually congenital because of anomalies of the müllerian duct system. Acquired cysts are paramedian in location and most commonly associated with BPH.

Pathology. Prostate cysts are benign.

**Imaging.** Prostate cysts are usually asymptomatic and found incidentally.

*Computed Tomography.* Prostate cysts are low-density lesions in the prostate. MRI and ultrasound are superior to CT in delineating prostate cysts.

*Magnetic Resonance Imaging.* Cysts are generally uniformly high in signal intensity on T2-weighted images secondary to their fluid content. These cysts demonstrate variable

signal intensity on T1-weighted images depending on the presence of infection or hemorrhage.

*Ultrasound.* Acquired prostate cysts are anechoic lesions that occur most commonly in the transitional zone as a result of degeneration of BPH. They also may be seen in the peripheral zone.

*Imaging Algorithm.* These cysts are usually discovered incidentally. No further imaging is required.

**Treatment.** Transurethral resection or aspiration should be considered the first line of management of symptomatic cysts. Open resection may also be required.

## What the Referring Physician Needs to Know: Prostate Cysts

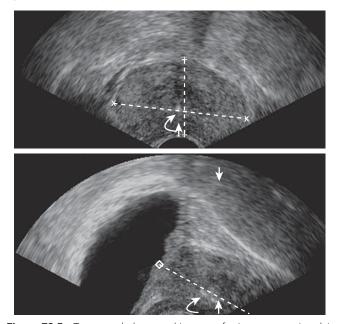
 Acquired cysts are usually incidental findings. Unless symptomatic, no treatment is required.

## Prostate Calcification

**Etiology.** Primary, or idiopathic, prostatic calcification develops in the acini of the prostatic parenchyma. The cause is unknown, and the relationship to infection is also unclear. Some believe that primary prostatic calcification develops by calcification of the corpora amylacea, forming "prostatic calculi" (Figure 73-5). These are small, round or ovoid bodies seen in the lumen of the prostatic acini that may be derived from desquamated epithelial cells and proteinaceous material.

Secondary prostatic calcification may be seen in association with BPH or carcinoma, infection, radiation therapy, and diabetes. Calculi also may develop in an abscess cavity or diverticulum.

**Prevalence and Epidemiology.** A common finding, prostate calcification increases with age, most prominently between the ages of 40 and 70 years.



**Figure 73-5** Transrectal ultrasound images of primary prostatic calcification (*arrows*) in the region of the corpora amylacea. *Dashed lines* are calipers measuring the size of the prostate.

**Clinical Presentation.** Most cases are asymptomatic. However, prostate calculi may cause obstruction, pain, infection, and hematuria.

Pathology. Calcification can be found in any part of the gland.

**Imaging.** Prostate calcifications are larger than prostate calculi. Calculi occur in the lumen of prostate acini. Calcification occurs in the parenchyma and may be focal or diffuse, involve a small or large area, and occur periurethrally or at the surgical capsule.

*Computed Tomography.* CT demonstrates high-density calcification within the prostate gland.

*Magnetic Resonance Imaging.* MRI is less sensitive than CT and ultrasound in the detection of prostate calcification. Calcifications are seen as areas of low signal intensity.

*Ultrasound.* Prostatic calcification has typical features on ultrasonography: it is echogenic, and associated acoustic shadowing may obscure visualization of the remainder of the gland.

**Differential Diagnosis.** Prostatic calcification is almost always asymptomatic. No clinical or laboratory data can determine its cause. The PSA level and fasting glucose value should be checked if the possibility of prostate cancer or diabetes is suspected.

**Treatment.** No medical treatment is required when prostate calcification is asymptomatic. Symptoms may occur in the setting of superimposed infection in which antibiotics are the mainstay of treatment. When obstructive or chronic infective symptoms occur, surgical treatment may be needed.

In those who are symptomatic, calculi may be removed transurethrally. Rarely, surgical prostatectomy may be indicated in patients with intractable infection.

## What the Referring Physician Needs to Know: Prostate Calcification

Prostate calcification is usually asymptomatic.

## **Key Points**

- Most benign prostate processes do not require radiologic investigation unless atypical signs or symptoms are present.
- Antibiotics are the mainstay of treatment for acute and chronic prostatitis. Drainage is usually indicated for prostatic abscess.
- Imaging tests alone cannot definitively differentiate prostatitis and prostate carcinoma.

## Malignant Focal Prostate Lesions

Prostate cancer is a common disease and an important health issue for men worldwide. The diagnosis and management of prostate cancer is highly complex, stemming from the uncertain natural history of the disease and its unpredictable biologic behavior. There is a high prevalence of the disease; autopsy series have revealed small prostate cancers in as many as 29% of men between ages 30 and 40 and 64% of men between ages 60 and 70.<sup>9</sup> However, a high proportion of prostate cancer fails to develop into clinically significant symptomatic cancer. There is no perfect method to determine which patients will have disease that will progress.<sup>10</sup> Factors such as a high PSA level, Gleason score, and stage are all useful for predicting outcome, but algorithms that combine stage, grade, and PSA level to predict pathologic stage or prognosis perform better than these individual factors alone.<sup>11</sup> Imaging plays an important contributory role in the management of prostate cancer.

## ETIOLOGY

The cause of prostate cancer is unknown. There are a number of risk factors, including increasing age (prostate cancer is rarely seen in men younger than age 40), ethnicity (African Americans are at greatest risk), diet, consumption of antioxidants, and a family history of prostate cancer. Recent genetic mapping studies have identified *RNASEL* and *MSR1* as potential prostate cancer susceptibility genes.<sup>12</sup>

## PREVALENCE AND EPIDEMIOLOGY

According to the National Cancer Institute Surveillance, Epidemiology, and End Results Program (seer.cancer.gov), a total of 220,800 new cases of prostate cancer were estimated in 2015, accounting for 13.3% of all new cancer cases. There were 27,540 estimated deaths from prostate cancer in 2015, resulting in 4.7% of all cancer deaths. Approximately 14% of men will develop prostate cancer at some point during their life.

Prostate cancer incidence increased dramatically in the early 1990s owing to earlier diagnosis with the introduction of PSA blood testing. Prostate cancer incidence continues to increase, although at a slower rate. This may be attributable to increased screening through PSA testing.<sup>15</sup> Although prostate cancer mortality rates have declined over the past decade, there is no evidence to link PSA screening to this decrease in mortality.<sup>16</sup>

## **CLINICAL PRESENTATION**

Prostate carcinoma is often asymptomatic. Symptomatic disease may manifest as prostatism and occasionally hematuria. Other manifesting symptoms may include bone pain and/or pathologic fractures related to bone metastases, uremia secondary to distal ureteral infiltration, and local hemorrhage resulting from tumor necrosis or obstruction. Digital rectal examination (DRE) may be normal or demonstrate an irregular, enlarged gland. Prostate cancer is characterized clinically by the serum PSA level; tumor, node, metastasis (TNM) stage; and Gleason score.

## Prostate-Specific Antigen

The PSA level is a strong indicator of stage and prognosis and is helpful in monitoring response to therapy. PSA serum levels must be interpreted carefully with regard to patient age, gland size, recent DRE or biopsy, and the presence of infection, all of which can increase the PSA level. Currently, a PSA serum threshold of 4.0 ng/mL is widely used as the threshold above which further investigations are performed for prostate carcinoma. The probability of detecting prostate cancer increases as the PSA rises. Between 0 and 2 ng/mL, 1% of patients have prostate cancer; between 2 and 4 ng/mL, 15% have prostate cancer; between 4 and 10 ng/mL, 25% have prostate cancer; and for a PSA level greater than 10 ng/mL, more than 50% will have prostate cancer.<sup>17</sup> Therefore, some have recommended the use of lower threshold values (<4 ng/mL) to avoid missing prostate cancers and to increase the likelihood that prostate cancers are detected at a curable stage.<sup>18</sup> Although this may lead to detection of more cancers, it also may result in overdiagnosis of cancers (especially in older men) that may not manifest clinically during the patient's lifetime.

The PSA density is obtained by dividing the PSA by the prostate size. This helps distinguish those with an abnormally high PSA from those with an elevated PSA secondary to BPH. A PSA density of 0.15 or greater has been proposed as a cutoff level for recommending prostate biopsy in men with serum PSA levels between 4 and 10 ng/mL and no suspicion of prostate cancer on DRE or transrectal ultrasonography (TRUS).<sup>19</sup> However, the correlation between PSA density and the presence of prostate cancer is not absolute.

PSA velocity is the rate of increase of the PSA level. A PSA velocity increase of greater than 0.75 ng/mL per year indicates a significant risk for prostate cancer regardless of the absolute serum PSA value.<sup>20</sup>

## PATHOLOGY

Prostate cancer most commonly occurs in the peripheral zone (70% of cancers), followed by the transitional zone (20%) and central zone (5%).

Ninety-five percent of prostate cancers are adenocarcinomas. Approximately 4% have transitional cell morphology and are thought to arise from the urothelial lining of the prostatic urethra. More rarely, a squamous cell type is found and, very rarely, a sarcoma (0.1% to 0.2%). A few cases have a neuroendocrine morphology believed to arise from neuroendocrine stem cells normally present in the prostate. Prostate cancer is graded histologically on a scale of 1 to 4 according to the cell differentiation and degree of anaplasia, as follows:

- *GX*: Grade cannot be assessed
- *G1:* Well differentiated (slight anaplasia) (Gleason 2 to 4)
- *G2:* Moderately differentiated (moderate anaplasia) (Gleason 5 to 6)
- *G3 to 4:* Poorly differentiated or undifferentiated (marked anaplasia) (Gleason 7 to 10)

Two thirds of prostate cancers have a mix of tumor grades. To determine the prognosis and aggressiveness of a tumor, a Gleason score is assigned histologically. Pathologists identify the two most common patterns of cells in the tissue and assign a Gleason grade to each on a scale of 1 to 5. The two grades represent the dominant and minor grade in the specimen and combine to make up the Gleason score. The higher the Gleason score, the more likely it is the cancer will grow and spread rapidly and the worse the prognosis, as follows:

- *Gleason score 2 to 4:* Well differentiated; minimal risk for death from prostate cancer in the following 15 years (indicates ~95% chance for surviving 15 years without aggressive treatment)
- *Gleason score 5 to 6:* Moderately well differentiated; modest risk for death from prostate cancer that increases slowly over at least 15 years of follow-up
- *Gleason score 7 to 10:* Moderately to poorly differentiated, with a 15-year survival rate of 15% to 40% even when cancer is diagnosed as late as 74 years of age

Atypical cells and prostatic intraepithelial neoplasia (PIN) diagnoses are made when a prostate biopsy specimen does not

look frankly neoplastic on histologic examination but the cells are abnormal. PIN can be further divided into low and high grades. The significance of low-grade PIN in relation to prostate cancer remains unclear, but the presence of atypical cells or high-grade PIN increases the likelihood of the presence of prostate cancer in the gland. There is a 30% to 50% likelihood of finding prostate cancer in a later biopsy specimen when highgrade PIN is initially discovered. For this reason, repeat biopsies are generally recommended.

## IMAGING

### Computed Tomography

CT has a limited role in assessing prostate cancer because it is usually unable to depict early-stage (T1 and T2) tumors (Figure 73-6). CT may demonstrate locally advanced disease with extracapsular extension, seminal vesicle involvement, and invasion into the mesorectum, rectum, bladder, and levator ani (Figure 73-7). Pelvic and abdominal lymph nodes also may be demonstrated. Evidence-based guidelines recommend the use of CT for distant prostate cancer staging in patients with a PSA greater than 20 ng/mL, Gleason score greater than 7, and/or clinical tumor stage T3 or higher.<sup>21</sup>

## Magnetic Resonance Imaging

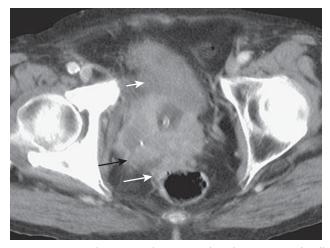
The initial role of prostate MRI was for locoregional staging in patients with biopsy-proved cancer (Figure 73-8). T1- and T2-weighted images provided anatomic information to help distinguish T2 and T3 disease (i.e., identify extracapsular extension) and evaluate for nodal disease (Boxes 73-1 and 73-2, Figures 73-9 to 73-13). Rapid growth of MRI technology and reader experience over the past 2 decades has led to a greatly expanded role for prostate MRI. The introduction of so-called multiparametric MRI has expanded the role of MRI in prostate cancer imaging to include tumor detection, localization, characterization, surveillance, and guidance for targeted biopsy.<sup>22</sup> The accuracy of prostate MRI in local staging has improved with time, most likely owing to improvements in MRI technology, better understanding of morphologic criteria used to



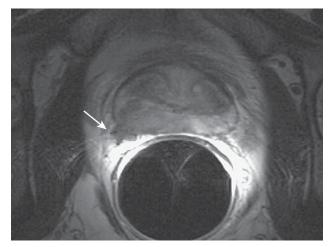
**Figure 73-6** Axial computed tomography image demonstrating an enlarged low-attenuation prostate gland. Prostate cancer was later confirmed histologically.

diagnose extracapsular extension or seminal vesicle invasion, and increased reader experience.<sup>23</sup>

There is currently no consensus regarding optimal patient preparation for prostate MRI. Most practices suggest the use of an enema before the examination, with evacuation immediately



**Figure 73-7** Axial computed tomography demonstrates locally advanced prostate cancer that has spread to the right pelvic sidewall *(black arrow),* the mesorectal fat, and the wall of the rectum *(long white arrow).* A urinary catheter is in place *(short white arrow)* because the tumor was causing obstruction at the bladder neck.



**Figure 73-8** Endorectal coil magnetic resonance image demonstrates a locally advanced prostate tumor (T3). Irregular, bulging low-signal tumor extends beyond the margin of the prostate posterolaterally on the right (*arrow*), compatible with extracapsular extension.

### BOX 73-1 FEATURES OF EXTRACAPSULAR EXTENSION OF PROSTATE CARCINOMA ON MAGNETIC RESONANCE IMAGING

- An irregular, spiculated, or angulated prostate margin
- Capsular retraction
- Asymmetry of the neurovascular bundle
- Tumor envelopment of the neurovascular bundle
- Obliteration of the rectoprostatic angle
- Tumor bulge into the periprostatic fat
- Broad tumor contact with the surface of the capsule
- Extracapsular tumor

### BOX 73-2 FEATURES OF SEMINAL VESICLE INVASION ON MAGNETIC RESONANCE IMAGING

- Disruption or loss of the normal architecture of the seminal vesicle
- Focal low signal intensity in the seminal vesicle
- Enlarged low signal intensity ejaculatory ducts
- Enlarged low signal intensity seminal vesicle
- Obliteration of the acute angle between the prostate and the seminal vesicle (best seen on sagittal images)
- Demonstration of direct tumor extension from the base of the prostate into and around the seminal vesicle

preceding the MRI to diminish the amount of stool and air in the rectum, which cause susceptibility artifact (particularly on diffusion weighted sequences). Some recommend abstinence from ejaculation for 3 days before prostate MRI to maintain seminal vesicle distention. An antispasmodic agent (e.g., glucagon) can be used to minimize bowel peristalsis, although it introduces increased cost and potential for adverse drug reactions. In the ideal scenario, it is universally recommended that the MRI is scheduled at least 6 weeks or more after TRUS biopsy to allow for resolution of postprocedural hemorrhage and inflammation.<sup>22</sup>

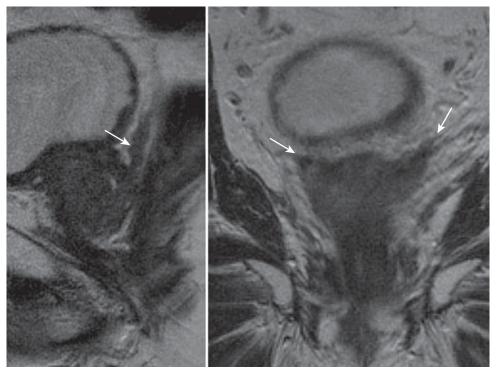
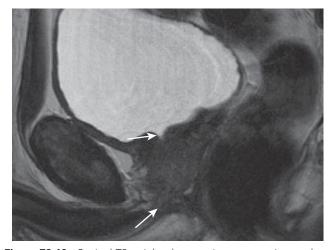
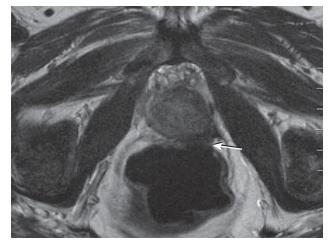


Figure 73-9 Coronal and sagittal T2-weighted magnetic resonance images demonstrating bilateral seminal vesicle invasion. The seminal vesicles are of abnormally low signal (arrows).



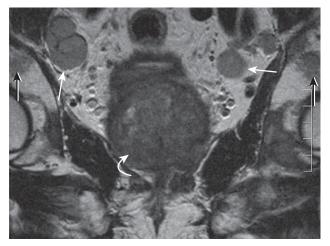
**Figure 73-10** Sagittal T2-weighted magnetic resonance image demonstrating extension into the bladder neck (*upper arrow*) and levator ani muscles (*lower arrow*) consistent with a locally advanced tumor.



**Figure 73-11** Axial T2-weighted magnetic resonance image demonstrating spread of a prostate tumor into the periprostatic fat, mesorectal fat, and the wall of the rectum (*arrow*).



Figure 73-12 Coronal T2-weighted magnetic resonance image demonstrating N1 nodal disease (nodes <2 cm) (arrow).



**Figure 73-13** Coronal T2-weighted magnetic resonance image demonstrating N2 nodal disease (>2 nodes <5 cm) (*straight white arrows*) (*curved arrow*, prostate cancer; *black arrows*, bone metastases).

Protocol Considerations. Protocols for optimal multiparametric evaluation of the prostate continue to evolve. The key is to obtain consistent image quality with an adequate signal-tonoise ratio (SNR) to allow for confident interpretation. At 1.5 T, most experienced readers think that insertion of an endorectal coil in addition to the use of a standard pelvic phased array radiofrequency coil is necessary to obtain adequate SNR in the prostate. Endorectal coil placement at 3 T produces even higher SNR, with improved image quality, higher spatial resolution, and significantly improved localization and staging performance for both experienced and less experienced radiologists.<sup>24</sup> However, the endorectal coil also can be associated with deformation of the prostate, increased cost and examination time, artifacts (specifically susceptibility), and patient discomfort (which may lead to reluctance to undergo prostate MRI). Some institutions now image exclusively at 3 T without the use of an endorectal coil. Individual centers should tailor their protocols to achieve optimal image quality as they deem appropriate.

Multiparametric Magnetic Resonance Imaging. The combination of anatomic and functional evaluation of the prostate

TABLE 73-1	System Characterization of Focal Peripheral Zone Lesions				
PI-RADS Category		Т2	DWI		
1 2		Uniform hyperintensity Linear, wedge- shaped, or diffuse hypointensity	No abnormality Indistinct ADC hypointensity		
3		Heterogeneous signal intensity or moderate hypointensity	Focal mild/ moderate ADC hypointensity		
4		Circumscribed, moderate hypointense focus/ mass (<1.5 cm)	Focal marked ADC hypointensity <1.5 cm		
5		Same as 4 but >1.5 cm or definite extracapsular extension	Same as 4 but >1.5 cm or definite extracapsular tumor		

**Prostate Imaging Reporting and Data** 

ADC, Apparent diffusion coefficient; DWI, diffusion weighted imaging; PI-RADS, Prostate Imaging Reporting and Data System.

constitutes the elements of multiparametric MRI (mpMRI). Integration of T2-weighting imaging, diffusion weighted imaging, and perfusion imaging (through dynamic contrastenhanced acquisitions) has led to a rapid growth in the understanding of the morphology, composition, and enhancement characteristics of prostate cancer and its mimics.

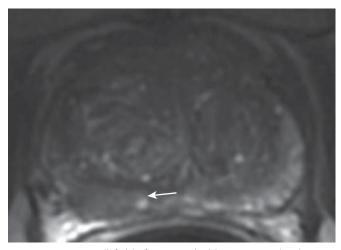
**T2-Weighted Imaging.** T2-weighted imaging is the workhorse of mpMRI because it demonstrates the zonal anatomy of the prostate while allowing identification and characterization of focal lesions. Multiplanar fast spin echo T2-weighted images of the prostate are typically obtained in small field-of-view (FOV) pulse sequences in axial, coronal, and sagittal planes. The axial and coronal sequences should be obtained in a plane oblique to the axis of the prostate to preserve the normal zonal architecture and prevent volume averaging. Large FOV axial (and possibly coronal) T2-weighted sequences are also obtained to the level of the aortic bifurcation to evaluate for nodal disease. T2-weighted sequences are also useful in detecting extracapsular extension and seminal vesicle invasion (Tables 73-1 and 73-2).

Tumors have different T2 characteristics whether they occur in the peripheral zone or transitional zone. Peripheral zone cancers typically manifest as a round or ill-defined T2 hypointense nodule (Figure 73-14). Because benign conditions such as postbiopsy hemorrhage, prostatitis, scarring/inflammation, and posttreatment changes can mimic the T2 hypointensity of tumors in the peripheral zone, correlation with other mpMRI characteristics (particularly diffusion weighted imaging) is critical. In the transitional zone, tumors are more difficult to differentiate from benign entities because of the various changes that occur in the setting of BPH. Transitional zone tumors are typically poorly marginated T2 hypointense lesions that may appear spiculated or lenticular (Figure 73-15). They lack the T2 hypointense capsule of BPH stromal nodules (see Chapter 72). Triplanar T2-weighted images are the

73-2	System Characterization of Focal Transitional Zone Lesions				
PI-RADS Category		T2	DWI		
1		Homogeneous intermediate intensity	No abnormality		
2		Circumscribed hypointense or heterogeneous encapsulated nodule (BPH)	Indistinct ADC hypointensity		
3		Heterogeneous signal intensity with obscured margins	Focal mild/ moderate ADC hypointensity		
4		Lenticular or noncircumscribed Moderately hypointense (<1.5 cm)	Focal marked ADC hypointensity <1.5 cm		
5		Same as 4 but >1.5 cm or definite extracapsular extension	Same as 4 but >1.5 cm or definite extracapsular tumor		

**Prostate Imaging Reporting and Data** 

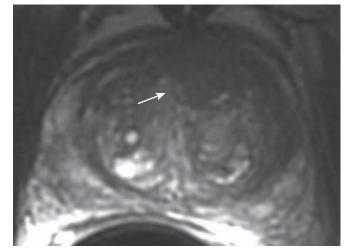
ADC, Apparent diffusion coefficient; BPH, benign prostatic hyperplasia; DWI, diffusion weighted imaging; PI-RADS, Prostate Imaging Reporting and Data System.



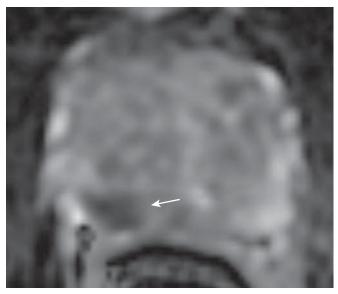
**Figure 73-14** Small field-of-view axial oblique T2-weighted image showing a focal hypointense nodule (*arrow*) in the peripheral zone of the right mid-gland in this patient—a Gleason 6 adenocarcinoma. Note the extracapsular extension at the level of the neurovascular bundle.

most important sequences for characterizing transitional zone tumors because BPH nodules can mimic carcinoma on diffusion and perfusion imaging.

**Diffusion Weighted Imaging.** DWI is a critical component of mpMRI of the prostate. DWI represents a functional assessment of the prostate by differentiating tissues with free and restricted diffusion of water molecules. Tissues with restricted diffusion are hyperintense on DWI sequences and hypointense on corresponding ADC maps. Neoplastic cells in prostate carcinoma contain high cell densities and abundance of intracellular and



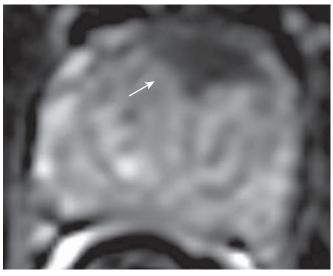
**Figure 73-15** Small field-of-view axial oblique T2-weighted image demonstrating focal lenticular hypointense signal (*arrow*) corresponding to a Gleason 6 adenocarcinoma in the anterior transitional zone of the mid-gland.



**Figure 73-16** Apparent diffusion coefficient map showing focal restricted diffusion (*arrow*) corresponding to the peripheral zone tumor in Figure 73-14.

intercellular membranes, resulting in restricted diffusion compared to normal tissues.

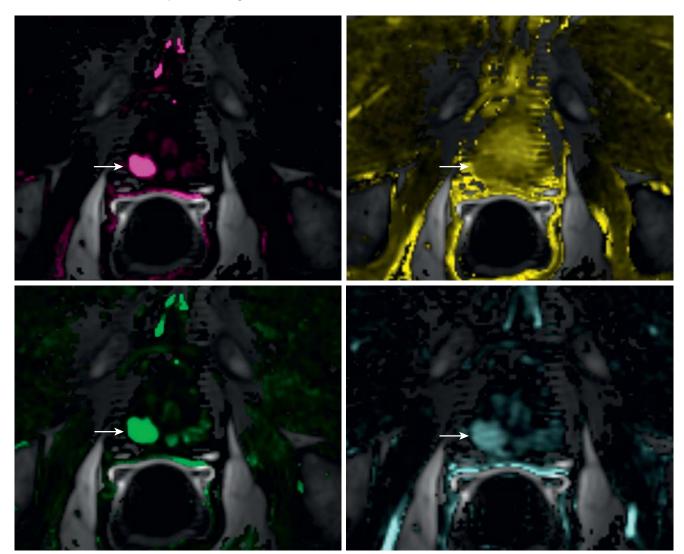
Restricted diffusion is best visualized on ADC sequences corresponding to DWI of high b-values. Close inspection of ADC sequences serves as a useful screening method for identifying prostate carcinoma, particularly within the peripheral zone (Figure 73-16). As a result of the overlap between malignant and benign focal lesions on T2-weighted imaging, the ADC sequence is usually considered the single most important sequence for characterizing peripheral zone tumor. In fact, expert prostate imagers recommend measuring peripheral zone tumor on the ADC sequence.<sup>22</sup> Although less specific compared to the peripheral zone, DWI is also useful in characterizing transitional zone cancers (Figure 73-17). Regardless of location, DWI has been found to significantly improve the sensitivity



**Figure 73-17** Apparent diffusion coefficient map demonstrating restricted diffusion (*arrow*) with lenticular morphology in this patient with transitional zone tumor (same patient as in Figure 73-15).

and specificity of T2-weighted imaging versus T2-weighted sequences alone.<sup>25,26</sup>

Dynamic Contrast-Enhanced (Perfusion) Imaging. The third component of mpMRI is dynamic contrast-enhanced (DCE) imaging or perfusion imaging. DCE imaging involves short rapid acquisitions of T1-weighted gradient echo images before, during, and after gadolinium administration. Although considered the least specific feature by many prostate imagers, DCE is an evolving technique that demonstrates the properties of angiogenesis and capillary leakiness in prostate tumors. Abnormal neoplastic tissues tend to show a rapid wash-in and washout of contrast, whereas normal tissues take up but retain contrast over time. Quantitative measurement and mapping of dynamic enhancement patterns can be used to characterize the properties of benign and malignant prostate tissue. Commercial products such as DynaCad (Invivo, Gainesville, FL) allow generation of color maps that display the wash-in or forward flux of contrast  $(k_{trans})$ , washout or reverse flux of contrast  $(k_{ep})$ , and total volume of contrast delivered (iAUGC) (Figure 73-18). Gadolinium time curves also can be processed from these color



**Figure 73-18** Perfusion maps generated from dynamic contrast-enhanced sequences in this patient with a Gleason 7 adenocarcinoma in the peripheral zone of the right mid-gland (arrows). Top left:  $k_{trans}$  (wash-in or forward flux); top right:  $V_e$  (extracellular volume fraction); bottom left:  $k_{ep}$  (washout or reverse flux); bottom right: iAUGC (area under the gadolinium concentration curve in the first 90 seconds).

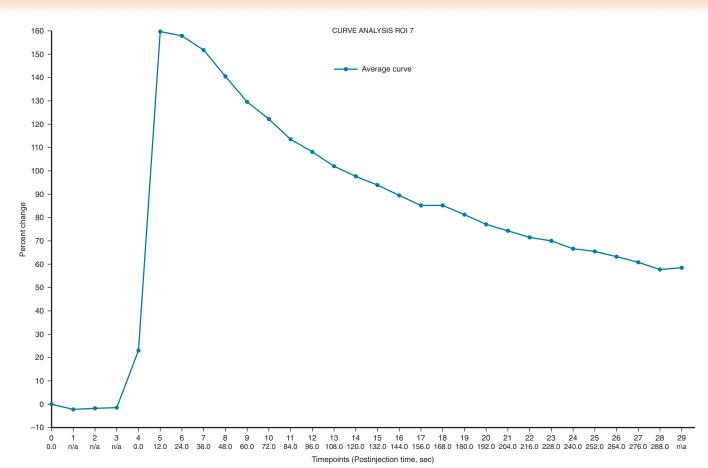


Figure 73-19 Time curve generated from the Gleason 7 cancer in the same patient as in Figure 73-18. This depicts a type 3 curve, which is the most suspicious for carcinoma because of its rapid wash-in and washout. *ROI*, Region of interest.

maps to depict the three classic enhancement curves: type 1 curve—persistent; type 2 curve—plateau; and type 3 curve—washout. Types 1 and 2 curves are classically associated with normal or benign tissue, whereas a type 3 curve is suspicious for malignancy (Figure 73-19).

Early studies on perfusion imaging have shown a significantly greater mean blood flow and interstitial volume of contrast agent distribution in prostate tumors than the mean blood flow measured in normal-appearing peripheral zone tissue.<sup>27</sup> Analysis of "wash-in" rates demonstrate increased sensitivity and specificity of peripheral zone cancer detection versus T2-weighted images alone.<sup>28</sup> These enhancement characteristics and enhancement curves can be used to increase the detection of prostate tumors.<sup>29</sup> Additionally, the combination of high spatial resolution DCE and T2-weighted imaging yields improves assessment of extracapsular extension and prostate cancer staging compared with either technique independently.<sup>30</sup>

## **Special Considerations**

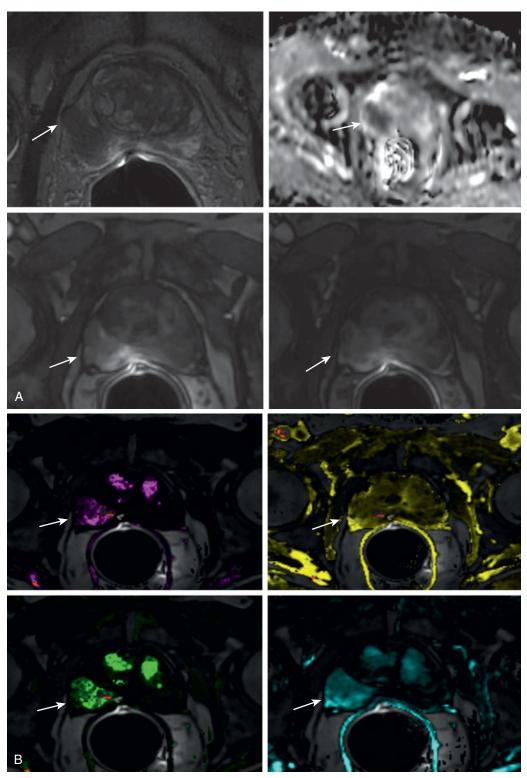
*Extracapsular Extension.* Extracapsular extension of prostate carcinoma is critical in tumor staging and subsequent patient management. mpMRI increases sensitivity for detecting extracapsular extension through the addition of DWI and DCE functional parameters (Figure 73-20).

*Neurovascular Bundle Involvement.* The neurovascular bundle is located posterolateral to the prostate gland (at the 5:00 and 7:00 positions). It is of low signal intensity on T1- and

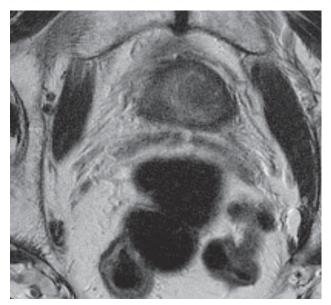
T2-weighted imaging and is surrounded by high-signal periprostatic fat. It is important to detect involvement of the neurovascular bundles because nerve-sparing surgery may be attempted in an effort to preserve potency if the neurovascular bundle is not involved.

**Posttreatment Magnetic Resonance Imaging.** The prostate decreases in volume and becomes low in signal intensity after irradiation and hormonal therapy, which should not be confused with tumor recurrence. The seminal vesicles also may demonstrate low signal intensity or irregular morphology (Figure 73-21).

**Standardization of Magnetic Resonance Imaging Reporting.** As the acquisition and interpretation of mpMRI has dramatically advanced in recent years, efforts have been made to standardize reporting. Developed by an expert prostate workgroup, Version 2 of the Prostate Imaging Reporting and Data System (PI-RADS) was recently published to reflect the most recent recommendations for reporting of mpMRI based on T2-weighted, DWI, and DCE imaging of prostate lesions in the peripheral and transitional zones.<sup>22</sup> T2-weighted and DWI characteristics are graded on a scale of 1 to 5 according to size and morphology while DCE patterns are scored according to the presence or absence of focal enhancement corresponding to T2-weighted/DWI abnormalities. See Tables 73-1 and 73-2 for characterization of focal prostate lesions according to T2-weighted and DWI PI-RADS criteria.



**Figure 73-20** Gleason 8 adenocarcinoma in the peripheral zone of the right mid-gland (arrows) demonstrating T2 hypointensity (top left, A), restricted diffusion (top right, A), early arterial enhancement (bottom left, A), and washout (bottom right, in A). Perfusion maps show increased k<sub>trans</sub> (top left, B), V<sub>e</sub> (top right, B), k<sub>ep</sub> (bottom left, B), and iAUGC (bottom right, B).



**Figure 73-21** Axial T2 magnetic resonance image demonstrating irregular seminal vesicles of low signal intensity after hormonal therapy and radiation therapy for prostate cancer.

### Additional Magnetic Resonance Imaging Techniques

*Magnetic Resonance Spectroscopy.* MR spectroscopy measures citrate, creatine, and choline to provide specific information regarding prostate metabolism. Prostate cancer is characterized by an elevated choline level (a normal cell membrane constituent that is elevated in many tumors) and/or a reduced citrate level (a constituent of normal prostate tissue) at MR spectroscopy. MR spectroscopy can improve tumor visualization and determination of tumor extent while increasing staging accuracy.<sup>31</sup> Correlation has been reported between metabolite ratios (e.g., choline and creatine over citrate ratio) and the histologic grade of prostate cancer. MR spectroscopy measurement of prostate tumor (choline + creatine)/citrate and tumor volume may even correlate with pathologic Gleason score. Thus, MR spectroscopy has potential for the noninvasive assessment of prostate cancer aggressiveness.<sup>32</sup>

*Magnetic Resonance Lymphangiography.* Nodal staging currently relies on assessment of lymph node size and shape. Neither CT nor MRI can reliably demonstrate cancer within lymph nodes that are not enlarged. The relatively new technique of MR lymphangiography demonstrates potential to detect metastases in such nodes. Lymphotropic ultrasmall superparamagnetic iron oxide (USPIO) nanoparticles are taken up by macrophages present within normal lymph nodes. T1 and T2\*-susceptibility effect of iron oxide leads to reduced signal intensity, or "negative enhancement," within a node. In metastatic lymph nodes, cancer cells replace macrophages, resulting in a lack of USPIO particle uptake. This technique allows the detection of small and otherwise undetectable lymph node metastases in patients with prostate cancer.<sup>33</sup>

## Ultrasound

Transrectal ultrasound is superior to transabdominal ultrasound for prostate evaluation. Prostate cancer most commonly appears as a hypoechoic lesion in the peripheral gland. Other ultrasound features of prostate cancer include gland asymmetry, irregular contour, and heterogeneous echotexture. Prostate cancer may have a nodular and/or infiltrative pattern of spread, which may extend along the capsule. TRUS has not shown superiority to DRE in assessing extracapsular extension.<sup>34</sup>

## Nuclear Medicine

Radionuclide bone scans have a high sensitivity but low specificity for metastatic prostate cancer (Figures 73-22 and 73-23). The American College of Radiology recommends bone scintigraphy when the PSA level is greater than 10 ng/mL and the Gleason score is greater than 6.<sup>35</sup> The American Urological Association (AUA)<sup>36</sup> and the American Joint Committee on Cancer<sup>37</sup> recommend bone scintigraphy when the PSA level is greater than 20 ng/mL.

#### **Prostate Biopsy**

**Transrectal Ultrasound–Guided Biopsy.** TRUS-guided prostate biopsy is considered the gold standard for tumor localization and diagnosis. Standard sextant biopsy involves a total of 12 random core samples of the prostate, two each from the base, mid-gland, and apex bilaterally. A single biopsy session has a sensitivity of 70% to 80% for the detection of cancer. This increases with the number of biopsy sessions (up to 99% with four biopsies).<sup>38</sup> TRUS-guided biopsy is widely available, safe, well tolerated, and relatively inexpensive. However, limitations include false-negative biopsy and incorrect risk stratification (errors of undersampling) as well as detection of clinically insignificant tumor (error of oversampling).<sup>39</sup> The false-negative rate can reach 30% to 40%.<sup>40</sup>

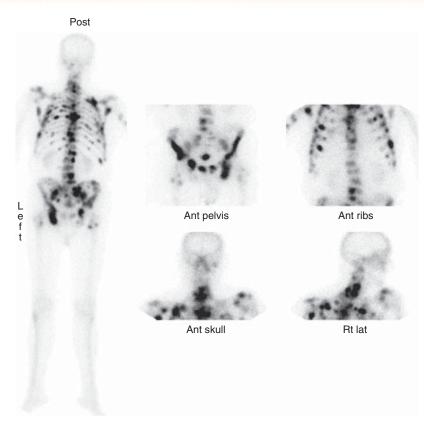
**Fusion Biopsy.** Fusion biopsy is a technique under active clinical and research investigation that allows targeting of focal suspicious prostate lesions through image fusion of mpMRI and TRUS volumetric data. Once a suspicious focal lesion(s) is identified by the radiologist on mpMRI, the lesion(s) can be targeted for fusion biopsy by drawing a region of interest that is later fused into the real-time TRUS data set by the urologist performing the biopsy (Figure 73-24). Targeted biopsy of areas likely to contain clinically significant cancer can be performed in addition to the standard random sextant biopsy. This offers potential to decrease false-negative biopsy findings, improve risk classification, limit repeat biopsy, and reduce overdetection.<sup>39</sup>

## Imaging Algorithms

When a patient has been identified on screening with an abnormal DRE or PSA level, the next step is typically TRUS biopsy (Figure 73-25). If a biopsy sample is positive, MRI staging may be considered. In patients with negative standard sextant biopsy results despite rising PSA levels, a fusion biopsy can be performed to sample the most suspicious area(s). Bone scintigraphy should be considered if the PSA level is above 10 to 20 ng/ mL, and CT should be considered if the PSA is above 20 ng/mL.

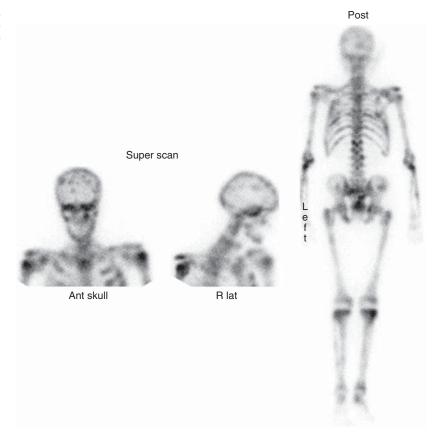
## DIFFERENTIAL DIAGNOSIS

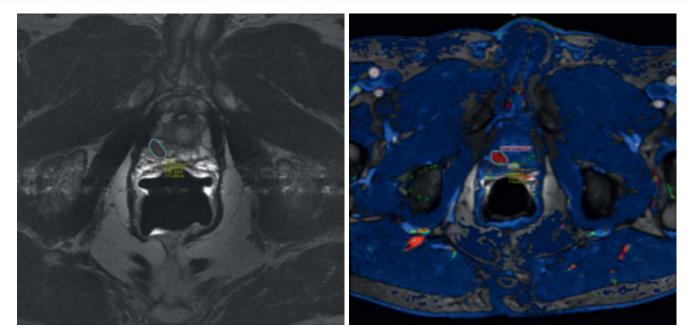
An elevated PSA level is suggestive of prostate cancer. However, the PSA value may be elevated in benign conditions such as BPH and prostatitis. The probability of prostate cancer is 1% with a PSA level between 0 and 2 ng/mL, 15% with a PSA level between 2 and 4 ng/mL, 25% with a PSA level between 4 and 10 ng/mL, and more than 50% with a PSA level greater than 10 ng/mL.<sup>17</sup> Local prostate cancers can be difficult to differentiate from



**Figure 73-22** Bone scintiscan demonstrating vertebral, rib, and pelvis uptake consistent with diffuse bone metastases. *Ant,* Anterior; *Post,* posterior; *Rt,* right.

**Figure 73-23** Bone scintiscan demonstrating a "superscan." All the radiotracer has been taken up by the bone metastases. Normal renal uptake and urinary excretion of tracer are not evident. *Ant,* Anterior; *Post,* posterior; *R lat,* right lateral.





**Figure 73-24** Axial oblique T2-weighted and perfusion map images portraying demarcation of the tumor in Figures 73-18 and 73-19 by a region of interest, which was targeted by the urologist at fusion biopsy.

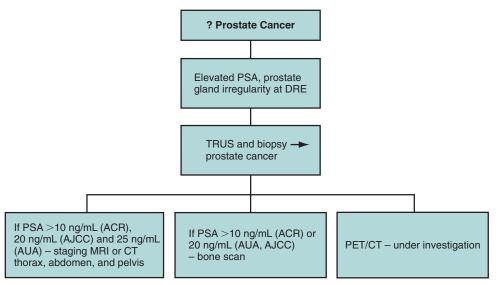


Figure 73-25 Prostate cancer algorithm. ACR, American College of Radiology; AJCC, American Joint Commission on Cancer; AUA, American Urological Association; CT, computed tomography; DRE, digital rectal examination; MRI, magnetic resonance imaging; PSA, prostate-specific antigen; TRUS, transrectal ultrasound.

prostatitis and BPH on imaging alone. TRUS sextant and/or fusion biopsy is often necessary for histologic diagnosis.

## TREATMENT

## Medical Treatment

The choice of therapy for prostate cancer depends on multiple factors, including patient age and life expectancy, comorbidity, and patient preference. Multiple therapeutic strategies are available to men who have clinically localized prostate cancer, including radical surgery, external-beam irradiation, prostate brachytherapy, cryosurgery, and watchful waiting with or without hormonal ablative therapy.

External-beam irradiation can be used as a definitive treatment for localized prostate cancer and is widely accepted as the treatment of choice in men who have advanced disease.

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Brachytherapy is most effective in patients who have lower grade cancers (Gleason score <7, PSA <10 ng/mL, and stage T1 to T2). This group has outcomes similar to those with radical prostatectomy and external-beam irradiation.

Watchful waiting is an alternative to definitive treatment in patients who have a life expectancy of less than 10 years. The rationale for this approach stems from the fact that increasing numbers of older men are being diagnosed with prostate cancer as the result of PSA screening. If disease progresses, palliative or active therapy is begun, depending on patient choice and physical condition.

Available forms of hormonal ablation include estrogens, luteinizing hormone–releasing hormone agonists, and direct androgen-blocking medications to suppress circulating androgens. This type of treatment has been used predominantly in men with advanced prostate cancer.

### Surgical Treatment

Radical prostatectomy is the gold standard for treatment of men who have clinically localized prostate cancer with a life expectancy of 10 years or greater. The 5-year progression-free survival rate after radical prostatectomy approaches 80% regardless of tumor stage or Gleason score. In patients who have Gleason 6 organ-confined disease, the 10-year biochemical progressionfree survival rate is between 91% and 97%.<sup>41</sup>

### What the Referring Physician Needs to Know

- PSA elevation can occur in a number of processes, but prostate cancer remains the diagnosis of interest because of its high prevalence.
- Differentiation between clinically significant and insignificant cancer drives patient management.
- The rapid development and growth of advanced MRI techniques have led to improved prostate characterization and continues to be an area of active research.
- Fusion biopsy is an emerging technology, allowing for targeted biopsy of suspicious focal prostate lesions.

### **Key Points**

- Prostate cancer is common and biologically heterogeneous. Imaging plays an important role in diagnosis and staging.
- Recent advances in multiparametric MRI have not only improved lesion characterization but also allowed for targeting of focal suspicious lesions on TRUS.
- Further clinical experience and standardization of prostate MRI reporting are required.

### **SUGGESTED READINGS**

American College of Radiology: MR Prostate Imaging Reporting and Data System version 2.0. <a href="http://www.acr.org/Quality-Safety/Resources/">http://www.acr.org/Quality-Safety/Resources/</a> PIRADS/>, (Accessed 03.15.). Bjurlin MA, Meng X, Le Nobin J, et al: Optimization of prostate biopsy: the role of magnetic resonance imaging targeted biopsy in detection, localization and risk assessment. *J Urol* 192:648–658, 2014. Kutikov A, Guzzo TJ, Malkowicz SB: Clinical approach to the prostate: an update. *Radiol Clin North Am* 44:649–663, 2006.

### REFERENCES

- Krieger JN, Nyberg L, Nickel JC: NIH consensus definition and classification of prostatitis. JAMA 282:236–237, 1999.
- Anothaisintawee T, Attia J, Nickel JC, et al: Management of chronic prostatitis/chronic pelvic pain syndrome: a systematic review and network meta-analysis. *JAMA* 305:78–86, 2011.
- 3. Benway BM: Bacterial prostatitis. Urol Clin North Am 35:23–32, 2008.
- 4. Nagel KN, Schouten MG, Hambrock T, et al: Differentiation of prostatitis and prostate cancer by using diffusion-weighted MR imaging and MR-guided biopsy at 3T. *Radiology* 267:164– 172, 2013.
- 5. Barozzi L, Pavlica P, Menchi I, et al: Prostatic abscess: diagnosis and treatment. *AJR Am J Roentgenol* 170:753–757, 1998.
- Thornhill BA, Morehouse HT, Coleman P, et al: Prostatic abscess: CT and sonographic findings. *AJR Am J Roentgenol* 148:899–900, 1987.
- Collado A, Palou J, Garcia-Penit J, et al: Ultrasound-guided needle aspiration in prostatic abscess. *Urology* 53:548–552, 1999.
- Naik KS, Carey BM: The transrectal ultrasound and MRI appearances of granulomatous prostatitis and its differentiation from carcinoma. *Clin Radiol* 54:173–175, 1999.
- Sakr WA, Grignon DJ, Crissman JD, et al: High grade prostatic intraepithelial neoplasia (HGPIN) and prostatic adenocarcinoma between the ages of 20-69: an autopsy study of 249 cases. *In Vivo* 8:439–443, 1994.
- 10. Albertsen PC, Hanley JA, Gleason DF, et al: Competing risk analysis of men aged 55 to 74

years at diagnosis managed conservatively for clinically localized prostate cancer. *JAMA* 280: 975–980, 1998.

- Partin AW, Mangold LA, Lamm DM, et al: Contemporary update of prostate cancer staging nomograms (Partin Tables) for the new millennium. Urology 58:843–848, 2001.
- Routh JC, Leibovich BC: Adenocarcinoma of the prostate: epidemiological trends, screening, diagnosis, and surgical management of localized disease. *Mayo Clin Proc* 80:899–907, 2005.
- 13. Deleted in review.
- 14. Deleted in review.
- 15. Jemal A, Clegg LX, Ward E, et al: Annual report to the nation on the status of cancer, 1975-2001, with a special feature regarding survival. *Cancer* 101:3–27, 2004.
- Thompson IM, Pauler DK, Goodman PJ, et al: Prevalence of prostate cancer among men with a prostate-specific antigen level < or = 4.0 ng per milliliter. N Engl J Med 27(350):2239–2246, 2004.
- Catalona WJ, Partin AW, Slawin KM, et al: Use of the percentage of free prostate-specific antigen to enhance differentiation of prostate cancer from benign prostatic disease: a prospective multicenter clinical trial. *JAMA* 279:1542– 1547, 1998.
- Krumholtz JS, Carvalhal GF, Ramos CG, et al: Prostate-specific antigen cutoff of 2.6 ng/mL for prostate cancer screening is associated with favorable pathologic tumor features. Urology 60:469–473, 2002.

- Bazinet M, Meshref AW, Trudel C, et al: Prospective evaluation of prostate-specific antigen density and systematic biopsies for early detection of prostatic carcinoma. *Urology* 43:44–51, 1994.
- D'Amico AV, Chen MH, Roehl KA, et al: Preoperative PSA velocity and the risk of death from prostate cancer after radical prostatectomy. *N Engl J Med* 351:125–135, 2004.
- O'Dowd GJ, Veltri RW, Orozco R, et al: Update on the appropriate staging evaluation for newly diagnosed prostate cancer. J Urol 158:687–698, 1997.
- American College of Radiology: MR Prostate Imaging Reporting and Data System version 2.0. <a href="http://www.acr.org/Quality-Safety/Resources/PIRADS/">http://www.acr.org/Quality-Safety/Resources/PIRADS/</a>, (Accessed 03.15.).
- Hricak H: Imaging prostate cancer: a multidisciplinary perspective. *Radiology* 243:28–53, 2007.
- Heijmink SW, Fütterer JJ, Hambrock T, et al: Prostate cancer: body-array versus endorectal coil MR imaging at 3 T—comparison of image quality, localization, and staging performance. *Radiology* 244:184–195, 2007.
- 25. Haider MA, van der Kwast TH, Tanguay J, et al: Combined T2-weighted and diffusion-weighted MRI for localization of prostate cancer. *AJR Am J Roentgenol* 189:323–328, 2007.
- Shimofusa R, Fujimoto H, Akamata H, et al: Diffusion-weighted imaging of prostate cancer. *J Comput Assist Tomogr* 29:149–153, 2005.
- Buckley DL, Roberts C, Parker GJM, et al: Prostate cancer: evaluation of vascular characteristics with dynamic contrast-enhanced T1-weighted MR imaging—initial experience. *Radiology* 233: 709–715, 2004.

### 922 PART 8 Urogenital Imaging

- Kim JK, Hong SS, Choi YJ, et al: Wash-in rate on the basis of dynamic contrast-enhanced MRI: usefulness for prostate cancer detection and localization. *J Magn Reson Imaging* 22:639–646, 2005.
- 29. Engelbrecht MR, Huisman HJ, Laheij RJ, et al: Discrimination of prostate cancer from normal peripheral zone and central gland tissue by using dynamic contrast-enhanced MR imaging. *Radiology* 229:248–254, 2003.
- Bloch BN, Furman-Haran E, Helbich TH, et al: Prostate cancer: accurate determination of extracapsular extension with high-spatial-resolution dynamic contrast-enhanced and T2-weighted MR imaging: initial results. *Radiology* 245:176– 185, 2007.
- Westphalen AC, Coakley FV, Qayyum A, et al: Peripheral zone prostate cancer: accuracy of different interpretative approaches with MR and MR spectroscopic imaging. *Radiology* 246:177– 184, 2007.

- 32. Zakian KL, Sircar K, Hricak H, et al: Correlation of proton MR spectroscopic imaging with Gleason score based on step-section pathologic analysis after radical prostatectomy. *Radiology* 234:804–814, 2005.
- Harisinghani MG, Barentsz J, Hahn PF, et al: Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. *N Engl J Med* 348:2491–2499, 2003.
- 34. Smith JA, Scardino PT, Resnick MI, et al: Transrectal ultrasound versus digital rectal examination for the staging of carcinoma of the prostate: results of a prospective, multi-institutional trial. *J Urol* 157:902–906, 1997.
- Amis ES, Jr, Bigongiari LR, Bluth EI, et al: Pretreatment staging of clinically localized prostate cancer. *Radiology* 215(Suppl):703–708, 2000.
- Carroll P, Coley C, McLeod D, et al: Prostatespecific antigen best practice policy. II. Prostate cancer staging and post-treatment follow-up. Urology 57:225–229, 2001.

- Green FL, Page DL, Fleming ID, et al, editors: *AJCC Cancer Staging Manual*, New York, 2002, Springer-Verlag.
- Roehl KA, Antenor JA, Catalona WJ: Serial biopsy results in prostate cancer screening study. *J Urol* 167:2435–2439, 2002.
- Bjurlin MA, Meng X, Le Nobin J, et al: Optimization of prostate biopsy: the role of magnetic resonance imaging targeted biopsy in detection, localization and risk assessment. *J Urol* 192:648– 658, 2014.
- 40. Sedelaar JP, Vijverberg PL, De Reijke TM, et al: Transrectal ultrasound in the diagnosis of prostate cancer: state of the art and perspectives. *Eur Urol* 40:275–284, 2001.
- Pound CR, Partin AW, Epstein JI, et al: Prostatespecific antigen after anatomic radical retropubic prostatectomy: patterns of recurrence and cancer control. Urol Clin North Am 24:395–406, 1997.

# 74 Seminal Vesicle Lesions

CARMEL CRONIN | JOSEPH R. GRAJO

# Imaging

Traditionally, the seminal vesicles were evaluated with seminal vesiculography. This has largely been replaced by computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (Figure 74-1).<sup>1</sup>

### COMPUTED TOMOGRAPHY

The seminal vesicles are of soft tissue attenuation (Figure 74-2). Cysts and small masses that do not deform the seminal vesicle are not well seen. Large masses or inflammatory change associated with infection or abscess can be appreciated. Calcification is clearly seen.

### MAGNETIC RESONANCE IMAGING

MRI is a valuable tool in evaluating the seminal vesicles owing to its multiplanar imaging capabilities and superb soft tissue contrast resolution (Figure 74-3). It clearly demonstrates cystic lesions and is more accurate for staging of solid neoplasms than CT or ultrasound.

### ULTRASOUND

Transrectal ultrasound (TRUS) is rapid, inexpensive, and generally well tolerated. It is superior to CT because it better delineates the internal structure of the seminal vesicles. It also does not require the administration of ionizing radiation and can be used to guide seminal vesicle biopsy or aspiration.

# **Specific Lesions**

### SEMINAL VESICLE CYST

### Etiology

Seminal vesicle cysts may be congenital or acquired. They manifest as a mass between the rectum and base of the bladder and may be associated with ejaculatory duct dilation. They are usually unilateral, unilocular, and resemble dilated seminal vesicles (Figure 74-4). Congenital cysts are often associated with ipsilateral genitourinary anomalies. An acquired cyst is usually associated with ejaculatory duct or seminal vesicle inflammation or obstruction such as prostatitis, seminal vesiculitis, or prostate surgery.

Associations with seminal vesicle cysts include the following:

• Autosomal dominant polycystic kidney disease in which the seminal vesicle cysts are usually bilateral

- Invasive local tumor or primary tumor of the seminal vesicle
- Infection or chronic prostatitis
- Benign prostatic hypertrophy
- Ejaculatory duct obstruction

### **Clinical Presentation**

Seminal vesicle cysts usually are asymptomatic but may manifest as obstruction, recurrent urinary tract infections (including epididymitis), and hematospermia.

### Pathology

Seminal vesicle cysts can occur in any part of the gland. They vary in size and are benign. Superimposed infection may be seen.

### Imaging

**Computed Tomography.** Cysts are well-defined hypoattenuating lesions on CT.

**Magnetic Resonance Imaging.** The MRI features of seminal vesicle cysts are similar to those of cysts in other locations, with low signal intensity on T1-weighted images and a unilocular smooth-walled lesion with uniform high intensity and a well-defined margin on T2-weighted images (see Figure 74-4). Hemorrhagic cysts have high signal intensity on both T1- and T2-weighted images.

**Ultrasound.** Cysts are seen as anechoic masses (Figure 74-5). TRUS can be used to guide needle placement for drainage or contrast studies to more fully delineate the lesion.<sup>2</sup>

### Differential Diagnosis

The main differential diagnosis is müllerian duct cyst.

### Treatment

No medical treatment is required for seminal vesicle cysts. When seminal vesicle cysts are large, they may cause pain and local obstruction. Draining such cysts may relieve discomfort.

## SEMINAL VESICLE OBSTRUCTION

### Etiology

Seminal vesicle obstruction is defined as a seminal vesicle with an anteroposterior diameter of more than 15 mm, length longer than 50 mm, and large anechoic areas containing sperm on aspiration.<sup>3</sup> Seminal vesicle obstruction may be congenital because of an ectopic ureter or acquired secondary to a local

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mass. It is important to recognize because it is associated with pain and male infertility.

### **Clinical Presentation**

The obstruction may be asymptomatic or painful when the gland becomes enlarged.

### Pathology

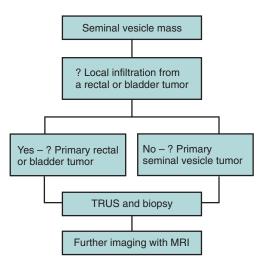
When seminal vesicle obstruction is due to congenital causes, it is most often unilateral. When acquired, it may be unilateral or bilateral. The seminal vesicles are usually normal histologically but may become secondarily infected.

### Imaging

**Computed Tomography.** CT will show an enlarged seminal vesicle.

**Magnetic Resonance Imaging.** The enlarged seminal vesicle is of normal signal intensity unless infected or infiltrated by tumor.

**Ultrasound.** Ultrasound will show an enlarged seminal vesicle.



**Figure 74-1** Imaging algorithm for a seminal vesicle mass. *MRI*, Magnetic resonance imaging; *TRUS*, transrectal ultrasound.

### **Differential Diagnosis**

No clinical or laboratory data aid in the diagnosis. Tumor marker levels may be elevated when the obstruction is caused by a malignant mass.

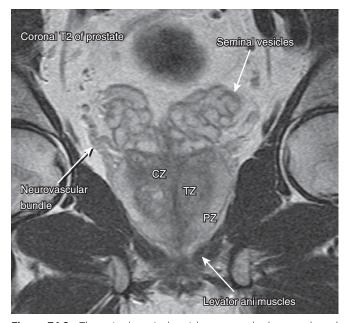
### Treatment

There is no medical treatment for seminal vesicle obstruction. Surgery or image-guided aspiration may be required to treat symptomatic obstruction.

### SEMINAL VESICULITIS AND ABSCESS

### Etiology

Infection of the seminal vesicles is most often secondary to acute or chronic prostatitis or acute epididymitis, although it



**Figure 74-3** The paired seminal vesicles are perched posterolateral and superior to the prostate gland as seen on this T2-weighted coronal image demonstrating superior soft tissue contrast resolution. *CZ*, Central zone; *PZ*, peripheral zone; *TZ*, transitional zone.

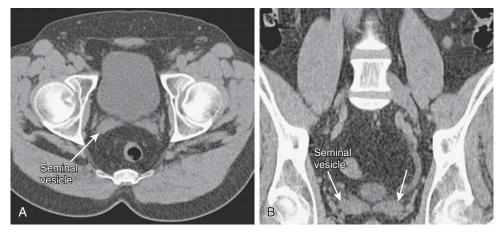
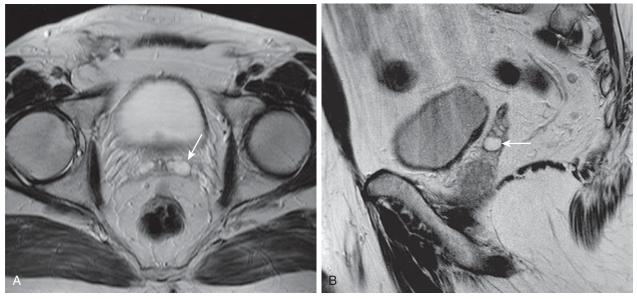


Figure 74-2 A and B, On computed tomography the seminal vesicles are of soft tissue attenuation and form a "bow-tie" appearance posterior to the prostate.



**Figure 74-4** Axial (A) and sagittal (B) T2-weighted magnetic resonance images demonstrate a left seminal vesicle cyst (*arrows*). Seminal vesicle cysts manifest as a mass between the rectum and base of the bladder and may be associated with ejaculatory duct dilation. They are usually unilateral and unilocular and resemble dilated seminal vesicles.

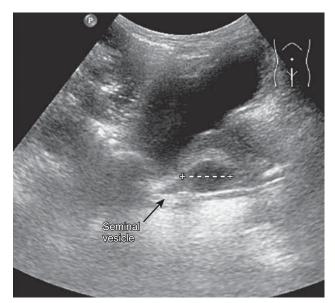


Figure 74-5 Ultrasound image of a seminal vesicle cyst.

may occur independently. The anaerobic organisms that cause prostatitis are the usual cause of seminal vesiculitis. *Mycobacterium tuberculosis* and *Schistosoma* are the most common causes in developing countries. Seminal vesiculitis may progress to a seminal vesicle abscess. Like prostate abscess, seminal vesicle abscess is more frequent in those with diabetes mellitus, chronic indwelling urinary catheter, and recent urinary tract intervention. Seminal vesiculitis and abscess may be associated with cysts and calcification of the seminal vesicles. Chronic bacterial vesiculitis is rare and difficult to diagnose.<sup>4</sup>

### **Clinical Presentation**

The cause of seminal vesiculitis is similar to other causes of pelvic infection such as prostatitis or cystitis; these infections may occur simultaneously.

### Pathology

The disorder is most often unilateral but may be bilateral. Infection and inflammation are found on histologic examination.

### Imaging

**Computed Tomography.** In the acute setting, the seminal vesicles may appear normal or asymmetrically enlarged. Surrounding inflammation also may be visualized. When abscess formation occurs, the involved seminal vesicle is enlarged, of low attenuation, or fluid-filled. Chronic infection causes wall thickening, contraction, and intraluminal or wall calcification on cross-sectional images.

**Magnetic Resonance Imaging.** Seminal vesiculitis and seminal vesicle abscess demonstrate low signal intensity on T1-weighted images. Signal intensity is higher than the normal seminal vesicle on T2-weighted images. Both enhance with gadolinium.

**Ultrasound.** In vesiculitis, TRUS may demonstrate enlargement of seminal vesicles (>14 mm thick) and thickened septa. Seminal vesicle abscess has features similar to those of abscesses elsewhere—a collection of heterogeneous but predominantly low echogenicity.

**Imaging Algorithm.** Seminal vesiculitis usually does not require investigation unless treatment fails, infection recurs, or there is concern that a mass is present.

### Differential Diagnosis

Seminal vesicle abscesses and infection are diagnosed clinically by a positive ejaculate culture. Imaging is not usually required in the investigation of infection.

### Treatment

Antibiotic therapy is the first-line treatment for seminal vesiculitis. A short trial of antibiotic treatment may be performed for small abscesses. If the seminal vesicle abscess fails to respond

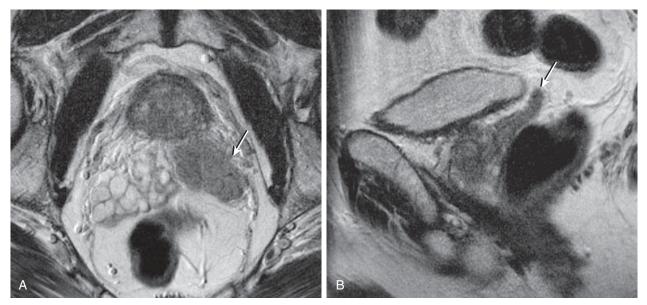


Figure 74-6 Axial (A) and sagittal (B) T2-weighted magnetic resonance images of prostate cancer (arrows) invading the left seminal vesicle. The seminal vesicle is of low signal intensity on T2-weighted imaging owing to infiltration by tumor.

rapidly to antibiotics, transrectal or perineal aspiration and, if necessary, surgery to remove the seminal vesicles may be required.

# MALIGNANT TUMORS OF THE SEMINAL VESICLES

### Etiology

Primary malignant tumors are rare and usually unilateral. Adenocarcinoma and sarcoma have been reported. Secondary malignancy of the seminal vesicles is much more common and may be due to hematogeneous spread or local invasion by malignant tumors of the prostate, rectum, or bladder (Figures 74-6 and 74-7). Locally invasive tumor is more likely to involve both seminal vesicles, and it may be difficult to identify the organ of origin.<sup>5,6</sup>

### Prevalence and Epidemiology

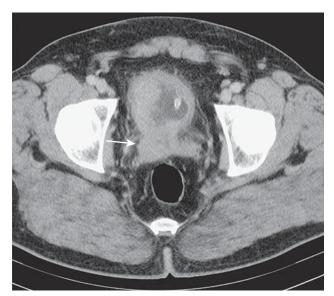
Primary seminal vesicle adenocarcinoma is very rare. It manifests in men older than 50 years of age. Sarcoma of the seminal vesicles is even less common.

### **Clinical Presentation**

The diagnosis of primary seminal vesicle neoplasm can be difficult because these lesions usually do not cause symptoms until late in their course and because symptoms are often nonspecific. Presenting signs and symptoms include urinary retention, dysuria, hematuria, and hematospermia.

### Pathology

Adenocarcinoma is the usual histologic type of primary seminal vesicle malignancy; however, epithelial stromal tumors, sarcomas (leiomyosarcoma, angiosarcoma, müllerian adenosarcoma-like tumor), phylloides tumor, and choriocarcinoma of the seminal vesicles are all reported. Invasion from the prostate, rectum, or other organ should be ruled out (see Figures 74-7 to 74-9).

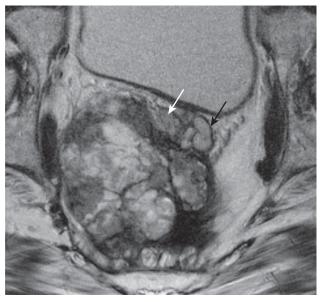


**Figure 74-7** Axial contrast-enhanced computed tomography image of a bladder cancer invading the right seminal vesicle (*arrows*). The seminal vesicle is enlarged by tumor.

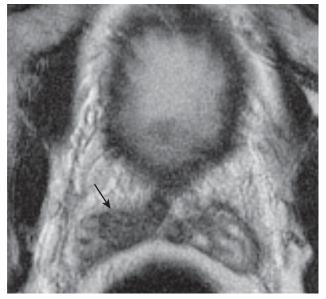
### Imaging

**Computed Tomography.** Primary tumors are centered on and predominantly confined to the seminal vesicles, whereas secondary tumors are centered on the prostate, bladder, or rectum. However, CT cannot reliably distinguish among tumor, chronic inflammation, and amyloid.

**Magnetic Resonance Imaging.** On MRI, a seminal vesicle tumor appears as a heterogeneous mass of intermediate signal on T1-weighted imaging and as heterogeneous high signal intensity on T2-weighted imaging. As with CT and TRUS, MRI cannot distinguish between benign and malignant solid masses.



**Figure 74-8** Axial T2-weighted magnetic resonance image of a large mucinous rectal carcinoma invading the right and part of the left seminal vesicle (*white arrow*). The lateral part of the left seminal vesicle appears normal (*black arrow*).



**Figure 74-9** Axial T2-weighted magnetic resonance image in a patient with prostate adenocarcinoma. The area of low signal intensity within the right seminal vesicle (*arrow*) was confirmed to be amyloid on pathologic evaluation.

**Ultrasound.** Solid tumors of the seminal vesicle may be isoechoic to the prostate but relatively hyperechoic to the normal seminal vesicle. There are no imaging characteristics indicative of a solid mass being benign or malignant.

### Differential Diagnosis

Because prostate cancer involving the seminal vesicle often cannot be distinguished from a primary seminal vesicle cancer, the prostate-specific antigen (PSA) level should be measured. In primary seminal vesicle malignancy, serum levels of markers for prostate cancer (i.e., PSA, prostatic acid phosphatase) are normal and the level of serum carcinoembryonic antigen is elevated. Positive staining for Ca-125 has been reported and may be useful to distinguish this from other tumors, such as those arising from the prostate or bladder.<sup>7</sup>

### Treatment

Advanced cancers, not amenable to surgical treatment, may be treated palliatively with chemotherapy. Seminal vesicle neoplasms manifest late and usually are not amenable to curative resection at the time of diagnosis.

### BENIGN TUMORS OF THE SEMINAL VESICLES

### Etiology

Causes of benign tumors include cystadenoma, fibroma, and leiomyoma. Cystadenomas usually are an incidental finding in elderly men. They are usually multilocular and may mimic seminal vesicle cysts.

### Clinical Presentation

Benign seminal vesicles are usually asymptomatic unless they cause local obstruction.

### Pathology

Benign tumors are usually unilateral. The pathologic findings vary according to the causative lesion.

### Imaging

**Computed Tomography.** CT poorly defines the internal structure of the seminal vesicle. CT may demonstrate a unilateral or bilateral mass. Local invasion is not a feature of these benign lesions.

**Magnetic Resonance Imaging.** Cystadenomas are multilocular and may mimic seminal vesicle cysts on MRI.

**Ultrasound.** Cystadenomas are multilocular and may mimic seminal vesicle cysts on TRUS. Solid tumors may be hypoechoic or hyperechoic.

### **Differential Diagnosis**

The differential diagnosis is seminal vesicle cysts.

### Treatment

Masses that cannot be differentiated from primary malignant masses should be resected.

### SEMINAL VESICLE CALCIFICATION

### Etiology

Seminal vesicle calculi and calcification most commonly occur secondary to infection with *Neisseria gonorrhoeae*, *M. tuberculosis*, or *Schistosoma* or to seminal vesicle obstruction. Calcification is also seen in patients with diabetes.<sup>1</sup>

### Clinical Presentation

May be asymptomatic and incidental or manifest as pain secondary to obstruction, infection, hematospermia, or infertility.

### Pathology

Seminal vesicle calcification can be classified into calcification of the seminal vesicle wall or seminal vesicle calculi.

### 928 PART 8 Urogenital Imaging

Calcification may be secondary to or complicated by infection or obstruction.

### Imaging

**Computed Tomography.** CT accurately demonstrates the location of seminal vesicle calcification or calculi.

**Magnetic Resonance Imaging.** MRI has limited value in assessing calcifications.

**Ultrasound.** TRUS may demonstrate the location and degree of calcification, owing to its echogenicity and the presence of posterior acoustic shadowing. However, shadowing from calcification in the prostate may limit the use of ultrasound.

### **Differential Diagnosis**

The differential diagnosis for calcification are diabetes and infection.

### Treatment

No medical treatment is necessary except antibiotics when concomitant infection is present. Surgical resection of a calculus may be required if it is suspected to be causing recurrent infections, obstruction, and/or infertility.

