The Equine Acute Abdomen

Third Edition

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Preface

Colic is a clinical syndrome that has frustrated horse owners and veterinarians for centuries, and that remains the same today. In fact, colic continues to be at or near the top of the list of causes of death in horses. Advances made over the past three decades in recognition of colic as well as medical, anesthetic, and surgical techniques have significantly improved the prognosis for any horse presented with colic. For example, horses with even the most devastating forms of colic, such as large colon volvulus, can have an excellent prognosis for survival if they are treated early in the disease process.

This edition of *The Equine Acute Abdomen* details further advances in early recognition of colic, including recognition of pain using subtle behavioral signs, evaluation of biomarkers indicative of ensuing severe disease, advances in imaging the abdomen, and approaches to determining the prognosis. An area of equine practice that has changed the most since the previous edition of this book is critical care, with many hospitals now employing criticalists. Consequently, several chapters in this edition detail important advances in areas such as fluid therapy, nutrition, and the appropriate use of antimicrobial, anti-inflammatory, and prokinetic agents. There is also a comprehensive new section on colic in foals.

This edition of *The Equine Acute Abdomen* explores discoveries in exciting new areas related to colic, such as the role of intestinal stem cells and the microbiome. We expect that advances in these and other areas will likely have a vital role in our future understanding of the pathogenesis and consequences of colic. This edition additionally includes up-to-date information on the epidemiology, pathophysiology, and treatment of specific diseases that cause colic, as well as important topics that often receive less attention, such as colic in the donkey, grass sickness, and biosecurity.

Given the breadth of information covered in this edition, we hope that the reader will be better prepared to intervene when horses are presented with colic. It also is our hope that this edition will inform veterinarians about the latest advancements in critical care, introduce them to some of the current trends in equine colic research, and help them improve their ability to pre-empt or ameliorate colic.

Dedication

Dedicated to the horses we've learned from throughout our careers, including the ones we've treated on the clinic floor, worked with in the research laboratory, and partnered with to teach veterinary students.

About the Companion Website

This book is accompanied by a companion website:

www.wiley.com/go/blikslager/abdomen

The website includes:

- Animations
- Figures from the book as PowerPoint slides, to download

Part I

Normal Anatomy and Physiology

1

Gross and Microscopic Anatomy of the Equine Gastrointestinal Tract

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Introduction

Gaining a working knowledge of the equine gastrointestinal tract and associated intra-abdominal organs can be challenging, especially for inexperienced individuals. Experienced veterinarians who examine and treat horses with conditions characterized by acute abdominal pain (colic) know that the key to the diagnosis often lies in recognizing changes in anatomic structures or relationships among different organs. With this in mind, the focus of this chapter is the gross and microscopic structure of the horse's alimentary tract (Figure 1.1A, B, C, and D), starting with the esophagus. Because some conditions characterized by colic involve other organs within the abdomen, we have reviewed the relevant structural aspects of the liver, spleen, and pancreas. In compiling this information, our goal is to provide veterinary students and veterinarians with the foundational materials needed to understand clinical conditions that result in colic.

Esophagus

Gross Anatomic Features

The esophagus is the long muscular tube that connects the pharynx to the stomach. It is regionally subdivided into cervical, thoracic, and abdominal parts. Individual and breed variations exist, but in general the esophagus is positioned on the dorsal aspect of the trachea at the level of the 1st cervical vertebra, inclines to the left lateral surface of the trachea at the level of the 4th cervical vertebra, and is positioned ventrolateral to the trachea from the level of the 6th cervical vertebra up to and during passage through the thoracic inlet. The thoracic portion of the esophagus travels within the mediastinum and is positioned dorsal to the trachea to the level of the tracheal bifurcation. The esophagus passes dorsal to the base of the heart and continues caudally until it penetrates the diaphragm at the esophageal hiatus, accompanied by the dorsal and ventral vagal trunks. The abdominal portion of the esophagus is short and travels over the dorsal border of the liver, creating an esophageal impression, before joining the cardia of the stomach at an acute angle.

The esophagus is more superficial and therefore more accessible for surgery in the mid- to caudal-third of the left side of the neck ventromedial to the jugular groove. Deep cervical fascia ensheathes the esophagus as it passes along the neck and also forms the left carotid sheath enclosing the left common carotid artery, the left vagosympathetic trunk, and the left internal jugular vein (when present). These structures, along with the neighboring left recurrent laryngeal nerve and the left tracheal lymphatic trunk (embedded within the deep cervical fascia that ensheathes the trachea), are to be avoided during surgical approaches to the esophagus.

Microscopic Features

The esophagus is designed to facilitate the delivery of ingesta to the stomach. Longitudinally oriented folds occur along the length of the mucosa of the esophagus to allow for expansion of its lumen during the passage of a food bolus. The mucosa of the esophagus is considerably mobile upon the underlying submucosa. The tunica mucosa is composed of three layers, or laminae (Figure 1.2). The lamina epithelialis is nonkeratinized stratified squamous epithelium (Figure 1.3); mild to moderate keratinization of the epithelium may occur, depending on the nature of the swallowed material.

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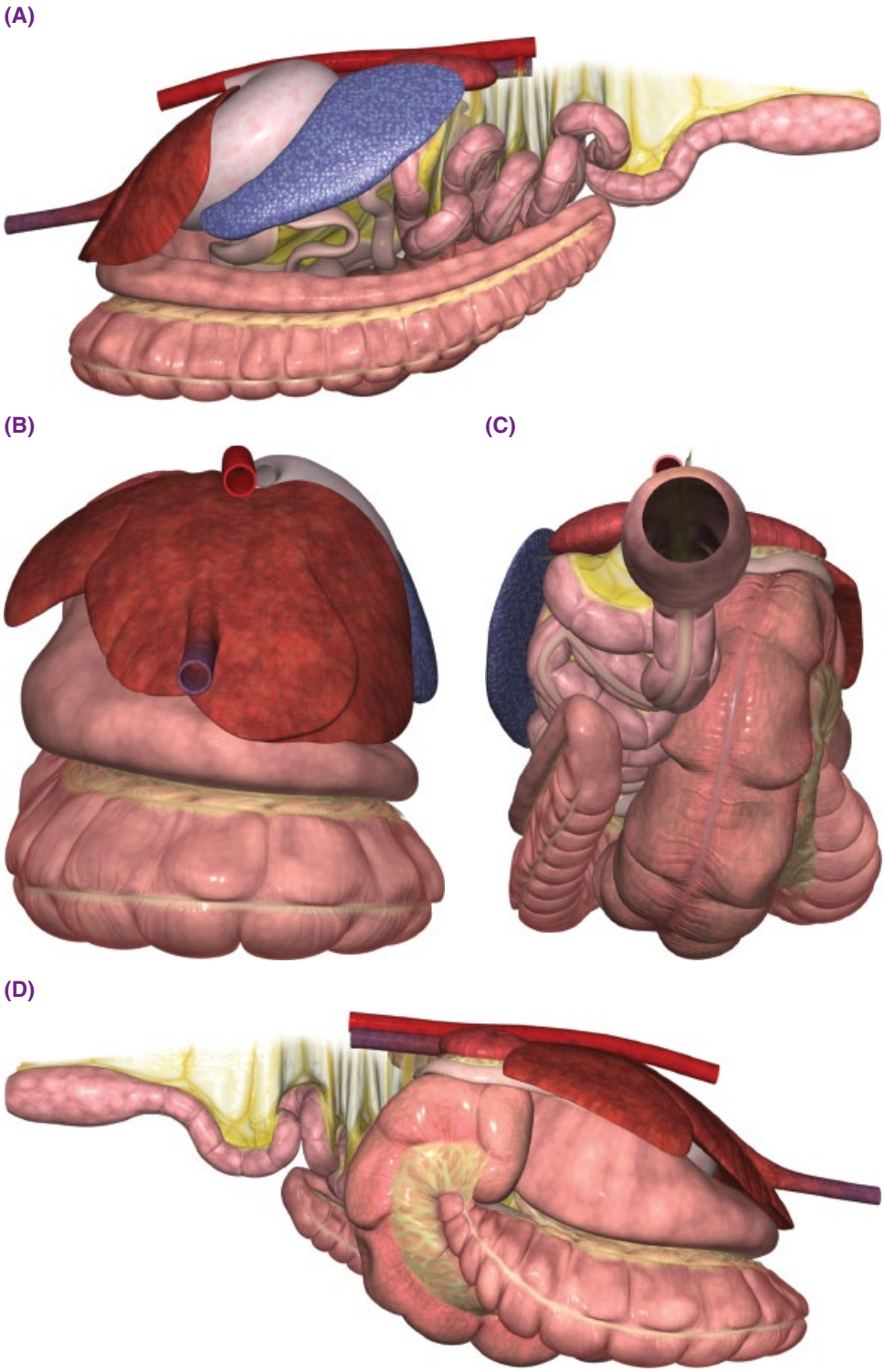

Figure 1.1 **(A)** The abdominal organs from the left side of the horse. **(B)** A view from the cranial-most aspect of the abdomen. **(C)** The abdominal organs visible from the caudal-most aspect. **(D)** The abdominal organs visible from the horse's right side. Source: Courtesy of The Glass Horse, Science In 3D.

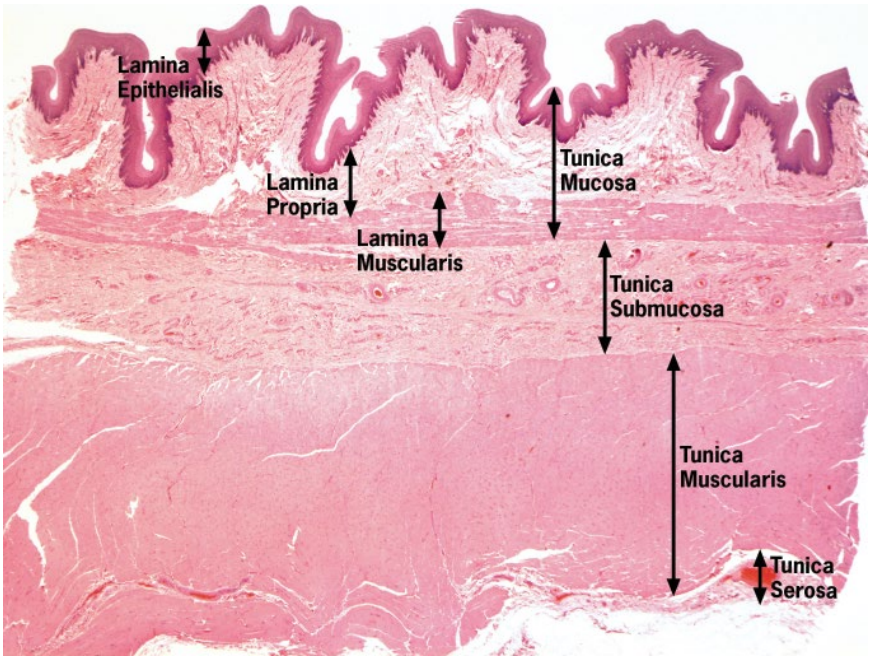

Figure 1.2 Full-thickness section of the thoracic esophagus. H&E stain.

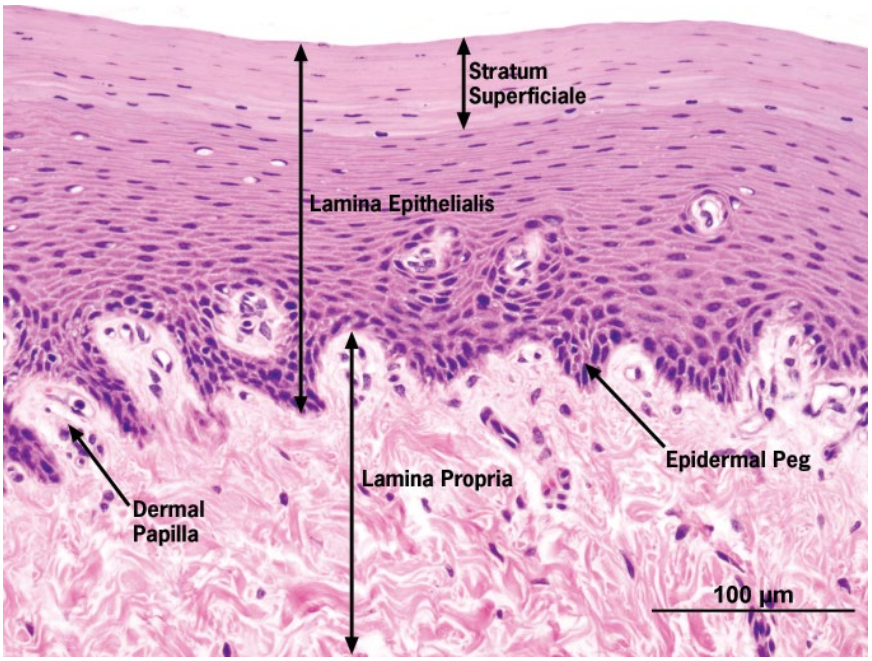

Figure 1.3 The lamina epithelialis of the esophagus. The epithelium is nonkeratinized with retention of nuclei throughout the most superficial layer (the stratum superficiale). The lamina propria is dense irregular connective tissue. The lamina propria and lamina epithelialis interdigitate via finger-like projections of the epidermis (epidermal pegs) and dermis (dermal papillae). H&E stain.

The lamina propria varies from loose to dense irregular connective tissue. The lamina muscularis mucosa consists of isolated bundles of longitudinally oriented smooth muscle in the cranial esophagus. The muscle bundles increase in density and coalesce into a distinct layer towards the caudal esophagus. Because the lamina muscularis mucosa serves as a demarcation between the mucosa and the submucosa, it is difficult to distinguish these layers where the muscularis is sparse or absent. The tunica submucosa is dense irregular connective tissue that contains prominent vasculature and the submucosal nerve plexus. Simple branching tubuloalveolar mucus-secreting submucosal glands are present at the pharyngoesophageal junction (Figure 1.4). The tunica muscularis is skeletal muscle in the cranial two-thirds of the esophagus and transitions into smooth muscle in the caudal third of the esophagus. There are two muscle layers in the tunica muscularis; however, the layers are not always distinguishable due to spiraling and interlacing of the muscle bundles. The cervical region of the esophagus

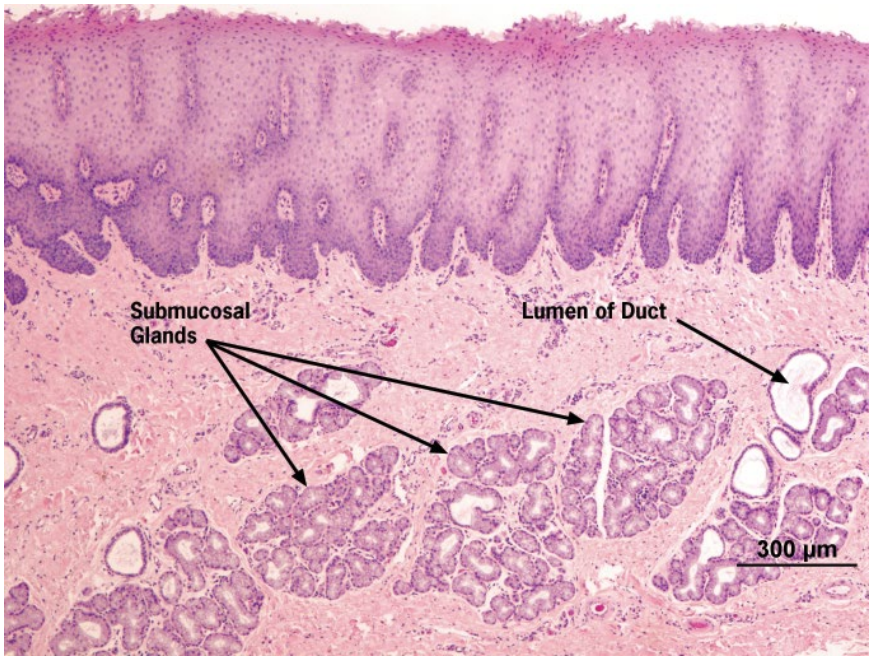

Figure 1.4 Esophageal submucosal glands. The mucous secretory products of the submucosal glands are ducted into the esophageal lumen. The larger clear spaces are sections of ducts. H&E stain.

has a tunica adventitia of dense irregular connective tissue that blends with the surrounding tissues. The thoracic and abdominal regions of the esophagus have a tunica serosa, which is mediastinal pleura and visceral peritoneum, respectively.

Esophagus–Stomach Junction

The true gastroesophageal junction in the equine is microscopically similar to the caudal esophagus with the addition of a thickening in the inner circular layer of the tunica muscularis that functions as a sphincter between the two organs. The combination of the muscular cardiac sphincter and the oblique angle at which the distal end of the esophagus joins the cardia of the stomach makes it exceptionally difficult for horses to vomit.

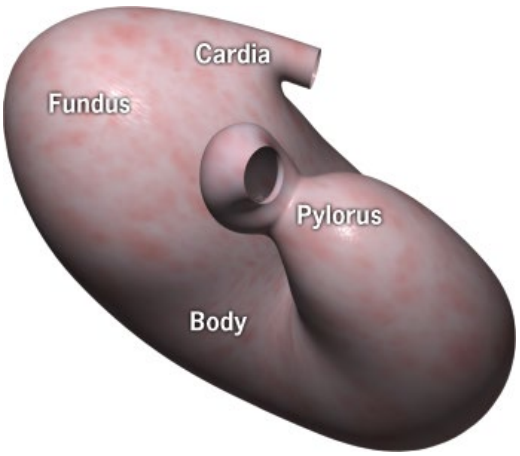

Figure 1.5 A view of the horse's stomach from the right side of the abdomen, permitting identification of the cardia, fundus, body, and pylorus. Source: Courtesy of The Glass Horse, Science In 3D.

Stomach

Gross Anatomic Features

The stomach is enclosed within the ribcage between the 9th and 15th ribs and is positioned in the left half of the abdomen, caudal to the diaphragm and liver and cranial to the spleen. It has four compartments, the cardia, fundus (saccus cecus), body, and pyloric regions (Figure 1.5). The cardia is the most cranial region and is firmly fixed to the diaphragm near the dorsal surface of the 11th rib. The fundus is dorsal to the cardia and is large and lined by a nonglandular mucosa. The body is the largest portion of the stomach and spans between the nonglandular region ventral to the cardia to the acute angle of the lesser curvature (the angular incisure). The pyloric region spans between the angular incisure to the duodenum and is subdivided into the pyloric antrum, canal, and the strong muscular sphincter, the pylorus. The pylorus is the only portion of the stomach located to the right of the median plane. The cardiac and pyloric regions are in close proximity due to the acute angle of the concave cranial surface of the stomach, the lesser curvature. The long convex greater curvature, extending between the cardia and the pylorus, defines the caudal surface of the organ. The parietal surface of the stomach lies against the diaphragm and

the left lobe of the liver and the visceral surface faces the intestines.

The stomach is attached to the abdominal wall and surrounding organs by dorsal and ventral mesogastria. The portions of the dorsal mesogastrium involving the stomach include the gastrophrenic and gastrosplenic ligaments and the greater omentum. The region of the greater curvature near the cardia is attached to the crura of the diaphragm by the gastrophrenic ligament. The gastrosplenic ligament connects the spleen to the left part of the greater curvature of the stomach. The greater omentum (epiploon) is a peritoneal fold that originates from the dorsal abdominal wall and attaches along the greater curvature of the stomach. This fold extends caudally, forming a flattened pouch referred to as the omental bursa. The omental bursa is accessed via a narrow slit, the epiploic (omental) foramen. The boundaries of the epiploic foramen are the caudate lobe of the liver dorsocranially, the caudal vena cava dorsally, the portal vein ventrally, and the right lobe of the pancreas caudoventrally. The lesser omentum is the largest portion of the ventral mesogastrium. It connects the lesser curvature of the stomach to the visceral surface of the liver (the hepatogastric ligament) and its free right edge connects the duodenum to the liver (hepatoduodenal ligament).

Microscopic Features

The equine stomach has both nonglandular and glandular regions. Surface area is increased in the stomach by rugae grossly and by gastric glands microscopically.

The nonglandular region of the stomach is microscopically similar to the caudal esophagus with a few exceptions. The lamina muscularis of the tunica mucosa in the stomach is organized into two distinct layers. The tunica muscularis is thicker in the stomach because of an additional layer of smooth muscle.

The junction of the nonglandular and glandular regions of the stomach forms a folded border, or margo plicatus (Figure 1.6). Microscopically, the margo plicatus is identified as an abrupt transition within the lamina epithelialis from a nonkeratinized stratified squamous epithelium to a simple columnar epithelium.

The glandular region of the stomach is further divided into cardiac gland, proper gastric gland, and pyloric gland regions. Microscopically, the distinction between these three regions may not be sharply demarcated, depending on where the tissue sample is taken and on the individual horse sampled. Mixing of the glandular regions may occur, some of which can be seen grossly. For example, small islands of proper gastric glands may be present in the pyloric gland region of the fresh, unfixed organ. The demarcation between proper gastric glands and pyloric glands can be seen and felt grossly because the proper gastric glands are taller than the pyloric glands and because they are colored differently in the fresh specimen.

The lamina epithelialis of the tunica mucosa of the glandular stomach is a simple columnar epithelium (Figure 1.7). This epithelium lines the entire surface of the glandular region of the stomach (Figure 1.8), including the gastric pits, and provides a protective function by secreting mucus. The lamina epithelialis also includes the epithelium lining the individual gastric glands, which invaginate into the lamina propria. The epithelium lining the gastric glands varies in cell type, depending on the

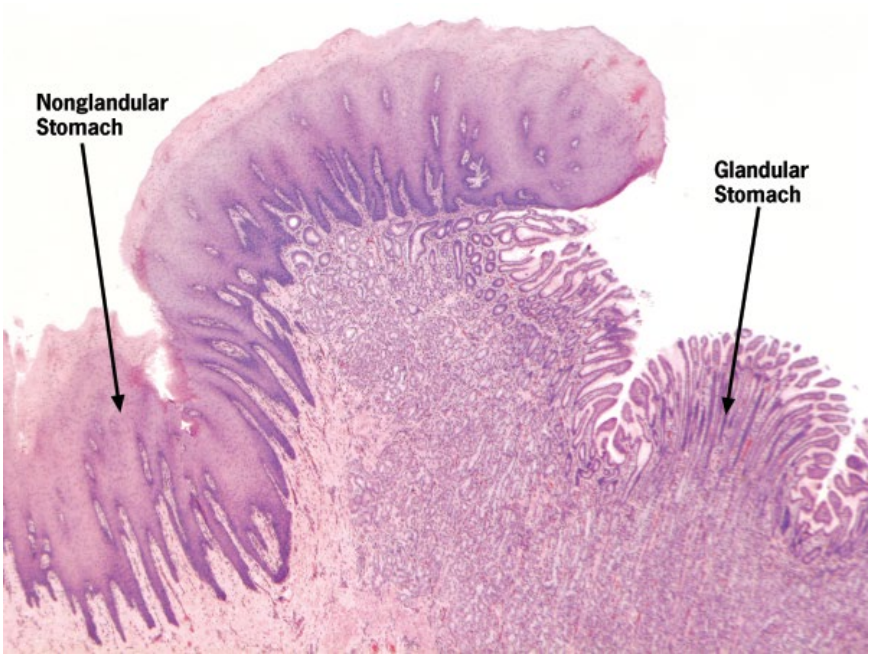

Figure 1.6 The junction of nonglandular and glandular regions of the equine stomach. The nonglandular region of the equine stomach slightly overlaps the glandular region of the stomach where the two adjoin, forming a folded border, or margo plicatus. H&E stain.

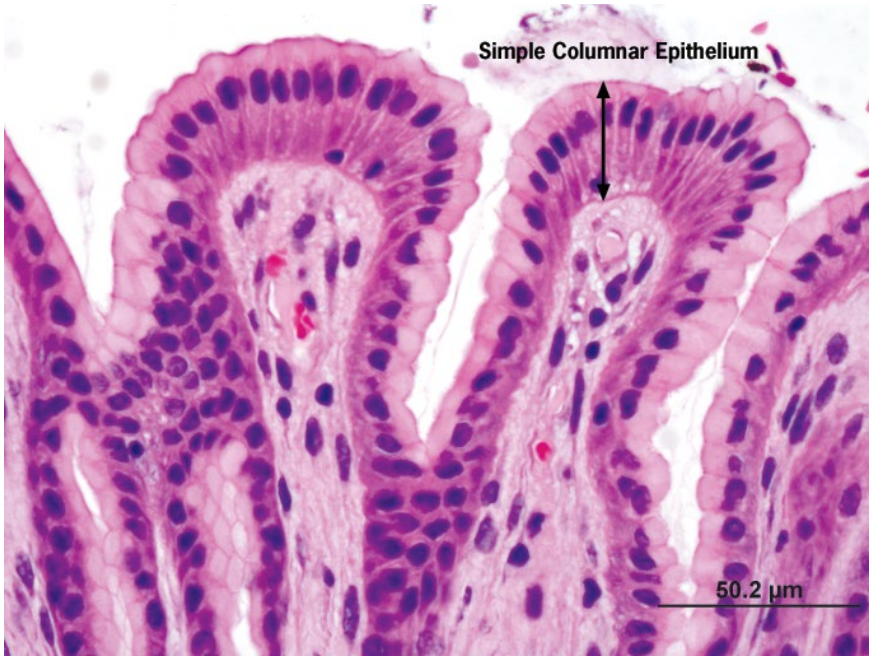

Figure 1.7 Simple columnar epithelium of the glandular portion of the equine stomach. This epithelium lines the surface of the glandular stomach and secretes a mucous product that is protective against the harsh acidic-fluid environment of the glandular stomach. H&E stain.

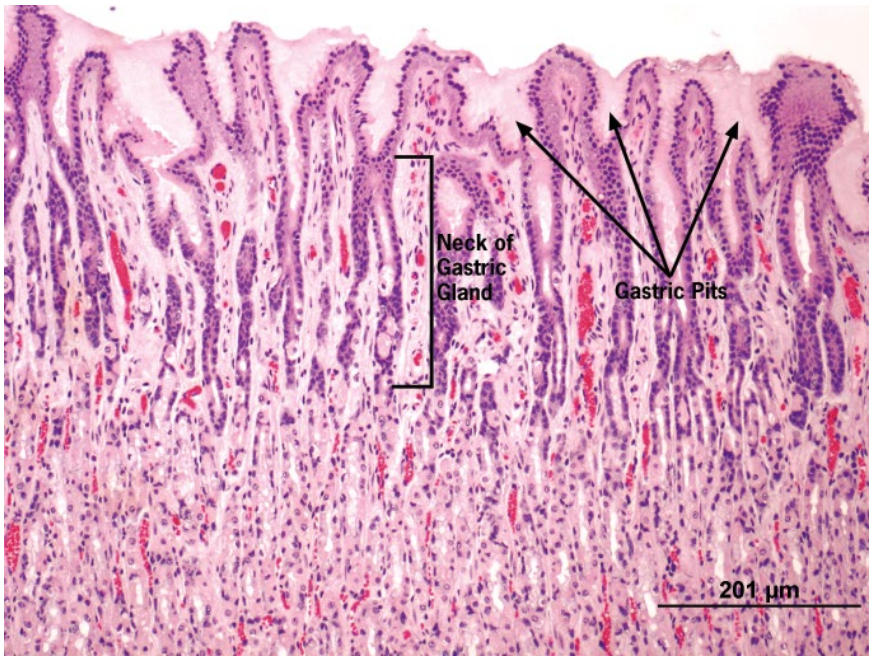

Figure 1.8 The gastric pits, necks, and upper portion of the proper gastric glands. The gastric pits in this image are filled with protective mucous, which is secreted by the simple columnar epithelium lining the surface and pits. Deep to the gastric pits are narrowings in the glands referred to as the necks. The necks of the gastric glands are where the stem cells are located. The secretory product of the surface mucous cells differs from the secretory product of the neck mucous cells in both composition and staining characteristics. H&E stain.

glandular region. Mitotic activity occurs in the neck region of all the gastric glands; daughter cells migrate and replenish both the surface epithelium and the epithelium lining the glands. The lamina propria is loose to dense irregular connective tissue, and in all regions is highly cellular, containing many lymphocytes, macrophages, plasma cells, and eosinophils. The lamina muscularis mucosa is an interwoven layer of smooth muscle bundles positioned perpendicular to one another. Many smooth muscle fibers extend adluminally from the lamina muscularis into the lamina propria. The tunica submucosa is typical, containing dense irregular connective tissue, prominent vasculature, and the submucosal nerve plexus. The tunica muscularis is composed of smooth muscle bundles arranged in oblique, circular, and longitudinal layers. The tunica serosa is visceral peritoneum.