### SEMINAL VESICLE AMYLOID

### Etiology

The deposition of amyloid in the seminal vesicles appears to be a phenomenon related most frequently to aging. It is common and usually a localized finding. Systemic amyloidosis is not present in most patients. It is important not to confuse seminal vesicle amyloid with a mass, metastasis, or local invasion from an adjacent prostate or rectal tumor.

### Prevalence and Epidemiology

The incidence of seminal vesicle amyloid increases with age, reaching 21% in men age 75 years and older.<sup>8</sup>

### **Clinical Presentation**

Isolated seminal vesicle amyloid is usually asymptomatic, unlike systemic amyloidosis, which involves many organs and systems in the body. It has been rarely associated with hematospermia and symptomatic enlargement of the seminal vesicle.

### Pathology

Seminal vesicle amyloid may be unilateral or bilateral. Local senile amyloid deposits are a common finding at autopsy. Deposits are bilateral and symmetric and occur subepithelially in the lamina propria of the seminal vesicles in aggregates varying in size from microscopic to grossly visible seminal vesicle wall thickening. When the amyloid deposits are due to systemic amyloidosis, the amyloid is located in the walls of blood vessels or within muscle rather than in a subepithelial location.<sup>9</sup>

### Imaging

**Computed Tomography.** CT will demonstrate focal or bilateral enlargement of the seminal vesicles.

**Magnetic Resonance Imaging.** Seminal vesicle amyloidosis is of low signal intensity on T2-weighted imaging, as is tumor invasion (see Figure 74-9). MRI may distinguish tumor invasion, although not with complete accuracy.<sup>10</sup> Unlike tumor, seminal vesicle amyloid does not enhance.<sup>11</sup>

**Ultrasound.** Amyloid is demonstrated as areas of low echogenicity that are indistinguishable from other seminal vesicle masses. TRUS may be helpful in distinguishing adjacent organ tumor spread from a focal seminal vesicle mass.<sup>12</sup>

### **Differential Diagnosis**

A normal PSA helps rule out prostate tumor invasion. However, even if the PSA value is elevated, the seminal vesicle pathologic process may still be amyloid and not metastatic prostate cancer. Biopsy helps confirm the diagnosis and rule out local invasion from tumors of adjacent organs.

### Treatment

No medical or surgical treatment is required. Because the radiologic appearance can be indistinguishable from that of tumor, TRUS-guided biopsy of the seminal vesicles should be considered in all cases of seminal vesicle mass or abnormality, particularly if the diagnosis has been made incidentally at MRI.<sup>13</sup>

### Key Point

• TRUS and MRI are the preferred modalities for investigating seminal vesicle pathology.

### REFERENCES

- King BF, Hattery RR, Lieber MM, et al: Seminal vesicle imaging. *Radiographics* 9:653–675, 1989.
- 2. Shabsigh R, Lerner S, Fishman IJ, et al: The role of transrectal ultrasonography in the diagnosis and management of prostatic and seminal vesicle cysts. *J Urol* 141:1206–1209, 1989.
- 3. Colpi GM, Negri L, Nappi RE, et al: Is transrectal ultrasonography a reliable diagnostic approach in ejaculatory duct sub-obstruction? *Hum Reprod* 12:2186–2191, 1997.
- 4. Sue DE, Chicola C, Brant-Zawadzki MN, et al: MR imaging in seminal vesiculitis. *J Comput Assist Tomogr* 13:662–664, 1989.
- Hoshi A, Nakamura E, Higashi S, et al: Epithelial stromal tumor of the seminal vesicle. *Int J Urol* 13:640–642, 2006.
- 6. Thyavihally YB, Tongaonkar HB, Gupta S, et al: Primary seminal vesicle adenocarcinoma presenting as isolated metastasis to penis responding to chemotherapy and hormonal therapy. *Urology* 69:778, 2007.
- Ormsby AH, Haskell R, Jones D, et al: Primary seminal vesicle carcinoma: an immunohistochemical analysis of four cases. *Mod Pathol* 13:46– 51, 2000.
- Coyne DJ, Kealy WF: Seminal vesicle amyloidosis: morphological, histochemical and immunohistochemical observations. *Histopathology* 22: 173–176, 1993.
- Pitkanen P, Westenmark P, Connwell GG, III, et al: Amyloid of the seminal vesicles: a distinctive and common localized form of senile amyloidosis. *Am J Pathol* 110:64–69, 1983.
- Kaji Y, Sugimura K, Nagaoka S, et al: Amyloid deposition in seminal vesicles mimicking tumor invasion from bladder cancer: MR findings. *J Comput Assist Tomogr* 16:989–991, 1992.
- Jager GJ, Ruijter ET, de la Rosette JJ, et al: Amyloidosis of the seminal vesicles simulating tumor invasion of prostatic carcinoma on endorectal MR images. *Eur Radiol* 7:552–554, 1997.
- Lawrentschuk N, Pan D, Stillwell R, et al: Implications of amyloidosis on prostatic biopsy. *Int J Urol* 11:925–927, 2004.
- Ramchandani P, Schnall MD, LiVolsi VA, et al: Senile amyloidosis of the seminal vesicles mimicking metastatic spread of prostatic carcinoma on MR images. *AJR Am J Roentgenol* 161:99– 100, 1993.

# **Erectile Dysfunction**

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# **Etiology**

Erectile dysfunction manifests clinically most commonly as impotence and less commonly as priapism. The causes of impotence can be psychogenic, endocrinologic, neurogenic, anatomic, infectious, pharmacologic, or vasogenic.<sup>1-3</sup> Vasogenic causes of erectile dysfunction include venous leak (aging, priapism, congenital, idiopathic) and arterial insufficiency (atherosclerosis, arterial stenosis or occlusion, perineal radiation, iatrogenic). Anatomic causes include phimosis and paraphimosis and fibrous plaques/scarring (from ischemia, Peyronie's disease, scleroderma, and chronic priapism). Priapism is an uncommon medical condition.<sup>4-6</sup> Anatomic and vascular causes of erectile dysfunction are curable by surgery and thus their accurate detection and characterization are clinically important.

# **Prevalence and Epidemiology**

With growing societal openness toward sexual dysfunction, more men are coming forward for evaluation and management of erectile dysfunction.<sup>3</sup> Traditionally, male impotence was considered to be psychogenic or an inevitable consequence of aging.<sup>3</sup> However, recent research indicates that arterial, venous, or mixed arteriovenous insufficiency plays a role in most cases of impotence.<sup>3</sup> Frequently, impotence is caused by a combination of psychogenic and organic factors.<sup>5</sup>

# **Clinical Presentation**

Impotent patients report inability to achieve penile erection, in contrast to priapism, in which patients present with persistent penile tumescence that is not associated with sexual desire or stimulation.<sup>4-6</sup> Other clinical manifestations related to causal or associated disease may predominate in these patients.

# Pathophysiology

Penile erection is a neurovascular phenomenon resulting from arterial dilatation, sinusoidal relaxation, and venous outflow restriction. Arterial compliance and adequate blood inflow are essential to achieve erection, and restriction of venous outflow is essential to preserve it.<sup>2</sup> Parasympathetic nerve stimulation via the S2-S4 nerve roots causes erection of the penis, and sympathetic nerve stimulation via the T11-L2 roots causes its detumescence.<sup>1</sup>

During erection, cholinergic stimulation causes relaxation of the smooth muscles surrounding the lacunar spaces of corpora

cavernosa. This reduces peripheral vascular resistance and increases arterial inflow. Relaxation of the smooth muscles of the cavernous and helicine arteries causes their dilatation.<sup>1-3</sup> When the sinusoids are expanded and engorged with blood, emissary veins are mechanically compressed against the unyield-ing tunica albuginea, which helps to maintain sinusoidal distention and penile erection.<sup>1-4</sup>

During detumescence, sympathetic neural activity causes contraction of the smooth muscles of the helicine arteries and the lacunae with a resultant decrease in arterial inflow. This results in collapse of the lacunae, with loss of erection.<sup>1</sup>

# Pathology

Organic impotence is most commonly due to vascular pathologic processes. Venous incompetence or failure of the venoocclusive mechanism of outflow restriction has been recognized as a major factor and may be its most common cause.<sup>3</sup> Venous leakage may be spongiosal<sup>7</sup> and may result from deterioration of the tunica albuginea, which is worsened by repeated and prolonged erections as a result of high pressure in the corpora cavernosa.<sup>2</sup> Venous leakage also may result from aging or priapism or be congenital or idiopathic.7 Both the cavernosal and para-arterial veins play an important role in the circulation of the corpora cavernosa and may be responsible for recurrence of venous leakage after deep dorsal venous stripping surgeries.8 Arterial disease within the proximal pelvic or segmental penile arteries can result in insufficient arterial inflow.<sup>2,3</sup> Arterial insufficiency may occur in isolation or be accompanied by venous leakage.<sup>3</sup> In patients older than 50 years of age, arterial insufficiency is usually caused by atherosclerosis affecting the iliac or internal pudendal arteries.<sup>5</sup> In young patients, traumatic focal stenosis or occlusion of the common penile artery in the region where it courses directly over the ischiopubic rami may result in erectile dysfunction. Perineal radiation therapy may affect the common penile artery close to the prostate gland.<sup>1</sup>

Other, less common causes of erectile dysfunction include anatomic abnormalities such as phimosis and paraphimosis.<sup>2</sup> Penile fibrosis within or adjacent to the tunica albuginea may cause painful erection, whereas fibrosis in the corpora cavernosa may prevent lacunar filling.<sup>1</sup> There are multiple causes of penile fibrosis, including ischemia, Peyronie's disease, and scleroderma.<sup>9</sup> Ischemic injury secondary to chronic priapism may result in fibrotic scarring and, hence, erectile dysfunction.<sup>6,9</sup> Priapism is most commonly caused by intrapenile injections of vasoactive drugs or by hypercoagulable states, including sickle cell disease and disseminated malignancy. Prolonged high-flow priapism secondary to arteriosinusoidal fistula (resulting from perineal or penile trauma) may also result in cavernosal ischemia, fibrosis, and erectile dysfunction.<sup>6</sup>

## Imaging

The penile-brachial index was used in the past for evaluation of vasculogenic impotence. However, this index may be affected by aortoiliac disease, even when penile hemodynamics are normal.<sup>2</sup> Techniques for evaluation of erectile dysfunction include duplex Doppler and color Doppler ultrasonography, dynamic infusion cavernosometry and cavernosography, and arteriography, including selective pudendal pharmacoangiography. At present, penile Doppler ultrasonography is the mainstay of imaging evaluation of impotence.<sup>3</sup>

### RADIOGRAPHY

Cavernosometry is usually performed in patients for whom venous surgery is being considered. The corpora cavernosa are cannulated with 25-gauge butterfly needles. Warm saline and low osmolar contrast material is infused via one corpus cavernosum, perfusing the other via anastomotic connections. Direct pressure measurements are obtained via the needle in the other corpus cavernosum. After baseline measurement of intracavernosal pressure and penile circumference, pharmacologic erection is produced by intracavernosal injection. Pressure and penile circumference monitoring is then performed for 10 minutes or until equilibrium occurs. If no erection is produced, heparinized saline is infused at increasingly rapid rates until intracavernosal pressure of 150 mm Hg is achieved. An infusion rate of less than 30 mL/min is considered normal. Venous outflow resistance also may be assessed by observing the rate of intracavernosal pressure fall after termination of intracavernosal saline infusion. With venous leakage, pressure falls rapidly. In cavernosography, 100 to 150 mL of contrast agent is infused into the corpus cavernosum to maintain 90 mm Hg of intracavernosal pressure. Fluoroscopy and spot films during the procedure may reveal the site of venous leak and provide the preprocedural anatomic information.<sup>1</sup>

Fibrous plaques and calcifications resulting from Peyronie's disease or scleroderma may be seen as filling defects within the corpora on cavernosography.<sup>9</sup>

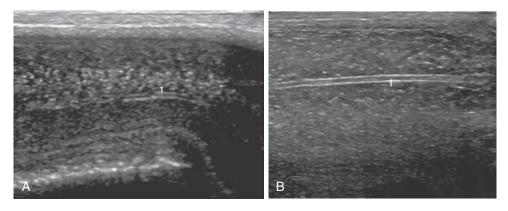
Selective internal pudendal pharmacoarteriography is usually performed before reconstructive arterial surgery or angioplasty. Intracavernosal injection of papaverine, nitroglycerin, or prostaglandin E1 (PGE<sub>1</sub>) is administered during the procedure. Aortoiliac arteriography is performed to evaluate for proximal atherosclerotic lesions and the patency of the inferior epigastric arteries, which are usually used for surgical revascularization.<sup>1</sup>

### MAGNETIC RESONANCE IMAGING AND COMPUTED TOMOGRAPHY

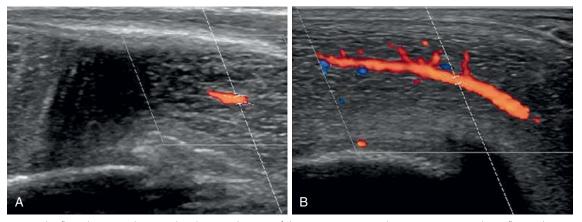
MRI and CT are useful alternatives for evaluation of arteriogenic impotence secondary to aortoiliac or small vessel disease and can be useful for evaluation of priapism secondary to venous thrombosis. It also can detect fibrotic plaques such as those resulting from Peyronie's disease and scleroderma.<sup>4</sup> When calcified, these plaques can be identified on CT.<sup>4</sup>

### ULTRASONOGRAPHY

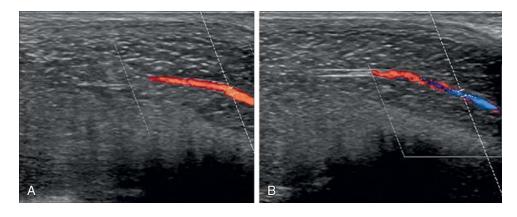
The ultrasound evaluation of erectile dysfunction uses Doppler estimation of cavernosal artery velocities to characterize arterial inflow. A high-frequency linear transducer is used with a mechanical standoff wedge to produce a favorable insonating angle. Optimization of "slow flow" sensitivity is crucial for the accurate depiction of diastolic flow and blood flow in the dorsal vein. Ultrasound evaluation of the flaccid penis is first performed to assess for structural anomalies and plaques.<sup>3</sup> Color Doppler imaging is used to identify the cavernosal artery before and after erection and determine its location and the flow direction.<sup>1,3</sup> Pharmacologic enhancement of erection can be achieved by injecting 30 to 60 mg of papaverine intracavernosally near the penile base.<sup>1,3</sup> Other agents used to induce erection include phentolamine and PGE<sub>1</sub>. Intracavernosal injection of PGE<sub>1</sub> is contraindicated in men who have conditions that predispose to priapism, such as sickle cell anemia, sickle cell trait, multiple myeloma, leukemia, cavernosal thrombosis, and tumors that are known to invade the cavernosa. Use of PGE<sub>1</sub> is also contraindicated in men with penile prostheses and relatively contraindicated in men with anatomic abnormalities of the penis.<sup>4</sup> The diameter of the cavernosal artery may be immeasurably small, at 0.6 mm in diameter before erection (Figure 75-1, A), and increases more than 75% in diameter, to an average of 1 mm in the erect penis (see Figure 75-1, B).<sup>1</sup> Both cavernosal arteries are intermittently imaged with Doppler ultrasonography at 5-minute intervals from 1 to 25 minutes after pharmacologic induction of erection or until waveform progression ceases.<sup>1</sup>



**Figure 75-1** The diameter of this cavernous artery measured 0.6 mm in the flaccid penis (A) and 1 mm at full erection (B).



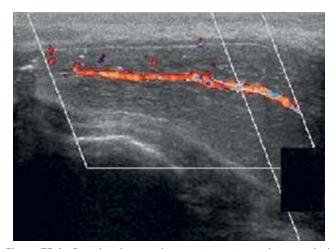
**Figure 75-2** A, In the flaccid penis, color Doppler ultrasound image of the cavernous artery demonstrates monophasic flow with minimal diastolic flow. B, With the onset of erection or after papaverine injection there is an increase in both systolic and diastolic flow in the cavernous artery.



**Figure 75-3** A and B, With continuing erection, cavernous artery enddiastolic flow declines to zero and then reverses.

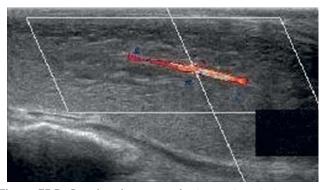
The normal peak systolic velocity in the erect penis ranges from 35 to 60 cm/s.<sup>1</sup> In the flaccid penis, Doppler ultrasonography demonstrates monophasic flow with minimal diastolic flow (Figure 75-2, *A*). With the onset of erection or after papaverine injection, there is an increase in both systolic and diastolic flow (see Figure 75-2, *B*). As the intracavernosal pressure increases, a dicrotic notch appears at the end of systole accompanied with the decrease in diastolic flow. With further increases in intracavernosal pressure, end-diastolic flow diminishes to zero and then reverses (Figure 75-3). Thus, a high-resistance waveform should be seen in the cavernosal artery at erection, with little or no diastolic flow.<sup>1,3,5</sup> Peak systolic velocities of 11 to 20 cm/s and over 35 cm/s are typical in the normal cavernosal and dorsal arteries before and after intracavernosal PGE<sub>1</sub> injection.<sup>5</sup> The venous outflow occlusive mechanism is most functional at full penile rigidity with adequate arterial inflow. Consequently, a high-resistance waveform with little or no diastolic flow should be seen in the cavernosal artery at erection.<sup>1</sup>

Doppler criteria used to diagnose impaired venous outflow occlusion include an arterial end-diastolic velocity of greater than 5 cm/s (Figure 75-4). It should be stressed that the diagnosis of venous incompetence can be made only if the peak systolic velocity exceeds 25 cm/s. Transient dorsal vein flow is normal, but persistent dorsal vein flow during erection reflects veno-occlusive failure. Persistent dorsal vein flow throughout the examination has 80% sensitivity and 100%



**Figure 75-4** Doppler ultrasound image in a patient with venous leak causing impotence. Note high diastolic flow velocity (end-diastolic volume >5 cm/s) in the cavernous artery at 20 minutes after intracavernosal papaverine injection.

specificity for venous leakage at cavernosography. The combination of persistent dorsal vein flow and elevated end-diastolic flow is 93% accurate for venous leakage when correlated with cavernosography.<sup>3,5</sup> Doppler criteria used to diagnose arterial insufficiency include a peak systolic velocity of less than 25 cm/s



**Figure 75-5** Doppler ultrasonography in arteriogenic impotence. Peak systolic velocity in the right cavernous artery was 19 cm/s 20 minutes after intracavernosal papaverine injection.

(Figure 75-5).<sup>1,3,5</sup> Secondary diagnostic criteria include failure of cavernosal artery dilatation and asymmetry of cavernosal flow velocities exceeding 10 cm/s.<sup>1,3</sup>

Fibrotic plaques appear as focal areas of increased echogenicity and also may show posterior acoustic shadowing, if calcified.<sup>1</sup>

### IMAGING ALGORITHM

The first objective is to rule out a vasculogenic cause for the erectile dysfunction.<sup>1</sup> Ultrasonography with color and pulsed wave Doppler imaging is the first imaging modality. Although

### SUGGESTED READINGS

Fitzgerald SW, Erickson SJ, Foley WD, et al: Color Doppler sonography in the evaluation of erectile dysfunction. *Radiographics* 12:3–17, 1992.

### REFERENCES

- 1. Zagoria RJ: Genitourinary radiology: the requisites, ed 2, St. Louis, 2004, Mosby, pp 312-351.
- Lue TF, Hricak H, Marich KW, et al: Vasculogenic impotence evaluated by high-resolution ultrasonography and pulsed Doppler spectrum analysis. *Radiology* 155:777–781, 1985.
- Fitzgerald SW, Erickson SJ, Foley WD, et al: Color Doppler sonography in the evaluation of erectile dysfunction. *Radiographics* 12:3–17, 1992.
- Pretorius ES, Siegelman ES, Ramchandani P, et al: MR imaging of the penis. *Radiographics* 21:S283– S299, 2001.

Lue TF, Hricak H, Marich KW, et al: Vasculogenic impotence evaluated by high-resolution ultrasonography and pulsed Doppler spectrum analysis. *Radiology* 155:777–781, 1985.

Doppler imaging can be useful in diagnosing venous incompetence, cavernosography is usually necessary in patients for whom venous surgery is being considered. Cavernosography provides direct anatomic information regarding the site of the leak. It is also required to diagnose failure of venous outflow occlusion in patients in whom arterial insufficiency precludes indirect Doppler sonographic assessment. Selective internal pudendal pharmacoarteriography and aortoiliac arteriography are performed in those with significant arterial disease before reconstructive surgery or angioplasty.<sup>1</sup>

### What the Referring Physician Needs to Know

- Erectile dysfunction may be due to insufficient arterial inflow or impaired venous outflow obstruction.
- Doppler ultrasonography is the first-line imaging test to evaluate for vasculogenic causes of erectile dysfunction.

### **Key Points**

- Doppler ultrasonography imaging should be continued for 25 minutes to fully assess for arterial and venous dysfunction.
- If Doppler ultrasonography is abnormal, further imaging can demonstrate the specific site of the lesion. The site of venous leakage can be determined with cavernosography, and the site of arterial stenosis can be determined with arteriography.

Zagoria RJ: *Genitourinary radiology: the requisites*, ed 2, St. Louis, 2004, Mosby, pp 312–351.

- Bertolotto M, Serafini G, Savoca G, et al: Color Doppler US of the postoperative penis: anatomy and surgical complications. *Radiographics* 25:731– 748, 2005.
- Bertolotto M, Quaia E, Mucelli FP, et al: Color Doppler imaging of posttraumatic priapism before and after selective embolization. *Radiographics* 23:495–503, 2003.
- Chen SC, Hsieh CH, Hsu GL, et al: The progression of the penile vein: could it be recurrent? J Androl 26:53–60, 2005.
- Hsu GL, Hsieh CH, Wen HS, et al: Penile venous anatomy: an additional description and its clinical implication. J Androl 24:921–927, 2003.
- 9. Rifkin MD: The urethra and penis. In *Diagnostic imaging of the lower genitourinary tract*, New York, 1985, Raven Press.

# 76

# Penile Trauma and Miscellaneous Penile Lesions

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# **Etiology**

Penile lesions can be categorized by cause (Box 76-1).<sup>1</sup>

### PENILE TRAUMA

Penile fracture is usually caused by the exertion of axial forces on the erect penis, causing a tear of the tunica albuginea, resulting in subcutaneous extrusion of blood. This injury usually occurs during vigorous sexual intercourse. Self-inflicted injury by forceful downward bending of the erect penis to achieve detumescence, direct blunt trauma to the erect penis, and bite injuries are other causes of penile injury.

Blunt trauma to the flaccid penis usually does not cause penile fracture but may cause an extratunical or cavernosal hematoma. Intracavernosal hematomas also may occur in longdistance cyclists.<sup>2</sup>

### PENILE MALIGNANCY

The irritative effect of smegma in uncircumcised men is presumed to be an important cause of penile squamous cell carcinoma (SCC). Human papillomavirus types 16 and 18 are also reported in association with penile SCC. Chronic inflammation or urethral stricture may result in anterior urethral carcinoma.<sup>3</sup>

### **BENIGN PALPABLE MASSES**

Cowper's duct syringocele results from the cystic dilatation of the main duct of the bulbourethral gland of Cowper. Penile hemangiomas and penile root neurofibromas are the other benign neoplasms of the penis.<sup>3</sup>

### **PEYRONIE'S DISEASE**

The cause of Peyronie's disease is unknown and possibly multifactorial. The disease results in chronic inflammation, which leads to fibrosis and focal thickening of the tunica albuginea.

### **ERECTILE DYSFUNCTION**

Impotence is discussed in Chapter 75.

### PRIAPISM

Priapism can be divided into low-flow and high-flow subtypes. Venous, low-flow, ischemic priapism is due to vascular stasis

and decreased penile venous outflow. Causes include sickle cell disease or trait, other blood dyscrasias, neurologic abnormalities such as syphilis, brain tumors, brain and spinal cord injury, trauma, medication for erectile dysfunction (particularly if administered intracavernosally), other drugs such as antidepressants, and illicit drugs (particularly cocaine). Arterial, high-flow, nonischemic priapism is caused by perineal or penile blunt trauma with direct cavernosal artery injury and resultant formation of an arterial-lacunar fistula.<sup>4</sup> It also may be caused by intracavernosal injections.

# **Prevalence and Epidemiology**

Penile trauma is fairly uncommon but important because of its relative urologic emergency.<sup>5,6</sup> Penile fracture is defined as rupture of a corpus cavernosum and its surrounding fibroelastic sheath, the tunica albuginea.<sup>2,6</sup> Typically, a tear occurs in only one of the corpora cavernosa and its surrounding tunica albuginea; however, corpus spongiosum and urethral involvement may occur in approximately 20% of penile fractures.<sup>2,6</sup>

SCC is the most common penile malignancy. It usually arises in the glans but also may arise in the urethra. Other urethral malignancies include transitional cell carcinoma and adenocarcinoma. Penile sarcomas are uncommon. Penile SCC is one of the most commonly seen malignancies in Asia and Africa but is rare in the United States, where African-American men are affected twice as often as white men. In children, rhabdomyosarcoma is the most common malignant tumor of the lower genitourinary tract, including the penis.

Peyronie's disease is uncommon, accounting for 0.3% to 0.7% of all urologic disorders. It occurs most often in the fourth to sixth decades of life and occasionally in men younger than 20 years of age.<sup>7</sup>

Impotence is common and is discussed in Chapter 75. Priapism can be arterial/high flow (nonischemic) or venous/low flow (ischemic).<sup>8</sup> Low-flow priapism is a urologic emergency.

## **Clinical Presentation**

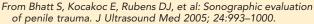
Most cases of penile fracture have a typical clinical history. The patient reports hearing a cracking or popping sound and experiences a sharp pain followed by rapid detumescence, swelling, ecchymosis, deformity, and deviation of the penis to the side opposite the injury. Patients with spongiosal and urethral injury may present with inability to urinate, hematuria, dysuria, and extravasation of urine and/or urethrorrhagia.<sup>2,6</sup>

SCC typically begins as focal thickening or ulceration of the glans.<sup>3</sup> Urethral carcinomas manifest with urinary complaints.

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76	Penile	Trauma	and	Miscellaneous	Penile	Lesions	935
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BOX 10-1	PENILE PAT	HOLOGIC PR	OCESSES
<ul> <li>Acute</li> <li>Tumor</li> <li>Inflami</li> <li>Infection</li> <li>Erection</li> <li>Impote</li> <li>Priapis</li> </ul>	rauma rating or sharp tr bending accider 's mation ons e dysfunction ence sm perative penis		



Cowper's duct syringocele may manifest as postvoid dribbling, urinary frequency, weak stream, or hematuria.<sup>3</sup>

Peyronie's disease may result in painful induration or plaques along the penis. It may cause penile deformity in erection and difficulty during sexual intercourse.<sup>3,7</sup>

In patients with low-flow priapism, the penis is fully erect and painful. This is a urologic emergency. Patients with highflow priapism usually develop a painless partial erection and are able to increase rigidity with sexual stimulation. Because the clinical presentation of high-flow priapism is not as dramatic as that of the low-flow type, it is occasionally recognized days or even months after the onset of symptoms. Treatment of highflow priapism is not an emergency because the risk for vascular damage with irreversible impotence is low. However, reduced potency may result in patients with long-standing untreated disease.<sup>4</sup>

# Pathology

Penile fractures usually occur in the proximal shaft or midshaft.<sup>2</sup> Rupture of the corpus cavernosum usually occurs in a transverse plane, in the ventral portion of the corpus cavernosum,<sup>2</sup> and typically involves less than half of the circumference of the erectile body.<sup>6</sup>

Penile SCC most commonly arises in the glans. Urethral carcinomas in males mostly arise in the bulbous and membranous portions of the urethra, followed by the fossa navicularis.<sup>3</sup>

### TRAUMA

The thickness of the tunica albuginea decreases from 2 mm to 0.5 to 0.25 mm during erection. External force applied to erect penile tissue causes a sudden rise in intracorporeal pressure, resulting in further distention and strain of the already thinned tunica albuginea, thereby causing a tear.<sup>2,6</sup> Spongiosal and urethral injuries are associated with a higher rate of complications.<sup>6</sup>

Cavernosal hematomas may result from injury to the subtunical venous plexus or smooth muscle trabeculae in the absence of complete tunical disruption. Intracavernosal hematomas are usually bilateral, resulting from injury to the cavernosal tissue when the base of the penile shaft is crushed against the pelvic bones.<sup>2</sup>

TABLE 76-1	Staging of Penile Tumors		
Stage	Characteristics		
I	Tumor localized to the glans penis		
II	Tumor invading the corpora without nodal or distant metastases		
111	Tumor involving the corpora and local lymph nodes		
IV	Distant metastases		

From Rifkin MD: The urethra and penis. In Diagnostic Imaging of the Lower Genitourinary Tract, New York, 1985, Raven Press.

### VASCULAR INJURIES

Rupture of the dorsal penile vessels may mimic penile fracture, but deformation and immediate detumescence do not occur because of the intact tunica albuginea. The hematoma may be superficial or deep to Buck's fascia depending on the site of vascular injury. Thrombosis of the superficial and deep dorsal penile veins is a rare urologic emergency, and the clinical and ultrasonographic appearance can mimic penile fracture.<sup>2</sup>

A cavernous arterial-lacunar fistula may develop after perineal or penile trauma, leading to high-flow priapism.<sup>2,4</sup>

### MALIGNANCY

Localized SCC (without cavernosal invasion or spread to lymph nodes) has a 3-year survival of 93%.<sup>3</sup> This rate decreases markedly once there is spread of disease beyond the superficial layers of the penis.

Leiomyosarcoma may arise from the smooth muscle of the glans or one of the corpora cavernosa. Leiomyosarcomas metastasize very early if arising from a corpus cavernosum. Rhabdomyosarcomas are usually very aggressive.

Penile lymphoma is an extremely rare neoplasm. It is usually secondary to retrograde hematogenous or lymphatic spread or direct extension from a neighboring organ. The most commonly affected site is the penile shaft, followed by the glans. Diffuse large cell lymphoma is the most common histologic subtype.<sup>9</sup> Staging of penile tumors is described in Table 76-1.

### PEYRONIE'S DISEASE

Peyronie's disease (induration penis plastica)<sup>7</sup> is characterized by chronic inflammation, which leads to fibrosis and focal thickening of the tunica albuginea. The plaques in this disease may or may not calcify.<sup>3</sup> Repeated microtrauma, hormonal dysfunction, metabolic disorders such as diabetes and gout, and a general fibroplastic disposition may play a role in pathogenesis of the disease. It begins as vasculitis and perivasculitis, which is followed by sclerosis, hyalinization, and then, occasionally, calcification. Localized irregularity or thickening of the tunica albuginea is suggestive of plaque.<sup>7</sup>

### PRIAPISM

Low-flow priapism characterized by inadequate venous outflow leading to tissue ischemia is a urologic emergency leading to permanent erectile dysfunction. It usually occurs after intrapenile injections of vasoactive drugs or is seen in men with sickle cell disease or disseminated malignancy. High-flow priapism is due to unregulated penile arterial inflow via an arteriocavernous fistula. Oxygenated blood in the corpora is diagnostic of this fistula. Usually, the venous outflow is maintained, preventing complete erection, stasis, and hypoxia.<sup>4,8</sup>

# Imaging

Because definitive diagnosis on the basis of clinical examination can be difficult in patients with penile trauma, various imaging methods may be used to diagnose and evaluate the exact location and extent of penile injury.<sup>2</sup> In particular, imaging may be needed in those with atypical clinical presentation or severe local pain or swelling precluding thorough physical examination.<sup>6</sup> Ultrasonography is the primary modality for crosssectional imaging of the penis<sup>3</sup> and is very useful for evaluating penile trauma. The integrity of the tunica albuginea as well as the extent and location of a tunical tear can be shown. Associated vascular injuries also can be shown by color or power Doppler techniques.<sup>2</sup>

MRI may be useful when ultrasonography is nondiagnostic or cannot be used because of severe pain and swelling of the injured penis.<sup>6</sup>

Uncomplicated infection and inflammation usually do not require imaging. When a complication such as an abscess arises, imaging may help evaluate its anatomic relationship to the corpora and urethra.<sup>3</sup>

Penile tumors are usually visible on physical examination; thus, imaging is rarely used for diagnosis but is useful for staging.<sup>3</sup>

### RADIOGRAPHY

Penile prostheses and calcified plaques of Peyronie's disease can be seen with radiography.<sup>3</sup> In traumatic injuries of the penis, retrograde urethrography may be used to detect urethral injury (Figure 76-1). However, this is an invasive technique and the result may be falsely negative.<sup>2</sup>

Cavernosography can be used to show a cavernosal tear but is invasive, has potential complications, and has a small risk for false-negative results when a corporeal defect seals early because of clotting.<sup>2</sup>

### COMPUTED TOMOGRAPHY

Penile prostheses (Figure 76-2) and calcified plaques (Figure 76-3) of Peyronie's disease can be easily seen on computed tomography (CT). CT is useful for staging of penile malignancies, for follow-up after surgery, and for the evaluation of post-surgical complications.<sup>3</sup>

### MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) is an excellent imaging method for evaluation of penile trauma. However, it is not considered routine for the evaluation of penile trauma because of high cost and restricted availability.<sup>2</sup> It should be used when ultrasonography is nondiagnostic or cannot be performed because of severe pain and swelling.<sup>6</sup> With the patient in the supine position, the penis is taped against the abdominal wall and a surface coil applied. Multiplanar T1-weighted, T2-weighted, and postcontrast T1-weighted images are acquired.<sup>6</sup>



**Figure 76-1** Retrograde urethrogram showing contrast extravasation from the penile urethra suggesting a urethral tear. The patient had sustained a penile fracture during sexual intercourse.



**Figure 76-2** Axial computed tomography image of the perineum showing an inflatable penile prosthesis.



**Figure 76-3** Axial computed tomography image showing a calcified plaque in the tunica albuginea of the penis in a patient with Peyronie's disease.

MRI can accurately reveal the presence, location, and extent of a tunical tear. Because the tunica albuginea is seen as having low signal intensity on both T1- and T2 weighted images, MRI is very suitable for the evaluation of its integrity (Figures 76-4 to 76-6) and so is particularly helpful in determining the need for surgical intervention. Injuries associated to the adjacent structures, particularly the corpus spongiosum and urethra, are also demonstrated. In patients without penile fracture, MRI can show an intact tunica albuginea and the presence of an intracavernosal or extratunical hematoma.<sup>6</sup>



**Figure 76-4** T1-weighted coronal magnetic resonance image of the penis showing discontinuity of the tunica albuginea (penile fracture) with an adjacent complex hyperintense hematoma.

### 76 Penile Trauma and Miscellaneous Penile Lesions 937

MRI is not primarily used for imaging penile tumors because they are usually visible on physical examination. MRI may be useful for pretreatment evaluation of penile lymphoma, for the detection of pelvic lymphadenopathy for staging penile malignancy, and postoperatively to evaluate postsurgical complications and deep or local recurrence of malignancy.<sup>3,9</sup>

On MRI, a Cowper's duct syringocele is seen as a T2-hyperintense midline oval structure at the base of penis adjacent to the ventral aspect of the bulbous urethra. MRI also can show the relationship of an inflammatory mass or abscess to the corporeal bodies and urethra.<sup>3</sup>

In low-flow priapism resulting from cavernous thrombosis, the affected cavernosal segment is distended with thrombotic blood and may compress the contralateral corpus cavernosum. The MR signal intensity of the affected segment depends on the age of the thrombus.<sup>3</sup>

On MRI, Peyronie's disease is seen as focal thickening of the tunica albuginea and is best evident on T2-weighted images. MRI localizes and depicts the extent of the fibrous plaques. After intravenous administration of gadolinium, enhancement of the plaque has been shown to correlate with the presence of active inflammation.<sup>3,7</sup>

Many inflatable penile prostheses are MR compatible. They appear T2 hyperintense because they contain fluid. MRI can be used to assess prosthesis-related complications.<sup>3</sup>

### ULTRASONOGRAPHY

Ultrasonography is the preferred imaging technique for evaluation of penile trauma because it allows evaluation of normal and pathologic structures smaller than 1 mm and the sensitivity



**Figure 76-5** Axial T2-weighted magnetic resonance image of the penis showing discontinuity of the tunica (penile fracture) surrounding the ventral corpus spongiosum.



**Figure 76-6** Sagittal T1-weighted magnetic resonance image of a penile fracture showing discontinuity of the tunica albuginea and disruption of the corpora with associated hematoma.

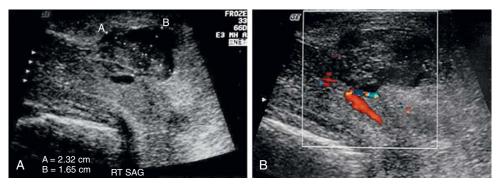


Figure 76-7 Gray-scale (A) and color Doppler (B) ultrasound images of the penis show discontinuity of the thin echogenic tunica and an adjacent complex hematoma.

of color Doppler analysis to slow flow allows full evaluation of penile vascularity.<sup>2</sup>

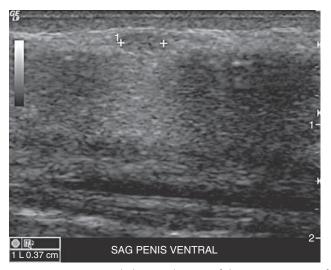
Ultrasonography shows an irregular hypoechoic or hyperechoic defect at the site of cavernosal rupture. Interruption of the thin echogenic line of the tunica albuginea and associated hematoma helps identify the exact location of rupture on ultrasound examination (Figure 76-7). In the acute phase, cavernosal hematomas appear as hyperechoic or complex masses, which later become cystic and often have septations. Cavernosal damage can cause fibrosis, which appears as poorly defined, echogenic scar replacing erectile tissue.<sup>2</sup>

In urethral and spongiosal trauma, sonourethrography shows the continuity of the anterior urethral lining. Real-time examination of the urethra during instillation of fluid may demonstrate extravasation through a ruptured urethral wall. The presence of air in the cavernosal bodies in the absence of external penetrating trauma is an indirect sign of urethral injury. Ultrasonography may show edema or hematoma of the corpus spongiosum after penile trauma. However, small isolated corpus spongiosal injuries may not be detected by ultrasonography.<sup>2,8</sup>

Venous injury with resultant posttraumatic dorsal arteriovenous fistula may show increased venous pressures and dilatation of the involved vein. In cases of thrombosis of the superficial and deep dorsal penile veins, ultrasonography shows a noncompressible dorsal vein. If the veins are ruptured, an associated adjacent hematoma may be present.<sup>2</sup>

Calcified and noncalcified plaques of Peyronie's disease can be seen on ultrasound evaluation and their location and extent demonstrated with accuracy (Figure 76-8).<sup>3</sup> However, ultrasonography cannot reliably distinguish between active inflammatory and quiescent stages of the disease, in contrast to MRI.<sup>7</sup> After surgery, ultrasonography can demonstrate patches on the tunica albuginea (as interruptions of normal echogenic tunica) or hyperechoic dermal/saphenous grafts used for penoplasty.<sup>8</sup>

For the evaluation of high-flow priapism, color Doppler ultrasonography has replaced arteriography as the imaging modality of choice. In patients with recent arterial laceration, gray-scale ultrasonography shows an irregular, but well-circumscribed, hypoechoic region, secondary to tissue injury or distended lacunar spaces in the corpus cavernosum. In high-flow priapism, the arterial-lacunar fistula bypasses the helicine arteries and appears as an aliasing color blush extending into the cavernosal tissue and as a turbulent high-velocity flow on color duplex ultrasonography.<sup>2,4,8</sup> Increasing the color Doppler



**Figure 76-8** Parasagittal ultrasound image of the penis in a case of Peyronie's disease shows a 3.7-mm isoechoic focal plaque-like thickening of the tunica albuginea.

velocity scale reduces aliasing of the color blush, which allows for localization of the cavernosal artery tear as a focal area with very high velocity flow.<sup>4</sup> Alternatively, the only finding in highflow priapism may be high cavernosal arterial flow in the absence of sexual stimulation.<sup>2</sup>

After therapeutic angiographic embolization, color Doppler imaging can be used to confirm successful embolization by demonstrating the disappearance or reduction in the size of a fistula or to identify unsuccessful treatment by showing patent collateral feeding vessels or persistent flow in the embolized artery. Long-term follow-up imaging with color Doppler ultrasonography is useful to exclude recurrent fistula and recanalization of the embolized cavernosal artery.<sup>4</sup>

In patients with low-flow or ischemic priapism, color Doppler ultrasonography shows absent or markedly reduced flow in the cavernosal arteries.<sup>8</sup>

Corporeal cylinders, the scrotal pump, and connecting tubing of inflatable devices are well visualized on ultrasonography. The abdominal reservoir also may be visualized if it is superficial and is best visualized when it has maximum volume (i.e., with the penis in the flaccid state). During routine ultrasonography of the pelvis, the full abdominal reservoir can be mistaken for a bladder diverticulum or a loculated fluid collection. Inflating the prosthesis decreases the reservoir volume, confirming the true nature of the fluid.

Infection can be a devastating complication of a penile prosthesis and may require antibiotic therapy and prosthetic removal. Associated inflammation results in corporeal fibrosis and penile shortening, which can make reimplantation difficult. Ultrasonography can be useful in identifying the extent of fibrotic changes, which manifest as focal or diffuse hyperechogenicity of the cavernosa.<sup>8</sup>

In patients with surgical revascularization for impotence, ultrasonography allows evaluation of the anastomosis between the inferior epigastric and dorsal penile arteries or vein. It also can be used to detect patency of the anastomosis and rare complications such as aneurysmal dilatation of the anastomosis.<sup>8</sup>

The neophallus created for sex reassignment appears heterogeneous on ultrasonography, reflecting the echogenicity of the explanted subcutaneous and muscular tissue. The neourethra manifests as an anechoic tubular structure after the instillation of saline solution into the lumen. Occasionally, hair growth in the neourethra can be seen. The vessels of the neophallus can be evaluated with color Doppler imaging. A prosthesis in a neophallus can be evaluated on ultrasonography and has the same appearance as in a native penis.<sup>8</sup>

# POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY

Positron emission tomography with CT (PET-CT) may be used in evaluation and staging of penile malignancies.

## **Differential Diagnosis**

Thrombosis of the superficial and deep dorsal penile veins is a rare urologic emergency and clinically may mimic penile fracture.<sup>2</sup> Epithelioid sarcoma may manifest as focal induration and may mimic Peyronie's disease clinically.<sup>3</sup>

## Treatment

In penile fractures, early surgical intervention can prevent delayed complications such as fibrous plaque formation and angulation of the penis.<sup>6</sup> Surgical repair consists of evacuation of any hematoma and repair of the tunical defect.<sup>5</sup>

Partial penectomy is performed for malignancies that involve the glans penis. Radical or total penectomy with or without cystoprostatectomy is done for the malignant lesions that involve the proximal shaft or the posterior urethra. In cases of SCC, penectomy with a 2-cm disease-free margin often achieves good postoperative survival.<sup>3</sup>

Surgical incision of the obstructed duct in Cowper's duct syringocele is usually curative.<sup>3</sup>

Surgical intervention is indicated in advanced Peyronie's disease and may involve penile shortening, straightening, or lengthening procedures.<sup>7</sup>

Treatment of high-flow priapism usually involves superselective embolization of the torn artery. Less commonly, surgical repair (ligation of the internal pudendal or cavernosal artery with microsurgical closure of the fistula) or conservative management with close follow-up is the method of management.<sup>2,4</sup>

In surgical correction of low-flow priapism, the engorged corpora cavernosa are connected with the glans, corpus spongiosum, or veins.

Phallic reconstruction surgery can be used for sex reassignment or for correction of congenital penile malformations.<sup>8</sup>

### What the Referring Physician Needs to Know

- In penile trauma, the integrity of the tunica albuginea is the most important factor in determining the necessity for surgical intervention.
- If a penile fracture is present, accurate assessment of the location and severity of rupture of the tunica albuginea is essential for the surgeon to determine the optimal site and extent for an incision.

### **Key Points**

- Surgical repair is generally recommended for patients with a suspected tear of the tunica albuginea or with urethral injury.
- Penile malignancy is usually diagnosed clinically, and imaging is used for staging the disease.
- The plaques of Peyronie's disease are best seen with ultrasonography or MRI.
- Low-flow priapism is a urologic emergency.

### SUGGESTED READINGS

Bertolotto M, Quaia E, Mucelli FP, et al: Color Doppler imaging of posttraumatic priapism before and after selective embolization. *Radiographics* 23: 495–503, 2003. Bhatt S, Kocakoc E, Rubens DJ, et al: Sonographic evaluation of penile trauma. *J Ultrasound Med* 24:993–1000, 2005. Pretorius ES, Siegelman ES, Ramchandani P, et al: MR imaging of the penis. *Radiographics* 21:S283– S299, 2001.

### REFERENCES

- 1. Rifkin MD: The urethra and penis. In *Diagnostic imaging of the lower genitourinary tract*, New York, 1985, Raven Press.
- Bhatt S, Kocakoc E, Rubens DJ, et al: Sonographic evaluation of penile trauma. J Ultrasound Med 24:993–1000, 2005.
- Pretorius ES, Siegelman ES, Ramchandani P, et al: MR imaging of the penis. *Radiographics* 21:S283– S299, 2001.
- Bertolotto M, Quaia E, Mucelli FP, et al: Color Doppler imaging of posttraumatic priapism before
- and after selective embolization. *Radiographics* 23:495–503, 2003.
- 5. El-Taher AM, Aboul-Ella HA, Sayed MA, et al: Management of penile fracture. *J Trauma* 56:1138–1140, 2004.
- Choi MH, Kim B, Ryu JA, et al: MR imaging of acute penile fracture. *Radiographics* 20:1397–1405, 2000.
- Helweg G, Judmaier W, Buchberger W, et al: Peyronie's disease: MR findings in 28 patients. *AJR Am J Roentgenol* 158:1261–1264, 1992.
- Bertolotto M, Serafini G, Savoca G, et al: Color Doppler US of the postoperative penis: anatomy and surgical complications. *Radiographics* 25:731– 748, 2005.
- Chiang KH, Chang PY, Lee SK, et al: MR findings of penile lymphoma. Br J Radiol 79:526–528, 2006.



# Imaging of the Scrotum

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# **Technical Aspects**

Scrotal imaging has been one of the undeniable success stories of modern radiology.<sup>1</sup> The scrotum is predominantly imaged for two clinical indications: the painless scrotal mass and the acute scrotum. Both conditions predominantly affect young men in the second through fourth decades of life. Rapid and accurate diagnosis is the goal of all imaging.<sup>2,3</sup> Among several imaging modalities available, ultrasonography and magnetic resonance imaging (MRI) are used predominantly, whereas computed tomography (CT), angiography, and nuclear medicine studies are rarely used as primary imaging modalities for disorders of the scrotum.

### **ULTRASONOGRAPHY**

Ultrasonography is undoubtedly the mainstay and is invariably the first and often the only imaging modality necessary.4 However, MRI can be useful as a problem-solving tool when ultrasonographic findings are equivocal or suboptimal.<sup>5</sup>

Scrotal ultrasonography is performed with the patient in the supine position and the scrotum supported by a rolled towel placed between the thighs. Optimal results are obtained with a high-frequency (7- to 10-MHz) linear-array transducer. Scanning is performed most often with the transducer in direct contact with the skin, but, if necessary, a stand-off pad can be used for evaluation of superficial lesions.

The testes are examined in at least two planes, along transverse and long axes. The size and echogenicity of each testis and epididymis are compared with those of the opposite side. Color Doppler and pulsed-wave Doppler imaging parameters are optimized to display low-flow velocities to demonstrate blood flow in the testes and surrounding scrotal structures. Power Doppler imaging also may be used to demonstrate intratesticular flow in patients with an acute scrotum. In patients being evaluated for an acute scrotum, the asymptomatic side should be scanned initially to set the gray-scale and color Doppler gain settings to allow comparison with the affected side. Transverse images with portions of each testis on the same image should be acquired in gray-scale and color Doppler modes. Scrotal skin thickness is evaluated. The structures within the scrotal sac are examined to detect extratesticular masses or other abnormalities. In patients with small palpable nodules, scans should include the area of clinical concern. A finger should be placed beneath the nodule and the transducer placed directly over the nodule for scanning. Alternatively, a finger can be placed on the

nodule and the transducer opposite to allow visualization of the lesion. Additional techniques such as use of the Valsalva maneuver or upright positioning can be used as needed for venous evaluation.6

### MAGNETIC RESONANCE IMAGING

For MRI of the scrotum, a folded towel is placed between the patient's legs to elevate the scrotum and penis. A local surface coil is used. The penis is dorsiflexed over the pubis and a pad placed over it to retain its position. It is important to take time with positioning and ensure patient comfort, because any movement either voluntary or from cremasteric contraction may degrade image quality.<sup>4</sup> A typical imaging protocol consists of large field-of-view (FOV) axial pelvic imaging to assess the inguinal canal and bowel for hernias and to detect ascites. The origins of the renal vessels should be included to allow evaluation of the lymph node drainage of the testes. A high-resolution T2-weighted fast spin-echo sequence (FOV of 10 to 12 cm, imaging matrix  $256 \times 256$ ) is used in the axial, sagittal, and coronal planes to image the scrotum. A high-resolution, axial, T1-weighted spoiled gradient echo sequence may be used to identify hemorrhage.

Gadolinium-enhanced imaging is not routinely used but can be performed in selected instances. Use of contrast material can aid in differentiating between a benign cystic lesion and a cystic neoplasm and can help assess for areas of absent or reduced testicular perfusion, such as in segmental testicular infarct. When gadolinium-enhanced imaging is indicated, a fat-saturated T1-weighted spoiled gradient echo sequence is obtained.7

## **Pros and Cons**

Modern ultrasonography provides high-resolution images of the scrotum and its contents, is relatively inexpensive and quick to perform, has no known bioeffects, and allows dynamic maneuvers such as the Valsalva maneuver to be incorporated into the examination. However, ultrasound imaging requires skill and is therefore operator dependent.

MRI provides excellent tissue detail. Contrast-enhanced MRI may allow diagnosis of some benign masses that are indeterminate on ultrasonography.<sup>5</sup> MRI also may aid detection of undescended testes that are not visualized on ultrasonography.8 In the acute scrotum, MRI can help diagnose testicular torsion; and when dynamic contrast-enhanced MRI is used in

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combination with T2- and T2\*-weighted images, testicular necrosis may be diagnosed.9 MRI is more expensive, takes slightly longer to perform, and cannot be used in patients with pacemakers, implants, and claustrophobia.

## **Controversies**

The field strength of MRI used in clinical practice and diagnostic radiofrequency coils are regarded as safe, and no harmful effects have been recorded. However, the potential effects are of some concern, because radiofrequency radiation increases tissue temperature and spermatogenesis is particularly susceptible to temperature-related impairment. Conflicting reports exist about the effects of MRI on the testis itself. However, it is unlikely that the relatively mild transient increase in scrotal temperature produced by a routine diagnostic MRI examination will cause significant damage. Thus, MRI should be used when there is a significant diagnostic advantage over ultrasonography.4

## **Normal Anatomy**

normal vascularity in a testis.

The normal adult testis is ovoid and measures 3 cm in anteroposterior dimension, 2 to 4 cm in width, and 3 to 5 cm in length. Each testis normally weighs between 12.5 and 19.0 g. Both the size and weight of the testes normally decrease with age.<sup>10,11</sup>

On ultrasonography the normal testis is slightly echogenic with a homogeneous echotexture. The testis is surrounded by a

fibrous band, the tunica albuginea, which is often not visualized in the absence of intrascrotal fluid (Figure 77-1). The tunica is often seen as an echogenic structure where it invaginates posteriorly into the testis to form the mediastinum.

The epididymis is a tubular curved structure consisting of a head, body, and tail that lies posterolateral to the testis and measures 6 to 7 cm in length. On ultrasonography, it is isoechoic to hyperechoic to the normal testis and has equal or diminished vascularity. The epididymal head is the largest and most easily identified portion of the epididymis. It lies superolateral to the upper pole of the testis and is an important landmark during the ultrasound examination (Figure 77-2). It is composed of 8 to 12 efferent ducts converging into a single larger duct in the body and tail. This single duct becomes the vas deferens and continues in the spermatic cord (Figure 77-3).

On MRI the normal testis has a homogeneous appearance, with intermediate signal intensity on T1-weighted images and high signal intensity on T2-weighted images relative to skeletal muscle. The tunica albuginea appears as low signal intensity on T1- and T2-weighted images. The relatively high signal intensity of the testis on T2-weighted images allows excellent contrast from solid lesions, which invariably have lower T2 signal intensity. T1-weighted images are useful for depicting tissues and substances of high signal intensity, such as fat and methemoglobin. The epididymis has signal intensity characteristics similar to those of testicular parenchyma on T1-weighted images but lower signal intensity on T2-weighted images. Intravenous administration of gadolinium results in hyperintensity of the epididymis relative to the testis (Figure 77-4).<sup>12</sup>

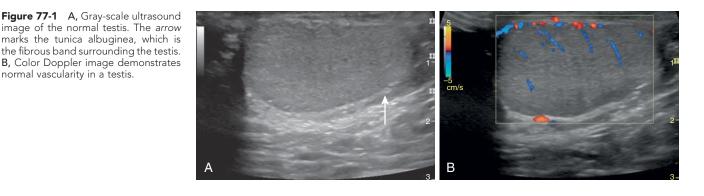
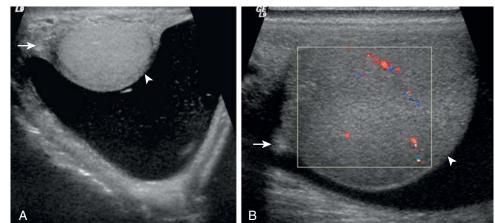


Figure 77-2 A, Normal epididymal head. Transverse gray-scale ultrasound image shows the normal pyramidal head of the epididymis (arrow), which is slightly hyperechoic compared with the testes (arrowhead) and lies along the posterolateral aspect of the testis. B, Transverse gray-scale ultrasound image demonstrates the normal, slightly hyperechoic epididymal body (arrow) closely apposed to the testis (arrowhead). The epididymal body is easily visualized in this patient owing to the presence of a large hydrocele.



### 942 PART 8 Urogenital Imaging

From the mediastinum, numerous fibrous septa extend into the testis, dividing it into 250 to 400 wedge-shaped lobuli, each of which consists of one to three seminiferous tubules. There are approximately 840 tubules per testis. As the tubules course centrally, they join other seminiferous tubules to form 20 to 30 larger ducts, known as the tubuli recti. The seminiferous tubules open via the tubuli recti into dilated spaces called the rete testis within the mediastinum. The rete testis, a network of epitheliumlined spaces embedded in the fibrous stroma of the mediastinum, drains seminal fluid into the epididymis through 10 to 15 efferent ductules.

Four testicular appendages have been described: the appendix testis, the appendix epididymis, the vas aberrans, and the

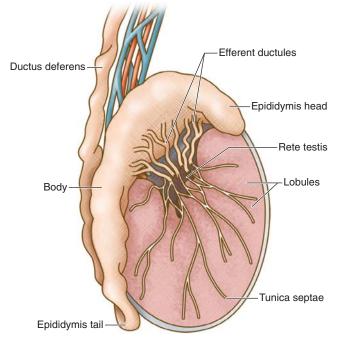


Figure 77-3 Drawing of normal testicular anatomy.

paradidymis (Figure 77-5). These are remnants of embryonic ducts (paramesonephric and mesonephric ducts).

The appendix testis is present in up to 92% of cases in a postmortem series, is identified sonographically in up to 80% of cases, and is more readily visible when a hydrocele is present. It is attached to the upper pole of the testis in the groove between the testis and the epididymis.

The appendix epididymis is attached to the head of the epididymis and has been encountered unilaterally in 34% and bilaterally in 12% of testes in postmortem series and is best seen in the presence of a hydrocele.<sup>13,14</sup>

The spermatic cord comprises the vas deferens, testicular artery, cremasteric artery, deferential artery, pampiniform plexus, genitofemoral nerve, and lymphatic vessels and begins at the deep inguinal ring and descends vertically into the scrotum.

The right and left testicular arteries, branches of the abdominal aorta, arise just distal to the renal arteries and provide the primary vascular supply to the testes. They enter the spermatic cord at the deep inguinal ring and continue along the posterior surface of the testis, penetrating the tunica albuginea where the capsular arteries form and course through the tunica vasculosa, located beneath the tunica albuginea. Branches arising from the capsular arteries carry blood toward the mediastinum, where they divide to form the recurrent rami that carry blood away from the mediastinum into the testis. A transmediastinal arterial branch of the testicular artery is present in approximately half of normal testes; it courses through the mediastinum to supply the capsular arteries and is usually accompanied by a large vein.<sup>15</sup>

The deferential artery, a branch of the superior vesical artery, and the cremasteric artery, a branch of the inferior epigastric artery, supply the epididymis, vas deferens, and peritesticular tissue. Waveforms of normal capsular and intratesticular arteries show high levels of antegrade diastolic flow, reflecting the low vascular resistance of the testis.<sup>16,17</sup>

Venous drainage of the testes is via the pampiniform plexus of draining veins, which is formed around the upper half of the epididymis in a variable fashion and continues as the testicular vein through the deep inguinal ring. The right testicular vein empties into the inferior vena cava, and the left testicular vein empties into the left renal vein.<sup>6</sup>

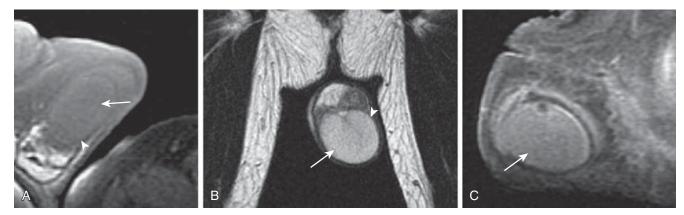


Figure 77-4 A, The normal testis (arrow) appears homogeneous and isointense to muscle on T1-weighted magnetic resonance imaging, with the tunica albuginea appearing hypointense (arrowhead). B, The normal testis (arrow) is hyperintense on T2-weighted MR imaging, with the tunica albuginea hypointense (arrowhead). C, The normal testis enhances homogeneously after administration of gadolinium (arrow).

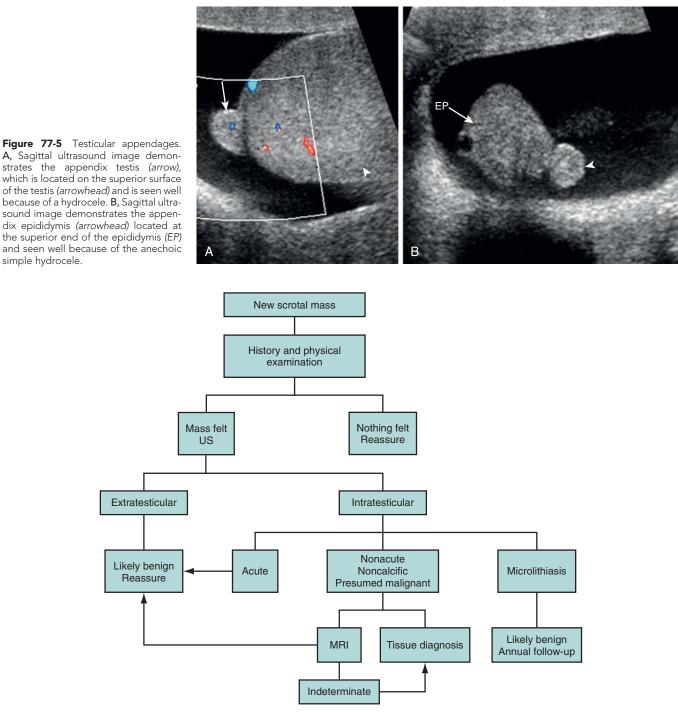


Figure 77-6 Algorithmic approach to the diagnosis and management of a new scrotal mass. MRI, Magnetic resonance imaging; US, ultrasound.

# Diagnosis

When evaluating a scrotal mass, the three most important questions to answer are (1) is the mass intratesticular or extratesticular? (2) is it cystic or solid? and (3) is it acute? With rare exceptions, intratesticular solid masses should be considered malignant. If the mass is extratesticular and cystic, the lesion is almost certainly benign and a specific diagnosis is often possible. Extratesticular solid masses are also most likely benign, with the prevalence of malignancy being approximately 3%. Unfortunately, there is considerable overlap in the sonographic appearances of many solid extratesticular masses, precluding a specific diagnosis in most cases. Localizing the abnormality to the epididymis, spermatic cord, or paratesticular location can shorten the differential diagnosis. Further refinement can sometimes be made on the basis of patient history and specific imaging characteristics, with MRI being helpful in selected cases.<sup>18</sup> An algorithmic approach to the differential diagnosis of scrotal masses is outlined in Figure 77-6.

### **Key Points**

- Ultrasonography is the mainstay of scrotal imaging.
- Ultrasound always should be performed in conjunction with the clinical history and physical examination.
- MRI may be helpful in selected cases.
- Origins of the renal vessels should be included in an MRI protocol for scrotal imaging to assess the lymphatic drainage of the testes.

### **SUGGESTED READINGS**

- Choyke PL: Dynamic contrast-enhanced MR imaging of the scrotum: reality check. *Radiology* 217:14–15, 2000.
- Dogra VS, Gottlieb RH, Oka M, et al: Sonography of the scrotum. *Radiology* 227:18–36, 2003.

### REFERENCES

- Choyke PL: Dynamic contrast-enhanced MR imaging of the scrotum: reality check. *Radiology* 217:14–15, 2000.
- 2. Buckley JC, McAninch JW: Diagnosis and management of testicular ruptures. *Urol Clin North Am* 33:111–116, 2006.
- 3. Moul JW: Timely diagnosis of testicular cancer. *Urol Clin North Am* 34:109–117, 2007.
- 4. Rifkin MD, Cochlin DL: *Imaging of the scrotum and penis*, London, 2002, Martin Dunitz.
- Muglia V, Tucci S, Jr, Elias J, Jr, et al: Magnetic resonance imaging of scrotal diseases: when it makes the difference. *Urology* 59:419–423, 2002.
- 6. Dogra VS, Gottlieb RH, Oka M, et al: Sonography of the scrotum. *Radiology* 227:18–36, 2003.
- Kim W, Rosen MA, Langer JE, et al: US MR imaging correlation in pathologic conditions of the scrotum. *Radiographics* 27:1239–1253, 2007.

Kim W, Rosen MA, Langer JE, et al: US MR imaging correlation in pathologic conditions of the scrotum. *Radiographics* 27:1239–1253, 2007.

- Extratesticular cystic masses are almost certainly benign, and a specific diagnosis is often possible.
- Intratesticular solid masses are considered malignant, with rare exceptions.

- Frush DP, Sheldon CA: Diagnostic imaging for pediatric scrotal disorders. *Radiographics* 18: 969–985, 1998.
- Watanabe Y, Nagayama M, Okumura A, et al: MR imaging of testicular torsion: features of testicular hemorrhagic necrosis and clinical outcomes. J Magn Reson Imaging 26:100–108, 2007.
- 10. Krone KD, Carroll BA: Scrotal ultrasound. Radiol Clin North Am 23:121–139, 1985.
- 11. Trainer TD: Histology of the normal testis. *Am J Surg Pathol* 11:797–809, 1987.
- Kubik-Huch RA, Hailemariam S, Hamm B: CT and MRI of the male genital tract: radiologicpathologic correlation. *Eur Radiol* 9:16–28, 1999.
- Rolnick D, Kawanoue S, Szanto P, et al: Anatomical incidence of testicular appendages. *J Urol* 100:755–756, 1968.

- Muglia V, Tucci S, Jr, Elias J, Jr, et al: Magnetic resonance imaging of scrotal diseases: when it makes the difference. *Urology* 59:419–423, 2002.
- Rumack CM, Wilson SR, Charboneau JW: Diagnostic ultrasound, ed 3, St. Louis, 2004, Mosby.
- Fakhry J, Khoury A, Barakat KL: The hypoechoic band: a normal finding on testicular sonography. AJR Am J Roentgenol 153:321–323, 1989.
- Middleton WD, Bell MW: Analysis of intratesticular arterial anatomy with emphasis on transmediastinal arteries. *Radiology* 189:157–160, 1993.
- Middleton WD, Thorne DA, Melson GL: Color Doppler ultrasound of the normal testis. AJR Am J Roentgenol 152:293–297, 1989.
- Woodward PJ, Schwab CM, Sesterhenn IA: Extratesticular scrotal masses—radiologicpathologic correlation. From the archives of the AFIP. *Radiographics* 23:215–240, 2003.



# Benign and Malignant Testicular Lesions

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# Benign Testicular Lesions

### ETIOLOGY AND CLINICAL PRESENTATION

Benign scrotal or testicular swellings and masses have many etiologies and different clinical presentations, as listed in Tables 78-1 and 78-2. Of palpable nodules, 31% to 47% are benign at surgery.<sup>1-3</sup>

### IMAGING

### Testicular Torsion, Testicular Infarction, and Torsion of the Testicular Appendage

Testicular torsion occurs when the spermatic cord is twisted, compromising the blood flow to and from the testis. Torsion can be classified as intravaginal or extravaginal. Intravaginal torsion occurs when the mesenteric attachment of the spermatic cord on the testis is narrow, allowing the testis to rotate within the cavity of the tunica vaginalis like a "bell clapper." It typically affects males between the ages of 12 and 18 years, probably owing to the fivefold increase in testicular volume at puberty. Extravaginal torsion, in which the entire testis, epididymis, and tunica vaginalis twist in a vertical axis, is rare and is typically seen prenatally (75%) or in neonates.<sup>4</sup> Intravaginal torsion is characterized by pain of sudden or insidious onset, whereas extravaginal or neonatal torsion may be completely asymptomatic, and a unilateral mass in the inguinal region or high scrotum may be the only manifestation. The extent of the spermatic cord twist and its duration are the two most important factors. The initial disruption of blood supply will be to the venous and lymphatic drainage, rather than to the arterial supply of the testes, and venous infarction occurs earlier and at lesser levels of torsion.<sup>4</sup>

**Magnetic Resonance Imaging.** Magnetic resonance imaging (MRI) has been used to differentiate subacute testicular torsion from epididymitis with a high degree of accuracy.<sup>5</sup> On MRI, an enlarged spermatic cord (secondary to edema) with no increase in cord vascularity (seen as lack of vascular flow voids) and a "whirlpool pattern" and "torsion knot" (best seen on T2-weighted coronal views) are specific for torsion.<sup>4</sup>

Contrast-enhanced MRI can help in the diagnosis of segmental testicular infarction (Figure 78-1). Dynamic contrastenhanced subtraction MRI can diagnose testicular torsion and detect testicular necrosis with a high degree of sensitivity and accuracy.<sup>6</sup> **Ultrasonography.** On ultrasonography, the initial appearance of the testis is hypoechoic and enlarged secondary to congestion accompanied by a small hydrocele. Later, increased echogenicity and heterogeneity can be seen from hemorrhagic change. The epididymis also may be involved (Figure 78-2). A small hypoechoic testis, with an enlarged echogenic epididymis, is seen with a chronic missed torsion. There may be an abrupt change in caliber of the spermatic cord below the point of torsion.<sup>4</sup> Ultrasound demonstration of the "whirlpool" sign in the spermatic cord with absent or reduced flow distal to the whirlpool is a reliable indicator of torsion.<sup>7</sup> Skin thickening may manifest as venous congestion.

Color Doppler imaging allows visualization of intratesticular blood flow, which is either reduced or absent in torsion. This distinction may be less apparent when orchitis is complicated by testicular infarction. Technical factors, including equipment and operator experience, may limit the quality of the study. A useful caveat to use in such conditions is to compare the findings with the contralateral normal testis. Color Doppler flow is difficult to detect in testes less than 1 mL in volume (i.e., in children). Techniques including power Doppler imaging and the use of contrast agents may improve detection of intratesticular flow.<sup>4</sup>

The most common cause of scrotal pain in a young child is torsion of the testicular appendix. The ultrasound appearance of the twisted testicular appendage has been described as an avascular hypoechoic or echogenic mass adjacent to a normally perfused testis and surrounded by an area of increased color Doppler flow.<sup>8,9</sup>

**Nuclear Medicine.** Traditionally, testicular scintigraphy has been used in the assessment of testicular torsion, but this method suffers from the constraints of limited access out of hours, complex equipment needs, and prolonged examination times.<sup>4</sup>

**Imaging Algorithm.** An imaging algorithm for testicular torsion, adapted from the American College of Radiology Appropriateness Criteria for Acute Scrotal Pain without Antecedent Mass or Trauma is proposed in Figure 78-3 and Table 78-3.<sup>10,11</sup>

# Epididymitis, Epididymo-Orchitis, and Testicular Abscess

Epididymitis is the most common cause of acute scrotal pain in postpubertal men. In 20% of patients, testicular extension

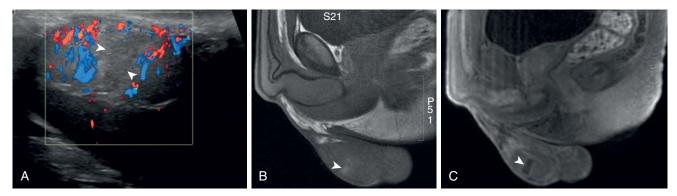
### 946 PART 8 Urogenital Imaging

TABLE 78-1 Causes of Acu	ite Scrotal Swelling		
Condition	Symptoms	Signs	Comments
Torsion	Acute onset of severe pain, usually postpubertal	Pain not relieved by scrotal elevation, high-riding testis, absent cremasteric reflex	Surgical emergency
Epididymo-orchitis	Severe acute onset of pain, older age group	Edema, tenderness, erythema	Positive urinalysis
Torsion of appendix testis	Gradual onset of pain, usually prepubertal	Tenderness localized to anterosuperior testis, cremasteric reflex preserved	Managed conservatively
Trauma	History of injury	Depends on severity of injury	May result in infarction, rupture, or torsion of testis.
Infarction	Depends on cause	Not specific	Possible causes include torsion, epididymo-orchitis, vasculitis, hypercoagulable states, sickle cell disease.
Abscess	Pain, fever, failure to improve with antibiotics in case of abscess secondary to epididymo- orchitis	Febrile; tender, swollen scrotum Signs may be masked in patients with acquired immunodeficiency syndrome	Known complication of mumps, smallpox, scarlet fever, influenza, typhoid, and sinusitis. Fournier's gangrene may extend to involve the testis.
Hematocele/pyocele	Depends on cause	Edematous and swollen in the acute phase, scrotal skin thickening, calcification when chronic	Hematoceles occur after trauma, including iatrogenic trauma. Pyoceles form from rupture of an abscess into, or infection of, a hydrocele.
Incarcerated inguinal hernia	Sudden irreducibility of inguinal hernia with pain	Nonreducible, edematous, red inguinal mass	Usually presents in the setting of a preexisting inguinal hernia.

#### TABLE 78-2 **Causes of Nonacute Scrotal Swelling** Condition Symptoms Signs Comments Hydrocele Painless mass that may Transillumination positive Reactive hydrocele may be associated with increase slowly in size epididymo-orchitis or other inflammation. Testicular cyst None Usually nonpalpable Incidental finding on ultrasonography. More common on the left; Varicocele Scrotal swelling, infertility Sudden onset of a right-sided varicocele, or "bag of worms" feel on any irreducible varicocele, may be due to palpation, pronounced on retroperitoneal pathology (e.g., renal cell Valsalva maneuver carcinoma) compressing the testicular vein. Epidermoid Painless mass or none Palpable mass or none Often removed surgically because it may be difficult to differentiate from malignancy. cvst Tubular ectasia Incidentally discovered; may be associated with None None of rete testis prior infection, trauma, or scrotal surgery Adrenal rests Often manifest as Bilateral scrotal masses Usually associated with elevated corticotropin bilateral scrotal swelling level Asymptomatic or may Spermatocele Discrete soft mass near Arises from obstructed efferent ductules usually manifest as small focal epididymis, freely moving in patients with prior vasectomy. scrotal lump and superior to testis with positive transillumination Testicular Incidental diagnosis, may be premalignant, Asymptomatic None microlithiasis follow-up imaging is often advised. Scrotal pearl Asymptomatic or may Hard nodule may or may Generally idiopathic and benign; may be from a torsed appendix testis. manifest as nodular not be felt. swelling

results in epididymo-orchitis. Primary orchitis may result from infectious agents such as mumps. Epididymitis in older men usually results from a lower urinary tract infection with the common causative organisms being *Escherichia coli*, *Pseudomonas*, and *Klebsiella*. In younger men, organisms such as *Chlamydia* and *Neisseria gonorrhoeae* are more common etiologic agents. Rarely, tuberculosis may cause epididymo-orchitis. Mild repetitive trauma to the scrotum such as caused by riding a bicycle also may cause mild noninfective "mechanical" epididymo-orchitis.<sup>9,12,13</sup>

Testicular abscess is usually a complication of epididymoorchitis, although it may also result from undiagnosed testicular



**Figure 78-1** Segmental testicular infarction. **A**, Color Doppler ultrasound image in a 24-year-old man with acute onset of scrotal pain shows a focal area of hypovascularity (*arrowheads*) surrounded by areas of normal vascularity. **B**, On magnetic resonance (MR), this area is T1 hyperintense (*arrowhead*) relative to the normal testicular parenchyma. **C**, Postcontrast sagittal T1-weighted MR image shows a well-defined focal perfusion defect (*arrowhead*), confirming the diagnosis of segmental testicular infarction.

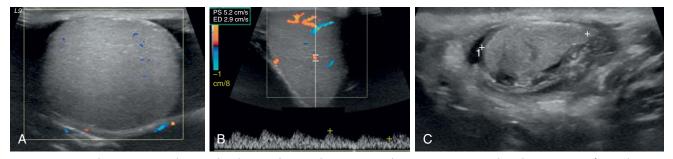


Figure 78-2 Testicular torsion. A, Color Doppler ultrasound image shows an avascular testis in a young male with acute onset of scrotal pain over the past 6 hours. B, Color Doppler image of the contralateral testis revealed normal vascularity. C, Gray-scale image of the symptomatic side revealed an enlarged and hypoechoic epididymis secondary to ischemia.

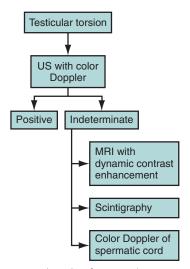


Figure 78-3 Imaging algorithm for testicular torsion. *MRI*, Magnetic resonance imaging; *US*, ultrasound.

torsion, gangrenous or infected tumor, or primary pyogenic or outcome of primary orchitis. A testicular abscess may complicate into pyocele or a fistula to the skin.<sup>9</sup>

**Magnetic Resonance Imaging.** MRI is not used as a primary modality, but epididymo-orchitis may be diagnosed in suspected cases of torsion based on increased vascularity of the spermatic cord, epididymis, and testis. **Ultrasonography.** Ultrasound findings of acute epididymitis include diffuse or focal involvement with low echogenicity or, rarely, high echogenicity (if there is coexisting hemorrhage), and increased blood flow on color Doppler imaging. There is usually evidence of inflammation in the rest of the testis, as well in the form of generalized swelling and hyperemia (Figure 78-4).<sup>9,12</sup> Associated findings, such as reactive hydrocele or pyocele and scrotal wall edema, can further support the diagnosis. Testicular ischemia and infarction may occur when the vascularity of the testis is compromised by venous occlusion. Changes of chronic epididymo-orchitis include persistent swelling of the epididymis as a heterogeneous mass and a striated appearance of the testis.<sup>9,12</sup>

Primary orchitis such as that secondary to mumps may have nonspecific findings and mimic tumor and transient torsion/ detorsion. However, the presence of increased venous flow suggests orchitis, because intratesticular venous flow is usually difficult to detect in normal testes.<sup>14</sup>

Testicular abscess is most commonly seen as an irregular, hypoechoic to anechoic mass with areas of mixed echogenicity. It is usually distinguished from tumors on the basis of clinical symptoms.<sup>9</sup>

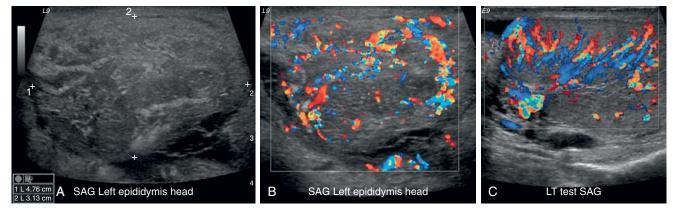
### Testicular Trauma

The primary causes of scrotal trauma include blunt, penetrating, degloving, and thermal injuries. Blunt scrotal trauma is by far the most common cause of testicular injury and usually results from athletic injury, motor vehicle accident, or assault. The right testis is more commonly injured than the left. Testicular trauma may result in testicular hematoma, traumatic

TABLEAccuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Testicular Torsion, Testicular78-3Infarction, and Torsion of the Testicular Appendage

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Modality	Accuracy	Limitations	Pitfalls
MRI	93%-100%	Motion sensitive, requires more time to perform than ultrasonography, skill to interpret, relatively expensive	T2*-weighted images may not be sensitive for detection of late contrast enhancement and are vulnerable to susceptibility artifacts that result from the air/tissue interface, which may distort images and hamper accurate measurement of signal intensity. <sup>10</sup>
Ultrasonography	89%-100%	Lower sensitivity in prepubertal and younger children	Blood flow can be preserved in torsion and detorsion, when hyperemia can be mistaken for orchitis.
Nuclear medicine	90% sensitivity 60% specificity	Cannot be applied to small children Lower availability of trained personnel to perform and interpret the examination	Hyperemic epididymis may be misinterpreted as a halo, producing false-positive study. <sup>11</sup> Photon-deficient areas secondary to hydrocele, spermatocele, uncommonly edematous appendix testis, and rarely an inguinal hernia can be mistaken for an avascular testis.

Remer EM, Francis IR, Baumgarten DA, et al: Acute onset of scrotal pain: without trauma, without antecedent mass. ACR Appropriateness Criteria, 2007. <a href="http://www.arrs.org">http://www.arrs.org</a>.



**Figure 78-4** Epididymo-orchitis. A 61-year-old man with scrotal pain. A, Sagittal gray-scale ultrasound image demonstrates a markedly enlarged heterogeneous epididymal head. B, Color Doppler image shows increased vascularity in the enlarged epididymal head. C, Transverse image of the testis demonstrates marked testicular hyperemia.

hydrocele or hematocele, testicular fracture, rupture, and infarction.  $^{\rm 15}$ 

**Magnetic Resonance Imaging.** MRI is generally not used to evaluate primary testicular trauma, although it may be performed for concomitant penile trauma.

**Ultrasonography.** Ultrasonography is ideal for the assessment of scrotal trauma because it provides rapid and accurate assessment of scrotal contents and their integrity. Hematoma maybe intratesticular or extratesticular and appear hyperechoic (acutely), heterogeneous (subacute), or predominantly hypoechoic (chronic) (Figure 78-5). Without surgical exploration, intratesticular hematoma has a poor prognosis.<sup>14</sup>

Hydrocele is commonly seen with trauma (Figure 78-6). Simple hydroceles usually appear uniformly hypoechoic. Rupture of the bulbar urethra may result in leakage of urine into the scrotum, mimicking a hydrocele.<sup>15</sup> Hematocele (blood within the tunica vaginalis) also may occur in trauma. Heterogeneity of the testicular parenchyma with associated hematocele suggests testicular rupture. A testicular fracture is a break in the continuity of the testicular parenchyma with an intact tunica albuginea. A testicular rupture involves discontinuity of the tunica albuginea with extrusion of testicular parenchymal contents into the scrotal sac. Testicular rupture necessitates emergent surgery, whereas testicular fracture with preserved vascularity may be managed conservatively. Testicular fracture without preserved vascularity also necessitates emergent surgery, owing to the presence of testicular ischemia. Heterogeneous testicular parenchymal echotexture, with focal hyperechoic or hypoechoic areas, corresponds to areas of hemorrhage or infarction (Figure 78-7).<sup>15-17</sup> Contour abnormality is the single most important predictor of testicular rupture.<sup>9,15-17</sup>

### Hydrocele, Hematocele, and Pyocele

Hydrocele is the most common cause of unilateral or bilateral diffuse painless scrotal enlargement. Congenital hydrocele results from a patent processus vaginalis resulting in open communication between the scrotal sac and peritoneum. It usually resolves by 18 months of age. Acquired hydroceles are the result of trauma, epididymitis, and torsion. Blood, pus, or urine may

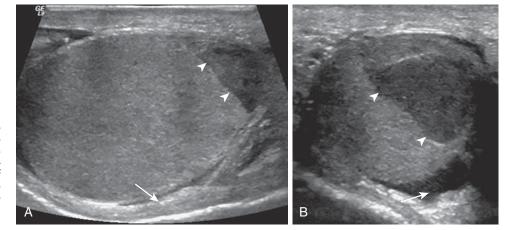
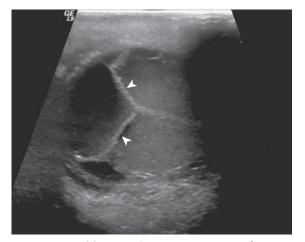


Figure 78-5 Testicular hematoma. A, Sagittal gray-scale ultrasound image of the testis in a young man struck in the scrotum with a baseball bat shows a testicular parenchymal hematoma (arrowheads) with edema and thickening of the scrotal skin (arrow). B, Transverse ultrasound image of the testis shows the testicular hematoma (arrowheads) and a small hematocele (arrow).



**Figure 78-6** Scrotal hematocele. Transverse image of a testis with adjacent multiseptated collection (*arrowheads*) with internal echoes. Surgery confirmed an organizing chronic scrotal hematoma.

accumulate in the tunica vaginalis spaces. Hematoceles and pyoceles are less common than simple hydroceles.<sup>9,12</sup>

**Magnetic Resonance Imaging.** MRI is not generally used to evaluate hydroceles, hematoceles, or pyoceles.

**Ultrasonography.** Hydroceles are characteristically anechoic collections with good sound transmission anterolateral to the testis because of the attachment of the testis to the epididymis and scrotal wall posteriorly. Low-level echoes from fibrin bodies or cholesterol crystals may occasionally be visualized (Figure 78-8). Both hematoceles and pyoceles are complex fluid collections that may contain multiple internal septa and debris (see Figure 78-6).<sup>9</sup>

**Nuclear Medicine.** Although radionuclide studies were traditionally used to diagnose hydrocele, this is no longer done.<sup>12</sup>

### Varicocele

A varicocele is a collection of abnormally dilated, tortuous, and elongated veins of the pampiniform plexus located posterior to the testis, accompanying the epididymis and the vas deferens within the spermatic cord. It can manifest as pain and/or swelling or may be detected incidentally during a workup for infertility. The cause of varicocele is unclear. Idiopathic varicoceles are thought to be due to incompetent valves in the testicular vein that permit retrograde passage of blood through the spermatic cord into the pampiniform plexus. Idiopathic varicoceles are more common on the left side where the testicular vein enters the left renal vein at a perpendicular angle. The right testicular vein enters obliquely into the inferior vena cava, and this appears to have some protective effect on the right side. Idiopathic varicoceles are bilateral in up to 70% of cases.

Secondary varicocele is uncommon. It is caused by compression of the renal vein by tumor or can result from an aberrant or obstructed renal vein. Because varicoceles are much less common on the right side, the finding of a right-sided varicocele in the absence of a left-sided varicocele should prompt further investigation to exclude an associated abdominal mass causing compressive symptoms. This also applies to older patients with a recent-onset varicocele. Secondary varicocele on the left may result from "nutcracker syndrome," in which the superior mesenteric artery compresses the left renal vein.<sup>9,18</sup>

**Radiography.** Although venography is still considered to be the gold standard, it is time consuming and invasive. A normal venogram is one in which a single testicular vein is seen up to the inguinal ligament and into the spermatic cord. If a varicocele is present, the internal spermatic vein will be enlarged and there will be reflux into the abdominal, inguinal, scrotal, or pelvic portions of the spermatic vein. There also will be venous collateralization and formation of anastomotic channels. Venography is now most commonly performed before definitive treatment with venous embolization.<sup>18</sup>

**Computed Tomography.** CT may be used to evaluate for abdominal and retroperitoneal masses as a cause of varicocele.

**Magnetic Resonance Imaging.** MR venography may be used when conventional venography is contraindicated or to demonstrate recurrent varicoceles after surgery.<sup>18</sup>

**Ultrasonography.** Ultrasonography is the primary modality for evaluation of varicoceles. The veins of the pampiniform plexus normally range from 0.5 to 1.5 mm in diameter, with a

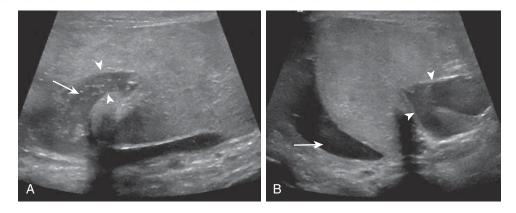
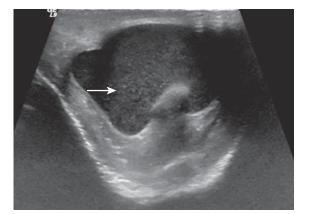


Figure 78-7 Testicular fracture. A, A young man presented with an enlarging scrotum after a severe motor vehicle accident. Sagittal gray-scale ultrasound image of the testis shows rupture of the tunica albuginea (arrowheads) with seminiferous tubules spliting out into the scrotal sac (arrow). B, Transverse image of the same testis shows the break in the tunica albuginea (arrowheads) with a hematocele (arrow).



**Figure 78-8** Chronic hydrocele with internal echoes (*arrow*) in an elderly man with chronic scrotal swelling.

main draining vein up to 2 mm in diameter. On ultrasound evaluation, a varicocele consists of multiple, serpentine, anechoic structures more than 3 mm in diameter, creating a tortuous collection located adjacent or proximal to the upper pole of the testis and the head of the epididymis. Performance of a Valsalva maneuver or examination with color Doppler imaging in the upright position is important because it causes an increase in vessel size and some varicoceles will only then become apparent (Figure 78-9). Rarely, varicoceles may be intratesticular, either in a subcapsular location or around the mediastinum testis.<sup>9,18,19</sup>

### Benign Cystic Scrotal Lesions

Cystic testicular lesions are usually benign and detected incidentally. Malignant testicular lesions can rarely show cystic degeneration secondary to hemorrhage or necrosis. An abnormal rind of parenchyma with increased echogenicity usually surrounds malignant cysts and provides a clue to the diagnosis. The common benign cystic scrotal lesions that can be characterized with ultrasonography include tunica albuginea cysts, intratesticular simple cysts, tubular ectasia of the rete testis, spermatocele, and epidermoid cysts.<sup>9,20</sup>

**Magnetic Resonance Imaging.** Simple cysts of the testis, epididymis, and tunica should have the same imaging features as a cyst elsewhere: low T1 and high T2 signal, imperceptible walls, and no enhancement. Epidermoid cysts are nonenhancing, with variable signal intensity on T1-weighted images. They are usually of high signal intensity on T2-weighted images, sometimes with internal foci of low signal intensity. There is a low signal intensity rim on T1- and T2-weighted sequences. The low-intensity outer rim is believed to be due to the outer fibrous capsule and adjacent compact keratin, whereas central hypointensity is believed to be due to dense central debris and rarely calcification.<sup>21</sup> Tubular ectasia of the rete testis has characteristic MRI features, but MRI is rarely needed because the ultrasound appearance is usually diagnostic. The lesion is uniformly of low intensity on T1-weighted sequences and isointense to hyperintense to testicular parenchyma on T2-weighted images (Figure 78-10). This lesion does not enhance after administration of gadolinium.<sup>22,23</sup>

**Ultrasonography.** Cysts of the tunica albuginea are located within the tunica. The mean age at presentation is approximately 40 years, and frequently patients may present with clinically palpable firm scrotal nodules, although they may be asymptomatic and incidentally discovered. They vary in size from 2 to 30 mm and are usually well defined, solitary, and unilocular (Figure 78-11) but may be multilocular. Complex tunica albuginea cysts may simulate a testicular neoplasm.

Simple testicular cysts are rare and usually detected incidentally in men 40 years of age or older. They are typically filled with serous fluid and may range from 2 to 18 mm. On ultrasonography, they are well-defined, anechoic with thin smooth walls and posterior acoustic enhancement. They are usually located near the mediastinum testis, suggesting that they may originate from the rete testis. Simple cysts usually require no treatment.

Epidermoid cysts represent 1% of all testicular tumors. They range from 1 to 3 cm in diameter, and most commonly manifest during the second to fourth decades with a painless testicular nodule or incidentally. The ultrasound appearance varies with maturity, compactness, and quantity of keratin present within the cyst. A target appearance, a solid mass with an echogenic rim, and a characteristic "onion ring" configuration with alternating layers of hyperechogenicity and hypoechogenicity have been described (Figure 78-12). These cysts are usually avascular. When an epidermoid cyst is suspected, testicular-sparing surgery by enucleation may be pursued rather than orchiectomy. MRI may be helpful in further characterizing the lesion preoperatively.

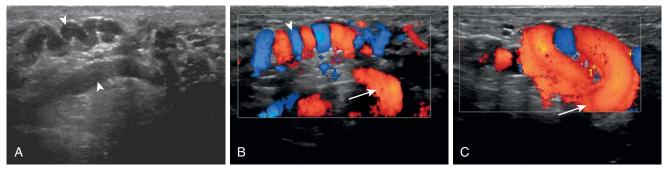


Figure 78-9 Elderly man with chronic varicocele. Gray-scale (A) and color Doppler (B) images show dilated and tortuous veins in the pampiniform plexus (*arrowheads*) with a dilated main draining vein (*arrow*) that dilates significantly with Valsalva maneuver (C).

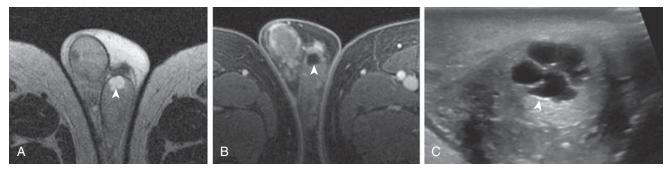
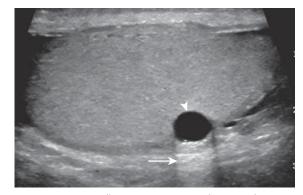


Figure 78-10 Cystic transformation of the rete testis. A, T2-weighted magnetic resonance image in the scrotum shows a small hyperintense lesion in the upper left testis (*arrowhead*) that does not enhance after administration of a contrast agent (B). C, Ultrasound image confirms the multiloculated nature of the lesion (*arrowhead*).



**Figure 78-11** Tunica albuginea cyst. Sagittal gray-scale image in a patient undergoing ultrasonography for a palpable scrotal abnormality reveals a cyst of the tunica albuginea (*arrowhead*). Note the increased through-transmission confirming the cystic nature of the lesion (*arrow*).

Tubular ectasia or cystic transformation of the rete testis is a benign condition that results from partial or complete obliteration of the efferent ductules. Variable-sized cystic lesions are seen in the region of the mediastinum testis with no associated soft tissue abnormality and no blood flow on color Doppler imaging. Most of these lesions occur in older men; they may be due to prior trauma or infection and are often bilateral and asymmetric. The characteristic location, appearance, and association with spermatoceles or epididymal cysts make a confident imaging diagnosis possible (Figure 78-13).<sup>9,20</sup>

Spermatoceles and epididymal cysts are both thought to result from dilation of the epididymal tubules, but the contents

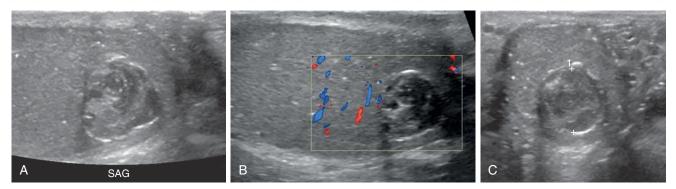
of these masses differ. Cysts contain clear serous fluid, whereas spermatoceles are filled with spermatozoa and sediment containing lymphocytes, fat globules, and cellular debris. Both lesions may result from prior episodes of epididymitis or trauma. Spermatoceles and epididymal cysts appear identical on ultrasonography, manifesting as anechoic, circumscribed masses with no or few internal echoes and with loculations and septations rarely seen (Figure 78-13). Intratesticular spermatoceles occur adjacent to the mediastinum testis and are indistinguishable from simple intratesticular cysts. Differentiation between spermatocele and simple cyst is rarely important from a clinical point of view.<sup>9,20</sup>

### **Classic Signs: Benign Cystic Scrotal Lesions**

- Simple testicular, epididymal, and tunical cysts: Resemble simple cysts elsewhere in the abdomen
- Tubular ectasia of the rete testis: Variable-sized cystic lesion in the region of the mediastinum with no associated soft tissue abnormality and no flow on color Doppler imaging
- Testicular epidermoid cyst: Whorled or onion skin appearance produced by alternating layers of compacted keratin and desguamated squamous cells

# Testicular Calcification and Scrotal Calcification ("Scrotal Pearls")

Testicular microlithiasis is characterized by small calcifications in the seminiferous tubules of the testis either unilaterally or



**Figure 78-12** Epidermoid cyst. **A**, Sagittal gray-scale ultrasound image of a testis in a 16-year-old boy with a palpable scrotal mass reveals an intratesticular lesion with rings of low and high echogenicity producing a characteristic "onion-ring" appearance. Enucleation revealed an epidermoid cyst. **B**, Sagittal color Doppler image confirms the avascular nature of the mass. **C**, Transverse gray-scale image confirms intraparenchymal location and demonstrates the "onion ring" appearance.

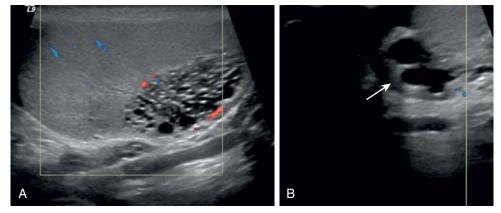
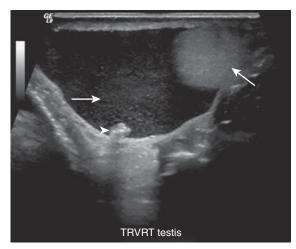


Figure 78-13 Dilated rete testis with epididymal cyst/spermatocele. A, Color Doppler image of a testis in an asymptomatic individual shows cystic transformation of the rete testis. B, Color Doppler image of the ipsilateral epididymis shows epididymal cysts/spermatoceles (arrow), which are frequently associated with tubular ectasia of the rete testis.

bilaterally. It has a prevalence of up to 2% in a symptomatic pediatric and adult population undergoing testicular ultrasonography.<sup>24</sup> It is thought that microlithiasis is due to defective Sertoli cell phagocytosis of degenerating tubular cells, which then calcify within the seminiferous tubules. In the diffuse form, nonshadowing hyperechoic foci (>2 mm) are diffusely scattered throughout the testicular parenchyma, usually of both testes and uncommonly of one testis only. Limited microlithiasis is defined as fewer than five small calcifications in any single plane of imaging. The cause and significance of limited microlithiasis are unknown.

Most often, testicular microlithiasis is an incidental finding in an otherwise normal testis. However, testicular microlithiasis may be associated with cryptorchidism, Klinefelter's syndrome, Down syndrome, pulmonary alveolar microlithiasis, and subfertility. There is also an association with testicular germ cell neoplasms (both seminomatous and nonseminomatous), but the strength of this association is not clear. Because of the postulated association between testicular microlithiasis and testicular cancer, annual ultrasonography is recommended when microlithiasis is present.<sup>9,12,24</sup>

"Scrotal pearls," or extratesticular scrotal calcifications, arise from the surface of the tunica vaginalis and may break loose to migrate between the two layers of the tunica. Hydroceles facilitate the sonographic diagnosis of scrotal calculi (Figure 78-14).



**Figure 78-14** "Scrotal pearl." Gray-scale ultrasound image in a middle-aged man with remote history of acute scrotal pain shows a hyperechoic focus with posterior echoic shadowing (*arrowhead*) suggestive of a scrotal pearl from prior torsion of testicular appendage. It is well seen due to the hydrocele with internal echoes (*dashed arrow*). Also seen is part of the testis (*arrow*).

Figure 78-15 Diffuse microlithiasis. A, Sagittal gray-scale ultrasound image of a testis containing numerous punctuate hyperechoic foci consistent with diffuse microlithiasis. B, Transverse image of both testes showing bilateral diffuse microlithiasis.

hypoechoic intraparenchymal lesions (arrowheads) consistent with adrenal rests. **B**, Color Doppler images confirm the vascular nature of these lesions.

Figure 78-16 Testicular adrenal rests. A, Gray-scale sagittal ultrasound image in a young boy with known congenital adrenal hyperplasia shows multiple small

They may result from inflammation of the tunica vaginalis or torsion of the appendix testis or epididymis.<sup>9</sup>

**Ultrasonography.** In diffuse testicular microlithiasis, innumerable small hyperechoic foci are diffusely scattered throughout the testicular parenchyma. These foci are tiny (1 to 3 mm), rarely shadow, and occasionally show a comet-tail appearance (Figure 78-15).<sup>9</sup>

### Miscellaneous Lesions: Sperm Granuloma, Adrenal Rests, Inguinal Hernia

Sperm granulomas often found after vasectomy are thought to arise from extravasation of spermatozoa into the soft tissues surrounding the epididymis.

Adrenal rests are associated with patients inadequately treated for adrenogenital syndromes and arise from aberrant adrenal cortical cells that migrate with gonadal tissues in the fetus. In response to elevated levels of corticotropin, these rests can form tumor-like masses in up to 8% of patients with congenital adrenal hyperplasia. In the correct clinical setting and with consistent ultrasonographic findings, no further workup is necessary.

Inguinal hernias may occasionally manifest as a paratesticular mass. Often the diagnosis is made clinically, but ultrasonography is useful in the evaluation of atypical cases.<sup>9,19</sup>

**Ultrasonography.** The typical ultrasound appearance of a sperm granuloma is that of a solid, hypoechoic or heterogeneous mass that is usually located within the epididymis with or without calcification.

Adrenal rests are typically bilateral and multifocal hypoechoic lesions with occasional posterior acoustic shadowing (Figure 78-16). Many adrenal rests demonstrate spokelike vascularity with multiple peripheral vessels radiating toward a central point within the mass.

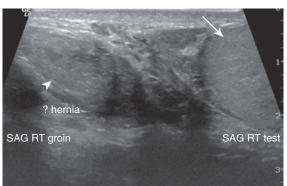
**Figure 78-17** Inguinal hernia. Sagittal ultrasound image of the right groin shows a hypoechoic masslike lesion (*arrowhead*) adjacent to the

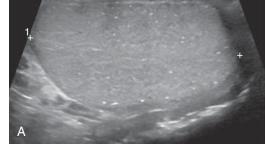
The presence of bowel loops with peristalsis extending along the inguinal canal is diagnostic of an inguinal hernia. Omentum and other fatty tissue may be seen as hyperechoic structures (Figure 78-17).<sup>9,19</sup>

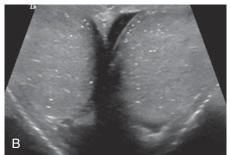
# Malignant Testicular Lesions ETIOLOGY

right testis (arrow) suggestive of an inguinal hernia.

In the majority of cases of testicular cancer, the cause is unclear. There is an increased incidence of cancer in undescended testes. The lifetime risk for death from testicular malignancy in men of any age with a history of cryptorchidism is approximately 9.7 times the risk in normal men. The risk for malignancy is increased in both the undescended testis and the contralateral normally descended testis.<sup>25</sup>







Genetic and environmental factors, trauma, endocrine abnormalities, previous infection, infertility, and testicular microlithiasis have been suggested as causative factors.<sup>26</sup>

### **CLINICAL PRESENTATION**

Testicular tumors generally manifest as painless enlargement of the testis or a palpable nodule, which may be discovered on self-examination by the patient or physical examination by a physician. It is the most common solitary neoplastic process in the 20- to 40-year-old male population and the fifth most frequent cause of death in men aged 15 to 34 years. Reactive hydroceles are associated with some tumors. Occasionally, acute pain may be the presenting symptom and may mimic an infectious or inflammatory process. Up to 19% of patients present with signs or symptoms of metastases. Back pain, abdominal mass, lymphadenopathy, and weight loss are the most common associated constitutional symptoms. Five percent of patients present with gynecomastia or breast tenderness.<sup>25-27</sup>

### PATHOPHYSIOLOGY AND PATHOLOGY

Most primary testicular neoplasms are of germ cell origin and are generally highly malignant. As a result, all intratesticular masses should be considered malignant until proved otherwise. There are many histologic subtypes of germ cell tumor, but it is of primary importance to make the distinction between two basic tumor types: seminomas and nonseminomatous germ cell tumors (NSGCTs), owing to the implications for treatment. Seminomas are more radiosensitive and carry a better prognosis, with an approximately 95% survival rate. NSGCTs are less radiosensitive and are usually treated with surgery and adjuvant chemotherapy.

Seminomas may remain localized for a long period and tend to first spread via lymphatics to para-aortic lymph nodes. NSGCTs metastasize early in comparison, usually via hematogeneous spread, typically to liver, lungs, and brain. Less common forms of testicular malignancy include sex cord/stromal tumors (Leydig cell, Sertoli cell, and granulosa cell tumors), lymphoma, leukemia, and metastases.

Seminoma is the most common germ cell tumor, accounting for 35% to 50% of all cases. It is also a common component of mixed germ cell tumors and is the most common tumor type in cryptorchid testes. Classic seminomas account for over 80% of all diagnosed cases of this cell type. Seminomas occur in slightly older patients than do other testicular neoplasms, with a peak incidence in the fourth and fifth decades. They rarely occur before puberty. Macroscopically, seminoma is a homogeneous solid, firm round or oval mass corresponding to its homogeneous appearance on ultrasound. Microscopically, there are sheets of relatively large cells with clear cytoplasm and densely staining nuclei. Spermatocytic seminomas occurring around the sixth decade are large, multinodular, fleshy, gelatinous, and hemorrhagic tumors. Microscopically, they have solid sheets of cells interrupted by pseudoglandular patterns. Spermatocytic seminomas do not metastasize, and thus radical orchidectomy is an adequate treatment.

NSGCT account for approximately 60% of all germ cell tumors. These malignancies are more aggressive than seminomas, and approximately one third of these patients have metastases at the time of presentation. They are uncommon before puberty and after the age of 50 years. Sonographic findings mirror their aggressive behavior, with heterogeneity and coarse calcifications often present.

Mixed germ cell tumors are the most common form of NSGCT and are the second most common primary testicular malignancy after seminoma, constituting almost 40% of all germ cell tumors. They contain nonseminomatous elements in various combinations. A tumor with both mixed seminomatous and nonseminomatous elements is considered an NSGCT because the nonseminomatous component most accurately reflects the response to treatment and overall prognosis. The most common combination is that of a teratoma and an embryonal cell carcinoma, previously known as teratocarcinoma.

Teratoma is a neoplasm composed of tissues that have differentiated along any of the three somatic pathways: ectodermal, mesodermal, or endodermal. Teratomas account for 5% to 10% of all testicular tumors. They have a bimodal incidence peak, representing approximately one third of testicular tumors in children but less than 7% of tumors in adults. They are common components of mixed germ cell tumors in adults. Teratomas are classified as mature or immature based on their degree of differentiation. Tumors are usually heterogeneous, firm, nodular, and well-circumscribed solid or cystic lesions depending on type of immature or mature elements, such as neural, glandular, and squamous tissues.

Embryonal cell carcinoma is a rare tumor, accounting for only 2% to 3% of pure germ cell tumors, although they are common components of mixed germ cell tumors. They occur in younger adults, with a peak incidence in the latter part of the second and the third decades. They may vary in size, color, and texture; are commonly hemorrhagic; and exhibit areas of cystic degeneration and necrosis.

Yolk sac (endodermal sinus) tumor is also known as the infantile form of embryonal cell carcinoma. This tumor occurs almost exclusively in children younger than 5 years of age and is the most common germ cell tumor in infants younger than 2 years, accounting for 60% of testicular neoplasms in this age group. Yolk sac tumors are characterized by multiple patterns of growth that recapitulate the yolk sac, allantois, and extraembryonic mesenchyme and may manifest as a soft mass involving the testis. It is locally aggressive, often metastasizes to distant organs, and is associated with serum elevation of alphafetoprotein in the majority of cases. Microscopically, these tumors are quite heterogeneous.

Pure choriocarcinoma is the rarest type of germ cell tumor, accounting for less than 0.5% of malignant primary testicular tumors, but is present in approximately 23% of all mixed germ cell tumors. It is composed of trophoblastic cells. The peak incidence is in the second and third decades. It is commonly associated with elevated levels of human chorionic gonadotropin (hCG) and frequently manifests as metastatic disease via hematogenous and lymphatic routes. Often patients have symptoms from hemorrhagic metastases to the central nervous system and lung. Macroscopically, these tumors manifest as hemorrhagic, necrotic masses. Microscopically, they exhibit an admixture of trophoblastic cells in varying proportions.

Gonadal stromal tumors, also known as sex cord/stromal tumors, are rare and generally benign tumors accounting for approximately 4% of all testicular neoplasms. The term *gonadal stromal tumor* refers to a neoplasm containing Leydig, Sertoli, thecal, granulosa, or lutein cells and fibroblasts in various degrees of differentiation. The majority of the stromal tumors are Leydig cell tumors. Leydig cell tumors account for 1% to 3% of all testicular neoplasms. They typically occur in young adults with varied presentation. A distinguishing clinical feature is gynecomastia and impotence secondary to hormone production. In children, they result in precocious virilization. Grossly, Leydig cell tumors are well-circumscribed, yellow-tan or brown-gray lobulated masses with occasional macroscopic hemorrhage or necrosis. Sertoli cell tumors are rare and account for less than 1% of all testicular tumors. They arise from the sustentacular cells lining the seminiferous tubules. Gynecomastia is evident in one third of patients. Grossly, Sertoli cell tumors are well circumscribed, solid, yellow-tan or white-tan with small areas of hemorrhage.

A specific subtype called large cell calcifying Sertoli cell tumor was described in 1980. It usually occurs in the pediatric age group and may be multifocal and bilateral. Their initial symptoms may be related to other associated conditions, which include pituitary adenoma, bilateral adrenocortical hyperplasia, cardiac myxoma, and other sex cord/stromal cell tumors. The tumors usually contain large areas of calcification.

Granulosa cell tumors are rare benign tumors and very rarely develop in the testis. They have a similar histologic resemblance to ovarian tumors of the same cell type.

Mixed undifferentiated sex cord/stromal cell tumors include elements of more than one identifiable sex cord/stromal cell type, and the exact cell of origin cannot be established with certainty. Grossly, these tumors are similar to other sex cord/ stromal neoplasms, with variable microscopic appearance.

Gonadal stromal tumors in conjunction with germ cell tumors are called gonadoblastomas, commonly occurring with cryptorchidism, hypospadias, and female internal secondary sex organs. The tumor may be large (up to 12 cm), solid gray-white, and well circumscribed with an admixture of germ cells and sex cord/stromal elements in a haphazard infiltrative pattern.

Testicular lymphoma may be primary (~50%) or secondary (~50%). Primary testicular lymphoma occurs primarily in men older than 60 years of age and is the most common testicular neoplasm in this age group. Bilateral involvement is rare. Secondary testicular lymphoma is the most common mechanism by which lymphoma involves the testis in children and usually occurs in the presence of extratesticular lymph node enlargement.

Metastases to the testes are rare but have been reported from prostate and lung carcinomas, usually in advanced disease.

### IMAGING

Locating the origin of a scrotal mass is critical because extratesticular masses are benign whereas virtually all intratesticular masses are considered malignant until proved otherwise. Ultrasonography is highly accurate in distinguishing intratesticular and extratesticular pathologic processes. Most malignant neoplasms are more hypoechoic than normal testicular parenchyma; however, hemorrhage, necrosis, calcification, or fatty change can produce areas of variable and increased echogenicity. In difficult cases, MRI may be useful to locate and characterize lesions.

### Computed Tomography

CT is used to stage testicular neoplasms and screen for retroperitoneal and mediastinal lymphadenopathy as well as lung and brain metastases.  $^{\rm 28}$ 

### Magnetic Resonance Imaging

Seminomas typically demonstrate moderate to low signal intensity compared with normal testicular tissue on T1-weighted images and are hypointense to normal testicular tissue on T2-weighted images. The tumor tissue enhances briskly and early after intravenous administration of a contrast agent. A pseudocapsule is sometimes visible around the tumor.

Nonseminomatous tumors are markedly heterogeneous. They may be isointense or hyperintense with hypointense foci. Reliable differentiation of tumor type by MRI is not possible. Cystic areas and calcifications can be identified. However, cystic change may occur in other NSGCT subtypes. Fat in teratomas may be seen as high signal intensity on T1-weighted images.

A "burned-out" testicular tumor may appear as a focal area of low signal intensity, with distortion of normal testicular architecture but no discernible mass.

### Lymphotropic Nanoparticle Enhanced Magnetic Resonance Imaging

The most important determinant of postorchidectomy therapy in patients with early-stage testicular cancer is regional lymph node involvement. Various modalities useful for evaluating the retroperitoneal nodes in patients with testicular cancer include retroperitoneal lymph node dissection, bipedal lymphangiography, and abdominal/pelvic computed tomography (CT). Unfortunately, none of these modalities is ideal. Lymphotropic nanoparticle-enhanced MRI is accurate for detecting nodal metastases in patients with testicular cancer and has yielded higher sensitivity and specificity compared with unenhanced MRI in a small pilot study.<sup>29</sup>

### Ultrasonography

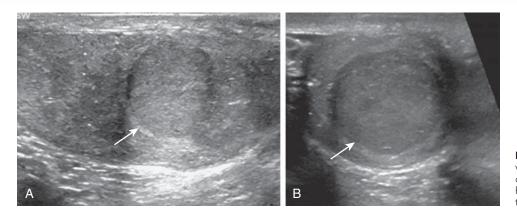
Seminomas are generally well visualized, uniformly hypoechoic, and easily differentiated from surrounding normal tissue (Figure 78-18). Some may develop cystic change as a result of necrosis or hemorrhage. Local invasion of the tunica albuginea may be difficult to determine. Many tumors have increased flow on color Doppler imaging. The flow patterns can include a diffuse increase, speckled increase, focal increase, or abnormal flow to the periphery of the lesion.

NSGCT are typically more heterogeneous than seminomas and may have both solid and cystic components. Coarse calcifications are common (Figure 78-19). It is not possible to differentiate between the various subtypes of NSGCT on ultrasonography. Both mixed NSGCT and embryonal cell carcinoma are similar, with cystic areas present in one third of tumors and possible echogenic foci with or without shadowing.

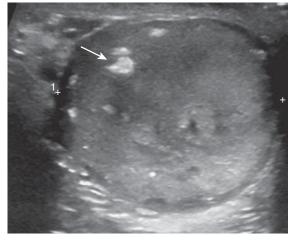
Teratomas are well-defined, markedly inhomogeneous masses containing solid and cystic areas of various sizes and appear similar to other NSGCTs (Figure 78-20). Dense echogenic foci causing acoustic shadowing result from focal calcification, cartilage, and immature bone. Macrocalcifications seen with teratomas are often suggestive of malignancy.

Gonadal stromal tumors are usually small, solid, and hypoechoic on ultrasonography. Cystic spaces from hemorrhage and necrosis are occasionally seen in larger lesions.

For occult primary tumors, ultrasonography is an important tool in patients with impalpable testicular tumors who present with retroperitoneal, mediastinal, or supraclavicular metastases. Ultrasonography approaches 100% sensitivity in its ability to identify impalpable testicular masses. Occasionally, in patients with proven germ cell tumor in the mediastinum or



**Figure 78-18** Sagittal (A) and transverse (B) gray-scale ultrasound images of the testis show a focal, well-defined homogeneous mass (*arrows*). Histopathology revealed a seminoma.



**Figure 78-19** Transverse gray-scale ultrasound image of a testis shows a heterogeneous, ill-defined mass with coarse calcifications (*arrow*). Histopathology revealed a nonseminomatous germ cell tumor with an approximately 70% embryonal cell carcinoma component.

retroperitoneum, no primary tumor is found on testicular ultrasonography. This may be due to tumor arising from germ cell rests at these extratesticular sites or a "burned-out" primary testicular tumor, where the tumor outgrows its blood supply and involutes. Sonographically, an echogenic focus with or without posterior acoustic shadowing may be seen. A repeat ultrasound examination in 3 months is usually suggested to confirm the absence of testicular involvement.

Lymphoma and leukemia are the most common malignancies to secondarily involve the testes. Lymphoma typically appears as hypoechoic and homogeneous nodules on ultrasound examination (Figure 78-21). Bilateral involvement occurs in approximately 20% of cases.<sup>1</sup> Leukemia of the testes has a variable appearance and may manifest as hypoechoic or hyperechoic nodules or diffuse infiltration of an entire testis.

Metastases to the testes are very rare and indistinguishable from other testicular tumors.

# Nuclear Medicine (Positron Emission Tomography and Computed Tomography)

Accurate staging and classification of patients into low- and high-risk groups is important because management differs between the two. At present, initial staging is based on clinical examination, tumor marker measurement, and CT. Based on conventional techniques, up to 50% of patients are understaged and approximately 25% are overstaged. CT is most commonly performed for staging purposes, but it has a false-negative rate up to 59% and a false-positive rate up to 40%. 18Ffluorodeoxyglucose–labeled positron emission tomography (FDG-PET) has been investigated for the staging of testicular tumors. Many studies have confirmed the superiority of FDG-PET over CT alone. The limitation of FDG-PET is its inability to detect disease in small lymph nodes because of its limited spatial resolution.<sup>30-34</sup>

Many patients with metastatic disease have residual masses after treatment. In patients with seminoma, the differentiation of fibrosis and necrosis from viable tumor is particularly important, because the treatment of patients with residual disease is difficult. CT and other conventional imaging modalities are unable to differentiate between necrosis/fibrosis and viable tumor. FDG-PET has been used to detect viable tumor in residual masses after treatment. Also, FDG-PET detects relapse earlier than CT.<sup>33-38</sup>

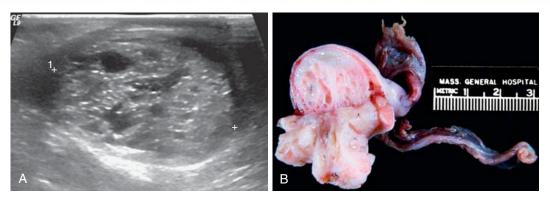
## Imaging Algorithm for Scrotal Mass

Ultrasonography is the modality of choice for evaluation of a palpable testicular mass. The key is to determine if the palpable lesion is intratesticular or extratesticular. All intratesticular masses are considered malignant until proved otherwise, whereas most extratesticular masses are benign. MRI may be helpful as a problem-solving tool when testicular ultrasonography is indeterminate.

### DIFFERENTIAL DIAGNOSIS

When encountering acute versus chronic onset of scrotal pain, accurate prior history helps narrow the differential diagnosis. Testicular tumor serum markers can improve the specificity of an imaging diagnosis of a testicular lesion. Urinalysis findings suggestive of infection support a diagnosis of infectious epididymo-orchitis.

Most testicular tumors manifest as a testicular mass, and histologic analysis after orchiectomy is required to diagnose the specific type. The tumor marker beta-hCG is elevated in 40% to 60% of patients with testicular cancer, including all patients with choriocarcinoma and approximately 10% with seminoma. Alpha-fetoprotein is elevated in 50% to 70% of patients with testicular tumors, particularly those with yolk sac or embryonal component. Other tumor markers that may be elevated include lactate dehydrogenase and alkaline phosphatase.<sup>39</sup>



**Figure 78-20** A, Sagittal image in a 6-month-old boy with testicular swelling shows a solid and cystic mass that completely replaces the testis. B, Gross pathology specimen shows a smooth tan-purple surface with the cut surface revealing a shiny pink-gray solid and cystic mass that replaces the normal testicular parenchyma. Histopathology revealed cartilage, bone, fat, and neuroectodermal cells consistent with a teratoma. (*Courtesy Jonathan Murnick, MD.*)

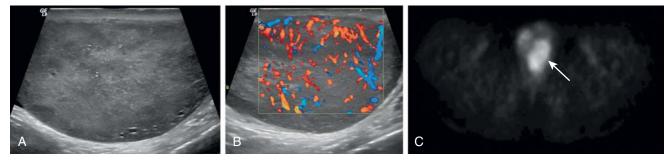


Figure 78-21 A and B, Sagittal images show diffuse involvement of a unilateral testis by lymphoma, manifest as hypoechoic areas with increased vascularity on the color Doppler image (B). C, Positron emission tomography with computed tomography performed for staging reveals increased fluorodeoxyglucose uptake in the left testis (arrow). (Courtesy Jonathan Murnick, MD.)

### TREATMENT

Epididymitis, epididymo-orchitis, and most benign testicular lesions need no treatment or can be managed medically. Some benign testicular lesions need surgery, including testicular torsion, severe testicular trauma, and testicular masses that are indeterminate on imaging.

For malignant testicular tumors after radical orchiectomy, clinical staging is considered the first step in management. Several cycles of chemotherapy are administered for earlystage NSGCT, the response to which is monitored with levels of tumor markers. For patients with stage 1 seminoma, treatment options include surveillance (with treatment being reserved for those who experience relapse), adjuvant retroperitoneal radiation therapy, and adjuvant chemotherapy. The cure rate for patients with stage 1 disease is 100%. For stage 2 seminoma patients, postorchiectomy treatment options include radiation therapy, chemotherapy, and, in rare cases, retroperitoneal node dissection. Radiation therapy is the choice of treatment with low-bulk disease, and cisplatin-based chemotherapy regimens are used in patients with more advanced disease.<sup>39</sup>

### What the Referring Physician Needs to Know

- The key distinction to be made in patients with acute nontraumatic scrotal pain is to differentiate between testicular torsion, which is a surgical emergency, and scrotal infection, which is managed medically.
- Testicular rupture requires surgical repair, whereas testicular injury without rupture may be managed conservatively.
- Ultrasonography is the primary imaging modality for a suspected testicular neoplasm and is able to accurately

determine if there is a mass and whether the mass is intratesticular or extratesticular.

 CT is the primary imaging modality used to screen for metastases. In a young male patient with bulky retroperitoneal lymphadenopathy and no known primary tumor, ultrasonography of the testes should be performed to assess for a primary testicular tumor.

#### **Key Points**

- Testicular torsion may have preserved blood flow. It is important to assess color Doppler flow in the testis with settings optimized for low flow detection. MRI with dynamic contrast enhancement may be used in indeterminate cases.
- Heterogeneous echotexture with deformity of the testicular contour in the setting of trauma is the most important sonographic sign of testicular rupture.
- An epidermoid cyst may be treated with testicular-sparing enucleation rather than orchidectomy if suspected preoperatively.
- Seminomas are exquisitely sensitive to radiation therapy, and cure rates of 100% can be achieved with stage 1 disease after orchiectomy. Nonseminomas are treated with chemotherapy after orchiectomy.

#### **SUGGESTED READINGS**

- Aso C, Enriquez G, Fite M, et al: Gray-scale and color Doppler sonography of scrotal disorders in children: an update. *Radiographics* 25:1197–1214, 2005.
- Dogra V, Bhatt S: Acute painful scrotum. Radiol Clin North Am 42:349–363, 2004.

#### REFERENCES

- Haas GP, Shumaker BP, Cerny JC: The high incidence of benign testicular tumors. J Urol 136:1219–1220, 1986.
- 2. Barnhouse K, Powers A, Smith PC: Clinical inquiries: how should you further evaluate an adult with a testicular mass? *J Fam Pract* 56:851–853, 2007.
- Carmignani L, Gadda F, Gazzano G, et al: High incidence of benign testicular neoplasms diagnosed by ultrasound. J Urol 170:1783–1786, 2003.
- Sidhu PS: Clinical and imaging features of testicular torsion: role of ultrasound. *Clin Radiol* 54:343–352, 1999.
- Trambert MA, Mattrey RF, Levine D, et al: Subacute scrotal pain: evaluation of torsion versus epididymitis with MR imaging. *Radiology* 175: 53–56, 1990.
- Watanabe Y, Nagayama M, Okumura A, et al: MR imaging of testicular torsion: features of testicular hemorrhagic necrosis and clinical outcomes. J Magn Reson Imaging 26:100–108, 2007.
- Vijayaraghavan SB: Sonographic differential diagnosis of acute scrotum: real-time whirlpool sign, a key sign of torsion. J Ultrasound Med 25:563–574, 2006.
- American College of Radiology: Acute onset of scrotal pain: without trauma, without antecedent mass. <a href="http://www.acr.org/SecondaryMainMenu">http://www.acr.org/SecondaryMainMenu</a> Categories/quality\_safety/app\_criteria/pdf/Expert PanelonUrologicImaging/AcuteOnsetofScrotal PainWithoutTraumaWithoutAntecedentMass Doc2.aspx>, Revised 2007 (Accessed 22.03.08.).
- 9. Rumack CM, Wilson SR, Charboneau JW: *Diagnostic ultrasound*, ed 3, St. Louis, 2004, Mosby.
- Watanabe Y, Dohke M, Ohkubo K, et al: Scrotal disorders: evaluation of testicular enhancement patterns at dynamic contrast-enhanced subtraction MR imaging. *Radiology* 217:219–227, 2000.
- 11. Paushter D: *Testicular torsion*. <http://www .emedicine.com/RADIO/topic683.htm>,(Accessed 22.03.08.).
- 12. Rifkin MD, Cochlin DL: Imaging of the scrotum and penis, London, 2002, Martin Dunitz.
- DiMare M: Acute epididymitis. *Medscape* 2007. <<u>http://www.emedicine.com/emerg/topic166</u> .htm>, (Accessed 23.03.08.).

*graphics* 21(Spec No.):S273–S281, 2001. Woodward PJ, Sohaey R, O'Donoghue MJ, et al: From the archives of the AFIP. Tumors and tumorlike

Dogra V, Gottlieb RH, Rubens DJ, et al: Benign

intratesticular cystic lesion: US features. Radio-

lesions of the testis: radiologic-pathologic correlation. *Radiographics* 22:189–216, 2002.

- 14. Dogra V, Bhatt S: Acute painful scrotum. *Radiol Clin North Am* 42:349–363, 2004.
- 15. Deurdulian C, Mittelstaedt CA, Chong WK, et al: US of acute scrotal trauma: optimal technique, imaging findings, and management. *Radiographics* 27:357–369, 2007.
- Buckley JC, McAninch JW: Use of ultrasonography for the diagnosis of testicular injuries in blunt scrotal trauma. J Urol 175:175–178, 2006.
- Kim SH, Park S, Choi SH, et al: Significant predictors for determination of testicular rupture on sonography: a prospective study. J Ultrasound Med 26:1649–1655, 2007.
- Beddy P, Geoghegan T, Browne RF, et al: Testicular varicoceles. *Clin Radiol* 60:1248–1255, 2005.
- 19. Rubenstein RA, Dogra VS, Seftel AD, et al: Benign intrascrotal lesions. *J Urol* 171:1765– 1772, 2004.
- Dogra VS, Gottlieb RH, Rubens DJ, et al: Benign intratesticular cystic lesions: US features. *Radiographics* 21(Spec No.):S273–S281, 2001.
- Cho JH, Chang JC, Park BH, et al: Sonographic and MR imaging findings of testicular epidermoid cysts. *AJR Am J Roentgenol* 178:743–748, 2002.
- 22. Rouviere O, Bouvier R, Pangaud C, et al: Tubular ectasia of the rete testis: a potential pitfall in scrotal imaging. *Eur Radiol* 9:1862– 1868, 1999.
- Tartar VM, Trambert MA, Balsara ZN, et al: Tubular ectasia of the testicle: sonographic and MR imaging appearance. *AJR Am J Roentgenol* 160:539–542, 1993.
- Miller FN, Rosairo S, Clarke JL, et al: Testicular calcification and microlithiasis: association with primary intra-testicular malignancy in 3,477 patients. *Eur Radiol* 17:363–369, 2007.
- 25. Rumack CM, Wilson SR, Charboneau JW: *Diagnostic ultrasound*, ed 3, St. Louis, 2004, Mosby.
- Rifkin MD, Cochlin DL: *Imaging of the scrotum and penis*, London, 2002, Martin Dunitz.
   Moul JW: Timely diagnosis of testicular cancer.
- Urol Clin North Am 34:109–117, abstract vii, 2007.
- Williams MB: Testicular seminoma. <a href="http://www.emedicine.com/Med/topic2250.htm">http://www.emedicine.com/Med/topic2250.htm</a># section~References>, (Accessed 20.06.08.).

- 29. Harisinghani MG, Saksena M, Ross RW, et al: A pilot study of lymphotrophic nanoparticleenhanced magnetic resonance imaging technique in early stage testicular cancer: a new method for noninvasive lymph node evaluation. Urology 66:1066–1071, 2005.
- Albers P, Bender H, Yilmaz H, et al: Positron emission tomography in the clinical staging of patients with stage I and II testicular germ cell tumors. Urology 53:808–811, 1999.
- Hain SF, O'Doherty MJ, Timothy AR, et al: Fluorodeoxyglucose PET in the initial staging of germ cell tumours. *Eur J Nucl Med* 27:590–594, 2000.
- Kumar R, Zhuang H, Alavi A: PET in the management of urologic malignancies. *Radiol Clin North Am* 42:1141–1153, ix, 2004.
- Lassen U, Daugaard G, Eigtved A, et al: Wholebody FDG-PET in patients with stage I nonseminomatous germ cell tumours. *Eur J Nucl Med Mol Imaging* 30:396–402, 2003.
- 34. Spermon JR, De Geus-Oei LF, Kiemeney LA, et al: The role of (18)fluoro-2-deoxyglucose positron emission tomography in initial staging and re-staging after chemotherapy for testicular germ cell tumours. *BJU Int* 89:549–556, 2002.
- Becherer A, De Santis M, Karanikas G, et al: FDG-PET is superior to CT in the prediction of viable tumour in post-chemotherapy seminoma residuals. *Eur J Radiol* 54:284–288, 2005.
- Hain SF, O'Doherty MJ, Timothy AR, et al: Fluorodeoxyglucose positron emission tomography in the evaluation of germ cell tumours at relapse. Br J Cancer 83:863–869, 2000.
- Sanchez D, Zudaire JJ, Fernandez JM, et al: 18F-fluoro-2-deoxyglucose-positron emission tomography in the evaluation of nonseminomatous germ cell tumours at relapse. *BJU Int* 89:912–916, 2002.
- Malkowski B, Pluzanska K, Pietrzak T, et al: The comparison of the CT and PET/CT FDG in the diagnostics of testicular cancer. J Nucl Med Meeting Abstracts 48:385P, 2007.
- Vogelzang NJ, Scardino PT, Shipley WU, et al, editors: Comprehensive textbook of genitourinary oncology, ed 3, Philadelphia, 2006, Lippincott Williams & Wilkins.



# Imaging of Disorders of the Female Urethra

NAVEEN M. KULKARNI | SRINIVASA R. PRASAD | VENKATESWAR R. SURABHI

#### **Urethral Diverticulum**

#### ETIOLOGY

A urethral diverticulum is a focal outpouching of urethral tissue into the urethrovaginal space. It is thought to be due to postinflammatory dilatation and rupture of the periurethral glands (of Skene) into the urethra. Most urethral diverticula are acquired and occur in women between their third and sixth decades in age.<sup>1</sup> The estimated prevalence of urethral diverticula is 0.6% to 6% of adult women.<sup>2</sup> Congenital urethral diverticula are rare but have been reported in neonates and children.

#### PATHOPHYSIOLOGY

It is widely believed that most diverticula result from infection of the periurethral glands. Other causes include urethral trauma from vaginal childbirth, instrumentation, and surgery.

#### **CLINICAL PRESENTATION**

Women with urethral diverticula manifest a range of symptoms, including dysuria, increased urinary frequency, dyspareunia, and postvoid dribbling. Approximately 20% of patients are asymptomatic.<sup>3</sup> Physical examination can reveal periurethral "bogginess," a palpable cyst, and expression of mucus or pus through the urethral orifice.<sup>4</sup>

#### COMPLICATIONS

Urethral diverticula may be complicated by urinary incontinence (60%), recurrent urinary tract infections (30%), stone formation (10%), and, rarely, malignant transformation.<sup>4</sup> More than 100 cases of urethral cancer complicating a diverticulum have been reported. Unlike de novo urethral carcinomas in which squamous carcinomas are predominant, 60% of urethral carcinomas developing in urethral diverticula are adenocarcinomas.

#### IMAGING

Imaging is adjunct to clinical examination and endoscopy. Apart from diagnosis of urethral diverticula, it assists in preoperative planning if repair is being considered.

#### Radiography

Voiding cystourethrography (VCUG) is a commonly used technique to detect urethral diverticula (Figures 79-1 and 79-2),<sup>5</sup> with a sensitivity of 44% to 95%.<sup>3</sup> However, successful demonstration of a diverticulum depends on the patient voiding during the study. If the patient is unable to void under examination, a postvoid film may demonstrate the diverticulum.

Double-balloon urethrography is more sensitive than VCUG but is invasive and technically difficult, requiring a specialized catheter and expertise to perform and interpret.<sup>3</sup>

Both of these techniques are invasive, involve ionizing radiation, and may fail to demonstrate a urethral diverticulum with a narrow or sealed-off neck.

#### Computed Tomography

Computed tomography (CT) is the most sensitive modality to detect calculi that may develop within diverticula. CT also may be used to stage malignancy within a urethral diverticulum.

#### Magnetic Resonance Imaging and Ultrasonography

Endoluminal (transvaginal or transrectal) ultrasonography and magnetic resonance imaging (MRI) permit comprehensive evaluation of urethral diverticula, including assessment of size, number, location, and configuration (Figure 79-3).<sup>6</sup>

Ultrasonography is performed using a broadband 5- to 10-MHz linear array for transperineal scanning (transducer placed on the labia) and a broadband 5- to 9-MHz curved array for transvaginal scanning (transducer placed 1 to 2 cm in the vaginal introitus).

MRI for assessment of urethral diverticula may be performed with a surface or endoluminal (endovaginal or endorectal) coil. Transvaginal MRI is performed using a disposable endovaginal coil after intramuscular injection of 1 mg of glucagon (to prevent rectal contractions), axial and sagittal fast spin echo T2-weighted imaging, and unenhanced and gadoliniumenhanced axial spin echo T1-weighted imaging.<sup>6</sup>

Urethral diverticula occur most frequently along the posterolateral wall of the mid-urethra.<sup>4</sup> They appear as cystic paraurethral lesions on imaging (Figures 79-4 through 79-6). The diverticular neck is usually best demonstrated on endoluminal MRI. Fluid/fluid levels, internal echoes, or altered signal intensity may result from hemorrhage or superimposed infection. Malignant degeneration manifests as soft tissue mass within the diverticulum in this situation.

#### TREATMENT

Small asymptomatic diverticula may be managed expectantly. Acutely inflamed diverticula should be initially treated with

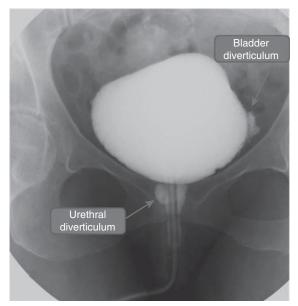
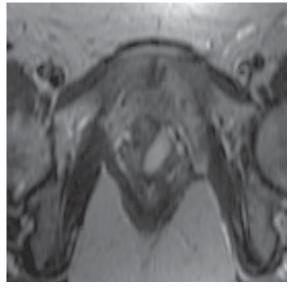


Figure 79-1 Voiding urethrocystogram shows urethral and urinary bladder diverticula.



**Figure 79-3** Axial T2-weighted magnetic resonance image of the perineum demonstrates urethral diverticulum.



Figure 79-2 Voiding urethrocystogram shows a urethral diverticulum.

antibiotics. Symptomatic or large urethral diverticula should be resected.<sup>1</sup> Endoluminal MRI or ultrasonography provides a useful roadmap by accurately identifying the diverticular configuration and neck. Recurrence may occur in up to 30% of patients, usually owing to inadequate excision of the diverticular neck.<sup>1</sup>

#### **Urethritis**

Acute urethritis in women is most frequently gonorrheal (*Neisseria gonorrhoeae*) or trichomonal (*Trichomonas vaginalis*) and less commonly is due to infection by *Chlamydia trachomatis*.<sup>7</sup>



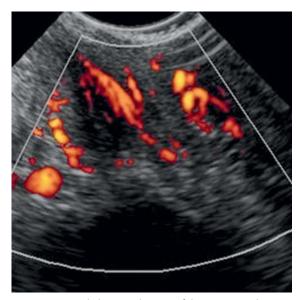
**Figure 79-4** Coronal transvaginal sonogram demonstrates multiple urethral diverticula as rounded anechoic structures.



**Figure 79-5** Axial endovaginal T2-weighted magnetic resonance image of the urethra demonstrates circumferential diverticulum.



Figure 79-6 Axial endovaginal T2-weighted magnetic resonance demonstrates a complex urethral diverticulum (*arrow*).



**Figure 79-7** Sagittal ultrasound image of the perineum demonstrates increased periurethral vascularity in a patient with urethritis.

It is characterized clinically by dysuria, frequency, and nocturia.<sup>7</sup> Diagnosis is usually based on clinical and laboratory workup.<sup>7</sup> The role of imaging is limited in the acute phase (Figure 79-7). Imaging plays a role in diagnosing complications such as postinflammatory urethral strictures and evaluation of the upper urinary tract for involvement by infection.

#### **Female Urethral Stricture**

Stricture of the female urethra is uncommon. It may be congenital or acquired. Traumatic causes include urethral injury from childbirth, iatrogenic injury, or injury sustained in a motor vehicle accident. Urethral stricture also may be caused by urethritis or urethral neoplasm. It manifests as persistent hesitancy in initiating urination and a slow urinary stream.

#### DIAGNOSIS

VCUG may demonstrate the stricture and provide a road map to surgeon, such as length of the stricture and proximity to the urinary bladder. Secondary changes of the bladder may be seen.

#### **Paraurethral Cysts**

Paraurethral cysts are classified into four groups: Skene's gland cyst, Gartner's duct cyst, müllerian remnant cyst, and epithelial inclusion cyst.

#### SKENE'S GLAND CYST AND ABSCESS

Skene's glands are the many small glands located in the lamina propria of the lower third of the female urethra. These glands drain into ducts that open at the lateral aspect of the external urethral orifice. Skene's gland cysts are very rare, and abscess is a rare complication of gonorrhea. Benign tumors such as villous adenomas and malignant tumors that resemble prostate cancer may arise from Skene's glands.<sup>8</sup>

#### GARTNER'S (MESONEPHRIC) DUCT CYST

Gartner's ducts are a remnant of the lower segment of the mesonephric ducts, which usually regress in the female. They course along the outer anterior aspect of the vaginal canal. Cystic dilatation of segments of these ducts results in Gartner's duct cysts, which are located on the anterolateral aspect of the vagina.<sup>9</sup> These cysts are lined by cuboid or low columnar epithelium and do not secrete mucus.

#### **MÜLLERIAN REMNANT CYST**

Anomalous reabsorption of the müllerian ducts in women may lead to development of a retention vaginal cyst anywhere in the proximal four fifths of the vagina, although the most typical location is along the anterolateral aspect of the vagina. The lining epithelium is characteristically that of a columnar, mucus-producing endocervical type.<sup>9</sup>

#### VAGINAL WALL INCLUSION CYSTS

Acquired inclusion cysts of the surface epithelium are the most common cystic lesions of the vagina.<sup>9</sup> They commonly occur in sites of trauma.

#### Urethrovaginal and Urethroperineal Fistulas

Urethrovaginal fistulas may develop secondary to pelvic fracture, obstetric or iatrogenic trauma, pelvic radiation, and pelvic malignancy. These fistulas manifest with urine leakage and urinary tract infections. Diagnosis usually can be made on physical examination, VCUG (Figure 79-8), and urethroscopy.

#### **Urethral Neoplasms**

Neoplasms involving the female urethra are extremely rare. Benign urethral tumors include leiomyoma, hemangioma, and nephrogenic adenoma. Malignant urethral tumors include squamous cell carcinoma (50%), adenocarcinoma (27%) (Figure 79-9), and



**Figure 79-8** Voiding urethrocystogram in a 40-year-old woman demonstrates a fistulous tract (*arrows*) between the urethra and the perineum consistent with urethroperineal fistula.

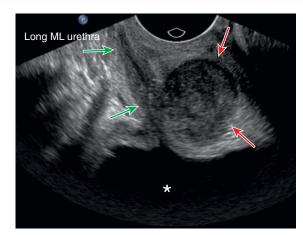


**Figure 79-9** Urethral adenocarcinoma. Axial contrast-enhanced computed tomography image of the perineum in a 45-year-old woman demonstrates a well-circumscribed urethral or periurethral multiseptated cystic lesion (*arrows*) indenting the vagina anteriorly.

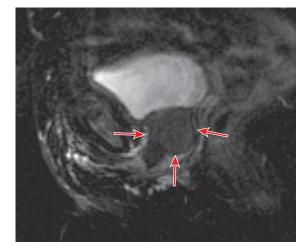
transitional cell carcinoma (22%), constituting the majority of ure thral cancers in women.  $^{\rm 10-12}$ 

# EPIDEMIOLOGY AND CLINICAL MANIFESTATIONS

Common risk factors for urethral cancers include human papillomavirus infection (transitional and squamous cell carcinomas) and urethral diverticula (adenocarcinoma). There is increased prevalence of urethral cancers (excluding transitional



**Figure 79-10** Urethral leiomyoma. Longitudinal transvaginal sonogram demonstrates a well-circumscribed mass (*red arrows*) closely related to the urethra (*green arrows*). The urinary bladder (*star*) is also seen. *ML*, Midline.



**Figure 79-11** Urethral leiomyoma. Sagittal T2-weighted magnetic resonance image of the perineum demonstrates a hypointense mass (*arrows*) closely related to the urethra at the bladder base.

cell carcinoma) among African-American women. Up to 50% of women with urethral cancers manifest late with metastatic disease.<sup>10-12</sup>

Women with urethral tumors may present with an anterior vaginal/urethral mass, dysuria, hematuria, or urethral obstruction. Urethral carcinomas are rare heterogeneous tumors that typically occur in postmenopausal women.

#### IMAGING

At imaging, leiomyomas appear as well-circumscribed tumors with uniform contrast enhancement (Figures 79-10 through 79-12).<sup>11</sup> Urethral carcinomas typically show heterogeneity secondary to hemorrhage and necrosis, especially when large (Figure 79-13).<sup>10</sup> Additionally, findings of locoregional or distant metastases may be found. Urethral adenocarcinomas may be seen in association with diverticula.

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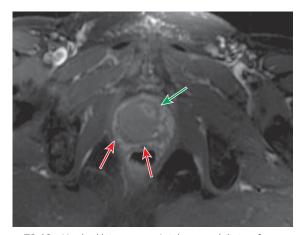
#### TREATMENT AND PROGNOSIS

Treatment of urethral malignancies is stage dependent. Surgery is the primary mode of treatment for all cancers. A multimodality approach incorporating radiation therapy and chemotherapy is required for advanced cancers. Overall survival rates of approximately 50% for distal urethral cancers and 6% for proximal urethral cancers have been reported.<sup>10-12</sup>

#### What the Referring Physician Needs to Know: Urethral Diverticulum

See Table 79-1.

- VCUG is usually the first test in evaluation of the female urethra.
- High-resolution MRI and ultrasonography provide a roadmap to the surgeon about the location, size, configuration, and neck of urethral diverticula.
- Incomplete resection of the neck is an important cause of recurrence of urethral diverticulum after surgery.



**Figure 79-12** Urethral leiomyoma. Axial postgadolinium fat-saturated T1-weighted magnetic resonance image of the perineum demonstrates a well-circumscribed mass (*red arrows*) isointense to muscle, arising from the posterior wall of the urethra (*green arrow*).

#### **Key Points**

- Urethral diverticula in women are rare. Patients may be asymptomatic or present with nonspecific manifestations.
- Imaging is essential to establish the diagnosis, characterize and localize different urethral diseases, and provide a road map when surgery is considered.
- Endoluminal MRI and ultrasonography provide valuable information that affects successful treatment.



**Figure 79-13** Urethral squamous cell carcinoma. Sagittal ultrasound image of the perineum demonstrates a solid hyperechoic mass replacing the urethra.

TABLE 79-1 Imaging Techniques in Evaluation of Female Urethra		
Imaging Method	Pros	Cons
Voiding cystourethrography	Method of choice for evaluating female urethra Useful in postoperative evaluation	Limited evaluation of urethral tumors and complex diverticula Periurethral tissues cannot be imaged
Transperineal and transvaginal ultrasonography	Absence of radiation exposure	Time and cost constraints
CT urethrography	Useful for the detection of urethral calculi	Radiation exposure Lacks the sensitivity and specificity to evaluate urethral strictures
Endovaginal and endorectal MRI and MR urethrography	Periurethral tissues visualized Excellent modality for diagnosing and characterizing urethral diverticula	Cost constraints Not widely available

CT, Computed tomography; MRI, magnetic resonance imaging.