The cardiac gland region is narrow and borders a portion of the margo plicatus. Cardiac glands are simple coiled tubular glands with some branching in the fundus of the glands. The length of the cardiac glands varies, particularly where the glands are juxtaposed against the

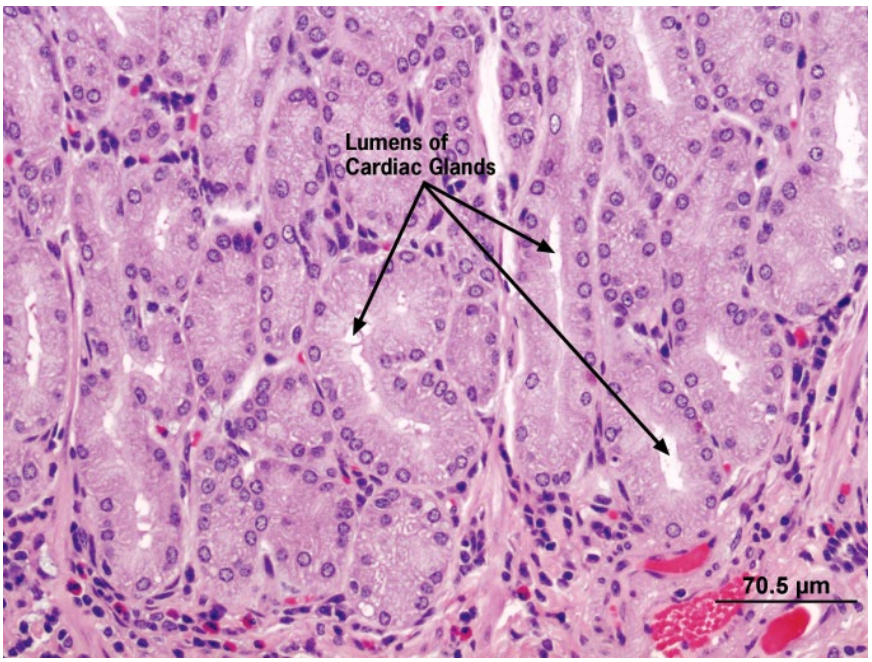

Figure 1.9 The deep portion of the cardiac glands from the equine glandular stomach. This image illustrates the body and base (fundus) of the cardiac glands. Cardiac glands are coiled tubular glands, therefore the glands will appear to be in many different planes when sectioned, and it will be difficult to trace the lumen of any one gland. The epithelium lining the glands secretes mucin, and the glandular secretory product is mucous. The vacuolation of the epithelial cytoplasm is due to mucin granules. Note the basally positioned nuclei of the glandular epithelium. H&E stain.

margo plicatus. The glands are shortest immediately adjacent to the margo plicatus; otherwise, the glands are similar to the proper gastric glands in depth. The cardiac glands are primarily mucus secreting (Figure 1.9). Chief cells and parietal cells are increasingly present within the cardiac glands as they transition into proper gastric glands. Enteroendocrine cells are present in the cardiac glands, but require special stains to be identified using light microscopy.

The proper gastric gland region occupies approximately two-thirds of the body of the equine stomach. Proper gastric glands are long simple tubular glands that are straight but have some coiling and branching at the fundus of the glands. Proper gastric glands are divided into an isthmus (the funnel-shaped opening of the gastric pit into the neck), a short neck, a long body, and a fundus, or base. The gastric pits overlying the proper gastric glands tend to be shallower than the pits overlying the cardiac glands and pyloric glands, but this varies throughout the glandular stomach. The cells of the proper gastric glands include mucous neck cells, parietal cells, chief cells, and enteroendocrine cells (Figure 1.10). In general, parietal cells predominantly populate the neck and upper to mid-portions of the body of the glands, whereas chief cells predominantly populate the lower portions of the body and the fundus of the glands. Mucus-secreting cells are also present in the proper gastric glands in the regions where the proper gastric glands are transitioning with the cardiac glands or the pyloric glands.

The pyloric gland region occupies the remaining one-third of the glandular stomach near the pylorus. Some of the pyloric glands border the margo plicatus. Pyloric glands are simple coiled tubular glands with some branching in the fundus of the glands. The pyloric glands are primarily mucus secreting (Figure 1.11), but may have scattered populations of parietal and chief cells, particularly near the junction of the pyloric glands with the proper gastric glands. Pyloric glands also have enteroendocrine cells.

The stomach joins the cranial part of the duodenum at the gastroduodenal junction.

Small Intestine

Gross Anatomic Features

The small intestine has three parts, the duodenum, jejunum, and ileum (Figure 1.12); these are suspended from the dorsal body wall by connecting mesentery, the mesoduodenum, mesojejunum, and mesoileum, respectively. The mesojejunoileum (collectively referred to as "the mesentery") attaches to the dorsal body wall ventral to the first lumbar vertebra. The celiac and cranial mesenteric arteries enter the mesentery at this site, and the stalk-like mass is referred to as "the root of the mesentery," which can be palpated via rectal examination.

The duodenum is approximately 1 m in length and is attached to the dorsal body wall by a short mesentery, the mesoduodenum. The duodenum is regionally subdivided into cranial, descending, and ascending parts. The cranial part is defined by a bulbous double curvature, the duodenal sigmoid flexure, which lies ventral to

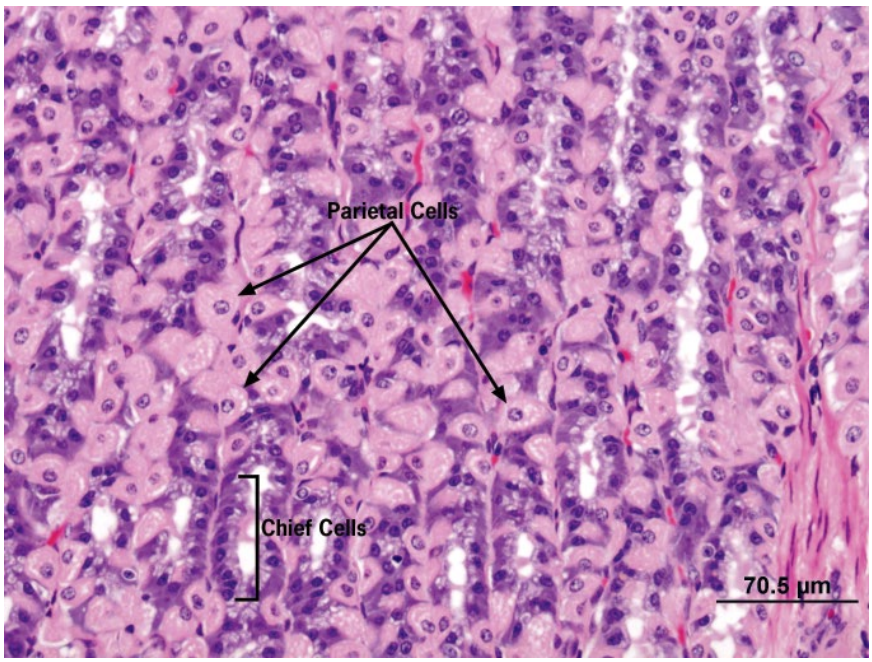

Figure 1.10 A portion of the proper gastric glands from the equine glandular stomach. This image illustrates the middle portion of the body of the proper gastric glands. Many eosinophilic parietal cells are visible; however, there are also many basophilic staining chief cells. The large parietal cells have a moth-eaten appearance due to the extensive canalicular system of the cells. The parietal cells produce and transport hydrogen and chloride ions into the cell canaliculi, where the ions combine to form hydrochloric acid. The chief cells produce proenzymes, particularly pepsinogen. H&E stain.

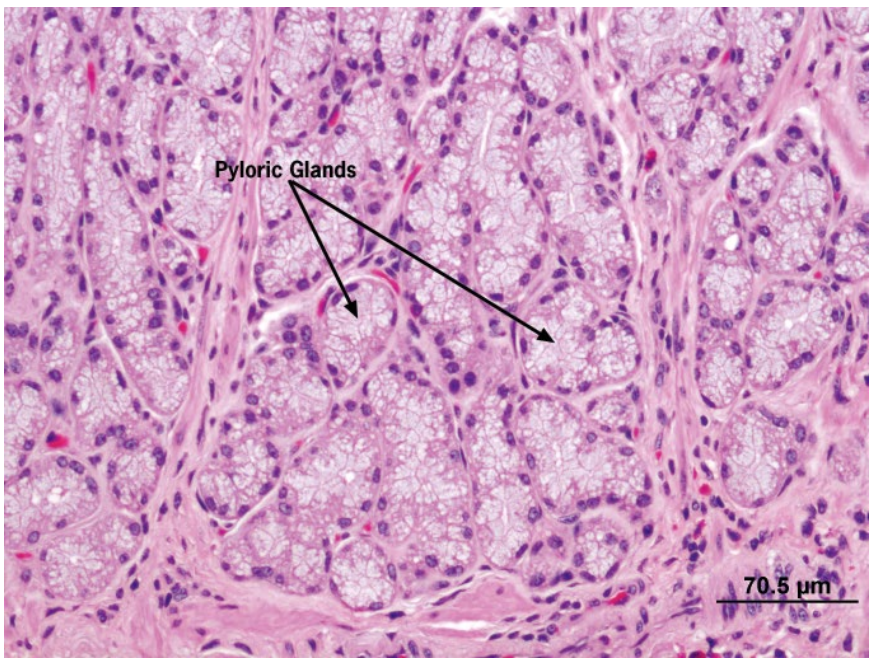

Figure 1.11 The deep portion of the pyloric glands from the equine glandular stomach. This image illustrates the body and base (fundus) of the pyloric glands. Pyloric glands are very similar to cardiac glands in that they both are coiled tubular glands that secrete mucous. H&E stain.

the liver in the region of the hepatic portal vein. The major and minor duodenal papillae are located opposite each other in the second bend of the flexure and the body of the pancreas fits snugly within the second concavity of this flexure. A sharp bend, the cranial duodenal flexure, marks the beginning of the descending part, which passes caudally and is located dorsally on the right side of the abdomen. At its caudal flexure (sometimes referred to as the short transverse part of the duodenum) at the caudal pole of the right kidney, the duodenum turns medially and passes from right to left around the base of the cecum, caudal to the root of the mesentery. The short ascending duodenum then passes cranially on the left of the mesentery to transition into the jejunum ventral and medial to the left kidney. The duodenojejunal junction and flexure are attached to the transverse colon by the duodenocolic fold.

At the duodenojejunal junction, the mesentery of the jejunum begins increasing in length. There are approximately 25 m of jejunum in the adult horse and because of

the long mesentery; the coils of jejunum have considerable mobility. The majority of the jejunal coils reside in the left dorsal abdomen where they freely mix with those of the descending colon. The mobility of the jejunum within the abdomen increases the odds of untoward events such as incarceration within the epiploic foramen, inguinal canal, or rents in the mesentery and volvulus via twisting around the root of the mesentery.

The short terminal portion of the small intestine is the ileum, which is approximately 50 cm in length. The ileum has a thick muscular wall that delivers ingesta through the dorsomedial wall of the cecum via the ileal papilla, a protrusion of the ileum into the lumen of the cecum. The ileocecal fold attaches the ileum to the dorsal band of the cecum.

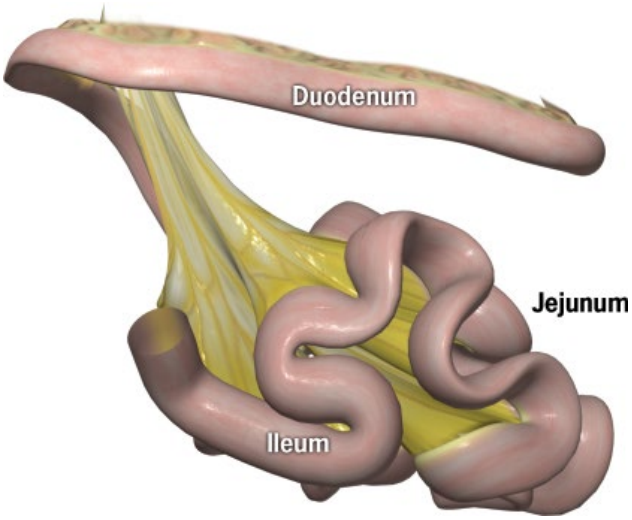

Figure 1.12 The duodenum, jejunum, and ileum, as viewed from the right side of the horse. Note the short mesoduodenum and long jejunal mesentery. Source: Courtesy of The Glass Horse, Science In 3D.

Microscopic Features

In the small intestine, the surface area is grossly increased by the sheer length of the organ and by plicae circulares (circular folds). Surface area is increased microscopically by villi and by microvilli. The microvilli are referred to as the striated border. Microscopically, the three divisions of the small intestine are similar. In the tunica mucosa, the lamina epithelialis lining the villi is made up of simple columnar cells that are interspersed with unicellular mucous glands, or goblet cells. The simple columnar cells are absorptive, and are referred to as enterocytes. The simple columnar epithelium also lines the intestinal glands (crypts of Lieberkühn).

The small intestinal glands are simple tubular glands that may coil and have some branching in the fundic region. The intestinal glands invaginate into the lamina propria. Cell division takes place in the fundic region of the intestinal glands; undifferentiated cells mature into goblet cells and enterocytes as they migrate toward the villi. In horses, another cell type, the acidophilic granular cell (Paneth cell) is also derived from the stem cells in the fundic region of the intestinal glands (Figure 1.13). Acidophilic granular cells occur in all divisions of the small intestine and are thought to play a role in mucosal immunity. Enteroendocrine cells are also present in the small intestinal glands. The lamina propria has variable cellularity, including but not limited to plasma cells,

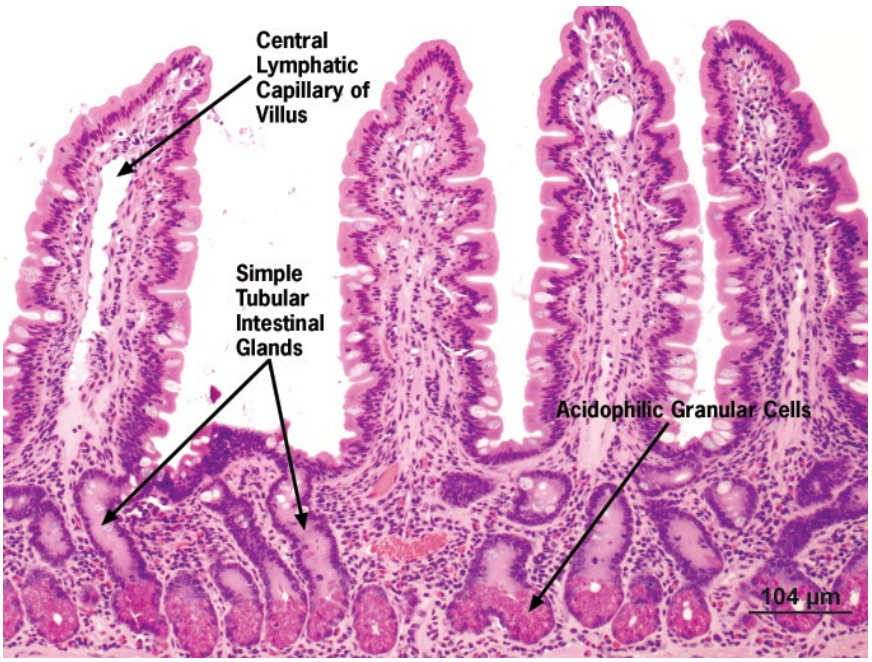

Figure 1.13 The villi and intestinal glands of the equine jejunum. The small intestinal glands are simple tubular glands that empty into the intestinal lumen at the base of the villi. The bright eosinophilic-staining cells in the fundic region of these glands are the acidophilic granular (Paneth) cells. Lymphatic capillaries (central lacteals) are located within the lamina propria of the villi. H&E stain.

lymphocytes, macrophages, and granulocytes, particularly eosinophils. The lamina propria within the villi has both blood capillaries and lymph capillaries (lacteals). The lamina muscularis mucosa is present and gives off smooth muscle fibers that extend adluminally into the villi. Contraction of these fibers allows for shortening of the villi and is thought to aid in emptying the capillaries, which become engorged during digestion.

In general, the villi in the duodenum are blunt and wide whereas in the jejunum they are long and slender and in the ileum they are club-shaped. In the tunica submucosa, submucosal glands extend throughout the duodenum and into the jejunum (Figure 1.14). The submucosal glands are simple branching tubuloacinar glands that empty into the fundus of the intestinal glands (Figure 1.15). The glands predominantly contain mucous adenomeres with some serous adenomeres occurring occasionally. Gut-associated lymphoid tissue (GALT) occurs throughout the equine small intestine (Figure 1.16). GALT includes both nodular lymphoid tissue (primarily B cells) and diffuse lymphoid tissue (primarily T cells), which often occur together in aggregates

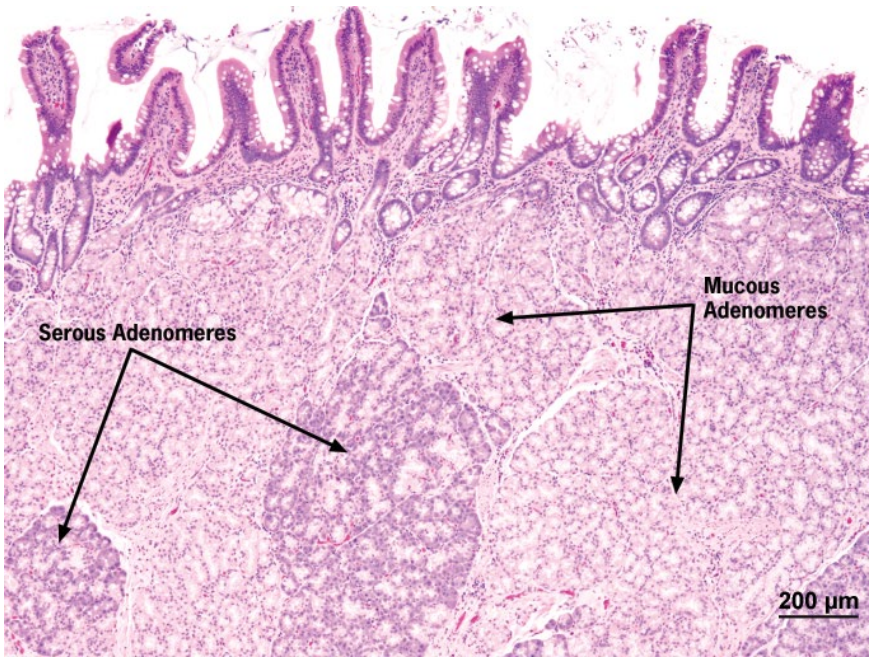

Figure 1.14 The submucosal glands of the equine jejunum. The submucosal glands are primarily composed of mucous adenomeres (light staining regions); however, serous adenomeres (darker staining regions) do occur. H&E stain.

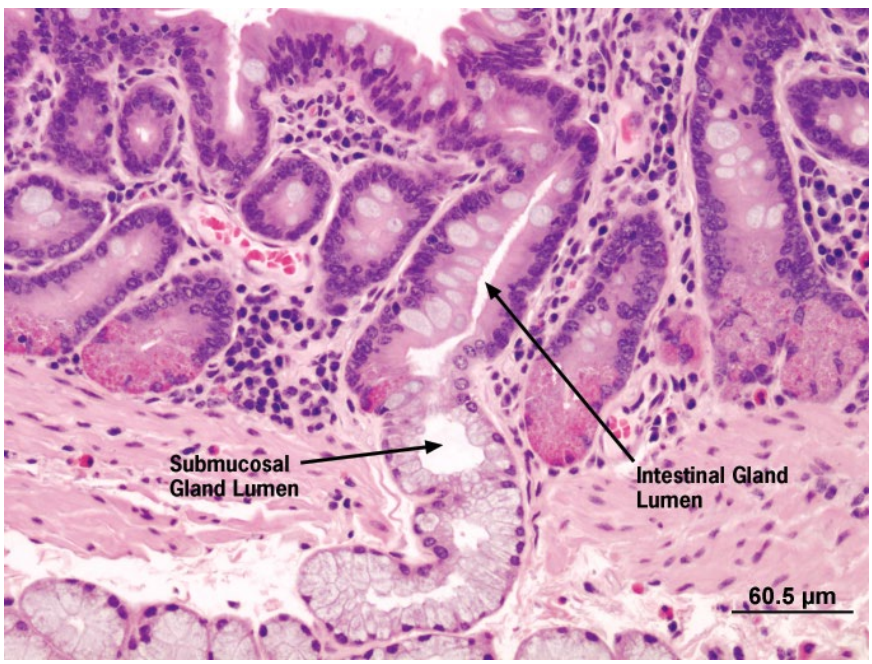

Figure 1.15 The junction of the submucosal and intestinal glands. The submucosal glands are not ducted directly to the intestinal lumen, but empty into the fundic region of the intestinal glands. H&E stain.

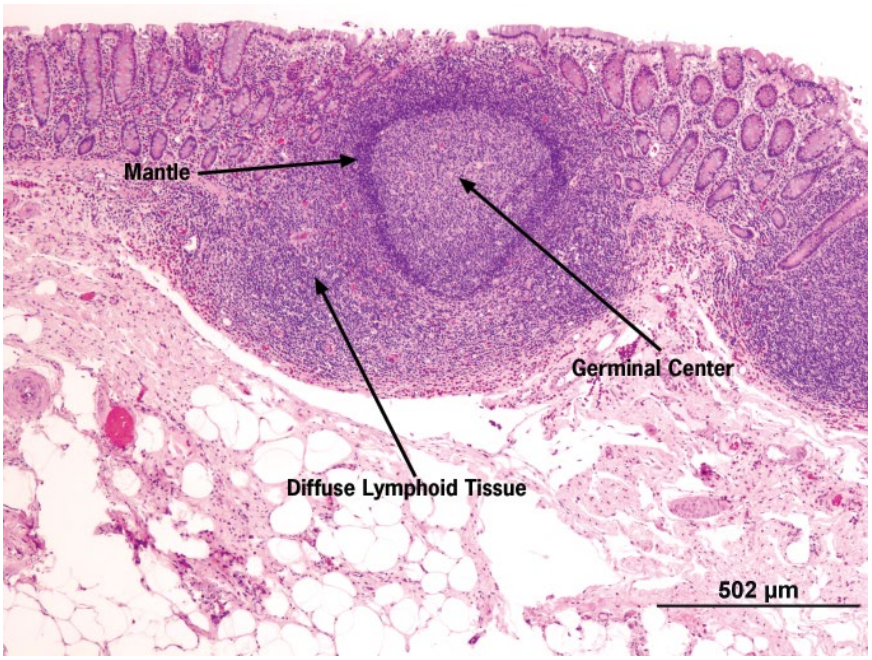

Figure 1.16 Gut-associated lymphoid tissue (GALT). GALT may be found throughout the tubular digestive tract. GALT is composed of nodular (primarily B cells) and diffuse (primarily T cells) lymphoid tissue. The nodular lymphoid tissue in this image of the ventral colon is undergoing proliferation in response to antigenic stimulation, forming a lighter staining central germinal center surrounded by a darker staining mantle of nonproliferative, nonreactive B cells. Surrounding the nodule is diffuse lymphoid tissue. H&E stain.

(Peyer's patches). Lymphoid aggregates are grossly visible as thickened regions in the intestinal wall; the mucosa overlying these aggregates has a pitted surface. Microscopically, the aggregates are located in the tunica submucosa and extend adluminally into the tunica mucosa. The lamina muscularis is often disrupted by the lymphocytic infiltration. The lamina epithelialis overlying the pits is lacking in goblet cells and contains specialized epithelial cells known as microfold cells ("M" cells) that play a role in the immune process of monitoring intestinal antigens (Dellmann and Eurell, 1998).

Large Intestine

Gross Anatomic Features

The large intestine includes the cecum, colon, rectum, and anal canal.

The cecum is a large comma-shaped fermentation vat that can accommodate 30 L or more of ingesta. The cecum is 1 m or more in length and is subdivided into a base, body, and apex (Figure 1.17). The base is wide and curves dorsally from beneath the caudal ribs to the right paralumbar fossa. Developmentally, the portion of the base cranial and ventral to the ileal papilla is part of the ascending colon, but this is not conventionally recognized. The body curves cranioventrally and has lesser and greater curvatures. The blind, pointed apex is located within the concavity of the sternal flexure of the ventral colon. The cecum is attached dorsally to the ventral surface of the right kidney, the pancreas, and the dorsal abdominal wall at the root of the mesentery.

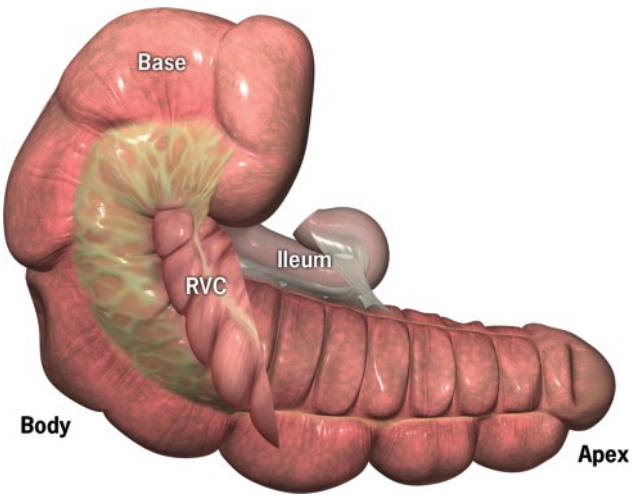

Figure 1.17 The cecum, terminal ileum, and proximal portion of the right ventral colon (RVC) as viewed from the right side of the horse. The ileocecal fold is evident where it attaches the antimesenteric border of the ileum to the cecum, as are the base, body, and apex of the cecum. Source: Courtesy of The Glass Horse, Science In 3D.

The cecum has sacculations (haustra ceci) and four longitudinal bands (teniae ceci). The cecal arteries, veins, and lymphatic vessels pass through the mesentery overlying the medial and lateral cecal bands. The dorsal band of the cecum serves as the point of attachment for the ileocecal fold. The ventral cecal band is the most easily palpated band per rectum, running from the base toward the apex of the cecum; this band is almost entirely exposed, being concealed only where the cecum is attached to the dorsal body wall. A strong triangular fold

of tissue, the cecocolic fold, attaches the lateral band of the cecum to the right ventral colon.

The ascending colon (large colon) is long and capacious, accommodating 80 or more liters of ingesta, and is folded into two horseshoe-shaped lengths of intestine, one dorsally and the other ventrally positioned, with the toes of the shoes pointed cranially. The ascending colon originates on the right side of the abdomen along the lesser curvature of the base of the cecum at the cecocolic ostium, located near the costochondral junctions of the last two ribs. It also terminates on the right side of the abdomen at the junction of the right dorsal colon with the transverse colon (Figure 1.18A, B, and C). With the exception of its origin and termination, the majority of the ascending colon is potentially freely mobile within the abdominal cavity, making the ascending colon prone to displacement and volvulus.

After its origin at the cecocolic ostium, the right ventral colon curves cranioventrally along the ventral abdomen until it reaches the sternum, where it is deflected to the left of the midline at the sternal flexure. From the sternal flexure, the left ventral colon continues caudally along the ventral abdominal floor. In the vicinity of the pelvic inlet, the left ventral colon makes a dorsally directed hairpin turn (the pelvic flexure) to become the left dorsal colon. When it contains ingesta, the pelvic flexure can be palpated during the rectal examination. The left dorsal colon continues cranially, dorsal to the left ventral colon, until it reaches the diaphragm (the dorsal diaphragmatic flexure) where it is deflected to the right of the midline. The right dorsal colon continues caudally, dorsal to the right ventral colon. At the base of the cecum, the right dorsal colon is deflected medially to continue as the transverse colon. The terminal portion of the right dorsal colon is dilated (ampulla coli).

The right and left ventral colons have an average diameter of approximately 25 cm. The most pronounced changes in the diameter occur at the pelvic flexure, where the diameter decreases to approximately 8 cm, and at the junction between the ampulla coli and the transverse colon, where the diameter changes from approximately 50 cm in the right dorsal colon to approximately 8 cm in the transverse colon. These large-to-small diameter changes are frequent sites of impaction.