#### 964 PART 8 Urogenital Imaging

#### SUGGESTED READINGS

- Debaere C, Rigauts H, Steyaert L, et al: MR imaging of a diverticulum in a female urethra. *J Belg Radiol* 78:345–346, 1995.
- Elsayes KM, Mukundan G, Narra VR, et al: Endovaginal magnetic resonance imaging of the female urethra. *J Comput Assist Tomogr* 30:1–6, 2006.
- Hricak H, Secaf E, Buckley DW, et al: Female urethra: MR imaging. *Radiology* 178:527–535, 1991.Kawashima A, Sandler CM, Wasserman NF, et al:
- Imaging of urethral disease: a pictorial review. *Radiographics* 24(Suppl 1):S195–S216, 2004.

#### REFERENCES

- Hosseinzadeh K, Furlan A, Torabi M: Pre- and postoperative evaluation of urethral diverticulum. AJR Am J Roentgenol 190:165–172, 2008.
- Romanzi LJ, Groutz A, Blaivas JG: Urethral diverticulum in women: diverse presentations resulting in diagnostic delay and mismanagement. J Urol 164:428–433, 2000.
- 3. Keefe B, Warshauer DM, Tucker MS, et al: Diverticula of the female urethra: diagnosis by endovaginal and transperineal sonography. *Am J Roentgenol* 156:1195–1197, 1991.
- 4. Patel AK, Chapple CR: Female urethral diverticula. *Curr Opin Urol* 16:248–254, 2006.

- Morikawa K, Togashi K, Minami S, et al: MR and CT appearance of urethral clear cell adenocarcinoma in a woman. J Comput Assist Tomogr 19:1001– 1003, 1995.
- Pavlica P, Bartolone A, Gaudiano C, et al: Female paraurethral leiomyoma: ultrasonographic and magnetic resonance imaging findings. *Acta Radiol* 45:796–798, 2004.
- Perera ND, Senanayake L, Vithana VH, et al: An unusual presentation of female urethral leiomyoma. *Ceylon Med J* 50:31–33, 2005.
- Prasad SR, Menias CO, Narra VR, et al: Crosssectional imaging of the female urethra: technique and results. *Radiographics* 25:749–761, 2005.
- Rovner ES: Urethral diverticula: a review and an update. *Neurourol Urodyn* 26:972–977, 2007.
- Lee JW, Fynes MM: Female urethral diverticula. Best Pract Res Clin Obstet Gynaecol 19:875–893, 2005.
- Prasad SR, Menias CO, Narra VR, et al: Crosssectional imaging of the female urethra: technique and results. *Radiographics* 25:749–761, 2005.
- Simpson T, Oh MK: Urethritis and cervicitis in adolescents. *Adolesc Med Clin* 15:253–271, 2004.
- Dias P, Hillard P, Rauh J: Skene's gland abscess with suburethral diverticulum in an adolescent. *J Adolesc Health Care* 8:372–375, 1987.
- Eilber KS, Raz S: Benign cystic lesions of the vagina: a literature review. J Urol 170:717–722, 2003.
- Amin MB, Young RH: Primary carcinomas of the urethra. Semin Diagn Pathol 14:147–160, 1997.
- Ikeda R, Suga K, Suzuki K: MRI appearance of a leiomyoma of the female urethra. *Clin Radiol* 56:76–79, 2001.
- 12. Stragier J, Van Poppel H, Mertens V, et al: Adenocarcinoma of the rectum with a solitary metastasis to the urethra in a female. *Eur J Surg Oncol* 20:696–697, 1994.

# 80

# Imaging of Disorders of the Male Urethra

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#### Trauma

#### ETIOLOGY

Urethral trauma may result from blunt, penetrating, or iatrogenic injury. The spectrum of urethral injuries includes contusion, partial or complete disruption, and urethral injury and may involve either the anterior or posterior urethral segment. Blunt anterior urethral injuries are commonly associated with perineal straddle injury, whereas posterior urethral injuries are usually a consequence of the shearing forces involved with a pelvic fracture.<sup>1</sup> Penetrating injuries, including gunshot injuries, may involve both the anterior and posterior urethral segments.<sup>1</sup>

#### PREVALENCE AND EPIDEMIOLOGY

Blunt trauma causes the vast majority of injuries to the posterior urethra. Urethral disruption occurs in approximately 10% of pelvic fractures. Almost all membranous urethral disruptions related to blunt trauma have an associated pelvic fracture.<sup>2</sup> Urethral injuries associated with pelvic fractures are much less common in females because of its shorter length and greater mobility in relation to the pubic arch.<sup>3</sup> Anterior urethral injuries commonly occur as a result of straddle injuries and rarely follow anterior pubic rami and penile fractures.

#### **CLINICAL PRESENTATION**

Inability to urinate, blood at the meatus, and a palpable bladder are the classic findings of urethral disruption. Other symptoms may include frank hematuria, a high-riding prostate on rectal examination, decrease in urinary stream, spraying or double stream, and postvoid dribbling. Inability to pass a urethral catheter may be the first indication of urethral injury. In delayed presentation, induration in the area of a posttraumatic stricture may be palpable.<sup>1</sup>

#### PATHOPHYSIOLOGY

The male urethra is anatomically subdivided at the level of the urogenital diaphragm into anterior (penile and bulbar portions) and posterior segments (membranous and prostatic portions), and the mechanism of urethral injury also may be classified along these lines. Posterior urethral injury is usually caused by a massive shearing force that results in concomitant pelvic fracture. Membranous urethral disruptions are associated with multiple organ injury, whereas anterior urethral injuries usually occur in isolation. Causes of anterior urethral injuries include straddle trauma crushing the immobile bulbous urethra against the pubic rami or a penile fracture leading to a laceration through the adjacent urethra. Iatrogenic injuries affect both anterior and posterior segments of the urethra.<sup>4</sup>

#### IMAGING

#### Radiography

Retrograde urethrography (RUG) is the study of choice in diagnosing urethral injuries.<sup>5</sup> It is accurate, simple, and may be performed rapidly in the trauma setting. Extravasation of contrast agent from partial or complete disruption of the urethra is usually readily identified at urethrography. RUG permits assessment of the integrity of the anterior urethra and demonstrates gross extravasation from the posterior urethra. However, voiding cystourethrography (VCUG) may be required to completely evaluate the posterior urethra.

Several classifications of the anatomic site of urethral injury have been described. On the basis of RUG findings, Colapinto and McCallum<sup>6</sup> described three types of posterior urethral injuries in 1977 (type I, II, and III injuries). Subsequently, in 1997, Goldman and associates<sup>7</sup> proposed a new, expanded anatomic classification for the purposes of comparing treatment strategies and outcomes after blunt urethral trauma (Figures 80-1 and 80-2, Table 80-1).

#### Computed Tomography

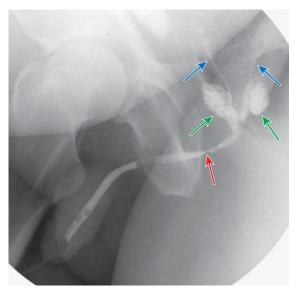
Although computed tomography (CT) is ideal for imaging upper urinary tract and bladder injuries, it has a limited role in the diagnosis of urethral injuries. Nonetheless, a recent retrospective radiographic comparison of CT findings in patients with urethrographically proved urethral injuries demonstrated CT findings of prostatic apex elevation and contrast agent extravasation above or below the urogenital diaphragm in various subclasses of urethral injury.<sup>8</sup>

#### Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) may have a role in evaluating complex cases, particularly when the posterior urethra is involved and delayed repair is being planned. MRI has the advantages of demonstrating periurethral tissues and of



**Figure 80-1** Combined retrograde urethrography and micturition cystourethrography demonstrates complete transection of the urethra with stricture formation.



**Figure 80-2** Retrograde urethrography demonstrates stricture of the membranous urethra (red arrow) with reflux of contrast medium into the seminal vesicles (green arrows) and vas deferens (blue arrows).

demonstrating the posterior urethra even if there is a distal stricture.

In patients with urethral injury, MRI can assess the length of urethral injury, position of the prostatic apex, and prostatic dislocation. A combination of T1- and T2-weighted images can differentiate between soft tissue edema, fibrosis, and hematoma.

TABLE 80-1	Classification of Male Urethral Injuries	
Types Urethr		Findings
Type I		Posterior urethra stretched but intact; no extravasation
Type II	l	Partial or complete posterior urethral disruption with tear of the membranous urethra above urogenital diaphragm; extravasation into extraperitoneal pelvis
Type II	I	Partial or complete combined anterior and posterior urethral disruption with disruption of the urogenital diaphragm; extravasation into the extraperitoneal pelvis and perineum
Type I	V	Bladder neck injury
Type I	VA	Injury to the bladder base with periurethral extravasation simulating a bladder neck injury (may be difficult to distinguish from type IV injury radiologically)
Туре ∖	/	Partial or complete pure bulbous urethral disruption, due to straddle injury
From G	Jaman SM	Sandlar CM Carriera IN Ir McGuira El: Blunt

From Goldman SM, Sandler CM, Corriere JN, Jr, McGuire EJ: Blunt urethral trauma: a unified, anatomical mechanical classification. J Urol 157:85–89, 1997.

However, conventional MRI cannot assess the patency of the urethral lumen.<sup>9,10</sup> (Table 80-2).

#### Ultrasonography

Urethral ultrasonography has limited diagnostic use in the acute setting.

#### Imaging Algorithm

Any male patient with urethral injury and/or any of the clinical findings described earlier should have RUG to evaluate for urethral disruption (see Table 80-2).

#### TREATMENT

#### **Complete Posterior Urethral Disruption**

The method chosen in the management of a posterior urethral injury should minimize the chances for the debilitating complications of incontinence, impotence, and urethral stricture and avoid opening or infecting the pelvic hematoma. The ideal method of management is still controversial. Timing of the intervention typically is classified as "immediate" treatment when it takes place less than 48 hours after injury, as "delayed primary" treatment after 2 to 14 days, and as "deferred" treatment 3 months or more after injury. When urethral injury is suspected, urethral catheterization is discouraged to prevent the potential conversion of a partial into a complete urethral injury. Instead, a suprapubic catheter should be placed.

**Immediate Surgical Repair.** Primary suturing of the severed urethral ends, although once commonly performed, has been abandoned because of high rates of postoperative impotence and incontinence. Other problems with primary suturing are potential release of the pelvic hematoma tamponade (risking uncontrolled bleeding), excessive urethral débridement and subsequent stricture, and the possibility of converting an incomplete to complete urethral injury during dissection.

TABLE 80-2			
Imagir	ng Method	Pros	Cons
Retrog uret	rade hrography	Gold standard for diagnosing anterior urethral strictures Provides excellent evaluation of the anterior urethra	Stricture length in the bulbar urethra is often underestimated. Radiation exposure. Limited evaluation of urethral tumors and complex diverticula. Periurethral tissues cannot be imaged.
Voidin cyste	g ourethrography	Provides excellent evaluation of the posterior urethra in men Useful in postoperative evaluation	Limited evaluation of the anterior urethra, urethral tumors and complex diverticula. Periurethral tissues cannot be imaged.
Sonou	rethrography	More accurate in the bulbar urethra Absence of radiation exposure	Time and cost constraints.
CT ure	thrography	Useful for the detection of urethral calculi	Radiation exposure. Lacks the sensitivity and specificity to evaluate urethral strictures.
MR ure	ethrography	Periurethral tissues visualized, allowing evaluation (e.g., for spread of inflammation and tumor)	Cost constraints. Not widely available.

CT, Computed tomography; MR, magnetic resonance.

**Deferred Treatment.** In the acute trauma setting, when the urethra is injured and the bladder is distended, a suprapubic tube usually can be placed percutaneously, typically by Seld-inger technique. When gross hematuria is present, a cystogram should be performed. If the bladder is empty (from recent micturition or concomitant bladder injury), the suprapubic tube is placed by open cystotomy and the bladder is explored for concomitant bladder injuries.

Over 3 to 6 months after posterior urethral injury, the hematoma slowly reabsorbs, the prostate descends into a more normal position, and scar tissue at the urethral disruption site becomes stable and mature. This frequently results in urethral stricture, which may require delayed open urethroplasty or urethrotomy. The major advantage of deferring treatment of urethral injury is a low reported incidence of long-term impotence and incontinence.

**Primary Realignment.** Primary realignment by minimally invasive methods has become a common contemporary management option, particularly at high-volume trauma centers. Urethral realignment employs actual realignment by endoscopic guidance of flexible cystoscopes. The urethral catheter usually is maintained for 4 to 6 weeks and acts as a guide that allows the distracted urethral ends to come together, in the same plane, as the pelvic hematoma slowly reabsorbs. These minimally invasive techniques can be performed immediately or in a delayed fashion.

#### Complete Anterior Urethral Disruption

Suprapubic catheter placement is required. This injury requires close observation because infection, tissue necrosis, or fasciitis may manifest in a delayed fashion. These complications may require tissue débridement of devitalized tissue, subcutaneous drainage, or intravenous antibiotics. Preservation of urethral tissue should be maximized so as to facilitate subsequent reconstruction.

#### Partial Anterior and Posterior Urethral Disruption

Incomplete lacerations usually heal spontaneously. Primary management is urinary diversion by suprapubic catheter, although anecdotal evidence suggests that passage of a urethral catheter may be equally efficacious. VCUG is obtained after 2 weeks of urinary diversion. Subsequent urethral scarring is usually minimal. When strictures do occur, they are usually short and often can be managed successfully by urethrotomy.

#### Male Urethral Neoplasms

#### ETIOLOGY

Chronic inflammation associated with urethral stricture and repeated/frequent urethritis predispose to urethral malignancy.

#### PREVALENCE AND EPIDEMIOLOGY

Male urethral tumors are uncommon, accounting for less than 1% of all urologic cancers.<sup>11</sup>

Benign urethral tumors are rare. An adenomatous polyp is the most common benign tumor of the urethra and is usually seen in young males. Malignant urethral tumors usually occur in men older than 50 years of age. The most common malignant tumor of the urethra is squamous cell carcinoma, which comprises 78% of cancers. Other malignant tumors include transitional cell carcinoma (15%), which is the most common form in the prostatic urethra, adenocarcinoma (6%), clear cell carcinoma (Figure 80-3), cloacogenic carcinoma, and malignant melanoma.<sup>11,12</sup> Approximately 60% of cancers occur in the bulbomembranous portion of the urethra, 30% in the penile urethra, and 10% in the prostatic urethra.

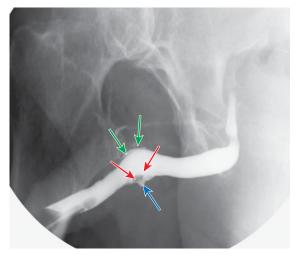
#### **CLINICAL PRESENTATION**

Presenting symptoms of urethral malignancy include bleeding, a palpable mass, and obstructive voiding symptoms.

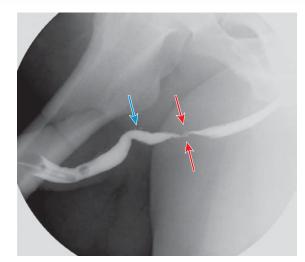
#### PATHOLOGY

Urethral malignancy may spread by direct extension to adjacent structures such as the corpora and prostate or via lymphatics. The anterior urethra drains to superficial and deep inguinal nodes, and occasionally to external iliac nodes. The posterior urethra drains to pelvic nodes.

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**Figure 80-3** Urethral metastasis. Retrograde urethrography in a patient with prostatic carcinoma demonstrates a polypoid filling defect (red arrows) with penetrating ulcer or pseudodiverticulum (blue arrow) within the anterior urethra. There is also dilation of the urethra (green arrows) at this point.



**Figure 80-4** Acute gonococcal urethritis with stricture formation. Retrograde urethrography demonstrates a stricture of the anterior urethra (red arrows) with irregularity of the urethral outline (blue arrow).

#### IMAGING

#### Radiography

Primary tumors may be detected as a focal irregular narrowing on urethrography.

## Computed Tomography and Magnetic Resonance Imaging

CT and MRI are routinely used in the staging of urethral cancer.<sup>13</sup> MRI also may be helpful in planning treatment.<sup>10</sup> On MRI, urethral tumors are isointense to hypointense relative to the corpora and demonstrate mild enhancement.<sup>10</sup> Local extension is best assessed on T2-weighted images. MRI is highly accurate (82%) in assessing extension of the tumor to the periurethral adipose tissue, best demonstrated on T1-weighted images. However, associated inflammatory changes can result in overestimation of extent of the tumor (see Table 80-2).

#### TREATMENT AND PROGNOSIS

Treatment of urethral malignancies is stage dependent. Surgery is the primary mode of treatment for all cancers. A multimodality approach incorporating radiotherapy and chemotherapy is required for advanced cancers. Prognosis depends on tumor stage and location. Overall survival rates of approximately 50% for distal urethral tumors and 6% for proximal tumors have been reported.

#### Inflammatory and Infectious Conditions of the Male Urethra

Urethritis caused by sexually transmitted microorganisms is a significant source of morbidity in the United States. Common causative organisms are Neisseria gonorrhoeae and nongono-coccal organisms, of which Chlamydia trachomatis is the most common. Ureaplasma urealyticum, Mycoplasma hominis, and Mycoplasma genitalium also are implicated.<sup>14-17</sup> Clinical manifestations of urethritis vary from nonspecific symptoms



**Figure 80-5** Chronic gonococcal stricture. Retrograde urethrography demonstrates a smooth stricture involving the anterior urethra (arrows).

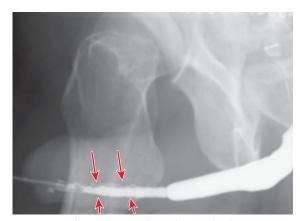


Figure 80-6 Urethritis. Retrograde urethrography demonstrates irregularity of the distal anterior urethra and filling of glands of Littre (arrows).

to dysuria, urethral discharge, or pruritus of the urethral meatus.<sup>14-17</sup>

Urethritis is usually diagnosed by clinical and laboratory findings. Imaging is not indicated in uncomplicated cases, such as stricture formation from *Gonococcus* urethritis (Figures 80-4 to 80-6). RUG demonstrates irregularity of the urethral outline in the acute phase and multiple strictures in the chronic phase.<sup>14-17</sup>

### URETHRAL CONDYLOMATA ACUMINATA (URETHRAL WARTS)

Condylomata acuminata of the urethra are almost always preceded by lesions on the skin. Urethral involvement occurs in 0.5% to 5% of male patients. They are wart-like papillomas caused by human papillomavirus and are usually transmitted by direct sexual contact.<sup>18</sup> Patients commonly report dysuria, urethral discharge, and bloody spotting from the urethra.

#### Imaging and Treatment

Examination of the urethral meatus often reveals a small, protruding papilloma. RUG and urethroscopy reveal them as multiple small filling defects (Figure 80-7). Lesions may become infected and ulcerated. Urethral lesions are treated with intraurethral instillation of antimicrobial therapy (e.g., 5-fluorouracil).

Rarely, giant condylomata (Buschke-Löwenstein tumors) involving the glans penis and urethra may be seen. Surgical excision is the treatment of choice for these large lesions.<sup>18</sup>

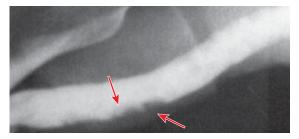


Figure 80-7 Condylomata acuminata. Retrograde urethrography demonstrates multiple filling defects (arrows) within the anterior urethra.

#### CHRONIC URETHRAL STRICTURE

RUG is the initial investigation of choice. Cross-sectional imaging can be used if needed. The surgical method for repairing a bulbar urethral stricture is selected according to the length of the stricture. In patients with short congenital anomalies of the mucosal membrane, endoscopic urethrotomy is the solution of choice. Strictures of 1 to 2 cm are treated using an end-to-end anastomosis, those of 2 to 3 cm by augmented anastomotic urethroplasty, and those of more than 3 cm by an augmented dorsal or ventral onlay graft urethroplasty. In patients with strictures larger than 6 cm involving both penile and bulbar urethra or associated with local adverse conditions, a two-stage urethroplasty or mesh graft urethroplasty is mandatory.<sup>19</sup>

#### What the Referring Physician Needs to Know: Urethral Trauma

• Location of urethral injury (anterior and/or posterior urethra) and degree of extravasation are the important factors to determine radiologically.

#### Key Points: Urethral Trauma

- A high index of suspicion should be maintained; when urethral injury is considered possible, RUG should be performed.
- MRI may be helpful in assessing complex cases before delayed urethral repair.
- Primary management of urethral disruption is urinary diversion by suprapubic catheter placement.

#### SUGGESTED READINGS

- Bircan MK, Sahin H, Korkmaz K: Diagnosis of urethral strictures: is retrograde urethrography still necessary? *Int Urol Nephrol* 28:801–804, 1996.
- Kawashima A, Sandler CM, Wasserman NF, et al: Imaging of urethral disease: a pictorial review. *Radiographics* 24(Suppl 1):S195–S216, 2004.

Obenauer S, Plothe KD, Ringert RH, et al: Imaging of genitourinary trauma. *Scand J Urol Nephrol* 40:416–422, 2006.

Pavlica P, Barozzi L, Menchi I: Imaging of male urethra. *Eur Radiol* 13:1583–1596, 2003. Pavlica P, Menchi I, Barozzi L: New imaging of the anterior male urethra. *Abdom Imaging* 28:180– 186, 2003.

#### REFERENCES

- 1. Chapple C, Barbagli G, Jordan G, et al: Consensus statement on urethral trauma. *BJU Int* 93:1195–1202, 2004.
- 2. Zingg EJ, Casanova GA, Isler B, et al: Pelvic fractures and traumatic lesions of the posterior urethra. *Eur Urol* 18:27–32, 1990.
- Venn SN, Greenwell TJ, Mundy AR: Pelvic fracture injuries of the female urethra. *BJU Int* 83:626–630, 1999.
- 4. Morey AF: Consensus statement on urethral trauma. *J Urol* 174:968–969, 2005.
- Uehara DT, Eisner RF: Indications for retrograde cystourethrography in trauma. *Ann Emerg Med* 15:270–272, 1986.
- Colapinto V, McCallum RW: Injury to the male posterior urethra in fractured pelvis: a new classification. J Urol 118:575–580, 1977.
- Goldman SM, Sandler CM, Corriere JN, Jr, et al: Blunt urethral trauma: a unified, anatomical mechanical classification. *J Urol* 157:85–89, 1997.

- Ali M, Safriel Y, Sclafani SJ, et al: CT signs of urethral injury. *Radiographics* 23:951–963, discussion 963-956, 2003.
- Kim B, Kawashima A, LeRoy AJ: Imaging of the male urethra. Semin Ultrasound CT MR 28:258– 273, 2007.
- Ryu J, Kim B: MR imaging of the male and female urethra. *Radiographics* 21:1169–1185, 2001.
- 11. Shirkhoda A, Salmanzadeh A, Jafri SZ, et al: Urethral leiomyosarcoma: evaluation by MRI with pathologic correlation. *J Comput Assist Tomogr* 24:423–425, 2000.
- Ohtani M, Yanagizawa R, Shoji F, et al: Leiomyoma of the male urethra. *Eur Urol* 8:372–373, 1982.
- Kubik-Huch RA, Hailemariam S, Hamm B: CT and MRI of the male genital tract: radiologicpathologic correlation. *Eur Radiol* 9:16–28, 1999.

- Greenberg SH: Male reproductive tract sequelae of gonococcal and nongonococcal urethritis. *Arch Androl* 3:317–319, 1979.
- 15. Osegbe DN, Amaku EO: Gonococcal strictures in young patients. *Urology* 18:37–41, 1981.
- 16. Pec J: [Post-gonorrheal strictures of the urethra in men]. *Bratisl Lek Listy* 86:378–383, 1986.
- Rusakov VI, Mitusov VV, Gul'iants ES: [Role of inflammation in the development of urethral strictures in men]. *Vestn Dermatol Venerol* 64– 65, 1985.
- Gross G, Ikenberg H, Petry KU, et al: [Condyloma acuminata and other HPV-associated diseases of the genitals, anus and urethra]. *Hautarzt* 58:179–186, 2007.
- Angermeier KW, Jordan GH, Schlossberg SM: Complex urethral reconstruction. Urol Clin North Am 21:567–581, 1994.

81

# Peritoneal Fluid Collections, Peritonitis, and Peritoneal Abscess

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#### **Peritoneal Fluid Collections**

#### ETIOLOGY

Ascites is the abnormal accumulation of fluid in the peritoneal cavity. There are numerous causes of ascites, including congenital, infective, inflammatory, and neoplastic diseases. In the United States the most common causes are liver disease and malignancy. In many parts of the world, tuberculosis is an important cause. The main causes of ascites and their frequency in the United States are listed in Table 81-1.

#### PREVALENCE AND EPIDEMIOLOGY

The term *ascites* does not specify the type of fluid accumulated within the peritoneal cavity. Ascites may be further classified as in Table 81-2 into infected, chylous, hemorrhagic, and neoplastic fluid.

#### SPECIFIC TYPES

#### Chylous Ascites

Chylous ascites is a milky fluid that is rich in triglycerides secondary to leakage of lymph into the peritoneal cavity. In the United States the most common cause of chylous ascites is malignancy, of which lymphoma accounts for 30% to 50% of cases. Other associated neoplasms include breast, esophageal, pancreatic, colon, renal, testicular, ovarian, and prostate cancer, as well as lymphangiomyomatosis, a more common cause in children. Approximately 0.5% to 1% of cirrhotic patients with ascites have chylous instead of serous fluid.

Trauma, surgery, or radiotherapy to the abdomen may damage lymphatic channels and lead to chylous ascites. Worldwide, infectious causes such as tuberculosis and filariasis (parasitic infection caused by *Wuchereria bancrofti*) are more common than neoplastic causes.

Paracentesis typically shows a cloudy milky aspirate. Triglyceride content of more than 0.1 g/L is diagnostic of chylous ascites. When the cause of chylous ascites is unclear, computed tomography (CT) of the abdomen and pelvis may be useful to evaluate for lymphadenopathy.

#### Hemorrhagic Ascites

Persons with hemorrhagic ascites have a red blood cell count greater than 50,000/mm<sup>3</sup>. The normal red blood cell count of

peritoneal fluid is less than 1000/mm<sup>3</sup>. There are several causes of hemorrhagic ascites. Bloody ascites occurs in approximately 5% of patients with cirrhosis.<sup>1</sup> In such patients, hemoperitoneum may occur spontaneously or after a traumatic paracentesis. In the more common setting of traumatic paracentesis, the ascitic fluid will clot, in contrast to nontraumatic bloody ascites, in which the red cells are lysed and the fluid does not clot on standing. The presence of nontraumatic bloody ascites in a cirrhotic patient raises concern for an underlying malignancy such as hepatocellular carcinoma. Approximately 20% of ascitic fluid aspirations in patients with malignant ascites are bloody.<sup>2</sup>

Trauma is clearly an important cause of hemoperitoneum (to be discussed). Other less common causes of hemorrhagic ascites are peritoneal dialysis, tuberculosis, rupture of vascular tumor such as hepatic adenoma, sarcoidosis, and vasculitis such as Henoch-Schönlein purpura.

#### PATHOPHYSIOLOGY

There are three theories that explain the genesis of ascites. The diminished effective volume theory<sup>3</sup> and overflow theory<sup>4</sup> differ in whether abnormal renal sodium retention precedes or follows the accumulation of ascites. The peripheral arterial vasodilation theory<sup>5</sup> combines aspects of both the volume and overflow theories and is the most widely accepted.

#### IMAGING

#### Radiography

Plain films are insensitive to ascites until at least 500 mL of fluid has accumulated. Indirect and nonspecific signs are abdominal haziness, bulging of the flanks, indistinct psoas margin, and increased separation of bowel loops. More specific signs include separation of lateral liver contour from the thoracoabdominal wall (Hellmer's sign), separation of the ascending and descending colon from the properitoneal fat line, and symmetric density on either side of the urinary bladder (the "Mickey Mouse" sign).

#### Ultrasonography

Ultrasonography detects as little as 10 mL of fluid. It is of help in assessing patency and flow pattern of portal or hepatic veins and in guiding paracentesis (Table 81-3). Peritoneal fluid is seen in the pelvic cul-de-sac in normal females in all phases of the menstrual cycle. Features that differentiate simple from complicated ascites on imaging studies are shown in Table 81-4

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and illustrated in Figure 81-1. The findings of simple ascites does not exclude infection or tumor. Gallbladder wall thickening is seen in 82% of cases of benign ascites, whereas only 5% of malignant ascites show this finding.<sup>6</sup> Ascites may cause artifacts as a result of reflection of the ultrasonic sound waves at the liver/fluid interface. Pericolonic epiploic appendages may simulate peritoneal metastases.

Hemoperitoneum may have differing appearances depending on transducer frequency and duration of hemorrhage. At

TABLE 81-1	Causes of Ascites in U.S. Clinical	Practice
Cause		Percentage
Cirrho	sis	81
Maligr	ancy	10
Heart failure		3
Tubero	culosis	2
Dialysi	s	1
Pancre	atic disease	1
Others	5	2

Data from Runyon BA, Montano AA, Akriviadis EA, et al: The serum-ascites albumin gradient is superior to the exudatetransudate concept in the differential diagnosis of ascites. Ann Intern Med 1992; 117:215–220.

Type         Characteristics           Infected         Attenuation of fluid collection ≥20 HU Loculated Rim enhancing Air ±           Chylous         Fat/fluid level (discussed           (discussed         Fluid/fluid level in text)           Density equal to that of water           Hemorrhagic (discussed         High density fluid or clotted blood Density ≥50 in text)           Neoplastic         Solid mass or metastatic nodules Abundant fluid May or may not be loculated	TABLE 81-2	Types and Characteristics of Complex Ascites		
Interfactor of finite concertion         Loculated         Rim enhancing         Air ±         Chylous       Fat/fluid level         (discussed       Fluid/fluid level         in text)       Density equal to that of water         Hemorrhagic       High density fluid or clotted blood         (discussed       Density ≥50         in text)       (Density may vary as blood may be clotted or lysed)         Retroperitoneal spread ±       Neoplastic         Solid mass or metastatic nodules         Abundant fluid	Туре		Characteristics	
(discussed in text)Fluid/fluid level Density equal to that of waterHemorrhagic (discussed in text)High density fluid or clotted blood Density ≥50 (Density may vary as blood may be clotted or lysed) Retroperitoneal spread ±NeoplasticSolid mass or metastatic nodules Abundant fluid	Infecte	ed	Loculated Rim enhancing	
(discussed Density ≥50 in text) (Density may vary as blood may be clotted or lysed) Retroperitoneal spread ± Neoplastic Solid mass or metastatic nodules Abundant fluid	(disc	ussed	Fluid/fluid level	
Abundant fluid	(disc	ussed	Density ≥50 (Density may vary as blood may be clotted or lysed)	
	Neopla	astic	Abundant fluid	

HU, Hounsfield units.

2- to 3-MHz acute hemorrhage is anechoic with increased through-transmission. With increasing frequency of transducer, the hemorrhage appears echogenic. After the first 4 days, with hematoma lysis, internal echoes either fill the collection or layer dependently. With time, hematoma becomes an anechoic seroma.

#### Computed Tomography

It is difficult to characterize the underlying cause of ascites based on CT attenuation of ascitic fluid. Simple ascites has a density of 0 to 30 Hounsfield units (HU). However, CT cannot differentiate among bile, urine, and serous fluid within the ascites. Chylous ascites has density less than 0 HU (Figure 81-2). Hemoperitoneum usually has a density higher than 30 HU (see later). CT is not sensitive to the presence of semisolid material within the ascitic fluid (Figure 81-3). This is particularly true with severe acute pancreatitis, in which peripancreatic necrosis is difficult to differentiate from inflammatory fluid based on CT density.<sup>7</sup> Magnetic resonance imaging (MRI) is superior in demonstrating solid material within the ascitic fluid (see Figure 81-3). However, CT is better at showing small amounts of gas within collections.

The sensitivity of CT for detecting early subperitoneal metastases is low. In a study of 24 patients, the sensitivity of CT for peritoneal metastases less than 1 cm was 20% to 33% compared with 85% to 90% of gadolinium-enhanced MRI.<sup>8</sup> Despite these potential pitfalls, in most institutions, CT is the principal imaging technique for detecting peritoneal disease and assessing the cause of unexplained ascites.

The CT appearance of blood in the peritoneal cavity depends on its duration. Owing to its high protein content, unclotted peritoneal blood usually has a measured attenuation of 30 to 45 HU; the attenuation may be lower in an anemic patient. Blood that has clotted has an attenuation of 45 to 70 HU. A sentinel clot is blood clotted adjacent to the bleeding site (Figure 81-4). Narrow CT windows may be required to detect this clot. Layering of dense blood in the presence of ascites is often seen (Figure 81-5). Active arterial extravasation shows higher density of 80 to 200 HU on a contrast-enhanced study. The presence of active extravasation usually mandates invasive therapy, whereas most other cases of hemoperitoneum may be treated conservatively.<sup>9</sup>

#### Magnetic Resonance Imaging

The reader is referred to the section on peritonitis for a discussion of MRI techniques for the assessment of peritoneal disease.

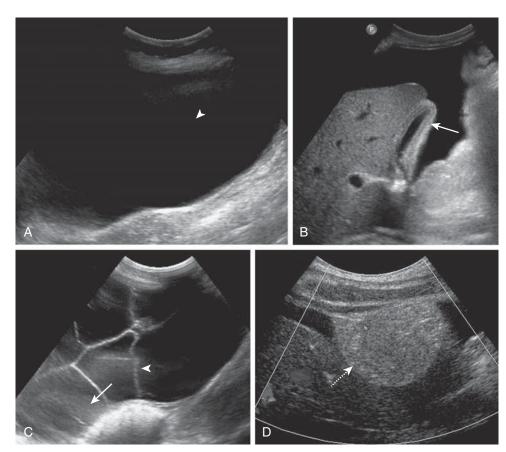
81-3 Accuracy,	Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Peritoneal Fluid		
Modality	Accuracy	Limitations	Pitfalls
Ultrasonography	Can detect as little as 10 mL of ascites Can assess portal and hepatic venous flow Portable	Overlying bowel gas, patient body habitus, limited evaluation of peritoneal masses	Artifacts from reflection of fluid-solid interfaces. Epiploic appendages can be mistaken for peritoneal metastases.
СТ	The best single test for determining site and nonliver cause of ascites	Cannot detect low-density soft tissue in ascitic fluid Low sensitivity for serosal bowel metastases	A collection with considerable amount of solid tissue (e.g., in setting of pancreatic necrosis) may appear as simple fluid collection.
MRI	Good overview of ascites	Ill patients may not tolerate long scan.	Standing wave artifact on 3.0-T MRI.

CT, Computed tomography; MRI, magnetic resonance imaging.

TABLE         Differentiation of Simple and Complex Ascites on Imaging Tests		
Imaging Type	Simple Ascites*	Complicated Ascites <sup>†</sup>
Ultrasonography (see Figure 81-1)	Anechoic Acoustic enhancement Fills the space between organs and bowel without mass effect Mobile with patient's position change Compresses with transducer pressure Thickened gallbladder <sup>6</sup> Diffuse smooth thickening of small bowel without nodularity	Internal echoes Septa: Multiple septa suggest tuberculosis or pseudomyxoma Fluid displaces bowel and solid organs Scalloping of solid organ surface (liver, spleen) suggests pseudomyxoma Loops of bowel matted together Fluid in the lesser sac <sup>18</sup> Loculated fluid collections Lack of thickening of gallbladder <sup>6</sup> Peritoneal solid or cystic masses suggest malignant disease or less likely tuberculosis
СТ	Uniform attenuation of 0 to 20 HU Bowel floats freely in midabdomen Ascites that does not extend onto the lesser sac	Loculated collections Peritoneal thickening or abnormal enhancement Peritoneal, omental masses or nodularity Attenuation >20 HU or variable attenuation Enhancement of peritoneal fluid on delayed phases
MRI	Fluid that is uniformly low signal on T1 weighting and very high signal on T2 weighting	Higher signal fluid on T1 weighting Debris within fluid Loculated fluid

*CT*, Computed tomography; *HU*, Hounsfield units; *MRI*, magnetic resonance imaging. \*Simple ascites denotes transudative fluid as seen in liver disease and cardiac failure.

<sup>†</sup>Complex ascites indicates the presence of infection, inflammation, or neoplasm. Hemorrhagic ascites is dealt with separately in the text.



**Figure 81-1** Ultrasound images of simple and "complicated" ascites. A and B, A 44-year-old man presented with alcoholic cirrhosis. Peritoneal fluid (*arrowhead*, A) is anechoic without debris, consistent with simple ascites of chronic liver disease. The gallbladder (*arrow*, B) is thickened. C and D, A 54-year-old woman presented with ovarian cancer. The ascites shows septation (*arrowhead*, C) and debris (*arrow*, C). A peritoneal mass (*dashed arrow*, D) with vascular flow is seen. These findings are consistent with complicated ascites of peritoneal carcinomatosis.

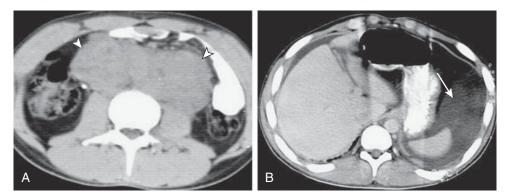
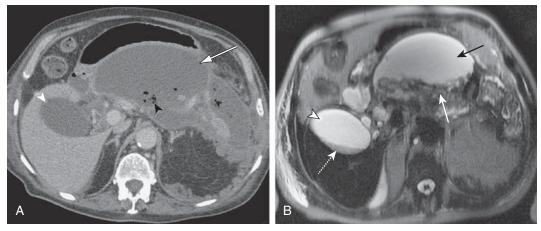
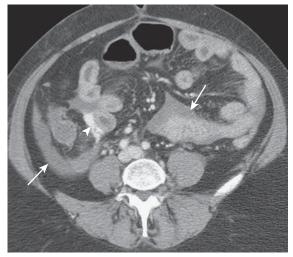


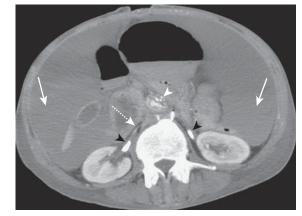
Figure 81-2 Chylous ascites. A, Axial computed tomography (CT) in a 19-year-old man with extensive retroperitoneal adenopathy (arrowheads) from testicular cancer. Retroperitoneal lymph node dissection was performed. B, CT performed 3 months after surgery shows low-density ascites (arrow). Chylous ascites was found on paracentesis, indicating lymphatic leakage into the peritoneal cavity after lymph node dissection.



**Figure 81-3** Computed tomography (CT) versus magnetic resonance imaging (MRI) for complex fluid collections. A 44-year-old man presented with alcoholic pancreatitis and fever. **A**, Axial CT shows large peripancreatic collection (*arrow*) with gas (*black arrowhead*). This was suggestive of a peripancreatic abscess. There is also a homogeneous collection in the liver (*white arrowhead*). **B**, T2-weighted MRI performed 10 hours later shows debris (*white arrow*), which was not detectable on CT, within the large peripancreatic collection (*black arrow*). The solid material represented fat necrosoma, as demonstrated on subsequent surgery. On the other hand, the gas is not as well seen on MRI. The intrahepatic collection (*arrowhead*) also shows dependent debris (*dashed arrow*) on MRI that was not identifiable on CT.



**Figure 81-4** Sentinel clot. Axial computed tomography image in a 49-year-old woman after a motor vehicle accident. Dense blood (*arrow-head*) is seen adjacent to a thick-walled bowel loop. This sentinel clot suggests the site of bowel-mesenteric trauma. There is dense fluid in the mesentery (*arrows*), indicating hemoperitoneum, which is not as dense as the sentinel clot.



**Figure 81-5** Hemoperitoneum in a 57-year-old diabetic man who had laparotomy for infective aortitis. The patient became hypotensive after aortic graft placement. This axial computed tomography image shows aortic graft (white arrowhead), collapsed inferior vena cava (dashed arrow), and evidence of layered hemoperitoneum (solid arrows), indicating massive peritoneal bleeding. Bilateral ureteral stents (black arrowheads) are seen. Intravesical pressure was elevated at 28 mm Hg, indicating elevated intra-abdominal pressure in keeping with abdominal compartment syndrome. Emergency decompressive laparotomy was performed, and the patient survived.

Acute blood that contains deoxyhemoglobin is isointense and hypointense on T1- and T2- weighted sequences, respectively. Subacute blood containing methemoglobin is hyperintense on T1-weighted images. Initially, methemoglobin is intracellular and appears hypointense on T2-weighted sequences; as the red cells lyse, the signal is increased. Hemorrhage that is several days old is hypointense on all sequences owing to the presence of hemosiderin, which also causes susceptibility artifacts on gradient echo sequences.

#### SPECIFIC LESIONS

#### Mesenteric Trauma

Bowel and mesenteric injuries are found in 5% of patients undergoing laparotomy for blunt abdominal trauma.<sup>10</sup> Diagnostic peritoneal lavage has a sensitivity exceeding 90% for the detection of hemoperitoneum but does not accurately delineate which organ has been injured, does not detect retroperitoneal injury, and makes subsequent CT assessment difficult. CT is the best noninvasive method of detecting bowel and mesenteric injury with specificity of more than 95% and sensitivity of 70% to 95%.<sup>10,11</sup> Table 81-5 gives the CT findings of bowel and mesenteric trauma (Figures 81-4 and 81-6). Of note, bowel and mesenteric injuries often coexist.

#### Abdominal Compartment Syndrome

Compartment syndrome is well known in the extremities, where increased pressure within a closed fascial space depresses



**Figure 81-6** Mesenteric injury in a 53-year-old woman after a vehicular accident. Axial computed tomography (CT) image shows thick-walled enhancing loop of distal ileum (*dashed arrow*) and dense peritoneal fluid indicating hemoperitoneum (*solid arrow*). There is soft tissue stranding surrounding a mesenteric vessel (*arrowhead*), which is a sensitive but not specific indicator of mesenteric trauma. The conglomeration of CT signs indicated significant bowel and mesenteric trauma.

capillary perfusion pressure to a level that cannot maintain tissue viability. The effects of elevated intra-abdominal pressure are less well recognized. Normally, intra-abdominal pressure is approximately 5 mm Hg. The intra-abdominal pressure may increase with acute and substantial accumulation of fluid within the abdomen (Table 81-6). Abdominal compartment syndrome (ACS) is defined as intra-abdominal pressure of at least 20 mm Hg, with dysfunction of at least one thoracoabdominal organ, usually pulmonary or renal insufficiency.<sup>12,13</sup> In contrast, a more gradual rise in abdominal pressure, such as in normal pregnancy or in ascitic accumulation in liver disease or ovarian cancer, does not normally result in ACS. Laparoscopy with pneumoperitoneum may cause elevated intra-abdominal pressure, but the effect is transient and not to the degree required to cause ACS. The definitive test for ACS is indirect measurement of abdominal pressure using a transurethral probe inserted in the urinary bladder. CT signs (see Figures 81-5 and 81-7; Box 81-1)<sup>13-15</sup> are neither sensitive nor specific for ACS. However, when a combination of these findings is present in the appropriate clinical setting or if the signs are seen to worsen on sequential imaging studies, the radiologist should raise the possibility of ACS. As in other compartment syndromes, the definitive treatment of ACS is decompressive surgery.

#### ANALYSIS OF ASCITIC FLUID

The macroscopic appearance may be helpful in determining the cause. Uncomplicated ascitic fluid is usually a pale shade of yellow and is clear. Cloudy ascites may be seen in patients with liver disease owing to the presence of neutrophils, but this finding is not specific for infection. Chylous ascites typically has a milky appearance (see later). Malignant tumors or traumatic taps may produce bloody ascites. Dark-brown fluid may indicate the presence of bile.

TABLE 81-6	Cause of Abdominal Compartment Syndrome	
Poten	tial Causes	Specific Conditions Increasing Risk
Traum	а	Grade V liver injury Hemoperitoneum Penetrating trauma
Abdominal surgery		Surgery in obese patients Liver transplantation Repair of large incisional hernia
Pancreatitis		Hemorrhagic pancreatitis Large amount of pancreatic ascites
Massiv	e fluid resuscitation	More than 5 L within 24 hr

TABLE 81-5	Computed Tomography Features of Mesenteric and Bowel Injury		
Injury		Specific CT Signs	Less-Specific CT Signs
	nteric injury (see Figures 81-4 81-6)	Mesenteric arterial extravasation Irregularity of mesenteric vessels with surrounding soft tissue density Abrupt termination of mesenteric vessel Hemoperitoneum without solid organ injury	Mesenteric fat haziness (sensitive but not specific) Mesenteric hematoma Ascites or retroperitoneal fluid collection
Bowel	injury	Bowel wall discontinuity Extravasation of orally introduced contrast agent Pneumoperitoneum (without penetrating injury or prior diagnostic lavage)	Bowel wall thickening Abnormal bowel wall enhancement

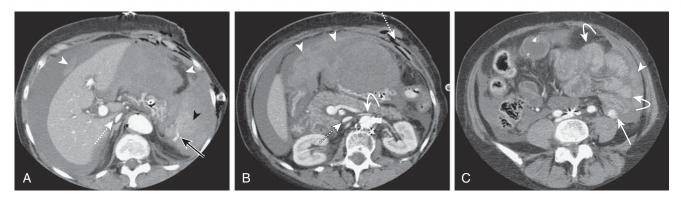


Figure 81-7 Abdominal compartment syndrome. Axial computed tomography (CT) images in a 76-year-old woman after a motor vehicle accident. A to C, Spleen is nonenhancing (black arrowhead), with active arterial extravasation (black arrow). Grade 5 splenic injury was diagnosed. There is abdominal distention with large hematoma (white arrowheads) that displaces posteriorly and effaces the stomach. A sentinel clot (white arrow, C) is seen adjacent to a bowel loop indicating the site of most severe mesenteric injury. Gas and fluid are seen to track in the left rectus sheath (dashed white arrows), suggesting a seat-belt injury. Bowel wall shows increased enhancement (curved arrows, C). The inferior vena cava (dashed arrows) and renal veins (curved arrow, B) are flattened. These findings are also seen with severe hypotension (shock bowel), and imaging diagnosis of abdominal compartment syndrome cannot be made with certainty. However, at the time of the CT scan the patient was on pressor agents and had normal renal function and blood pressure (hence the decision to use an intravenous contrast agent). In addition, intravesical pressure was elevated, at 26 mm Hg. The patient underwent emergency laparotomy for splenectomy and evacuation of peritoneal hemorrhage.

#### BOX 81-1 **IMAGING FEATURES OF ABDOMINAL COMPARTMENT SYNDROME**

- Elevated diaphragm
- Rounded configuration of abdominal wall (anteroposterior-tolateral girth ratio >0.8)
- Rapid increase in ascites (serial scans)
- Hemoperitoneum
- Flattened inferior vena cava
- Flattened renal veins
- Mosaic liver perfusion •
- Increased bowel enhancement
- Increased gastric wall enhancement
- Gastric distention
- Reduced diastolic flow in portal, hepatic, or renal veins on ultrasonography

These computed tomography signs are neither sensitive nor specific. Alternative diagnoses such as hypotension, shock, bowel injury, and multiple-organ failure in severe pancreatitis may mimic the findings of abdominal compartment syndrome. Awareness of the clinical situation is required for raising the diagnosisfor example, most patients with abdominal compartment syndrome have normal blood pressure.

Ascites was previously divided into either an exudate (>25 g/L of total protein content) or transudate (<25 g/L of protein). However, the serum ascites-albumin gradient has been found to be more helpful than the exudate-transudate concept in assessing the cause of ascites.<sup>16</sup> The gradient is obtained by subtracting the ascitic albumin level from the serum level. A gradient of more than 1.1 g/dL indicates portal hypertension with a degree of accuracy purported to be 97%.<sup>16</sup>

#### TREATMENT

#### Paracentesis

The mainstay of treatment of ascites, after medical therapy such as regulation of salt intake and diuretic therapy, is paracentesis. Many clinicians avoid performing paracentesis because of coagulopathy and fear of hemorrhagic complications. The number of patients who require red cell transfusion for

#### TABI F **Types of Peritonitis** 81-7 Noninfectious Infectious

#### Less common, and causes include chemical peritonitis, which may be secondary to peritoneal contamination by pancreatic or biliary secretions or by ruptured dermoid (see Figure 81-8), granulomatous peritonitis (secondary to foreign bodies such as talc), and sclerosing encapsulating peritonitis associated with continuous ambulatory peritoneal dialysis.

Bacterial peritonitis is the most common cause of peritonitis; mycobacteria and fungi may rarely cause peritonitis.

paracentesis-related bleeding is less than 1%.<sup>17</sup> The American Association of Liver Diseases does not recommend prophylactic fresh frozen plasma or platelet transfusion before paracentesis.

Before needle puncture, it is customary to use Doppler ultrasonography to check that there is no abdominal wall varix at the site of needle entry and an image of the site of puncture is obtained.

#### Other Treatment Options

Patients with ascites requiring repeated paracentesis should be considered for a transjugular intrahepatic portosystemic shunt (TIPS). If liver function is poor, patients should also be considered for liver transplantation. Peritoneovenous shunts (LeVeen or Denver) or surgical portosystemic shunts have very limited indications, even in those with refractory ascites.

#### Peritonitis and Peritoneal Abscess

Peritonitis is defined as diffuse inflammation of the parietal and visceral peritoneum. It may be primary (spontaneous bacterial peritonitis) or secondary to infectious or noninfectious causes (Table 81-7, Figure 81-8).

An abscess is an infected fluid collection. Peritoneal abscess usually occurs secondary to inflammation of an abdominal organ or after abdominal surgery.

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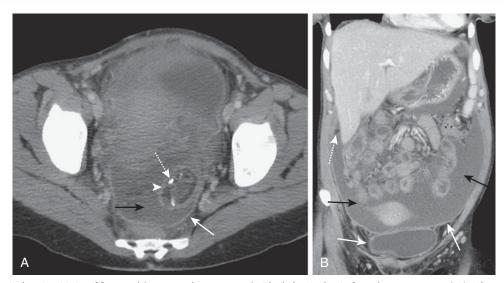


Figure 81-8 Chemical peritonitis in a 22-year-old woman who presented with abdominal pain 2 weeks postpartum. A, Axial computed tomography shows a left adnexal mass (arrowhead), which contains calcification (dashed arrow) and fat, in keeping with a dermoid. There is peritoneal fluid (black arrow) and peritoneal enhancement (solid white arrow). B, Coronal reformatted image shows the extent of peritoneal fluid (black arrows) and peritoneal enhancement (solid white arrow) indicating peritonitis. Note the fat globule (dashed arrow) in the peritoneum from ruptured dermoid.

#### **CLINICAL PRESENTATION**

The presenting features of spontaneous bacterial peritonitis include unexplained fever, abdominal pain or tenderness, and altered mental status. Patients with secondary bacterial peritonitis are usually more ill and minimize abdominal movements that cause discomfort. Abdominal wall rigidity and rebound tenderness are specific signs of peritoneal infection or inflammation. A sign that is often discussed in the clinical literature is pain worsened when an examiner lightly bumps the stretcher or bed on which the patient is lying. The absence of this "shake tenderness" may be taken as a reassuring sign that peritonitis is unlikely to be present. Other signs include fever, rigors, and diminished bowel sounds.

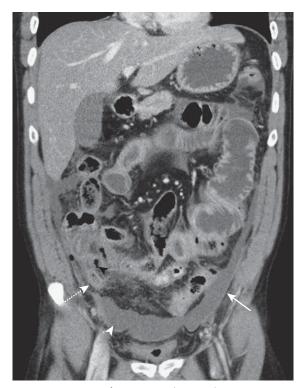
#### SPECIFIC LESIONS

See Table 81-8 and Figure 81-9 for specific lesions of peritonitis.

#### **Tuberculous Peritonitis**

Peritoneum is rarely involved by *Mycobacterium tuberculosis*, usually evidence of gastrointestinal tuberculosis.

**Diagnosis.** In tuberculous peritonitis, a chest radiograph may show evidence of old tuberculosis in 20% to 30% of patients. In "wet" tuberculous peritonitis, CT shows large-volume free or loculated ascites (Figure 81-10). The fluid is of higher density (25 to 50 HU) than simple ascites owing to increased protein and cellular content. Enlarged mesenteric lymph nodes with low-density centers may be seen (Figure 81-11). Tuberculous chylous ascites may produce a characteristic fat/fluid level on CT but is rare. The "dry" form of tuberculous peritonitis manifests as peritoneal thickening, omental masses or caking, dense adhesions, and tethered loops of bowel (Figure 81-12). CT features that favor tuberculosis over malignancy include mesenteric nodules larger than 5 mm, relative lack of nodular omental and peritoneal thickening, and the presence of peritoneal or

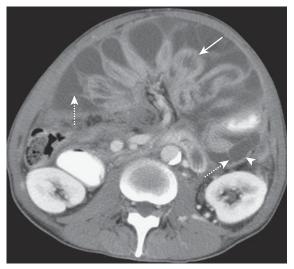


**Figure 81-9** Peritonitis from ruptured appendicitis in a 29-year-old man who presented with acute abdominal pain. Coronal reformatted computed tomography image shows a thickened appendix (*dashed arrow*), periappendiceal abscess containing gas (*black arrowhead*), peritoneal fluid in the pelvis (*white arrowhead*), and peritoneal enhancement (*white arrow*). A ruptured appendix with peritonitis was suspected and proven at subsequent surgery.

splenic masses with a low-density center or calcification.<sup>19-21</sup> On ultrasound, fine mobile fibrinous strands may be seen in the ascitic fluid.<sup>22</sup> The gold standard for diagnosis is culture of mycobacteria from ascitic fluid or peritoneal biopsy performed under direct visualization, usually laparoscopically.

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TABLESpecific81-8	Specific Lecience at Veritabilic			
Types	Characteristics	Diagnosis	Treatment	
Spontaneous bacterial peritonitis	An ascitic fluid infection without an obvious intra-abdominal source. Seen in 10%-20% cirrhotic inpatients	No radiologic feature can differentiate simple ascites from spontaneous bacterial peritonitis.	Antibiotics and paracentesis	
Secondary bacterial peritonitis	Due to pathologic process involving intra-abdominal organs Occasionally, peritonitis secondary to extension of retroperitoneal disease, such as a perinephric abscess Individual causes of secondary peritonitis discussed in the chapters that deal with organ of origin	CT signs of peritonitis are peritoneal thickening and enhancement. This is most visible in the pelvic peritoneum. Inflammation of the source organ may also be evident (see Figure 81-9). Bowel perforation may cause a localized abscess or widespread pneumoperitoneum and peritonitis.	Treat underlying cause	
Tuberculous peritonitis	Peritoneum is rarely involved by Mycobacterium tuberculosis, usually evidence of gastrointestinal tuberculosis	(discussed in text)	Treat underlying cause	
Fungal peritonitis	Most common risk factor peritoneal dialysis Fungi responsible for 2% to 13% of cases especially <i>Candida albicans</i> and <i>Candida parapsilosis</i>	Limited literature on the imaging appearances of fungal peritonitis	Treat underlying cause	
Sclerosing encapsulating peritonitis	Sclerosing encapsulating peritonitis is almost always a complication of peritoneal dialysis and is characterized by peritoneal thickening and eventually bowel obstruction.	(discussed in text)	Cessation of peritoneal dialysis and commencement of hemodialysis. Nutritional support and surgery for bowel obstruction may be required.	



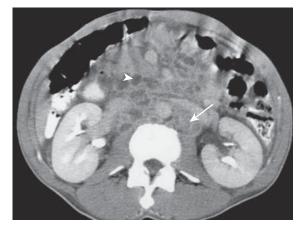
**Figure 81-10** "Wet" form of peritoneal tuberculosis in a 43-year-old Nigerian man who presented with weight loss. Axial computed tomography image shows loculated fluid collections (*arrowhead*) containing septa (*dashed arrows*). Small bowel loops are mildly thick-walled (*solid arrow*). Carcinomatosis was suspected, but peritoneal tuberculosis was eventually diagnosed.

Treatment. The underlying cause is treated.

#### Sclerosing Encapsulating Peritonitis

Sclerosing encapsulating peritonitis is almost always a complication of peritoneal dialysis and is characterized by peritoneal thickening and eventually bowel obstruction. It is estimated to have a prevalence of 1% to 7% in peritoneal dialysis patients.

**Diagnosis.** The clinical presentation of sclerosing encapsulating peritonitis is usually recurrent abdominal pain and



**Figure 81-11** Mesenteric adenopathy in a 27-year-old man with tuberculosis who presented with night sweats and weight loss. Axial computed tomography shows mesenteric (*arrowhead*) and retroperitoneal (*arrow*) low-density adenopathy. There is no significant ascites or omental thickening.

symptoms of bowel obstruction. The effectiveness of peritoneal dialysis in maintaining low creatinine levels may be diminished.

Ultrasound findings include tethering of bowel to the abdominal wall and thickened peritoneum. The CT findings are listed in Table 81-9 and shown in Figures 81-13 and 81-14.<sup>23,24</sup> The CT findings of dialysis-induced sclerosing encapsulating peritonitis may be similar to those of peritoneal tuberculosis (which may also cause sclerosing encapsulating peritonitis) and pseudomyxoma peritonei.

**Treatment.** Treatment of sclerosing encapsulating peritonitis is cessation of peritoneal dialysis and commencement of hemodialysis. Nutritional support and surgery for bowel obstruction

### TABLEComputed Tomography Findings of<br/>Sclerosing Encapsulating Peritonitis

Computed Tomography Findings	Comment
Peritoneal thickening	Usually diffuse smooth thickening is seen. Nodular thickening is less common.
Peritoneal calcification	May be fine and speckled or diffuse and conglomerate. May encase loops of bowel causing cocoon appearance (see Figure 81-13).
Peritoneal enhancement	This is usually more marked than in bacterial peritonitis.
Loculated fluid collections	Seen in 90% of cases.
Tethering or matting of the small bowel	Bowel tethering is usually posterior to loculated collections (see Figure 81-14).
Thickening of the bowel wall	
Calcification of bowel wall	This feature is not usually seen in other diseases such as tuberculosis and pseudomyxoma peritonei.
Calcification of liver and splenic capsule	

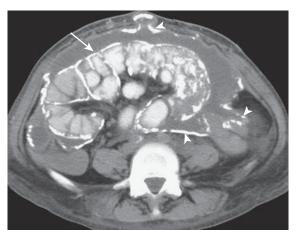


**Figure 81-12** "Dry" form of peritoneal tuberculosis in a 36-year-old Indian immigrant with fever and abdominal pain. Axial computed tomography shows diffuse omental nodularity (*arrowhead*), loculated peritoneal fluid (*dashed arrow*), and smooth peritoneal enhancement (*solid arrow*). These appearances could be due to peritoneal carcino matosis. Tuberculosis was proved on omental biopsy. In our experience, patients with peritoneal tuberculosis typically present with mixed "wet" and "dry" forms and this differentiation is not clinically useful.

may be required. The prognosis of advanced sclerosing encapsulating peritonitis is poor, with mortality as high as 80%.

#### Peritoneal Abscess

Imaging tests cannot reliably differentiate an uninfected fluid collection from an early abscess. Features that suggest an abscess include a thickened, enhancing wall and air within the peritoneal collection (Figure 81-15). Mild thickening and enhancement of the wall of a peritoneal collection does not necessarily indicate infection, and the finding may be due to inflammation, as seen in pancreatitis and the postoperative state. The presence



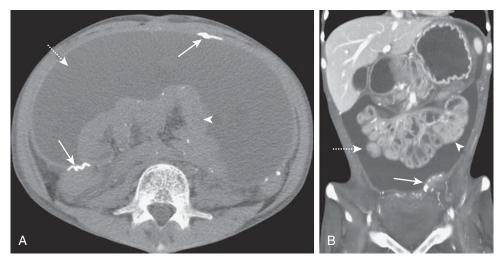
**Figure 81-13** Sclerosing encapsulating peritonitis, advanced stage, in a 58-year-old woman with a history of peritoneal dialysis. Axial computed tomography shows dense calcification of the peritoneum (*arrowheads*) and of the serosal surface of bowel (*arrow*). The bowel is not obstructed. The calcification encapsulates the bowel, hence the names sclerosing encapsulating peritonitis or "cocoon" abdomen.

of gas bubbles in a peritoneal collection is a highly specific but insensitive sign for an abscess. Occasionally, air may be found within a collection owing to fistulous communication to bowel. Another potential pitfall is the use of hemostatic bioabsorbable sponges (e.g., Gelfoam), which may mimic an abscess in the immediate postoperative situation.<sup>25</sup> Features that suggest the presence of such sponges include curvilinear strips of air density material that resolve within a few days after surgery (Figure 81-16).

**Treatment.** Abscess drainage is commonly performed under imaging guidance. CT guidance is used for most collections lying deep in the peritoneum, between bowel loops, or in the retroperitoneum. Ultrasonography may be used for a large peritoneal collection in which the superficial surface of the collection is clearly visible by ultrasonography. Ultrasonography is also used for transrectal, transvaginal, and transperineal drainage.<sup>26,27</sup> Appropriate precautions should be undertaken if there is coagulopathy or risk factors for bleeding (Table 81-10). In most cases, abscess drainage can be performed under conscious sedation. Conscious sedation also may be employed in children undergoing percutaneous abscess drainage.<sup>28</sup>

The pathway of the needle is determined by ultrasonography or a noncontrast CT study. If ultrasonography is used, subsequent wire and catheter placement is visualized fluoroscopically. When performing a transgluteal approach, choose a path that is as medial as possible to reduce the risk for injury to the sciatic nerve. A direct trocar approach may be used for large superficial collections, with no organs close to the catheter track. The catheter used will depend on local preferences. A report comparing multiple drainage catheters, ex vivo, indicated that nitinol-reinforced catheters had better flow rates.<sup>29</sup> Drains are left in place until the output reduces to less than 10 mL per 24 hours, despite regular lavage.

Complications of abscess drainage are uncommon and include bleeding or transient symptomatic bacteremia. Intracavitary fibrinolytic drugs are safe and help break down septa and hemorrhagic debris to improve drainage, obviating the need for surgery in some cases.<sup>30</sup>



**Figure 81-14** Sclerosing encapsulating peritonitis, early stage. Axial (A) and coronal reformatted (B) images show foci of peritoneal calcification (*solid arrows*) and moderate amount of ascites (*dashed arrows*). There are small foci of calcification on the bowel surface but not as impressive as in Figure 81-13. Bowel (*arrowheads*) is displaced posteriorly by the dense ascites and does not freely float. The patient had a 5-year history of peritoneal dialysis.



**Figure 81-15** Abscess. An 18-year-old man presented after a gunshot wound to the abdomen and subsequent surgical resection of bowel. Coronal reformatted computed tomography (CT) image shows a left peritoneal collection with thick, smooth enhancing walls (*arrows*) and a gas bubble (*arrowhead*). This abscess was drained using CT guidance.

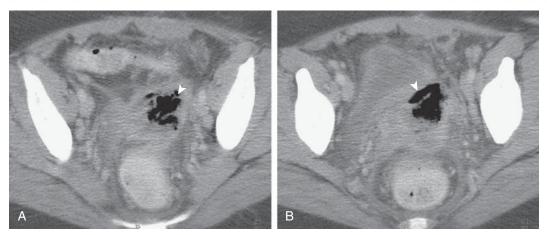
### TABLE Preprocedure Assessment for Percutaneous 81-10 Abscess Drainage

Optimizing Treatment Options
>50,000/µL: platelet transfusion required for lower platelet count.
<1.5. If it is >1.5, fresh frozen plasma is given. In cirrhotic patients, factor VII is given intravenously 15 minutes before the procedure.
Procedure performed 2 hours after stopping heparin.
Procedure performed 24 hours after stopping heparin.
Procedure performed 5 days after cessation of heparin. If it needs to be performed earlier, platelet transfusion is given.
Given intravenously 30 minutes before procedure.

These are guidelines. If a procedure needs to be performed emergently, the guidelines may be waived after discussion with the referring team. The increased risk for bleeding is discussed with the patient or guardian during informed consent.

#### What the Referring Physician Needs to Know

- It is not necessary to check laboratory values for coagulation before paracentesis unless there is clinically obvious disseminated intravascular coagulation.
- Albumin infusion is not required if the paracentesis volume is 5 L or less. Albumin infusion of 6–8 g/L of fluid aspirated is given for larger volumes of paracentesis.
- CT findings of posttraumatic hemoperitoneum do not necessitate surgery; however, acute arterial extravasation or presence of abdominal compartment syndrome is an indication for emergency surgery.
- Percutaneous image-guided abscess drainage is a safe and effective technique.
- Intra-abscess fibrinolytic drugs are safe and help break down septa and hemorrhagic debris to improve drainage, obviating the need for surgery in some cases.



**Figure 81-16** Gelfoam bioabsorbable sponge simulating abscess. During several types of surgery, including hysterectomy and partial resection of liver or kidneys, Gelfoam sponges are used to reduce hemorrhage. These are intentionally left after surgery and expected to be absorbed in a few days. A postoperative computed tomography (CT) in the first week may result in these sponges, which contain entrapped air, to be mistaken for abscess. A and B, Axial computed tomography (CT) in a 46-year-old woman after hysterectomy shows striplike air-containing structures (*arrowheads*) at the operative bed surrounded by fluid. This is the typical appearance of Gelfoam and does not indicate abscess. Subsequent CT study (not shown) demonstrated disappearance of Gelfoam.

#### **Key Points**

- Gallbladder wall thickening in the presence of ascites is usually suggestive of simple ascites from liver disease or cardiac failure.
- The most common causes of chylous ascites are malignant retroperitoneal adenopathy and lymph node dissection.
- A sentinel clot sign in the presence of hemoperitoneum and abdominal trauma provides an indication of the site of the bleeding.
- Radiologists need to be aware of a constellation of signs that may be seen in abdominal compartment syndrome.
- Of cirrhotic inpatients, 10% to 20% have spontaneous bacterial peritonitis.
- No radiologic feature can differentiate simple ascites from spontaneous bacterial peritonitis.
- In cases of peritoneal tuberculosis, a chest radiograph may show evidence of old tuberculosis in 20% to 30% of

patients, whereas features of active tuberculosis are much less common.

- The distinction among peritoneal tuberculosis, mesothelioma, and carcinomatosis is usually not possible on imaging studies.
- Sclerosing encapsulating peritonitis is almost always a complication of peritoneal dialysis and is characterized by peritoneal thickening and eventually bowel obstruction.
- Mild thickening and enhancement of the wall of a peritoneal collection does not necessarily indicate infection, and the finding may be due to inflammation, as seen in pancreatitis and the postoperative state.
- Surgically intentionally placed hemostatic bioabsorbable sponges (e.g., Gelfoam) may mimic an abscess on postoperative CT.

#### SUGGESTED READINGS

- Brofman N, Atri M, Hanson JM, et al: Evaluation of bowel and mesenteric blunt trauma with multidetector CT. *Radiographics* 26:1119–1131, 2006.
- Lubner M, Menias C, Rucker C, et al: Blood in the belly: CT findings of hemoperitoneum. *Radiographics* 27:109–125, 2007.
- Olafsson S, Blei AT: Diagnosis and management of ascites in the age of TIPS. *AJR Am J Roentgenol* 165:9–15, 1995.
- Patel A, Lall CG, Jennings SG, et al: Abdominal compartment syndrome. *AJR Am J Roentgenol* 189:1037–1043, 2007.
- Runyon BA, Montano AA, Akriviadis EA, et al: The serum-ascites albumin gradient is superior to the exudate-transudate concept in the differential diagnosis of ascites. *Ann Intern Med* 117:215–220, 1992.

#### REFERENCES

- DeSitter L, Rector WG, Jr: The significance of bloody ascites in patients with cirrhosis. *Am J Gastroenterol* 79:136–138, 1984.
- Runyon BA, Hoefs JC, Morgan TR: Ascitic fluid analysis in malignancy-related ascites. *Hepatol*ogy 8:1104–1109, 1988.
- Witte MH, Witte CL, Dumont AE: Progress in liver disease: physiological factors involved in the causation of cirrhotic ascites. *Gastroenterol*ogy 61:742–750, 1971.
- Henriksen JH: The "overflow" theory of ascites formation: a fading concept? Scand J Gastroenterol 18:833–837, 1983.
- 5. Schrier RW, Arroyo V, Bernardi M, et al: Peripheral arterial vasodilation hypothesis: a proposal for the initiation of renal sodium and water retention in cirrhosis. *Hepatology* 8:1151–1157, 1988.
- 6. Tsujimoto F, Miyamoto Y, Tada S: Differentiation of benign from malignant ascites by

sonographic evaluation of gallbladder wall. *Radiology* 157:503–504, 1985.

- Morgan DE, Baron TH, Smith JK, et al: Pancreatic fluid collections prior to intervention: evaluation with MR imaging compared with CT and US. *Radiology* 203:773–778, 1997.
- 8. Low RN, Barone RM, Lacey C, et al: Peritoneal tumor: MR imaging with dilute oral barium and intravenous gadolinium-containing contrast

#### 982 PART 8 Urogenital Imaging

agents compared with unenhanced MR imaging and CT. *Radiology* 204:513–520, 1997.

- Lubner M, Menias C, Rucker C, et al: Blood in the belly: CT findings of hemoperitoneum. *Radiographics* 27:109–125, 2007.
- Brofman N, Atri M, Hanson JM, et al: Evaluation of bowel and mesenteric blunt trauma with multidetector CT. *Radiographics* 26:1119–1131, 2006.
- 11. Mirvis SE, Gens DR, Shanmuganathan K: Rupture of the bowel after blunt abdominal trauma: diagnosis with CT. *AJR Am J Roentgenol* 159:1217–1221, 1992.
- 12. Ivatury RR, Diebel L, Porter JM, et al: Intraabdominal hypertension and the abdominal compartment syndrome. *Surg Clin North Am* 77:783–800, 1997.
- Patel A, Lall CG, Jennings SG, et al: Abdominal compartment syndrome. *AJR Am J Roentgenol* 189:1037–1043, 2007.
- Epelman M, Soudack M, Engel A, et al: Abdominal compartment syndrome in children: CT findings. *Pediatr Radiol* 32:319–322, 2002.
- Pickhardt PJ, Shimony JS, Heiken JP, et al: The abdominal compartment syndrome: CT findings. AJR Am J Roentgenol 173:575–579, 1999.
- Runyon BA, Montano AA, Akriviadis EA, et al: The serum-ascites albumin gradient is superior to the exudate-transudate concept in the

differential diagnosis of ascites. *Ann Intern Med* 117:215–220, 1992.

- McVay PA, Toy PT: Lack of increased bleeding after paracentesis and thoracentesis in patients with mild coagulation abnormalities. *Transfusion* 31:164–171, 1991.
- Gore RM, Callen PW, Filly RA: Lesser sac fluid in predicting the etiology of ascites: CT findings. *AJR Am J Roentgenol* 139:71–74, 1982.
- Rodriguez E, Pombo F: Peritoneal tuberculosis versus peritoneal carcinomatosis: distinction based on CT findings. J Comput Assist Tomogr 20:269–272, 1996.
- Ha HK, Jung JI, Lee MS, et al: CT differentiation of tuberculous peritonitis and peritoneal carcinomatosis. *AJR Am J Roentgenol* 167:743–748, 1996.
- 21. Jadvar H, Mindelzun RE, Olcott EW, et al: Still the great mimicker: abdominal tuberculosis. *AJR Am J Roentgenol* 168:1455–1460, 1997.
- 22. Kedar RP, Shah PP, Shivde RS, et al: Sonographic findings in gastrointestinal and peritoneal tuberculosis. *Clin Radiol* 49:24–29, 1994.
- Stafford-Johnson DB, Wilson TE, Francis IR, et al: CT appearance of sclerosing peritonitis in patients on chronic ambulatory peritoneal dialysis. J Comput Assist Tomogr 22:295–299, 1998.
- 24. George C, Al-Zwae K, Nair S, et al: Computed tomography appearances of sclerosing

encapsulating peritonitis. *Clin Radiol* 62:732-737, 2007.

- Sandrasegaran K, Lall C, Rajesh A, et al: Distinguishing gelatin bioabsorbable sponge and postoperative abdominal abscess on CT. AJR Am J Roentgenol 184:475–480, 2005.
- Maher MM, Gervais DA, Kalra MK, et al: The inaccessible or undrainable abscess: how to drain it. *Radiographics* 24:717–735, 2004.
- 27. Varghese JC, O'Neill MJ, Gervais DA, et al: Transvaginal catheter drainage of tuboovarian abscess using the trocar method: technique and literature review. *AJR Am J Roentgenol* 177:139– 144, 2001.
- Gervais DA, Brown SD, Connolly SA, et al: Percutaneous imaging-guided abdominal and pelvic abscess drainage in children. *Radiographics* 24:737–754, 2004.
- Macha DB, Thomas J, Nelson RC: Pigtail catheters used for percutaneous fluid drainage: comparison of performance characteristics. *Radiology* 238:1057–1063, 2006.
- Beland MD, Gervais DA, Levis DA, et al: Complex abdominal and pelvic abscesses: efficacy of adjunctive tissue-type plasminogen activator for drainage. *Radiology* 247:567–573, 2008.

# **82**

# Non-neoplastic Conditions of the Peritoneum and Neoplastic Conditions of the Mesentery and Omentum

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# Non-neoplastic Conditions of the Peritoneum

In many of the diseases discussed in this chapter the diagnosis is often initially raised on computed tomography (CT) or magnetic resonance imaging (MRI). However, in most cases, it is not possible to make a categorical diagnosis based on the imaging findings alone and it is necessary to correlate with clinical findings and laboratory tests.

In this section we discuss peritoneal diseases that are not classified as infectious diseases or neoplasms. This diverse group of diseases may be categorized as peritoneal fat-based lesions, peritoneal involvement in multiple-organ disease, and fibrosisrelated conditions.

#### PERITONEAL FAT-BASED DISEASES

#### Mesenteric Panniculitis

Mesenteric panniculitis is an idiopathic condition with mesenteric fatty infiltration, chronic inflammation (with lymphocytes, macrophages), and fibrosis. Fat necrosis and calcification may occur less commonly. The disease is thought to be a continuum of mesenteric lipodystrophy (where fat necrosis predominates), to mesenteric panniculitis (with chronic inflammation), to retractile mesenteritis (where fibrosis predominates).<sup>1</sup>

Mesenteric panniculitis is twice as common in males than in females. The typical manifestation is one of chronic abdominal pain, fever, and weight loss. Alternatively, the patient may be asymptomatic and the finding is seen incidentally on CT. The CT features of mesenteric panniculitis and retractile mesenteritis are listed in Table 82-1 and shown in Figures 82-1 and 82-2.<sup>2</sup> The differential diagnosis of these conditions is presented in Table 82-2.

In some patients (reports range from 1% to 70%), the presence of mesenteric panniculitis is a sign of malignancy elsewhere. In the absence of malignancy, most patients with mesenteric panniculitis have a favorable prognosis and may be managed conservatively with follow-up CT. Experience of specific treatment is limited. Mesenteric panniculitis involving the mesocolon has been suggested to have a more aggressive course, and surgical treatment is often required. Retractile mesenteritis has a poorer prognosis, mainly owing to bowel ischemia.

#### Epiploic Appendagitis, Segmental Omental Infarction, and Omental Torsion

Epiploic appendices are pedunculated protuberances of adipose tissue arranged in parallel rows along the antimesenteric border of colon. Each appendage is supplied by one or two small arteries from the colonic vasa recta and drained by a single vein. Given the tenuous vascular supply and narrow neck, these appendages are at risk for ischemia or torsion, resulting in inflammation and infarction.

Epiploic appendagitis is usually primary without an associated bowel pathologic process. Uncommonly, it can be secondary to inflammation of adjacent organs (e.g., resulting in appendicitis, cholecystitis, and diverticulitis).<sup>3</sup>

The typical clinical picture of primary epiploic appendagitis is nonspecific lower abdominal pain that usually subsides within 1 week.<sup>4</sup> The pain may worsen with abdominal stretching or coughing. The CT findings of primary epiploic appendagitis are fairly specific (Figure 82-3 and Table 82-3).<sup>3,5</sup> Because epiploic appendagitis may be secondary to bowel inflammation, it is important to exclude associated appendicitis and diverticulitis before making the diagnosis of primary epiploic appendagitis. Like epiploic appendagitis, segmental omental infarction belongs to the spectrum of fat-based peritoneal and mesenteric conditions. CT findings are shown in Table 82-3 and Figure 82-4. Differentiation between epiploic appendagitis and segmental omental infarction is not clinically necessary because conservative therapy with analgesics is all that is required for both conditions. Rarely, laparoscopic surgery may be required in persistently symptomatic segmental omental infarction. Infrequently, segmental omental infarction may be mistaken for a fatty tumor such as liposarcoma. The lack of a well-defined outline and typical site of segmental omental infarction, as well as the clinical presentation, usually help differentiate this entities.4,5

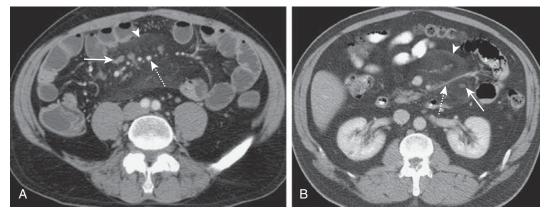
Omental torsion is another cause of acute abdominal pain. It may be idiopathic or secondary to adhesions or tumor. The classic CT sign is a whirling pattern of curvilinear streaks in the omental fat with central hyperdense vascular structure (Figure 82-5). However, the "whirl" sign is not always present, and, if not, differentiation from omental infarction is difficult. It is useful if the diagnosis can be made on CT, because the condition may be treated conservatively.

#### TABLE Computed Tomography Features of Mesenteric Panniculitis and Retractile Mesenteritis

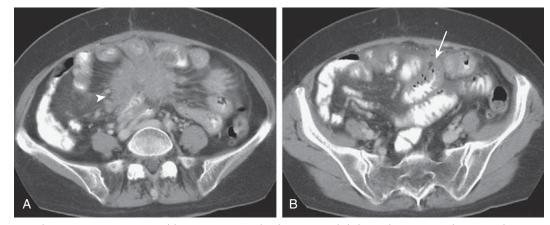
Computed	Tomography	Feature
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#### Comment

MESENTERIC PANNICULITIS	
Increased density of mesenteric fat	Root of mesentery most affected Extension into distal mesentery and retroperitoneum less common
Mesenteric vessels encased by increased density fat	No vessel constriction or displacement
Scattered soft tissue mesenteric nodules	<10 mm (<5 mm in 80% of cases)
"Fat ring" sign	Low-density fat surrounding mesenteric nodules and vessels is seen in >75% of cases; however, not specific and may be seen in mesenteric lymphoma
"Pseudocapsule" sign	Thin (<3 mm) capsule seen around expanded misty mesentery in 50% of cases; however, sign not specific and may be seen with liposarcoma
RETRACTILE MESENTERITIS	
Mesenteric fibrosis	Indrawing and tethering of mesenteric vessels and bowel
Bowel ischemia	Seen in severe retractile mesenteritis
Disappearance of "fat ring" and "pseudocapsule" signs	When fibrosis becomes more prominent, some features of mesenteric panniculitis disappear

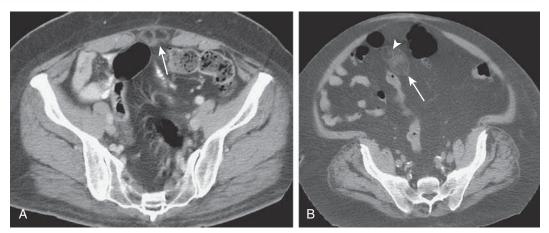


**Figure 82-1** Mesenteric panniculitis. Contrast-enhanced axial computed tomography images in a 52-year-old woman with abdominal pain (A) and a 58-year-old man with known lung cancer (B). In both cases, the root of the mesentery is expanded and has a misty appearance (*arrowheads*). There are small lymph nodes (*arrows*) with a ring of low-density fat around them ("fat ring" sign). The mesenteric vessels (*dashed arrows*) have increased density fat around them but are not stenosed.



**Figure 82-2** Retractile mesenteritis. A 71-year-old woman presented with nausea and abdominal pain. **A**, Axial computed tomography (CT) image shows a 5-cm soft tissue mass (*arrowhead*) in the mesentery with spiculated outline and indrawing and tethering of small bowel loops. **B**, Axial CT image shows thick-walled small bowel (*arrow*). The patient underwent laparotomy and was found to have ischemic small bowel, which was resected. The differential diagnosis for the CT finding includes carcinoid tumor and desmoid.

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**Figure 82-3** Epiploic appendagitis. Axial computed tomography images in a 50-year-old woman undergoing staging for known breast cancer (A) and a 69-year-old man with pelvic pain (B). Epiploic appendagitis appears as a fat density ovoid lesion with peripheral soft tissue rim (arrows). There may be central hyperdensity as a result of a thrombosed epiploic vein (arrowhead, B). The lesions are found on the antimesenteric border of the colon, usually anterior or lateral to the colon. The colonic wall is not thickened. Epiploic appendagitis is usually less than 5 cm and does not have mass effect.

TABLE 82-2		gnosis of Mesenteric Retractile Mesenteritis	
MESE	NTERIC PANNICULI	ГІЅ	
Liposa Lymph		Unusual CT findings, such as nodules >10 mm, retroperitoneal extension, displacement of vasculature, mass effect, or invasion of bowel and rapid increase in size of nodules on follow-up imaging, require biopsy.	
Cushin dise	ig's syndrome/ ase	Variation in fat distribution may be caused by corticosteroid excess, with increased volume of mesenteric fat. Nodules are uncommon in Cushing's disease. Drugs such as lamivudine (Epivir) taken for human immunodeficiency virus infection, may cause increased volume and density of mesenteric fat on CT.	
RETRACTILE MESENTERITIS (SPICULATED MESENTERIC MASS)			
Carcin	oid tumor	Biopsy is required if there is no	
Desmo	pid tumor	evidence of carcinoid (known tumor, positive on octreotide scan)	
Mesen	iteric tuberculosis	or tuberculosis (positive cultures).	
Peritor	neal mesothelioma		
CT, Con	nputed tomography.		

## PERITONEAL INVOLVEMENT IN CHRONIC MULTIPLE-ORGAN DISEASE

#### Amyloidosis

Amyloidosis refers to the extracellular deposition of protein fibrils. Classification of amyloidosis is still evolving. Primary amyloidosis and amyloidosis associated with myeloma show light-chain immunoglobulin deposition (AL type). Amyloidosis associated with chronic dialysis shows immunoglobulin (beta-2 microglobulin) deposition. Amyloidosis secondary to chronic inflammation, such as rheumatoid arthritis, osteomyelitis, and tuberculosis, shows deposition of acute-phase reactant serum amyloid A (AA type). In less common cases of

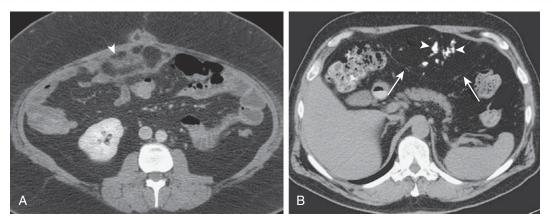
# TABLE<br/>82-3Computed Tomography Findings of<br/>Epiploic Appendagitis and Segmental<br/>Omental Infarction

Computed Tomography Finding Features or Characteristics	Epiploic Appendagitis	Segmental Omental Infarction (see Figure 82-4)
Size	1-5 cm	Usually 3-15 cm
Location	Immediately adjacent to colon	Anterior to transverse colon
Shape	Ovoid or clover leaf Hyperdense rim	Amorphous, no clear outline
Side predominance	More common on left	More common on right
Mass effect	Nil	May displace transverse colon posteriorly or parietal peritoneum anteriorly
Central dot sign <sup>4,5</sup> : Due to thrombosis of central vein or small hemorrhage	Seen in 50%	Not seen
Follow-up scans	Fibrous band or focus of calcification	Often dense calcification and/or fibrosis (see Figure, 82-4, <i>B</i> )

amyloidosis, neuroendocrine peptides such as calcitonin or cytoskeleton proteins such as keratin may be deposited. The CT findings are listed in Table 82-4. $^6$ 

#### Whipple's Disease

Although Whipple's disease has an infectious cause, it is typically classed with other infiltrative diseases because its imaging manifestations may overlap. The causative organism is a grampositive bacillus, *Tropheryma whippelii*, which is usually found in soil.<sup>7</sup> CT findings are presented in Table 82-4 and shown in Figure 82-6.<sup>8</sup>



**Figure 82-4** Segmental omental infarction. A, Axial computed tomography (CT) image in a 26-year-old patient with multiple endocrine neoplasia type I and prior Whipple's procedure. An area of the omentum (*arrowhead*) shows a thickened outline and increased central density. Bowel is displaced posteriorly. These are typical features of segmental omental infarction. B, A 65-year-old man presented with metastatic renal cancer requiring regular staging. CT shows an expanded segment of omentum with thin rim (*arrows*). There is calcification within the omentum (*arrowheads*) that had been stable for 4 years, indicating chronic omental infarction.



**Figure 82-5** Omental torsion. Axial computed tomography image in a 39-year-old woman with acute right lower quadrant pain. The omentum is swollen (arrowhead) with a central hyperdense structure (dashed arrow) and whirling pattern of curvilinear streaks (solid arrows). The appearance is classic for omental torsion. The patient was managed conservatively.

*Mycobacterium avium-intracellulare* in patients with acquired immunodeficiency syndrome may cause CT findings similar to those of low-density lymphadenopathy and bowel wall thickening. Diagnosis of Whipple's disease is made by small bowel biopsy and demonstration of lipid-laden macrophages containing bacterial fragments that stain with periodic acid–Schiff.

#### Systemic Mastocytosis

Mastocytosis is a rare disease characterized by excessive proliferation of mast cells in the skin, bone marrow, and other organs.

The 2001 World Health Organization classification of mastocytosis divides this disease into at least five groups.<sup>9</sup> Some groups are associated with hematologic neoplasms or sarcomas. Imaging of systemic mastocytosis includes a skeletal scintigraphic survey and radiographic and endoscopic gastrointestinal evaluation. Bone scintigraphy appears to correlate well with the progression of bone marrow disease in systemic mastocytosis and may help identify a subgroup of patients with an aggressive clinical course. CT findings are discussed in Table 82-4 and shown in Figure 82-7.

#### Sarcoidosis

Sarcoidosis is a multisystem disorder of unknown cause characterized by the accumulation of CD4+ T lymphocytes, mononuclear phagocytes, and noncaseating granulomas. Abdominal CT findings are listed in Table 82-4 and shown in Figure 82-8.

#### Extramedullary Hematopoiesis

Extramedullary hematopoiesis is an ectopic hematopoiesis that occurs as a compensatory response to insufficient bone marrow hematopoiesis. Although any tissue of mesenchymal origin may show extramedullary hematopoiesis, the liver and spleen are the most common sites in the abdomen. Occasionally, the kidneys may be involved. In such cases, CT shows homogeneously and poorly enhancing perinephric masses that appear to engulf the kidneys without architectural distortion, a finding similar to that in renal lymphoma.<sup>10</sup> Serosal and mesenteric implants may occur, possibly as a result of rupture of hepatosplenic nodules.<sup>11</sup> On CT these implants may be mistaken for lymphadenopathy or metastatic disease (Figure 82-9).

#### Eosinophilic Gastroenteritis

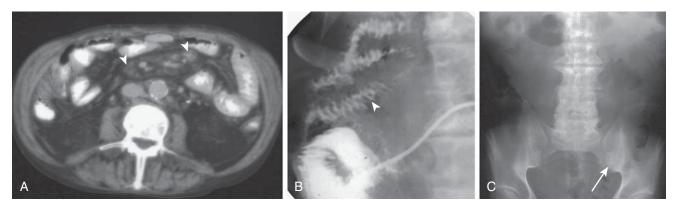
Eosinophilic gastroenteritis is an uncommon disorder with eosinophilic infiltration of different layers of the abdominal gastrointestinal tract.

To make the diagnosis of eosinophilic gastroenteritis it is necessary to have gastrointestinal symptoms, eosinophilic infiltration of the gastrointestinal tract ( $\geq$ 20 eosinophils per high power field), lack of eosinophilic infiltration in other organs, and no evidence to support other conditions associated with eosinophilia, such as drug allergy, parasitic infection, or malignancy. The stomach is the most affected organ in eosinophilic gastroenteritis, followed by the duodenum. The small and large bowels are less commonly affected. Eosinophilic gastroenteritis may be classified into mucosal, muscular, and subserosal subtypes. The mucosal and submucosal forms are discussed elsewhere. The subserosal type manifests as ascites

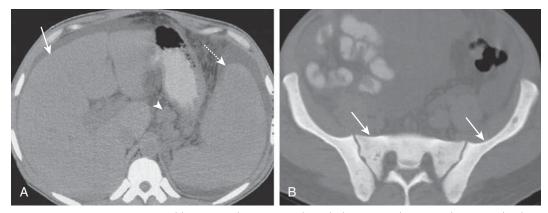
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TABLE 82-4 Computed To	mography Findings in	Systemic Diseases	That Occasionally Involve	e the Peritoneum
Finding	Amyloidosis	Whipple's Disease	Mastocytosis	Sarcoidosis
Bowel wall or fold thickening	Bowel involved in 80% of primary, 60% of secondary disease <sup>34</sup>	Seen Sometimes pneumatosis	Seen in 40%-60% of type 1 disease	Very rare. Gastric wall thickening sometimes seen
Lymphadenopathy	Occasionally seen	Low-density adenopathy <sup>12,35,*</sup>	Common in type 3 disease, especially periportal	Upper abdominal and retroperitoneal in 40%
Peritoneal thickening	Seen	Seen	Omental thickening <sup>6</sup>	Very rare (20 cases reported) <sup>36</sup> May mimic peritoneal carcinomatosis
Ascites	Seen	Seen	Common in types 2 and 3	Rare; ascites in sarcoid patient more commonly due to cardiac or hepatic disease than to sarcoid <sup>35</sup>
Mesenteric calcification	Typically seen <sup>35,37</sup>	Rare	Rare	Rare
Hepatosplenomegaly (HSM)	Seen	Not common	Often seen	10%-15% have diffuse HSM
Specific computed tomography (CT) findings	No specific CT findings	Low-density adenopathy, sacroiliitis	Diffuse or multifocal hot spots on bone scan; sclerotic or lytic bone lesions on CT	Pulmonary involvement in 90% 75% have low-density hepatic lesions and 80% have splenic lesions

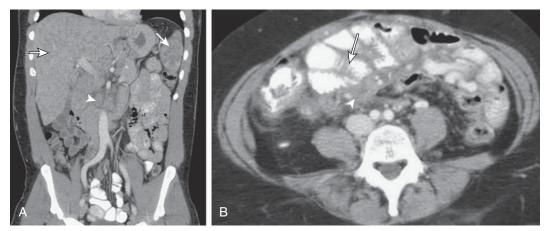
\*The differential diagnosis for low-density adenopathy includes testicular cancer (nonseminomatous), treated lymphoma, tuberculosis, and cavitary mesenteric lymph node syndrome. Extramedullary hematopoiesis causes low-density masses that simulate adenopathy.



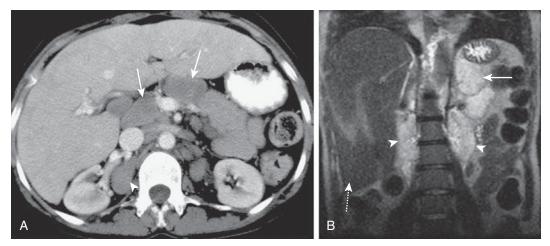
**Figure 82-6** Whipple's disease in a 62-year-old man with unexplained fever and weight loss. **A**, Axial computed tomography shows mixed low-density and higher density mesenteric adenopathy (*arrowheads*). This was initially thought to be due to lymphoma. **B**, Small bowel follow-through was performed for investigation of concomitant malabsorption. There is evidence of fold and wall thickening (*arrowhead*) of the small bowel. **C**, Abdominal radiograph on same patient shows asymmetric sacroiliitis, worse on the left (*arrow*). Whipple's disease is a cause of seronegative spondyloarthropathy.



**Figure 82-7** Systemic mastocytosis in a 54-year-old woman with urticaria and weight loss. **A**, Axial computed tomography shows hepatomegaly (*solid arrow*), splenomegaly (*dashed arrow*), moderate-volume adenopathy (*arrowhead*), and ascites. Change in liver and splenic size is helpful in assessing response to therapy. **B**, Bone window shows diffuse osteosclerosis (*arrows*). These features are highly suggestive of systemic mastocytosis, which was proved on bone marrow and skin biopsies.



**Figure 82-8** Abdominal sarcoidosis. **A**, A 43-year-old man presented with known sarcoidosis. Coronal reformatted abdominal computed tomography image shows numerous small low-density lesions in the liver and spleen (*arrows*), as well as moderate-volume adenopathy (*arrowhead*). These findings remained stable over 3.5 years of follow-up. They are consistent with sarcoidosis and represent the most common presentation of this disease in the abdomen. **B**, A 48-year-old woman presented with known sarcoidosis and abdominal cramping. Axial computed tomography shows dense mesenteric soft tissue (*arrowhead*) enveloping bowel loops, which show thickened folds (*arrow*). The peritoneal biopsy showed noncaseating granuloma.



**Figure 82-9** Extramedullary hematopoiesis in a 16-year-old girl with homozygous sickle cell anemia. Axial computed tomography scan (A) and coronal T2-weighted magnetic resonance image (B) show several peritoneal masses of low density and high signal intensity (*solid arrows*) around the celiac artery and the hepatic hilum and retroperitoneal masses (*arrowheads*). These simulate lymphadenopathy. However, in this patient the lesions were foci of extramedullary hematopoiesis. Note the absence of spleen from autosplenectomy and moderately enlarged liver (*dashed arrow*, B).

but cannot be diagnosed on imaging studies.<sup>12</sup> Paracentesis usually shows a sterile exudative effusion containing as many as 95% eosinophils.

#### Castleman's Disease

Castleman's disease (also known as angiofollicular lymph node hyperplasia or giant lymph node hyperplasia) may be unicentric or multicentric. These two subtypes have different biologic behavior and are discussed separately.

Unicentric Castleman's disease is usually a benign lymphoproliferative disorder of young adults and generally curable with surgical resection. The most common site is the mediastinum. In the abdomen, the retroperitoneum, mesentery, porta hepatis, and pancreas are affected.<sup>13</sup> Peripheral lymphadenopathy is unusual, and laboratory abnormalities are seen in less than 25%. Up to 15% of patients with unicentric Castleman's disease have the plasma cell histologic type. Approximately half of these patients present with fever and have anemia or an elevated erythrocyte sedimentation rate.

In contrast to unicentric disease, multicentric disease has a poor prognosis. A strong association has been found between multicentric Castleman's disease and human herpesvirus 8, which is also the etiologic factor of Kaposi's sarcoma. Most patients with multicentric Castleman's disease die of fulminant infection or malignancy. Approximately 30% of patients with multicentric disease develop non-Hodgkin's lymphoma or Kaposi's sarcoma. There is also a strong association with POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes).

On CT or MRI, well-defined enhancing nodal masses are seen (Figure 82-10).<sup>13</sup> Larger masses (typically >5 cm) may show necrosis. The degree of enhancement may be lower on the plasma cell variant. Adjacent organ invasion is uncommon, except in multicentric Castleman's disease.

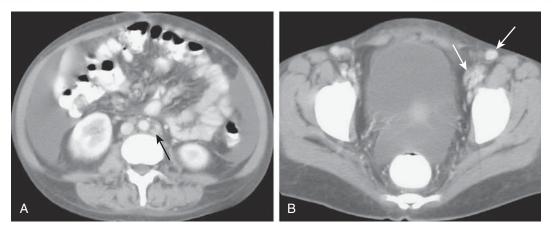
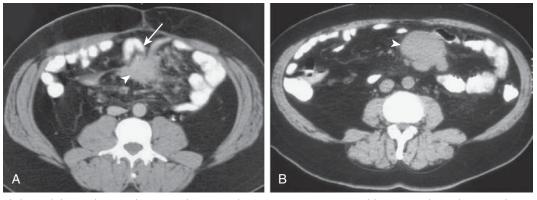


Figure 82-10 Mediastinal Castleman's disease diagnosed on thoracoscopy in a 67-year-old woman. A and B, Axial computed tomography images of the abdomen and pelvis show enhancing lymph nodes (*arrows*) in the retroperitoneum and inguinal region. Ascites is also present. The appearances are typical for this disease.



**Figure 82-11** Abdominal desmoid. **A**, Axial computed tomography (CT) image in a 44-year-old woman with Gardner's syndrome and total colectomy. There is a spiculated mass (*arrowhead*) in the mesentery with adherent bowel loop (*arrow*) anteriorly. In addition to desmoids, patients with Gardner's syndrome have a predilection for multiple tumors, including osteoma and fibroma. **B**, Axial CT image in a 47-year-old woman. A smooth, rounded soft tissue mass in the mesentery (*arrowhead*) was proved at biopsy to be desmoid. A smooth contour is more common than the spiculated appearance shown in **A**.

#### FIBROSIS-ASSOCIATED CONDITIONS

Retractile mesenteritis (see earlier), mesenteric fibromatosis (desmoid tumor), and inflammatory pseudotumor are linked by the presence of fibroblasts or fibrosis in the mesentery. However, they are distinct in cause and biologic behavior.

#### Mesenteric Fibromatosis (Abdominal Desmoid)

Mesenteric fibromatosis is a locally aggressive fibroproliferative process that has the capacity to infiltrate or recur but is considered benign because it does not metastasize.

Desmoid tumors have a predilection for surgical sites (e.g., the mesentery or abdominal wall after colectomy or at the site of ilioanal pouch anastomosis). Sporadic abdominal desmoids are associated with somatic mutations of the beta-catenin gene. In patients with familial adenomatosis coli there is an inactivating germline mutation in the adenomatous polyposis coli gene. Both gene mutations result in increased transcription of betacatenin protein, which causes cellular adherence and explains the biology of desmoid tumors.

The CT and MRI findings of desmoids are nonspecific.<sup>14-16</sup> The contour is smooth in approximately two thirds of cases. Spiculated lesions may mimic carcinoid tumors (Figure 82-11). The lesions are usually of low signal intensity on T1-weighted precontrast sequences and show variable signal on T2-weighted sequences.<sup>17</sup> The enhancement pattern is variable from none to mild homogeneous or heterogeneous enhancement. Previous CT and MRI reports have indicated that strong enhancement is unusual and that most tumors enhance to the same degree as skeletal muscle.<sup>14,16</sup> However, a recent MRI study indicates that strong enhancement is often seen.<sup>16</sup> Necrosis is uncommon.

#### Inflammatory Pseudotumor

Inflammatory pseudotumor (also called inflammatory myofibroblastic tumor or plasma cell granuloma) is a benign, chronic inflammatory disorder of unknown cause that may manifest as a mesenteric mass indistinguishable from a neoplasm. The lungs and orbits are the most common sites of this lesion. Mesenteric and omental pseudotumor accounts for approximately 40% of extrapulmonary cases. Small bowel mesentery (distal ileum), transverse mesocolon, and greater omentum are the most common sites in the abdomen. Solid abdominal organs including the liver, kidneys, and pancreas may be affected less commonly.<sup>9</sup>

On ultrasonograms, the lesions are solid with mixed echopattern. Prominent vascularity may be seen on Doppler interrogation. The CT appearance is nonspecific.<sup>18,19</sup> Although

most mesenteric pseudotumors have a smooth contour, occasionally an irregular outline is seen. Bowel invasion is rare. Central calcification may be seen. Enhancement is variable.

#### Neoplastic Conditions of the Mesentery and Omentum

#### ETIOLOGY

The peritoneum is the lining of mesothelial cells that drapes the abdominal and pelvic walls as well as vital organs contained within, enclosing the peritoneal cavity. It has a rich blood supply and lymphatic drainage. The omentum and mesentery are specialized folds of peritoneum.

Neoplasms of the peritoneum can be divided into primary and secondary types. Primary peritoneal neoplasms arise from the peritoneum itself, whereas secondary peritoneal neoplasms originate from adjacent or remote organs.

#### PREVALENCE AND EPIDEMIOLOGY

Primary peritoneal neoplasms are rare. The most common of these is peritoneal mesothelioma, which has a reported incidence of two cases per million.<sup>20</sup> Other primary neoplasms arising from the mesentery and omentum include cystic mesothelioma, serous surface papillary carcinoma, desmoplastic small round cell tumor, and leiomyomatosis peritonealis disseminata.

Secondary neoplasms of the peritoneum are more common than primary tumors but are uncommon overall. When present, metastatic disease to the peritoneum implies a poor prognosis. The most common primary tumors to metastasize to the peritoneum are ovary, breast, and gastrointestinal tract tumors. Peritoneal metastases are often discovered by imaging or at surgery and require biopsy for definitive diagnosis. When biopsy yields poorly differentiated adenocarcinoma and a primary tumor site is not found, the tumor is usually categorized as adenocarcinoma of an unknown primary tumor rather than primary peritoneal adenocarcinoma.<sup>21,22</sup>

#### **CLINICAL PRESENTATION**

Patients with peritoneal cancer usually present with diffuse abdominal pain, weight gain, and/or abdominal distention secondary to bowel obstruction or ascites. Occasionally they may present with weight loss. Thrombocytosis is common at presentation and is a poor prognostic indicator. Recent literature shows that patients with secondary peritoneal carcinomatosis can present with other hematologic manifestations, such as disseminated intravascular coagulation, distal emboli, or hemolytic anemia.<sup>23,24</sup> Therefore, a high index of suspicion for peritoneal carcinomatosis should be present when a patient with a primary tumor known to metastasize to the peritoneal cavity presents with such signs and symptoms.

Clinical presentations vary depending on the specific pathologic process of the patient's underlying peritoneal disease.<sup>24</sup>

#### NORMAL ANATOMY

The peritoneum is a thin, vascular layer of mesothelium and connective tissue that covers the wall of the abdominal and pelvic cavities and viscera. The parietal peritoneum is attached directly to the abdominal wall, and the visceral peritoneum drapes or lines the visceral organs. The space between these two layers is termed the peritoneal cavity and normally contains approximately 50 mL of serous fluid.

The peritoneum is divided into spaces by various peritoneal folds, known as ligaments. The omentum is a specialized peritoneal fold that originates along the stomach and is divided into the lesser and greater omentum. Special folds of the peritoneum, the mesentery and mesocolon, connect the small bowel and colon to the posterior abdominal wall and serve as a conduit for vascular supply and lymphatic drainage to the intestines.

#### PATHOPHYSIOLOGY

Primary tumors of the omentum and mesentery arise from the mesothelial cells of the peritoneum.

Malignant mesothelioma is an aggressive primary tumor of the peritoneum and accounts for 30% to 45% of all mesotheliomas.<sup>25</sup> Like mesothelioma arising from the pleural surface; malignant mesothelioma of the peritoneum is associated with asbestos exposure. However, cases also have been reported after abdominal radiation therapy. Peritoneal mesothelioma is typically treated with surgical resection and intraperitoneal chemotherapy but has a dismal prognosis with a median survival time of 8 to 12 months after diagnosis.<sup>25</sup>

Cystic mesothelioma is a cystic tumor of the mesothelial cells of the peritoneum. It is not as aggressive as malignant mesothelioma, commonly affects women of reproductive age, and has a predilection for the pelvis. On CT it appears as a noncalcified multiloculated cystic pelvis mass. Histologically, the disease manifests as multiple cysts lined with mesothelium. The prognosis is usually good, but the tumor recurs in up to 50% of cases.<sup>26</sup>

Serous surface papillary carcinoma is a primary peritoneal cancer that commonly occurs in postmenopausal women. Histologically it resembles papillary serous ovarian carcinoma. The presence of calcifications can help differentiate it from malignant mesothelioma. Treatment is usually with intraperitoneal chemotherapy.<sup>27,28</sup>

Desmoplastic small round cell tumor is a highly aggressive neoplasm that usually occurs in young adults and metastasizes early and extensively. The tumor is usually identified by immunohistochemical staining, and the prognosis is very poor.

Primary peritoneal tumors of mesenchymal origin are rare and include liposarcomas, hemangiomas, lymphangiomas, neurogenic tumors, and malignant fibrous histiocytomas.

Secondary malignancy of the omentum and mesentery is most commonly from ovarian, breast, and gastrointestinal tract primary tumors. It may result from direct spread (e.g., ovary, pancreas, and gastrointestinal cancers), lymphatic spread (e.g., lymphoma), or hematogenous spread (e.g., melanoma, breast, and lung cancer). Peritoneal involvement is often discovered by imaging and confirmed with peritoneal biopsy. The presence of peritoneal carcinomatosis at the time of diagnosis is a poor prognostic indicator and may alter management. Carcinoma of an unknown primary tumor is usually a poorly differentiated adenocarcinoma that has a very poor prognosis.

#### IMAGING

Imaging plays a central role in the detection, characterization, and staging and restaging of neoplasms involving the mesentery and omentum. The preferred diagnostic imaging modalities are CT, MRI, and positron emission tomography with CT (PET/CT), all of which have excellent ability to detect peritoneal lesions 1 cm and greater. However, their sensitivity and specificity for detecting peritoneal lesions less than 1 cm is much lower, with an estimated sensitivity of CT for nodules less than 1 cm as low as 15%.<sup>23</sup>

#### Radiography

Plain film radiography has a limited role in evaluation of patients with peritoneal neoplasms. Large-volume ascites may be detected (Figure 82-12). Gastrointestinal fluoroscopy can be a useful tool to study complications of peritoneal neoplasms (Figure 82-13).

#### Computed Tomography

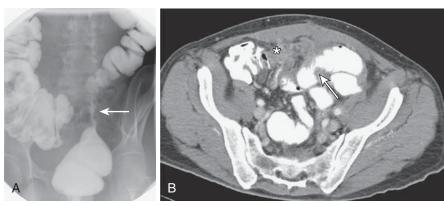
CT is the cornerstone modality in evaluating neoplasms of the omentum and mesentery (Figure 82-14). CT excels in detecting metastatic nodules 1 cm and greater, with sensitivity ranging from 60% to 79%, but sensitivity falls significantly for nodules smaller than 1 cm.

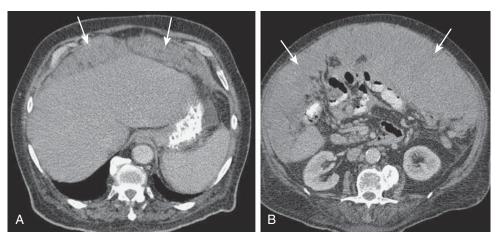
CT performed for evaluation of malignancy involving the omentum or mesentery should be performed with intravenous and enteric contrast media. This allows separation of peritoneal disease from bowel, which can be difficult in an unenhanced scan.



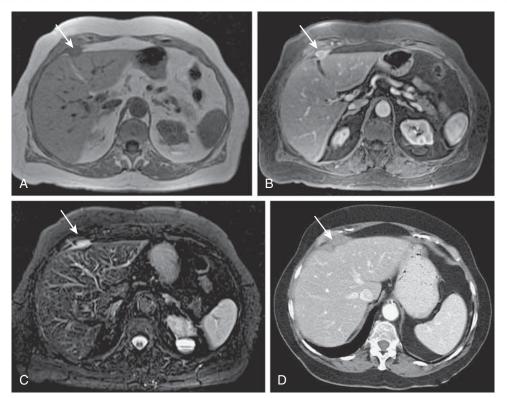
**Figure 82-12** A 39-year-old man with abdominal distention. Frontal abdominal radiograph shows centrally displaced bowel from large-volume ascites (*arrow*).

**Figure 82-13** A 60-year-old man with previous resection of adenocarcinoma of the transverse colon presented with abdominal pain and nausea. A, A single-contrast barium enema demonstrates irregular segmental narrowing (*arrow*) of rectosigmoid colon. This was initially thought to represent a metachronous lesion. B, Computed tomography confirmed a soft tissue mass in the rectosigmoid region (*arrow*) and peritoneal implants elsewhere (*asterisk*).





**Figure 82-14** A 56-year-old man presented with primary malignant mesothelioma of the abdomen. Computed tomography of the abdomen with intravenous and enteric contrast material demonstrates extensive confluent soft tissue attenuation within the upper peritoneum anterior to the liver (so-called omental caking) (*arrows*). This extended inferiorly into the pelvis.



**Figure 82-15** A 67-year-old woman presented with known ovarian cancer. Axial T1-weighted precontrast (A), T1-weighted fat-saturated postcontrast (B), and fat-saturated T2-weighted (C) images show an enhancing peritoneal deposit anterior to the liver, near the falciform ligament. Note the decreased conspicuity of the same implant on the corresponding computed tomography scan (D).

#### Magnetic Resonance Imaging

MRI has specificity similar to that of CT for the detection of omental and mesenteric malignancies. It has slightly higher sensitivity than CT. Subtracting the precontrast T1-weighted image from the gadolinium (Gd)-enhanced T1-weighted gradient echo image increases the conspicuity of tumor implant enhancement located within the peritoneum and along the bowel serosa (Figure 82-15).

The limiting factors of MRI are image degradation from patient motion because of long image acquisition times and artifacts resulting from misregistration during image subtraction. Overall, MRI offers little advantage over CT in sensitivity, specificity, or accuracy in studying omental and mesenteric pathology.

As with CT, MRI should be performed with intravenous administration of a contrast agent. Both precontrast and post-contrast MRI sequences are typically obtained to demonstrate enhancement.

#### Ultrasonography

Ultrasonography is of limited use in the evaluation of patients with neoplasms involving the mesentery and omentum. Occasionally, peritoneal nodules can be seen in patients undergoing ultrasound evaluation for ascites (Figure 82-16). Ultrasonography is widely used to guide diagnostic paracentesis or occasionally to guide peritoneal biopsy.

#### Nuclear Medicine

General nuclear medicine (not including PET) plays a limited role in evaluating neoplasms of the mesentery and

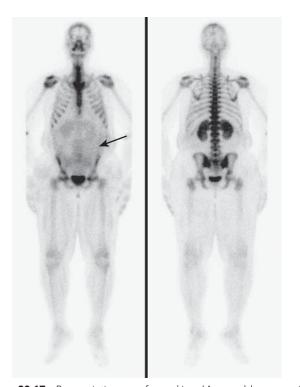


**Figure 82-16** A 46-year-old man presented with known peritoneal metastasis from colorectal cancer. Ultrasonography was performed to confirm ascites and guide paracentesis. Sagittal gray-scale image demonstrates ascites and a peritoneal soft tissue nodule (*arrow*) in the right lower quadrant that corresponded to the patient's known peritoneal carcinomatosis.

omentum. However, an incidental subtle finding on a nuclear medicine scan may suggest the presence of peritoneal metastasis (Figure 82-17).

#### Positron Emission Tomography With Computed Tomography

The advent of 18F-fluorodeoxyglucose (FDG)-PET fused with CT (PET/CT) has revolutionized oncologic imaging. PET/CT



**Figure 82-17** Bone scintiscan performed in a 64-year-old woman with breast cancer reveals increased uptake in the spine, ribs, and pelvis, consistent with diffuse osseous metastatic disease. There is also abnormal diffuse uptake in the abdomen, suggesting peritoneal spread (*arrow*), which was confirmed at surgery.

is performed after intravenous administration of FDG. Patients should refrain from excessive motion and talking to minimize soft tissue FDG uptake, because this may the mimic pathologic process. An unenhanced CT scan (attenuation correction CT) is now routinely obtained and fused with the PET to help localize the exact region of abnormal FDG uptake.<sup>29</sup>

The current role of PET/CT in peritoneal cancer is to detect active disease when conventional imaging is inconclusive or negative in the presence of elevated serum tumor markers in the posttherapy patient (Figure 82-18). PET is limited by relatively low spatial resolution and in identifying tumors that are hypocellular or have low glucose metabolism.

PET/CT has become integral in the management of cancer patients for staging, restaging, monitoring therapy/assessing therapy, and guiding intervention. It can be used to evaluate tumors of the mesentery and omentum. Although its overall sensitivity for detecting these tumors is similar to that of CT and MRI, PET may be more sensitive for evaluating peritoneal nodules of 0.6 to 1.0 cm.<sup>29,30</sup>

#### Dual-Energy Computed Tomography

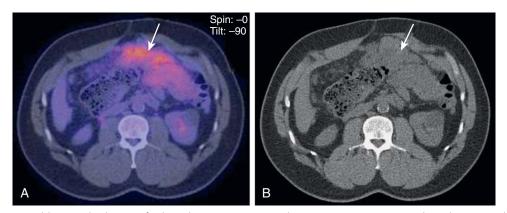
Dual-energy CT is a rapidly evolving technique. It increases the lesion conspicuity, which is helpful for staging (Figure 82-19).

#### Imaging Algorithm

As previously discussed, plain radiographs, ultrasonography, and general nuclear medicine are not suited for the evaluation of neoplasms of the omentum and mesentery. However, they can give clues to a peritoneal malignancy, which can be confirmed by the use of another cross- sectional imaging modality (Table 82-5).

#### **Classic Signs**

- There are no classic radiographic signs for neoplasms of the omentum or mesentery.
- One should look for soft tissue density in the peritoneum.



**Figure 82-18** A 54-year-old man with a history of colon adenocarcinoma. Fused positron emission tomography with computed tomography (PET/ CT) axial image (A) shows diffuse fluorodeoxyglucose uptake in confluent soft tissue density in the anterior abdomen (*arrow*), consistent with metabolically active peritoneal carcinomatosis. The volume and extent of disease are more readily seen on PET/CT than on the attenuation correction CT (B).

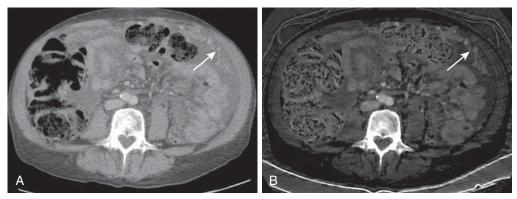


Figure 82-19 Single-energy versus dual-energy computed tomography (CT) scan. A, Single-energy axial CT in a 63-year-old man presenting with pain in the general abdomen and known case of liver cancer, shows faint omental nodules (*arrow*). B, lodine images show increased conspicuity of omental nodules (*arrow*), with iodine uptake helping to characterize the nodule and differentiate from surrounding ascites.

# TABLEAccuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Neoplastic Conditions of the<br/>Mesentery and Omentum

Modality	Accuracy	Limitations	Pitfalls
Radiography	Of limited use	Cannot evaluate mesentery or omentum	Hard to detect peritoneal nodules or masses unless they cause mass effect on viscera or cause bowel obstruction
СТ	Very good at detecting nodules >1 cm	Sensitivity falls significantly with nodules <1 cm	May miss small nodules
MRI	Similar specificity as CT Sensitivity increased with gadolinium-enhanced subtraction imaging	Not sensitive for nodules <1 cm Motion artifacts and long scan times	May miss small nodules
Ultrasonography	Limited value	Better sensitivity when ascites is present, but even then sensitivity is poor	Not the study of choice
Nuclear medicine	Little utility	Does not directly image mesentery or omentum	Not the study of choice
PET/CT	May have better sensitivity than CT and MRI in detecting nodules between 0.6 cm and 1.0 cm	Misregistration and artifacts related to normal FDG uptake can be problematic.	May miss small nodules because of issues with image resolution, misregistration, and physiologic bowel uptake. Physiologic bowel activity can limit detection of serosal implants. False-negative result from hypocellular or hypometabolic tumors.

CT, Computed tomography; FDG, fluorodeoxyglucose; MRI, magnetic resonance imaging; PET, positron emission tomography.

#### DIFFERENTIAL DIAGNOSIS

In the absence of a known primary malignancy, the differential diagnosis of a neoplasm in the mesentery or omentum is extensive. Metastases to the peritoneum are more common than primary malignancy.

When considering a focal lesion of the omentum or mesentery, one should keep non-neoplastic or inflammatory causes in the differential diagnosis. Typically imaging is used to diagnose malignancy of the omentum and mesentery. Imaging plays a key role in guiding biopsy to obtain tissue for histologic analysis. Immunohistochemical analysis and study of various tissue-specific cytokeratins also allude to a particular pathologic entity.

#### TREATMENT

#### **Medical Treatment**

In general, the prognosis for malignancies of the mesentery and omentum is poor. Medical treatment usually consists of intraperitoneal chemotherapy; however, response varies depending on the cause of the malignancy.

#### Surgical Treatment

Many institutions combine surgical therapy with chemotherapy as treatment for omental and mesenteric cancer. The combination of surgical debulking or cytoreductive surgery and intraperitoneal chemotherapy has been shown to increase survival to a greater extent than intraperitoneal chemotherapy alone.<sup>31-33</sup>

### **Key Points**

- Mesenteric panniculitis demonstrates increased volume of the proximal mesenteric root with increased-density fat that envelops, without constricting, mesenteric vessels. Small soft tissue nodules are also seen.
- Epiploic appendagitis is a cause of abdominal pain and manifests on CT as a small (<5 cm) lesion of increased fat density adjacent to the colon. It is a self-limiting disease.
- The differential diagnosis of a spiculated mesenteric lesion includes carcinoid, desmoid tumor, peritoneal tuberculosis, and mesothelioma.
- The differential diagnosis of low-density mesenteric masses or adenopathy includes tuberculosis, metastases from germ cell tumors, treated lymphoma, Whipple's disease, and extramedullary hematopoiesis.
- Primary peritoneal neoplasms are rare.

- Prognosis of primary peritoneal malignancy is generally poor.
- The presence of omental or mesenteric metastasis from a known primary is a poor prognostic indicator for overall patient survival.
- Early detection and aggressive therapy with a combination of cytoreductive surgery and intraperitoneal chemotherapy may improve longevity but are typically not curative.
- CT, MRI, and PET/CT are the imaging modalities of choice for the detection, characterization, and staging of neoplasms involving the omentum and mesentery.
- Image-guided or surgical biopsy of a peritoneal lesion is often the first step in diagnosis. When carcinoma is diagnosed, but a primary site is not found, the diagnosis of carcinoma of an unknown primary tumor is established.

### SUGGESTED READINGS

- Friedman S, Janowitz HD: Systemic amyloidosis and the gastrointestinal tract. Gastroenterol Clin North Am 27:595–614, vi, 1998.
- Horton KM, Corl FM, Fishman EK: CT of nonneoplastic diseases of the small bowel: spectrum of disease. J Comput Assist Tomogr 23:417–428, 1999.
- Pickhardt PJ, Bhalla S: Unusual nonneoplastic peritoneal and subperitoneal conditions: CT findings. *Radiographics* 25:719–730, 2005.
- Singh AK, Gervais DA, Hahn PF, et al: Acute epiploic appendagitis and its mimics. *Radiographics* 25:1521–1534, 2005.

# REFERENCES

- Horton KM, Lawler LP, Fishman EK: CT findings in sclerosing mesenteritis (panniculitis): spectrum of disease. *Radiographics* 23:1561– 1567, 2003.
- 2. Daskalogiannaki M, Voloudaki A, Prassopoulos P, et al: CT evaluation of mesenteric panniculitis: prevalence and associated diseases. *AJR Am J Roentgenol* 174:427–431, 2000.
- 3. Singh AK, Gervais DA, Hahn PF, et al: Acute epiploic appendagitis and its mimics. *Radiographics* 25:1521–1534, 2005.
- McClure MJ, Khalili K, Sarrazin J, et al: Radiological features of epiploic appendagitis and segmental omental infarction. *Clin Radiol* 56:819–827, 2001.
- Ghahremani GG, White EM, Hoff FL, et al: Appendices epiploicae of the colon: radiologic and pathologic features. *Radiographics* 12:59– 77, 1992.
- Horger M, Vogel M, Brodoefel H, et al: Omental and peritoneal involvement in systemic amyloidosis: CT with pathologic correlation. *AJR Am J Roentgenol* 186:1193–1195, 2006.
- Wilson KH, Blitchington R, Frothingham R, et al: Phylogeny of the Whipple's-disease–associated bacterium. *Lancet* 338:474–475, 1991.
- Rijke AM, Falke TH, de Vries RR: Computed tomography in Whipple disease. J Comput Assist Tomogr 7:1101–1102, 1983.
- Uysal S, Tuncbilek I, Unlubay D, et al: Inflammatory pseudotumor of the sigmoid colon mesentery: US and CT findings (2004:12b). *Eur Radiol* 15:633–635, 2005.
- Georgiades CS, Neyman EG, Francis IR, et al: Typical and atypical presentations of extramedullary hematopoiesis. *AJR Am J Roentgenol* 179:1239–1243, 2002.
- 11. Scott WW, Jr, Fishman EK: Extramedullary hematopoiesis mimicking the appearance of

- carcinomatosis or peritoneal mesothelioma: computed tomography demonstration. *Gastrointest Radiol* 15:82–83, 1990.
- Horton KM, Corl FM, Fishman EK: CT of nonneoplastic diseases of the small bowel: spectrum of disease. J Comput Assist Tomogr 23:417–428, 1999.
- Meador TL, McLarney JK: CT features of Castleman disease of the abdomen and pelvis. *AJR Am J Roentgenol* 175:115–118, 2000.
- Einstein DM, Tagliabue JR, Desai RK: Abdominal desmoids: CT findings in 25 patients. *AJR Am J Roentgenol* 157:275–279, 1991.
- Lee JC, Thomas JM, Phillips S, et al: Aggressive fibromatosis: MRI features with pathologic correlation. *AJR Am J Roentgenol* 186:247–254, 2006.
- 16. Quinn SF, Erickson SJ, Dee PM, et al: MR imaging in fibromatosis: results in 26 patients with pathologic correlation. *AJR Am J Roent-genol* 156:539–542, 1991.
- 17. Azizi L, Balu M, Belkacem A, et al: MRI features of mesenteric desmoid tumors in familial adenomatous polyposis. *AJR Am J Roentgenol* 184:1128–1135, 2005.
- Brown G, Shaw DG: Inflammatory pseudotumours in children: CT and ultrasound appearances with histopathological correlation. *Clin Radiol* 50:782–786, 1995.
- Narla LD, Newman B, Spottswood SS, et al: Inflammatory pseudotumor. *Radiographics* 23: 719–729, 2003.
- Jeong YJ, Kim S, Kwak SW, et al: Neoplastic and nonneoplastic conditions of serosal membrane origin: CT findings. *Radiographics* 28:801–817, 2008.
- Pavlidis N, Fizazi K: Cancer of unknown primary (CUP). Crit Rev Oncol Hematol 54: 243–250, 2005.

- 22. Ghosh L, Dahut W, Kakar S, et al: Management of patients with metastatic cancer of unknown primary. *Curr Probl Surg* 42:12–66, 2005.
- Pickhardt PJ, Bhalla S: Primary neoplasms of peritoneal and sub-peritoneal origin: CT findings. *Radiographics* 25:983–995, 2005.
- Levy AD, Arnáiz J, Shaw JC, et al: From the archives of the AFIP. Primary peritoneal tumors: imaging features with pathologic correlation. *Radiographics* 28:583–607, quiz 621-622, 2008.
- Bridda A, Padoan I, Mencarelli R, et al: Peritoneal mesothelioma: a review. *Med Gen Med* 9:32, 2007.
- Sugarbaker P, Yan T, Zappa L, et al: Thin-walled cysts as a pathognomonic CT finding in cystic mesothelioma. *Tumori* 94:14–18, 2008.
- Alberti N, Serrano-Egea A, García-García E, et al: Primary papillary serous carcinoma of the peritoneum: report of a case with diagnosis by fine needle aspiration and immunocytochemistry. *Acta Cytol* 51:203–206, 2007.
- Puvaneswary M, Proietto T: Primary papillary serous carcinoma of the peritoneum: four cases and review of computed tomography findings. *Australas Radiol* 48:421–425, 2004.
- Bybel B, Brunken R, Shah SN, et al: PET and PET/CT imaging: what clinicians need to know. *Cleve Clin J Med* 73:1075–1087, 2006.
- Gunn AJ, Brechbiel MW, Choyke PL: The emerging role of molecular imaging and targeted therapeutics in peritoneal carcinomatosis. *Expert Opin Drug Deliv* 4:389–402, 2007.
- Al-Shammaa HA, Li Y, Yonemura Y: Current status and future strategies of cytoreductive surgery plus intraperitoneal hyperthermic chemotherapy for peritoneal carcinomatosis. World J Gastroenterol 14:1159–1166, 2008.
- 32. Facchiano E, Scaringi S, Kianmanesh R, et al: Laparoscopic hyperthermic intraperitoneal

chemotherapy (HIPEC) for the treatment of malignant ascites secondary to unresectable peritoneal carcinomatosis from advanced gastric cancer. *Eur J Surg Oncol* 34:154–158, 2008.

- Nam JH, Kim YM, Jung MH, et al: Primary peritoneal carcinoma: experience with cytoreductive surgery and combination chemotherapy. *Int J Gynecol Cancer* 16:23–28, 2006.
- Allen HA, III, Vick CW, Messmer JM, et al: Diffuse mesenteric amyloidosis: CT, sonographic, and pathologic findings. J Comput Assist Tomogr 9:196–198, 1985.
- Pickhardt PJ, Bhalla S: Unusual nonneoplastic peritoneal and subperitoneal conditions: CT findings. *Radiographics* 25:719–730, 2005.
- 36. Bourdillon L, Lanier-Gachon E, Stankovic K, et al: Lofgren syndrome and peritoneal involve-

ment by sarcoidosis: case report. *Chest* 132:310–312, 2007.

37. Coumbaras M, Chopier J, Massiani MA, et al: Diffuse mesenteric and omental infiltration by amyloidosis with omental calcification mimicking abdominal carcinomatosis. *Clin Radiol* 56:674–676, 2001.



# Neoplastic and Non-neoplastic Conditions of the Abdominal Wall

OSCAR M. RIVERO | MANUEL F. GRANJA | DIEGO A. AGUIRRE

Cross-sectional imaging modalities including ultrasonography, computed tomography (CT), and magnetic resonancy imaging (MRI) provide good anatomic detail of the abdominal wall and allow evaluation of pathologic processes in this area. Ultrasonography is frequently used as the first imaging modality to explore a palpable abdominal mass.<sup>1</sup>

# **Non-neoplastic Conditions**

# ABDOMINAL WALL INFLAMMATION, INFECTION, AND FLUID COLLECTION

# Etiology

Inflammatory processes involving the abdominal wall include diffuse edema (Figure 83-1), infections such as cellulitis or abscess, and sterile collections (seroma or liquefying hematoma)<sup>1</sup> (Figure 83-2).

Fluid collections of the abdominal wall commonly result from trauma, postsurgical wound complication, or extension from an intra-abdominal source (Figures 83-3 and 83-4).<sup>2-4</sup>

Abdominal wall infections also can manifest as necrotizing fasciitis. This condition is considered a true surgical emergency.<sup>5</sup>

### Prevalence and Epidemiology

Spontaneous infection of the abdominal wall is infrequent in the general population. It is more commonly seen in patients with diabetes mellitus, immunosuppressant therapy, sepsis, surgery, trauma, atherosclerosis, alcoholism, obesity, and malnutrition.<sup>1,3,6</sup>

# **Clinical Presentation**

Clinical recognition of fluid collections or inflammatory processes can be difficult, and patients may present with fever, pain, and skin changes.<sup>3,6</sup>

## Pathology

Pathologic and laboratory findings vary according to the specific type of infection.

# Imaging

Infectious involvement of the abdominal wall may manifest as cellulitis with poorly defined inflammatory changes in the subcutaneous fat tissue or as a well-defined collection (abscess).<sup>4,7</sup> CT and MRI provide key information regarding the nature and extent of the infection.<sup>3</sup>

**Radiography.** Conventional radiographs have no role in assessing infection and collections of the abdominal wall.

**Computed Tomography.** On CT, abscesses appear as lowattenuation fluid collections, often with enhancing margins and gas or gas/fluid levels.<sup>2</sup> Diffuse inflammatory stranding of adjacent structures also is seen. Necrotizing fasciitis can be seen as soft tissue gas dissecting fascial planes in a characteristic appearance.<sup>5</sup> CT plays an important role in guiding percutaneous aspiration or drainage procedures.

**Magnetic Resonance Imaging.** Abscesses are often heterogeneous but generally appear hypointense on T1-weighted sequences and hyperintense on T2-weighted sequences with peripheral enhancement and inflammatory changes in the adjacent tissues.<sup>3,8</sup>

**Ultrasonography.** Fluid collections complicated by infection or hemorrhage have a complex appearance on ultrasound with echoes and internal septa.<sup>1</sup>

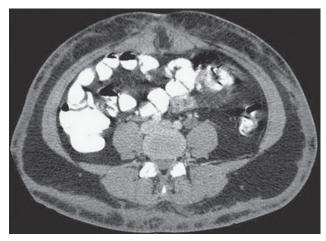
**Imaging Algorithm.** Ultrasonography is the mainstay for diagnosis of abdominal wall abscesses; however, in obese or postoperative patients, in whom ultrasound evaluation is limited, multidetector CT (MDCT) or MRI should be considered (Table 83-1).

Classic Signs: Abdominal Wall Inflammation, Infection, and Fluid Collections

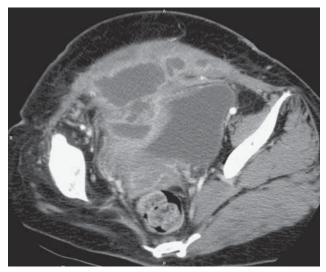
- Cellulitis appears as diffuse inflammatory changes involving the skin and subcutaneous tissue.
- Abscesses appear as fluid collections, with enhancing margins and surrounding inflammatory changes.

## Differential Diagnosis

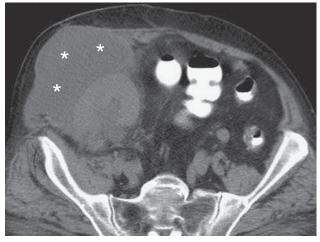
Differential diagnosis of abdominal wall collections includes uninfected seroma, hematomas, and abscess. Image-guided



**Figure 83-1** Postsurgical diffuse fat stranding. Axial contrast-enhanced computed tomography image of the abdomen shows diffuse subcutaneous fat stranding in a 32-year-old woman 2 days after abdominoplasty. Note diffuse thickening of the subcutaneous tissue, with no fluid collections.



**Figure 83-3** Abdominal wall abscess. Axial contrast-enhanced computed tomography image of the abdomen shows a complex pelvic collection extending into the abdominal wall in a 41-year-old woman that was secondary to pelvic inflammatory disease.



**Figure 83-2** Abdominal wall seroma. Axial unenhanced computed tomography image of the abdomen shows an abdominal wall fluid collection (seroma, *asterisks*), located superficial to a renal transplant in the right iliac fossa.



**Figure 83-4** Abdominal wall seroma and mesh. Axial contrastenhanced computed tomography image of the abdomen demonstrates a well-defined ventral wall seroma *(asterisks)*, manifesting after ventral hernia repair with mesh *(arrowheads)*, in a 51-year-old man.

TABLE	Accuracy, Limitations, and Pitfalls of the Modalities Used in Imaging of Abdominal Wall Inflammation,
83-1	Infection, and Fluid Collections

Modality	Accuracy	Limitations	Pitfalls
Radiography	Limited availability of	Not useful	
СТ	source literature for comparing accuracy of	lonizing radiation	
MRI	different imaging modalities for detecting non-neoplastic pathology of the abdominal wall	Expensive and not widely available Limited spatial resolution Limited on postoperative patients Patient-limiting factors (e.g., claustrophobia, pacemaker)	
Ultrasonography		Obesity, significant scarring, patients with acute abdominal pain Operator dependent Requires high-frequency transducer	If near field is overlooked, abdominal wall pathologic process may be missed.

CT, Computed tomography; MRI, magnetic resonance imaging.

aspiration with bacteriologic analysis may be needed to differentiate between these entities.<sup>1</sup>

### Treatment

Therapy includes antimicrobial therapy and percutaneous drainage. Surgical management is usually required in severe conditions or in cases of necrotizing fasciitis.<sup>9</sup>

# TRAUMATIC ABNORMALITIES, INCLUDING ABDOMINAL WALL HEMATOMA

### Etiology

Traumatic injuries include laceration, contusion, hematoma, and muscle tear. Abdominal wall hematomas may be associated with trauma, anticoagulation therapy, and blood dyscrasias. Abdominal wall hematomas commonly involve the anterior or anterolateral muscle groups.<sup>2</sup>

Groin, or retroperitoneal hematoma may occur as a complication of arterial or venous catheterization.<sup>10</sup>

### Prevalence and Epidemiology

Trauma may result in abdominal wall abnormalities that can be detected on imaging studies, including abdominal wall



**Figure 83-5** Abdominal wall rupture. Axial contrast-enhanced computed tomography image demonstrating traumatic rupture of the right posterolateral abdominal wall (*arrowheads*) in a 23-year-old man after blunt trauma to the abdomen. Note discontinuity of the abdominal wall in this region.

laceration (Figure 83-5), hematoma, contusion, and muscular tear (Figure 83-6).<sup>7,11</sup>

# **Clinical Presentation**

Above the arcuate line, wall hematomas are confined within the rectus sheath, they are oval (Figure 83-7), and they manifest with pain and tenderness. Below the arcuate line and because of the absence of the posterior rectus sheath, the hematoma is unconfined; it can leak and dissect posteriorly into the extraperitoneal spaces, across the midline in the prevesical space (Retzius's space), or laterally into the flank, predisposing to hypovolemic shock secondary to uncontained blood loss (Figure 83-8).<sup>12-14</sup>

# Pathology

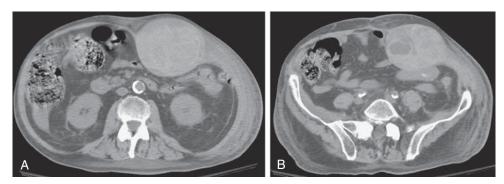
Trauma may affect skin, subcutaneous tissues, and muscles of the abdominal wall.

#### Imaging

**Computed Tomography.** On CT, acute hematoma is hyperdense relative to muscle because of clot formation. Attenuation values decrease with time as breakdown of blood products



**Figure 83-6** Ruptured rectus abdominis muscle. Axial contrastenhanced computed tomography image in a 36-year-old man showing rupture of the right rectus abdominis muscle (*arrowheads*) after blunt abdominal trauma, with herniation of extraperitoneal fat into the subcutaneous tissue.



**Figure 83-7** Abdominal wall hematoma. Axial unenhanced computed tomography images of the abdomen through the (A) lower pole of the kidneys and (B) level of the umbilicus in a 62-year-old anticoagulated patient that show a left rectus abdominis muscle hematoma. Note heterogeneous density of the hematoma with multiple fluid-fluid levels and moderate stranding in the subcutaneous fat.



**Figure 83-8** Rectus sheath hematoma. Axial unenhanced computed tomography image of the abdomen in a 59-year-old man demonstrating a rectus sheath hematoma occurring below the arcuate line. Note extension of the hematoma to the prevesical space (of Retzius).

occurs. Chronic hematoma may be isodense or hypodense relative to surrounding muscle.<sup>12,15</sup>

A classification method for rectus sheath hematoma has been described on the basis of CT findings, as follows<sup>12,13</sup>:

- Type 1: The hematoma is unilateral and intramuscular.
- *Type 2:* The hematoma is intramuscular, as it is in type 1, but blood is also present between the muscle and the transversalis fascia. It may be unilateral or bilateral. No blood is seen in the prevesical space.
- *Type 3:* The hematoma may or may not affect the muscle; blood products are seen between the muscle and the fascia transversalis, as well as in the prevesical space.

**Magnetic Resonance Imaging.** MRI is very useful in the diagnosis of abdominal wall hematoma, especially when the CT findings are nonspecific. Acute hematomas appear isointense relative to muscle on T1-weighted images and hypointense on T2-weighted images. Subacute hematomas demonstrate high signal intensity on both T1- and T2-weighted images.<sup>15</sup>

**Ultrasonography.** Hematomas appear as a nonspecific complex fluid collection with internal echoes and septations.<sup>1</sup>

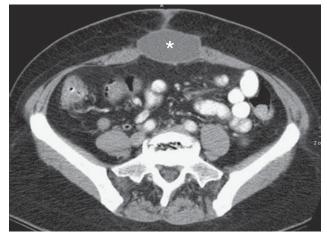
**Imaging Algorithm.** Ultrasonography is the mainstay for diagnosis of suspected abdominal wall hematoma; however, in obese or postoperative patients, in whom ultrasound evaluation is limited, MDCT should be considered (see Table 83-1). In the acute setting, MDCT provides key information regarding hematoma size and extension into the abdominal cavity.

### Classic Signs: Traumatic Abnormalities, Including Abdominal Wall Hematoma

- Hematomas appear as heterogeneous fluid collections. Rectus sheath hematomas occurring above the arcuate line are contained within the muscular fascia. Below the arcuate line, hematoma may extend into the prevesical space, becoming uncontained (Figure 83-9).
- CT and MRI show a heterogeneous fluid collection with fluid/fluid levels (hematocrit effect).
- Ultrasonography demonstrates a complex collection.



**Figure 83-9** Abdominal wall hematoma. Axial contrast-enhanced computed tomography image of the abdomen demonstrates a hematoma in the anterior abdominal wall in a 32-year-old woman after cesarean section. The hematoma is below the arcuate line, demonstrates hematocrit effect (*asterisks*), and is associated with extraperitoneal extension of the hematoma into the space of Retzius (*arrowheads*).



**Figure 83-10** Abdominal wall seroma. Axial contrast-enhanced computed tomography image of the abdomen demonstrating a homogeneous fluid collection in the midline anterior abdominal wall (*asterisk*) in a 42-year-old woman after left colectomy. Note the homogeneous density of the fluid collection and absence of inflammatory changes in adjacent subcutaneous tissue.

## **Differential Diagnosis**

Abdominal wall hematoma may mimic other pathologic processes leading to acute abdomen.<sup>7</sup> It may be confused with other fluid collections, such as infected or uninfected seroma (Figure 83-10) or abscesses.<sup>1</sup>

### Treatment

In hemodynamically stable conditions, conservative measures are the mainstay of treatment.<sup>13</sup> If the patient becomes unstable or cannot be controlled with conservative measures, surgical intervention or transcatheter embolization may be considered.<sup>13</sup>

# **ENDOMETRIOMAS**

# Etiology

Endometriomas form when functional endometrial tissue is located outside the uterine cavity. This may occur after surgical procedures that disrupt the uterine cavity (e.g., cesarean section), allowing endometrial tissue to be seeding.<sup>16</sup> In these cases, endometriomas may be located within the abdominal wall at the site of the surgical incision.

### Prevalence and Epidemiology

In most cases, ectopic endometrial tissue is located within the pelvis, associated with the ovaries, uterine ligaments, and pelvic peritoneal folds.<sup>5</sup>

### **Clinical Presentation**

Most patients present with a palpable mass in the region of a surgical scar. A history of cyclic pain associated with menses may be present.

## Pathophysiology

Two leading theories exist for endometriosis. One hypothesis suggests that mesenchymal cells with multipotential properties may undergo metaplasia into endometriosis. The other theory states that endometrial cells may be transported to ectopic sites, forming an endometrioma. When these cells are stimulated by estrogens, they may proliferate and become symptomatic.<sup>16</sup>

### Pathology

Extrapelvic endometriosis has been described in nearly all body cavities and organs, but the abdominal wall is the most frequent location, occurring in approximately 0.8% of patients with endometriosis.<sup>16-20</sup>

### Imaging

The ultrasound, CT, and MRI features of abdominal wall endometriosis are nonspecific. Endometriomas appear as a solid mass in the abdominal wall with hypervascular component.<sup>16,18</sup>

**Computed Tomography.** The major role of CT is to demonstrate a solid, enhancing mass in the abdominal wall.<sup>16</sup>

**Magnetic Resonance Imaging.** MRI may show high signal intensity on T1- and T2-weighted images resulting from hemorrhage.<sup>20</sup> Nevertheless, abdominal wall endometrioma may be nonspecific—hypointense or isointense to muscle on T1-weighted images and hyperintense on T2-weighted images and enhance after contrast administration.<sup>16</sup>

**Ultrasonography.** On ultrasonography, endometriomas tend to be solid, hypoechoic lesions within the abdominal wall; they show internal vascularity on Doppler studies. Cystic changes may occur and are probably secondary to intralesional bleeding during menstruation.

**Imaging Algorithm.** Ultrasonography is the primary modality in the evaluation of abdominal wall masses (see Table 83-1). Because of its nonspecific solid appearance, additional imaging with MDCT or MRI is important to confirm local extent. Image-guided biopsy should be considered to exclude malignancy.

#### **Classic Signs: Endometriomas**

- A nonspecific, solid hypervascular mass is located within the abdominal wall.
- Presentation tends to be at the surgical incision site after pelvic surgery.
- Appearance on MDCT and MRI is similar to that of soft tissue tumors; thus, histologic assessment is usually necessary.