There are four longitudinal bands on the right and left ventral colons (two in the mesocolon, two free), one on

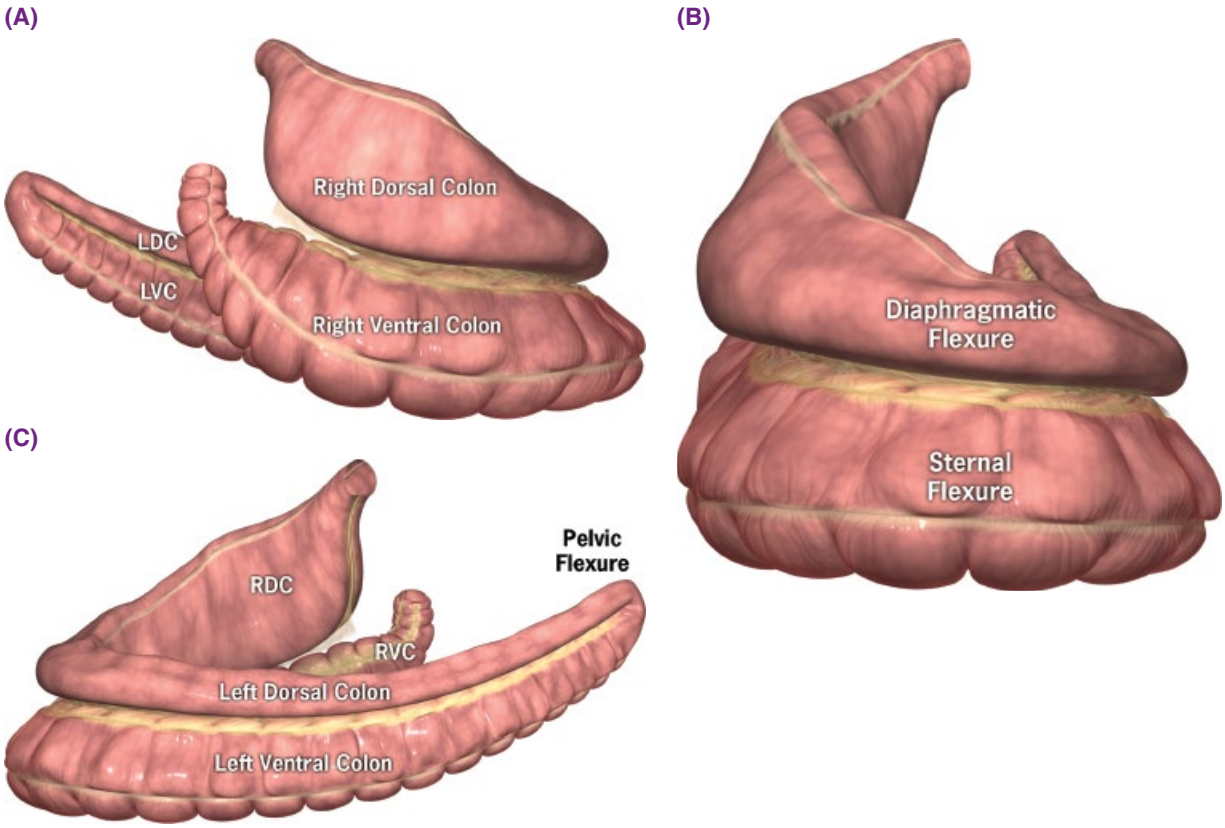

Figure 1.18 **(A)** The large colon, as viewed from the right side of the horse. The left ventral (LVC) and left dorsal (LDC) colons are evident towards the caudal aspect of the horse's abdomen. **(B)** The large colon from the cranial-most aspect of the abdomen, depicting the sternal flexure in the ventral colon and the diaphragmatic flexure in the dorsal colon. **(C)** The large colon, as viewed from the left side of the horse. The right ventral (RVC) and right dorsal (RDC) colons are identified. Source: Courtesy of The Glass Horse, Science In 3D.

the pelvic flexure and the left dorsal colon (in the mesocolon), and three on the right dorsal colon (one in the mesocolon, two free). The right and left ventral colons are sacculated and the left and right dorsal colons are smooth (lack sacculations).

The transverse colon is a short segment that connects the ascending (large) and descending (small) colons (Figure 1.19). It passes from right to left cranial to the root of the mesentery, and has a diameter of approximately 8 cm. It is fixed in position by its short mesenteric attachment to the dorsal wall of the abdominal cavity. The transverse colon has two longitudinal bands, one mesenteric and one antimesenteric.

The terminal 3–4 m of large intestine comprises the descending (small) colon and rectum (Figure 1.20). The descending colon is located within the left caudodorsal abdomen; it has a diameter of approximately 8 cm and contains a variable number of fecal balls. The descending colon is sacculated and has two longitudinal bands, one on the mesenteric surface and the other band on the antimesenteric surface. The antimesenteric band is wide and is palpable per rectum. Characteristically, the mesentery of the descending colon contains a large amount of fat, making identification of the mesenteric vessels difficult.

The rectum is approximately 25 cm in length, beginning at the pelvic inlet and terminating at the anal canal. Initially, the rectum is supported by the mesorectum; the caudal portion of the rectum is retroperitoneal. The terminal portion of the rectum is dilated (the rectal ampulla), which provides a storage site for fecal balls prior to defecation and is useful during palpation.

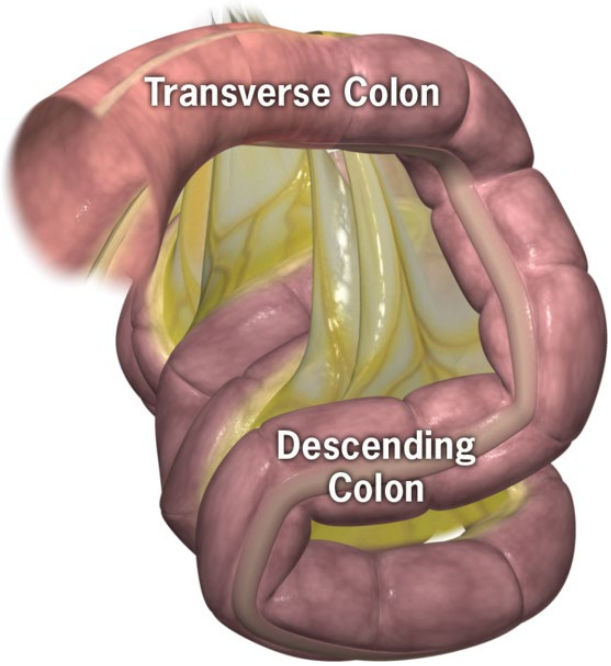

Figure 1.19 The transverse colon and initial portion of the descending colon as viewed from the cranial aspect of the abdomen. Source: Courtesy of The Glass Horse, Science In 3D.

Microscopic Features

Microscopically, the divisions of the large intestine are very similar. Longitudinal folds increase the surface area of the large intestine. In the tunica mucosa, the luminal surface is smooth in comparison to the small intestine, as there are no villi. The lamina epithelialis is made up of simple columnar epithelium; however, in the large intestine the enterocytes may be difficult to differentiate due to the increased number of goblet cells, particularly in the intestinal glands. The intestinal glands are simple tubular glands that are straight with little coiling or branching (Figure 1.21). The intestinal glands invaginate into the lamina propria, which has varying cellularity. The lamina muscularis mucosa is present. The tunica submucosa may contain lymphoid aggregates. The tunica muscularis has the most variation of all the tunics in the large intestine. The inner circular layer of smooth muscle is typical. The outer longitudinal layer of smooth muscle in the tunica muscularis is comparatively thin, except where it forms thickened longitudinal bands called teniae. The teniae are reinforced with elastic fibers. The walls of the large intestine bulge out in-between the bands and form sacculations called haustra. The number of bands varies within the different regions of the large intestine.

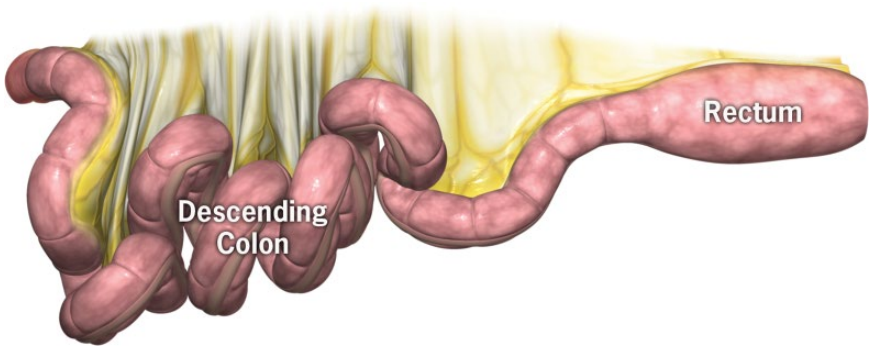

Figure 1.20 The descending colon and rectum as viewed from the horse's left side. Source: Courtesy of The Glass Horse, Science In 3D.

Liver

Gross Anatomic Features

The liver is positioned beneath the ribs, with approximately 60% of the liver to the right of the median plane. The long axis of the organ is positioned obliquely; the caudodorsal surface lies on the right of the median plane adjacent to the right kidney and the cranioventral surface lies on the left of the median plane near the costochondral junctions of the 6th or 7th ribs. The parietal surface is adjacent to the diaphragm. The visceral surface of the liver contains impressions made by the stomach, cecum, colon, duodenum, and right kidney. The liver is fixed in position by six ligaments and by the pressure of the surrounding organs; this pressure is thought to contribute to atrophy of the right lobe (sometimes the left lobe) in older horses. The liver is divided into left, right, caudate, and quadrate lobes (Figure 1.22A and B).

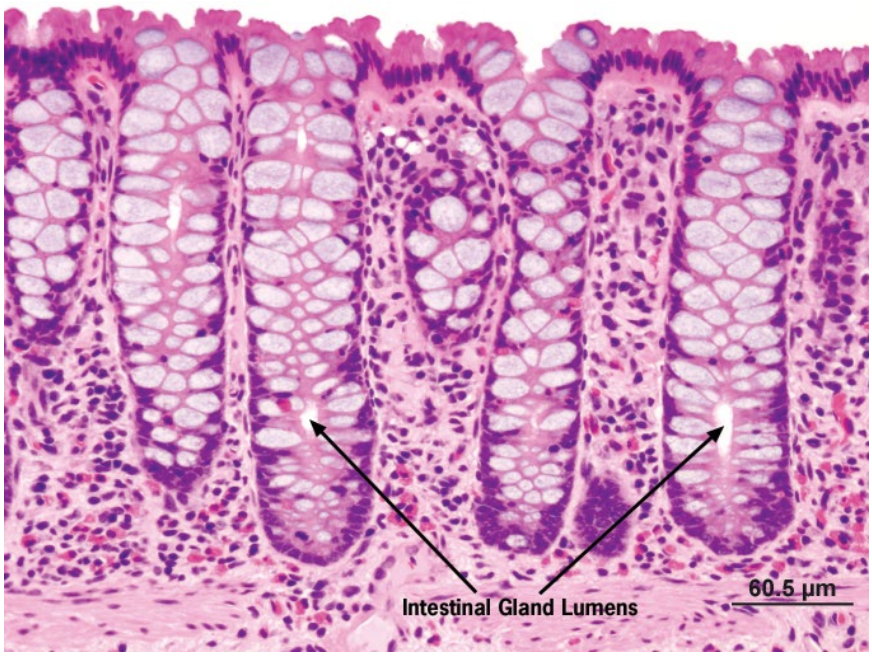

Figure 1.21 The intestinal glands of the equine descending colon. The large intestinal glands are simple straight tubular glands. The bright eosinophilic-staining cells in the lamina propria are eosinophils. H&E stain.

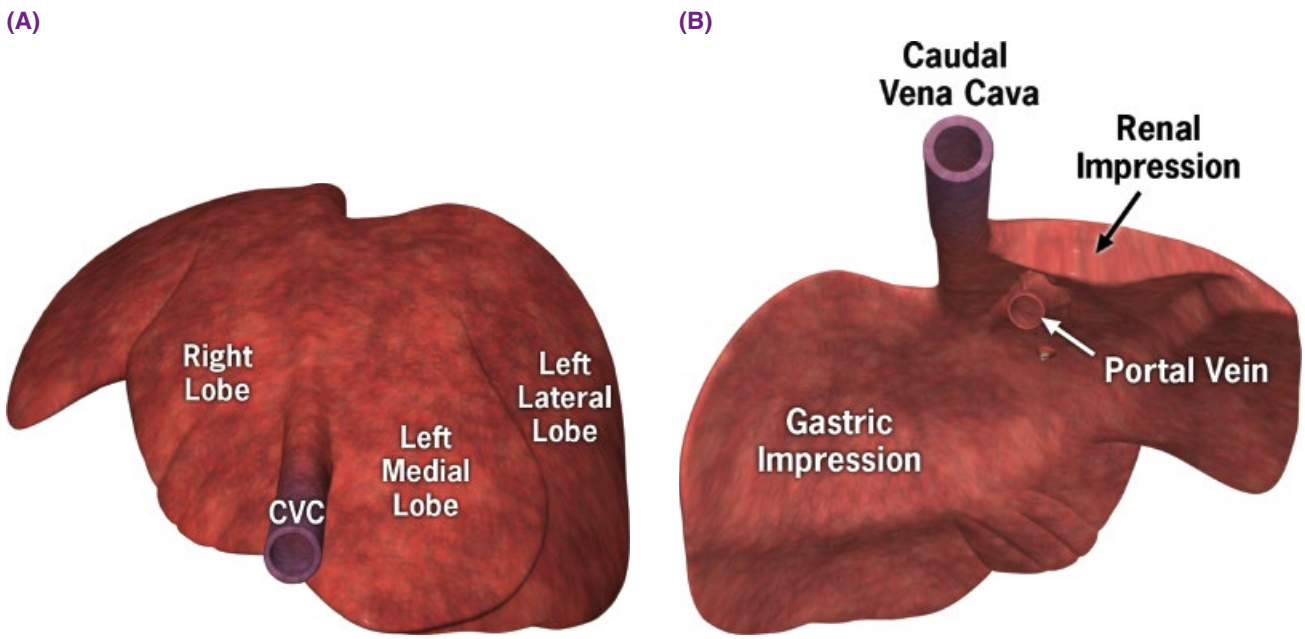

Figure 1.22 **(A)** The liver and caudal vena cava (CVC) as viewed from the cranial-most aspect of the abdomen. **(B)** The liver, caudal vena cava, and portal vein from a ventrocaudal point of view. Source: Courtesy of The Glass Horse, Science In 3D.

The left lobe is subdivided into left lateral and left medial lobes; the left medial lobe is separated from the quadrate lobe by the umbilical fissure for the passage of the falciform and round ligaments. The right lobe is not subdivided. The caudate process is positioned dorsal to the caudal vena cava and together these structures form the dorsal boundary of the epiploic foramen. The ventral boundary of the epiploic foramen is formed by the pancreas and the portal vein. The epiploic foramen is a potential site for strangulation obstruction of the distal jejunum and ileum. The proximal portion of the duodenum is attached to the medial portion of the right lobe by the mesoduodenum, through which the bile duct passes from the portal fissure of the liver to the proximal duodenum. The mesoduodenum is continued by a band of fibrous tissue that attaches the right dorsal colon to the visceral surface of the liver.

Spleen

Gross Anatomic Features

The spleen is part of the immune system rather than the digestive system. However, the fact that the ascending colon commonly becomes displaced dorsal to the renosplenic ligament necessitates inclusion of the spleen in any discussion relating to colic in horses. In the adult horse, the spleen is positioned against the left abdominal wall, with its wide dorsal base ventral to the last three ribs and its narrow ventral apex directed cranioventrally near the distal extremity of the 10th rib (Figure 1.23). The cranial margin of the spleen is concave, while the caudal margin is convex. The caudal margin, which initially runs parallel to the costal arch, can be palpated per rectum in adult horses. The dorsal portion of the spleen is attached to the left crus of the diaphragm and the left kidney by the phrenicosplenic and renosplenic ligaments, respectively (Figure 1.24). These ligaments form a "shelf" upon which the ascending colon can become lodged when displaced.

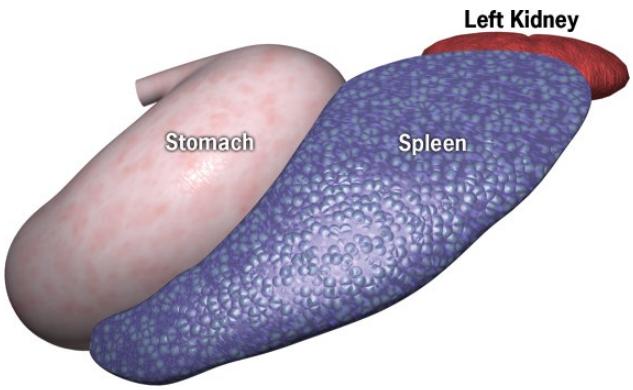

Figure 1.23 The spleen, stomach, and left kidney as viewed from the left side of the horse. Source: Courtesy of The Glass Horse, Science In 3D.

Pancreas

Gross Anatomic Features

Although acute pancreatitis appears to be a rare occurrence in the horse, there is recent evidence that pancreatic injury may occur in horses with acute intestinal obstruction. For this reason, a brief description of the pancreas is included as a final component of this chapter.

The pancreas is primarily positioned to the right of the median plane and completely surrounds the portal vein. The majority of the pancreas is situated adjacent to the stomach and liver, the cecal base, right dorsal colon, transverse colon, and cranial flexure of the duodenum (Figure 1.25). It has left and right lobes and a body. The right lobe follows the descending duodenum and extends to the right kidney; the left lobe is attached to the stomach wall. The pancreatic duct runs adjacent to the bile duct and enters the duodenum at the hepatopancreatic ampulla. A smaller accessory pancreatic duct enters the duodenum at the minor duodenal papilla, a short distance from the major papilla.

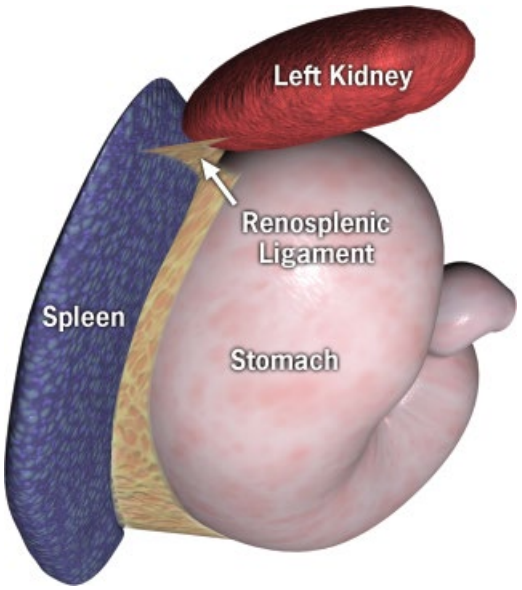

Figure 1.24 The spleen, stomach, and left kidney as viewed from the caudal aspect of the abdomen. The renosplenic ligament as well as the gastrosplenic ligament connecting the spleen to the stomach are evident. Source: Courtesy of The Glass Horse, Science In 3D.

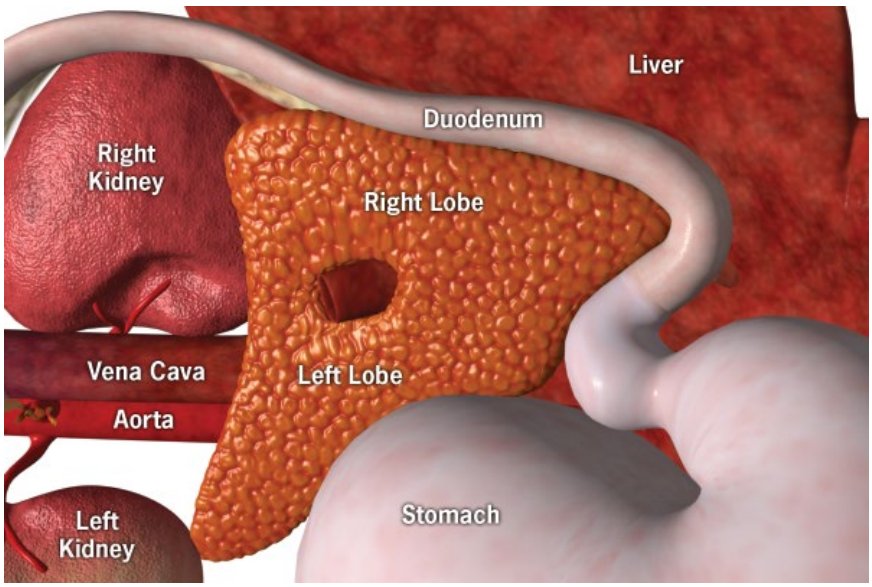

Figure 1.25 The pancreas is confluent between the stomach, duodenum, and liver, extending to the right kidney with the left lobe extending along the right dorsal and transverse colons to the left kidney.

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2

Intestinal Epithelial Stem Cells

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The intestine is a complex organ composed of multiple layers each having distinct functions. These layers include: an outer serosa, two muscular layers (an inner circular layer and outer longitudinal layer separated by the myenteric nerve plexus), the submucosa, and the innermost mucosal layer (Figure 2.1) (Dellmann, 1987). The mucosa is further divided into three distinct layers: (i) the muscularis mucosa, a thin layer of smooth muscle that demarcates the mucosa from submucosa; (ii) the lamina propria, a layer mixed of connective tissue and a complex capillary system; and (iii) the innermost epithelial layer. This innermost layer is composed of a single columnar epithelial cell lining that directly interfaces with the intestinal lumen and its contents. Noxious luminal contents are prevented access to the bloodstream by the critical barrier created by these cells. These cells must simultaneously form a barrier as well as transport nutrients (small intestine) and water (large intestine) (Kararli, 1995). In order to maintain this cellular barrier, this epithelial cell lining remains in a dynamic and rapid state of cellular turnover that continues throughout life. During homeostatic conditions, cell loss is balanced by cell renewal. A new intestinal lining is created every 5–7 days. This capacity of self-renewal is attributed to adult or somatic stem cells that reside within the intestinal mucosal lining deep within the base of each crypt of Lieberkühn (Figure 2.2A). Intestinal stem cells are distinct from the more commonly known mesenchymal stem cells used in equine orthopedic research and therapy in that their capacity to differentiate is restricted. Intestinal stem cells self-renew, as is required of all stem cells; however, unlike mesenchymal stem cells that can give rise to multiple tissue types (bone, cartilage, connective tissue, and fat cells), intestinal stem cells only differentiate into cells of intestinal epithelial lineage.

A recent study has characterized the discrete intestinal epithelial cell lineages that exist in the horse (Gonzalez et al., 2015). Two main intestinal epithelial cell lineages exist: secretory and absorptive cells (Figure 2.2B). Absorptive enterocytes are the most abundant cell type and are distributed along the entire length of the small and large intestine. Maintenance of normal systemic health depends on the absorption of nutrients and water by this cell type. The secretory cell lineage consists of Paneth, enteroendocrine, and goblet cells. Paneth cells are restricted to the small intestine and are present within the crypt base interspersed between the stem cells. Historically, these cells are known to secrete antimicrobial peptides such as lysozyme. However, recent research has demonstrated that these cells appear to be critical to maintaining normal stem cell function and are particularly critical during times of intestinal injury (Clevers & Bevins, 2013; Sato et al., 2011b). Normal gut function also depends on the secretion of hormones by enteroendocrine cells. Multiple subtypes of enteroendocrine cells exist dispersed along the length of the small and large intestine and each secretes unique hormones. Finally, goblet cells are located along the length of the small and large intestine and secrete mucus into the lumen. This mucus layer aids in both nutrient absorption and creates a protective covering on the surface of the epithelial cells (Figure 2.3). All of these mature postmitotic cells types are critical to intestinal homeostasis and overall systemic health and are derived from intestinal stem cells (see Figure 2.2).

Intestinal epithelial stem cells were first identified by transmission electron microscopy in 1974 (Cheng & Leblond, 1974). However, the specific characterization of these cells has only recently been accomplished using gene and protein biomarkers (Barker et al., 2007). The identification of Lgr5 as a biomarker of a fast cycling population of stem cells, also known as the crypt-base columnar (CSC) stem cell, was an important discovery (Barker et al., 2007). Subsequently, an exponential increase in research and publications in the area of intestinal stem cell biology occurred. The discovery of other

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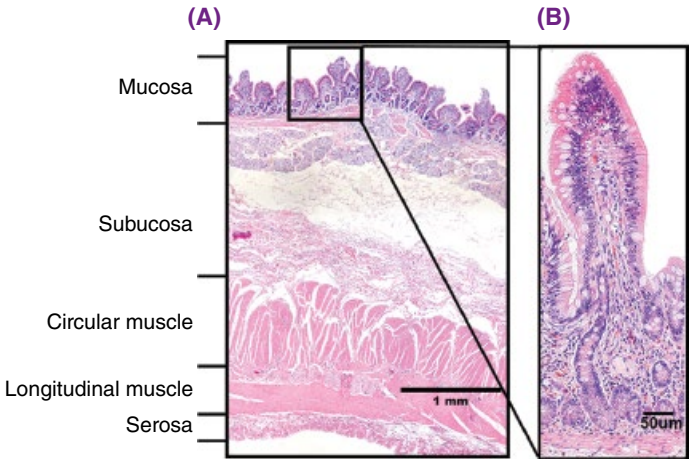

Figure 2.1 Intestinal layers. H&E stained section of an equine small intestinal biopsy. The intestine is composed of five main layers **(A)**. The inner most mucosal layer is magnified **(B)**.

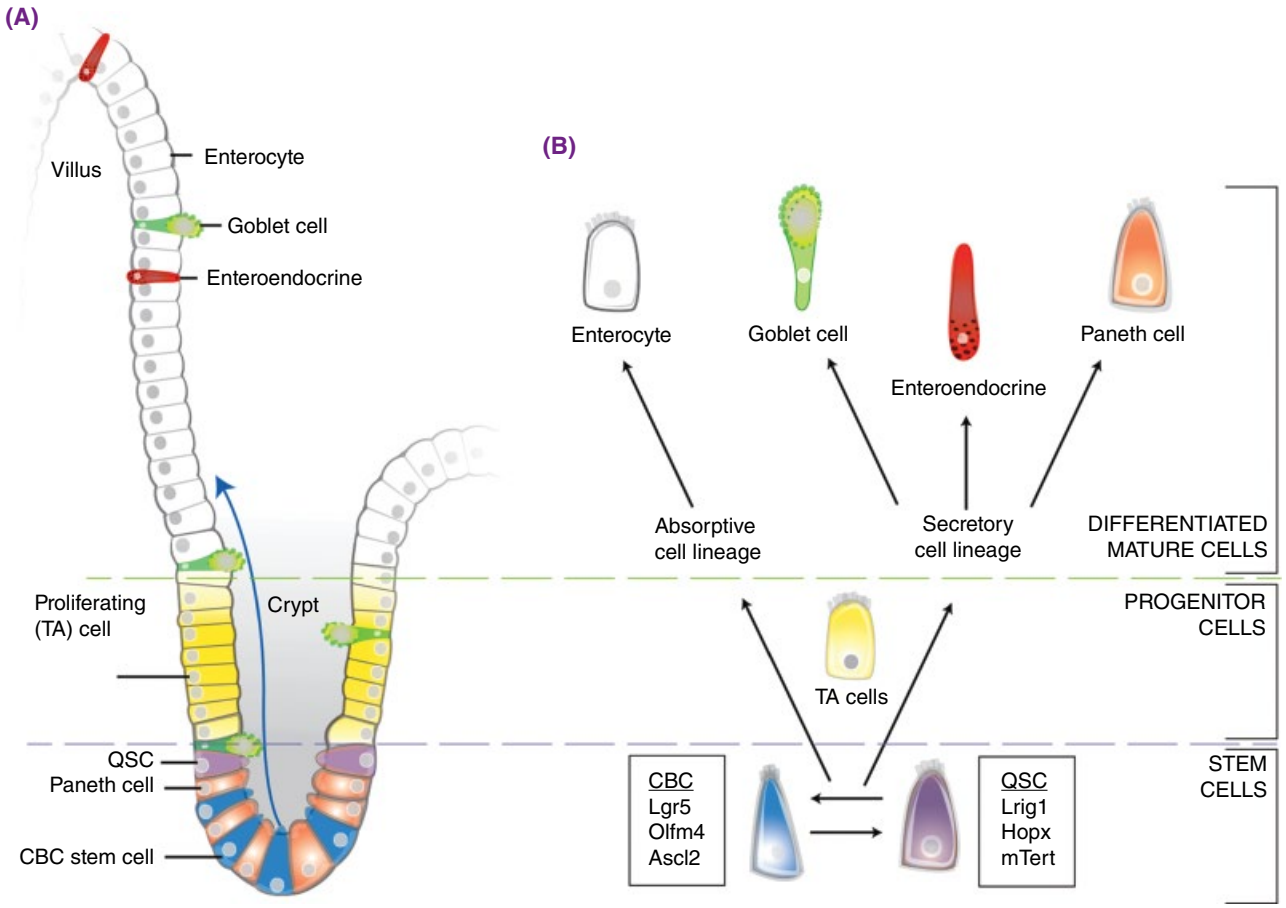

Figure 2.2 Intestinal epithelial architecture and distinct cell populations. **(A)** Schematic representation of the crypt–villus axis. **(B)** Two populations of intestinal stem cells exist with each expressing distinct gene biomarkers. Both stem cell populations have the capacity to differentiate into mature, active intestinal epithelial cells. CBC, crypt-base columnar (cell); QSC, quiescent stem cell; TA, transit amplifying (cell). Source: Gonzalez, 2015. Reproduced with permission of John Wiley & Sons.

important biomarkers for cellular identification have subsequently occurred and include: Olfm4, Ascl2, and Sox9 (see Figure 2.3, Table 2.1) (Formeister et al., 2009; Powell et al., 2012; van der Flier, Haegebarth et al., 2009a; van der Flier, van Gijn et al., 2009b). An antibody against SOX9 protein has been shown to cross-react with equine tissue (Figures 2.3 and 2.4) (Gonzalez et al., 2015). However, SOX9 expression is not restricted to CBC stem cells and is also expressed in the proliferating transit amplifying pool of cells as well as Paneth cells. A separate,

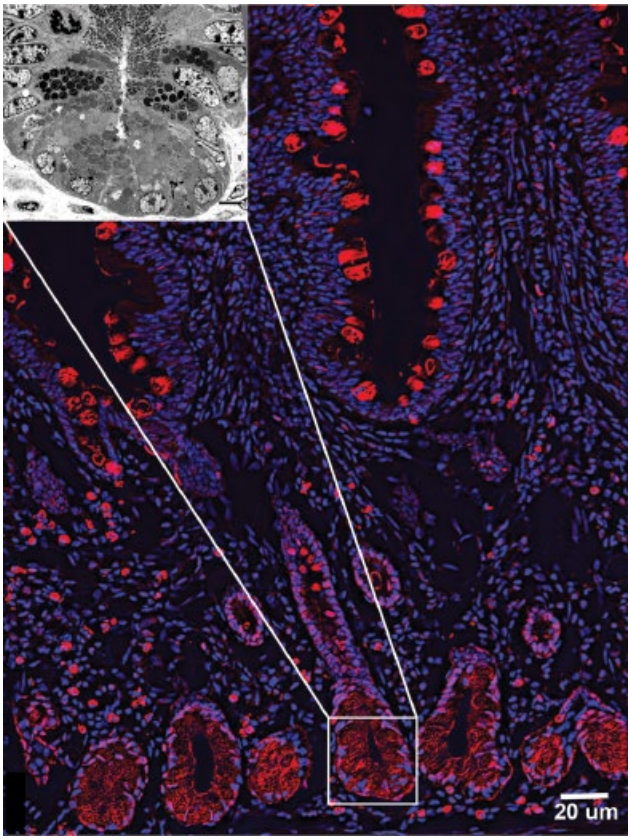

Figure 2.3 Immunofluorescence and transmission electron microscopy of jejunal crypt base. Epithelial cells with pink nuclei express the protein SOX9 that has been associated with progenitor cells. Cells with red cytoplasm express MUC2, a protein associated with mucin. All remaining nuclei appear blue. Red blood cells are autofluorescent and appear as small red dots within the lamina propria. Inlay: transmission electron microscopic image of a crypt base. Small funnel-shaped stem cells are interdigitated between Paneth cells with large electron dense cytoplasmic granules, scale bar 5 µm.

Table 2.1 Intestinal stem cell biomarkers.

Crypt-base columnar (active) stem cells	Slow cycling (reserve or quiescent) stem cells
Lgr5	Hopx
Olfm4	Lrig1
Ascl2	mTert
Sox9	Bmi1

slower cycling or reserve stem cell population, the quiescent stem cells (QSC), also has been described and is identified using biomarkers such as Bmi1, Hopx, Lrig1, and mTert (see Table 2.1) (Montgomery et al., 2011; Powell et al., 2012; Takeda et al., 2011; Yan et al., 2012). Unfortunately, no antibodies against protein biomarkers of QSC have yet been found to cross-react with equine tissue. Despite evidence that distinguishes these two cells types, in other species it is clear that cells expressing biomarkers attributed to either fast or slow cycling stem cells have the capacity to differentiate into all four post-mitotic, mature epithelial cell types. Recent advances in the field of intestinal stem cell biology have enabled detailed study of the stem cell niche as the potential source of a novel therapeutic target to enhance intestinal mucosal regeneration (Markel et al., 2008; Lin and Barker, 2011).

Stem cells are a renewable source of mature epithelial cells in the gut. Understanding their function is critical to developing clinical applications and improving the outcome in cases of severe mucosal injury. Treatments that hasten expansion of stem cells may provide a means of improving tissue regeneration. Mouse studies have demonstrated the capacity of the intestinal epithelial stem cell compartment to expand after resection, radiation, and doxorubicin treatment (Dekaney et al., 2007; Dekaney et al., 2009; Hua et al., 2012; Van Landeghem et al., 2012). Intestinal biopsies obtained from equine clinical cases with severe ischemic injury demonstrate that progenitor cells are maintained in these tissues, albeit in reduced numbers (see Figure 2.4) (Kinnin et al., 2014). Therefore, it may be possible in the future to activate the remaining stem cells to stimulate mucosal repair in tissue that otherwise may be resected. Another potential therapeutic intervention is stem cell engraftment into areas of damage. Techniques to grow intestinal stem cells in culture have been developed in mice, pigs, and humans and most recently in the horse (Sato et al., 2009; Gonzalez et al., 2013; Sato et al., 2011a; Jacobs et al., 2014). Intestinal stem cells in these cultures develop three-dimensionally and consist of crypt-like structures, all mature epithelial cell types, as well as a pseudo-lumen where dead cells are extruded. These "mini guts" have actually been shown to adhere to denuded epithelium in mouse colon (Yui et al., 2012). Despite these significant advances in the field, intestinal stem cells have yet to be used clinically.

Few medical advances have been made to treat intestinal compromise in horses in recent years despite the fact that colic is the leading known cause of death. Furthermore, within a hospitalized population, cases of colic can be the most costly. In 1998, the cost of colic was estimated to be US$115 million (USDA, 1998). Additionally, damage to the intestinal mucosa is a component of most severe causes of colic. Diffuse inflammatory disease or strangulating lesions of the small intestine and colon commonly result in variable degrees of epithelial loss and therefore barrier compromise. Epithelial cell loss extending beyond 50% of the crypt in the large intestine, has been associated with poor outcome in colic cases (van Hoogmoed et al., 2000). This poor outcome is likely associated with loss of the

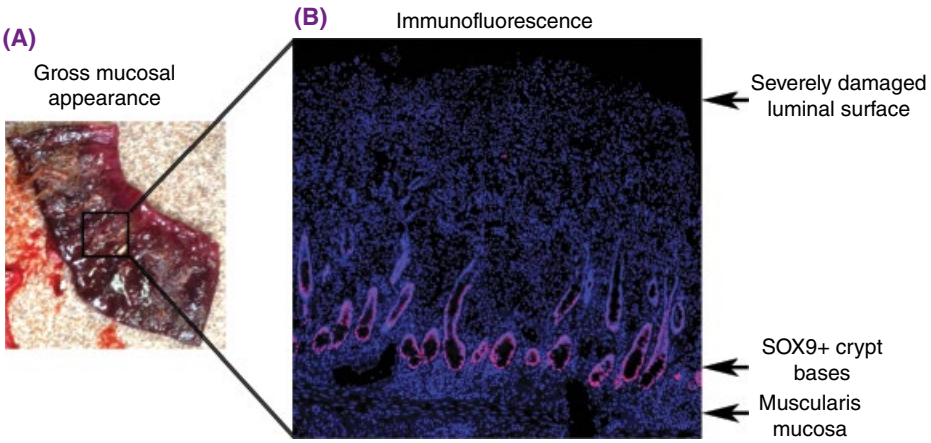

Figure 2.4 Tissue expression of a progenitor cell biomarker following severe ischemic injury. **(A)** Gross mucosal appearance of strangulated equine small intestine. **(B)** Mucosal biopsy (tissue shown in A) processed for immunofluorescence that shows $SOX9^{+}$ progenitor cells present within the crypt base despite complete loss of villus architecture at the luminal surface.

progenitor pool of cells that reside within the crypt (Gonzalez et al., 2014; Smith et al., 2013).

Further research is needed in order to harness the therapeutic potential of intestinal stem cells. Hastening mucosal repair is critical to prevent and treat the sequelae of severe intestinal injury seen in horses with sepsis, bacteremia, laminitis, ileus, and diarrhea. Intestinal stem cell research may hold the key to the discovery of novel and progressive therapies that, in conjunction with existing treatments, will shorten recovery times and facilitate enhanced repair following severe mucosal damage.

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3

Gastric Secretory Function

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Stomach Anatomy and Physiology

The dorsal fundus of the equine stomach is lined with nonglandular stratified squamous epithelium that is confluent with the lining of the esophagus (Figure 3.1). This lining is highly sensitive to acid, which can damage the cells within minutes of exposure (Widenhouse et al., 2002). The gastric squamous epithelium has multiple cell layers covered by a superficial cornified layer (Figure 3.2), and limited mucosal protection is primarily achieved by tight junctions between cells that form a barrier to acid. This is not a highly effective barrier, and exposure to even weak organic acids (acetic, propionic) can damage the barrier, particularly when the pH is low (acidic) (Nadeau & Andrews, 2002). A hydrophobic phospholipid layer has been described on the surface of the equine gastric squamous mucosa, and this may provide some protection against acid injury (Ethell et al., 2000). In addition to these mechanical protective factors, saliva provides a natural mechanism of neutralizing acid as well as coating the epithelium (Bouchoucha et al., 1997).

In neonatal foals, the developing gastric squamous epithelium is thin and possibly more susceptible to acid injury than mature epithelium (Murray & Mahaffey, 1993). As part of normal gastric development in neonates, during the first month of life the epithelium becomes thicker, which is influenced by exposure to hydrochloric acid. The developing epithelium may resist acid less effectively than more mature gastric squamous epithelium, predisposing it to peptic injury.

An irregular raised ridge, the margo plicatus, separates the squamous compartment from the glandular compartment of the stomach. Most equine gastric ulcers occur in the squamous mucosa in close proximity to this border, because this area of squamous mucosa comes into most frequent contact with acidic gastric contents.

The ventral gastric mucosa is a highly differentiated glandular tissue that has many cell types, including those that secrete hydrochloric acid and digestive enzymes, and cells that stimulate and inhibit acid secretion (Figure 3.3). The glandular mucosa is not only highly differentiated, but the distribution of cells varies by region. The oxyntic (acid-secreting) portion of the glandular mucosa is in the region of the body of the stomach. This is where acid-secreting parietal cells, pepsinogen-secreting chief cells, histamine-secreting cells, and some somatostatin-secreting cells are located. These cells are aligned vertically from the lumen to the muscularis mucosa, such that the secreted hydrochloric acid is transported along channels toward the luminal surface. As the glandular mucosa transitions from the body to the antrum, there are fewer oxyntic glands, and these are absent in the antrum itself. Within the mucosa of the antrum there are abundant mucus- and mucin-secreting cells, as well as endocrine cells (Figure 3.4). Gastrin-secreting G cells are located in this region of the stomach.

The glandular mucosa also contains highly developed self-protective mechanisms. Unique to the glandular mucosa is the ability to form a bicarbonate-rich protective mucus layer within which a pH gradient reduces the acidity at the mucosal surface to near neutral levels. Phospholipids in the mucus help repel gastric acid, and these phospholipids can be found in the secretory channels of the gastric gland.

Gastric Secretory Function

Hydrochloric acid is secreted by parietal cells via H^+,K^+-ATPase pumps, of which there are more than 1 million per cell. The H^+,K^+-ATPase pumps utilize the phosphorylation of adenosine triphosphate (ATP) to exchange water-solvated protons (protonated water, hydroxonium

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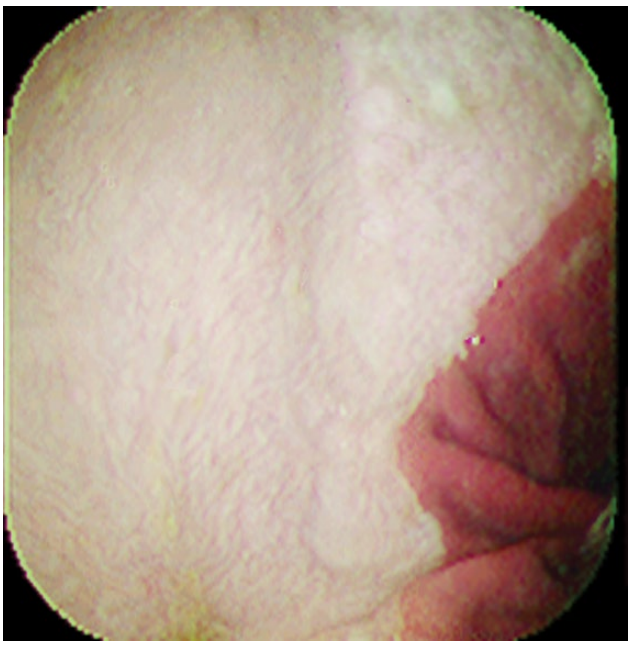
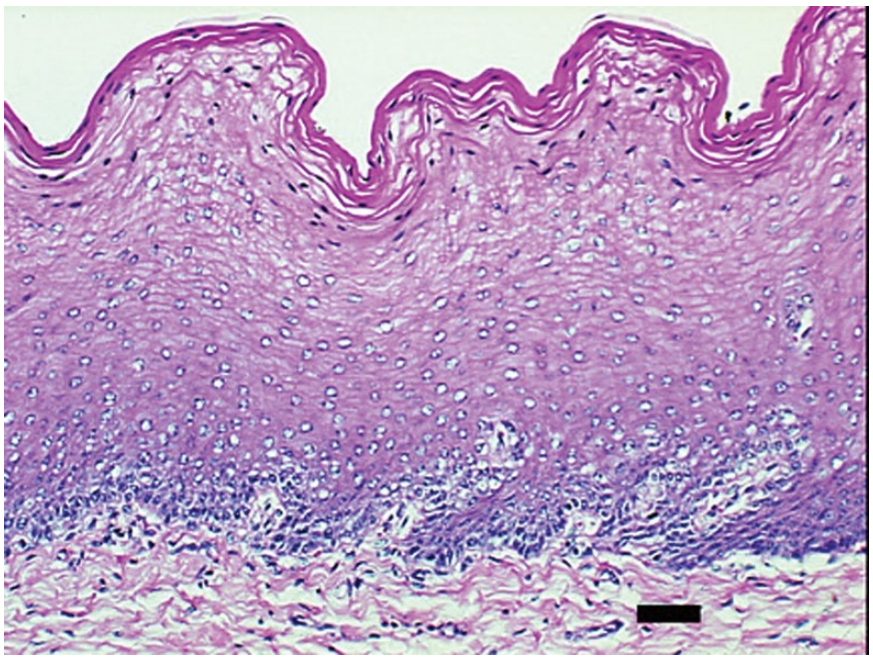


Figure 3.1 Endoscopic view of the normal equine stomach, with the squamous epithelial lining on the left and glandular mucosal lining shown along the right side of the photograph.

ion, H_3O^+) for potassium ions. In conjunction with parallel potassium and chloride ion conductances, this ATPase is responsible for the secretion of hydrochloric acid into the secretory canaliculus of the parietal cell, the enclosed space reaching a pH of near 1.0 (Rabon & Reuben, 1990). In the resting parietal cell, these pumps reside within the membranes of vesicles in the cell cytoplasm. When activated by histamine and gastrin, the parietal cells alter their shape and the vesicles merge with the outer cell membrane to form secretory canaliculi.

The equine stomach secretes hydrochloric acid continuously, even when the foal or horse is not eating (Campbell-Thompson & Merritt, 1990). Gastric acid secretion is pronounced as early as 2 days of age in neonatal foals (Sanchez et al., 1998). Gastric acidity is lowest when the horse eats (Murray & Schusser, 1993) or the foal nurses, because eating stimulates the secretion of bicarbonate-rich saliva that can neutralize some gastric acid, and roughage or milk absorb gastric secretions so that they do not contact the mucosal surface. Once a horse stops eating or a foal ceases nursing, the gastric pH can rapidly decrease to less than 2.0, and the acidity will remain high until eating or nursing resumes (Sanchez et al., 1998; Murray & Schusser, 1993).

Figure 3.2 Microscopic appearance of the equine gastric squamous mucosa, with periodic acid–Schiff staining. Layers of keratinized epithelial cells line the luminal surface of the mucosa. Cell proliferation occurs in the basal layers adjacent to the lamina propria, and over time cells move towards the luminal surface and become keratinized.



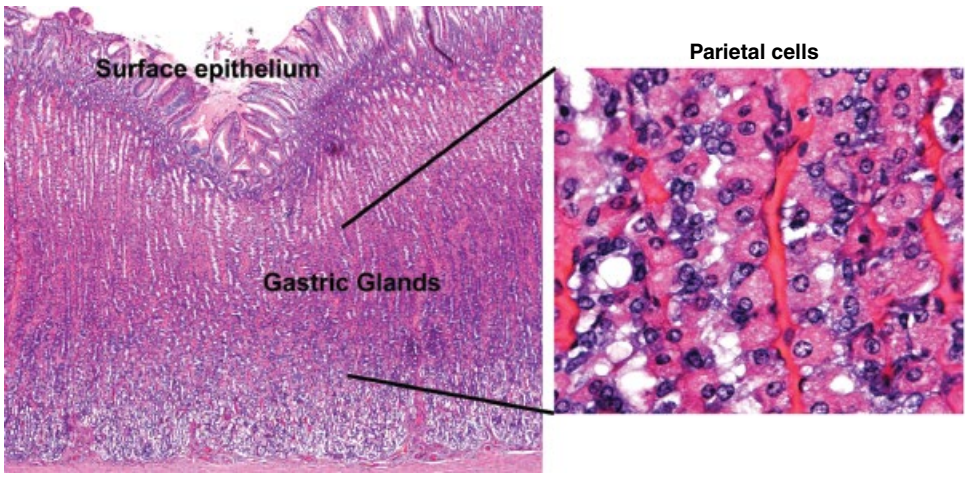


Figure 3.3 Microscopic appearance of the equine gastric glandular (oxyntic) mucosa stained with H&E. The acid-secreting gastric glands lie deep to mucus-secreting cells on the surface. The area of the gastric glands is enlarged to show the parietal cells arranged in parallel.

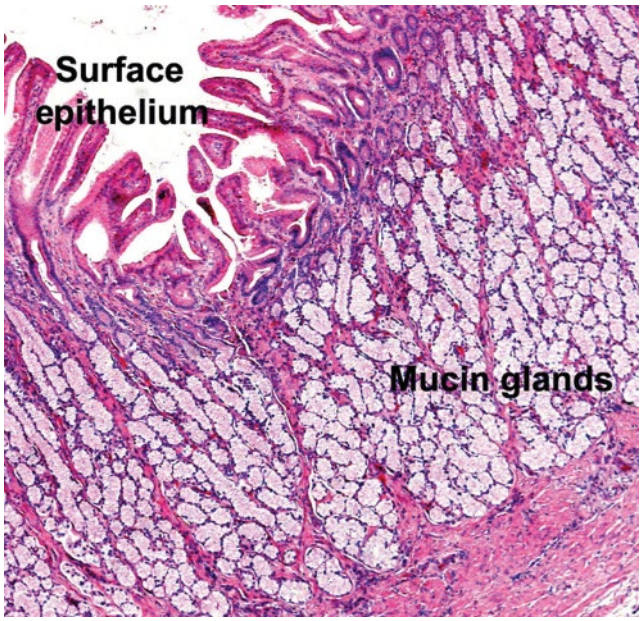


Figure 3.4 Microscopic appearance of the equine gastric glandular (antral) mucosa. There are abundant mucosal mucin-secreting glands and an absence of parietal cells.

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4

Small Intestinal Function

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Digestive Physiology: Anatomy

Digestion and absorption of nutrients take place predominantly in the proximal half of the small intestine so that the ileum is exposed to a relatively low nutrient load (Figure 4.1). The digestive/absorptive units of the small intestinal mucosa are finger-like projections of the epithelial surface, the villi (Figure 4.2), whereas secretory function is largely confined to the crypts (Xu et al., 2012). Villus height and crypt depth decline from the proximal to the distal segments of the intestine. As enterocytes move up the crypt–villus axis, they progressively differentiate to take on absorptive and digestive functions (Figure 4.3). For example, there is a gradient of RNA abundance from the villus base to the tip with six times more of the D-glucose transporter SGLT1 being present in mature cells near the tip than in the immature cells at the base (Hwang et al., 1991). A similar gradient for amino acid absorption has been demonstrated by autoradiographic methods in equine jejunum (Figure 4.4). Although the crypts of both small and large intestines have zones of proliferation, migration, and differentiation, only the small intestine has villi with unique digestive and absorptive capabilities (Figure 4.5).

The apical surface of a mature enterocyte is also arranged to form microvilli, which is described as a brush border (Figure 4.6). Enzymes that complete digestion of carbohydrates (disaccharidases) and proteins (peptidases) and render them absorbable are located within the microvilli. The microvillar membrane also contains various specific transport systems for absorbing digestive end products into the enterocyte. An aqueous layer approximately 35 μm thick, called the unstirred water layer, and glycocalyx coat the brush border of surface epithelial cells presenting additional barriers to movement of solutes (see Figure 4.6) (Wilson et al., 1971). Enterocytes are connected to each other by tight junctions, which restrict the transmucosal flux of large molecules, although these tight junctions are permeable to water and many low-molecular weight substances. Tight junctions are composed of integral membrane proteins such as occludin and a family of proteins called the claudins (Figure 4.7). These proteins are attached on their cytoplasmic surface to a plaque of proteins that facilitate regulation of the tight junction, such as zonula occludens-1 (ZO-1), and the cytoskeleton (Marchiando et al., 2010). Research has shown that tight junctions may be physiologically regulated during transport functions in order to enhance mucosal transport. For example, Na^+-glucose transport via SGLT1 results in activation of myosin light chain kinase, which results in cytoskeletal contraction and opening of the tight junction (Turner et al., 1997). Other studies have shown that tight junctions can be regulated during repair from ischemic injury by physiologic factors such as prostaglandins (Blikslager et al., 2007). The space between cells is called the paracellular space, which may also play a role in creating a barrier to diffusion, depending upon how collapsed or dilated it is (Gawenis et al., 2004).

Intraluminal Digestion

In the small intestine, dietary carbohydrates, fats, and proteins are broken down by pancreatic enzymes, and the products of carbohydrate and protein digestion are hydrolyzed further by brush border enzymes (Figure 4.8) (Wright et al., 2012; Ganapathy, 2012). Hydrogen ions in the duodenum trigger the release of secretin from S cells, which stimulates the pancreas and liver to secrete HCO_3^- and water (see Figure 4.8) (Liddle, 2012). Bicarbonate neutralizes H^+ ions in the proximal small intestine and thereby prevents acid-pepsin damage to the duodenal mucosa, provides a functional pH for pancreatic and

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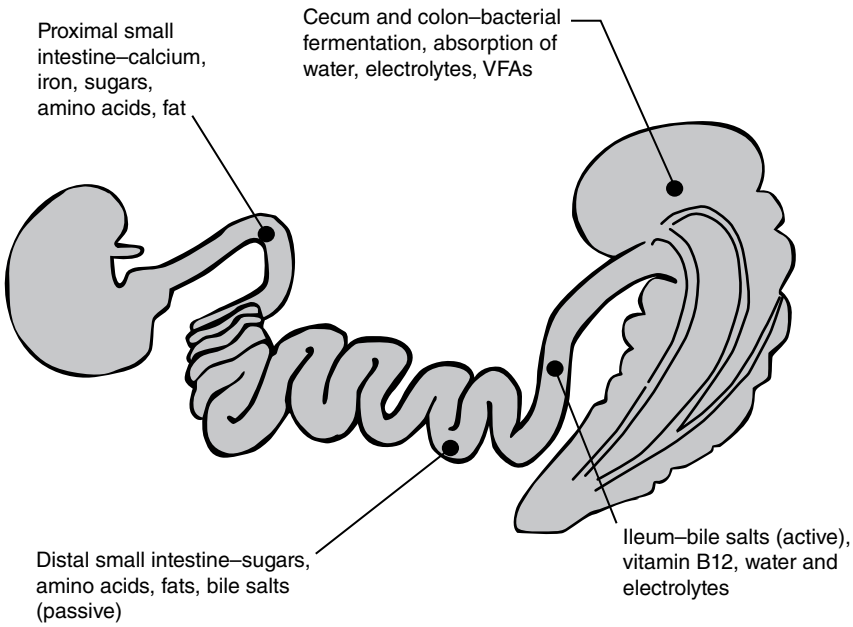

Figure 4.1 Distribution of major sites of absorption in the equine small intestine based on information from other species.

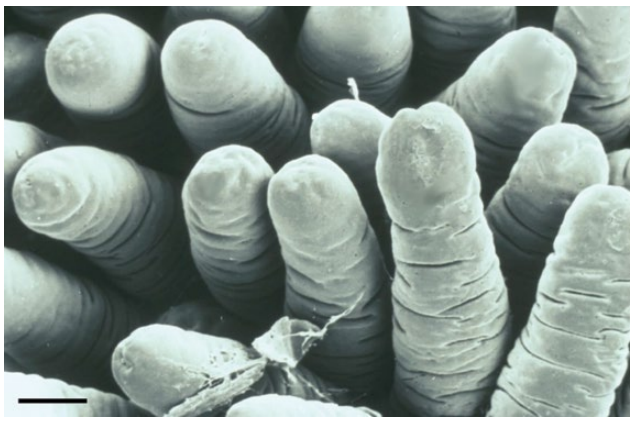

Figure 4.2 Typical appearance of jejunal villi in equine small intestine on scanning electron microscopy. Bar = 100 µm.

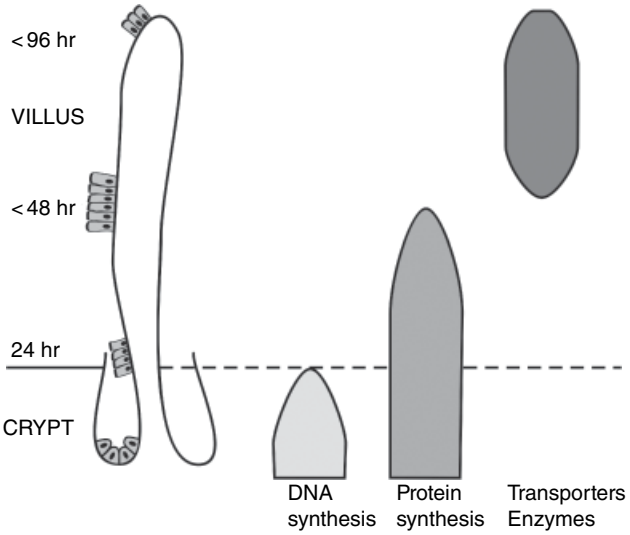

Figure 4.3 Distribution of different activities in the small intestinal crypt and villus, demonstrating steps in the maturation of epithelial cells leading to the development of transporters and enzymes in the upper third of villi.

brush border enzymes, and increases solubility of bile acids and fatty acids (Chen & Davidson, 2012). Proteins and fats in the duodenum stimulate the release of cholecystokinin (CCK) from endocrine cells, which causes the pancreas to secrete enzymes for the digestion of carbohydrates, fats, and proteins, as well as cofactors (colipase) that aid in enzymatic digestion (see Figure 4.8) (Liddle, 2012; Wright et al, 2012; Ganapathy, 2012). Trypsinogen, the precursor form (zymogen) of trypsin, must reach the small intestine to be activated by the brush border enzyme enterokinase. Trypsin can also activate trypsinogen, but this occurs at a much slower rate than activation by enterokinase. All other zymogens can only be activated by trypsin. The principal pancreatic enzymes are amylase for starch digestion, trypsin, chymotrypsin, carboxypeptidase, and elastase for protein digestion, and lipase and colipase for fat digestion (Liddle, 2012).

Basal pancreatic secretions in the horse are profuse and apparently continuous (10–12 L/100 kg body weight/day), but they can be increased rapidly as the horse eats (Alexander, 1969). The concentration of HCO_3^- is low and does not exceed that of Cl^- at any rate of secretion, so that Cl^- remains the predominant inorganic anion in the horse's pancreatic secretion at all rates of flow (Alexander, 1969). As a result, pancreatic secretion may provide a source of anion (Cl^-) for exchange with HCO_3^- in the terminal ileum to buffer contents prior to fermentation in the colon (Argenzio, 1990). Although content and output

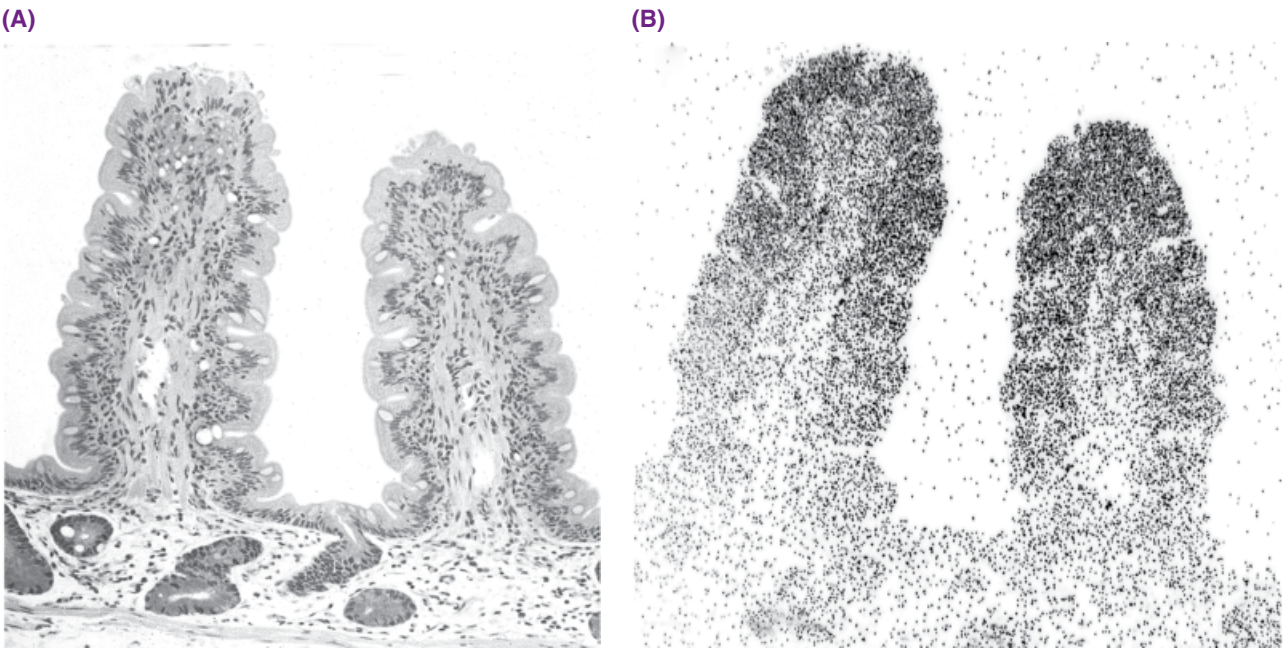

Figure 4.4 Autoradiographic location of transport sites for L-alanine in villi from equine jejunum, with section stained with H&E **(A)** and unstained section **(B)**. Note that silver grains that identify tritiated L-alanine are concentrated towards the villus tip.