# Differential Diagnosis

Imaging findings of abdominal wall endometrioma are nonspecific, and a wide spectrum of disorders should be considered in the differential diagnosis, including neoplasms (e.g., sarcoma, desmoid tumor, lymphoma, or metastasis) and non-neoplastic causes (e.g., suture granuloma, ventral hernia, hematoma, or abscess).<sup>16,20</sup>

### Treatment

Pharmacologic therapies with hormonal agents such as progestogens are indicated. If medical treatment of abdominal wall endometriosis fails, surgical excision is the treatment of choice.<sup>16,19</sup>

# VARICES

### Etiology

Abdominal wall varices are dilated subcutaneous veins that form part of a portosystemic shunt secondary to portal hypertension.<sup>21</sup>

# Prevalence and Epidemiology

In the setting of chronic liver disease, varices are common, occurring in up to 20% to 35% of patients.<sup>22</sup>

### **Clinical Presentation**

Abdominal wall varices are mainly asymptomatic.

# Pathophysiology

Cirrhosis is the most common cause of intrahepatic portal hypertension and accounts for the majority of cases of portal hypertension in the West. Postsinusoidal and posthepatic causes of portal hypertension include portal and splenic vein thrombosis or hepatic diseases, Budd-Chiari syndrome, and inferior vena cava obstruction.

### Pathology

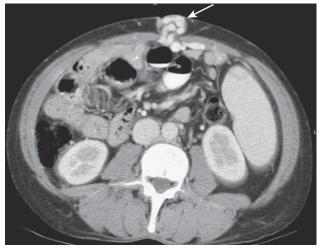
The left portal vein communicates with the systemic epigastric veins near the umbilicus via paraumbilical venous channels (Cruveilhier-Baumgarten syndrome).

### Imaging

Varices are easily identified on cross-sectional imaging modalities. They are located in the subcutaneous tissue or wall musculature and have a characteristic tubular shape (Figure 83-11).<sup>22</sup>

**Computed Tomography.** Abdominal wall varices appear as subcutaneous, enhancing tubular structures near the umbilicus.<sup>22</sup>

**Magnetic Resonance Imaging.** Varices have a similar appearance on MR images as they do on CT scans.



**Figure 83-11** Abdominal wall varices. Axial contrast-enhanced computed tomography image of the abdomen demonstrating multiple periumbilical varices (*arrow*) in a 48-year-old man with cirrhosis man. In such cases, periumbilical varices may simulate an abdominal wall hernia.

**Ultrasonography.** On Doppler ultrasonography, abdominal wall varices appear as fluid-filled dilated tubular structures, with intraluminal venous flow near the umbilicus.<sup>22</sup>

**Nuclear Medicine.** Abdominal varices result in pooling of technetium-99m–tagged red blood cells within the dilated vessels. Radiotracer localization may mimic scintigraphic findings of acute gastrointestinal hemorrhage. Clinical suspicion and careful evaluation of scintigraphic gastrointestinal bleeding studies will avoid false-positive interpretations.<sup>23</sup>

**Imaging Algorithm.** Ultrasonography is the mainstay for diagnosis of abdominal wall masses, including varices; however, if ultrasound evaluation is limited, MDCT or MRI should be considered (see Table 83-1).

### **Classic Signs: Varices**

- Dilated tubular structures, located within the abdominal wall, demonstrate slow flow on Doppler ultrasonography.
- Slow filling, with delayed enhancement after administration of a contrast agent, can be seen.

### Differential Diagnosis

Abdominal wall varices may simulate hernias, abdominal wall tumors, or excessive scarring after previous surgery (Figure 83-12).

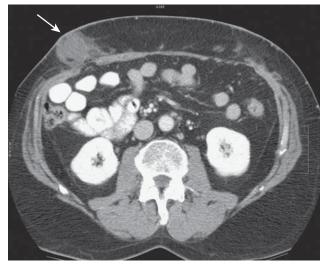
### Treatment

Abdominal wall varices are incidental findings and generally do not require medical treatment; however, these varices may bleed and require surgical ligation.

# **PSEUDOANEURYSMS**

# Etiology

Pseudoaneurysms arise from disruption to the arterial wall, resulting from inflammation, trauma, or iatrogenic causes such as surgical procedures, percutaneous biopsy, or drainage.<sup>24</sup>



**Figure 83-12** Abdominal wall granuloma. Axial contrast-enhanced computed tomography image of the abdomen demonstrates a soft tissue nodule in the ventral abdominal wall (*arrow*) in a 55-year-old patient after spigelian hernia repair. The nodule represented excessive fibrotic tissue after prior surgery.

A pseudoaneurysm is a pulsatile hematoma in the soft tissues with persistent communication between the artery and the extraluminal space.<sup>25,26</sup>

# Pathophysiology

A pseudoaneurysm lacks endothelial lining and differs from a hematoma in that it has direct communication with the arterial lumen.<sup>24</sup>

### Pathology

Pseudoaneurysms predominantly involve the common femoral artery and usually manifest within 2 cm of the arterial puncture site.

# Imaging

Femoral artery pseudoaneurysm causes a localized groin mass with heterogeneous appearance on unenhanced images due to blood products communicating with the arterial lumen.

**Radiography.** Angiography remains the standard of reference for the diagnosis of pseudoaneurysms despite the advent of new imaging technologies.

**Computed Tomography.** Contrast-enhanced CT and CT angiography show a contrast-filled sac. A low-attenuation area within the pseudoaneurysm indicates partial thrombosis. The donor artery adjacent to the pseudoaneurysm can usually be seen communicating with it.<sup>27,28</sup>

**Magnetic Resonance Imaging.** On MRI, pseudoaneurysms have an appearance similar to that on CT. MR angiography is a valuable tool assessing pseudoaneurysms in patients with allergy to iodinated contrast agents.<sup>24</sup>

**Ultrasonography.** A pseudoaneurysm is a cystic structure that typically demonstrates direct communication with the arterial lumen. Swirling of echogenic blood may be seen within the

Document téléchargé de ClinicalKey.fr par Faculte de Medecine de Tunis août 30, 2016. Pour un usage personnel seulement. Aucune autre utilisation n'est autorisée. Copyright ©2016. Elsevier Inc. Tous droits réservés. pseudoaneurysm cavity on real-time examination. On Doppler examination, arterial flow is seen within the pseudoaneurysm. To-and-fro flow between the artery and the pseudoaneurysm also is usually evident.

**Imaging Algorithm.** Ultrasonography is the mainstay for detection and visualization of pseudoaneurysms and associated hematoma (see Table 83-1). Moreover, it permits evaluation of the neck and lumen of the pseudoaneurysm; and, in most cases, ultrasound-guided compression results in complete thrombosis of the pseudoaneurysm. For cases in which additional information is needed, MDCT and/or MRI may be performed.

#### **Classic Signs: Pseudoaneurysms**

- Pseudoaneurysm is a contained vascular perforation.
- On contrast-enhanced studies, pseudoaneurysms show contained contrast extravasation, with a neck (pseudoaneurysm inlet) at the site of vessel perforation.

#### Differential Diagnosis

A hematoma or any inflammatory or neoplastic process may produce a groin mass and local mass effect.<sup>28</sup>

### Treatment

**Medical Treatment.** Ultrasound-guided percutaneous injection of thrombin is an alternative procedure that many authors suggest as the therapeutic method of choice. Technical success rates with this method in the setting of postcatheterization pseudoaneurysms are greater than 90%.<sup>24,29,30</sup>

**Surgical Treatment.** Endovascular management permits exclusion of pseudoaneurysms from the circulation and includes two broad categories: embolization and stent placement.

# **Neoplastic Conditions**

### **ETIOLOGY**

Both primary and secondary neoplasms of the abdominal wall are relatively uncommon. Benign primary tumors include lipoma, neuroma, neurofibroma, and desmoid tumor, which do not typically metastasize but can be locally aggressive. Malignant primary tumors include the spectrum of soft tissue sarcomas. Metastases to the abdominal wall are more common than primary malignancy, and periumbilical involvement may occur secondary to intraperitoneal spread.

### PREVALENCE AND EPIDEMIOLOGY

Abdominal wall neoplasms are rare, accounting for less than 2% of adult malignant tumors. Some subcutaneous lesions may be a manifestation of systemic disease, such as neurofibromas in neurofibromatosis or lipomas in lipomatosis.

The most common primary neoplasm of the abdominal wall is a desmoid tumor, a benign entity with aggressive local behavior.<sup>31</sup> Primary malignant lesions, most commonly sarcomas, occur infrequently and metastatic melanoma is the most frequent secondary malignancy.<sup>32</sup>

### **CLINICAL PRESENTATION**

Although large masses are generally discovered by inspection and palpation, small tumors may be difficult to detect clinically, particularly in obese patients or in those with surgical scars or indurated tissue.

### PATHOPHYSIOLOGY

Malignant primary tumors tend to originate from connective tissues of the abdominal wall, whereas metastases tend to involve subcutaneous tissue but may occur in any compartment of the abdominal wall.

### PATHOLOGY

Pathologic findings vary greatly, according to the specific type of neoplasm.

### IMAGING

### Computed Tomography

MDCT is the mainstay of diagnostic imaging to assess patients with suspected abdominal wall lesions owing to its widespread availability, excellent spatial resolution, and relative lack of susceptibility to motion artifact. Multiplanar and three-dimensional CT reformatted images provide excellent anatomic assessment of these lesions, which is useful when planning operative intervention.

### Magnetic Resonance Imaging

Because of its superior soft tissue contrast, MRI provides important information regarding tumor extension and is particularly useful to facilitate accurate preoperative local staging and surgical planning.

### Ultrasonography

Although ultrasonography is highly operator dependent, it is relatively inexpensive, noninvasive, and widely available, playing an important role in the evaluation of patients with suspected abdominal wall masses.

Ultrasonography provides important information regarding lesion location and extent and may be used for percutaneous image-guided biopsy or percutaneous treatment. The primary limitation of ultrasonography is that it does not demonstrate deep extension of large abdominal wall lesions and may not accurately delineate the relationship of these lesions to underlying bowel.

# Positron Emission Tomography With Computed Tomography

Positron emission tomography with CT (PET/CT) is recommended for staging metastatic disease. Abdominal wall metastases shows avid uptake of 18F-fluorodeoxyglucose (FDG), allowing differentiation from benign nodules. FDG uptake of soft tissue sarcomas is variable, and thus the role of PET/CT in this setting is limited.

#### Imaging Algorithm

The most useful diagnostic imaging techniques for suspected abdominal wall tumors are MDCT, MRI, and ultrasonography, all of which show high anatomic detail, tumor location, and local extension (Table 83-2).

TABLE         Accuracy a           83-2         Accuracy a	and Limitations of the Modalities Used in I	maging of Neoplastic Conditions of the Abdominal Wall
Modality	Accuracy	Limitations
Radiography	Limited availability of source literature	Not useful for small lesions
СТ	for comparing accuracy of different imaging modalities for detecting	Ionizing radiation
MRI	abdominal wall neoplastic lesions	Expensive and not widely available Limited on postoperative patients Patient-limiting factors (e.g., claustrophobia, pacemaker)
Ultrasonography		Obesity, significant scarring, patients with acute abdominal pain Operator dependent
PET/CT		Most wall metastases demonstrate avid FDG uptake. Benign primary lesions do not show FDG uptake.

CT, Computed tomography; FDG, fluorodeoxyglucose; MRI, magnetic resonance imaging; PET, positron emission tomography.

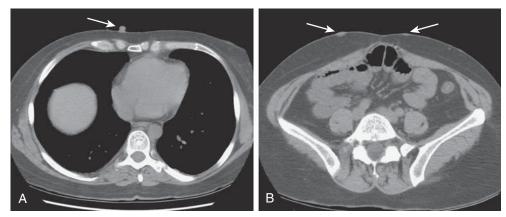


Figure 83-13 Neurofibromatosis. Axial nonenhanced computed tomography images of (A) the lower thorax and (B) abdomen demonstrate multiple soft tissue cutaneous nodules in the anterior abdominal wall (arrows), representing neurofibromas in a 32-year-old man with type 1 neurofibromatosis.

Ultrasonography may be used as the primary imaging modality in patients with suspected abdominal wall lesions. MDCT and MRI are particularly useful to assess local extension and involvement of intra-abdominal structures.

### Imaging of Specific Lesions

**Benign Abdominal Wall Tumors.** Benign abdominal wall tumors are frequent incidental findings on abdominal imaging. This category includes lipoma, neuroma, neurofibroma, and other less common tumors, such as hemangioma and lymphangioma.<sup>33,34</sup>

Lipomas may manifest in the subcutaneous tissue or in the muscular planes. When there is a soft tissue component or an increase in size, malignant degeneration (liposarcoma) should be suspected.<sup>33</sup>

Neurofibromas occur most frequently in patients with neurofibromatosis, manifesting as multiple, small, and well-defined lesions in the subcutaneous tissue of the abdominal wall (Figure 83-13).

Less frequent benign neoplasms include intramuscular hemangiomas, which are vascular lesions arising within the skeletal muscles. They manifest as a painful mass, and there is a slight female predominance.<sup>35-37</sup> Lymphangiomas occur infrequently in the abdominal wall.

*Computed Tomography.* Benign neoplasms have a variable appearance on CT. Lipomas are well-defined, fat-containing lesions located in the subcutaneous tissue or muscular planes



**Figure 83-14** Abdominal wall lipoma. Axial contrast-enhanced computed tomography image demonstrating an abdominal wall lipoma (*arrowheads*) in the left iliac fossa, deep to the external oblique muscle.

(Figure 83-14). When thick, enhancing septations or soft tissue components are seen, malignant degeneration should be suspected.<sup>33</sup>

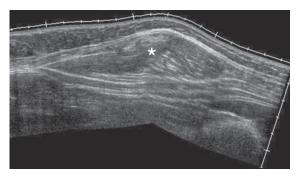
Neurofibromas are well-defined, enhancing soft tissue lesions, with no malignant features.

The appearance of abdominal wall hemangioma on CT is nonspecific and is typically a soft tissue density mass in the abdominal wall musculature. Classically, lymphangiomas appear as low-density lesions, involving and expanding the adjacent muscles, with delayed enhancement. *Magnetic Resonance Imaging.* Lipomas follow fat signal on T1- and T2-weighted images and suppress homogeneously on fat-suppressed images, with no enhancing septations. Neurofibromas are best visualized on delayed, fat-suppressed postgado-linium images and demonstrate well-defined margins and delayed enhancement.

Intramuscular hemangiomas are isointense to surrounding muscle on T1-weighted images and hyperintense on T2-weighted images, showing slow enhancement after administration of a contrast agent.<sup>36,37</sup>

Lymphangiomas follow the appearance of fluid, demonstrating low signal on T1-weighted images and high signal on T2-weighted images. Because of the interstitial nature of gadolinium-based contrast media, they demonstrate delayed homogeneous enhancement.

*Ultrasonography.* The ultrasound appearance of benign abdominal wall neoplasms is variable and usually nonspecific. Lipomas usually appear as highly echogenic, well-marginated lesions in the abdominal wall (Figure 83-15). Neurofibromas appear as nonspecific, well-defined, hypoechoic solid lesions. Hemangiomas and lymphangiomas have a variable appearance and may manifest as a hypoechoic mass or with multiple hypoechoic tubular-like structures with no significant flow on Doppler interrogation.



**Figure 83-15** Abdominal wall lipoma. Ultrasound image of an abdominal wall lipoma (*asterisk*) shows a well-marginated lesion, isoechoic to the subcutaneous fat.

*Positron Emission Tomography With Computed Tomography.* Although useful in differentiating benign from malignant abdominal wall tumors, the role of PET/CT in specific diagnosis of abdominal wall neoplasms is limited.

**Desmoid Tumors and Deep Fibromatosis.** Desmoid tumor, also known as deep fibromatosis or aggressive fibromatosis, is a rare, benign tumor entity associated with familial adenomatous polyposis and Gardner's syndrome. Although rare, desmoids are the most common primary neoplasm of the abdominal wall.<sup>31,38-41</sup>

Desmoid tumors arise from connective tissue and may occur at multiple anatomic sites, preferentially involving the aponeurosis of the rectus abdominis muscle (Figure 83-16), internal oblique, and, less frequently, external oblique muscles.

*Computed Tomography.* A variable-attenuation soft tissue mass is present that causes retraction, angulation, and distortion of adjacent structures, with infiltrative margins and a variable enhancement pattern (Figure 83-17).



**Figure 83-16** Desmoid tumor. Axial contrast-enhanced computed tomography image of the abdomen demonstrating an ill-defined, enhancing soft tissue mass (*arrowheads*), with infiltrative margins, arising from the sheath of the left rectus abdominis muscle in a 41-year-old woman.

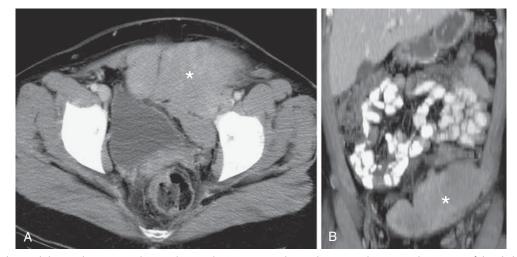


Figure 83-17 Advanced desmoid tumor. Axial (A) and coronal (B) contrast-enhanced computed tomography images of the abdomen in a 35-yearold woman show an enhancing soft tissue mass involving the left anterolateral abdominal wall musculature (*asterisks*), with advanced local spread. Local excision revealed a desmoid tumor.

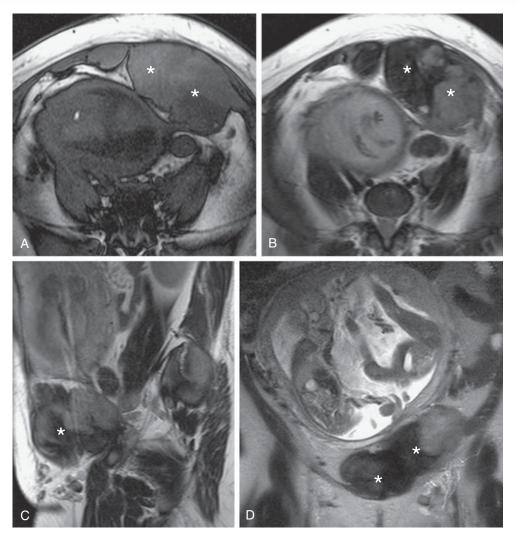


Figure 83-18 Desmoid tumor. Axial (A and B) T1-weighted, gradient recalled echo and (C) sagittal T1-weighted and (D) coronal T2-weighted magnetic resonance images of the lower abdomen demonstrate a heterogeneous mass (*asterisks*) expanding the left-sided rectus abdominal muscle in a 30-year-old pregnant patient (note twin pregnancy) with a desmoid tumor.

*Magnetic Resonance Imaging.* These tumors are hypointense to muscle on T1-weighted images, with variable signal intensity on T2-weighted images depending on proportions of cellular versus fibrous components (Figure 83-18).<sup>41</sup> Variable enhancement occurs after contrast agent administration. MRI is useful to determine tumor resectability.

*Ultrasonography.* On ultrasonography, an ill-defined soft tissue mass of variable echogenicity is seen that has infiltrative margins.

*Positron Emission Tomography With Computed Tomography.* Because of its low metabolic activity, these tumors do not demonstrate FDG uptake.

**Soft Tissue Sarcomas.** Soft tissue tumors of the abdominal wall, although clinically similar to one another, have many distinct histologic subtypes. Soft tissue sarcomas are mesenchymal neoplasms that make up 1% of adult malignancies. Fewer than 5% of these uncommon lesions occur in the abdominal wall. They have a high incidence of local recurrence (25%) and have a propensity for distant metastases, accounting for a substantial mortality rate of 50%.<sup>32,42</sup>

For optimal treatment planning and outcome, histologic diagnosis of the primary tumor is essential. In general, the treatment of choice is surgical resection with an adequate margin of uninvolved tissue.

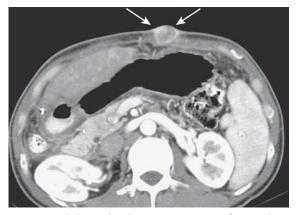
Dermatofibrosarcoma protuberans is the most frequently occurring soft tissue sarcoma of the abdominal wall. It is a low-grade soft tissue tumor, with tendency for local recurrence and metastasis to distant sites. The tumor typically manifests as a discrete, firm subcutaneous nodule that is adherent to the skin but not attached to the underlying fascia or musculature.<sup>32</sup> Less common abdominal wall soft tissue sarcomas include malignant fibrous histiocytoma, fibrosarcoma, synovial sarcoma, liposarcoma, rhabdomyosarcoma, leiomyosarcoma, and others.<sup>32,43</sup>

**Computed Tomography.** On CT there is an ill-defined soft tissue mass that shows retraction, angulation, and distortion of adjacent structures, with an infiltrative pattern and variable enhancing pattern (Figure 83-19).

*Magnetic Resonance Imaging.* MRI will show an ill-defined, soft tissue mass demonstrating infiltrative margins and a variable enhancement pattern.



**Figure 83-19** Abdominal wall sarcoma. Contrast-enhanced computed tomography image shows an enhancing soft tissue mass (*asterisk*) arising from the left lateral wall musculature, with slightly ill-defined margins in a 56-year-old woman. Histologic diagnosis demonstrated a primary soft tissue sarcoma of the abdominal wall.



**Figure 83-20** Abdominal wall metastasis at site of surgical incision. Axial contrast-enhanced computed tomography image demonstrating a soft tissue mass in the anterior abdominal wall (*arrows*), at the incision site for previous right hemihepatectomy for hepatocellular carcinoma in a 52-year-old man with cirrhosis.

*Ultrasonography.* Ultrasound evaluation shows an illdefined, soft tissue mass with variable echogenicity and infiltrative margins.

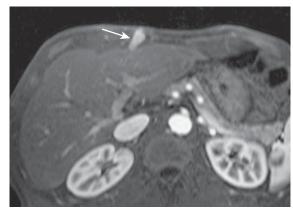
*Positron Emission Tomography With Computed Tomography.* Abdominal wall sarcomas have variable FDG uptake.

**Abdominal Wall Metastases.** Metastases to the abdominal wall are not uncommon, and, although they may occur as an isolated finding, they are more frequently seen in patients with widespread metastatic disease.

Abdominal wall metastases are most frequently secondary to hematogenous spread and involve the abdominal wall muscles or subcutaneous fat. Local spread via surgical incisions (Figure 83-20), tract of percutaneous needle biopsy (Figure 83-21), or port sites after laparoscopy also may occur, particularly in colonic, ovarian, gastric, gallbladder, renal, and hepatic neoplasms.<sup>44-47</sup>

Malignancies that spread intraperitoneally, such as ovarian and gastrointestinal malignancies, tend to involve the umbilical area, producing a periumbilical mass known as Sister Mary Joseph's nodule (Figure 83-22).<sup>48,49</sup>

The abdominal wall also may be locally invaded by malignancies arising from the pleura, peritoneum, or diaphragm (mesothelioma, rhabdomyosarcoma, or fibrosarcoma) or intraabdominal organs (colonic carcinoma) (Figure 83-23).



**Figure 83-21** Seeding via needle biopsy tract. Axial postgadolinium fat-suppressed T1-weighted gradient recalled echo image demonstrates an arterially enhancing nodule in the anterior abdominal wall (*arrow*), 2 months after needle biopsy of right-sided hepatocellular carcinoma (not shown) in a 48-year-old man with cirrhosis. The enhancing nodule represents a metastasis in the needle biopsy track. The patient underwent liver transplant during the interval.

Metastatic melanoma represents the most frequent malignant subcutaneous nodule in the abdominal wall, although it may involve different compartments of the abdominal wall (Figure 83-24). Less common metastases to the abdominal wall include carcinoma of the lung, kidney, breast, and colon. Lymphomatous involvement of the abdominal wall is not uncommon, manifesting as soft tissue thickening with or without local lymphadenopathy (Figure 83-25).<sup>50</sup>

**Computed Tomography.** Abdominal wall metastases appear as well-defined, soft tissue lesions located in the subcutaneous tissue or muscular planes. They demonstrate variable enhancement after contrast agent administration. When large enough, abdominal wall metastases may invade adjacent structures.

*Magnetic Resonance Imaging.* Metastases appear as soft tissue lesions with variable enhancement pattern.

*Ultrasonography.* Abdominal wall metastases are solid lesions of variable echogenicity occurring in the subcutaneous tissue or muscular plane. Ultrasonography is useful when image-guided biopsy or intervention is considered.

*Positron Emission Tomography With Compute Tomography.* Most abdominal wall metastases demonstrate avid FDG uptake. However, small lesions (<5 mm) may not be visible on PET.

# DIFFERENTIAL DIAGNOSIS

Based on clinical data and physical examination, several abdominal wall pathologic processes may be misdiagnosed, including benign and malignant neoplasms, non-neoplastic pathologic processes, and hernias.<sup>34,51</sup>

The differential diagnosis of multiple soft tissue abdominal wall lesions includes metastases and benign tumors such as neurofibromas. Aggressive behavior such as rapid growth or local invasion, as well as a history of widespread metastatic disease, favor malignant tumors. For solitary lesions, tumor growth and clinical findings that suggests local invasion indicate desmoid tumor or primary sarcoma.

Ultrasonography, MDCT, and MRI provide important information regarding the nature of the lesion, number, and local features, thus guiding differential diagnosis. Multiple solid lesions

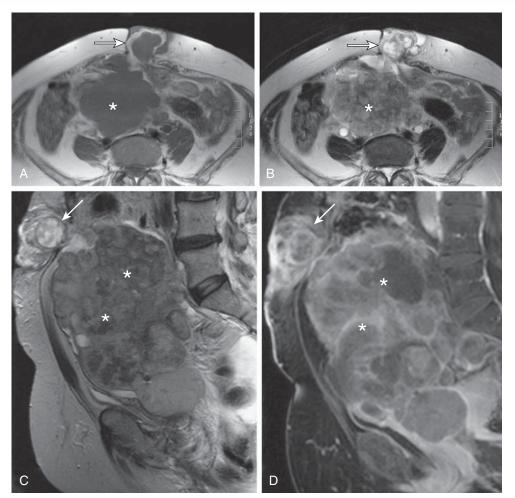


Figure 83-22 Periumbilical metastatic nodule. Axial (A) T1- and (B) T2-weighted and sagittal (C) T2-weighted and (D) postgadolinium T1-weighted fat-suppressed magnetic resonance images demonstrate a complex pelvic mass (*asterisks*) and a periumbilical node (*arrows*), secondary to peritoneal spread of ovarian carcinoma in a 62-year-old woman.

may be metastases, unless occurring in a patient with a known phakomatosis. A solitary lesion with no aggressive local features most probably represents a benign or low-grade neoplasm.

For many cases, imaging features and clinical data are nonspecific and tissue sampling is necessary to make a specific diagnosis.

# TREATMENT

### Medical Treatment

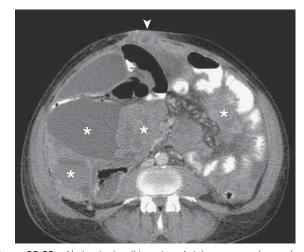
Benign abdominal wall tumors, except desmoids, require no further intervention. Although desmoids are considered benign, their locally aggressive behavior and tendency to relapse requires multidisciplinary treatment, typically consisting of surgery, irradiation, and pharmacologic treatment.

Soft tissue sarcomas have a high tendency to recur after surgery and tend to metastasize early during the clinical course.

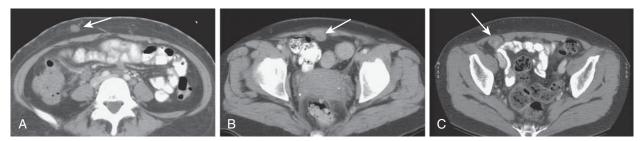
Abdominal wall metastases usually appear in patients with widespread metastatic disease, so systemic or palliative therapy typically is recommended.

### Surgical Treatment

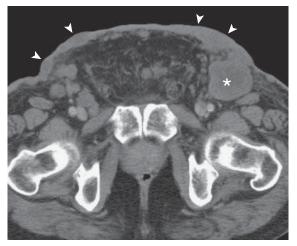
The treatment of choice for aggressive soft tissue tumors is surgical resection with adequate margins of uninvolved tissue; even then, these lesions have a tendency to recur.<sup>32</sup>



**Figure 83-23** Abdominal wall invasion. Axial contrast-enhanced computed tomography image of the abdomen demonstrating extensive intra-abdominal spread of a gastrointestinal tumor (*asterisks*) and local invasion of the anterior abdominal wall (*arrowhead*) in a 51-year-old woman.



**Figure 83-24** Melanoma metastases to the abdominal wall. Axial contrast-enhanced computed tomography images demonstrate the variable distribution of these lesions. A, Subcutaneous metastasis (*arrow*) in a 64-year-old man. B, Metastasis located at the deep aspect of the right rectus abdominis muscle (*arrow*) in a 42-year-old woman. C, Metastasis (*arrow*) to the external iliac lymph node chain, in close proximity to the abdominal wall muscles in a 45-year-old woman.



**Figure 83-25** Abdominal wall lymphoma. Axial contrast-enhanced computed tomography through the lower abdomen demonstrates inguinal lymphadenopathy (*asterisk*) and irregular abdominal wall thickening (*arrowheads*) secondary to lymphomatous involvement in a 61-year-old woman with non-Hodgkin's lymphoma.

### What the Referring Physician Needs to Know

# Abdominal Wall Inflammation, Infection, and Fluid Collections

- Inflammatory disease of the abdominal wall commonly results from a postsurgical wound infection and is less commonly spontaneous or an extension of an intraabdominal source.
- Noninfected collections may occur after surgery or trauma.
- An abscess is a complex fluid collection, with enhancing margins and peripheral inflammatory changes.

# Traumatic Abnormalities, Including Abdominal Wall Hematoma

- Traumatic injuries include laceration, hematoma, and contusion of the abdominal wall.
- The position of the hematoma relative to the arcuate line is important, because hematomas occurring above the arcuate line are contained, whereas those occurring below may extend into the pelvis, resulting in severe blood loss.

### Endometriomas

- Abdominal wall endometriosis should be suspected in patients with cyclic focal pain and tenderness of the abdominal wall, particularly after cesarean section or other uterine surgery.
- Imaging appearance is nonspecific; thus, tissue sampling is almost always necessary to make the diagnosis.
- If medical treatment fails, surgical excision should be considered.

### Varices

• Abdominal wall varices are frequently present in patients with recanalized paraumbilical veins secondary to portal hypertension.

### **Pseudoaneurysms**

- Noninvasive diagnostic modalities should be included in the initial workup.
- A complete workup to determine the location of the pseudoaneurysm and evaluate surrounding structures and relevant vascular anatomy for therapeutic decision is needed, and this may include ultrasonography, CT, or MRI.

#### **Neoplastic Conditions**

- Metastases to the abdominal wall are more common than primary malignancy.
- Desmoid tumor is benign but locally aggressive, demonstrating an infiltrative pattern of growth and a high tendency to recur.
- Primary malignant lesions are rare.
- Abdominal wall metastases usually appear in patients with widespread metastatic disease and reach the abdominal wall via hematogenous, lymphatic, or intraperitoneal spread or via direct extension.
- Metastatic melanoma is the most frequent metastasis to the abdominal wall.

### **Key Points**

# Abdominal Wall Inflammation, Infection, and Fluid Collections

- Localized fluid collections in the abdominal wall are seromas, abscesses, or liquefying hematomas.
- Imaging studies confirm the presence of fluid collections, provide information regarding communication with intra-abdominal content, and may guide percutaneous aspiration or drainage procedures.

# Traumatic Abnormalities, Including Abdominal Wall Hematoma

- Hematomas may be associated with trauma, anticoagulation therapy, blood dyscrasia, or muscular strain associated with vigorous coughing.
- It is important to define anatomic location of the hematoma in relation to the arcuate line.
- Most of the abdominal wall hematomas are treated conservatively. If bleeding is uncontrollable, surgical or radiologic intervention may be necessary.
- Aspiration or drainage of wall hematomas should be avoided, because percutaneous procedures may induce rebleeding or introduce infection.

# Endometriomas

- Abdominal wall endometriomas occur in women of reproductive age, usually after uterine surgery.
- On imaging, an abdominal wall endometrioma is a solid, vascular mass, with or without blood components.

• Imaging appearance is nonspecific, thus tissue sampling is almost always necessary.

### Varices

- Abdominal wall varices are usually incidental findings, reflecting collateral circulation, secondary to portal hypertension or chronic venous obstruction.
- Imaging appearance of abdominal wall varices is characteristic; moreover, CT and MRI usually identify the cause for varices.
- In cases of portal hypertension, varices tend to be localized in the periumbilical area.

### **Pseudoaneurysms**

- Pseudoaneurysms arise from disruption in arterial wall continuity, owing to inflammation, trauma, or iatrogenic causes such as angiography.
- Femoral artery pseudoaneurysm causes a localized vascular groin mass.
- Symptomatic pseudoaneurysms, and pseudoaneurysms with persistent inflow (i.e., persistent communication with vascular lumen), should be treated.
- As a result of technologic advances in ultrasound-guided and endoluminal management of pseudoaneurysms, there is a trend toward minimally invasive management of pseudoaneurysms.
- Ultrasonography, CT, and MRI are the most widely used diagnostic imaging modalities.

# SUGGESTED READINGS

- Berna JD, Garcia-Medina V, Guirao J, et al: Rectus sheath hematoma: diagnostic classification by CT. *Abdom Imaging* 21:62–64, 1996.
- Berna JD, Zuazu I, Madrigal M, et al: Conservative treatment of large rectus sheath hematoma in patients undergoing anticoagulant therapy. *Abdom Imaging* 25:230–234, 2000.
- Bloom RA, Gomori JM, Fields SI, et al: Abdominal wall lipoma: CT and MRI appearance. *Comput Med Imaging Graph* 15:37–39, 1991.
- Cho KC, Patel YD, Wachsberg RH, et al: Varices in portal hypertension: evaluation with CT. *Radiographics* 15:609–622, 1995.
- Ghahremani GG, Gore RM: CT diagnosis of postoperative abdominal complications. *Radiol Clin North Am* 27:787–804, 1989.
- Goldberg SR, Halvorsen RA, Neifeld JP: Vascular tumors of the abdominal wall. *Am J Surg* 187:553–556, 2004.
- Grouwels P, Verswijvel G, Vandevenne J, et al: Abdominal wall desmoid tumor. *JBR-BTR* 90: 190–191, 2007.

- Hensen JH, Van Breda Vriesman AC, Puylaert JB: Abdominal wall endometriosis: clinical presentation and imaging features with emphasis on sonography. AJR Am J Roentgenol 186:616–620, 2006.
- Khati NJ, Enquist EG, Javitt MC: Imaging of the umbilicus and periumbilical region. *Radiographics* 18:413–431, 1998.
- Lee JC, Thomas JM, Phillips S, et al: Aggressive fibromatosis: MRI features with pathologic correlation. AJR Am J Roentgenol 186:247–254, 2006.

Morgan R, Belli AM: Current treatment methods for postcatheterization pseudoaneurysms. J Vasc Interv Radiol 14:697–710, 2003.

- Park CM, Kim SH, Moon MH, et al: Recurrent ovarian malignancy: patterns and spectrum of imaging findings. *Abdom Imaging* 28:404–415, 2003.
- Schlemmer M: Desmoid tumors and deep fibromatoses. *Hematol Oncol Clin North Am* 19:565–571, vii-viii, 2005.
- Sharif HS, Clark DC, Aabed MY, et al: MR imaging of thoracic and abdominal wall infections:

comparison with other imaging procedures. *AJR Am J Roentgenol* 154:989–995, 1990.

- Shiu MH, Weinstein L, Hajdu SI, et al: Malignant soft-tissue tumors of the anterior abdominal wall. *Am J Surg* 158:446–451, 1989.
- Soyer P, Pelage JP, Dufresne AC, et al: CT of abdominal wall implantation metastases after abdominal percutaneous procedures. J Comput Assist Tomogr 22:889–893, 1998.
- Stojadinovic A, Hoos A, Karpoff HM, et al: Soft tissue tumors of the abdominal wall: analysis of disease patterns and treatment. *Arch Surg* 136:70– 79, 2001.
- Teo HE, Peh WC, Shek TW: Case 84: desmoid tumor of the abdominal wall. *Radiology* 236:81– 84, 2005.
- Trerotola SO, Kuhlman JE, Fishman EK: CT and anatomic study of postcatheterization hematomas. *Radiographics* 11:247–258, 1991.
- Woodward PJ, Sohaey R, Mezzetti TP, Jr: Endometriosis: radiologic-pathologic correlation. *Radiographics* 21:193–216, questionnaire 288-194, 2001.

#### **REFERENCES**

- Gokhale S: Sonography in identification of abdominal wall lesions presenting as palpable masses. J Ultrasound Med 25:1199–1209, 2006.
- 2. Goodman P, Raval B: CT of the abdominal wall. *AJR Am J Roentgenol* 154:1207–1211, 1990.
- Sharif HS, Clark DC, Aabed MY, et al: MR imaging of thoracic and abdominal wall infections: comparison with other imaging procedures. *AJR Am J Roentgenol* 154:989–995, 1990.
- Ghahremani GG, Gore RM: CT diagnosis of postoperative abdominal complications. *Radiol Clin North Am* 27:787–804, 1989.
- Virmani V, Sethi V, Fasih N, et al: The Abdominal wall lumps and bumps: cross-sectional imaging spectrum. *Can Assoc Radiol J* 65:9–18, 2014.
- 6. Stamenkovic I, Lew PD: Early recognition of potentially fatal necrotizing fasciitis: the use of
- frozen-section biopsy. N Engl J Med 310:1689–1693, 1984.
- Donnelly LF, Frush DP: Cross-sectional imaging of abnormalities of the abdominal wall in pediatric patients. *AJR Am J Roentgenol* 176:1233– 1239, 2001.
- Weinreb JC, Cohen JM, Maravilla KR: Iliopsoas muscles: MR study of normal anatomy and disease. *Radiology* 156:435–440, 1985.

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- 9. Marron CD, McArdle GT, Rao M, et al: Perforated carcinoma of the caecum presenting as necrotising fasciitis of the abdominal wall, the key to early diagnosis and management. *BMC Surg* 6:11, 2006.
- Trerotola SO, Kuhlman JE, Fishman EK: CT and anatomic study of postcatheterization hematomas. *Radiographics* 11:247–258, 1991.
- Donnelly LF, Johnson JF, 3rd: Unilateral abdominal wall hypoplasia: radiographic findings in two infant girls. *Pediatr Radiol* 25:278–281, 1995.
- Berna JD, Garcia-Medina V, Guirao J, et al: Rectus sheath hematoma: diagnostic classification by CT. *Abdom Imaging* 21:62–64, 1996.
- Cil BE, Turkbey B, Canyigit M, et al: An unusual complication of carotid stenting: spontaneous rectus sheath hematoma and its endovascular management. *Diagn Interv Radiol* 13:46–48, 2007.
- 14. Berna JD, Zuazu I, Madrigal M, et al: Conservative treatment of large rectus sheath hematoma in patients undergoing anticoagulant therapy. *Abdom Imaging* 25:230–234, 2000.
- Khati NJ, Enquist EG, Javitt MC: Imaging of the umbilicus and periumbilical region. *Radiographics* 18:413–431, 1998.
- Hensen JH, Van Breda Vriesman AC, Puylaert JB: Abdominal wall endometriosis: clinical presentation and imaging features with emphasis on sonography. AJR Am J Roentgenol 186:616– 620, 2006.
- Patterson GK, Winburn GB: Abdominal wall endometriomas: report of eight cases. *Am Surg* 65:36–39, 1999.
- Coley BD, Casola G: Incisional endometrioma involving the rectus abdominis muscle and subcutaneous tissues: CT appearance. AJR Am J Roentgenol 160:549–550, 1993.
- Seydel AS, Sickel JZ, Warner ED, et al: Extrapelvic endometriosis: diagnosis and treatment. *Am J Surg* 171:239, 1996.
- Woodward PJ, Sohaey R, Mezzetti TP, Jr: Endometriosis: radiologic-pathologic correlation. *Radiographics* 21:193–216, questionnaire 288-194, 2001.
- Cho KC, Patel YD, Wachsberg RH, et al: Varices in portal hypertension: evaluation with CT. *Radiographics* 15:609–622, 1995.
- 22. De Gaetano AM, Lafortune M, Patriquin H, et al: Cavernous transformation of the portal vein: patterns of intrahepatic and splanchnic collateral circulation detected with Doppler sonography. AJR Am J Roentgenol 165:1151– 1155, 1995.
- 23. Moreno AJ, Byrd BF, Berger DE, et al: Abdominal varices mimicking an acute gastrointestinal

hemorrhage during technetium-99m red blood cell scintigraphy. *Clin Nucl Med* 10:248–251, 1985.

- Saad NEA, Saad WEA, Davies MG, et al: Pseudoaneurysms and the role of minimally invasive techniques in their management. *Radiographics* 25:S173–S189, 2005.
- Altin RS, Flicker S, Naidech HJ: Pseudoaneurysm and arteriovenous fistula after femoral artery catheterization: association with low femoral punctures. *AJR Am J Roentgenol* 152: 629–631, 1989.
- Fellmeth BD, Roberts AC, Bookstein JJ, et al: Postangiographic femoral artery injuries: nonsurgical repair with US-guided compression. *Radiology* 178:671–675, 1991.
- 27. Busquets AR, Acosta JA, Colon E, et al: Helical computed tomographic angiography for the diagnosis of traumatic arterial injuries of the extremities. *J Trauma* 56:625–628, 2004.
- Soto JA, Munera F, Morales C, et al: Focal arterial injuries of the proximal extremities: helical CT arteriography as the initial method of diagnosis. *Radiology* 218:188–194, 2001.
- Morgan R, Belli AM: Current treatment methods for postcatheterization pseudoaneurysms. J Vasc Interv Radiol 14:697–710, 2003.
- La Perna L, Olin JW, Goines D, et al: Ultrasoundguided thrombin injection for the treatment of postcatheterization pseudoaneurysms. *Circulation* 102:2391–2395, 2000.
- Grouwels P, Verswijvel G, Vandevenne J, et al: Abdominal wall desmoid tumor. *JBR-BTR* 90:190–191, 2007.
- 32. Stojadinovic A, Hoos A, Karpoff HM, et al: Soft tissue tumors of the abdominal wall: analysis of disease patterns and treatment. *Arch Surg* 136:70–79, 2001.
- Bloom RA, Gomori JM, Fields SI, et al: Abdominal wall lipoma: CT and MRI appearance. *Comput Med Imaging Graph* 15:37–39, 1991.
- Marinis A, Vassiliou J, Kannas D, et al: Endometriosis mimicking soft tissue tumors: diagnosis and treatment. *Eur J Gynaecol Oncol* 27:168– 170, 2006.
- Goldberg SR, Halvorsen RA, Neifeld JP: Vascular tumors of the abdominal wall. *Am J Surg* 187:553–556, 2004.
- Huff TN, Geiger XJ, Duffy GP, et al: Case report: endometrioma of the abdominal wall. *Clin Orthop Relat Res* 463:221–224, 2007.
- Saad DF, Shehata BM, Patrick E, et al: Intramuscular hemangioma of the abdominal wall. *J Pediatr Surg* 41:601–602, 2006.
- Schlemmer M: Desmoid tumors and deep fibromatoses. *Hematol Oncol Clin North Am* 19:565– 571, vii-viii, 2005.

- Kaplan DB, Levine EA: Desmoid tumor arising in a laparoscopic trocar site. *Am Surg* 64:388– 390, 1998.
- Lee JC, Thomas JM, Phillips S, et al: Aggressive fibromatosis: MRI features with pathologic correlation. *AJR Am J Roentgenol* 186:247–254, 2006.
- Teo HE, Peh WC, Shek TW: Case 84: desmoid tumor of the abdominal wall. *Radiology* 236:81– 84, 2005.
- Shiu MH, Weinstein L, Hajdu SI, et al: Malignant soft-tissue tumors of the anterior abdominal wall. *Am J Surg* 158:446–451, 1989.
- Karadag O, Altundag K, Elkiran ET, et al: Anterior abdominal wall synovial sarcoma: a rare presentation. Am J Clin Oncol 28:323–324, 2005.
- 44. Baron MA, Ladonne JM, Resch B: Abdominal wall metastasis from ovarian cancer after laparotomy: a case report. *Eur J Gynaecol Oncol* 23:561–562, 2002.
- Soyer P, Pelage JP, Dufresne AC, et al: Abdominal wall metastatic tumor seeding along a percutaneous abscess drainage tract. *AJR Am J Roentgenol* 171:1643–1644, 1998.
- Tarantino L, Francica G, Esposito F, et al: Seeding from hepatocellular carcinoma after percutaneous ablation: color Doppler ultrasound findings. *Abdom Imaging* 31:69–77, 2006.
- Goshen E, Davidson T, Aderka D, et al: PET/CT detects abdominal wall and port site metastases of colorectal carcinoma. *Br J Radiol* 79:572–577, 2006.
- Kim CK, Park BK, Choi JY, et al: Detection of recurrent ovarian cancer at MRI: comparison with integrated PET/CT. J Comput Assist Tomogr 31:868–875, 2007.
- Park CM, Kim SH, Moon MH, et al: Recurrent ovarian malignancy: patterns and spectrum of imaging findings. *Abdom Imaging* 28:404–415, 2003.
- Bozas G, Anagnostou D, Tassidou A, et al: Extranodal non-Hodgkin's lymphoma presenting as an abdominal wall mass: a case report and review of the literature. *Leuk Lymphoma* 47:329–332, 2006.
- Wong KT, Lee PS, Chan YL, et al: Paraffinoma in anterior abdominal wall mimicking liposarcoma. *Br J Radiol* 76:264–267, 2003.

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# **Abdominal Wall Hernias**

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# **Etiology**

Abdominal wall hernias, or external hernias (where abdominal contents protrude beyond the abdominal cavity), include inguinal, femoral, umbilical, incisional, spigelian, epigastric, lumbar, and obturator hernias.<sup>1,2</sup> All abdominal wall hernias consist of a peritoneal sac that protrudes through a weakness or defect in the muscular layers of the abdomen. The defect may be congenital or acquired. Weakness of the transversalis fascia, which is the layer immediately outside peritoneum, is the main cause of abdominal wall hernias, especially in the groin.<sup>2-4</sup>

# **Prevalence and Epidemiology**

Abdominal wall hernias are a common clinical problem, especially in elderly patients because of the weakness of the abdominal wall and conditions that increase intra-abdominal pressure. Abdominal wall hernias represent a frequent imaging finding in the abdomen; thus, their actual prevalence and distribution are probably underestimated in the published literature.<sup>5,4</sup>

# **Clinical Presentation**

Most abdominal wall hernias are asymptomatic; however, in the United States, surgery for complications of an external hernia is one of the most common emergent procedures in patients older than 50 years of age.<sup>7</sup> Between 4% and 6% of all diagnosed hernias require emergent surgical repair and are commonly associated with older age, femoral or scrotal location, greater 30-day reoperation risk, and decrease overall survival.<sup>5,8,9</sup> Prompt diagnosis is desirable, because delayed treatment is associated with greater morbidity.<sup>10</sup>

# Pathophysiology

Hernias can occur in any portion of the abdominal wall; however, inguinal, umbilical, epigastric, para-umbilical, incisional, and femoral hernias were the most commonly reported hernias in a recent review by Dabbas and colleagues<sup>11</sup> (Figure 84-1). They usually manifest at points of weakness of the abdominal wall, where no muscle is present, along the midline, in the linea semilunaris on each side, and in the inferior lumbar space.

Abdominal wall hernias may be acquired or congenital. Acquired hernias are more frequently seen in patients who are obese or elderly or in those with previous trauma or surgery. Congenital hernias include indirect inguinal hernias and gastroschisis and omphalocele, occurring lateral to or at the umbilicus, respectively.

# Imaging

In the past, the diagnosis of a hernia was made clinically or by means of plain radiographs or barium studies. Increasingly, diagnosis is made by computed tomography (CT) or ultrasonography.<sup>1,12</sup> Cross-sectional imaging is required when the clinical presentation is misleading or inconclusive or in the presurgical assessment of the contents of an incarcerated hernia.

# RADIOGRAPHY

Small, noncomplicated abdominal wall hernias are not seen on conventional radiographs. In some cases, such as in patients with a large wall defect or large hernia sac, the hernia may be visible. In these cases, air-, fluid-, or stool-filled loops are seen in abnormal locations in the abdomen, most frequently in the inguinal or umbilical area (Figure 84-2).

In some cases of complicated abdominal wall hernia, such as bowel incarceration or strangulation, conventional radiographs allow detection of signs of mechanical ileus, bowel loop enlargement, thickening of intestinal folds and air/fluid levels.<sup>12</sup>

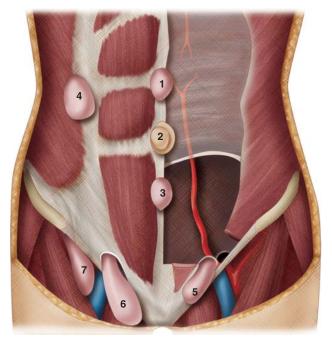
In the past, the diagnosis of abdominal wall hernias was confirmed with barium studies or intraperitoneal administration of iodinated contrast agents.<sup>3,14</sup> In current clinical practice, conventional radiography, barium studies, and herniography no longer play a pivotal role in the diagnosis of abdominal wall hernias.

## COMPUTED TOMOGRAPHY

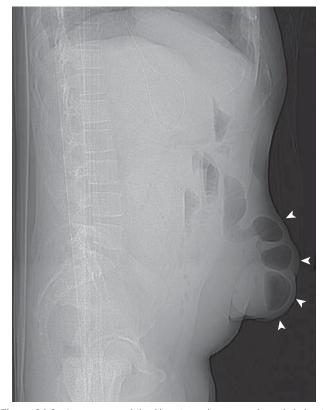
For abdominal wall hernias, CT shows the specific anatomic site of the hernial sac; its shape, connections, and contents; and characteristics of the wall defect. Hernias can be distinguished from masses of the abdominal wall (e.g., tumor, hematoma, abscess, undescended testis, and aneurysm). CT also allows assessment for the presence of complications (e.g.,

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**Figure 84-1** Diagram of the anterior abdominal wall, depicting site of abdominal wall hernias: 1, supraumbilical hernia; 2, umbilical hernia; 3, infraumbilical hernia; 4, spigelian hernia; 5, direct inguinal hernia; 6, indirect inguinal hernia; 7, femoral hernia.



**Figure 84-2** Large paraumbilical hernia as shown on a lateral abdominal radiograph in a 66-year-old man. Note the air-filled colonic loops herniating into the subcutaneous tissue (*arrowheads*) through a paraumbilical defect. Abdominal wall hernias are seen infrequently on conventional radiographs.



**Figure 84-3** Axial reformatted contrast-enhanced computed tomography image demonstrates a strangulated left indirect inguinal hernia. Note the C-shaped, thick-walled, herniated small bowel loops associated with moderate mesenteric fat stranding. Also note the contralateral displacement of the inferior epigastric vessels (arrowhead).

incarceration, bowel obstruction, volvulus, and strangulation) (Figure 84-3).<sup>4,7,15-19</sup>

Most CT protocols for hernia evaluation include oral and intravenous contrast agent administration. However, owing to the high resolution of modern CT scanners, intravenous use of a contrast agent may not be necessary, especially in patients with abnormal renal function. Some authors advocate image acquisition while the patient performs the Valsalva maneuver to increase intra-abdominal pressure, which may aid in demonstrating some hernias, particularly those involving the ventral abdominal wall.<sup>20</sup>

Multidetector row CT (MDCT) is now widely available and is pivotal in assessing patients with suspected abdominal wall hernia. It has a short acquisition time, good coverage, and excellent resolution. Moreover, three-dimensional information and multiplanar reformatted images provide excellent anatomic depiction of abdominal wall anatomy and useful information for surgical planning. MDCT is considered the first imaging choice when complications of abdominal wall hernias are suggested.

# MAGNETIC RESONANCE IMAGING

The role of magnetic resonance imaging (MRI) in assessing the abdominal wall is evolving. MRI can detect and characterize hernias with a sensitivity of 91%, specificity of 92%, positive predictive value of 97%, and negative predictive value of 79% considering laparoscopy as the gold standard. Useful sequences include coronal three-dimensional T1-weighted images without fat saturation during Valsalva maneuver and, at rest, axial turbo spin echo T2-weighted and axial short tau inversion recovery (STIR) comparing both groins.<sup>21-26</sup>

# ULTRASONOGRAPHY

Ultrasonography is a relatively inexpensive, noninvasive, and widely available modality that plays a pivotal role in evaluating

TABLE 84-1	Accuracy, L	imitations, and Pitfalls of the	Modalities Used in Imaging of Abdominal Wall Hern	ias
Modal	ity	Accuracy	Limitations	Pitfalls
Radiog CT MRI	ıraphy	There is limited availability of source literature for comparing accuracy of different imaging modalities for detecting abdominal wall hernias.	Not useful for small defects Ionizing radiation Expensive and not widely available Limited spatial resolution Limited on postoperative patients Patient-limiting factors (e.g., claustrophobia, pacemaker)	
Ultrasc	pnography		Body habitus, significant scarring of overlying tissues, patients in distress Operator dependent Requires high-frequency transducer	Lipoma of the spermatic cord or abdominal wall

CT, Computed tomography; MRI, magnetic resonance imaging.

patients with suspected abdominal wall hernias. No patient preparation is required. Ultrasonography allows dynamic evaluation (e.g., during Valsalva maneuver) to confirm herniation of intra-abdominal contents through a wall defect. However, when necessary, it requires flotation pads to achieve best resolution and avoid the "bang effect" of direct transducer placement on the skin.<sup>27,28</sup>

# **IMAGING ALGORITHM**

Ultrasonography should be used as the primary imaging modality in asymptomatic patients with suspected abdominal wall hernia on physical examination and in children and women of child-bearing age.<sup>21</sup> Ultrasonography is particularly useful in thin patients and may add information regarding complications in patients with acute presentation. However, its utility in obese patients or in patients with abdominal wall scarring may be limited.

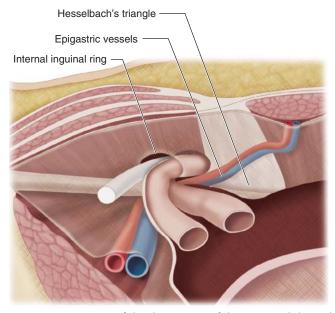
MDCT provides excellent anatomic detail and is particularly useful in patients who are obese or who have significant abdominal wall scarring and when physical examination is limited. In addition, because the entire abdomen is visualized, MDCT may detect subtle signs of complications such as bowel obstruction, incarceration, and strangulation. Hence, MDCT is the imaging modality of choice in patients with suspected complicated abdominal wall hernia. (Tables 84-1 and 84-2).

# **Imaging of Specific Lesions**

## **INGUINAL HERNIAS**

Inguinal hernias represent the most common type of abdominal wall hernias. They may occur in children (indirect most common) and adults (direct and indirect) and manifest medial (direct) or lateral (indirect) to the inferior epigastric vessels. Regardless of age, inguinal hernias are more common in males than in females. In children, most inguinal hernias develop because the peritoneal extension accompanying the testis fails to obliterate. In adults, they are caused by acquired weakness and dilation of the internal inguinal ring,<sup>4</sup> which is a defect in the fascia transversalis.

Indirect inguinal hernias are more commonly seen in men, where the hernia sac passes through the internal or deep inguinal ring into the scrotum, anteromedially to the spermatic cord, and lateral to the epigastric vessels (Figure 84-4). In females, an indirect inguinal hernia follows the round ligament into the



**Figure 84-4** Diagram of the deep aspect of the anterior abdominal wall depicting a left indirect inguinal hernia. The hernia sac protrudes through the internal inguinal ring, located lateral to the epigastric vessels. Note Hesselbach's triangle, located medial and inferior to the epigastric vessels.

labia majora. In some cases, indirect herniated content may pass all the way into the scrotum (known as a complete hernia) and may contain intestine (small bowel or colon), mesenteric fat, the appendix, foreign bodies, bladder, ureter, or any peritoneal cavity content (fluid, air).

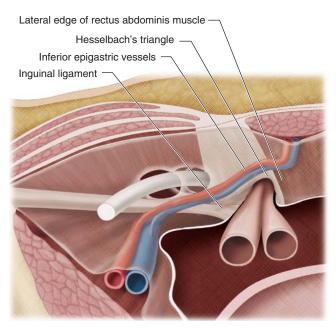
Direct inguinal hernias are located medial to the inferior epigastric vessels, are thought to be acquired, appear between 30 and 40 years of age, and are often bilateral. They run lateral to the remains of the obliterated umbilical artery and are contained by the aponeurosis of the external oblique muscle (Figure 84-5). Unlike the indirect inguinal hernias, the direct hernia sac lies behind the spermatic cord and is unlikely to reach the scrotum.

### Radiography

In some cases, including those with large wall defects or large hernia sacs, inguinal hernias may be visible as air-, fluid- or stool-filled bowel loops in the inguinal area.

TABLE     Key Imaging Findings of Abdominal Wall Hernias						
Hernia Type	Imaging Features	Preferred Modality	Clinical Significance			
INGUINAL HEI	INGUINAL HERNIAS					
Indirect	Lateral to epigastric vessels	US or MDCT	Common in men; may pass into the scrotum			
Direct	Medial to epigastric vessels	US or MDCT	Often bilateral; do not pass into the scrotum or labia majora			
Femoral	Medial to femoral vessels	MDCT	High tendency to incarcerate			
VENTRAL HER	NIAS					
Umbilical	Around the umbilicus	US or MDCT	Prone to incarceration and			
Hypogastric	Below the umbilicus—midline	US or MDCT	strangulation			
Epigastric	Above the umbilicus—midline	US or MDCT				
Paraumbilical	Lateral to the umbilicus	MDCT	Related to diastasis of rectus abdominis muscles			
Spigelian	Linea semilunaris	MDCT	High frequency of incarceration			
LUMBAR HER	VIAS					
Superior	Below the 12th rib	MDCT	Asymptomatic; strangulation is			
Inferior	Above iliac crest	MDCT	uncommon			
INCISIONAL H	ERNIAS					
Parastomal	Lateral to stoma site	MDCT	May cause bowel obstruction			
PELVIC HERNI	AS					
Obturator	Through obturator foramen	MDCT	Prone to incarceration and			
Sciatic	Through sciatic foramen	MDCT	strangulation			
Perineal	Through pelvic floor	MDCT	Most frequent; no emergent treatment required			
OTHER HERNI	OTHER HERNIAS					
Richter	Herniation of antimesenteric wall of the bowel—usually femoral hernia	MDCT	Prone to incarceration and			
Littre	Herniation of Meckel's diverticulum—inguinal hernias	MDCT	strangulation			
Interparietal	Between fascial planes of abdominal wall	MDCT				

MDCT, Multidetector computed tomography; US, ultrasonography.



**Figure 84-5** Diagram of the deep aspect of the anterior abdominal wall depicting a left direct inguinal hernia. The hernia sac protrudes through Hesselbach's triangle, which is bounded by the inferior epigastric vessels, lateral edge of the rectus abdominis muscle, and inguinal ligament.

# Computed Tomography

CT allows visualization of the following:

- Abdominal wall defect
- Hernia sac, medial (direct inguinal hernia [Figure 84-6]) or lateral (indirect inguinal hernia [see Figure 84-3]) to the epigastric vessels in the inguinal region
- Hernia content, which may include intra-abdominal fat, bowel loops, appendix, foreign bodies, bladder, and ascites In cases in which the hernia sac contains bowel loops, signs

of incarceration, obstruction, or strangulation should be sought.

# Magnetic Resonance Imaging

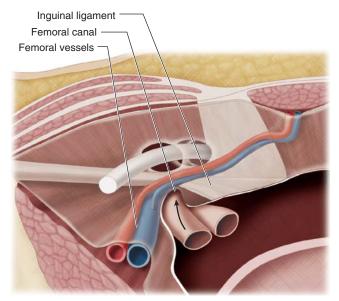
Visualization of abdominal wall discontinuity and the hernia sac with intra-abdominal contents may be seen on MRI.

# Ultrasonography

Ultrasonography allows visualization of abdominal wall discontinuity and protrusion of intra-abdominal contents into the subcutaneous tissue. Assessment should be made of hernial sac content and, in males, the degree of extension into the scrotum. Dynamic evaluation should be performed during Valsalva's maneuver, in which the hernia sac should become larger, unless the contents are incarcerated. Because the superficial and inferior epigastric vessels are not easily seen on ultrasonography, distinction between direct and indirect inguinal hernias may not be possible.



**Figure 84-6** Axial unenhanced computed tomography image demonstrating herniation of mesenteric fat through the internal inguinal ring (*arrowhead*).



**Figure 84-7** Diagram of the deep aspect of the anterior abdominal wall depicting a left femoral hernia. The hernia sac protrudes through the femoral canal (*arrow*) medial to the femoral vessels and inferior to the inguinal ligament.

## **FEMORAL HERNIAS**

Femoral hernias are far less frequent than inguinal hernias and are especially rare in children. They occur more commonly in women and, for unclear reasons, have a tendency to be right sided.<sup>19</sup> They arise from a defect in the attachment of the transversalis fascia to the pubis and thus occur medial to the femoral vein and posterior to the inguinal ligament (Figure 84-7).<sup>20</sup> They are difficult to differentiate clinically from inguinal hernias and have a tendency to incarcerate.<sup>5,19</sup>

### Computed Tomography

The hernia sac is located medial to the femoral vessels, protruding into the upper thigh (Figure 84-8). CT helps differentiate hernia from other causes of an inguinal mass, such as lymph node, hematoma, abscess, pseudoaneurysm, arteriovenous fistula, lipoma, hydrocele, saphenous varix, or undescended



**Figure 84-8** Axial unenhanced computed tomography image through the pelvis demonstrates a right femoral hernia, containing small bowel loops with no signs of complication in a 65-year-old man. Note the hernia sac (*arrow*) located medial to the femoral vessels (*arrowhead*).

testis. CT permits identification of complications, principally incarceration, owing to small size of hernia defect.

### Magnetic Resonance Imaging

Abdominal wall discontinuity and hernia sac and contents located medial to the femoral vessels can be seen on MRI.

#### Ultrasonography

Ultrasonography can show a mass medial to the femoral vein, but femoral hernias are difficult to identify in obese patients.

# **VENTRAL HERNIAS**

Ventral hernias include all hernias through the anterior and lateral abdominal wall, aside from inguinal hernias. Midline defects include umbilical, paraumbilical, epigastric, and hypogastric hernias.

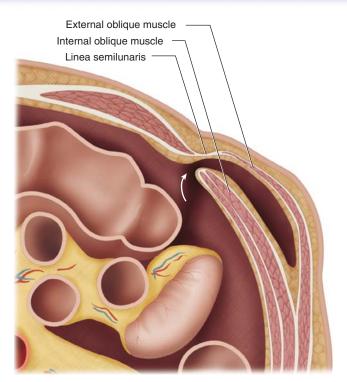
In adults, umbilical hernias are by far the most common ventral hernias; they are usually small and are particularly common in women. Risk factors include multiple pregnancies, ascites, obesity, and large intra-abdominal masses.<sup>12,19,20</sup>

Paraumbilical hernias are large abdominal defects through the linea alba in the region of the umbilicus, usually related to diastasis of the rectus abdominis muscles. Epigastric and hypogastric hernias occur in the linea alba, above or below the umbilicus, respectively.

Strangulation and incarceration of midline hernias is frequent. Clinical diagnosis is difficult: physical examination is limited, especially in obese patients, and symptoms are nonspecific.

Lateral defects include a spigelian hernia, which is a rare, acquired anterior hernia through the linea semilunaris. It is a fibrous union of the rectus sheath with the aponeuroses of the transverse and oblique abdominal muscles that extends from the level of the ninth costal cartilage to the symphysis pubis. These hernias occur lateral to the rectus muscle and below the umbilicus and are almost always found just above the point where the inferior epigastric vessels pierce the posterior wall of the rectus sheath.

The hernial sac protrudes through the aponeurosis of the transversus abdominis and the internal oblique muscles and



**Figure 84-9** Diagrammatic axial view of the abdomen at the level of the umbilicus depicting an interparietal spigelian hernia. Note the hernia sac (*arrow*) protruding through the linea semilunaris without exiting into the subcutaneous tissue, herniating between the internal and external oblique muscles.

dissects laterally, beneath an intact external oblique aponeurosis and muscle (Figure 84-9). When the external oblique aponeurosis is also defective, the hernial sac can be subcutaneously located and can be confused with lipoma of the abdominal wall if the muscular defect is not recognized (Figure 84-10). This is a complete spigelian hernia. Spigelian hernias have a high frequency of incarceration.

### Computed Tomography

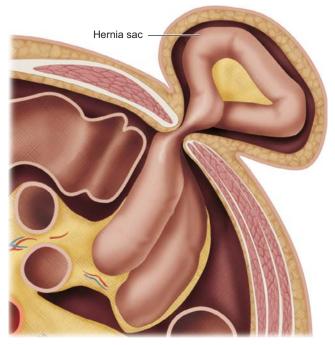
On CT, diastasis and atrophy of the rectus abdominis muscles with protrusion of intra-abdominal contents into the abdominal wall may be frequently seen in midline hernias (Figure 84-11). The most frequently herniated intra-abdominal content is omental fat, although hernia sacs also may contain small or large bowel loops and, less frequently, portions of the stomach or the liver.

CT permits identification of complications, principally incarceration, owing to the small size of hernia defect.

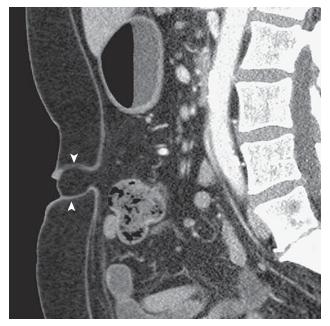
Spigelian hernias demonstrate protrusion of mesenteric fat through a defect in the linea semilunaris, between the rectus abdominis and aponeuroses of the transversus abdominis and internal oblique muscles (Figure 84-12). The subcutaneous hernia sac can be confused with an abdominal wall lipoma if the muscular defect is not recognized. Clinical diagnosis is very difficult in these patients.

# Magnetic Resonance Imaging

The MRI features of a ventral hernia are very similar to those on MDCT. MRI is useful for differentiating ventral wall hernias from lipomas or other soft tissue masses.



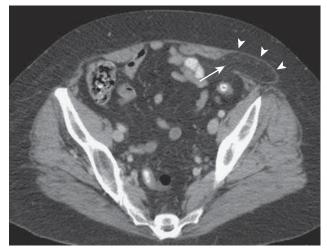
**Figure 84-10** Diagrammatic axial view of the abdomen at the level of the umbilicus depicting a complete spigelian hernia. As in incomplete hernias the hernia sac protrudes through the linea semilunaris. However, in complete hernias the hernia sac protrudes through the complete thickness of the wall musculature.



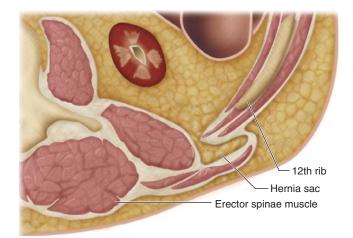
**Figure 84-11** Sagittal contrast-enhanced computed tomography image shows an umbilical hernia (*arrowheads*) containing intraabdominal fat with no signs of complications in a 44-year-old man with umbilical pain and a difficult physical examination.

## Ultrasonography

Ultrasonography can show a hernia sac on the ventral abdominal wall protruding through the linea semilunaris or the linea alba. This modality is particularly useful for imaging thin patients and children. It permits dynamic evaluation of the



**Figure 84-12** Axial contrast-enhanced computed tomography image below the level of the umbilicus demonstrating an incomplete spigelian hernia through the linea semilunaris on the left side of the abdomen. Note the hernia sac (*arrow*) contained beneath the external oblique muscle (*arrowheads*).



**Figure 84-13** Diagrammatic axial view of the abdomen through the superior lumbar triangle. Note the hernia sac containing retroperitoneal fat herniating through the superior lumbar triangle, bordered by the internal oblique muscle anteriorly, the 12th rib superiorly, and the erector spinae muscle posteriorly.

hernia during Valsalva maneuver, for better delineation of wall defect, content, and assessment for incarceration. It is limited in evaluating atrophy or diastasis of the rectus abdominis muscles, particularly in obese patients or in those with excessive abdominal scarring.

# LUMBAR HERNIAS

Lumbar hernias occur through defects in the lumbar muscles or the posterior fascia, below the 12th rib and above the iliac crest. Herniation may occur through the superior (Grynfeltt-Lesshaft [more frequent]) or through the inferior (Petit [less frequent]) lumbar triangle. They usually occur after surgery or trauma.

The superior lumbar triangle is defined by the internal oblique muscle anteriorly, the 12th rib superiorly, and the erector spinae muscle posteriorly (Figure 84-13). The inferior lumbar triangle

is bordered by the external oblique muscle anteriorly, the iliac crest inferiorly, and the latissimus dorsi muscle posteriorly. Diffuse lumbar hernias also may occur, usually after flank incisions for kidney operations, and may contain bowel loops, retroperitoneal fat, kidneys, or other viscera.

Lumbar hernias are usually asymptomatic. Because the neck of the hernias is wide, strangulation is uncommon. It is postulated that they occur more frequently in women because of the wider female pelvis.<sup>1,12</sup>

## Computed Tomography

CT clearly demonstrates herniation of intra-abdominal contents through the abdominal wall in the lumbar triangles, demonstrating the size of the abdominal defect and the contents (Figure 84-14). Lumbar hernias may demonstrate intraperitoneal or extraperitoneal contents. Multiplanar capabilities of MDCT permit excellent anatomic depiction of the wall defect in the inferior or superior lumbar triangles.

# Magnetic Resonance Imaging

The appearance of a lumbar hernia on MRI is very similar to that seen on MDCT. Because of its multiplanar capabilities, MRI also demonstrates clearly the exact anatomic location of the wall defect in the lumbar area.

#### Ultrasonography

Lumbar hernias are difficult to identify on ultrasonography, particularly in obese patients, but may become visible when the hernia sac is large.

# INCISIONAL AND OTHER HERNIAS

Incisional hernia is a delayed complication of abdominal surgery and occurs in 0.5% to 13.9% of patients. Most incisional hernias develop during the first months after surgery, and now they have become the most common hernia repair procedure.<sup>5,16,20,29</sup>

Parastomal hernias are commonly seen after end-colostomy (4% to 48.1%) and end-ileostomy (1.8% to 28.3%).<sup>30</sup>

Less frequent hernias include the interparietal, Richter, and Littre types. Interparietal or interstitial hernia refers to a hernia sac located in the fascial planes between the abdominal wall muscles, without exiting into the subcutaneous tissue; this hernia type occurs most commonly in the inguinal region (see Figure 84-9). Richter's hernia is a type of abdominal wall hernia for which only part of the antimesenteric wall of the bowel becomes incarcerated in the hernia defect; this is frequently associated with femoral hernias (Figure 84-15). A Littre's hernia is an inguinal hernia containing a Meckel's diverticulum. All of these uncommon abdominal hernias are particularly prone to incarceration and strangulation.

### Computed Tomography

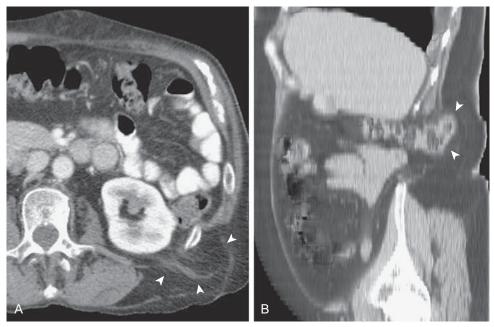
CT demonstrates the wall defect at the location of previous abdominal surgery. In parastomal hernias, CT shows bowel loops protruding through the wall defect at the stoma site. For interparietal hernias, CT demonstrates the hernia sac between the abdominal wall muscles, without exiting into the subcutaneous tissue (see Figure 84-15).

# Magnetic Resonance Imaging

The appearance of incisional hernias on MRI is similar to that on MDCT. For small wall hernias, MRI is less useful than MDCT (Figure 84-16).

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**Figure 84-14** A, Axial contrast-enhanced computed tomography (CT) image through the mid-pole of the left kidney demonstrating a superior lumbar hernia in a 61-year-old man. Note herniation of the retroperitoneal fat into the subcutaneous tissue (*arrowheads*). B, Sagittal reformatted contrast-enhanced CT image in a different patient demonstrates a superior lumbar hernia (*arrowheads*) containing large bowel loops, with no signs of complications.



**Figure 84-15** Axial contrast-enhanced computed tomography image demonstrating herniation of the antimesenteric border of the transverse colon through a paraumbilical incisional defect in a 43-year-old woman. Note that only part of the circumference of the transverse colon is herniated (*arrowheads*), characteristic of a Richter type of hernia.

## Ultrasonography

Because of scarring, detection and visibility of incisional hernias is limited on ultrasound evaluation. Also, detection of interparietal, Richter's, and Littre's hernias is very limited.

# PELVIC HERNIAS

Pelvic hernias usually occur in elderly women secondary to acquired weakness of the pelvic floor. Sciatic (Figure 84-17) and obturator (Figure 84-18) hernias are rare and usually manifest as herniation of small bowel loops or ureters through the sciatic or obturator foramen, respectively. Perineal hernias manifest more frequently and occur adjacent to the anus or labia majora or in the gluteal region.



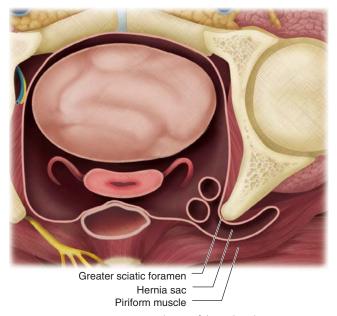
**Figure 84-16** Axial T2-weighted magnetic resonance imaging (MRI) of the abdomen demonstrates an incisional type of ventral hernia in the right upper quadrant. Note herniation of the hepatic flexure of the colon (*arrowheads*). Incidentally, there is a simple cyst in the left kidney (*asterisk*). MRI shows abdominal wall anatomy in great detail and clearly depicts the abdominal wall defect and hernia content.

# Computed Tomography

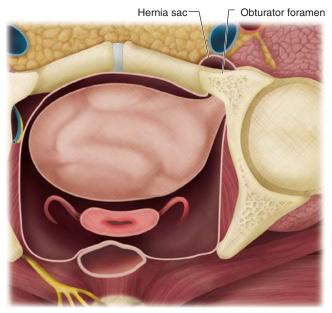
On CT, sciatic hernias can be seen to pass through the greater or lesser sciatic foramen, most commonly involving the small bowel or the distal ureter. Obturator hernias pass through the obturator foramen, extending between the pectineal and obturator muscles (Figure 84-19). Perineal hernias occur through the pelvic floor, adjacent to the anus and labia majora or in the gluteal region.

# Magnetic Resonance Imaging

The multiplanar capabilities of MRI permit adequate depiction of pelvic hernias; however, small pelvic hernias may not be evident.



**Figure 84-17** Diagrammatic axial view of the pelvis depicting a sciatic hernia. The hernia sac protrudes through the greater sciatic foramen. Note posterior displacement of the piriform muscle, which also exits through the sciatic foramen.



**Figure 84-18** Diagrammatic axial view of the pelvis depicting an obturator hernia. The hernia sac protrudes through the obturator foramen.

# Ultrasonography

Ultrasonography is of limited use in identifying and localizing pelvic hernias.

# COMPLICATIONS OF ABDOMINAL WALL HERNIAS

The most common abdominal wall hernia complications are incarceration, strangulation, and bowel obstruction. Although complications can be detected on clinical evaluation, at least



**Figure 84-19** Axial unenhanced computed tomography image through the lower pelvis demonstrating small bowel loops herniating through the left-sided obturator foramen. Note fluid-filled small bowel loops (*asterisk*) located between the obturator and pectineus muscles (*arrowheads*).

47% of patients with abdominal wall hernias can present without typical physical examination findings (no palpable inguinal defect or reducible mass).<sup>21,31</sup> Imaging studies are required when the clinical presentation is misleading or inconclusive or when preoperative assessment of the hernia or secondary obstruction is required.<sup>32</sup>

# **Bowel Obstruction**

After adhesions, abdominal wall hernias are the second leading cause of small bowel obstruction and account for 10% to 15% of all small bowel obstructions. Most cases of bowel obstruction secondary to wall hernias occur after incarceration and strangulation. In these cases, bowel obstruction occurs with the transition point at the level of the hernia.

# Incarceration

Incarceration refers to an irreducible hernia. It is diagnosed clinically when a hernia cannot be reduced or pushed back manually. The diagnosis of incarceration cannot be made with imaging alone but can be suggested when herniation occurs through a small defect and the hernia sac has a narrow neck (Figure 84-20). Impending strangulation of incarcerated hernias should be suspected when there is free fluid within the hernia sac, bowel wall thickening, or luminal dilation.<sup>32</sup>

### Strangulation

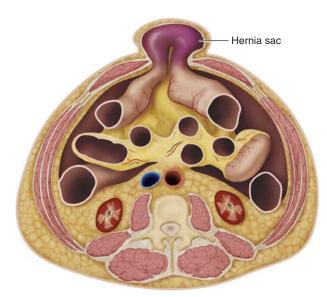
Hernia strangulation refers to ischemia caused by compromised blood supply. It usually occurs when the hernia defect obstructs the afferent and efferent bowel loops, creating a closed loop of herniated bowel (Figure 84-21). Strangulated abdominal wall hernias are associated with a high operative fatality rate (6% to 23%).<sup>33</sup>

#### Trauma

Hernias may be complicated by trauma in two ways: a hernia may be caused by trauma (traumatic hernia), or there may be trauma to a previously existing hernia. The most common locations are areas of relative anatomic weakness—the lumbar region and the lower abdomen.<sup>7</sup>



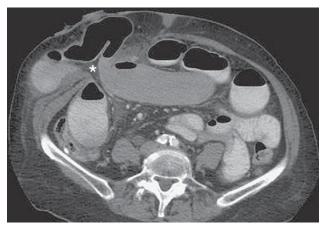
**Figure 84-20** Incarcerated hypogastric incisional hernia. Axial contrast-enhanced computed tomography image demonstrates an incarcerated midline incisional hernia (*arrowheads*) at the level of the hypogastrium in a 48-year-old woman, presenting with abdominal pain. Note the relatively small hernia defect compared with the caliber of herniated bowel loops.



**Figure 84-21** Diagrammatic axial view of the abdomen depicting a strangulated paraumbilical hernia. Note the hernia sac containing small bowel loops, which demonstrate abnormal perfusion secondary to strangulation at the neck of the hernia.

The patient with previously known abdominal wall hernia who presents after high-impact trauma should be scrutinized for the presence of fluid within the hernia sac, bowel wall thickening, asymmetric bowel wall enhancement, vessel engorgement, and fat stranding within the hernia sac or in surrounding soft tissues. These findings should alert the radiologist to traumatic injury of a preexisting abdominal wall hernia, which usually requires operative management.

**Computed Tomography.** Key CT findings of bowel obstruction include dilated bowel proximal to the hernia and normalcaliber, reduced-caliber, or collapsed bowel distal to the obstruction. The degree of caliber change helps predict the



**Figure 84-22** Axial contrast-enhanced computed tomography image demonstrating a strangulated spigelian hernia in a 63-year-old man who presented with bowel obstruction. Note the narrow hernia neck (*asterisk*) and dilatation of herniated bowel loops in a C-shaped configuration.

grade of obstruction.<sup>34,35</sup> Other findings may include tapering of the afferent and efferent limbs at the hernia defect, dilatation of the herniated loops, and "fecalization" of small bowel contents proximal to the obstruction.

MDCT findings of strangulation are those of closed-loop obstruction and ischemia. Closed-loop findings include dilated, fluid-filled, U- or C-shaped loops of bowel entrapped within the hernia sac and proximal obstruction (Figure 84-22). Findings of ischemia include wall thickening, abnormal mural hypoattenuation or hyperattenuation and enhancement, mesenteric vessel engorgement, fat obliteration, mesenteric haziness, and ascites (see Figure 84-3). MDCT permits reliable diagnosis and assessment of traumatic hernias, including characterization of hernia content, visualization of disrupted abdominal muscle layers, and identification of associated intraabdominal injuries. It also permits visualization of findings within a hernia sac that could represent injury to a preexisting abdominal wall hernia.

**Magnetic Resonance Imaging.** MRI is rarely used in the acute setting of suspected complication of an abdominal wall hernia.

**Ultrasonography.** Ultrasound evaluation may show fluid in the hernia sac, abnormal wall thickening of the herniated bowel loops, and even the transition point in cases of strangulation, with proximal bowel dilatation. However, clinicians and radiologists should not rely on ultrasonography alone to exclude the presence of a complicated abdominal wall hernia.

# WALL HERNIA REPAIRS

Several surgical procedures are employed in the repair of abdominal wall hernias, ranging from open or laparoscopic suture repair to the use of a mesh.<sup>36-39</sup> Complications such as hernia recurrence, fluid collections, or infection may occur after abdominal wall hernia repair.

# Computed Tomography

According to the components, the mesh material may or may not be visible on MDCT. Mesh made of polypropylene,

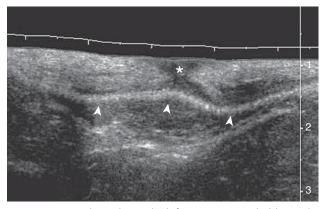


Figure 84-23 High-resolution, high-frequency sagittal oblique ultrasound image of the abdominal wall through the umbilicus in a 45year-old man after umbilical hernia repair with mesh. Note the thin echogenic line (arrowheads) located deep to the abdominal wall, corresponding to the mesh. Also note the umbilicus, with no recurrent hernia (asterisk).

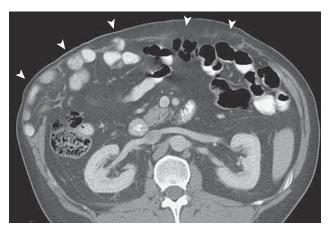


Figure 84-24 Axial contrast-enhanced computed tomography image shows abdominal wall eventration (arrowheads). Bowel loops herniate into the subcutaneous tissue, and no anterior abdominal wall is seen.

consisting of 0.44-mm-thick monofilaments, is not visible on CT owing to its intermediate attenuation, which is similar to that of surrounding tissues. In contrast, mesh made of expanded polytetrafluoroethylene, a high-attenuation 1-mm macrofilament, is visible as a linear high-attenuation structure.

MDCT provides important information regarding the presence of postoperative fluid collections, such as seroma, hematoma, or abscess (showing multiple septations, air locules, enhancing rim, and fat stranding in surrounding tissues) or recurrent hernias.

### Magnetic Resonance Imaging

The role of MRI for the evaluation of hernia repairs is limited, particularly for visualization of the mesh and for detection of recurrent hernias. However, it may provide information regarding the presence and extension of postoperative fluid collections.

### Ultrasonography

Ultrasonography may demonstrate mesh as an echogenic linear band, located deep to the abdominal wall (Figure 84-23). However, it may become invisible if surrounded by fibrous tissue that demonstrates similar echogenicity. However, ultrasonography is a valuable method to detect postoperative fluid collections and infections. Seromas characteristically demonstrate anechoic fluid; when complicated by hemorrhage or infection, they appear more complex, with septations and/or layering and low-level echoes representing blood cells or debris. Moreover, fluid collections may be aspirated percutaneously under ultrasound guidance.

# **Differential Diagnosis**

Based on physical examination, several abdominal wall pathologic processes may be clinically misdiagnosed as hernias, including benign (lipomas, hemangiomas, fibromas) and malignant tumors (metastases, primary sarcomas, and desmoid tumors). Other pathologic processes that may mimic wall hernias on physical examination include eventration (Figure 84-24), gas collections within the abdominal wall, enlarged inguinal lymph nodes, undescended testis, and enlarged vessels in the abdominal wall.

The MDCT and ultrasound appearance of wall hernias is characteristic, providing specific diagnosis according to the anatomic location. Dynamic imaging during a Valsalva maneuver may provide additional information by augmenting the wall defect and hernia sac content, confirming the diagnosis.

# Treatment

Surgical treatment is recommended for most patients with abdominal wall hernias, with the aim of avoiding complications. Medical treatment or clinical observation is reserved for patients with significant comorbidities, in whom surgical treatment may be contraindicated.

To prevent acute complications, external hernias are usually repaired electively, and surgical correction of hernias is currently the most frequent major operation performed by general surgeons in the United States.<sup>40</sup>

### What the Referring Physician Needs to Know

- Abdominal wall hernias are a frequent imaging finding; and although most are asymptomatic, they usually require surgical treatment to prevent complications.
- Abdominal wall hernias may occur anywhere in the abdominal wall; however, groin and ventral hernias are the most common sites.
- MDCT and ultrasonography play a major role in accurately identifying wall hernias, extent of the wall defect, hernia sac contents, and presence of complications. MDCT is the modality of choice for evaluating the complications of abdominal wall hernias.
- The most common complication of abdominal wall hernia is bowel obstruction, secondary to incarceration or strangulation. Incarceration refers to an irreducible hernia, and strangulation refers to ischemia caused by a compromised blood supply.
- Hernias secondary to high-impact trauma tend to occur in the areas of relative anatomic wall weakness-the lumbar region and lower abdomen.
- Abdominal wall hernia repairs may be visible on MDCT or ultrasound imaging. MDCT is particularly useful for detecting hernia recurrence.

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### **Key Points**

- Inguinal hernias: Most frequent wall hernias
- Direct inguinal hernias: Medial to inferior epigastric vessels; usually occur in adults
- Indirect inguinal hernias: Lateral to inferior epigastric vessels; occur in children and adults
- Femoral hernias: Difficult to diagnose; medial to femoral vessels; high frequency of incarceration
- Ventral hernias: Most frequently at the linea alba or linea semilunaris
- SUGGESTED READINGS
- Aguirre DA, Casola G, Sirlin C: Abdominal wall hernias: MDCT findings. AJR Am J Roentgenol 183:681-690, 2004.
- Aguirre DA, Santosa AC, Casola G, et al: Abdominal wall hernias: imaging features, complications, and diagnostic pitfalls at multi-detector row CT. Radiographics 25:1501–1520, 2005.
- Bennett HF, Balfe DM: MR imaging of the peritoneum and abdominal wall. Magn Reson Imaging Clin N Am 3:99-120, 1995.
- Harrison LA, Keesling CA, Martin NL, et al: Abdominal wall hernias: review of herniography and

#### REFERENCES

- 1. Aguirre DA, Casola G, Sirlin C: Abdominal wall hernias: MDCT findings. AJR Am J Roentgenol 183:681-690, 2004.
- 2. Miller PA, Mezwa DG, Feczko PJ, et al: Imaging of abdominal hernias. Radiographics 15:333-347, 1995.
- 3. Harrison LA, Keesling CA, Martin NL, et al: Abdominal wall hernias: review of herniography and correlation with cross-sectional imaging. Radiographics 15:315-332, 1995.
- 4. Lee GH, Cohen AJ: CT imaging of abdominal hernias. AJR Am J Roentgenol 161:1209-1213, 1993
- 5. Beadles CA, Meagher AD, Charles AG: Trends in emergent hernia repair in the United States. JAMA Surg 150:194-200, 2015.
- 6. Kingsnorth A, LeBlanc K: Hernias: inguinal and incisional. Lancet 362:1561-1571, 2003.
- 7. Killeen KL, Girard S, DeMeo JH, et al: Using CT to diagnose traumatic lumbar hernia. AJR Am J Roentgenol 174:1413-1415, 2000.
- 8. Abi-Haidar Y, Sanchez V, Itani KM: Risk factors and outcomes of acute versus elective groin hernia surgery. J Am Coll Surg 213:363-369, 2011.
- 9. Hernández-Irizarry R, Zendejdas B, Ramirez T, et al: Trends in emergent inguinal hernia surgery in Olmsted County, MN: a population-based study. Hernia 16:397-403, 2012.
- 10. Yu CY, Lin CC, Yu JC, et al: Strangulated transmesosigmoid hernia: CT diagnosis. Abdom Imaging 29:158-160, 2004.
- 11. Dabbas N, Adams K, Pearson K, et al: Frequency of abdominal wall hernias: is classical teaching out of date? JRSM Short Rep 2:5, 2011.
- 12. Aguirre DA, Santosa AC, Casola G, et al: Abdominal wall hernias: imaging features, complications, and diagnostic pitfalls at multi-detector row CT. *Radiographics* 25:1501–1520, 2005.
- 13. Lassandro F, Iasiello F, Pizza N, et al: Abdominal hernias: radiological features. World J Gastrointest Endosc 3:110-117, 2011.
- 14. Toms AP, Dixon AK, Murphy JM, et al: Illustrated review of new imaging techniques in the diagnosis of abdominal wall hernias. Br J Surg 86:1243-1249, 1999.

correlation with cross-sectional imaging. Radiographics 15:315-332, 1995.

- Ianora AA, Midiri M, Vinci R, et al: Abdominal wall hernias: imaging with spiral CT. Eur Radiol 10:914-919, 2000.
- Meuwly JY, Gudinchet F: Sonography of the thoracic and abdominal walls. J Clin Ultrasound 32:500-510, 2004.
- Miller PA, Mezwa DG, Feczko PJ, et al: Imaging of abdominal hernias. Radiographics 15:333-347, 1995.

- Umbilical hernias: Most frequent ventral hernia; more frequent in women
- Lumbar hernias: Usually asymptomatic (wide neck, strangulation is uncommon)
- Incisional hernias: A delayed complication of surgery; more common in vertical than transverse incisions
- Pelvic hernias: Most frequent in elderly women owing to acquired weakness of the pelvic floor

Zarvan NP, Lee FT, Jr, Yandow DR, et al: Abdominal hernias: CT findings. AJR Am J Roentgenol 164:1391–1395, 1995.

2003.

- 15. Goodman P, Balachandran S: Postoperative atrophy of abdominal wall musculature: CT demonstration. J Comput Assist Tomogr 15:989–993, 1991.
- 16. Ghahremani GG, Iimenez MA, Rosenfeld M, et al: CT diagnosis of occult incisional hernias. AJR Am J Roentgenol 148:139–142, 1987.
- 17. Goodman P, Balachandran S: CT evaluation of the abdominal wall. Crit Rev Diagn Imaging 33:461-493, 1992.
- 18. Ianora AA, Midiri M, Vinci R, et al: Abdominal wall hernias: imaging with spiral CT. Eur Radiol 10:914-919, 2000.
- Zarvan NP, Lee FT, Jr, Yandow DR, et al: 19. Abdominal hernias: CT findings. AJR Am J Roentgenol 164:1391-1395, 1995.
- 20. Emby DJ, Aoun G: CT technique for suspected anterior abdominal wall hernia. AJR Am J Roentgenol 181:431-433, 2003.
- 21. Miller J, Cho J, Michael M, et al: Role of imaging in the diagnosis of occult hernias. JAMA Surg 149:1077-1080, 2014.
- 22. Van den Berg JC: Inguinal hernias: MRI and ultrasound. Magn Res Imag Clin North Am 12:689-705, 2004.
- 23. van den Berg JC, de Valois JC, Go PM, et al: Dynamic magnetic resonance imaging in the diagnosis of groin hernia. Invest Radiol 32:644-647, 1997.
- 24. van den Berg JC, de Valois JC, Go PM, et al: Groin hernia: can dynamic magnetic resonance imaging be of help? Eur Radiol 8:270-273, 1998.
- 25. Musella M, Milone F, Chello M, et al: Magnetic resonance imaging and abdominal wall hernias in aortic surgery. J Am Coll Surg 193:392-395, 2001.
- 26. Bennett HF, Balfe DM: MR imaging of the peritoneum and abdominal wall. Magn Reson Imaging Clin N Am 3:99-120, 1995.
- 27. Moreno Gallego A, Aguayo JL, Flores B, et al: Ultrasonography and computed tomography reduce unnecessary surgery in abdominal rectus sheath haematoma. Br J Surg 84:1295-1297, 1997.
- 28. Meuwly JY, Gudinchet F: Sonography of the thoracic and abdominal walls. J Clin Ultrasound 32:500-510, 2004.

29. Singh P, Kaushik R, Sharma R, et al: Umbilical port hernia following laparoscopic cholecystectomy. J Minim Access Surg 2:29-30, 2006.

Rutkow IM: Demographic and socioeconomic aspects of hernia repair in the United States in

Toms AP, Cash CC, Fernando B, et al: Abdominal

Semin Ultrasound CT MR 23:143-155, 2002.

2003. Surg Clin North Am 83:1045-1051, v-vi,

wall hernias: a cross-sectional pictorial review.

- Carne P, Robertson GM, Frizelle FA, et al: Para-30. stomal hernia. Br J Surg 90:784–793, 2003.
- 31. Neblett WW, 3rd, Pietsch JB, Holcomb GW, Jr: Acute abdominal conditions in children and adolescents. Surg Clin North Am 68:415-430, 1988.
- 32. Rettenbacher T, Hollerweger A, Macheiner P, et al: Abdominal wall hernias: cross-sectional imaging signs of incarceration determined with sonography. AJR Am J Roentgenol 177:1061-1066, 2001.
- 33. Bendavid R: Complications of groin hernia surgery. Surg Clin North Am 78:1089-1103, 1998.
- 34. Boudiaf M, Soyer P, Terem C, et al: CT evaluation of small bowel obstruction. Radiographics 21:613-624, 2001.
- 35. Furukawa A, Yamasaki M, Takahashi M, et al: CT diagnosis of small bowel obstruction: scanning technique, interpretation and role in the diagnosis. Semin Ultrasound CT MR 24:336-352, 2003.
- 36. Koning GG, Wetterslev J, van Laarhoven CJ, et al: The totally extraperitoneal method versus Lichtenstein's technique for inguinal hernia repair: a systematic review with meta-analyses and trial sequential analyses of randomized clinical trials. PLoS ONE 8:52599, 2013.
- 37. Yang J, Tong N, Yao da J, et al: Laparoscopic or Lichtenstein repair for recurrent inguinal hernia: a meta-analysis of randomized controlled trials. ANZ J Surg 83:312-318, 2013.
- 38. Courtney CA, Lee AC, Wilson C, et al: Ventral hernia repair: a study of current practice. Hernia 7:44-46, 2003.
- Crespi G, Giannetta E, Mariani F, et al: Imaging 39 of early postoperative complications after polypropylene mesh repair of inguinal hernia. Radiol Med (Torino) 108:107-115, 2004.
- Rutkow IM: Surgical operations in the United 40. States: then (1983) and now (1994). Arch Surg 132:983-990, 1997.

85

# Response Evaluation Criteria in Solid Tumors, World Health Organization, and Other Response Criteria

NAVEEN M. KULKARNI | ANTHONY E. SAMIR

Monitoring the response of tumors to treatment has become an integral component of oncologic imaging. Imaging studies play a vital role in objective assessment by quantifying tumor response to a variety of physical and pharmaceutical treatments. Traditionally, therapeutic response has been assessed by conventional methods that involve serial tumor burden measurements according to the World Health Organization (WHO) and Response Evaluation Criteria in Solid Tumors (RECIST) criteria.<sup>1,2</sup> Computed tomography (CT) and magnetic resonance imaging (MRI) provide reliable and reproducible anatomic data to determine changes in tumor burden through treatment. However, the management of many tumors has extended beyond traditional chemotherapy and novel targeted therapies (such as antiangiogenic agents) have been introduced. With respect to targeted therapy, changes in tumor dimension may not be evident in the early course of treatment and measurement alone has been shown to have limitations. At the same time, to maximize the effectiveness of care, it is important to differentiate between responders and nonresponders as early as possible. Hence, monitoring effects from these expensive targeted therapies has introduced new expectations from imaging techniques. Conventional measurement-based methods are still widely used, but new techniques are being increasingly adopted. Emerging techniques such as positron emission tomography (PET or PET/CT) can be used to look at changes in tumor metabolism. There has been growing interest in the use of tumor viability measurement, dynamic contrast-enhanced imaging, or perfusion imaging to assess tumor vascular microenvironment and early antiangiogenic effects.<sup>3</sup> Other advances in MRI such as diffusion weighted imaging (DWI) are also evolving as biomarkers of cellular integrity. Despite availability of various imaging techniques, it is challenging to determine the most appropriate image biomarker to serve as a surrogate end point of treatment response. An ideal imaging biomarker should be noninvasive, objectively quantitative, reproducible, readily available, validated, and easy to implement in the clinical setting. This chapter discusses various established and emerging and evolving imaging biomarkers, the criteria of response evaluation, and their challenges.<sup>1-6</sup>

# Response Criteria Based on Tumor Burden Measurement

# WORLD HEALTH ORGANIZATION CRITERIA

Response evaluation with diagnostic imaging has continuously evolved since the late 1970s. It has been generally accepted that a decrease in tumor size correlates with treatment effect. In view of this, the WHO first published a set of tumor response criteria in 1981, which was mainly used in clinical trials in which tumor response was the primary end point. The WHO criteria for tumor burden assessment were based on summing bidimensional, or two-dimensional (2D), measurements. The WHO criteria received wide acceptance, but were soon realized to have potential pitfalls such as no information on minimum lesion size or the number of lesions to be selected in patients with multiple lesions, the type of imaging modality that should be used, and lack of clarity among some definitions of response criteria. For example, a 25% increase in the product of 2D diameters (progressive disease) was defined by some investigators as increase in any one lesion and by others as increase in the sum of all selected lesions.

It was observed that many research trials initiated by pharmaceutical companies often modified WHO criteria to address areas that lacked clarity and also to accommodate new technologies (such as multidetector CT [MDCT]), and this led to variability and potential for overestimation or underestimation in clinical trial results.<sup>1,2</sup>

# RESPONSE EVALUATION CRITERIA IN SOLID TUMORS CRITERIA

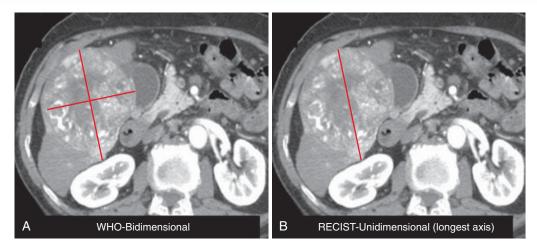
# RECIST 1.0

To address limitations of the WHO criteria, an International Working Committee was formed to standardize WHO criteria so that meaningful comparisons could be made among clinical trial studies. This led to the proposed RECIST criteria (version 1.0) in 2000. Important updates for RECIST criteria include adoption of unidimensional measurement (i.e., longest diameter) in RECIST versus bidimensional measurement in the WHO (Figure 85-1), specification on tumor type that should be selected as tumor target, number of tumor targets in total and per organ to be chosen, broadening of the cutoff point defining progressive disease, and recommending the type of imaging that should be used. Even with introduction of RECIST 1.0, some important questions and issues remained unaddressed, such as assessment of lymph nodes, role of new imaging modalities such as PET/CT and MRI and if fewer than 10 lesions can be assessed without affecting the conclusion on response assessment. The RECIST Working Group subsequently revised the original criteria, and RECIST version 1.1 was released in 2008<sup>1,2,7</sup> (Table 85-1).

### RECIST 1.1

The guidelines defining tumor measurements by RECIST are simple, easy to apply, and quantitative. Optimization of image

<sup>1029</sup> 



**Figure 85-1** Target lesion measurement according to the WHO and RECIST criteria. (A) With the WHO criteria, the longest tumor diameter and a second diagonal that is perpendicular and longest are obtained and multiplied (two-dimensional measurement). (B) With RECIST, only the longest diameter is obtained. On subsequent follow-up, the longest diameter measurement should follow any change in tumor shape and is independent of previous study results.

TABLE 85-1				
Key Fe	eatures	RECIST 1.1	RECIST 1.0	
Measu metl	rement hod	Longest tumor diameter for extranodal lesions	Longest tumor diameter	
	: lesion asurable on) size	At least 10 mm on CT	10 mm on spiral and 20 mm on conventional CT	
Numb targ lesic	et	Total of 5 and up to 2 lesions per organ	Total of 10 target lesions and up to 5 per organ	
Assess lymp node		ent of Short axis measurement Not specified recorded. Target nodal lesion ≥15 mm, ≥10 mm, and ≤15 mm pathologic		
	cation lisease gression	>20% increase in the sum of longest dimensions of target lesions (>5 mm absolute increase is required) and new lesions	>20% increase in the sum of target lesions (no absolute increase is required) and new lesions	
lmagin moc	ng Ialities	Chest x-ray, CT, and MRI	CT, MRI, and FDG-PET (PET included for lesion detection only.) Chest x-ray can be used but not preferred	

Data from Eisenhauer EA: Response evaluation: beyond RECIST. Ann Oncol 18(Suppl 9):ix29–ix32, 2007; and Eisenhauer EA, Therasse P, Bogaerts J, et al: New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 45:228–247, 2009.

CT, Computed tomography; FDG, fluorodeoxyglucose; MRI, magnetic resonance imaging; PET, positron emission tomography.

acquisition protocols at baseline and throughout follow-up examinations is essential for proper application of RECIST 1.1. Contrast-enhanced CT continues to be the most widely used modality. It is recommended to acquire CT images in the portal venous phase of contrast enhancement. For purposes of consistency, it is prudent to reconstruct 5-mm slices (or less) contiguously. To avoid partial volume averaging effects and inconsistent measurements of the same lesion (either target lesion or lymph node or non–lymph node) between serial examinations, the target lesion should be at least twice the slice thickness at baseline—that is, 10 mm if slice thickness is 5 mm. This principle is also applicable to MRI examinations. Measurements and comparisons should be performed on the same pulse sequence on serial studies.<sup>1,2</sup> Measurement on a chest radiograph is acceptable if the lesion is surrounded by pulmonary parenchyma, but is not preferred owing to the lack of 3D.<sup>2</sup>

# MEASURABILITY OF TUMOR BURDEN

### Target Lesion (Measurable Lesion)

Extranodal target lesions should meet the size criterion of 10 mm or greater in the longest dimension (see Figure 85-1). A lymph node is considered pathologically enlarged and measurable by RECIST 1.1 if the short axis measures 15 mm or greater on contrast-enhanced CT. At baseline and on subsequent posttreatment time points, the longest dimension of extranodal target lesions and short axis measurement of the node is used for assessing tumor burden and to monitor response.<sup>1,2</sup> With respect to bone lesions, either lytic or mixed lytic-blastic bone lesions with soft tissue components can be considered measurable lesions as long as the soft tissue component meets the definition of measurability. In RECIST 1.1, blastic bone lesions are considered nonmeasurable. When both cystic and solid metastases are present, solid lesions are preferred as selectable target lesions. Lesions located in a previously irradiated area are not considered target lesions unless there is demonstrable progression in lesion size.<sup>1,2,8</sup>

#### Nonmeasurable Lesion

This includes organ lesions with longest diameter less than 10 mm and lymph nodes 10 mm or greater to less than 15 mm short axis. Other truly nonmeasurable lesions include leptomeningeal disease, ascites, pleural or pericardial effusion, lung lymphangitis, and skin carcinomatosis. Lymph nodes with short axis less than 10 mm are considered nonpathologic and should not be recorded or followed.<sup>1,2</sup>

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	RECIST 1.1 Criteria for Tumor Response Assessment
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Complete response	Disappearance of all target lesions or lymph nodes decreased to <10 mm in the short axis
Partial response	>30% decrease in sum of longest diameters of target lesions
Progressive disease	>20% increase in sum of longest diameters of target lesions with an absolute increase of ≥5 mm; new lesions
Stable disease	None of the above

Data from Eisenhauer EA: Response evaluation: beyond RECIST. Ann Oncol 18(Suppl 9):ix29–ix32, 2007; and Eisenhauer EA, Therasse P, Bogaerts J, et al: New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 45:228–247, 2009.

### Tumor Response Evaluation

Measurable disease is defined by the presence of at least one target (measurable) lesion. At baseline, when more than one target lesion is present, all lesions up to a maximum of five lesions in total and a maximum of two lesions per organ representative of all involved organs should be identified as target lesions to record their measurement at baseline and each time point. It is preferable that the target lesion be clearly defined, be suitable for repeat measurement, and not have been previously treated with local-regional therapy. All other lesions and disease sites, including pathologic lymph nodes (as described earlier), are designated as nontarget lesions, and only their presence should be recorded at baseline. A sum of the longest diameters (SLD) for all target lesions is calculated, reported, and followed to assess response. When lesions are too small to measure, a default value of 5 mm is assigned. If they disappear completely, the measurement is recorded as 0 mm. When a target lesion fragments into multiple smaller lesions, the longest dimension of all fragmented portions are added to the sum. If target lesions coalesce, the longest dimension of the resulting coalescent lesion should be taken.<sup>1,2</sup>

Measurements are not required for nontarget lesions, which are followed as "present," "absent," or, uncommonly, "unequivocal progression." The appearance of unequivocal new lesions indicates disease progression. If there are unequivocal lesions, progression should be reassessed on follow-up examinations.

### **RESPONSE CATEGORIES**

### Target Lesion Evaluation

The defined response on imaging is categorized as CR (extranodal target lesions have disappeared, and all lymph nodes measure <10 mm in short axis), PR (at least a 30% decrease in SLD of tumor burden), PD (tumor burden increase of at least 20% with an absolute change in SLD of at least 5 mm), and SD (neither PR nor PD) (Table 85-2).<sup>1,2</sup>

### Nontarget Lesion Evaluation

Any nontarget lesions should be assessed only qualitatively at all time points even if they have measurable size. The responses are categorized as CR (disappearance of all nontarget lesions, normalization of tumor marker level and regression of pathologic lymph nodes to <10 mm in short axis), Non-CR/non-PD (persistence of one or more nontarget lesion(s) and/or maintenance of tumor marker level above the normal limits), and

# TABLE<br/>85-3Overall Responses for Possible Combinations<br/>of Tumor Responses in Target, Nontarget,<br/>and New Lesions Based on RECIST 1.1

Target Lesions	Nontarget Lesions	New Lesions	Overall Response
CR	CR	No	CR
CR	Non-CR/non-PD	No	PR
CR	NE	No	PR
PR	Non-PD or NE	No	PR
SD	Non-PD or NE	No	SD
PD	Any	Yes or No	PD
Any	PD	Yes or No	PD
Any	Any	Yes	PD
Not all evaluate	Non-PD	No	NE

Data from Eisenhauer EA: Response evaluation: beyond RECIST. Ann Oncol 18(Suppl 9):ix29-ix32, 2007; and Eisenhauer EA, Therasse P, Bogaerts J, et al: New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 45:228-247, 2009.

*CR*, Complete response; *NE*, not evaluable; *PD*, progressive disease; *PR*, partial response; *SD*, stable disease.

PD (unequivocal progression of existing nontarget lesions) (Table 85-3).<sup>1,2</sup>

### **Overall Response**

Based on response outcome of target and nontarget lesion(s) evaluation, overall response is evaluated (Table 85-3).<sup>1,2</sup>

Although RECIST has gained popularity in evaluating treatment response, it has inherent limitations such as subjectivity in lesion selection and inconsistent imaging protocol. Moreover, with targeted therapies, morphologic changes within tumors lag behind physiologic and molecular changes. Hence, RECIST is not suited to monitor early effects of these novel therapies.<sup>1,2</sup>

# Role of Volumetric and Functional Imaging

Due to lack of standardization, widespread availability, and being labor intensive (in the case of volumetric technique), the working group has not adopted these methods in response assessment by RECIST. The only exception is utility of fluorodeoxyglucose (FDG)-PET to complement CT in assessing disease progression. A positive follow-up FDG-PET with negative FDG-PET at baseline is considered disease progression. In the setting of positive follow-up FDG-PET and absent baseline FDG-PET, new disease site is confirmed where there is a correlate on CT, otherwise follow-up CT scan is recommended to confirm this (if confirmed, the date of abnormal FDG-PET scan will be the date of PD). A positive FDG-PET at follow-up that correlates to anatomically stable disease is not considered PD.<sup>1-3,7,9-11</sup>

# Response Assessment Based on Tumor Density Measurement

# CHOI CRITERIA

Tumor x-ray attenuation measured in Hounsfield units (HU) on contrast-enhanced CT can serve as an additional method for

TABLE 85-4	Choi Response Criteria		
Respo Categ		Definition	
CR		Resolution of all lesions and no new lesions	
PR		A decrease in size of ≥10% (longest dimension of tumor) or decrease in tumor attenuation (Hounsfield units) of ≥15%. No appearance of new lesions	
PD		≥10% increase in tumor size (longest dimension), does not meet PR tumor attenuation criteria and new lesions	
SD	None of the above		

Choi H: Critical issues in response evaluation on computed tomography: lessons from the gastrointestinal stromal tumor model. Curr Oncol Rep 7:307–311, 2005.

*CR*, Complete response; *NE*, not evaluable; *PD*, progressive disease; *PR*, partial response; *SD*, stable disease.

response assessment, as described by Choi.<sup>12</sup> Its role was first studied in gastrointestinal stromal tumors (GISTs) treated with imatinib mesylate.<sup>12</sup> Unlike regular chemotherapy, the targeted therapies differ in mechanism of action, such as inhibiting tumor angiogenesis. Tumors treated with targeted therapies may not demonstrate change in tumor burden as seen with standard cytotoxic therapies. Therefore, traditional criteria based on tumor burden assessment cannot be applied to assess response for tumors such as GISTs when treated with targeted therapies.<sup>12</sup>

Reduced tumor radiodensity on portal venous phase CT has shown a correlation with underlying tumor necrosis after therapy without substantial changes in tumor bulk. Tumor attenuation is measured by drawing a region of interest (ROI) circumscribing the margin of the tumor in the portal venous phase. The average Hounsfield units of the target lesions is computed before and after therapy. Response categories and definitions are provided in Table 85-4.<sup>12</sup> Hounsfield unit measurement has the advantage of being a simple approach, does not require expertise, and can be performed on a routine imaging workstation. The Choi response criteria have been used in assessment of other solid tumors. Some of the studies have suggested utility of Choi criteria in response evaluation of early metastatic renal cell carcinoma treated with sunitinib and in soft tissue sarcoma treated with chemotherapy and radiation therapy.<sup>12-14</sup>

# Modified Response Evaluation Criteria in Solid Tumors

Treatment assessment based on changes in tumor burden alone also can be misleading when applied to hepatocellular carcinoma (HCC). The management of HCC has evolved over many years, and recently novel therapeutic approaches have been introduced. There is growing interest in customizing treatment tailored to suit each individual patient, needing early and accurate assessment of tumor response to therapy. Conventional biomarker such as RECIST has been applied to HCC. However, with targeted treatment, response evaluation based on conventional RECIST alone can be less informative and lag behind biologic changes.<sup>15,16</sup> In 2008, expert groups convened by the European Association for the Study of the Liver (EASL) and American Association for the Study of Liver Diseases (AASLD) introduced the concept of including tumor enhancement in the arterial phase of contrast-enhanced imaging studies, which led Target Response Assessment by Modified RECIST for Hepatocellular Carcinoma (American Association for the Study of Liver Diseases–Journal of the National Cancer Institute Guidelines) and Comparison to <u>RECIST 1.1</u>

TABLE

85-5

Response Categories	mRECIST	RECIST 1.1
CR	Disappearance of arterial enhancement in all target lesions	Resolution of all target lesions
PR	>30% decrease in sum of longest diameters of viable—that is, arterial enhancing component in target lesions	>30% decrease in sum of longest diameters of target lesions
PD	>20% increase in sum of longest diameters of viable target lesions; new lesions meeting criteria of HCC (at least 1 cm, arterial enhancing and washout on portal venous phase)	>20% increase in sum of longest diameters of target lesions; absolute increase of ≥5 mm is required; new lesions
SD	Criteria not fulfilling any of the above categories	Criteria not fulfilling any of the above categories

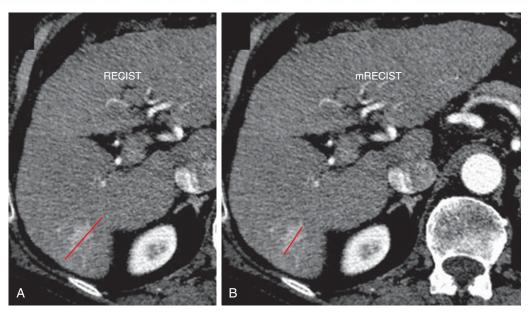
Data from Lencioni R, Llovet JM: Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. Semin Liver Dis 30:52–60, 2010; Lencioni R: New data supporting modified RECIST (mRECIST) for Hepatocellular Carcinoma. Clin Cancer Res 19:1312–1314, 2013; and Kim MN, Kim BK, Han KH, Kim SU: Evolution from WHO to EASL and mRECIST for hepatocellular carcinoma: considerations for tumor response assessment. Expert Rev Gastroenterol Hepatol 9:335–348, 2015.

*CR*, Complete response; *NE*, not evaluable; *PD*, progressive disease; *PR*, partial response; *SD*, stable disease.

to the modified RECIST (mRECIST) assessment (Table 85-5). Therefore, optimization of image acquisition protocols at the baseline and throughout follow-up examinations is an important prerequisite for proper application of mRECIST. Patients can be followed with either contrast-enhanced spiral CT, preferably with use of multislice scanners, or contrast-enhanced dynamic MRI. To maintain consistency in imaging, it is recommended to reconstruct 5-mm slices (or less) contiguously. To avoid partial volume averaging effects and inconsistent measurements of the same lesion on serial examinations, a target HCC lesion should be at least twice the slice thickness at baseline—that is, 10 mm if slice thickness is 5 mm. This is also applicable to MRI examinations. Measurements and comparisons should be performed on the same sequence on serial studies. To meet the criteria of target lesion, lesions should have discernible margins and show arterial enhancement to be selected as target lesions and should fulfill the RECIST 1.1 measurable lesion definition (Figure 85-2).<sup>16-19</sup>

The response categories for mRECIST are described in Table 85-5. A newly detected hepatic nodule that can be classified as HCC (at least 1 cm in longest dimension and demonstrates arterial enhancement with washout on portal venous or delayed phase) will be considered evidence of progression. Malignant portal vein thrombosis and HCC with infiltrative appearance without clearly definable margins should be considered nontarget lesions. A periportal lymph node greater than 20 mm in short axis can be considered malignant. During the course of

85 Response Evaluation Criteria in Solid Tumors, World Health Organization, and Other Response Criteria 1033



**Figure 85-2** Method of target lesion measurement by mRECIST for assessment for hepatocellular carcinoma and its comparison to RECIST. (A) According to RECIST, a target lesion on arterial-phase computed tomography is measured as its longest overall tumor diameter. (B) In mRECIST, only the longest viable tumor diameter (in this case, the arterially enhancing component) is measured, excluding any areas of necrosis.

treatment, when measurable tumor has met the criteria for response or stable disease and there is new or worsening ascites and pleural effusion, cytopathologic confirmation of malignancy is mandatory to diagnose disease progression.<sup>15-19</sup>

# Response Assessment Based on Fluorodeoxyglucose With Positron Emission Tomography: European Organization for Research and Treatment of Cancer Criteria

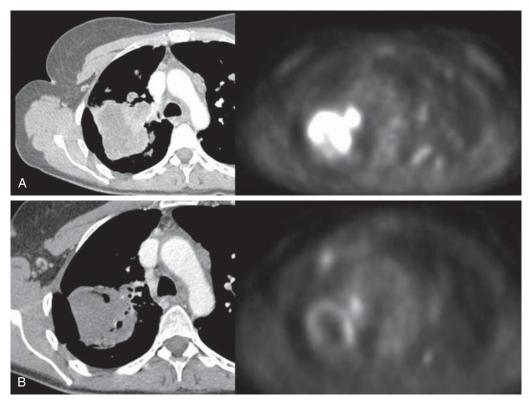
Typically, malignant lesions show intense 18F-FDG uptake and standardized uptake value (SUV) can serve as an important semi-quantitative imaging biomarker for assessment of tracer uptake in PET. To calculate SUV, tumor FDG activity concentration is measured during a 10- to 15-minute static scan, which is then normalized for the injection dose and patient weight, lean mass, or body surface area. There is growing evidence that in FDG-PET–positive tumors, early metabolic changes of treatment can be measured and also may predict long-term outcome.<sup>20,21</sup> Moreover, with targeted therapies, early response can be predicted by FDG PET, which is not possible by measuring tumor dimension alone (Figure 85-3). The European Organization for Research and Treatment of Cancer (EORTC) recommends the following criteria for PET imaging biomarker assessment<sup>22</sup>:

- *PD:* SUV increase of greater than 25%, visible increase in the extent of uptake by more than 20%, and the appearance of a new FDG-positive metastasis
- *SD:* Increase in SUV by less than 25% or decrease by less than 15% and no increase in extent of uptake (<20% in longest dimension)
- *PR*: Reduction of the SUV by 15% after one cycle of chemotherapy and greater than 25% after two or more cycles (reduction in extent of FDG uptake is not required)
- *CR:* Complete resolution of metabolically active tumor volume so that it is indistinguishable to background tissue

EORTC also suggested that the initial region of interest for SUV measurements should contain only viable tumor and be used consistently on all subsequent scans.<sup>23,24</sup> The role of PETbased response assessment criteria has been demonstrated in malignancies such as GISTs, bile duct tumors, and tumors of the esophagus and gastrointestinal tract.<sup>25-29</sup> Nevertheless, there are pitfalls in the EORTC criteria. The criteria do not specify how ROI are drawn and how to handle multiple lesions. The response criterion of 15% suggested for PR can be within expected test variability. Moreover, 18F-FDG is not a tumorspecific tracer and benign tissues, sites of inflammation, granulomata, and certain other nonmalignant conditions may also concentrate 18F-FDG. In addition, interscan reproducibility of SUV remains an important consideration because SUV can be influenced by several factors, including time from tracer injection to image acquisition, patient preparation, scan quality, ROI selection, and so on.

# Response Assessment Based on Fluorodeoxyglucose–Positron Emission Tomography: Positron Emission Tomography Response Criteria in Solid Tumors

The discrepancy between tumor response and decrease in tumor size is very apparent in tumors such as lymphoma and those treated with targeted agents. Little change in size on CT in spite of significant decrease in tumor enhancement and/or FDG uptake is common. Therefore, tumor metabolic response as an index of tumor response can be a better predictor of outcome than morphologic changes alone. Because of lack of standardization and reproducibility associated with qualitative FDG-PET response assessment, attempts were made to assess and validate quantitative PET information for effective therapy response assessment and not just use qualitative information. This led to the proposed PET Response Criteria in Solid Tumors 1.1 (PERCIST 1.1) criteria in 2009 incorporating quantitative



**Figure 85-3** Comparison of response assessment by tumor burden (RECIST) and metabolic (fluorodeoxyglucose (FDG)–positron emission tomography) activity of tumor. Right lung tumor before (A) and after (B) treatment with an antiangiogenic agent (bevacizumab) shows no significant change in tumor size (except for necrosis) but marked decrease in FDG uptake.

approaches to monitoring PET tumor response.<sup>24,30,31</sup> To maintain consistency in quantitative assessment across serial scans, PERCIST requires identical PET scans to be performed on the same scanner with similar patient preparation, comparable injected doses of FDG, and scan time after trace injection between baseline and follow-up scans. In comparison to standard body weight-normalized SUV, PERCIST recommends using SUL (SUV normalized to lean body mass) because it is less dependent on patient weight. It is suggested that SUL peak should be measured using 1.2-cm-diameter sphere producing 1-cm<sup>3</sup> volume spheric ROI centered over the area of highest uptake in the tumor. Tumor sizes should be noted and should be 2 cm or larger in diameter for accurate measurement, although smaller lesions of sufficient 18F-FDG uptake, including those not well seen anatomically, can be assessed. Treatment response is described as continuous variable and reports percentage changes in SUL for the peak lesion (which may not be the same lesion) at baseline and subsequent time points. It recommends the following criteria for response assessment<sup>24</sup>:

- *CR:* Refers to disappearance of all metabolically active tumors and no new FDG-avid lesions
- *PR:* 0.8-unit (>30%) decrease in SUL peak between the most intense lesion before treatment and the most intense lesion after treatment (may not be the same lesion)
- *PD*: A 0.8-unit (>30%) increase in SUL peak or the appearance of a new FDG-avid lesion

Difficulty in optimization and protocol standardization within and between institutions and response evaluation based on a single FDG-intense lesion are some of the challenges that have limited widespread application of quantitative assessment based response evaluation by PERCIST.

# **Response Criteria for Lymphoma**

Lymphoma is the most common primary hematopoietic malignancy. But size-based response evaluation of abnormal lymph nodes poses challenges. Unlike metastatic deposits to other organs, lymph nodes are normal anatomic structures that possess a measurable size. Currently, lymph node size is used to diagnose a lymph node as malignant, because larger lymph nodes are more likely to be malignant than smaller ones.<sup>8,32</sup> At the same time, it is known that even when involved by malignancy lymph node size may be normal. Application of established methods such as WHO and RECIST to monitor treatment response on imaging has presented unique challenges in lymphoma.<sup>1</sup> Unlike solid organ tumors, malignant nodes can shrink to normal or near normal size and may not disappear completely, limiting application of criteria based on conventional tumor burden. Similarly, posttreatment scarring at disease sites can continue to demonstrate a measurable lesion despite complete tumor cell resolution. Lymphoma also can manifest in manners that are challenging to assess objectively on traditional imaging techniques, such as diffuse infiltration of viscera, bone or bone marrow involvement without focal lesion, and overall increase in size. This led to introduction of the International Workshop Criteria (IWC) that was based on cross-sectional imaging (CT and also MRI) and was soon adopted as a standard approach with imaging (Table 85-6).<sup>3</sup>

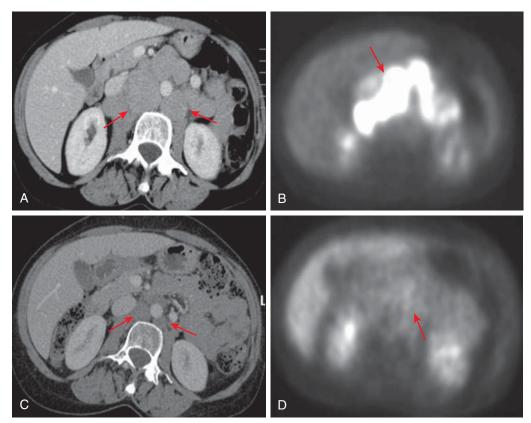
With experience in clinical trials, limitations of the CT-based IWC method, such as lack of functional or molecular information, became evident and important limitations of morphologic measurements were recognized. Notable among these is

	ernational Worksho	p Criteria		
85-6 Response	Definition	Nodal Mass	Spleen and Liver	Bone Marrow
CR	Disappearance of all evidence of disease	Return to normal size of lymphadenopathy	Not palpable, nodules disappeared	Infiltrate cleared on repeat biopsy; if indeterminate by morphology, immunochemistry should be negative
PR	Regression of measurable disease and no new sites	≥50% decrease in SPD of dominant masses	≥50% decrease in SPD of nodules; no increase in size of liver or spleen	Irrelevant if positive before therapy; cell type should be specified
Relapsed disease or PD	Any new lesion or increase by ≥50% of previously involved sites from nadir	Appearance of a new lesion(s) >1.5 cm in any axis, ≥50% increase in SPD of more than one node, or ≥50% increase in longest diameter of a previously identified node <1 cm in short axis	>50% increase from nadir in the SPD of any previous lesions	New or recurrent Involvement
SD	Failure to attain any o	of the above categories		

Data from Cheson BD, Horning SJ, Coiffier B, et al: Report of an international workshop to standardize response criteria for non-Hodgkin's lymphomas. NCI Sponsored International Working Group. J Clin Oncol 17:1244, 1999; and Cheson BD, Pfistner B, Juweid ME, et al: Revised response criteria for malignant lymphoma. J Clin Oncol 25:579–586, 2007.

NOTE: Lymph nodes are measured in short axis.

CR, Complete remission; CT, computed tomography; FDG, [18F] fluorodeoxyglucose; PD, progressive disease PET, positron emission tomography; PR, partial remission; SD, stable disease; SPD, sum of the product of the diameters.



**Figure 85-4** After completion of chemotherapy, contrast-enhanced computed tomography (CT) image shows residual tumor mass (*arrow*) with marked reduction in FDG uptake on corresponding PET image (*arrow*), highlighting the benefit of metabolic imaging over CT alone in response assessment of FDG-avid lymphoma.

posttreatment fibrosis or scarring manifesting as residual mass on CT, a finding observed in approximately 40% of patients with non-Hodgkin's lymphoma and an even higher number of those with Hodgkin's lymphoma. Active tumor tissue is present in 10% to 20% of such patients, but it is not possible to separate cases with and without residual disease on CT. Therefore, a need for a functional imaging approach was realized. Subsequently, the International Harmonization Project (IHP) criteria integrating IWC and PET for assessment of response to therapy for lymphoma was convened (see Figure 85-4 and Table 85-7).<sup>33,34</sup>

TABLEInternational Harmonization Project Criteria Integrating International Workshop Criteria and Positron85-7Emission Tomography With Computed Tomography for Assessment of Response to Therapy for Lymphoma

Response	Definition	Nodal Mass	Spleen and Liver	Bone Marrow
CR	Disappearance of all evidence of disease	<ol> <li>Positive FDG avid or PET before therapy: Mass of any size permitted if PET negative</li> <li>Variably FDG avid or PET negative: Regression to normal size on CT</li> </ol>	Not palpable, nodules disappeared	Infiltrate cleared on repeat biopsy; if indeterminate by morphology, immunochemistry should be negative
PR	Regression of measurable disease and no new sites	<ul> <li>≥50% decrease in SPD of up to six largest dominant masses; no increase in size of other nodes</li> <li>1. FDG avid or PET positive before therapy: One or more PET positive at previously involved site</li> <li>2. Variably FDG avid or PET negative: Regression on CT</li> </ul>	≥50% decrease in SPD of nodules (for single nodule in greatest transverse diameter); no increase in size of liver or spleen	Irrelevant if positive before therapy; cell type should be specified
Relapsed disease or PD	Any new lesion or increase by ≥50% of previously involved sites from nadir	Appearance of a new lesion(s) >1.5 cm in any axis, ≥50% increase in SPD of more than one node, or ≥50% increase in longest diameter of a previously identified node >1 cm in short axis Lesions PET positive if FDG-avid lymphoma or PET positive before therapy	>50% increase from nadir in the SPD of any previous lesions	New or recurrent involvement
SD	Failure to fulfill above categories	<ol> <li>FDG avid or PET positive before therapy: PET positive at prior sites of disease and no new sites on CT or PET</li> <li>Variably FDG-avid or PET negative: No change in size of previous lesions on CT</li> </ol>		

CR, Complete remission; CT, computed tomography; FDG, [18F]-fluorodeoxyglucose; PD, progressive disease; PET, positron emission tomography; PR, partial remission; SD, stable disease; SPD, sum of the product of the diameters.

Details of both IWC and IHP are beyond the scope of this chapter, and readers are referred to appropriate references. Tables 85-6 and 85-7 provide an overview of these two sets of response criteria.

# **Future Trends**

Advances in imaging technologies, contrast materials, and postprocessing methods have brought physiologic and functional assessment to imaging. Newer imaging techniques now possess the ability to detect changes in tumor microenvironment and tissue cytoarchitecture by capturing alterations in perfusion and oxygenation, as well as molecular changes. Modalities such as dynamic contrast-enhanced CT and MRI, which assess contrast material tumoral biodistribution to evaluate tissue microvascular changes; diffusion weighted MRI, which assess cellularity and its integrity; and magnetic resonance spectroscopy, for quantifying relative tissue chemical composition,<sup>3,6,35-37</sup> are all promising techniques for more accurate and precise tumor burden assessment.

#### **Key Points**

- Imaging remains central to monitoring treatment in solid tumor and lymphoid malignancies.
- Morphologic methods (e.g., RECIST) are most commonly used for response assessment.
- With the introduction of novel drugs such as targeted therapies, oncologic imaging expectations have changed.
- Functional imaging techniques such as PET are promising and increasingly used. Their role is evolving to complement morphologic methods. Routine availability, reproducibility, standardization, and validation are needed for widespread use.

# SUGGESTED READINGS

- Eisenhauer EA: Response evaluation: beyond RECIST. Ann Oncol 18(Suppl 9):ix29-ix32, 2007.
- Eisenhauer EA, Therasse P, Bogaerts J, et al: New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 45:228–247, 2009.
- Cheson BD, Horning SJ, Coiffier B, et al: Report of an international workshop to standardize response criteria for non-Hodgkin's lymphomas.

NCI Sponsored International Working Group. J Clin Oncol 17:1244, 1999.

- Cheson BD, Pfistner B, Juweid ME, et al: Revised response criteria for malignant lymphoma. *J Clin Oncol* 25:579–586, 2007.
- Lencioni R, Llovet JM: Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. *Semin Liver Dis* 30:52–60, 2010.
- Wahl RL, Jacene H, Kasamon Y, et al: From RECIST to PERCIST: evolving considerations for PET response criteria in solid tumors. J Nucl Med 50(Suppl 1):122S–1250S, 2009.

#### REFERENCES

- Eisenhauer EA: Response evaluation: beyond RECIST. Ann Oncol 18(Suppl 9):ix29–ix32, 2007.
- Eisenhauer EA, Therasse P, Bogaerts J, et al: New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer* 45:228–247, 2009.
- 3. Miles KA: Functional CT imaging in oncology. *Eur Radiol* 13(Suppl 5):M134–M138, 2003.
- Avril NE, Weber WA: Monitoring response to treatment in patients utilizing PET. *Radiol Clin North Am* 43:189–204, 2005.
- 5. Nathan PD, Vinayan A, Stott D, et al: CT response assessment combining reduction in both size and arterial phase density correlates with time to progression in metastatic renal cancer patients treated with targeted therapies. *Cancer Biol Ther* 9:15–19, 2010.
- Padhani AR, Husband JE: Dynamic contrastenhanced MRI studies in oncology with an emphasis on quantification, validation and human studies. *Clin Radiol* 56:607–620, 2001.
- Husband JE, Schwartz LH, Spencer J, et al: Evaluation of the response to treatment of solid tumours: a consensus statement of the International Cancer Imaging Society. Br J Cancer 90:2256–2260, 2004.
- Dorfman RE, Alpern MB, Gross BH, et al: Upper abdominal lymph nodes: criteria for normal size determined with CT. *Radiology* 180:319–322, 1991.
- Sohaib SA, Turner B, Hanson JA, et al: CT assessment of tumour response to treatment: comparison of linear, cross-sectional and volumetric measures of tumour size. *Br J Radiol* 73:1178–1184, 2000.
- Spaepen K, Stroobants S, Dupont P, et al: Prognostic value of positron emission tomography (PET) with fluorine-18 fluorodeoxyglucose ([18F]FDG) after first-line chemotherapy in non-Hodgkin's lymphoma: is [18F]FDG-PET a valid alternative to conventional diagnostic methods? J Clin Oncol 19:414–419, 2001.
- 11. Spira D, Vogel W, Bares R, et al: Volumeperfusion CT as an adjunct to whole-body contrast-enhanced CT for monitoring response to therapy in lymphoma. *Br J Haematol* 151:293, 2010.
- Choi H: Critical issues in response evaluation on computed tomography: lessons from the gastrointestinal stromal tumor model. *Curr Oncol Rep* 7:307–311, 2005.
- 13. Goh V, Ganeshan B, Nathan P, et al: Assessment of response to tyrosine kinase inhibitors in metastatic renal cell cancer: CT texture as a

predictive biomarker. Radiology 261:165-171, 2011.

- 14. van der Veldt AA, Meijerink MR, van den Eerweght AA, et al: Targeted therapies in renal cell cancer: recent developments in imaging. *Target Oncol* 5:95–112, 2010.
- Salvaggio G, Furlan A, Agnello F, et al: Hepatocellular carcinoma enhancement on contrastenhanced CT and MR imaging: response assessment after treatment with sorafenib: preliminary results. *Radiol Med* 119:215–221, 2014.
- Vouche M, Kulik L, Atassi R, et al: Radiologicalpathological analysis of WHO, RECIST, EASL, mRECIST and DWI: Imaging analysis from a prospective randomized trial of Y90 +/– sorafenib. *Hepatology* 58:1655–1666, 2013.
- Lencioni R, Llovet JM: Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. *Semin Liver Dis* 30:52–60, 2010.
- Lencioni R: New data supporting modified RECIST (mRECIST) for hepatocellular carcinoma. *Clin Cancer Res* 19:1312–1314, 2013.
- Kim MN, Kim BK, Han KH, et al: Evolution from WHO to EASL and mRECIST for hepatocellular carcinoma: considerations for tumor response assessment. *Expert Rev Gastroenterol Hepatol* 9:335–348, 2015.
- Torizuka T, Tamaki N, Inokuma T, et al: Value of fluorine-18-FDG-PET to monitor hepatocellular carcinoma after interventional therapy. J Nucl Med 35:1965–1969, 1994.
- Paudyal B, Oriuchi N, Paudyal P, et al: Early diagnosis of recurrent hepatocellular carcinoma with 18F-FDG PET after radiofrequency ablation therapy. *Oncol Rep* 18:1469–1473, 2007.
- Young H, Baum R, Cremerius U, et al: Measurement of clinical and subclinical tumour response using [18F]-fluorodeoxyglucose and positron emission tomography: review and 1999 EORTC recommendations. European Organization for Research and Treatment of Cancer (EORTC) PET Study Group. Eur J Cancer 35:1773–1782, 1999.
- Costelloe CM, Chuang HH, Madewell JE, et al: Cancer Response Criteria and Bone Metastases: RECIST 1.1, MDA and PERCIST. J Cancer 1:80– 92, 2010.
- Wahl RL, Jacene H, Kasamon Y, et al: From RECIST to PERCIST: evolving considerations for PET response criteria in solid tumors. *J Nucl Med* 50(Suppl 1):122S–1250S, 2009.
- Tixier F, Le Rest CC, Hatt M, et al: Intratumor heterogeneity characterized by textural features on baseline 18F-FDG PET images predicts

response to concomitant radiochemotherapy in esophageal cancer. J Nucl Med 52:369–378, 2011.

- Jadvar H, Henderson RW, Conti PS: [F-18]fluorodeoxyglucose positron emission tomography and positron emission tomography: computed tomography in recurrent and metastatic cholangiocarcinoma. J Comput Assist Tomogr 31:223– 228, 2007.
- Muller D, Wiedmann M, Kluge R, et al: Is 18F-FDG-PET suitable for therapy monitoring after palliative photodynamic therapy of nonresectable hilar cholangiocarcinoma? *Z Gastroenterol* 43:439–443, 2005.
- Thurau K, Palmes D, Franzius C, et al: Impact of PET-CT on primary staging and response control on multimodal treatment of esophageal cancer. World J Surg 35:608–616, 2011.
- Prior JO, Montemurro M, Orcurto MV, et al: Early prediction of response to sunitinib after imatinib failure by 18F-fluorodeoxyglucose positron emission tomography in patients with gastrointestinal stromal tumor. J Clin Oncol 27: 439–445, 2009.
- Zhou LL, Wang CC, Zhao JH, et al: The role of FDG-PET in staging of lymphoma and evaluation of therapeutic efficiency. *Zhonghua Xue Ye Xue Za Zhi* 30:233–623, 2009.
- Zijlstra JM, Landauer-van der Werf G, Hoekstra OS, et al: 18F-fluoro-deoxyglucose positron emission tomography for post-treatment evaluation of malignant lymphoma: a systematic review. *Haematologica* 91:522–529, 2006.
- Einstein DM, Singer AA, Chilcote WA, et al: Abdominal lymphadenopathy: spectrum of CT findings. *Radiographics* 11:457–472, 1991.
- 33. Cheson BD, Horning SJ, Coiffier B, et al: Report of an international workshop to standardize response criteria for non-Hodgkin's lymphomas. NCI Sponsored International Working Group. J Clin Oncol 17:1244, 1999.
- Cheson BD, Pfistner B, Juweid ME, et al: Revised response criteria for malignant lymphoma. *J Clin Oncol* 25:579–586, 2007.
- Ben-Haim S, Ell P: 18F-FDG PET and PET/CT in the evaluation of cancer treatment response. *J Nucl Med* 50:88–99, 2009.
- Patterson DM, Padhani AR, Collins DJ: Technology insight: water diffusion MRI: a potential new biomarker of response to cancer therapy. *Nat Clin Pract Oncol* 5:220–233, 2008.
- Koh DM, Collins DJ: Diffusion-weighted MRI in the body: applications and challenges in oncology. *AJR Am J Roentgenol* 188:1622–1635, 2007.



# **Image-Guided Therapy**

SURABHI BAJPAI | RAUL N. UPPOT

Increasing emphasis on tailoring of cancer treatment strategies to individual patients (i.e., personalized medicine) has enabled development of multiple therapeutic options in the management of malignant diseases of the abdomen and pelvis.<sup>1-5</sup> In particular, in patients with malignant hepatic and renal tumors, organ-directed treatment such as percutaneous ablation, intraarterial embolic therapies, and targeted radiation therapy have shown considerable promise in improving patient outcome.<sup>6-15</sup> Although surgical resection is considered the gold standard treatment option for management of these tumors, percutaneous ablative therapies offer a valuable therapeutic option in renal cell cancers and hepatic malignancies.<sup>12,14-17</sup> Intra-arterial therapies are effective treatment options in patients with locally advanced liver malignancy, and image-guided radiation treatments are suitable alternatives for unresectable hepatic malignancies or those that are difficult to ablate.<sup>6-10,18-23</sup>

Imaging has a crucial role in the successful delivery of therapy in patients selected to undergo image-guided loco-regional therapies.<sup>2,24-28</sup> The role of imaging before treatment is to determine tumor burden and staging; depict the anatomic relationships of tumor, particularly its proximity to critical structures; select the appropriate treatment option; and plan the treatment approach.<sup>2,12,24-29</sup> After loco-regional therapy, imaging is not only required to monitor therapeutic success and detect residual and recurrent disease but is also essential to detect procedure-related complications.<sup>24-28</sup> Continuing technologic advances in computed tomography (CT) and magnetic resonance imaging (MRI) not only permit reliable morphologic evaluation of hepatic and renal tumors but also enable functional assessment. Functional imaging techniques such as perfusion CT/MRI, diffusion weighted imaging (DWI), 18-fluorodeoxyglucose (FDG) with positron emission tomography (PET), and/or PET/CT enable evaluation of various physiologic properties of tumors, such as vascularity and metabolism, which are increasingly being used before and after loco-regional therapies. This chapter will briefly describe the role of imaging in preprocedural evaluation and postprocedural assessment of abdominal malignancies undergoing imageguided targeted therapies, with particular focus on hepatic and renal tumors

# **Image-Guided Treatment Options**

The past few decades have seen a substantial rise in the performance of image-guided loco-regional therapies for various tumors in the abdomen and pelvis. Prominent image-guided treatments include percutaneous image-guided ablation and intra-arterial therapies. Percutaneous image-guided ablative techniques include radiofrequency ablation (RFA), percutaneous ethanol injection, microwave ablation (MWA), cryoablation, laser ablation, and irreversible electroporation (IRE). Whereas percutaneous ablations are most commonly used for treatment of renal cell cancer and malignant liver lesions, intraarterial and image-guided radiation therapy are primarily offered in the management of hepatic malignancies.<sup>12,14,15,24-30</sup>

Percutaneous ablation is based on the principle of local tumor destruction through needle-guided administration of chemicals, heat, or electric current into the tumor while avoiding damage to the surrounding normal tissue.<sup>31-34</sup> Although percutaneous ethanol injection achieves tumor destruction through slow image-guided instillation of absolute or 95% alcohol into the tumor resulting in coagulative necrosis, RFA causes tumor death by generating heat through transmission of high-frequency alternating current (AC).<sup>33,35</sup> MWA works on the principle of tissue destruction through electromagnetic waves, with frequencies 90 kilohertz or greater inducing rapid molecular motion of cellular particles with heat generation and coagulative necrosis.<sup>34</sup> IRE is a nonthermal ablation technique in which tissue destruction is achieved by permanent cell membrane permeability increase induced by powerful high-voltage electric pulses (3 kilovolts).<sup>36</sup> Increased permeability permits transmembrane movement of water-soluble substances and ions, disrupting cellular homeostasis and causing cell death.<sup>36</sup> Most ablation procedures are percutaneous, although laparoscopic and intraoperative approaches are also used. Among the various ablative techniques, the collective experience with RFA is the largest and RFA has come to be considered a standard treatment option for local tumor control.<sup>17,2</sup>

In the treatment of hepatic malignancies, intra-arterial therapies such as transarterial chemoembolization (TACE) and selective internal radiation therapy (SIRT) are most frequently performed. These involve transarterial administration of different particles into vessels supplying the tumor to accomplish tissue destruction. Transarterial embolization techniques are possible as a result of the dual hepatic vascular supply (portal vein, 75%; hepatic artery, 25%), which enables selective intraarterial instillation of embolic agents and chemotherapeutic drugs into the tumor because hepatic tumor blood supply is preferentially arterial.<sup>17,18</sup> The intra-arterially administered substances cause obstruction of tumor feeding vessels and result in cell death while the normal liver parenchyma, which is supplied by the portal vein, is not damaged.<sup>17,18</sup> SIRT or radioembolization involves intra-arterial administration of micron-sized particles (20 to 60 microns) containing a radioisotope (yttrium-90 [<sup>90</sup>Y]), which delivers focused beta radiation to cause tumor destruction while minimizing radiation damage to the surrounding normal liver. In contrast to TACE, SIRT requires preservation of adequate perfusion to the tumor to enhance free radical-dependent cell death from radiotherapy.<sup>17,18,37</sup> In hepatocellular carcinoma (HCC), intra-arterial therapies are considered the first-line palliative therapy for inoperable cases with large or multifocal HCC without major vascular invasion or extrahepatic disease but with preserved liver function and performance status.<sup>17,18,37</sup> In hepatic metastases, intra-arterial

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therapies have a palliative role particularly in management of hepatic metastases from neuroendocrine tumor, breast cancer, and colon cancer.<sup>17,18,37</sup>

Image-guided radiation therapy is increasingly used for management of hepatic malignancies because novel threedimensional (3D) conformal radiation therapy allows targeted delivery of a high radiation dose to limited volumes of liver while limiting irradiation of residual functioning liver parenchyma.<sup>6,38</sup> These techniques use percutaneously placed radiopaque fiducials around the tumor to maintain high precision in radiation delivery leading to DNA damage and causing cell death.<sup>6,38</sup>

# **Imaging Protocol**

Dynamic contrast multidetector CT (MDCT) and gadoliniumenhanced MRI are considered the standard of care for preprocedural assessment of abdominal tumors before locoregional therapies, as well as for monitoring response to treatment.<sup>1,25,29,39-41</sup> Although CT and MRI are equally accurate in pretreatment evaluation, gadolinium-enhanced MRI is preferred for evaluation of hepatic malignancies because of higher specificity and superior soft tissue and contrast resolution.<sup>42</sup> For hepatic tumors, dynamic contrast-enhanced imaging with arterial phase, portal venous phase, and delayed phase is typically performed. In hepatic malignancies, particularly metastases from an extrahepatic primary, such as colorectal cancer, PET/ CT is increasingly used for pretreatment assessment to identify extrahepatic sites of disease and for accurate tumor staging.<sup>2</sup> For metastatic disease, PET/CT is also preferred over CT for evaluation of ablation zone and after SIRT therapy. Morphologic imaging studies such as CT and MRI are often insensitive compared to PET/CT for monitoring response after SIRT therapy because of the presence of necrosis, edema, hemorrhage, and cystic change.