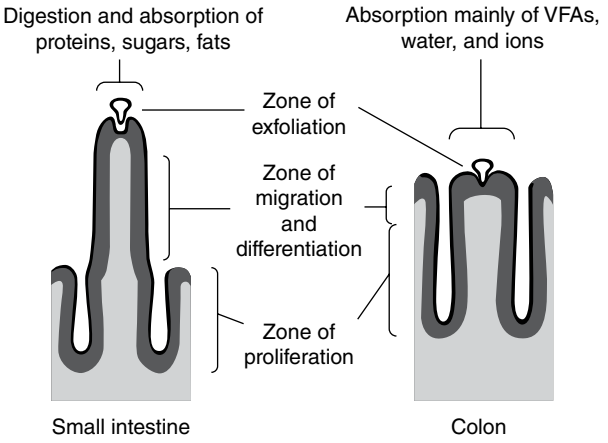

Figure 4.5 Structural differences in mucosa between small intestine and colon, particularly demonstrating villi in the small intestine with digestive and absorptive capabilities that are lacking in the colon.

of pancreatic enzymes is small in the horse compared with other animals (Alexander, 1969), digestion and absorption appear to be as efficient (Hintz, 1975).

Lipolysis in the small intestine requires emulsification of fat by bile salts, which allows the intestine to break the fat globules into minute particles by agitation, and thereby increase the surface area of lipids. The precursor of bile salts is cholesterol, which is converted in the liver to cholic acid or chenodeoxycholic acid (Dawson, 2012). These bile acids then combine principally with glycine and taurine to form glyco- and tauro-conjugated bile salts. Conjugation lowers the pK_a to below the physiologic range of intestinal pH, causing the conjugated bile acids to become anions (referred to as bile salts) rather than undissociated bile acids. In the ionized form, they are more soluble. Micelles form when the bile salts reach a particular concentration in the intestine, called the critical micellar concentration (CMC), and they aid in absorption (Dawson, 2012).

Approximately 94% of bile salts are reabsorbed by the small intestinal mucosa, pass to the liver, and then are resecreted in a process called enterohepatic circulation of bile (Dawson, 2012). Active transport by a Na^+-dependent process in the ileum (see Figure 4.1) and passive absorption by the jejunum combine to reclaim intraluminal bile. Secondary bile salts are produced from bacterial deconjugation and dehydroxylation of bile salts that are not absorbed in the small intestine and enter the colon. These secondary bile salts are relatively insoluble at the pH of colonic contents, and form precipitates that are excreted in feces. In a study assessing horses following jejunal or jejunoileal resection, the level of bile salts in the feces was significantly increased, presumably because of loss of bile salt transport (Little et al., 2005).

Absorption of Ions and Water

Reabsorption of ions and water by the intestine is critical to recover the large volume of digestive secretions from the salivary glands, pancreas, liver, stomach, and small intestine itself. Most of the small intestinal absorption of

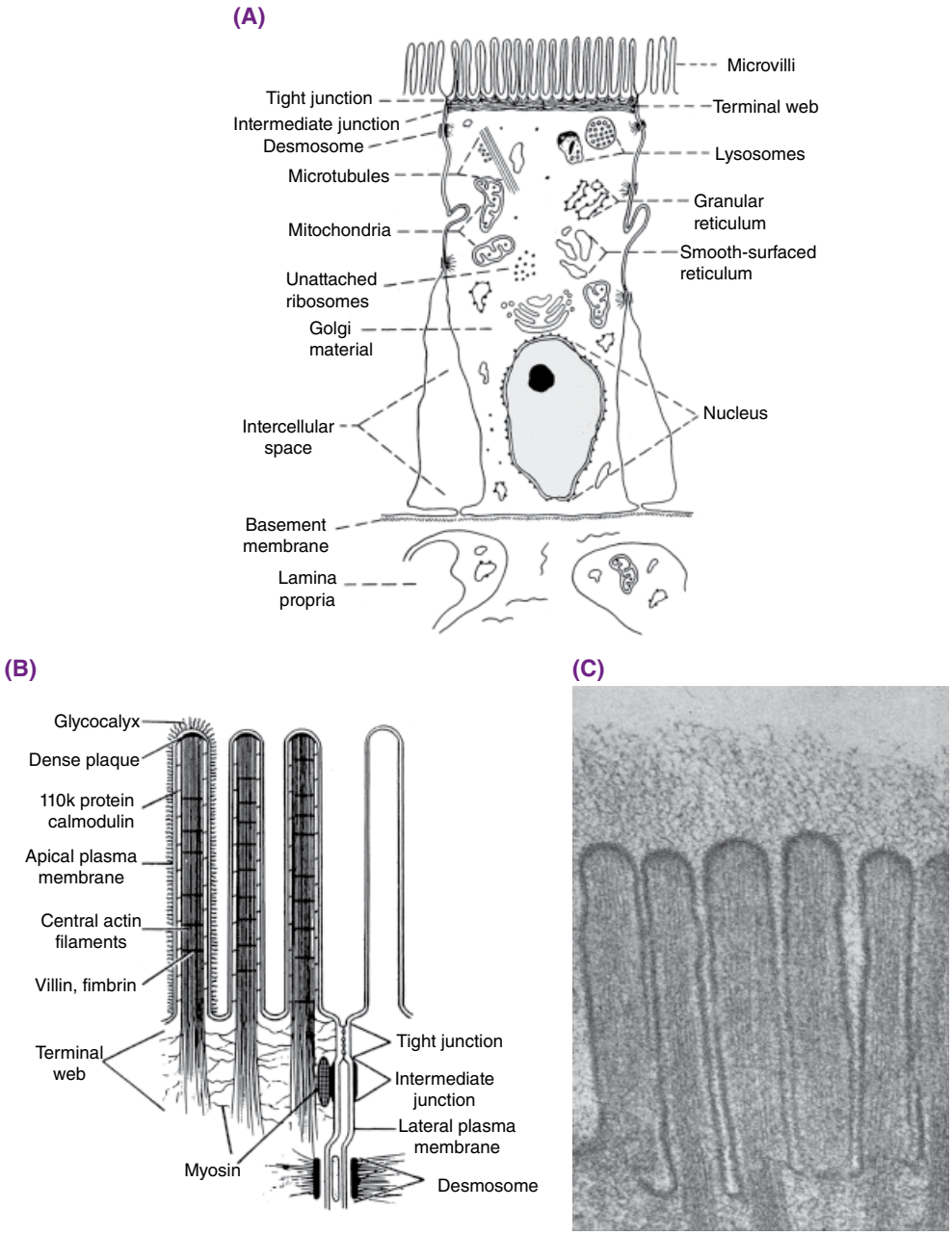

Figure 4.6 Typical absorptive epithelial cell or enterocyte in small intestine **(A)**, schematic of the structural features of the apical plasma membrane and junctional complexes of intestinal absorptive cells **(B)**, and transmission electron microscopic image of microvilli **(C)** with obvious actin filaments that form rootlets in the terminal web. Source: Johnson, 1987. Reproduced with permission of Elsevier.

water takes place in the distal third of the small intestine, but the bulk of intestinal water is absorbed by the large intestine (Argenzio, 1990). However, Na^+ absorption in the small intestine plays an important role in absorption of several nutrients and other ions.

The routes for transepithelial movement of ions and water are through the cells (transcellular) or between epithelial cells (paracellular) (Blikslager et al., 2007). The tight junction divides the epithelial cell into an apical and basolateral domain, so that the epithelial cells are polarized into distinct regions. This allows development of an electrochemical gradient across the epithelium, generated by the basolaterally located Na^+,K^+-ATPase. This "Na^+ pump" transports three Na^+ molecules out of the cell for every two molecules of K^+ that are transported into the cell, generating a negative intracellular potential difference of approximately –40 mV (the electrical gradient) and a low intracellular concentration of Na^+/high concentration of intracellular K^+ (the chemical gradient). Absorption of sodium in the small intestine takes place

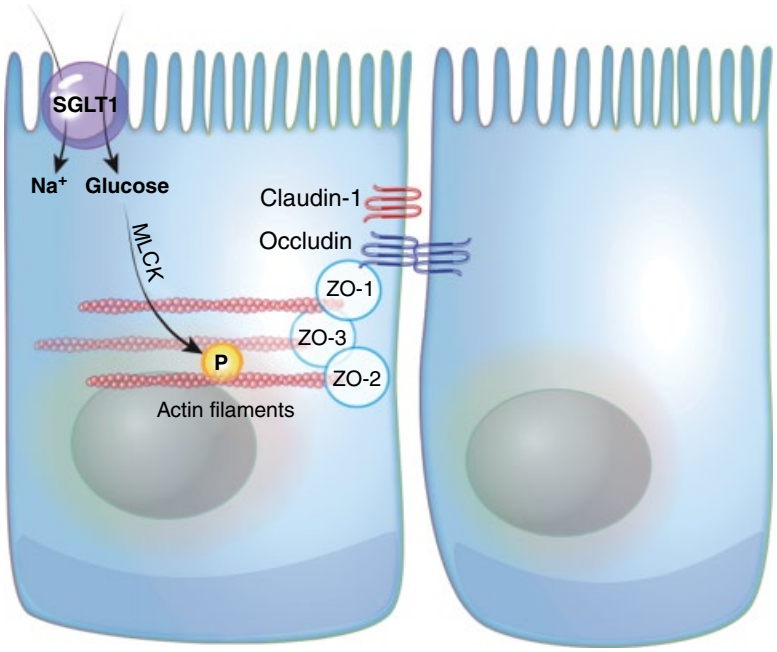

Figure 4.7 Illustration of the components that make up a tight junction, including integral membrane proteins such as occludin and claudins, and intracellular plaque proteins such as ZO-1. Note attachment of the tight junction via plaque proteins (ZO-1, ZO-2, ZO-3) to the cytoskeleton. When the myosin light chain of the actinomyosin cytoskeleton is phosphorylated by myosin light chain kinase (MLCK) in response to transport of Na^+ and glucose via SGLT1, the cytoskeleton contracts. This results in opening of the tight junction. © North Carolina State University.

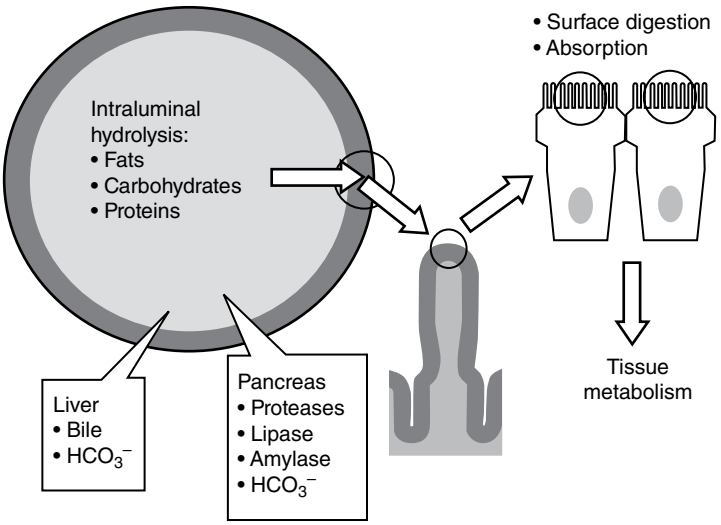

Figure 4.8 Interaction between intraluminal digestion, surface digestion, and absorption in small intestine, showing the contribution of liver and pancreas to the process.

primarily by Na^+–H^+ electroneutral transporters (NHEs) driven by the transepithelial electrochemical gradient (Figure 4.9). Of the NHEs, NHE2 and NHE3 are expressed in the apical membrane of intestinal epithelial cells, with NHE3 playing the dominant role. This was determined largely in knockout mice, in which knockout of NHE3 causes diarrhea because of intraluminal Na^+ absorption, whereas knockout of NHE2 has comparatively minimal effects on Na^+ absorption (Kato & Romero, 2011). The NHEs function in concert with Cl^-–HCO_3^- exchangers, of which there are two expressed in the apical epithelial membrane: down-regulated in adenoma (DRA) and anion exchanger 1 (AE1). The naming of DRA derives from the initial genetic identification of this AE in patients with congenital chloride diarrhea. Electroneutral absorption of NaCl is achieved by the functional link between NHE and AEs, via intracellular proteins such as NHE regulatory factors (NHERFs). AEs are also driven by the electrochemical gradient set up by basolateral Na^+,K^+-ATPase, in this case by expulsion of HCO_3^- from the relatively negative internal potential of the cell. In addition, because anion exchange is coupled to NHE function, the Na^+ gradient drives intracellular movement of Cl^- (Kato & Romero, 2011). The Na^+ gradient also energizes uptake of hexoses (glucose), amino acids, B vitamins, and bile acids by using individual Na^+-linked cotransporters such as SGLT1 (for glucose).

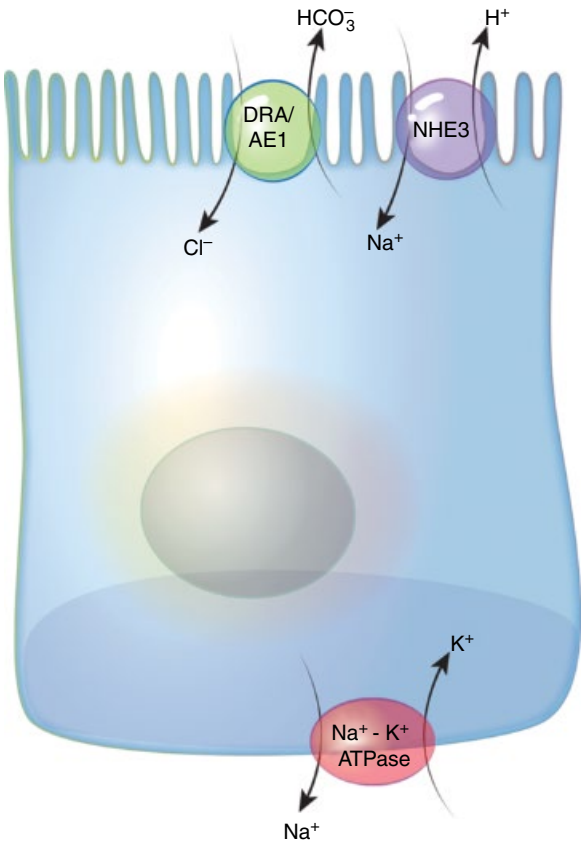

Figure 4.9 Mechanism of NaCl absorption in the small intestine. Na^+ enters the enterocyte via Na^+/H^+ exchangers 2 and 3 (primarily NHE3). These act in concert with anion exchangers (AEs), named AE1 and down-regulated in adenoma (DRA). NHEs and AEs are functionally linked, although this can be modified. The net result is absorption of NaCl electroneutrally. The Na^+ that enters the cell is then pumped out of the cell against an electrochemical gradient by the energy-dependent Na^+-K^+-ATPase. © North Carolina State University.

Water transport is passive, closely coupled to solute movement, and is primarily paracellular. However, a group of integral membrane proteins called aquaporins can also facilitate transcellular water transport in response to osmotic gradients (Verkman, 2011). As absorbed Na^+ is pumped across the basolateral membrane, it creates an osmotic gradient that draws water into the intercellular space (Figure 4.10). Although the tight junction favors this process by restricting backflow of absorbed water and electrolytes into the lumen, paracellular permeability and reverse flow through this route are actually high in the jejunum (Figure 4.11). Paracellular permeability decreases from jejunum to colon, so that Starling forces have much more influence on ion and fluid transport in the proximal bowel. Net water movement from lumen through the paracellular route "drags" ions and low-molecular weight substances with it; this transport mechanism is called solvent drag (Figure 4.12). Solvent drag or convection is another means by which small water soluble substrates, such as sugars and amino acids, are drawn across the epithelium (Pappenheimer, 1993). Fluid absorbed by the epithelium moves from the interstitium into the central lacteal of the villus (Chang & Rao, 1994). The villus contracts through the action of its smooth muscle fibers and "pumps" the fluid from the central lacteal into the deeper lymphatics (Chang & Rao, 1994).

Carbohydrate Absorption

Several brush border oligosaccharidases hydrolyze initial products of starch digestion derived from amylase, and the final monomeric D^+-isomer forms are produced by brush border disaccharidases (Figure 4.13). Sucrase

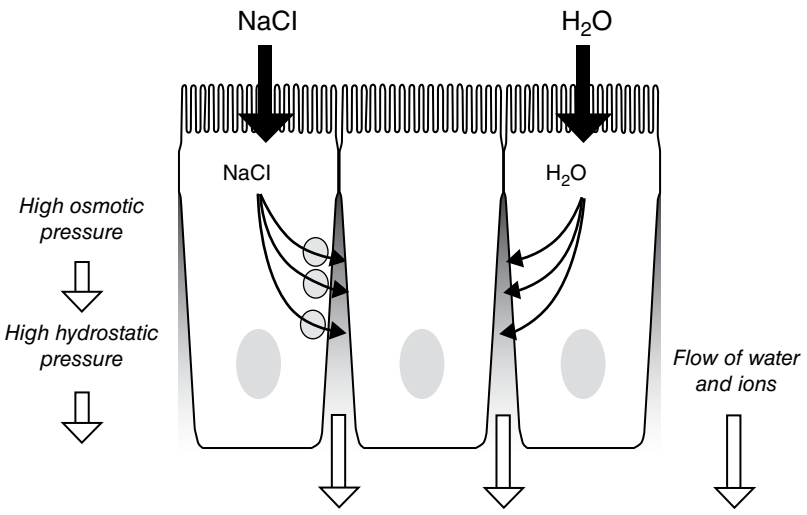

Figure 4.10 The standing gradient hypothesis invoked to explain water absorption. As absorbed Na^+ is pumped across the basolateral membrane, it creates an osmotic gradient that draws water into the intercellular space. As water accumulates in this space, it increases the hydrostatic pressure, and this pressure forces the water across the basolateral membrane towards the capillary. The tight junction favors this process by restricting backflow of absorbed water and electrolytes into the lumen.

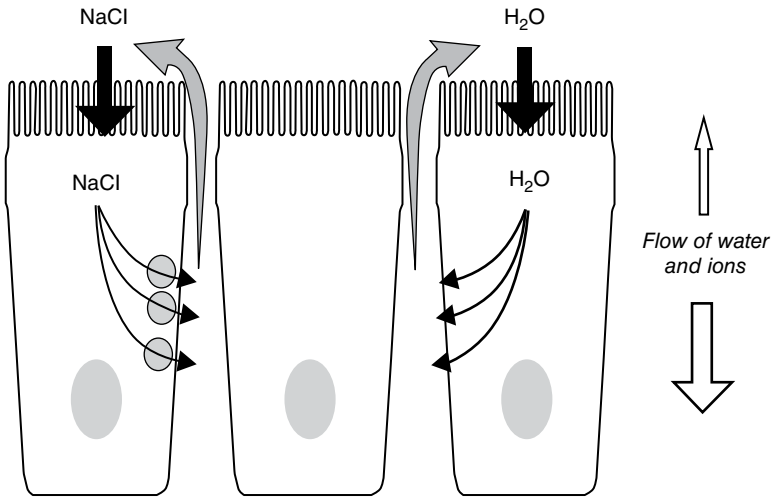

Figure 4.11 In a "leaky" epithelium, the tight junctions are sufficiently loose or permeable to allow back flux of some absorbed water and ions into the lumen, so that water absorption is less efficient (in the jejunum) than in a tight epithelium (colon).

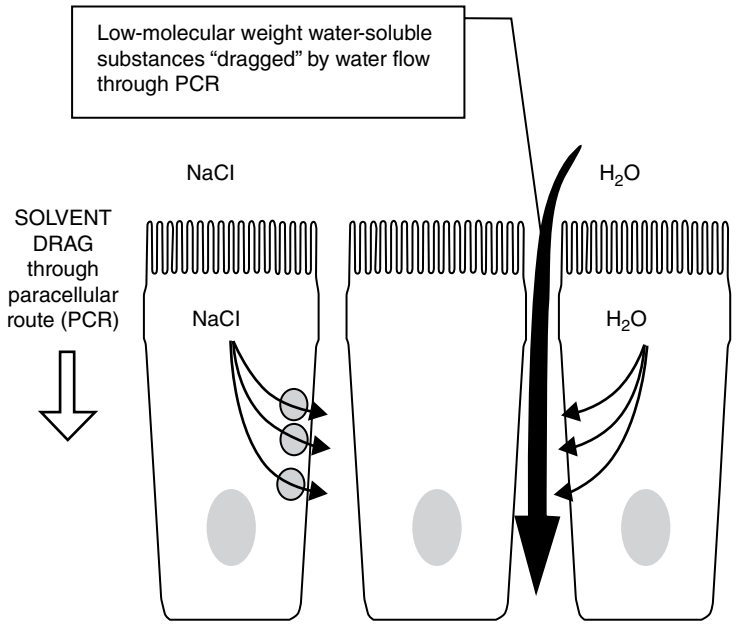

Figure 4.12 In an epithelium where the bulk flow of water is toward the basement membrane, low-molecular weight substances will be entrained to follow the absorbed water and be absorbed. This is called "solvent drag" and is analogous to a stream carrying material with it in the direction of the current flow.

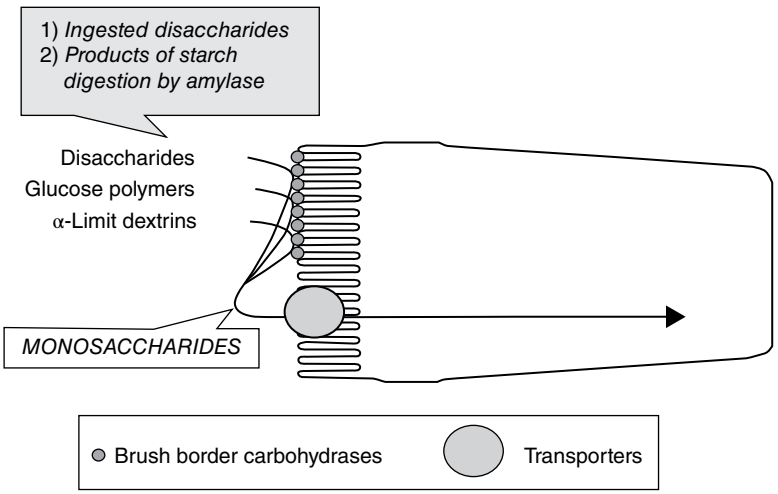

Figure 4.13 Surface hydrolysis of the carbohydrate polymers produced by intraluminal digestion and the subsequent absorption of the same as monosaccharides. Source: Johnson, 1987. Reproduced with permission of Elsevier.

activity is highest in the proximal small intestine of the horse on a grass-based diet, with activity levels comparable to those reported in other nonruminants (Dyer et al., 2002). Maltase activity is distributed evenly along the equine small intestine, and is higher than in other species (Dyer et al., 2002). Lactase activity is higher in equine jejunum than in other parts of equine small intestine, but decreases as the animal matures (Dyer et al., 2002).

The monosaccharides produced by brush border hydrolysis, such as D-glucose and D-galactose, are transported across the enterocyte membrane by SGLT1 (Figure 4.14). In horses maintained on conventional grass-based diets, the major site of D-glucose uptake by the SGLT1 transporter is the duodenum, followed by the jejunum, and then the ileum (Dyer et al., 2002). The D^+-isomer form of fructose moves from the lumen into the cell by facilitated diffusion through the glucose transport 5 (GLUT5) system, which is not Na^+-dependent (see Figure 4.14). The monosaccharides diffuse down their concentration gradient from the absorptive cell into the plasma through a GLUT2 passive transport mechanism and then enter the portal venous system (see Figure 4.14).

Protein Absorption

Brush border oligopeptidases break down the small neutral peptides yielded by pancreatic peptidases into constituent di- and tripeptides (~25%) or amino acids (~75%). Within the enterocyte, the peptides are hydrolyzed by soluble cytoplasmic oligopeptidases into constituent amino acids, which move passively into portal blood down a concentration gradient (Figure 4.15) (Ganapathy, 2012). Consequently, many di- and tripeptides are transported into the cell, but mostly free amino acids enter portal circulation (see Figure 4.15) (Ganapathy, 2012). The intestine has several distinct amino acid transport systems, with varying degrees of specificity for L^+-isomer forms of the amino acids and differences in Na^+ dependence (Ganapathy, 2012). Circulating and intraluminal amino acids can also be used by the intestinal epithelial cells as a source of metabolic fuel (Rhoads et al., 2000).

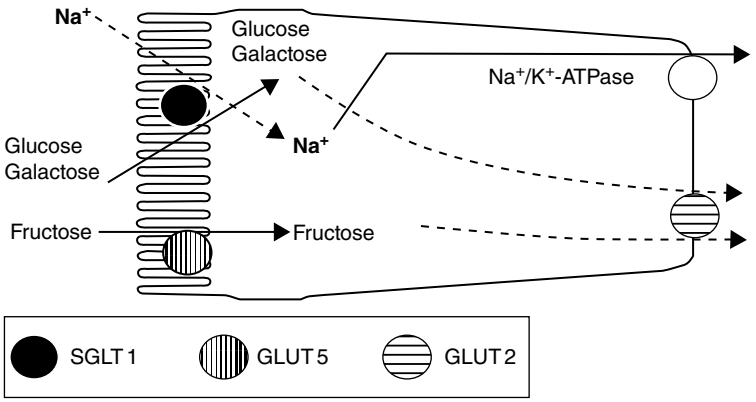

Figure 4.14 Monosaccharide transporters in intestinal epithelium, showing the Na^+-dependent process for glucose and galactose (SGLT1) and the Na^+-independent process for fructose (GLUT5) on the brush border and the basolateral transporter used by all three monosaccharides (GLUT2).

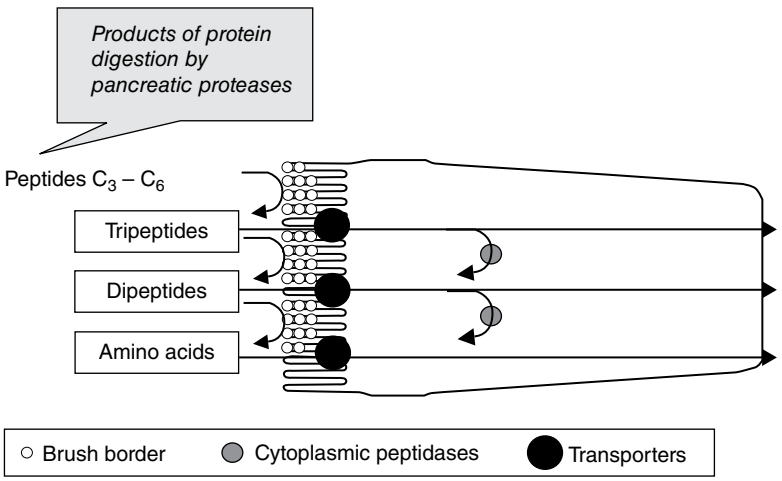

Figure 4.15 Surface hydrolysis of the protein polymers produced by intraluminal digestion and the subsequent absorption of the same as small peptides and amino acids. Source: Johnson, 1987. Reproduced with permission of Elsevier.

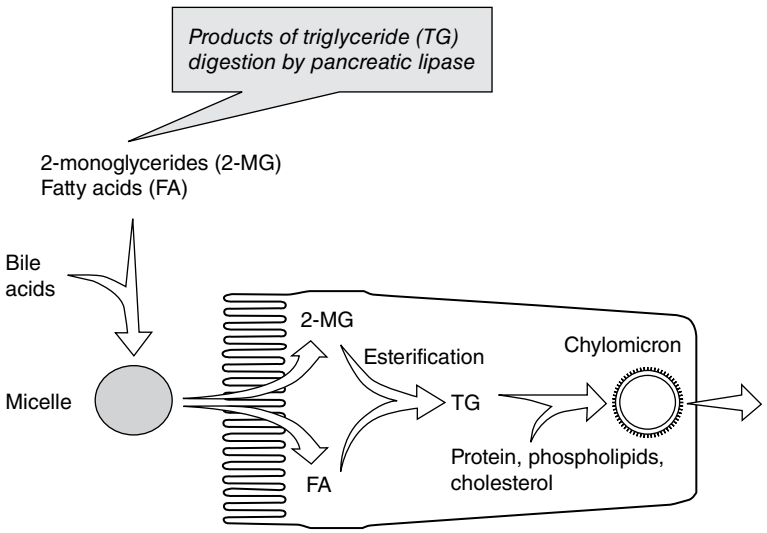

Figure 4.16 Role of micellar solubilization and chylomicron formation on absorption of 2-monoglycerides and fatty acids. Micelles allow these products to cross the unstirred aqueous layer to reach the apical membrane, and the chylomicrons are taken up by the lymphatics.