For renal tumors, the typical protocol includes an unenhanced, nephrographic phase and delayed phase acquisition.<sup>29,39-41</sup> The delayed phase is typically acquired to define the relationship of the tumor to the renal collecting system and detect urinary complications.<sup>29,39-41</sup> Subtraction imaging adds value as a complementary technique for precise determination of enhancement in the treatment zone.<sup>29,39-41</sup> Coronal and sagittal reformation images are also obtained. Irrespective of the technology used for surveillance, it is essential to maintain consistency in the imaging protocol performed at baseline before therapy and at different time points after therapy.<sup>29,41</sup> The initial timing of imaging assessment after various loco-regional therapies is generally 4 to 8 weeks after treatment. Following initial assessment of treatment response, subsequent imaging follow-up is performed to detect local tumor progression evidenced by recurrence and development of new local and distant sites of disease.<sup>25,26,29,41</sup> Our current practice includes posttreatment imaging follow-up at 1, 3, 6, 9, and 12 months, followed by imaging at longer intervals if no residual or recurrent disease is revealed.

# **Imaging: Pretreatment Evaluation**

Imaging is integral to the multidisciplinary care of patients diagnosed with hepatic or renal malignancy because patient selection is often carried out depending on the oncologic assessment, as well as the technical feasibility of various treatment options.<sup>25,26,29,41,42</sup> Detailed radiologic evaluation before therapy is crucial to selecting the most appropriate local or systemic approach—that is, surgical resection versus systemic chemotherapy versus loco-regional therapy.<sup>25,26,29,41,42</sup> Preprocedure imaging with CT or MRI allows tumor localization, depicts tumor margins and relationship to adjacent structures, and determines a safe path for percutaneous intervention, protecting and minimizing damage to adjacent normal and critical structures.\* Pretherapeutic evaluation also permits assessment of tumor vascularity and metabolic activity to ensure precise dose and delivery of targeted therapies. The next few paragraphs will discuss several points requiring careful attention during assessment before loco-regional therapies.

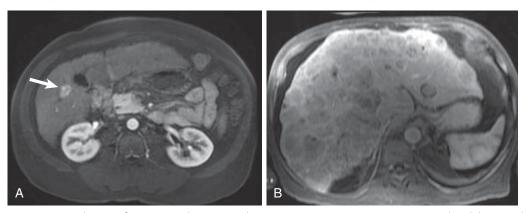
## **TUMOR STAGING**

A key function of imaging is the accurate determination of tumor stage, including evaluation of tumor size, number, location, presence of major vascular involvement, nodal disease, and distant metastases to select the most optimal targeted therapeutic option. In patients with hepatic tumors, the size and number of lesions dictate the type of loco-regional therapy with solitary tumors or fewer than 3 tumors being treated by percutaneous ablation or radiation therapy and multiple hepatic lesions are managed with intra-arterial therapies. For percutaneous ablation, tumor size has considerable influence on the treatment plan, including determination of types and number of electrode probes (single vs. clustered probes).<sup>24,42-45</sup> Tumor size is also a strong predictor of treatment success and survival for both hepatic and renal tumors.<sup>42,527,43,44</sup>

In patients with HCC, tumors 5 cm or less have a higher likelihood of achieving a favorable outcome with percutaneous ablation and in tumors less than 3 cm the outcomes after RFA reportedly match those with surgical resection (Figure 86-1).<sup>43,</sup> Large HCCs measuring more than 5 cm are generally not considered ideal candidates for percutaneous ablation, and surgical resection remains a favored option.<sup>27</sup> A combination of TACE and percutaneous ablation may benefit patients with tumors greater than 5 cm. Patients with multinodular or multifocal HCC and relatively preserved liver function without major vascular invasion or extrahepatic disease are often treated with intra-arterial therapies. In patients with oligometastatic liver disease (solitary tumor or <5 tumors measuring  $\leq$ 3 cm), ablative therapies, and image-guided radiation therapy are increasingly offered as an option to patients who refuse surgery or when surgery is contraindicated.<sup>8,26</sup> In these patients, RFA has shown some success in controlling tumor burden, with 5-year survival rates of 24% to 44% for tumors less than 5 cm and favorable outcome in metastases less than 3 cm (5-year survival rate of 55% to 56%).<sup>†</sup> Tumor recurrence rates after RFA in metastatic colorectal cancer vary from 6% to 40% and are relative to size, number, and location of lesions with worsening outcome for tumors greater than 5 cm.47 Higher rates of complete ablation can be achieved with MWA because of the larger zones of ablation achieved.<sup>25</sup> In patients in whom ablation is not feasible or an option, intra-arterial approaches such as TACE (with irinotecan) and SIRT therapy are other promising but less established approaches.17,18,25 In hepatocellular

<sup>\*</sup>References 24, 25, 29, 41, 43, 44.

<sup>&</sup>lt;sup>†</sup>References 8, 25, 26, 33, 46, 47.



**Figure 86-1** Tumor staging in selection of appropriate loco-regional treatment strategy in two patients. **A**, Axial gadolinium-enhanced magnetic resonance imaging (MRI) demonstrates a 2.1-cm arterially enhancing hepatocellular carcinoma (HCC) (*arrow*) in a 53-year-old man that was treated with radiofrequency ablation. **B**, Axial gadolinium-enhanced MRI in the portal venous phase demonstrates multiple lesions in both lobes of liver (biopsy-proved HCC) in a 79-year-old man that was treated with transarterial chemoembolization.

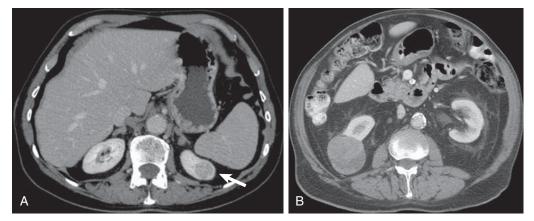


Figure 86-2 Solitary renal cell carcinoma (RCC) treated by percutaneous ablation. A, Axial nephrographic phase computed tomography (CT) demonstrates a 2.3-cm left upper pole RC (*arrow*) in a 72-year-old man treated with cryoablation. B, Axial nephrographic phase CT demonstrates a 4.5-cm right renal mid-pole RCC (*arrow*) in a 62-year-old woman treated with radiofrequency ablation with multiple sessions.

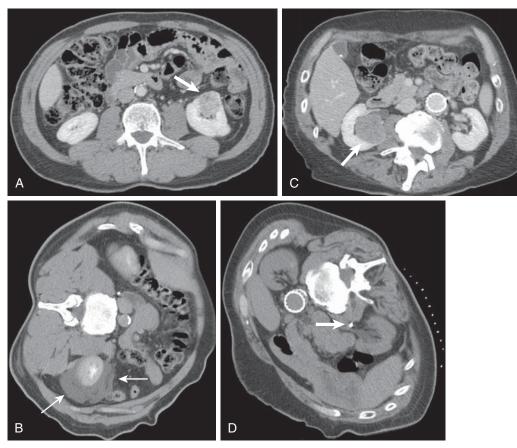
carcinoma, intra-arterial therapies are offered as the first-line palliative therapy for nonsurgical patients with large or multifocal HCC without major vascular invasion or extrahepatic disease but with preserved liver function and performance status (see Figure 86-1).<sup>17,18</sup>

In RCC, tumor size dictates treatment success, with optimal tumor size for percutaneous ablation being 4 cm or less or T1a tumors according to American Joint Committee on Cancer staging (Figure 86-2).<sup>12,29,48</sup> In tumors less than 3 cm, complete tumor necrosis can be achieved, resulting in successful treatment in 100% of cases.<sup>12,29,48</sup> Increasing tumor size limits treatment effectiveness with reduced likelihood of recurrence-free survival, thereby necessitating an increased number of ablation sessions to achieve an equivalent degree of necrosis.<sup>12,29,48</sup> Due to the ability to visualize the treatment zone, cryoablation decreases the number of sessions needed for successful treatment of the tumor. The tumor size also dictates the type of electrode, number of overlapping ablations, and number of treatment sessions. Whereas tumors measuring 1.5 cm can be treated with a single ablation with a cluster electrode, increasing

tumor size necessitates use of more electrodes, overlapping ablations, and multiple sessions.

## TUMOR LOCATION

Tumor location has a significant impact on loco-regional treatment strategy because it determines the type of therapy and the percutaneous approach to the tumor. Precise delineation of tumor location and its relationship to adjacent structures is mandatory before percutaneous ablation because it not only determines a safe trajectory to the tumor but also influences planning of the procedure, including patient position, type of electrode, and need for adjunctive procedures such as hydrodissection.<sup>49,50</sup> The anatomic relationship of the tumor to surrounding structures such as the stomach, duodenum, and colon should be ascertained before ablation because it not only limits the ability to perform complete ablation, thereby affecting treatment efficacy, but also potentially increases the complication rate, such gastrointestinal perforation.<sup>25,49,50</sup> Adjunctive procedures such as hydrodissection (or intraperitoneal instillation of



**Figure 86-3** Tumor location and its impact on planning procedural strategy for percutaneous ablation. **A**, Axial nephrographic phase computed tomography (CT) image shows a 2.9-cm left renal cell carcinoma (RCC) (*arrow*) in the anterior aspect with close proximity to the colon. **B**, Intraprocedural axial CT images showing instillation of peritoneal 5% dextrose solution to move the colon away (hydrodissection) from the kidney to facilitate successful radiofrequency ablation of the renal lesion (*arrows*). **C**, Axial nephrographic phase CT image shows a 3.6-cm central RCC (*arrow*) with close proximity to the renal pelvis and ureter. **D**, Intraprocedural axial CT image shows the ureter placed (*arrow*) for pyeloperfusion technique to limit collecting system injury.

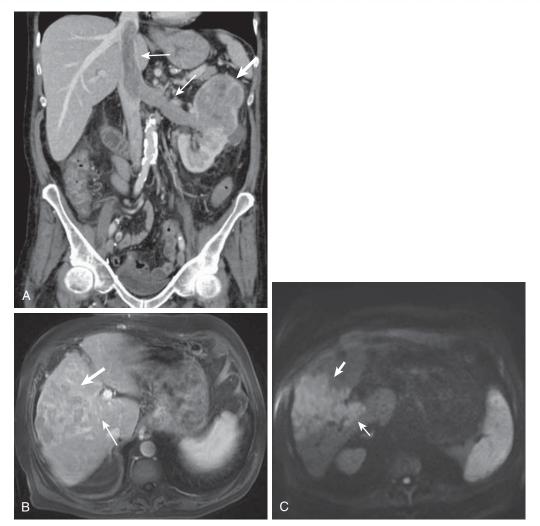
dextrose fluid before thermal ablation) is often performed in these circumstances to move the bowel loops away from the renal or hepatic tumor and thereby limit injury to these organs from ablation (Figure 86-3).<sup>25,49,50</sup> Additionally, other ablative procedures such as alcohol injection or IRE could be performed to limit adjacent organ injury.

Careful attention to the relationship of hepatic and renal tumors to structures with the liver and renal hilum is essential to avoid inadvertent injury to the biliary tract and renal collecting system or ureter, respectively.<sup>51</sup> Percutaneous ablation of tumors situated within less than 1 cm from large biliary ducts has been reported to cause biliary stenosis.<sup>25,42,47,51,52</sup> Similarly, ablation of central renal tumors could lead to collecting system injury, including infundibular or ureteral strictures and urinoma formation.<sup>29,51</sup> Retrograde pyeloperfusion is an effective adjunctive procedure used in percutaneous ablation of central renal tumors to minimize collecting system and ureteral injury<sup>29,</sup> (see Figure 86-3). Image-guided ablation of tumors close to the hepatic and renal vessels is feasible, and thermal injury to these vessels is limited because of blood flow.<sup>29,51</sup> However, this potentially can limit the efficacy of RFA as a result of possible "heat sink effect."32,44 This effect can lead to incomplete treatment of tumor tissue, and local recurrence rates of up to 48% have been reported for tumors close to large vessels.8,25,47 In exophytic renal

tumors, the "oven effect" of surrounding perinephric fat has been reported to "contain" heat within the tumor, leading to enhanced tumor ablation.<sup>13-15,29,53,54</sup> In patients scheduled for image-guided radiation treatment, close proximity of the hepatic tumors to structures such as breast, stomach, and small or large bowel can increase nontarget organ radiation injury and surgical placement of AlloDerm spacers (LifeCell, Bridgewater, NJ) to move the structures away from radiation field has been documented.<sup>55,56</sup>

# LOCAL TUMOR INVASION AND METASTATIC DISEASE

Loco-regional therapies generally are not indicated for locally advanced tumors with major vascular invasion because it adversely affects outcome and overall survival<sup>27,42,57</sup> (Figure 86-4). Multiplanar reformations and 3D reconstructed images are very useful to accurate depiction of vascular involvement (see Figure 86-4). Tumors with infiltrative margins are less likely to be successfully treated with percutaneous ablation compared with well-encapsulated tumors.<sup>43,44</sup> In hepatic malignancies, the presence of biliary involvement such as biliary invasion or duct dilatation should be identified before considering ablative or intra-arterial therapies, because these procedures increase the



**Figure 86-4** Pretreatment imaging to assess vascular involvement before loco-regional therapy. **A**, Contrast-enhanced coronal reformatted computed tomography image in a 62-year-old man with a large left renal cell carcinoma (*thick arrow*), with tumor thrombus extending into left renal vein and inferior vena cava (*thin arrows*). **B**, Axial gadolinium-enhanced magnetic resonance imaging (MRI) in a 63-yr-old man shows an infiltrative hepatocellular carcinoma (*thick arrow*) with tumor thrombus in the portal vein (*thin arrow*). **C**, Axial diffusion weighted MRI image obtained at b = 600 demonstrates hyperintensity within the thrombus (*thin arrow*), suggesting restricted diffusion. The presence of significant vascular involvement precludes ablative and intra-arterial therapies.

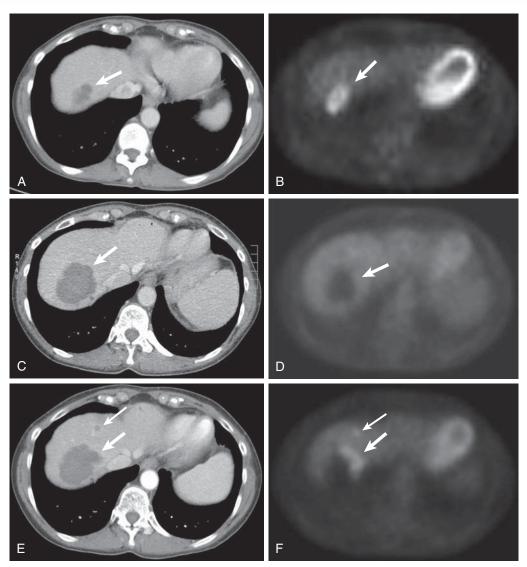
risk for biliary necrosis and infective complications. Presence of distant metastases adversely affects outcome and is a relative contraindication for loco-regional therapies because these treatment options are generally considered for local tumor control.<sup>42</sup>

## VASCULAR ANATOMY

Intra-arterial therapies such as TACE and SIRT necessitate evaluation of the arterial vascular anatomy before embolization procedures. Preprocedural evaluation of normal and variant vascular anatomy should be performed along with identification of preexisting vascular diseases such as arterial atherosclerosis for treatment planning.<sup>45</sup> During embolization procedures, it is crucial to identify collateral vascular supply to hepatic tumors to ensure complete tumor embolization.<sup>17,45</sup> Before the SIRT procedure, it is mandatory to perform a pre-SIRT baseline diagnostic angiogram to map the mesenteric vascular anatomy to identify normal and variant vascular anatomy and hepatofugal flow. This step is very important because prophylactic embolization of vessels such as gastroduodenal and right gastric arteries is required to prevent nontarget radioactive embolization of stomach and small bowel, which can result in intractable radiation ulcers. In addition, single-photon emission CT (SPECT) imaging with macroaggregated albumin particles injected into the hepatic artery is also performed to detect arteriovenous shunting into the gastrointestinal or pulmonary vasculature. Recognition of any collateral vasculature with liverdirected flow at the same time as the presence of any relevant arteriovenous fistulae should prompt embolization before SIRT therapy to improve treatment effectiveness. Severe lung shunting that cannot be treated by embolization is a contraindication to SIRT.

#### TUMOR METABOLISM

18-FDG PET is a noninvasive metabolic imaging technique used in the pretreatment and postprocedural evaluation of patients undergoing loco-regional therapies. PET/CT scanners, which combine the metabolic information of 18-FDG-PET



**Figure 86-5** Recurrent tumor and new lesion after percutaneous ablation of a colorectal liver metastases. A, Axial contrast enhanced computed tomography (CT) image in a patient with colon cancer shows a 2.5 cm hypodense hepatic metastasis in the dome of the liver (*arrow*) treated by radiofrequency ablation. **B**, Corresponding positron emission tomography (PET) image shows intense fluorodeoxyglucose (FDG) uptake (*arrows*). Follow up PET/CT was performed at 3 months. Axial contrast enhanced CT (**C**) show complete response (*arrow*) with no FDG uptake on PET image (*arrow* in **D**). Axial contrast enhanced CT (**E**) and corresponding PET image (**F**) performed 6 months later shows intense FDG uptake along the ablation zone (*thick arrows*), compatible with tumor recurrence. There is also a new FDG avid metastatic deposit adjacent to the ablation zone (*thin arrows*).

with the precise anatomic information provided by CT, allow precise lesion localization. Use of PET/CT for pretreatment evaluation is beneficial in tumors that demonstrate FDG uptake because this permits monitoring of treatment response (Figure 86-5). PET/CT is a useful tool for detection of unsuspected extrahepatic metastatic disease, which often precludes locoregional treatment options.<sup>58</sup> Although the utility of PET/CT in HCC is limited as a result of variable FDG uptake, PET/CT is very useful in patients with colorectal metastases treated with MWA, RFA, or TACE. PET/CT has been reported to be better than CT alone for detection of extrahepatic disease and improves staging in colorectal cancer, thyroid cancer, melanoma, and carcinoid tumors.<sup>59</sup> PET/CT, however, does not presently have a role in the pretreatment evaluation and staging of renal cell cancer.

#### ESTIMATION OF FUNCTIONAL RESERVE

The main advantages of loco-regional therapies are the benefits of limited damage to the surrounding normal hepatic and renal parenchyma and tumor destruction.<sup>25,26,45</sup> A favorable long-term outcome relies not only on successful tumor destruction but also on adequate residual functional parenchyma. There-fore, assessment of organ function is essential before undertak-ing loco-regional therapies. Whereas laboratory tests such as serum urea, creatinine, transaminases, and so forth can provide a reliable estimation of organ function, the value of imaging in determining functional reserve is often underestimated.<sup>25,26,45</sup> It is important to pay particular attention to renal or liver dysfunction during pretreatment assessment and appropriately comment on these facts in the radiology reports. Reliable

estimation of the functional reserve helps in triaging patients into surgery versus local ablative therapies. Patients with inadequate functional reserve might be poor surgical candidates because of the propensity to develop organ failure. This is important in patients with severe fibrosis or cirrhosis or with solitary kidney, in which ablative treatment is preferred because of suboptimal functional reserve.<sup>25,26,45</sup> Appropriate liver reserve is a prerequisite for SIRT procedures because hepatic parenchymal damage can result from radiation treatment.<sup>25,26,45</sup> In patients with liver cirrhosis, imaging can help in reliable determination of hepatic functional reserve by recognition of features such as ascites or hydrothorax, markers of portal hypertension such as splenomegaly, and esophageal or gastric varices.<sup>25,26,45</sup> Identification of these imaging features usually necessitates additional procedures before management of cancer, such as paracentesis, endoscopic variceal ligation, and so forth. Another factor in determination of background parenchymal changes is the impact of these changes on success of percutaneous ablative therapies.<sup>25,26,45</sup> For example, thermal ablation of hepatic tumors is likely to be more efficacious in the setting of background cirrhosis because of the insulating effect of the fibrotic liver (oven effect) leading to elevated intratumoral temperatures and longer cytotoxic effect.43,44

# **Imaging: Posttreatment Evaluation**

Imaging has a cardinal role in the postprocedural management of patient treatment with loco-regional therapies for malignancies of the abdomen and pelvis. The four principal goals of imaging follow-up after treatment are as follows<sup>25,26</sup>:

- 1. Define the expected normal changes at the treatment site
- 2. Identify abnormal changes such as residual disease or tumor recurrence
- 3. Permit recognition of treatment-related complications
- 4. Detect new areas of disease distant from the ablation zone, including extrahepatic disease

Early identification of residual recurrent disease and complications helps guide appropriate intervention and additional treatment sessions.<sup>25,26,29,41,60</sup> Typically, the first postprocedure imaging evaluation is performed 4 weeks after completion of treatment.<sup>25,25,26,60</sup> At this time, the patient is typically seen by an interventional radiology physician who reviews the imaging with the patient.<sup>29,41</sup> Subsequent follow-up imaging is performed more closely during the first year because of a higher likelihood of recurrence in the initial year after treatment.

# **IMAGING APPEARANCES**

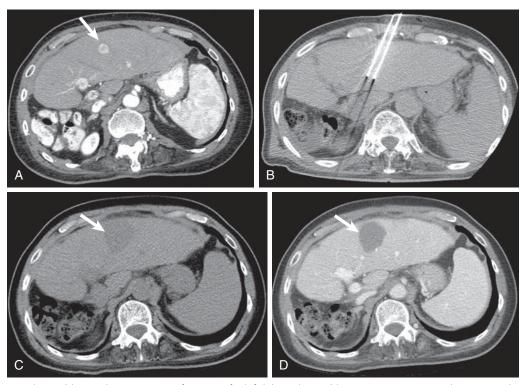
## Percutaneous Ablation

The imaging appearances after ablation of renal and hepatic tumors are similar. The expected changes vary in appearance based on the time elapsed after the procedure and evolve over time.<sup>25,26,60</sup> Irrespective of the ablative technology, it is important to remember that 5 to 10 mm of normal parenchymal tissue is included in the ablation zone to ensure a tumor-free margin and effectively eliminate the microscopic tumor invasion usually existent around the tumor periphery while preserving normal organ function. Therefore, the size of the final ablation zone is usually larger than the tumor dimensions before treatment.<sup>25,26,29,41,60</sup> The ablation zone in the immediate posttreatment scan classically appears as a nonenhancing region with areas of hyperdensity on CT resulting from the presence

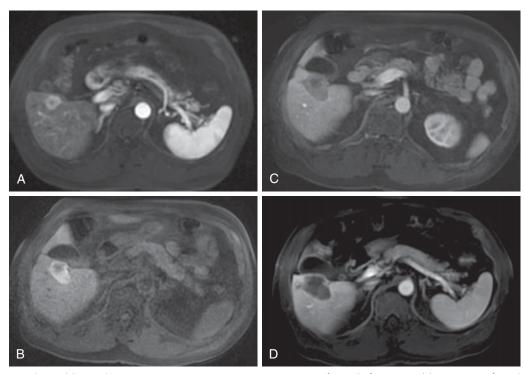
of proteinaceous material or hemorrhage<sup>29,41</sup> (Figures 86-6 and 86-7). Also very commonly seen are small air bubbles in the ablation zone secondary to tissue necrosis, including occasional small foci of gas in the portal vein.<sup>25,26,60</sup> In postcontrast images, completely treated hepatic tumor demonstrates a total lack of enhancement on arterial, portal venous, and delayed phase images. A thin rim of peripheral enhancement is often seen around the ablation zone that manifests a physiologic inflammatory response to thermal injury caused by granulation tissue surrounding the zone of intratumor coagulation necrosis. This benign rim enhancement is transient, with a uniform appearance and smooth inner margins, and should be differentiated from the irregular nodular enhancement of residual tumor seen at the periphery of the ablation zone.<sup>25,26,60</sup> On MRI, the hepatic ablation zone has a heterogeneous appearance on T1-weighted images with description of three zones: a central zone of hypointensity surrounded by a broad hyperintense zone capped by a hypointense band.<sup>25,26,28,60</sup> The hypointense band represents areas of sinusoidal congestion in the acute phase and fibrotic change in the subacute phase. On T2-weighted images, the treated zone appears predominantly hypointense because of dehydration and coagulative necrosis. However, hyperintense foci secondary to hemorrhage can be seen. After gadolinium administration, the ablation zone demonstrates absence of enhancement. It is not uncommon to see perfusional changes in the liver after ablation, which include wedge-shaped peripheral areas of arterial enhancement adjacent to the ablation zone resulting from arteriovenous shunting from ablation injury. When in doubt, the ablation zones can be observed on closeinterval follow-up examinations. Whereas recurrent tumors show interval growth, perfusional variants disappear or become smaller on follow-up imaging.

Despite similarities in appearance, certain imaging features are different in renal tumors after ablation, particularly in partially exophytic tumors.<sup>29,39,41</sup> In partially exophytic tumors, perinephric fat stranding is seen with thickening of the pararenal fascia (see Figure 86-8).<sup>29,39,41</sup> The ablation zone is usually formed by a combination of the ablated tumor and some necrotic renal parenchyma, which can be differentiated from surrounding enhancing normal renal parenchyma.<sup>29,39,41</sup> The parts of the ablation zone that do not abut normal renal parenchyma are bordered by relatively normal-appearing fat and a thin soft tissue attenuation rim or halo.<sup>29,39,41</sup> Even more centrally located tumors finally develop fat interposition between the ablated tissue and normal renal parenchyma. Over time, the ablation zone shows reduction in size secondary to fibrous tissue and nonenhancing scar formation and gradually involutes. Dystrophic calcification and capsular retraction in peripheral lesions also have been described.

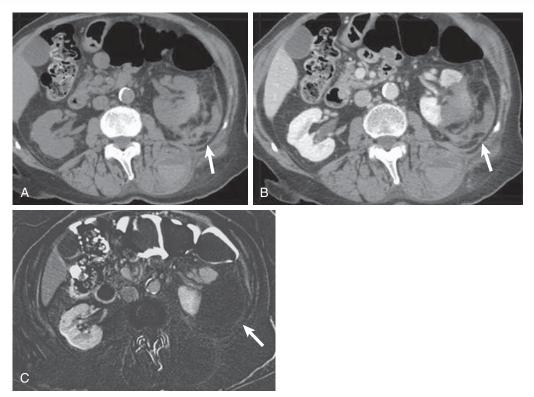
The spectrum of abnormal appearances includes immediate or delayed atypical changes that suggest inadequate treatment, progression, or procedure-related complications.<sup>25,26,28,60</sup> Prompt recognition of residual or recurrent disease after treatment is the primary intent of postprocedural imaging surveillance. Careful review of the images is required, and it is often helpful to review the pre-ablation and intraprocedural images to predict areas that demonstrate residual disease or recurrence. Recurrence following loco-regional therapy represents either local tumor progression at the margin of treatment zone or distant recurrence as a result of development of new tumor away from the ablation zone.<sup>61</sup> A new tumor focus also can develop in the contralateral kidney. Therefore, careful attention to the



**Figure 86-6** Expected postablation changes on CT after RFA of a left lobe colorectal liver metastases. **A**, Axial contrast enhanced CT showing the 2-cm left hepatic lobe metastatic lesion (*arrow*). **B**, Intraprocedural CT showing the RF probes within the left lobe lesion. **C**, Axial noncontrast CT image 1-month post RFA shows hyperdensity within the ablation zone (*arrows*) likely corresponding to a combination of hemorrhage, necrosis, and debris. **D**, Axial contrast enhanced CT image at 1-month post RFA shows the nonenhancing ablation zone (*arrows*) larger than the metastatic lesion indicative of complete treatment response.



**Figure 86-7** Expected postablation changes on magnetic resonance imaging (MRI) after radiofrequency ablation (RFA) of a right lobe hepatocellular carcinoma (HCC). A, Axial gadolinium-enhanced MRI shows a segment 5 HCC. B, One month after RFA, the ablation zone demonstrates heterogeneous areas of T1 hyperintensity. Axial gadolinium-enhanced MRI in the arterial (C) and portal venous phase (D) shows lack of enhancement within the ablation zone with a thin rim of peripheral enhancement, which is an expected finding.



**Figure 86-8** Expected postablation changes on computed tomography (CT) after radiofrequency ablation (RFA) of renal cell carcinoma (RCC). A, Axial noncontrast CT image shows the ablation zone after RFA of left renal RCC with heterogeneous hyperdense areas and perinephric fat stranding (*arrows*). Contrast-enhanced (**B**) and subtraction (**C**) images demonstrate lack of enhancement within the ablation zone indicating treatment response.

evaluation of the entire liver or both kidneys is important. Residual tumor from inadequate treatment generally appears as nodular enhancement in the treatment zone while tumor recurrence typically manifests as enhancing nodules after imaging confirmation of complete ablation previously. In primary and secondary hepatic tumors, the morphologic characteristics of recurrence are similar (Figure 86-9). However, HCC recurrences are better appreciated on arterial phase images whereas colorectal liver metastases are better identified on the portal venous phase.<sup>25,26</sup> Subtraction images are particularly helpful for identification of suspicious areas of nodular enhancement in both the liver and kidney.<sup>29,39,41</sup> It is particularly crucial to evaluate the vascular structures such as the portal vein or renal vein after ablation to identify vascular involvement or complications. After ablation of colorectal liver metastases, PET/CT is found to be superior to CT by allowing reliable differentiation of posttreatment changes from residual or recurrent malignant disease. However, PET/CT is limited in its ability to detect nodular recurrences and false positive results can occur in rare occasions of infective complications and abscess formation at the ablation site.<sup>52</sup> Mimics of neoplastic recurrence such as foreign body reaction and chronic infections can occur at the ablation zone and cause diagnostic challenges. In such situations, image-guided biopsy can be performed for confirmation of diagnosis.

#### Intra-Arterial Therapies

Interpretation of posttreatment changes after intra-arterial therapies can be difficult and requires a robust understanding of baseline imaging appearances and procedural details.<sup>18,25,26,62,63</sup>

It is particularly important to review the details of the angiography to anatomically localize the arterial territory treated by particle embolization.<sup>18,25,26,62,63</sup> Post-TACE imaging appearances can be categorized based on the administration of lipiodol during TACE procedure. Assessment of treatment response after lipiodol-TACE depends on the deposition of iodized oil on unenhanced CT and tumor size and enhancement characteristics on CT/MRI.<sup>25,26,62,63</sup> The tumoral areas with lipiodol uptake appear hyperattenuating on unenhanced CT, and the degree of lipiodol deposition within the tumor is proportional to the degree of tumor.<sup>25,26,62,63</sup> The lipiodol deposition limits the ability of CT to accurately detect residual viable tumor and therefore gadolinium-enhanced MRI is preferred for response assessment because the MRI signal intensity is not affected by lipiodol concentration<sup>25,26,62,63</sup> (Figure 86-10). Successfully treated tumors demonstrate nonenhancement on postcontrast CT/MRI. On MRI, treated tumors can have variable signal intensity on T1and T2-weighted images and necrotic tumors are generally hypointense on T2-weighted images, whereas hemorrhage and residual tumors are hyperintense on T2-weighted images.<sup>45</sup> In patients who undergo conventional TACE without lipiodol administration, dynamic contrast-enhanced CT is equally effective as MRI in monitoring treatment response.<sup>25</sup> Subtraction imaging is useful for assessment of contrast enhancement in postprocedural evaluation.

The imaging appearance after SIRT is manifested by reduction in tumoral enhancement on dynamic contrast-enhanced CT or MRI. In HCC, reduction in tumor enhancement is seen on both arterial and portal venous phases after successful radioembolization. Significant changes in tumor size might not be

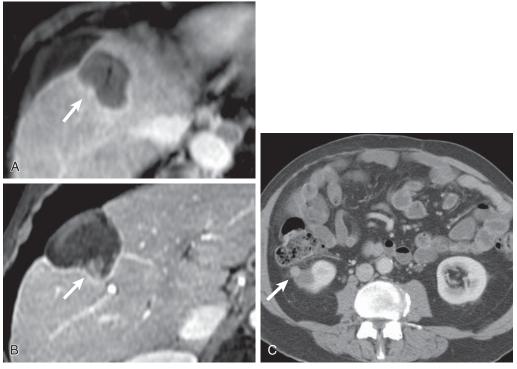
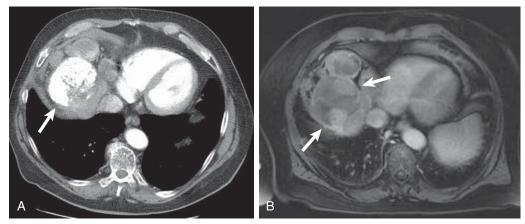


Figure 86-9 Expected rim enhancement versus abnormal nodular enhancement. A, Axial gadolinium-enhanced magnetic resonance imaging (MRI) after percutaneous ablation shows expected rim enhancement around the ablation zone that is due to inflammatory reaction (arrow). B, Axial gadolinium-enhanced MRI shows nodular enhancing lesion within the ablation zone suggestive of tumor recurrence (arrow). C, Axial contrast-enhanced computed tomography image after cryoablation of right renal cell carcinoma shows nodular recurrence in the ablation zone (arrow).



**Figure 86-10** Value of magnetic resonance imaging (MRI) in determination of treatment response after lipiodol-transarterial chemoembolization (TACE). **A**, Axial noncontrast computed tomography after lipiodol-TACE for dome hepatocellular carcinoma demonstrates heterogeneous deposition of lipiodol within the tumor (*arrow*), which limits assessment of enhancing tumor. **B**, Axial gadolinium-enhanced MRI better demonstrates enhancing nodules within the tumor, suggesting residual disease (*arrow*).

seen for a few months after treatment, and a transient peripheral rim of enhancement might be seen around the tumor secondary to local radiation effects, which may last for several months.<sup>25</sup> Varying degrees of transient local inflammatory changes can be seen within the liver outside the treated tumor and should not be confused with tumor progression. These manifestations include areas of periportal hypoattenuation secondary to perivascular edema, contralateral lobar hypertrophy and ipsilateral lobar atrophy, perihepatic ascites because of radiation effect on Glisson's capsule, and sympathetic pleural

effusion.<sup>25</sup> In patients with liver metastases treated with SIRT, PET/CT adds value by improved detection of treatment response.<sup>64</sup>

#### Image-Guided Radiation Therapy

After image-guided radiation therapy for hepatic malignancies, treatment changes are seen not only within the targeted tumor but also in the areas corresponding to the radiation zone. The zone of irradiation appears as a sharply demarcated region with the treated tumor appearing hypodense with peripheral rim

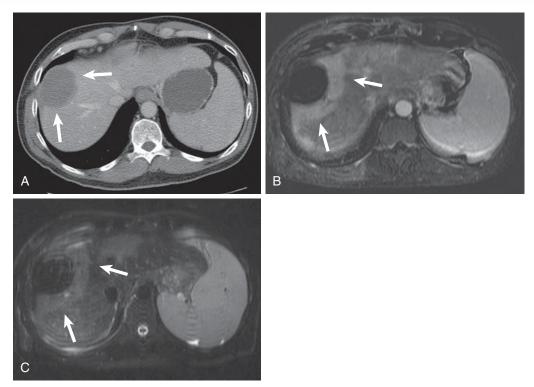


Figure 86-11 Proton beam therapy for hepatic dome colorectal liver metastases. A, Pretreatment axial contrast-enhanced computed tomography image shows a hypodense tumor in the dome of liver (arrows). B and C, Postradiation axial magnetic resonance imaging at 3 months shows the well-demarcated radiation zone (arrows) hyperintense on T2-weighted image with the tumor demonstrating T2 hypointensity and absence of enhancement of postgadolinium images.

enhancement.<sup>65</sup> After successful irradiation, there is gradual decline in the treated tumor while the surrounding irradiated hepatic parenchyma gradually shows increasing attenuation (initially isodense and then hyperdense) on contrast-enhanced CT.<sup>65</sup> Local treatment failure is evidenced by gradual increase in tumor size with lobulated thick heterogeneous enhancement of the irradiated tumor.<sup>65</sup> On MRI, the liver parenchyma in the zone of radiation demonstrates well-demarcated areas of T1 hypointensity and slight T2 hyperintensity as a result of increased free water content in the irradiated areas<sup>66</sup> (Figure 86-11). The irradiated areas demonstrate early, intense, and prolonged enhancement compared to that in the surrounding normal liver parenchyma because of impeded drainage of blood from hepatic venous obstruction secondary to radiation effects.<sup>66</sup> Complete treatment response is indicated by total lack of enhancement of the tumor within the radiation zone.

## MONITORING RESPONSE TO LOCO-REGIONAL THERAPIES

The main goal of loco-regional therapies, including percutaneous ablation or intra-arterial therapies, is to attain tumor destruction or necrosis of the targeted tumor tissue. Accordingly, after treatment, there might not be reduction in tumor size.<sup>25</sup> As a result, conventionally established tumor metric systems such as the World Health Organization (WHO) criteria and the Response Evaluation Criteria in Solid Tumors (RECIST), which were designed to assess tumor response to cytotoxic therapy causing tumor shrinkage, are well-suited to monitor response to loco-regional therapies.<sup>25</sup> In fact, they could even be misleading because image-guided therapies often lead to stabilization of tumor size or even tumor enlargement initially despite satisfactory tumor destruction resulting from lag time between treatment and change in tumor size.<sup>25</sup> Moreover, new lesions cropping up after targeted therapies such as percutaneous ablation do not signify treatment failure but rather indicate tumor progression.<sup>25</sup> In view of these inadequacies, new response criteria such as those from the European Association for the Study of the Liver (EASL) and the Modified Response Evaluation Criteria in Solid Tumors (mRECIST) were developed (Table 86-1). These criteria rely on the estimation of changes in dimensions of the viable tumor using dynamic contrast-enhanced CT or gadolinium-enhanced MRI and thereby assess the changes in size of intratumoral necrotic areas and not merely changes in tumor size. For primary hepatic tumors such as HCC, the viable tumor in the treatment zone is identified as enhancing areas on the arterial phase of contrastenhanced CT or gadolinium-enhanced MRI because this phase provides the maximal contrast between vascularized tumor tissue and nonenhancing necrotic tissue.<sup>25</sup> The size of the viable tumor should be determined without including intervening areas of necrosis.<sup>25</sup> Although initially reported in management of HCCs, liver metastases treated with loco-regional therapies also can be evaluated using these techniques. However, evaluation of hypovascular liver metastases is limited because these do not show arterial enhancement. In patients with colorectal metastases, PET/CT is preferred over CT for evaluation of the ablation zone for the same reason.

# COMPLICATIONS

Imaging is very important for the estimation of posttreatment complications after loco-regional therapies. Early identification of complications after loco-regional therapies is essential to institute immediate intervention. The complications after per-

TABLE <b>86-1</b>		Treatment Response Criteria for Loco-Regional Therapies		
Response		EASL	mRECIST	
Complete response (CR)		Total disappearance of enhanced areas	Total disappearance of intratumoral arterial enhancing areas	
Partial response (PR)		>50% decrease of enhanced areas	>30% decrease in sum of diameter of arterial enhancing areas	
Stable disease (SD)		Neither PR or PD criteria met	Neither PR or PD criteria met	
Progre dise	essive ase (PD)	>25% increase in the enhanced lesions	>20% increase in sum of arterial enhancing areas	

EASL, European Association for the Study of the Liver; *mRECIST*, modified Response Evaluation Criteria in Solid Tumors.

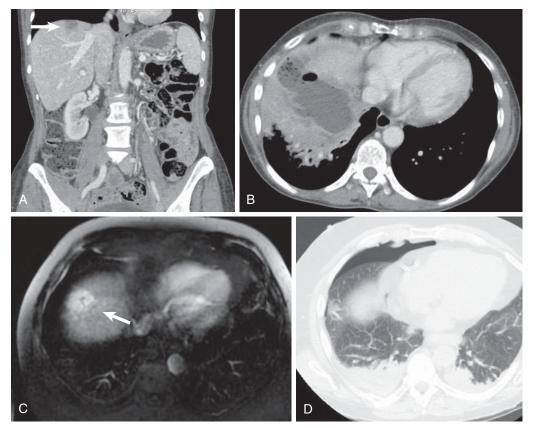
cutaneous ablation of the liver include hemorrhage, infection, pneumothorax, pleural effusion, hepatic insufficiency, arteriovenous fistula, biloma, and biliary stricture formation (Figure 86-12). Tumor seeding is a very rare complication of an ablation procedure; it is identified as enhancing tissue along the ablation track and must be differentiated from inflammatory response or infective complications. The complications of intra-arterial therapies include biliary (<10%, biliary necrosis, stricture, and cholecystitis), hepatic (0 to 4%, early transaminitis and acute liver failure, late fibrosis/cirrhosis with ascites, portal hypertension), radiation pneumonitis (<1%), access site injuries (hematoma), hepatic artery injury (dissection, thrombosis), nontarget embolization, infection (hepatic abscess), biliary strictures/ biloma, and hepatic failure. After renal ablation, the complications include perinephric hemorrhage, pneumothorax, ureteral injury, bowel injury, and track seeding.

# **Advanced Imaging Methods**

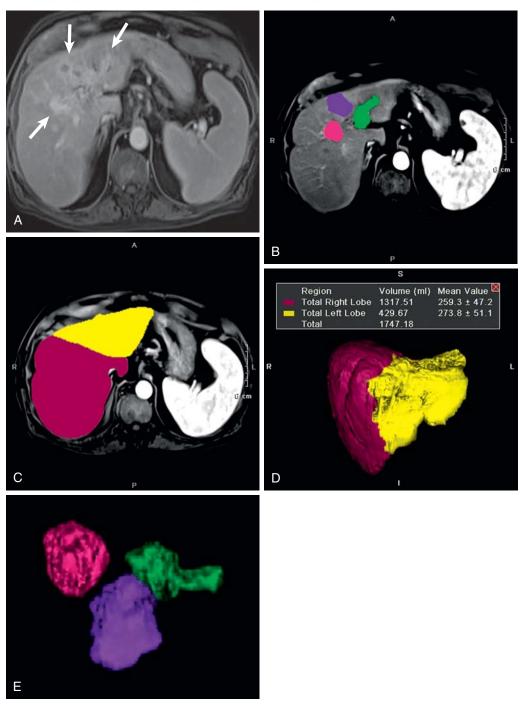
# POSTPROCESSING TECHNIQUES

# Tumor Volumetry

Volumetric methods play a crucial role in the evaluation of abdominal malignancies treated with loco-regional therapy. Segmentation methods allow estimation of tumor volume and liver volume to plan organ-directed therapies. For example, volumetric liver assessment is frequently performed for



**Figure 86-12** Complications after percutaneous ablative procedures. A, Coronal reformatted image in a 56-year-old man with colorectal liver metastasis (*arrow*) in the dome of liver treated by radiofrequency ablation (RFA). **B**, After RFA, an abscess developed at the ablation site. **C**, Gadolinium-enhanced magnetic resonance imaging shows a hepatic dome hepatocellular carcinoma (*arrow*) treated by microwave ablation. **D**, Postprocedure computed tomography image shows development of a small pneumothorax.



**Figure 86-13** Tumor volumetry to assess hepatic tumor burden to determine treatment dose before SIRT therapy. **A**, Axial gadolinium enhanced MR image demonstrates three heterogeneously enhancing HCC in the liver (*arrows*). **B**, Axial gadolinium enhanced MR image with color overlay showing determination of tumor volume using segmentation method with tumor depicted in color. **C**, Axial MR image with color overlay demonstrates segmentation method to measure liver volume with right lobe depicted in *red* and left lobe depicted in *yellow*. **D**, Volume rendered MR images demonstrating total liver with right lobe in *red* and left lobe in *yellow*. **E**, Volume rendered MR image of the tumor demonstrating the total tumor volume, left lobe tumor in *purple* and right lobe tumor in *pink*. Left portal vein is represented in *green*.

evaluation of functional liver residue when major hepatic resection (more than four segments) is planned.<sup>27,52,67</sup> In patients scheduled to undergo SIRT therapy, estimation of tumor burden and liver volume is an important prerequisite to calculate treatment dose (<sup>90</sup>Y) to limit toxicity to the normal liver<sup>67</sup> (Figure 86-13). Despite the widespread use of morphologic imaging studies such as CT and MRI for treatment evaluation, 2D tumor assessment has drawbacks. Conventional morphologic studies assume that tumors have spherical dimensions, and mRECIST criteria define threshold for partial response as 30% reduction in tumor diameter presuming that this corresponds to a 65% reduction in tumor volume.<sup>28</sup> 2D tumor volume estimates not only differ from concurrent 3D measurements but are also prone to interobserver variability both for measurement of tumor diameter and estimation of tumor necrosis.<sup>28</sup> Performing volumetric evaluation eliminates this limitation, and voxel-by-voxel volumetric analysis of tumor density and necrosis are more precise and reproducible than 2D measurements.<sup>28</sup> Volumetric quantification is particularly desirable when tumors are heterogeneous in the distribution of necrosis, which limits their accurate assessment using mRECIST.<sup>28</sup> Notwithstanding its immense benefits, volumetric measurements are not easily available and are not integrated completely into routine clinical practice.<sup>28</sup> In patients with colorectal liver metastases, reports indicate that volumetric increase in the ablation zone after the original postablation scan in colorectal liver metastases is highly predictive of ablation zone recurrence.

## Necrosis Quantification

Quantification of necrosis and viable tumor after loco-regional therapies has been shown to be accurate in determining treatment response.<sup>28,68,69</sup> In patients undergoing SIRT therapy, volumetric measurement of tumor necrosis has been reported to detect response earlier than the conventional response assessment criteria such as RECIST.<sup>64,67</sup> Moreover, preliminary studies demonstrate that tumor necrosis measurements correlate with survival.

## Dual-Energy Computed Tomography

Dual-energy CT (DECT) is technologic advancement in MDCT, which allows simultaneous acquisition of CT images using different photon energies. MDCT data acquisition at two different energies (generally 80 and 140 kilovoltage peak) allows tissue characterization, which improves lesion detection. The low kiloelectron volt monochromatic images and iodine-specific images generated from DECT acquisition has been shown to improve the conspicuity in the detection of both hypervascular and hypovascular liver lesions. The low-energy monochromatic images increase iodine conspicuity of the enhancing tumor and surrounding vasculature, thereby providing superior delineation of tumor margins and their relationship to adjacent vessels.<sup>70-73</sup>

Generally, posttreatment CT evaluation in the kidney or liver necessitates acquisition of both unenhanced and contrastenhanced CT images, which is essential to accurately characterize abnormal enhancement in the ablation zone for early recognition of residual or recurrent tumor. The diagnosis of viable noncontrast tumor in the heterogeneous ablation zone can be challenging at times because of the presence of hemorrhage, edema, or intralesional desiccation, which can be compounded by respiratory misregistration between the noncontrast and contrast scans.<sup>70</sup> The qualitative and quantitative iodine distribution images obtained from postprocessed DECT data sets can enable more accurate detection of residual and recurrent tumor (Figure 86-14). The iodine maps and images allow precise determination of the distribution of iodine within the ablation zone and therefore can theoretically improve the detection of abnormal enhancement within the heterogeneous ablation and improve detection of enhancing viable tumor after percutaneous ablation.<sup>74</sup> The conspicuity of the ablation zone has been shown to be better on iodine images than regular CT images and therefore could improve detection of viable tumor in ablation zone.

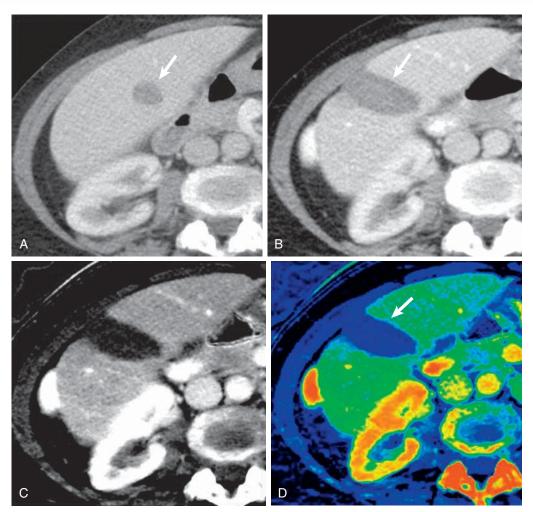
#### HEPATOBILIARY MAGNETIC RESONANCE CONTRAST AGENTS

Gadolinium-enhanced MRI is very sensitive for recognizing liver metastases and the introduction of hepatospecific contrast agents such as gadoxetate acid have increased their capability to detect and characterize hepatic lesions, particularly lesions less than 10 mm. MRI contrast agents such as gadoxetate disodium improve detection and characterization of metastases and HCC lesions on the delayed hepatobiliary phase images. Several studies have shown that, in spite of size, the detection of hepatic metastases is drastically improved with the gadoxetic-enhanced dynamic MRI scans as a result of superior liver-lesion contrast generated by hypointense metastases seen because of avid uptake of gadolinium by background normal liver.<sup>62,63,75</sup> Gadoxetic acid-enhanced MRI has been shown to have a high sensitivity (95%) and specificity (94%) for detection of liver lesions and reportedly results in change in surgical therapy in 14.5% of patients.<sup>62,63,75</sup> In our experience, radiation oncologists prefer gadoxetate-enhanced hepatobiliary phase MRI for facilitating more restricted delivery of therapy such as proton or x-ray radiation.

## FUNCTIONAL MAGNETIC RESONANCE TECHNIQUE

Diffusion weighted MRI imaging allows qualitative and quantitative evaluation of diffusion of water molecules in the tissues. Several studies have shown that DWI complements other MRI techniques in the detection and characterization of malignant lesions. Diffusion weighted MRI significantly improves the detection of colorectal liver metastases, particularly small (<1 cm) metastases that mimic intrahepatic vasculature, and highlight lesions close to the liver surface.<sup>76,77</sup> The combination of diffusion weighted MRI and gadoxetic acid-enhanced MRI has demonstrated better diagnostic accuracy and sensitivity (93%) in the detection of small HCCs (<2 cm).  $^{75}$  Diffusion weighted MRI also plays a cardinal role in tumor staging by enabling differentiation of bland and tumor thrombus with the mean apparent diffusion coefficient (ADC) of the tumor thrombus being significantly lower than that of bland thrombus (see Figure 86-4).75-78 Pretreatment diffusion weighted MRI forms a baseline for assessing changes in tumor cellular integrity after liver-directed therapy.

DWI, a functional imaging tool that measures tissue diffusivity of free water molecules, is potentially helpful in the monitoring of tumor response after intra-arterial therapies because successfully treated tumors show increased ADC values as a response to increasing water diffusion after cellular destruction. Early changes of increase in tissue diffusion on DWI after intraarterial therapy has been shown to be a predictive biomarker for favorable outcome or progression-free survival after TACE. Due to the lag time between successful treatment and changes in tumor dimension, DWI has been proposed to be a superior technique for evaluating response after SIRT therapy as early as 1 month after treatment in HCC.<sup>25</sup> After SIRT therapy, the necrotic tumor tissue is seen as significant increase in the ADC values.<sup>25</sup> DWI also might help distinguish posttreatment inflammation from viable tumor after SIRT therapy. Preliminary results have been published regarding the use of diffusion weighted MRI after hepatic RFA for detection of local tumor progression.<sup>79</sup> No obvious changes in ADC obtained from the



**Figure 86-14** Value of dual-energy computed tomography (CT) in monitoring response to percutaneous ablation. **A**, Axial contrast-enhanced CT image obtained in the portal venous phase shows a hypovascular liver metastasis (*arrow*). **B**, After radiofrequency ablation, axial contrast-enhanced CT image shows the ablation zone without obvious enhancement (*arrow*). **C** and **D**, Corresponding iodine image and color overlay iodine map substantially improves evaluation of the ablation zone (*arrow*), with no evidence of residual tumor or tumor recurrence.

therapies.

entire ablation zones were detected over time. However, ADCbased evaluation of signal alterations in the periphery of the ablation zone may be helpful in differentiation between local tumor progression, showing lower ADC values and nontumoral posttreatment tissue changes.<sup>25</sup>

#### **Key Point**

 Recognition and differentiation of normal posttreatment changes from residual or recurrent disease are necessary to prevent overcalling benign changes as abnormal, which in turn can result in unnecessary treatment.

# REFERENCES

- Adam R, De Gramont A, Figueras J, et al: The oncosurgery approach to managing liver metastases from colorectal cancer: a multidisciplinary international consensus. *Oncologist* 17:1225– 1239, 2012.
- 2. Bruix J, Sherman M: Management of hepatocellular carcinoma. *Hepatology* 42:1208–1236, 2005.
- Bruix J, Sherman M, Llovet JM, et al: Clinical management of hepatocellular carcinoma: conclusions of the Barcelona-2000 EASL conference. European Association for the Study of the Liver. J Hepatol 35:421–430, 2001.
- Fisher RA, Maluf DG, Wolfe L, et al: Is hepatic transplantation justified for primary liver cancer? J Surg Oncol 95:674–679, 2007.
- Fisher RA, Maroney TP, Fulcher AS, et al: Hepatocellular carcinoma: strategy for optimizing surgical resection, transplantation and pal:iation. *Clin Transplant* 16(Suppl 7):52–58, 2002.

What the Referring Physician Needs to Know

evaluation is essential for optimal results.

• Imaging is crucial in the successful management of

 Knowledge of the role of imaging in pretreatment planning, therapy guidance, and posttreatment

hepatobiliary and renal tumors with novel targeted

 Brock KK: Imaging and image-guided radiation therapy in liver cancer. Semin Radiat Oncol 21: 247–255, 2011.

- 7. Hur H, Ko YT, Min BS, et al: Comparative study of resection and radiofrequency ablation in the treatment of solitary colorectal liver metastases. *Am J Surg* 197:728–736, 2009.
- Mahnken AH, Pereira PL, de Baere T: Interventional oncologic approaches to liver metastases. *Radiology* 266:407–430, 2013.
- Ong SL, Gravante G, Metcalfe MS, et al: Efficacy and safety of microwave ablation for primary and secondary liver malignancies: a systematic review. Eur J Gastroenterol Hepatol 21:599–605, 2009.
- Park HC, Seong J, Tanaka M, et al: Multidisciplinary management of nonresectable hepatocellular carcinoma. *Oncology* 81(Suppl 1): 134–140, 2011.
- Clark HP, Carson WF, Kavanagh PV, et al: Staging and current treatment of hepatocellular carcinoma. *Radiographics* 25(Suppl 1):S3–S23, 2005.
- 12. Clark TW, Millward SF, Gervais DA, et al: Reporting standards for percutaneous thermal ablation of renal cell carcinoma. *J Vasc Interv Radiol* 20:S409–S416, 2009.
- Gervais DA, Arellano RS, Mueller PR: Percutaneous radiofrequency ablation of renal cell carcinoma. *Eur Radiol* 15:960–967, 2005.
- Gervais DA, McGovern FJ, Arellano RS, et al: Renal cell carcinoma: clinical experience and technical success with radio-frequency ablation of 42 tumors. *Radiology* 226:417–424, 2003.
- Zagoria RJ, Hawkins AD, Clark PE, et al: Percutaneous CT-guided radiofrequency ablation of renal neoplasms: factors influencing success. *AJR Am J Roentgenol* 183:201–207, 2004.
- Choueiri TK, Schutz FA, Hevelone ND, et al: Thermal ablation vs surgery for localized kidney cancer: a Surveillance, Epidemiology, and End Results (SEER) database analysis. Urology 78: 93–98, 2011.
- Kambadakone A, Ganguli S, Mueller PR: Interventional radiology in the management of hepatocellular carcinoma in liver cirrhosis. *Ann Gastroenterol Hepatol* 2:1–12, 2011.
- Kalva SP, Thabet A, Wicky S: Recent advances in transarterial therapy of primary and secondary liver malignancies. *Radiographics* 28:101–117, 2008.
- Kim M, Son SH, Won YK, et al: Stereotactic ablative radiotherapy for oligometastatic disease in liver. *Biomed Res Int* 2014:340478, 2014.
- Riaz A, Kulik LM, Mulcahy MF, et al: Yttrium-90 radioembolization in the management of liver malignancies. *Semin Oncol* 37:94–101, 2010.
- Tsochatzis EA, Germani G, Burroughs AK: Transarterial chemoembolization, transarterial chemotherapy, and intra-arterial chemotherapy for hepatocellular carcinoma treatment. *Semin Oncol* 37:89–93, 2010.
- 22. Ursino S, Greco C, Cartei F, et al: Radiotherapy and hepatocellular carcinoma: update and review of the literature. *Eur Rev Med Pharmacol Sci* 16:1599–1604, 2012.
- Wang N, Guan Q, Wang K, et al: TACE combined with PEI versus TACE alone in the treatment of HCC: a meta-analysis. *Med Oncol* 28:1038–1043, 2011.
- Boonsirikamchai P, Loyer EM, Choi H, et al: Planning and follow-up after ablation of hepatic tumors: imaging evaluation. *Surg Oncol Clin N Am* 20:301–315, viii, 2011.
- Crocetti L, Della Pina C, et al: Periintraprocedural imaging: US, CT, and MRI. *Abdom Imaging* 36:648–660, 2011.

- Schima W, Ba-Ssalamah A, Kurtaran A, et al: Post-treatment imaging of liver tumours. *Cancer Imaging* 7(Spec No A):S28–S36, 2007.
- Vauthey JN, Dixon E, Abdalla EK, et al: Pretreatment assessment of hepatocellular carcinoma: expert consensus statement. *HPB (Oxford)* 12:289–299, 2010.
- Yaghmai V, Besa C, Kim E, et al: Imaging assessment of hepatocellular carcinoma response to locoregional and systemic therapy. *AJR Am J Roentgenol* 201:80–96, 2013.
- 29. Uppot RN, Silverman SG, Zagoria RJ, et al: Imaging-guided percutaneous ablation of renal cell carcinoma: a primer of how we do it. *AJR Am J Roentgenol* 192:1558–1570, 2009.
- Gervais DA, McGovern FJ, Arellano RS, et al: Radiofrequency ablation of renal cell carcinoma. I. Indications, results, and role in patient management over a 6-year period and ablation of 100 tumors. AJR Am J Roentgenol 185:64–71, 2005.
- Bouza C, Lopez-Cuadrado T, Alcazar R, et al: Meta-analysis of percutaneous radiofrequency ablation versus ethanol injection in hepatocellular carcinoma. *BMC Gastroenterol* 9:31, 2009.
- Lencioni R, Cioni D, Della Pina C, et al: Hepatocellular carcinoma: new options for imageguided ablation. J Hepatobiliary Pancreat Sci 17:399–403, 2010.
- Lencioni R, Crocetti L, Pina MC, et al: Percutaneous image-guided radiofrequency ablation of liver tumors. *Abdom Imaging* 34:547–556, 2009.
- Liang P, Wang Y: Microwave ablation of hepatocellular carcinoma. Oncology 72(Suppl 1):124– 131, 2007.
- Livraghi T, Goldberg SN, Lazzaroni S, et al: Small hepatocellular carcinoma: treatment with radio-frequency ablation versus ethanol injection. *Radiology* 210:655–661, 1999.
- Narayanan G, Hosein PJ, Arora G, et al: Percutaneous irreversible electroporation for down-staging and control of unresectable pancreatic adenocarcinoma. J Vasc Interv Radiol 23:1613–1621, 2012.
- Bester L, Meteling B, Boshell D, et al: Transarterial chemoembolisation and radioembolisation for the treatment of primary liver cancer and secondary liver cancer: a review of the literature. *J Med Imaging Radiat Oncol* 58:341–352, 2014.
- Swaminath A, Dawson LA: Emerging role of radiotherapy in the management of liver metastases. *Cancer J* 16:150–155, 2010.
- Ortiz-Alvarado O, Anderson JK: The role of radiologic imaging and biopsy in renal tumor ablation. World J Urol 28:551–557, 2010.
- Schiller JD, Gervais DA, Mueller PR: Radiofrequency ablation of renal cell carcinoma. *Abdom Imaging* 30:442–450, 2005.
- 41. Wile GE, Leyendecker JR, Krehbiel KA, et al: CT and MR imaging after imaging-guided thermal ablation of renal neoplasms. *Radiographics* 27:325–339, discussion 39–40, 2007.
- Clasen S, Boss A, Schmidt D, et al: Magnetic resonance imaging for hepatic radiofrequency ablation. *Eur J Radiol* 59:140–148, 2006.
- 43. Gervais DA, Goldberg SN, Brown DB, et al: Society of Interventional Radiology position statement on percutaneous radiofrequency ablation for the treatment of liver tumors. *J Vasc Interv Radiol* 20:S342–S3427, 2009.
- 44. Gervais DA, Goldberg SN, Brown DB, et al: Society of Interventional Radiology position statement on percutaneous radiofrequency ablation for the treatment of liver tumors. *J Vasc Interv Radiol* 20:3–8, 2009.

- Brennan IM, Ahmed M: Imaging features following transarterial chemoembolization and radiofrequency ablation of hepatocellular carcinoma. Semin Ultrasound CT MR 34:336–351, 2013.
- Crocetti L, de Baere T, Lencioni R: Quality improvement guidelines for radiofrequency ablation of liver tumours. *Cardiovasc Intervent Radiol* 33:11–17, 2010.
- Hompes D, Prevoo W, Ruers T: Radiofrequency ablation as a treatment tool for liver metastases of colorectal origin. *Cancer Imaging* 11:23–30, 2011.
- Volpe A, Patard JJ: Prognostic factors in renal cell carcinoma. World J Urol 28:319–327, 2010.
- 49. Arellano RS, Garcia RG, Gervais DA, et al: Percutaneous CT-guided radiofrequency ablation of renal cell carcinoma: efficacy of organ displacement by injection of 5% dextrose in water into the retroperitoneum. *AJR Am J Roentgenol* 193:1686–1690, 2009.
- Clasen S, Pereira PL: Magnetic resonance guidance for radiofrequency ablation of liver tumors. *J Magn Reson Imaging* 27:421–433, 2008.
   Cantwell CP, Wah TM, Gervais DA, et al:
- 51. Cantwell CP, Wah TM, Gervais DA, et al: Protecting the ureter during radiofrequency ablation of renal cell cancer: a pilot study of retrograde pyeloperfusion with cooled dextrose 5% in water. J Vasc Interv Radiol 19:1034–1040, 2008.
- Guenette JP, Dupuy DE: Radiofrequency ablation of colorectal hepatic metastases. J Surg Oncol 102:978–987, 2010.
- Gervais DA, Arellano RS, McGovern FJ, et al: Radiofrequency ablation of renal cell carcinoma. II. Lessons learned with ablation of 100 tumors. AJR Am J Roentgenol 185:72–80, 2005.
- Zagoria RJ: Percutaneous image-guided radiofrequency ablation of renal malignancies. *Radiol Clin North Am* 41:1067–1075, 2003.
- Hedgire SS, Elmi A, Kambadakone AR, et al: MDCT imaging of AlloDerm biologic mesh spacers in the abdomen and pelvis: preliminary experience. *Clin Imaging* 38:279–282, 2014.
- Yoon SS, Chen YL, Kambadakone A, et al: Surgical placement of biologic mesh spacers prior to external beam radiation for retroperitoneal and pelvic tumors. *Pract Radiat Oncol* 3:199–208, 2013.
- Clasen S, Boss A, Schmidt D, et al: MR-guided radiofrequency ablation in a 0.2-T open MR system: technical success and technique effectiveness in 100 liver tumors. J Magn Reson Imaging 26:1043–1052, 2007.
- Dierckx R, Maes A, Peeters M, et al: FDG PET for monitoring response to local and locoregional therapy in HCC and liver metastases. Q J Nucl Med Mol Imaging 53:336–342, 2009.
- Sahani DV, Bajwa MA, Andrabi Y, et al: Current status of imaging and emerging techniques to evaluate liver metastases from colorectal carcinoma. *Ann Surg* 259:861–872, 2014.
- Crocetti L, Lencioni R: Thermal ablation of hepatocellular carcinoma. *Cancer Imaging* 8:19– 26, 2008.
- Zytoon AA, Ishii H, Murakami K, et al: Recurrence-free survival after radiofrequency ablation of hepatocellular carcinoma: registry report of the impact of risk factors on outcome. *Jpn J Clin Oncol* 37:658–672, 2007.
- 62. Kloeckner R, Otto G, Biesterfeld S, et al: MDCT versus MRI assessment of tumor response after transarterial chemoembolization for the treatment of hepatocellular carcinoma. *Cardiovasc Intervent Radiol* 33:532–540, 2010.

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- 63. Kubota K, Hisa N, Nishikawa T, et al: Evaluation of hepatocellular carcinoma after treatment with transcatheter arterial chemoembolization: comparison of Lipiodol-CT, power Doppler sonography, and dynamic MRI. *Abdom Imaging* 26:184–190, 2001.
- Miller FH, Keppke AL, Reddy D, et al: Response of liver metastases after treatment with yttrium-90 microspheres: role of size, necrosis, and PET. *AJR Am J Roentgenol* 188:776–783, 2007.
- 65. Jarraya H, Mirabel X, Taieb S, et al: Image-based response assessment of liver metastases following stereotactic body radiotherapy with respiratory tracking. *Radiat Oncol* 8:24, 2013.
- 66. Onaya H, Itai Y, Yoshioka H, et al: Changes in the liver parenchyma after proton beam radiotherapy: evaluation with MR imaging. *Magn Reson Imaging* 18:707–714, 2000.
- 67. Monsky WL, Garza AS, Kim I, et al: Treatment planning and volumetric response assessment for yttrium-90 radioembolization: semiautomated determination of liver volume and volume of tumor necrosis in patients with hepatic malignancy. *Cardiovasc Intervent Radiol* 34:306–318, 2011.
- Chalian H, Tochetto SM, Tore HG, et al: Hepatic tumors: region-of-interest versus volumetric analysis for quantification of attenuation at CT. *Radiology* 262:853–861, 2012.

- 69. Galizia MS, Tore HG, Chalian H, et al: MDCT necrosis quantification in the assessment of hepatocellular carcinoma response to yttrium 90 radioembolization therapy: comparison of two-dimensional and volumetric techniques. *Acad Radiol* 19:48–54, 2012.
- Agrawal MD, Pinho DF, Kulkarni NM, et al: Oncologic applications of dual-energy CT in the abdomen. *Radiographics* 34:589–612, 2014.
- Altenbernd J, Heusner TA, Ringelstein A, et al: Dual-energy-CT of hypervascular liver lesions in patients with HCC: investigation of image quality and sensitivity. *Eur Radiol* 21:738–743, 2011.
- 72. Kim KS, Lee JM, Kim SH, et al: Image fusion in dual energy computed tomography for detection of hypervascular liver hepatocellular carcinoma: phantom and preliminary studies. *Invest Radiol* 45:149–157, 2010.
- Robinson E, Babb J, Chandarana H, et al: Dual source dual energy MDCT: comparison of 80 kVp and weighted average 120 kVp data for conspicuity of hypo-vascular liver metastases. *Invest Radiol* 45:413–418, 2010.
- 74. Lee SH, Lee JM, Kim KW, et al: Dual-energy computed tomography to assess tumor response to hepatic radiofrequency ablation: potential diagnostic value of virtual noncontrast images and iodine maps. *Invest Radiol* 46:77–84, 2011.

- Park MJ, Kim YK, Lee MW, et al: Small hepatocellular carcinomas: improved sensitivity by combining gadoxetic acid-enhanced and diffusion-weighted MR imaging patterns. *Radiology* 264:761–770, 2012.
- Chandarana H, Taouli B: Diffusion and perfusion imaging of the liver. *Eur J Radiol* 76:348–358, 2010.
- Eccles CL, Haider EA, Haider MA, et al: Change in diffusion weighted MRI during liver cancer radiotherapy: preliminary observations. *Acta Oncol* 48:1034–1043, 2009.
- Catalano OA, Choy G, Zhu A, et al: Differentiation of malignant thrombus from bland thrombus of the portal vein in patients with hepatocellular carcinoma: application of diffusion-weighted MR imaging. *Radiology* 254:154–162, 2010.
- Park HJ, Kim SH, Jang KM, et al: Added value of diffusion-weighted MRI for evaluating viable tumor of hepatocellular carcinomas treated with radiotherapy in patients with chronic liver disease. AJR Am J Roentgenol 202:92–101, 2014.