Fat Absorption

Long- and medium-chain triglycerides are split into constituent fatty acids and monoglycerides by pancreatic lipase and colipase (Liddle, 2012). After lipolysis, the resulting long-chain fatty acids and 2-monoglycerides, as well as fat-soluble vitamins and cholesterol, must combine with bile acids to form a water-soluble mixed micelle (Figure 4.16) (Mansbach & Abumrad, 2012). A mixed micelle has the fat-soluble part of its components directed inward and the water-soluble portion directed outward. In this arrangement, micelles facilitate movement of lipids through the unstirred water layer to the intestinal epithelial cells, where they release their constituents for absorption (Mansbach & Abumrad, 2012). Because of their fat solubility, the released long-chain fatty acids and 2-monoglycerides can traverse the membrane down a concentration gradient. Fatty acids and 2-monoglycerides in the mucosal cell undergo re-esterification and formation of chylomicrons, which are taken up by the lymphatic system (see Figure 4.16) (Mansbach and Abumrad, 2012).

Iron Absorption

Iron has no avenue for excretion from the body so its transport must be closely regulated. The ferrous form of iron (Fe^{2+}) is absorbed better than the ferric form (Fe^{3+}), although the precise mechanism is not known (Figure 4.17) (Collins & Anderson, 2012). Some absorbed iron combines with an intracellular protein, called apoferritin, to form an iron complex called ferritin (see Figure 4.17). If no binding protein is available, absorbed ferrous iron is transported across the serosal border of the cell through transferrin receptors and is released to the circulation (see Figure 4.17) (Collins & Anderson, 2012).

If iron stores in the body are low, little iron enters the crypt cells from the blood (Figure 4.18). Consequently, little iron is available to stimulate synthesis of iron-binding proteins or ferritin in the crypt cell. As a result, cells migrating to the villus tip as mature cells are low in this protein (see Figure 4.18); however, the same cells are high in basolateral transferrin receptor (see Figure 4.18). Therefore, as ferrous iron enters the cell from the lumen, it is not bound and is free to enter the circulation and contribute to replenishing iron stores (Collins & Anderson, 2012). Conversely, a large iron store in the body causes the ferrous iron to diffuse from its high concentrations in blood into the crypt cell, where it induces synthesis of iron-binding proteins (see Figure 4.18). Consequently, the crypt cell migrates to the tip as a mature cell high in this protein. As ferrous iron enters the cell from the lumen, it is bound to the binding protein and stored. As the cell is exfoliated into the intestinal lumen from the villus tip, it takes its iron stores with it so this iron is lost to the body and not allowed to contribute to an existing high load (see Figure 4.18) (Collins & Anderson, 2012).

Calcium and Magnesium Absorption

Lumen-to-plasma flux of calcium is highest in the duodenum, but some is absorbed in the more distal small intestine, and some endogenous calcium is passively secreted in the jejunum (Kiela et al., 2012). A high concentration of dietary magnesium can decrease calcium absorption through competition for the calcium transport site. Absorbed calcium enters the cell down an electrochemical gradient from the lumen (Figure 4.19) and is transported through the cytoplasm complexed with the specific calcium-binding protein, calbindin D_{28K} (CaBP) (Kiela et al., 2012). This protein is regulated by

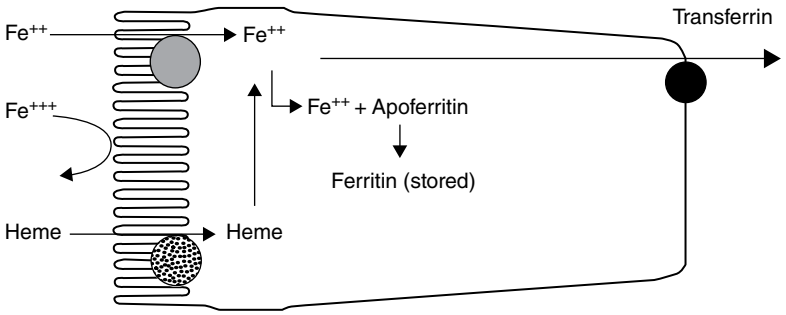

Figure 4.17 The ferrous form of iron (Fe^{2+}) is absorbed better than the ferric form (Fe^{3+}), and some absorbed iron combines with an intracellular protein, called apoferritin, to form ferritin. The nonbound ferrous iron is transported across the serosal border of the cell through transferrin receptors and is released to the circulation.

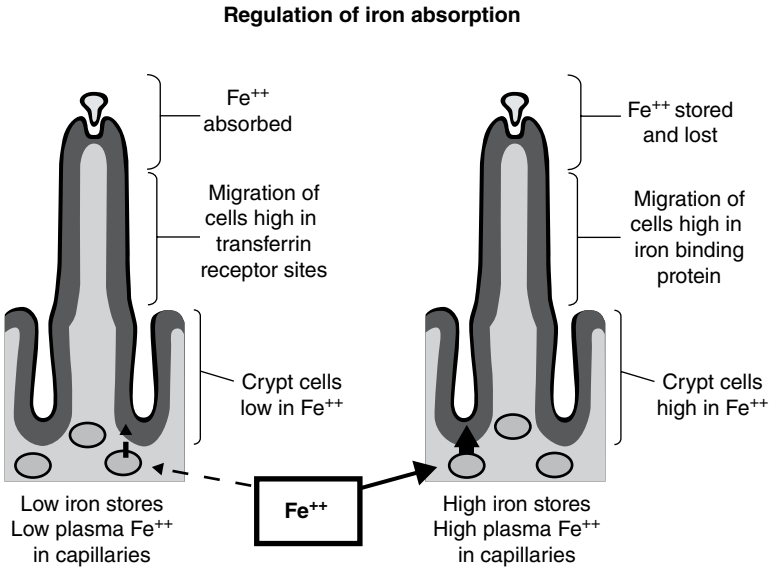

Figure 4.18 If iron stores are low in the body, little iron enters the crypt cells and little synthesis occurs of iron-binding proteins or ferritin, but the same cells will be high in basolateral transferrin receptor. Ferrous iron enters the cell from the lumen, is not bound, and is free to enter the circulation. Conversely, a large iron store in the body induces synthesis of iron-binding proteins in crypt cells and these migrate to the tip as mature cells high in this protein. Ferrous iron enters the cell from the lumen, is bound to the binding protein, and lost to the body as the cell is exfoliated from the villus tip.

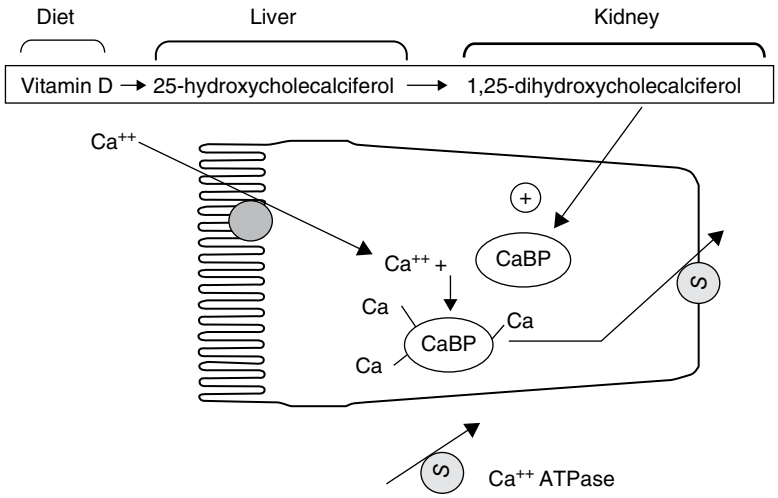

Figure 4.19 Absorbed calcium enters the cell down an electrochemical gradient from the lumen and is transported through the cytoplasm complexed with the specific calcium-binding protein, calbindin D_{28K} (CaBP). This protein is regulated by dietary vitamin D that has been converted to the biologically active form by the liver and kidney. Extrusion is against an electrochemical gradient mediated by the Ca^{2+}-ATPase.

the biologically active form of vitamin D, 1,25-dihydroxycholecalciferol (see Figure 4.19). Extrusion from the cell is against an electrochemical gradient mediated by the Ca^{2+}-ATPase (see Figure 4.19) (Kiela et al., 2012).

Magnesium absorption is of interest in horses because magnesium sulfate is used as a laxative in horses, and the extent of absorption could alter its laxative effects and the risk of magnesium toxicity (Henninger & Horst, 1997). Mean apparent magnesium absorption is approximately 70% for supplements fed to growing foals and 40–60% for magnesium fed to mature ponies. As in human beings, most is absorbed in the small intestine, primarily the proximal small intestine, and small amounts are absorbed in the colon (Hintz & Schryver, 1972).

Intestinal Secretion

Crypts of Lieberkühn are located over the entire surface of the small intestine and they secrete an almost pure extracellular fluid that maintains chyme in a fluid state, delivers secretory immunoglobulin A (IgAs), and flushes crypts of noxious and infectious agents. Intestinal water and electrolyte secretion are determined primarily by Cl^- movement, with movement of Na^+ and water following (Chang, 1996). In the gastrointestinal tract, the electroneutral Na^+–K^+–Cl^- (Na^+–Cl^- cotransporter or NKCC1 transporter; Figure 4.20) is responsible for moving Cl^- into the cell. The transporter that drives and energizes this process is the basolateral Na^+,K^+-ATPase, creating an inward chemical gradient for Na^+ via NKCC1. The cystic fibrosis transmembrane conductance regulator (CFTR, so named because its mutation in children with CF results in a failure to secrete fluid into the lumen) is the most important secretory Cl^- that is activated primarily by protein kinase A (PKA). This protein is ultimately activated by extracellular signals such as prostaglandin E_2 (PGE_2), which bind to G protein-linked receptors that release second messengers, particularly cyclic adenosine monophosphate (cAMP) (see Figure 4.20).

Intestinal secretion is under a degree of neural and eicosanoid tone, with cells of the lamina propria being the major sites of eicosanoid synthesis (Figure 4.21). A dynamic interplay between mucosa, the enteric nervous system, the central nervous system, and luminal contents, regulate secretion (Jones and Blikslager, 2002) (see Figure 4.21). Mediators produced by the enteric nervous system that promote secretion are acetylcholine, serotonin (5-hydroxytryptamine), substance P, and vasoactive intestinal peptide (VIP) (Jones & Blikslager, 2002; Argenzio, 1997).

Protective mucus is secreted by Brunner's glands, which are located in the first 9.6 m of the equine duodenum (Titkemeyer & Calhoun, 1955). The function of mucus from Brunner's glands is to protect the duodenal wall from digestion by gastric secretions. Mucus is also secreted in large quantities by mucus cells located extensively over the surface of the intestinal mucosa and in the crypts of Lieberkühn (Titkemeyer & Calhoun, 1955).

Function of the Ileum

The terminal portion of the ileum forms a papilla that projects into the cecum; the ileal orifice is in the center of the papilla, surrounded by the cecal musculature (Kotze, 1988), an annular fold of mucous membrane, and a venous network (Dyce & Hartman, 1973; Kotze, 1990). The lumen of the ileum decreases at the ileocecal junction and forms a papilla, but not a true sphincter (Dyce & Hartman, 1973; Kotze, 1988). A functional sphincter does exist and appears to contract in synchrony with

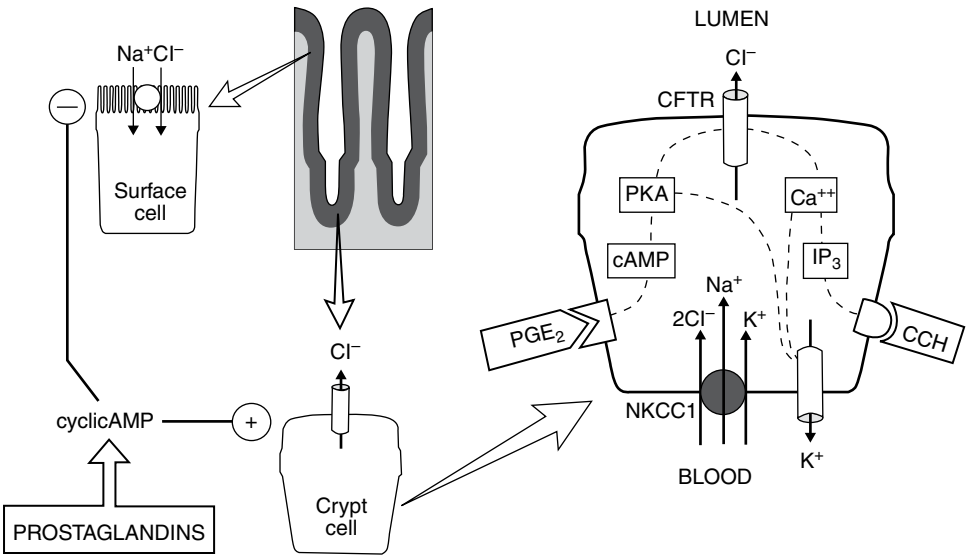

Figure 4.20 Effects of prostaglandins on ion transport in jejunal mucosa. Increased cyclic adenosine monophosphate (cAMP) activity in response to prostaglandin E_2 (or other cAMP agonists) stimulates Cl^- secretion by crypt cells and inhibits the electroneutral NaCl absorption by the surface epithelial cells. Chloride and water secretion are the net result. On the right is an expanded illustration of the process in a crypt cell. PGE_2 increases Cl^- secretion via the cystic fibrosis transmembrane conductance regulator (CFTR) by cAMP activation of protein kinase A (PKA), which phosphorylates CFTR. Carbachol (CCH) exerts its effects through inositol 1,4,5-triphosphate (IP_3) and calcium release from calcium stores, resulting in opening of CFTR via protein kinase C (PKC). In addition, molecules that signal via the second messenger Ca^{2+} also increasing basolateral K^+ efflux which has the effect of making the cell more electronegative. This has an additive effect on secretion of the anion Cl^-.

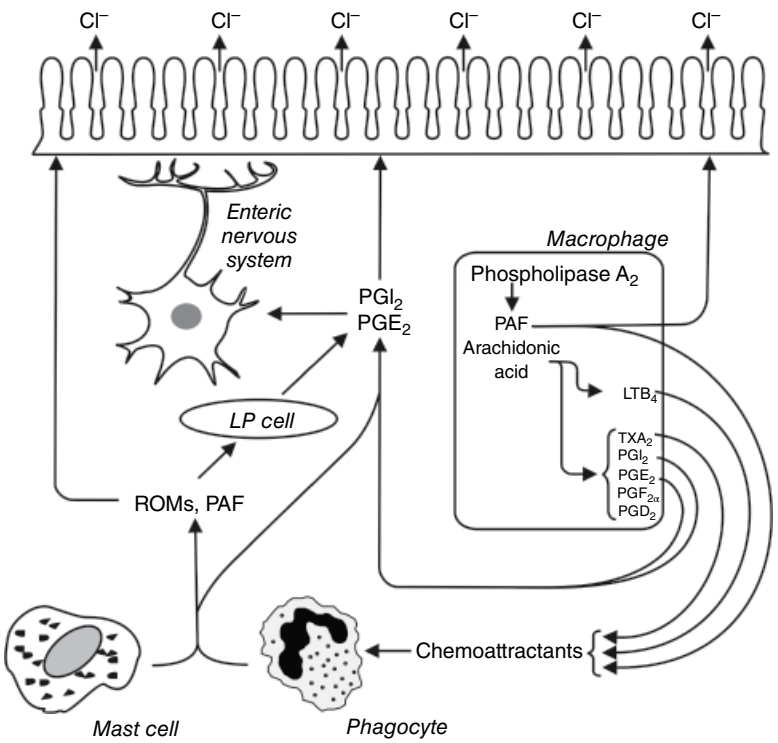

Figure 4.21 Proposed model for interaction between the immune system and the enteric nervous system in the regulation of Cl^- secretion. Stimulation of mast cells and phagocytes (neutrophils, eosinophils, macrophages) in the lamina propria by luminal or circulating stimuli causes them to release immune cell products, such as prostaglandins, reactive oxygen metabolites (ROM), and platelet-activating factor (PAF), and the last two could stimulate other lamina propria cells (LP cell) to produce prostaglandins. Prostaglandins stimulate Cl^- secretion. The final neurotransmitters involved are unknown, but acetylcholine and vasoactive intestinal peptide are possible candidates.

contractions of the cecal base (Coffin et al., 1997). Endoscopic studies of the cecal base of the horse have demonstrated that the ileal papilla is normally prominent and becomes even more prominent when the cecum is active (Dyce & Hartman, 1973). The muscle of the papilla is composed of three layers, an inner circular layer, a central longitudinal muscle layer from the ileum, and an outer layer formed from the circular muscle of the cecum and arranged into two semicircular lips (Dyce & Hartman, 1973; Kotze, 1988). It has been proposed that the venous network and annular fold of the papilla contribute to the ileal sphincter mechanism (Dyce & Hartman, 1973; Kotze, 1988). However, this theory is weakened by the observation that the veins are most engorged when the ileum is discharging its contents into the cecum (Dyce & Hartman, 1973).

The ileum appears to differ from the jejunum in its myoelectric activity and this might be related to its unique position at the junction of the small and large intestines. In the ileum of mature ponies, all phases of the migrating myoelectric complex (MMC) can be recorded, but irregular spiking activity (phase II) predominates during the interdigestive period (time between meals) (Ross et al., 1990). The migrating action potential complex (MAPC) can be recorded in the pony ileum (Ross et al., 1990), but not in the pony jejunum (Adams et al., 1984), as intense spike bursts of short duration that propagate rapidly aborally (Berry et al., 1986).

The MAPC immediately precedes retrograde cecal myoelectric activity 73% of the time, indicating a possible myoelectric coupling of the ileum and cecum, and may be responsible for transit of digesta from the ileum to the cecum (Ross et al., 1990). Also, ileal contents are discharged into the cecum in semisolid or liquid form, mostly at times when the cecum is inactive (Dyce & Hartman, 1973). Ileal and cecal filling appear to be more important in regulating ileocecal motility events in ponies than are stimuli associated with feeding (Ross et al., 1990).

Some evidence exists that local stimulation of chemoreceptors is important in the regulation of ileal motility in the horse. For example, at neutral pH, tonic activity of the human ileum, but not the jejunum, is increased by intraluminal short-chain fatty acids, whereas bile acids and lipids can induce ileal relaxation (Coffin et al., 1997). Likewise, the tone of the ileal papilla increases during contractions of the cecal base in horses, but not enough to prevent reflux of some cecal contents into the ileum (Roger et al., 1995). In the pony, serotonin and luminal fatty acids increase ileal peristalsis. The response to luminal acidification could be physiologically important because acidification of ileal contents by cecal reflux could stimulate ileal emptying of refluxed bacteria and cecal contents (Roger et al., 1995; Coffin et al., 1997). Through this response, ileal motility could augment the sphincter function of the ileal papilla in preventing reflux of cecal contents (Roger et al., 1995).

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5

Large Intestine Function

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Unlike the more proximal segments of the gastrointestinal tract, the large intestine is not a site in which digestion by endogenous enzymes cells takes place. In horses and other monogastric herbivores and omnivores, the large intestine provides the ideal environment for microbial growth, which favors fermentation and production of volatile fatty acids (VFAs). The large intestinal mucosa absorbs substantial amounts of VFAs, which serve as an important source of energy (Argenzio et al., 1974a). It is estimated that horses obtain as much as 30% of their energy requirements from VFAs produced by microorganisms in the cecum (Bergman, 1990). Because the horse's large colon is the main fermentation chamber (Argenzio et al., 1974b) and only about 25% of the energy requirements of horses fed a high-grain diet are supplied by glucose oxidation (Argenzio & Hintz, 1972), it is likely that VFAs supply much more than 50% of the horse's energy requirement. Microorganisms in the large bowel also synthesize vitamin K and water-soluble vitamins, which are likely absorbed, at least in part, and used as nutrients (Lewis, 1995; Argenzio, 1975). Furthermore, the large bowel absorbs large amounts of water and electrolytes from the intestinal contents, a process that is critical for water and electrolyte homeostasis (Argenzio et al., 1974a).

The complex functions as well as the enormous size, the high mobility, and the pronounced changes in diameter of the equine large intestine make this part of the gastrointestinal tract prone to malfunction (Argenzio, 1975). Although many aspects of equine large intestinal physiology await investigation, some major physiologic mechanisms have been elucidated.

Motility Patterns and Transit of Contents

Motility of the large intestine is complex, and several patterns have been identified (see Chapter 9). The purposes of these different motility patterns are to promote adequate mixing and contact of the intestinal contents with the mucosa, as well as to move the contents slowly enough to ensure that adequate time exists for fermentation and absorption. Emptying of the large intestine is also important as it provides space for additional ingesta entering from the small intestine. Transit of ingesta through the large intestine is considerably slower than through the small intestine. In a study in ponies, the majority of the marker of the liquid phase administered via nasogastric tube took less than 2 h to reach the cecum (Argenzio et al., 1974b). Conversely, in the same study and in a study in fistulated horses, it took more than 12 h for the majority of the marker of the liquid phase to be passed in the feces (Argenzio et al., 1974b; Lopes et al., 2004). Similarly, transit of particulate markers through the large intestine was considerably slower than their transit through the stomach and small intestine (Argenzio et al., 1974b).

Whereas the majority of the marker of the liquid phase and particulate markers administered via a cecal fistula left the cecum within 8 h, the majority of those markers were retained in the large colon for more than 24 h. Passage of the marker of the liquid phase and particulate markers through the descending colon was relatively rapid (Argenzio et al., 1974b).

Ingesta and gas move from the ileum into the cecum through the ileocecal valve, which impedes retrograde movement of liquid and particles into the ileum (Argenzio et al., 1974b). Characteristic (tinkling and splashing) sounds produced by ileocecal flow of small amounts of ingesta can be detected by auscultation over the right paralumbar fossa as frequently as one to three times per minute (Adams, 1999). Composition and volumes of ingesta and gas reaching the cecum vary considerably and depend on several factors, including the diet and the size of the horse. In horses eating only roughage, the water content of cecal ingesta exceeds 90% (Freeman, 2002; Sperber et al., 1992).

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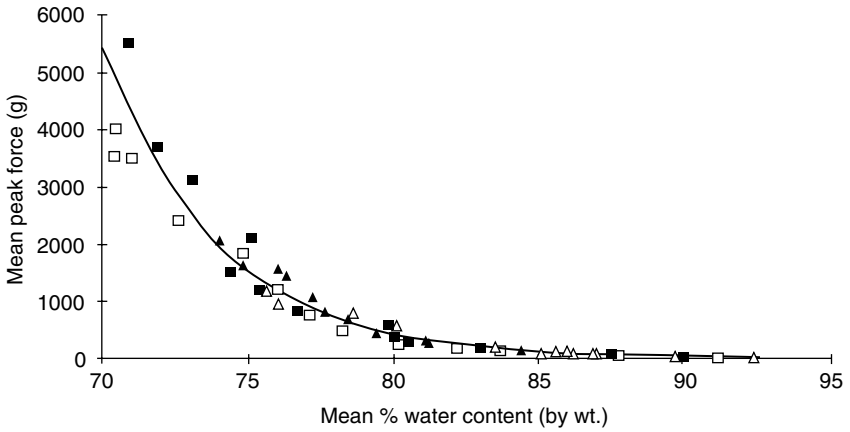

Figure 5.1 Plot of mean percent water content of ingesta of pigs versus mean peak force measured with a Stevens QTS 25 Texture Analyzer (Michael G. Brown & Associates, Pennsylvania, USA) as an indicator of ingesta viscosity. Source: Adapted from McRorie et al., 1998. Reproduced with permission of Springer.

Within the large intestine, ingesta are moved aborally by peristaltic contractions of the intestinal wall. These contractions create a pressure gradient to overcome resistance to ingesta flow. Throughout the cecum and large colon, there are local haustra-to-haustra mixing movements as well as retrograde propagation of coordinated contractions, which are thought to be important for delaying aboral transit. These motility patterns have been documented by electromyography, intraluminal manometry, auscultation, radiography after administration of positive contrast media, direct observation of the large intestine in horses undergoing laparotomy, scintigraphy after administration of radiolabeled markers, and endoscopy through cecal and colonic fistulas (Alexander, 1952; Lester et al., 1998; Ross et al., 1986, 1990; Sellers et al., 1982a, 1982b, 1984).

The cecum is partially filled with watery ingesta whereas the cecal base is filled with gas at a pressure that is slightly negative relative to atmospheric pressure. Changes in cecal shape and an effective outflow mechanism to the large colon accommodate the passage of additional ingesta and gas through the ileocecal valve as well as gas being produced within the cecum (Cottrell et al., 1998). Cecal contents are emptied into the right ventral colon through the cecocolic ostium. Coordinated contractions originate in the cecal body near the apex as often as every 2 min, and move toward the base, creating a pressure gradient that moves ingesta and gas (Ross et al., 1986, 1989, 1990). Then, muscular contractions form a constriction at the cecal base cranial to the ileocecal papilla. This constriction creates two separate compartments at the cecal base (cranial and caudal compartments), and is associated with the elevation of the ventral cecal base and opening of the cecocolic ostium. The last event in the cecal emptying mechanism is the contraction of the cranial compartment of the cecal base. Ingesta and gas are thus moved through the cecocolic ostium, although significant amounts of ingesta can move back to the cecal body instead of passing through the cecocolic ostium (Dyce et al., 1976; Roger et al., 1994). Because of the sigmoid configuration of the cecocolic junction, no reflux of ingesta occurs and only minor amounts of gas move from the colon to the cecum (Argenzio & Hintz, 1972; Dyce et al., 1976).

Within the large colon, resistance to flow of intestinal contents is increased at the pelvic flexure, which delays emptying of the ventral colon. Although a true sphincter is not present at the pelvic flexure, physiologically the ventral and dorsal colons are distinct compartments, and no reflux of liquid or particles occurs from the dorsal colon to the ventral colon (Argenzio et al., 1974b; Alexander, 1952). After leaving the large colon, the intestinal contents pass rapidly through the descending colon (Argenzio et al., 1974b). Intestinal contents undergo progressive dehydration as they move aborally through the large bowel. In a study of normal horses, hydration of contents decreased from about 92% in the cecum to 88% in the large colon and to 80% in the small colon (Freeman, 2002). In another study in fistulated horses eating only hay, water content of the ingesta from the right dorsal colon and feces was about 90% and 80%, respectively (Lopes et al., 2004). Although viscosity of large intestinal contents has not been studied in horses, a study in pigs has demonstrated that a decrease in water content is associated with an increase in viscosity of the ingesta (Figure 5.1) (McRorie et al., 1998). Furthermore, it has been clearly demonstrated in rabbits that ingesta viscosity is a major determinant of resistance to ingesta flow (Morel et al., 1990). In the descending colon, fecal balls smaller than the diameter of the colonic lumen are formed, thereby facilitating transit of the less hydrated intestinal contents. Secretion of large amounts of mucus in this segment also reduces the resistance to transit of contents through the descending colon and rectum (Guyton & Hall, 2000b).

Microbial Activity and Fermentation

Although relatively few studies of the equine microbiota have been performed (see Chapter 7), the available information indicates that the microbial activity in the equine

large intestine is similar to that in the bovine rumen. However, the differences in gastrointestinal anatomy render horses much less efficient at utilizing nutrients produced by the microbiota. For example, in contrast to the anatomic arrangement in ruminants, in the equine gastrointestinal tract the primary site for endogenous digestion and nutrient absorption (the small intestine) precedes the main site for microbial activity (the large intestine). Considering that there is normally no significant reflux of ingesta from the cecum to the ileum (Argenzio et al., 1974a) and that horses do not consistently practice coprophagy like other nonruminant herbivores, absorption of nutrients produced by the large intestinal microbiota may be limited by the lack of efficient mechanisms for digestion and absorption of several nutrients in the equine large intestine (Van Soest, 1994a; Soave & Brand, 1991; Ralston, 1986).

In ruminants, several species of bacteria, protozoa, and fungi coexist in the rumen. Usually, microorganisms are present in concentrations exceeding 10^9 cells/g of ruminal contents, and represent 50–90% of the rumen biomass. The rumen ecosystem has complex interactions among the microorganisms (e.g., competition for nutrients, predation, cross-feeding). As in any ecosystem, microbial populations are determined by the environmental conditions within the rumen, the availability of nutrients and the presence of negative interactions among organisms (e.g., predation) (Buddington & Weiher, 1999; Hoover & Miller, 1991; Van Soest, 1994a). The microorganisms are not evenly distributed throughout the rumen. Depending on factors such as the species, phase of the life cycle, and availability of nutrients, microorganisms can exist freely in the liquid phase of the ruminal contents, bound to solid particles, or attached to the ruminal mucosa. Microorganisms that utilize soluble nutrients (e.g., carbohydrates and proteins) are free in the liquid phase, while microorganisms that use insoluble nutrients (e.g., fiber) are bound to the solid particles. For organisms such as some protozoa, which have a relatively long life cycle, the turnover time of the ruminal liquid is too short, and binding to solid particles is the only way for them to stay in the rumen long enough to reproduce (Hoover & Miller, 1991; Van Soest, 1994b).

In the bovine rumen, extracellular enzymes produced by bacteria, fungi, and protozoa degrade complex carbohydrates. Simple carbohydrates, such as oligosaccharides and monosaccharides from feed or from degradation of complex carbohydrates, are engulfed and hydrolyzed by other microorganisms. The end products are VFAs (acetic, propionic, butyric, valeric, and isovaleric acids), lactic acid, carbon dioxide, and methane. These VFAs are absorbed by the rumen mucosa and are the main source of energy for ruminants. Rumen bacteria, fungi, and protozoa also have proteases, which rapidly degrade protein. Free amino acids and ammonia from the diet or from protein degradation are used by the microorganisms for synthesis of microbial protein and growth. In the small intestine, microbial proteins synthesized in the rumen and dietary proteins that evade microbial degradation are digested and absorbed to meet the animal's need. Fats are degraded by extracellular lipases released by bacteria and protozoa. The glycerol and fatty acids produced by fat degradation have different fates; glycerol is rapidly consumed by microorganisms, while fatty acids adhere to solid particles and are degraded at a slower rate. Long-chain fatty acids, especially if they are polyunsaturated, are toxic to bacteria and protozoa, and the intake of high levels of these compounds may reduce fiber digestion (Hintz et al., 1971; Argenzio & Armstrong, 1993). Besides their key role in digestion and protein synthesis, rumen microorganisms produce vitamins (i.e., vitamin K and the B vitamins), which are used as nutrients by the host (Buchanan-Smith et al., 2000). Furthermore, microbial fermentation produces heat that may help maintain body temperature when ambient temperature is low, but may become a problem when ambient temperature is high (Houpt, 1968).

Similar to the rumen, the equine large intestine is an anaerobic environment where contents are held for long periods (Figure 5.2) (Argenzio et al., 1974b; Argenzio, 1975). In the horse, the rich cecal and colonic microbiota are composed of large numbers of several species of bacteria, protozoa, and fungi (Bonhomme-Florentin, 1985, 1988; Daly et al., 2002; Gold et al., 1988; Julliand et al., 1999; Kern et al., 1973, 1974; Lin & Stahl, 1995; Linerode & Goode, 1970; Mackie & Wilkins 1988; Orpin, 1981; Sprouse & Garner, 1982; Sunvold et al., 1995; Costa et al., 2015; Ericsson et al., 2016). Microbial activity depends on the availability of nutrients and is reduced by fasting (Julliand et al., 2001; Kern et al., 1973; Garner et al., 1978; Goodson et al., 1988; Alexander, 1952).The microorganisms ferment hydrolyzable nutrients, such as sugars and protein that escape digestion and absorption in the proximal gastrointestinal tract, as well as indigestible complex molecules including cellulose and soluble fiber (Alexander, 1952; Bonhomme-Florentin, 1985, 1988; Julliand et al., 1999; Orpin, 1981; Sunvold et al., 1995). Because the proximal gastrointestinal tract does not produce enzymes that digest fiber, these molecules reach the large intestine intact. The main products of carbohydrate fermentation in the equine large intestine are VFAs (mainly acetic, propionic, and butyric acids) (Figure 5.3), which are well absorbed by the mucosa (Figure 5.4) (Argenzio, 1974a; Alexander, 1952; Julliand et al., 2001; Hintz et al., 1971; Stillions et al., 1970) and provide a major portion of needed energy (Bergman, 1990; Argenzio & Hintz, 1972; Argenzio, 1975). Small amounts of lactic acid are also produced in the large intestine, but are poorly absorbed and do not serve as a major nutrient for the horse. If large amounts of lactic acid were

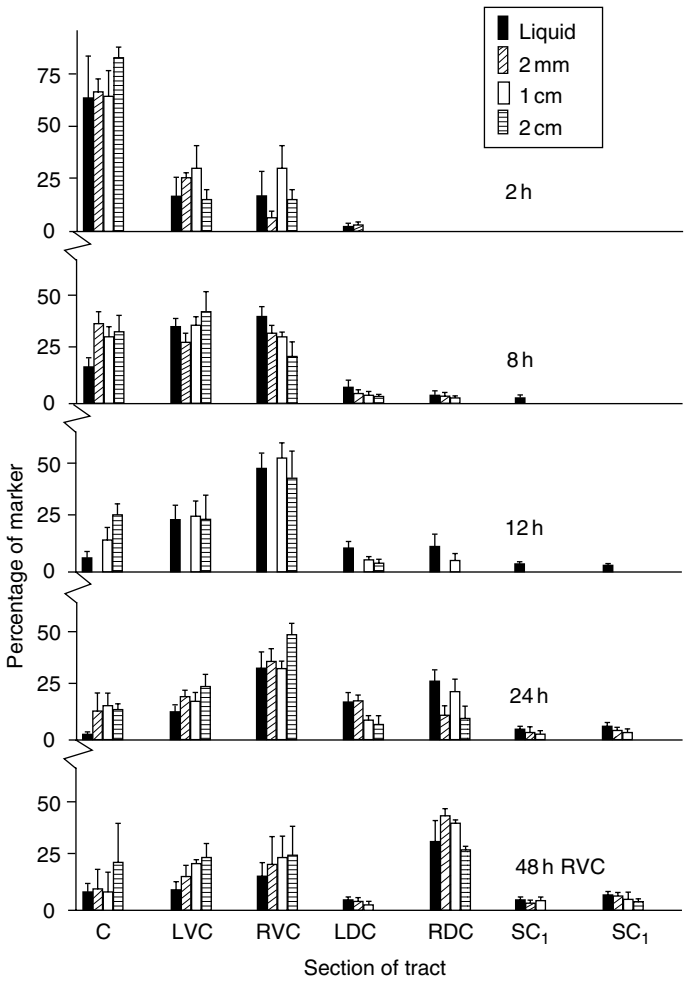

Figure 5.2 Percentage (± SE) of liquid and particulate markers (2 mm, 1 cm, and 2 cm) recovered from the large intestine of ponies euthanized 2, 8, 12, 24, and 48 h after receiving a dose of the markers via a cecal fistula. The 2 mm particulate marker was not given to animals sacrificed at the 12 h time point. C, cecum; LVC, left ventral colon; RVC, right ventral colon; LDC, left dorsal colon; RDC, right dorsal colon; SC_1, proximal small colon; SC_2, distal small colon. Source: Argenzio et al., 1974a. Reproduced with permission of the American Physiological Society.

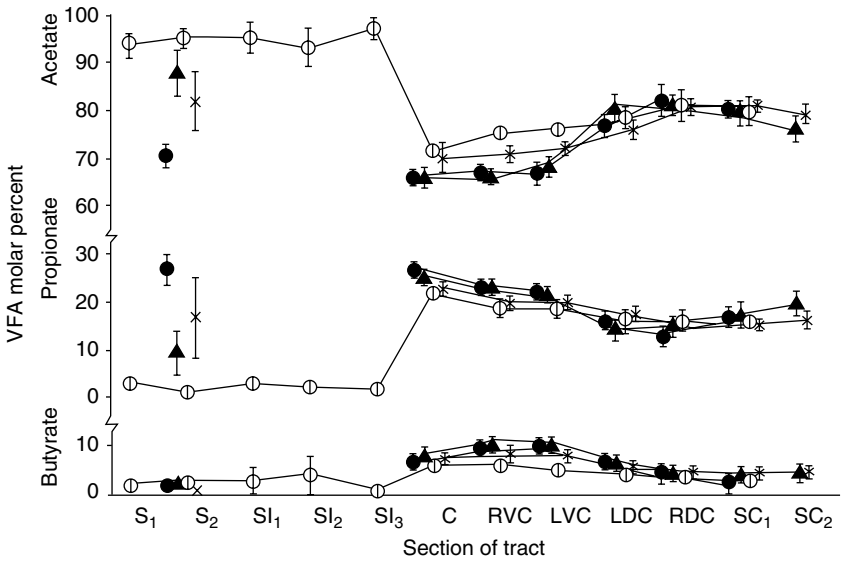

Figure 5.3 Mean relative proportions (± SE) of acetate, propionate, and butyrate in gastrointestinal contents of ponies sacrificed 0 h (closed circle), 2 h (closed triangle), 4 h (open circle), or 8 h (×) after feeding. S_1, cranial stomach; S_2, caudal stomach; SI_1, proximal small intestine; SI_2, middle small intestine; SI_3, distal small intestine; C, cecum; RVC, right ventral colon; LVC, left ventral colon; LDC, left dorsal colon; RDC, right dorsal colon; SC_1, proximal small colon; SC_2, distal small colon. Source: Argenzio et al., 1974b. Reproduced with permission of the American Physiological Society.

produced in the large intestine, this would lead to intraluminal acidosis and an increase in intraluminal osmolality (Argenzio et al., 1974a; Argenzio, 1990). The ratio of VFAs to lactic acid produced within the large intestine depends on the diet (e.g., more propionic and lactic acids are produced when grain is consumed) and intraluminal pH (e.g., lactic acid synthesis is increased when intraluminal pH falls) (Argenzio et al., 1974a; Julliand et al., 2001; Kern et al., 1973; Garner et al., 1978; Stillions et al., 1970; Argenzio, 1975). As has been documented to occur

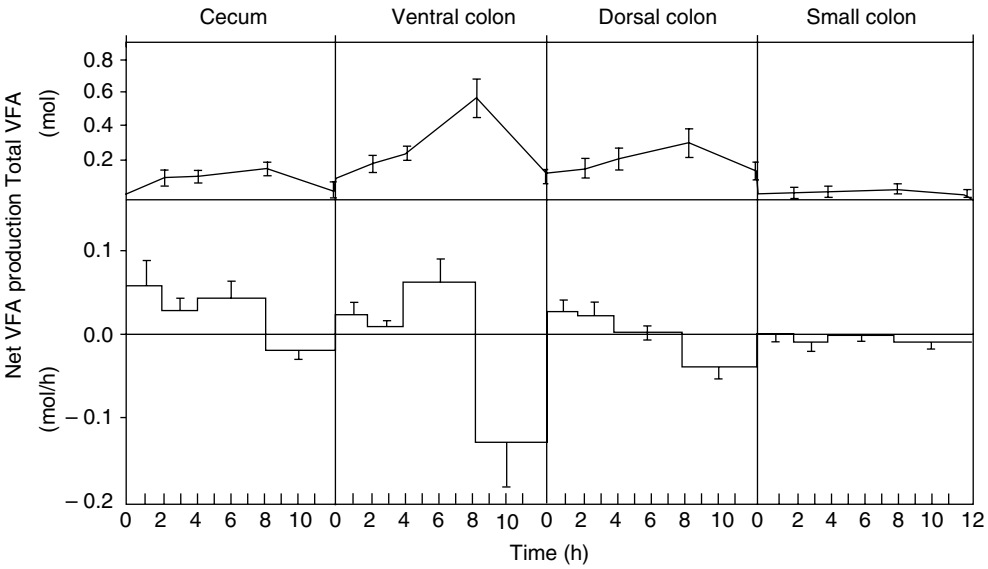

Figure 5.4 Content and net production (± SE) of volatile fatty acids (VFAs) in segments of the large intestine of ponies fed twice daily and euthanized 0, 2, 4, 6, 8, 10, and 12 h after feeding. Negative net production means absorption of VFAs. Source: Adapted from Argenzio et al., 1974b. Reproduced with permission of the American Physiological Society.

in ruminants, evidence exists that fat can be toxic to the equine microbiota. Recent studies have shown that the digestibility of fiber is decreased when horses consume large amounts of fat (Bush et al., 2001; Jansen et al., 2000, 2001, 2002).

Microorganisms in the equine large intestine also produce vitamin K and B vitamins, which constitute important nutrients for the horse (Lewis, 1995; National Research Council, 2007). Although the significance of the absorption of water-soluble vitamins produced by the colonic microbiota has been a subject of debate, recent studies in laboratory animals and humans clearly demonstrate that specialized systems for efficient uptake of B vitamins do exist in the large intestine (Said, 2013). These recent findings suggest that there is clinically significant absorption of water-soluble vitamins produced by the microbiota of the large intestine. Conversely, absorption of vitamin K in the large intestine appears to be much less significant and is thought to occur largely due to the lipid solubility of this vitamin. In mice, the main sites for absorption of vitamin K are the jejunum and ileum, but there is some uptake of vitamin K in the cecum (Goncalves et al., 2015). Conversely, colonic absorption of vitamin K is poor in laboratory animals (Goncalves et al., 2015; Groenen-van Dooren et al., 1995). Presently, no studies have been performed about vitamin absorption by the equine large intestine.

Unlike ruminants, horses are unable to use proteins produced by the gastrointestinal microorganisms as nutrients. In ruminants, proteins produced by microorganisms in the main fermentation chambers (i.e., the forestomachs) are digested and absorbed in the small intestine (Hoover & Miller, 1991). In horses, proteins produced by microorganisms in the main fermentation chambers (i.e., cecum and large colon) are not usable because the mucosa of the large intestine cannot absorb significant amounts of free amino acids or peptides. Because significant amounts of nonprotein nitrogen can be absorbed by the mucosa of the large intestine, synthesis of microbial protein, a process that consumes nonprotein nitrogen, has a role in nitrogen excretion (Bochroder et al., 1994). Microbial synthesis of protein traps nitrogen within the lumen of the large intestine and contributes to excretion of nitrogen in the feces (Argenzio, 1990; Van Soest, 1994a; Wootton & Argenzio, 1975).

Secretion and Absorption

Large amounts of water, electrolytes, and other solutes are secreted and/or absorbed by the equine large intestine (Argenzio et al., 1974a, 1974b; Argenzio & Stevens, 1975). Secretion and absorption by the large intestine have the following important roles: (i) to maintain ideal conditions for microbial growth in the intestinal lumen, which is particularly important for a monogastric herbivore such as the horse; (ii) to supply the body with nutrients, water, electrolytes, VFAs, and vitamins; (iii) to protect the mucosa against physical, chemical, and biological insults (e.g., damage due to friction of pieces of forage, acidity due to production of VFAs, and lactate); (iv) to maintain low viscosity of the ingesta and lubricate the mucosa to facilitate flow of intestinal contents; and (v) to excrete substances such as nitrogen and potassium.

Mucus Secretion

Mucus is secreted by the mucosa, which contains large numbers of goblet cells, especially in the small colon

(see Chapter 1). Secretion of mucus facilitates transit of the large intestinal contents by minimizing friction with the mucosa (Guyton & Hall, 2000b). This is likely more important in the final segments of the large intestine, where the intestinal contents gradually become drier and more viscous (McRorie et al., 1998; Freeman, 2002). Mucus also protects the mucosa against acids produced by microbial fermentation. Furthermore, mucus and other macromolecules (e.g., immunoglobulins, antimicrobial peptides) secreted by the mucosa are important in maintaining the integrity of the mucosa and protecting against pathogenic organisms and toxins (Guyton & Hall, 2000b; Hecht, 1999; Lamm, 1998).

Water and Electrolyte Secretion

Large amounts of electrolytes (primarily chloride, sodium, bicarbonate, and phosphate) and water are also secreted into the intestinal lumen. Secretion of water and electrolytes is important to maintain osmolality and pH within ranges that favor microbial growth and absorption of nutrients (Argenzio, 1990; Alexander & Hickson, 1970; Schryver, 1975). Secretion of water also is important to keep the viscosity of the ingesta low enough to facilitate ingesta flow and avoid the formation of impactions (Freeman, 2002; McRorie et al., 1998; Morel et al., 1990). Water secretion is a passive process driven by the osmotic gradients generated by secretion of solutes, primarily anions (HCO_3^- and Cl^-). Electrolyte secretion is initiated by an active mechanism of electrogenic secretion of chloride, which is present throughout the large intestine. This mechanism starts with chloride crossing the basolateral membrane into the cytoplasm through a Na^+–K^+–$2Cl^-$ cotransporter using an electrochemical gradient generated by the Na^+,K^+-ATPase. Chloride is then secreted into the lumen through chloride selective channels (largely the cystic fibrosis transmembrane conductance regulator) located on the apical membrane. Na^+ and K^+ cross the basolateral membrane back to the extracellular space via the Na^+,K^+-ATPase and K^+ selective channels, respectively. The electrogenic secretion of Cl^- is followed by Na^+ and K^+ secretion through the paracellular pathway (Figure 5.5) (Chang & Rao, 1994; Clarke & Argenzio, 1990; Giddings et al., 1974; Johnson, 2001).

Protein released into the lumen (i.e., mucus, sloughed cells) and nonprotein nitrogen (e.g., urea) secreted into the intestinal lumen are sources of nitrogen for the microbiota and represent a secondary means of nitrogen excretion (Argenzio, 1990; Wootton & Argenzio, 1975). Secretion of potassium also occurs and functions as a secondary excretion mechanism for this electrolyte (Chang & Rao, 1994; Agarwal et al., 1994). For several years, secretion of water and electrolytes was purported to occur at the crypts where the less mature epithelial cells are located, whereas absorption was performed by more mature cells located at the surface epithelium (Argenzio, 1990; Chang & Rao, 1994). However, the results of more recent studies suggest that this clear demarcation does not exist. In fact, both crypts and surface epithelium are able to absorb and secrete electrolytes and water in the presence of the appropriate stimulus (Sandle, 1998).

Fatty Acid Absorption

VFAs produced by microbial fermentation are rapidly absorbed by the mucosa of the large intestine (Argenzio et al., 1974a). Transcellular diffusion of protonated VFAs has been proposed as the main mechanism for the absorption of VFAs in the equine large intestine. However, because the pH (6.0–7.0) of the lumen of the equine large intestine is considerably higher than the pK_a of the VFAs (4.8), more than 99% of the VFAs are ionized. As a result, a source of H^+ is required for significant protonation of VFAs to occur, which maximizes their absorption (Bugaut, 1987). Dissociation of carbonic acid produced by hydration of CO_2 within the lumen and/or the epithelium as well as the ubiquitous cell membrane Na^+–H^+ exchange provide H^+ and create an acidic

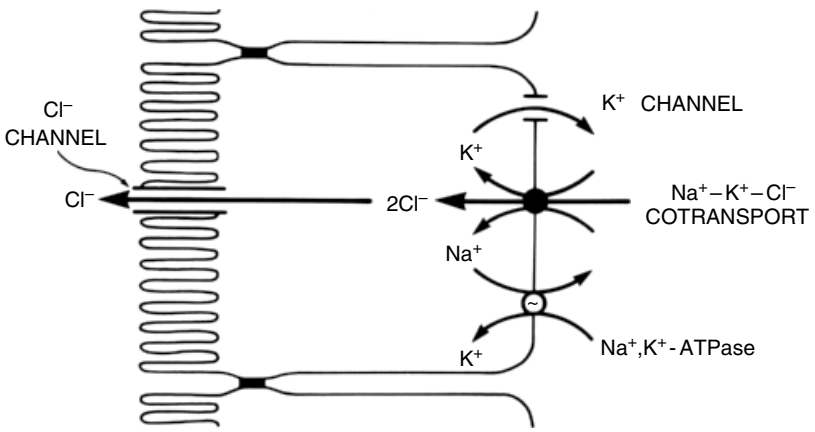

Figure 5.5 Electrogenic Cl^- secretion by colonocytes: active Cl^- secretion is followed by passive Na^+ and water secretion. ATPase, adenosine triphosphatase. Source: Barrett & Dharmsathaphorn, 1994, Fig. 17-9. Copyright McGraw-Hill Education. Reproduced with permission.

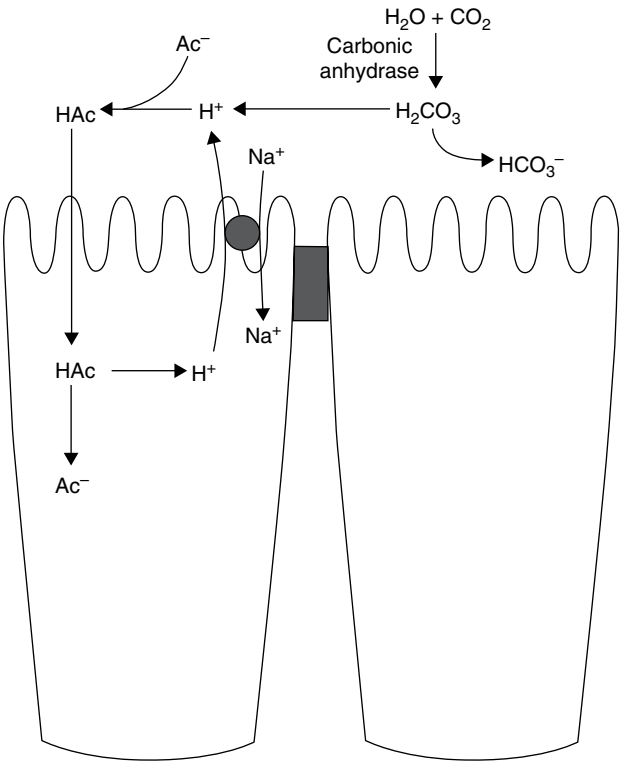

Figure 5.6 Absorption of volatile fatty acids (VFAs) in the protonated form by colonocytes. Ac^-, acetate ion; HAc, acetic acid. Source: Adapted from Argenzio, 1990.

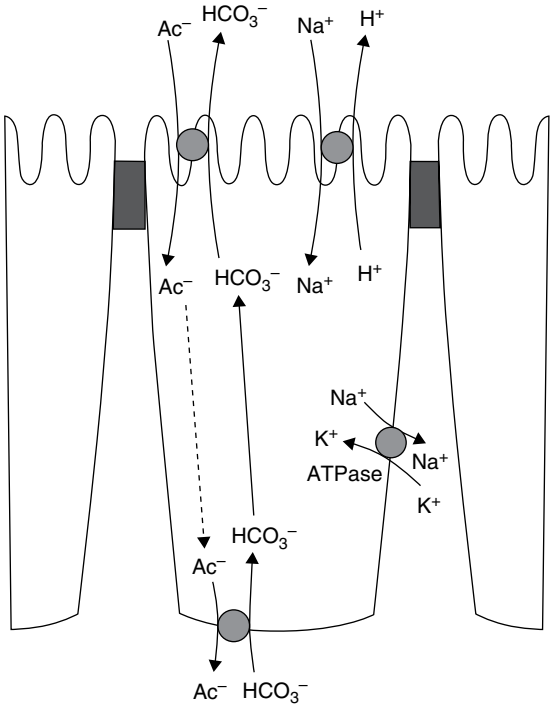

Figure 5.7 Absorption of volatile fatty acids (VFAs) in the ionized form by colonocytes. ATPase, adenosine triphosphatase. Source: Adapted from Sandle, 1998.

microclimate at the glycocalyx that favors protonation of VFAs (Figure 5.6) (Bugaut, 1987). Alternatively, it has been hypothesized that VFAs may be absorbed in the ionized form in exchange for bicarbonate (Figure 5.7) (Sandle, 1998). This hypothesis is supported by the identification of a VFA–HCO_3^- exchange mechanism in the apical membrane of mammalian colonocytes (Schroder et al., 2000). Bicarbonate appearing in the lumen during absorption of VFAs serves to buffer the colonic contents, counteracting the acidifying effect of the acids produced by microbial fermentation. This process may help prevent mucosal damage and avoid changes in the microbiota of the large intestine that would occur as the result of intraluminal acidosis. The intensity of the alkalinizing effect of absorption of VFAs is thought to be inversely related to the electroneutral absorption of sodium through a Na^+–H^+ exchange mechanism (Argenzio, 1990; Argenzio et al., 1977).

Recent research has shown that monocarboxilate transporter protein 1 (MCT1) is expressed on the luminal membrane of equine colonocytes, while MCT4 is expressed in the luminal membrane of the equine cecum (Nedjadi et al., 2014; Mykkanen et al., 2015). These findings suggest that MCT1 and MCT4 contribute to the uptake of VFAs in the equine large intestine (Mykkanen et al., 2015). It was also demonstrated that VFA transport through the luminal membrane of equine colonocytes is energized by the pH gradient and is not Na^+ dependent (Nedjadi et al., 2014).

In the horse, relative rates of transport of the absorbed VFAs through the intestinal mucosa are inversely proportional to their molecular weights (i.e., acetate > propionate > butyrate) (Argenzio et al., 1974b). Furthermore, extraction of glutamine from the blood by the large colon is modest compared with what occurs in the small intestine (Duckworth et al., 1992; Salloum et al., 1993) Collectively, these findings suggest that in horses, as in other species, butyrate is the main fuel for the colonocytes (Roediger, 1982). The VFAs absorbed but not used by the colonic mucosa pass to the liver via the splanchnic circulation. In the liver and other tissues, VFAs serve as fuel or are used as substrates for the synthesis of other fatty acids, glucose, triglycerides, and ketone bodies (Bergman, 1990; Argenzio & Hintz, 1970, 1971; Ford & Simmons, 1985; Ralston, 1990; Simmons & Ford, 1991).

Vitamin Absorption

Vitamin K and water-soluble vitamins produced by the microbiota of the equine large intestine can be utilized by the horse only if they are absorbed to a significant degree by the large intestinal mucosa. In other species, there is evidence of significant absorption of some of the water-soluble vitamins by the large intestinal mucosa,

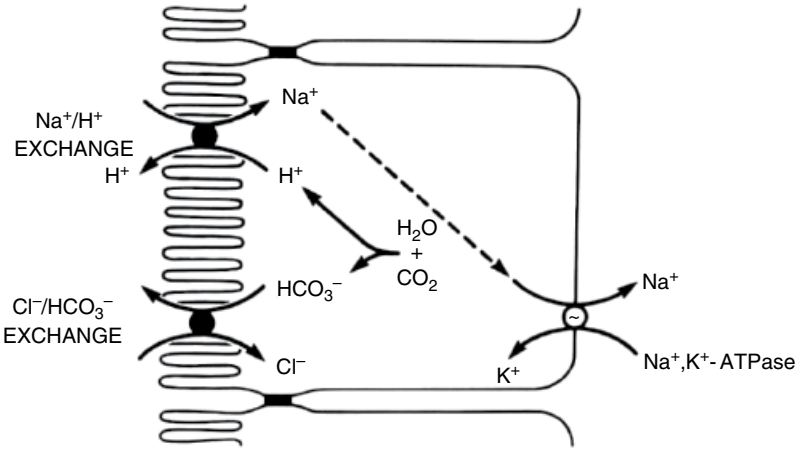

Figure 5.8 Electroneutral and electrogenic Na^+ absorption by the colonocytes: active Na^+ absorption is followed by passive Cl^- and water absorption. Water moves through via the transcellular pathway (through the tight junctions) and via the transcellular pathway (through aquaporins). ATPase, adenosine triphosphatase. Source: Barrett & Dharmsathaphorn, 1994, Fig. 17-12. Copyright McGraw-Hill Education. Reproduced with permission.

but absorption of vitamin K appears to be very limited and is mostly attributable to its lipid solubility.

Electrolyte Absorption

Large amounts of electrolytes, particularly sodium, potassium, chloride, and phosphorus, are absorbed by the mucosa of the equine large intestine (Argenzio & Stevens, 1975; Giddings et al., 1974; Schryver et al., 1972). Similar to what occurs in the small intestine, sodium is actively absorbed by the mucosa of the large intestine. The electrochemical gradient generated by the Na^+,K^+-ATPase on the basolateral membrane of the epithelium drives sodium absorption (Chang & Rao, 1994). Both electroneutral and electrogenic mechanisms for sodium absorption have been identified (Figure 5.8). Electroneutral absorption of sodium involves the exchange of sodium for another cation (i.e., hydrogen). This process may be coupled with the transport of VFAs and chloride that are absorbed in exchange for bicarbonate ions (Chang & Rao, 1994; Clarke & Argenzio, 1990; Argenzio et al., 1977). Electrogenic sodium absorption occurs by uncoupled entry of sodium through specific sodium channels, primarily the epithelial Na channel (Figure 5.9). This process is regulated by aldosterone and is inhibited by diuretics such as amiloride that close the sodium channels (Clarke & Argenzio, 1990; Clarke et al., 1992). This mechanism makes it possible for sodium to be absorbed against a large electrochemical gradient in the last portion of the large intestine (Argenzio, 1990; Clarke & Argenzio, 1990). While electroneutral absorption of sodium predominates in the oral segments of the large intestine (i.e., cecum and large colon), electrogenic sodium absorption predominates in the small colon (Clarke & Argenzio, 1990; Argenzio et al., 1977; Clarke et al., 1992). Potassium is also actively absorbed in the large intestine in exchange for H^+ via H^+,K^+-ATPase (Clarke & Argenzio, 1990; Barrett & Dharmsathaphorn, 1994). Throughout the large intestine, chloride is passively

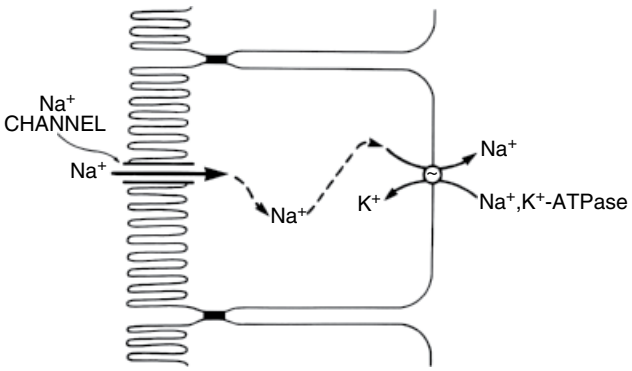

Figure 5.9 Electrogenic Na^+ absorption by the colonocytes. Active Na^+ absorption is followed by passive Cl^- and water absorption. Water moves through via the transcellular pathway (through the tight junctions) and via the transcellular pathway (through aquaporins). ATPase, adenosine triphosphatase. Source: Barrett & Dharmsathaphorn, 1994, Fig. 17-14. Copyright McGraw-Hill Education. Reproduced with permission.

absorbed following the absorption of cations (mainly sodium). As mentioned earlier, absorption of chloride occurs both by diffusion through the paracellular pathway and by a Cl^-–HCO_3^- exchange mechanism through the transcellular route (Clarke & Argenzio, 1990; Argenzio et al., 1977; Barrett & Dharmsathaphorn, 1994). The mechanism for phosphate absorption is not well known. In the large intestine of rats, diffusion of phosphate through the paracellular pathway is thought to be the primary mechanism (Hu et al., 1997).

Water Absorption

Large volumes of water are absorbed and secreted daily by the equine large intestine (Figure 5.10) (Argenzio et al., 1974b). This bidirectional movement of water occurs passively along hydrostatic, oncotic, and osmotic gradients (Barrett & Dharmsathaphorn, 1994). The hydrostatic gradients are produced by differences between interstitial and capillary hydrostatic pressures.

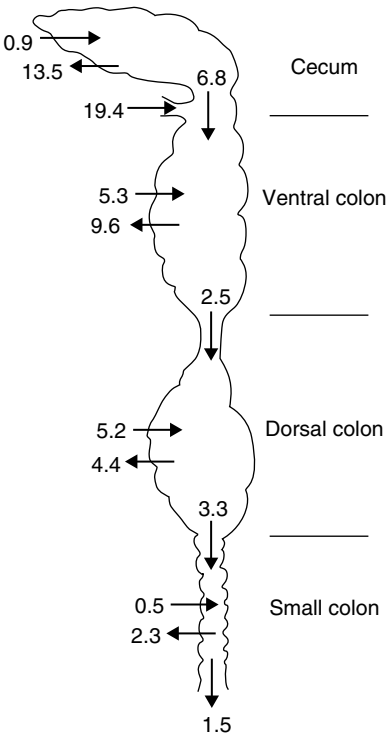

Figure 5.10 Daily net movement of water (in liters) through the large intestine of a 160 kg pony. Source: Adapted from Argenzio et al., 1974a, Fig. 8. Reproduced with permission of the American Physiological Society.

The oncotic gradients result from differences between interstitial and capillary oncotic pressures, which are dictated by the relative concentrations of macromolecules (e.g., proteins) within these compartments. The osmotic gradients depend on the concentration of all particles, including smaller particles (e.g., electrolytes, VFAs), within the various compartments (i.e., intestinal lumen, cytoplasm, interstitial space, and capillaries) and are highly affected by absorption, secretion, and intraluminal fermentation (Argenzio et al., 1974b; Johnson, 2001; Guyton & Hall, 2000a; Murray, 1988). Water moves toward the highest oncotic and osmotic pressures and away from the highest hydrostatic pressure (Guyton & Hall, 2000c; Murray, 1988). Thus, during absorption, movement of solute from the intestinal lumen increases the osmotic pressure within the interstitial space. This change in the osmotic gradient leads to absorption of water, which produces an increase in the hydrostatic pressure within the interstitial compartment, leading to movement of fluid from the interstitial space into the capillaries. The opposite changes occur during secretion of fluid (see Figure 5.8) (Giddings et al., 1974). Evidence exists that water moves by both transcellular (i.e., through cell membranes) and paracellular pathways (i.e., through tight junctions). Previous beliefs that movement of water through the gastrointestinal mucosa occurs predominantly by the paracellular pathway have been challenged by the discovery of cell membrane integral proteins, called aquaporins, which function as water channels (see Figure 5.8) (Ma & Verkman, 1999). In other mammals, several types of aquaporins (e.g., AQP3, AQP4, and AQP8) are expressed in the gastrointestinal tract, including the mucosa of the large intestine (Ma & Verkman, 1999). Although few studies have been conducted, evidence exists regarding the importance of aquaporins for water absorption by the mucosa of the large intestine. In one study, stools of AQP4 knockout mice had greater water content than stools from wild-type mice, although no differences in cecal contents were detected. Furthermore, the colon of the AQP4 knockout mice was less permeable to water and the absorptive response to intravenous administration of peptide YY was reduced when compared with those of the wild-type mice. These findings strongly suggest that aquaporins have a major role in water absorption by the mucosa of the large intestine (Wang et al., 2000). Additional studies, including some in horses, must be performed to improve our understanding of the mechanisms involved in water secretion and absorption in the large intestine.

Control of Secretion and Absorption

Control of secretion and absorption by the large intestinal mucosa is complex. Indirect control is exerted by mechanisms regulating other functions that affect secretion and absorption (e.g., hydrostatic pressure in capillaries of the mucosa, motility of the large intestine) (Chang & Rao, 1994). Secretion and absorption are also regulated by direct control of the epithelial cells through autocrine, paracrine, endocrine, immunologic, or neurocrine mechanisms. Neurons, hormone-secreting and immunologic cells located in the large intestine close to the target cells (i.e., epithelial cells), cells located away from the mucosa (e.g., the enteric nervous system), and cells located outside the gastrointestinal tract (e.g., sympathetic and parasympathetic nervous systems, endocrine glands) can exert control over these mechanisms. These regulatory cells function as sensors or are connected to other cells having the capacity to respond to stimuli (e.g., intraluminal antigens, low systemic blood pressure, hyperkalemia) (Chang & Rao, 1994; Barrett & Dharmsathaphorn, 1994). The regulatory cells release messengers (e.g., hormones, neurotransmitters, cytokines, nitric oxide) that bind to specific receptors in the epithelial cells (Chang & Rao, 1994; Barrett & Dharmsathaphorn, 1994; Izzo et al., 1998; Kitamura et al., 1984). Receptor binding activates intracellular mechanisms, leading to the activation of secretory or absorptive pathways. Several steps in these intracellular pathways have been identified, and different extracellular messengers may trigger different intracellular mechanisms mediated

by cyclic adenosine monophosphate (cAMP), cyclic guanosine monophosphate (cGMP), or calcium (Chang & Rao, 1994; Barrett & Dharmsathaphorn, 1994).

Sympathetic stimuli have proabsorptive effects on the large intestinal mucosa, whereas parasympathetic stimuli and locally secreted prostaglandins have the opposite effects (Chang & Rao, 1994; Barrett & Dharmsathaphorn, 1994; Clarke & Argenzio, 1990; Clarke et al., 1992; Argenzio & Clarke, 1989; Hubel, 1985). Considering the importance of the large intestine in the homeostasis of sodium and water, it is not surprising that mechanisms regulating sodium and water metabolism can have direct effects on the secretory and absorptive processes in the large intestine. For example, activation of the renin–angiotensin–aldosterone system in response to hypovolemia decreases secretion and increases absorption of NaCl and water in the large bowel (Clarke et al., 1992; Jansson et al., 2002; Levens, 1985; Sneddon et al., 1993). The putative mediators of these effects on the large intestine are catecholamines, angiotensin II, and aldosterone. Catecholamines, which are cosecreted (by the adrenal glands) with aldosterone, promote water absorption in the colon (Kendrick et al., 2002). The results of experimental studies indicate that angiotensin II increases electroneutral absorption of Na^+; however, a physiologic role of angiotensin II on Na^+ and water absorption independent of aldosterone release has not been proven (Levens, 1985). Aldosterone increases electrogenic absorption of Na^+ by promoting the expression of Na^+ channels and Na^+,K^+-ATPase on the apical membrane of colonocytes (Barbry & Hofman, 1997). Results of one in vitro study with colonic mucosa from ponies suggest that aldosterone enhances both electrogenic and electroneutral absorption of Na^+ by the colonic mucosa (Clarke et al., 1992). In another study, intravenous administration of aldosterone to horses led to a 72% reduction in fecal excretion of Na^+ at 9 h and an increase in K^+ excretion in feces from 3 h after treatment (Jansson et al., 2002).

Another mechanism involved in controlling water and electrolyte metabolism occurs via the release of vasopressin (antidiuretic hormone, ADH) by the pituitary gland in response to an increase in extracellular osmolality (Sneddon et al., 1993; Guyton & Hall, 2000a; Houpt et al., 1989). In laboratory animals, ADH promotes water absorption in the large intestine (Vicentini-Paulino, 1992). Considering that aquaporins are expressed in the large intestinal mucosa (Murray, 1988), ADH may act via the same mechanism operating in the kidney by promoting the insertion of aquaporins into epithelial cell membranes (Guyton & Hall, 2000b). Sodium and water metabolism are also affected by atrial natriuretic peptide (ANP), which may act on the large intestinal mucosa. ANP is a hormone released by the heart in response to stretching of the atrial wall that occurs during an expansion in plasma volume (Meyer, 1995). ANP reduces sodium and water absorption in the colon of laboratory animals (Argenzio & Armstrong, 1993; Schulman et al., 1996) suggesting a physiologic role for ANP in the regulation of Na^+ and water by the large intestine. Currently, no studies exist regarding the effects of ADH and ANP on large bowel absorption in horses.

Because of the enormous capacity of the equine large intestine and its ability to absorb large amounts of electrolytes and water, the large intestine is thought to function as a reservoir of water and electrolytes (Meyer, 1995; Sneddon et al., 1992). This reservoir can be utilized whenever necessary (e.g., to correct dehydration produced by exercise). The capacity of the reservoir depends on the diet, which may affect the water-holding capacity of intestinal contents. In one study, horses fed only hay had about 1.5 times more water in their gastrointestinal tracts than horses fed hay and grain (Meyer, 1995). The results of another study indicated that, after endurance exercise, horses eating only hay had lower plasma concentrations of protein and higher concentrations of potassium than horses eating hay and grain (Danielsen et al., 1995). These findings suggest that feeding only hay maximizes the capacity of the large intestine to function as a reservoir of water and electrolytes.

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6

Liver Function

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The liver is one of the largest organs in the body (second only to the skin), and constitutes approximately 1.5% of the body weight of the adult horse. The liver performs many essential body functions, and has a major role in the regulation of nutrient distribution. The majority of the nutrients absorbed from the gastrointestinal tract pass directly to the liver by way of the hepatic portal vein. Blood from the hepatic portal vein mixes with blood from the hepatic artery in the hepatic sinusoids, thus bathing the hepatocytes with a mixture of arterial blood and venous blood that has come mainly from the gut and spleen. One of the main functions of the liver is the maintenance of homeostasis, and it acts as a filter between the gut and the systemic circulation. Seventy percent of the blood flow to the liver comes from the hepatic portal vein, and the liver is the most important organ for the metabolism of orally administered drugs and gut-derived toxins or bacteria. The liver also adjusts the carbohydrate, protein, and lipid concentrations entering the bloodstream from the gastrointestinal tract, thereby maintaining constant blood levels of nutrients and responding to special circumstances (e.g., exercise, pregnancy, disease, and so on) (Barton, 2004; Friedman & Keefe, 2012; Divers, 2015).

Other major functions of the liver (Sisson & Grossman, 1953; Cunningham, 1997; Sherlock & Dooley, 2001; Gelberg & Cooper, 2002; O'Grady, 2002; Burrows & Westaby, 2002; Barton, 2004; Friedman & Keefe, 2012; Divers, 2015) include:

- Supplies bile salts and bicarbonate to assist in digestion.
- Synthesizes a large number of specialized proteins (including albumin, coagulation factors, and acute phase proteins), carbohydrates, and lipids.
- Excretes larger and more hydrophobic physiologic metabolites, foreign substances, and drugs (detoxification).

Bile Acid Metabolism and Excretion of Bile

Bile consists of several components, including conjugated bilirubin, bile acids, cholesterol, lecithin, water, and electrolytes. The bile released by the hepatocytes enters the bile canaliculi and is transported via the bile ducts and hepatic ducts to the intestine. The right and left hepatic ducts unite to form the common bile duct which along with the pancreatic duct empties into the duodenum via the major duodenal papilla, which is located on a raised mucosal fold (Dyce et al., 2010). Because the horse does not have a gallbladder, bile passes continuously into the duodenum.

Bile acids constitute 90% of the organic portion of bile. The primary bile acids, cholic and chenodeoxycholic acids, are synthesized from cholesterol in the liver, conjugated with taurine to form bile salts, and then excreted by an active transport mechanism into the bile canaliculi. Once excreted into the lumen of the intestinal tract, cholate and chenodeoxycholate may be reabsorbed or degraded by bacteria, forming the secondary bile acids deoxycholate or lithocholate. Another active transport mechanism in the distal ileum ensures that bile salts are conserved after they have fulfilled their digestive function. More than 95% of the conjugated bile acids are reabsorbed by the ileum and returned to the liver via enterohepatic circulation. Bile acids are estimated to be recycled at least 38 times a day

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in healthy ponies (Burrows & Westaby, 2002). Bile salts are powerful detergents, solubilizing lipids by enclosing them in bile salt aggregates called micelles.

Bilirubin is the breakdown product of tetrapyrroles that function as electron transport pigments. The majority of bilirubin is formed from hemoglobin and myoglobin. Macrophages (Kupffer cells) in the spleen, liver, and bone marrow engulf the pigments and convert them to biliverdin. Biliverdin is converted to bilirubin, which is released from the cells as free, insoluble bilirubin (also called indirect-reacting or unconjugated bilirubin). Unconjugated bilirubin is bound to albumin in the plasma and transferred to the hepatocytes. At the surface of the hepatocyte, the bilirubin is transferred from albumin to ligandin, which transports the bilirubin intracellularly. Within the hepatocyte, the bilirubin is conjugated with glucuronide in the endoplasmic reticulum. The conjugated bilirubin (also called direct-reacting bilirubin) is water soluble and is excreted into the bile canaliculi. Therefore, when liver and biliary tract function are normal, very little conjugated bilirubin enters the circulation. However, when biliary tract disease or obstruction is present, concentrations of conjugated bilirubin increase in the plasma.

Within the intestinal tract, conjugated bilirubin is converted by the microflora to urobilinogen and stercobilin, which are responsible for causing the feces to turn yellow-brown. In horses and other herbivores, the presence of chlorophyll pigments in the ingesta masks the color of urobilinogen (Barton, 2004). Urobilinogen is absorbed by the intestine and transported back to the liver as part of the enterohepatic circulation. The liver extracts most of this urobilinogen, but a small amount is excreted in the urine, and can be detected by urinalysis.

Protein Metabolism

The liver receives amino acids from the gut (via the hepatic portal vein) and the muscles, and regulates their concentrations in the plasma by controlling the rate of gluconeogenesis and transamination (O'Grady, 2002; Barton, 2004). The liver also converts ammonia to urea via the urea cycle. The liver is the major site of synthesis of almost all the plasma proteins, and for many is the principal site of their degradation. Plasma proteins synthesized in the liver include albumin, clotting factors V, VII, VIII, IX, fibrinogen, antithrombin III, protein C, transport factors (e.g., haptoglobin, transferrin, cerruloplasmin, and so on), and acute phase reactants (e.g., fibrinogen, amyloid A, hepcidin, alpha- and beta-globulins).

A close relationship exists between the muscles, liver, and gut with respect to amino acid flux. Muscle contributes the biggest source of protein turnover, and the liver is responsible for extensively modifying the blood amino acid composition. The aromatic amino acids – phenylalanine, tyrosine, and methionine – are preferentially processed to urea, whereas the branched-chain amino acids – valine, leucine, and isoleucine – are selectively passed to the periphery, where they are predominantly metabolized by muscle. This selectivity can be lost in horses with severe liver disease, and it is possible that the resulting change in the ratio of these two groups of amino acids may alter cerebral neurotransmitter metabolism and contribute to the pathophysiology of hepatic encephalopathy.

The liver is capable of transamination of amino acids (i.e., transfer an amino group of one amino acid to an alpha-ketoacid, thus forming a new amino acid and a new ketoacid). Thus, if there is an excess of amino acids or if carbohydrates are unavailable to be used as an energy source, the liver will deaminate amino acids to convert them to pyruvate, acetoacetate, and so on, which may be oxidized for energy, or used to form glucose by gluconeogenesis. Gluconeogenesis is under endocrine control.

All tissues and intestinal microflora generate ammonia, which is subsequently released into the circulation. The liver has a major role in eliminating ammonia from the circulation by converting ammonia and glutamine into urea in the hepatocyte mitochondria via the Krebs–Henseleit cycle (or urea cycle). The urea is released into the circulation as blood urea nitrogen, which is excreted by the kidneys. Failure to eliminate ammonia from the circulation is associated with encephalopathy due to liver disease (Burrows & Westaby, 2002; Divers, 2015).

Carbohydrate Metabolism

The liver acts as a gate for the large amounts of glucose and other monosaccharides delivered from the gut (via the hepatic portal vein) during digestion, by storing them as glycogen, and is also the main source of glucose during starvation. Initially, glycogenolysis is the principal metabolic pathway used, but as the glycogen stores become depleted, gluconeogenesis assumes greater importance. The main substrates for this pathway are lactate, pyruvate, volatile fatty acids, such as propionate, glucogenic amino acids (such as alanine from muscle), and glycerol (from lipolysis in fat stores). The control of carbohydrate metabolism is mainly hormonal (insulin, glucagons, catecholamines, and glucocorticoids). In liver disease, the supply of glucose by gluconeogenesis is generally well preserved, and hypoglycemia is only usually a problem in acute hepatic failure (Divers, 2015).

Lipid Metabolism

The major plasma lipids are cholesterol, cholesterol esters, phospholipids, and triglycerides. These are highly insoluble in water, and are carried in macromolecular complexes of lipid and protein carriers (apoproteins) called plasma lipoproteins. Only the intestine and liver synthesize and secrete plasma lipoproteins. The four main classes of plasma lipoproteins have different sizes and densities:

- Chylomicrons are produced by the mucosal cells of the small intestine during dietary fat absorption, and are the main carriers of triglyceride.
- Very low-density lipoproteins are produced by the liver and intestine, and have a core that contains 50–60% triglyceride.
- Low-density lipoproteins (LDL) are formed in plasma by catabolism of very low-density lipoproteins. They have a higher protein content and lower triglyceride proportion than the very low-density lipoproteins.
- High-density lipoproteins (HDL) are synthesized by the liver and intestine, and are also made in the plasma. They have the highest protein content and lowest triglyceride concentration.

Short-chain fatty acids can also be absorbed directly from the gastrointestinal tract, bound to albumin, and transported to the liver via the hepatic portal vein. The liver will also take up albumin-bound fatty acids released from adipose tissue.

The liver has several different roles in lipid metabolism, most of which are under endocrine control (principally via insulin and glucocorticoids). The primary role is to esterify free fatty acids into triglycerides for export to other tissues as lipoproteins (especially very low-density lipoproteins). The liver can also oxidize free fatty acids to acetyl coenzyme A via the tricarboxylic acid cycle to produce energy. The acetyl coenzyme A can be used to synthesize other fatty acids, cholesterol, steroids, and ketone bodies (acetoacetate and alpha-hydroxybutyrate). Peripheral tissues can use ketone bodies as an energy source. Acetyl coenzyme A can also be synthesized by the liver from glucose and amino acids, thereby enabling lipids to be produced from carbohydrates and proteins.

Detoxification and Drug Metabolism

The liver is responsible for the detoxification (biotransformation) and clearance of many endogenous (e.g., ammonia, bilirubin, steroid hormones) and exogenous (e.g., plant toxins, insecticides, mercaptans) compounds and many drugs. In general, the more lipophilic and the higher the molecular weight, the more likely the substance is to be cleared by the liver rather than the kidneys. Such hepatic clearance usually involves metabolic biotransformation with or without conjugation. In liver disease, alterations of drug handling can induce clinically important consequences by changing drug concentrations and half-life.

Storage

Several vitamins and trace minerals are stored in the liver, including the fat-soluble vitamins (vitamins A, D, E, and K), vitamin B12, copper, selenium, molybdenum, and iron.

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7

The Equine Intestinal Microbiota

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Introduction

The intestinal tract of the horse is home to a vast, diverse, and poorly understood population of microbes, otherwise known as microbiota. Comprised predominantly of bacteria, with lesser numbers of Archaea, viruses, fungi, and eukaryotes (intestinal parasites), the population interacts closely with the host.

The size and complexity of the intestinal microbiota are astounding. It has been estimated that the human gut microbiota contains approximately 10 times more cells than are present in the host. When the total genetic makeup of the microbiota (the microbiome) is considered, the number of genes contained by the host is outnumbered on an order of closer to 100 : 1 (Zhao, 2010). How these microbes and this "second genome" influence horse health is poorly understood, but their role is undeniably important.

In reality, the body can be considered as having a "love–hate" relationship with the microbiota. The gut microbiota plays critical roles in nutrition, metabolism, and a wide range of other functions and is absolutely required for health; however, it can also be involved with, or a direct cause of, a myriad of diseases. As the horse and its gut microbiota coevolved, a balance had to be struck to maintain horse and microbial health. The same type of balance must be established within the individual horse. This microbial population must interact with the body, but at the same time, the host must develop adequate immunologic tolerance of the accompanying massive immunologic onslaught. For both the horse's sake and for its own survival, the microbiota must provide benefits to maintain the horse's health and prevent the opportunistic pathogens amongst the microbiota from causing disease. As knowledge advances in horses and other species, it is becoming abundantly clear that deficiencies in these functions and balances are at the root of many infectious and inflammatory conditions, with increasing evidence of a role in other conditions such as allergy, metabolic disease, neoplasia, and obesity (Schwiertz et al., 2010; Sanz et al., 2010; Bisgaard et al., 2011).

The "Normal" Intestinal Microbiota

Understanding what constitutes "normal" is critical for any assessment of the role of the microbiota in disease. However, this can be complicated because of the complexity of the microbiota and the size of the horse's gastrointestinal tract. Culture-based methods have historically been used to evaluate the bacterial microbiota, but trying to characterize a population that consists of billions of bacteria from hundreds or thousands of distinct species *per gram of ingesta* or *feces* is rather futile. When problems with differential bacterial growth (e.g., a small number of species that grow exceptionally well on routine culture media) and the inability of routine methods to cultivate a large percentage of the microbiota are included, it is clear that culture-based studies provide a superficial, and misleading, assessment of the microbiota with marked underestimation of richness (number of species present), composition, and diversity. While culture media that are better able to grow most components of the intestinal microbiota have very recently been described (but not yet used in horses), nonculture-dependent methods are required for adequate study of such a complex environment. The most important advance in gastrointestinal microbiology has been development of cost-effective and high throughput next-generation sequence-based methods. This has revolutionized the study of microbiotas in various species, including the horse.

However, even with improvements in the ability to characterize the bacterial microbiota, problems remain.

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There may not be one "normal," as the microbiota might vary between different populations based on factors such as diet, management, breed, age, geographic region, and other factors. The potential for functional redundancy (whereby different microbes can achieve the same function) adds another layer of complexity since different overall gut microbiotas could be functionally similar. Study methods can add another layer of variability since there are no standard approaches. Additionally, viruses, Archaea and fungi have received limited attention, in part because of added difficulties characterizing those populations. The role of these in gut and systemic health is less clear (apart from a limited number of known viral pathogens). A final factor that cannot be overlooked is what "intestinal" really means, when referring to the intestinal microbiota. The equine gastrointestinal tract is a highly variable environment, with corresponding high variability in microbial inhabitants. Fecal samples are used for the vast majority of studies since collection of samples from other intestinal locations is not usually possible. While feces provide a good reflection of the composition of large and small colon, it is less predictive of the composition of more proximal compartments (Costa et al., 2015a). Thus, it must be remembered that most studies are actually evaluating the "fecal microbiota," something that may or may not accurately reflect the composition at the targeted intestinal site, particularly the stomach and small intestine. All these factors notwithstanding, understanding of the gut microbiota of healthy horses has profoundly increased in recent years. These advances can be considered both ground-breaking and superficial, as it is likely that current methods will be supplanted by newer techniques that can evaluate not just the organisms present but also what they might be (e.g., shotgun metagenomics) or are (e.g., transcriptomics, proteomics) doing.

Intestinal Microbiota of Healthy Horses

The intestinal microbiota of the horse contains a wide range of diverse bacteria. Species estimates are variable but range from the hundreds to many thousands. These include members of more than 20 different phyla; however, members of the phyla Firmicutes, Bacteroidetes, "Proteobacteria," Actinobacteria, and Verrucomicrobia dominate (Figure 7.1) (Costa et al., 2012, 2015a, 2015b, 2015c; Fernandes et al., 2014; O'Donnell et al., 2013; Proudman et al., 2015; Steelman et al., 2012). Relative abundances (proportions) of these phyla vary between studies, based on both biology and methodology. Studies

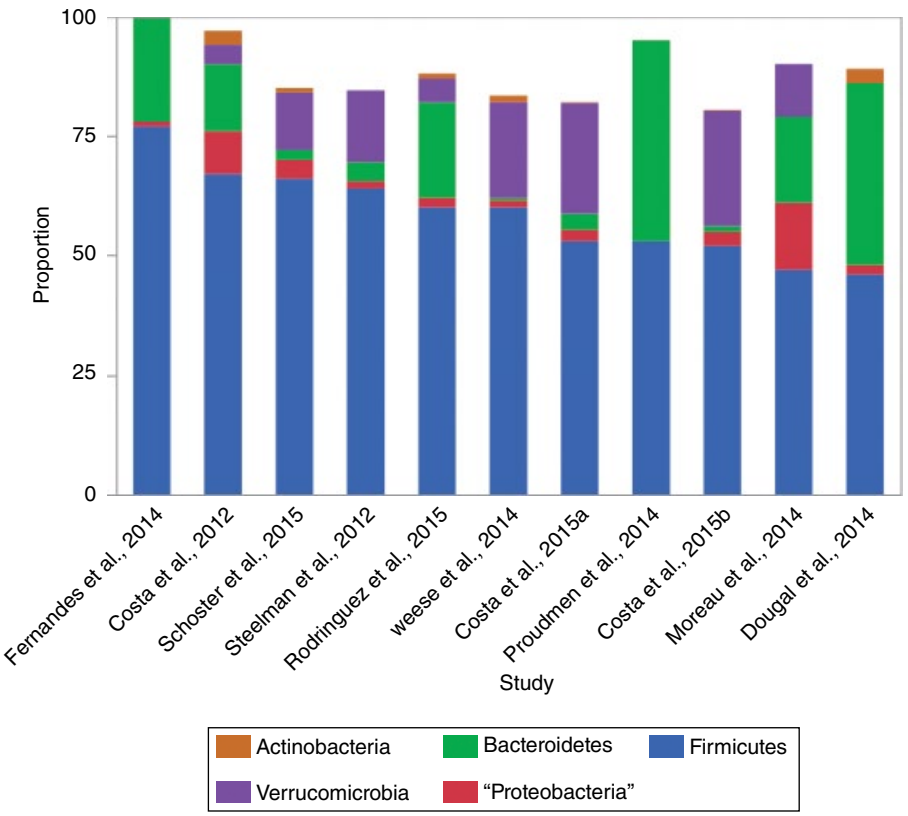

Figure 7.1 Phylum distribution of the equine intestinal microbiota.

based on 454 sequencing tend to report greater proportions of Bacteroidetes and minimal Verrucomicrobia while studies using newer Illumina sequencing identify fewer Bacteroidetes and more Verrucomicrobia. Regardless of the method, Firmicutes is the most common phylum in horses. This phylum of Gram-positive bacteria (including Clostridia, one of the dominant classes, and Clostridiales, a prominent order) is receiving increasing attention as its role in health becomes apparent. This can contradict typical (superficial) perceptions of the microbiota, particularly the "bad" nature of clostridia and the desire to limit their numbers.

The normal microbiota is not a static population. It changes throughout life in response to various processes, and the ability of the microbiota to change and adapt is probably important for maintaining health. At the time of birth, the intestinal tract is essentially sterile, yet exposure to microbes from the mare and environment result in rapid colonization. A remarkably rich and diverse microbiota is present in foals within the first 24 h of life (Costa et al., 2015b), and this continues to evolve during early life. These changes are probably highly influenced by diet and environmental exposures, based on the foal's exploratory behavior and transition to ingestion of higher fiber foods. What constitutes a true "adult" microbiota is not clear; however, the microbiota tends to be relatively stable by approximately 60 days of age (Costa et al., 2015b). Events such as antimicrobial exposure (Costa et al., 2015c), diet change (Proudman et al., 2015; Fernandes et al., 2014) and pregnancy (Weese et al., 2014) have been shown to impact the microbiota in the absence of overt gastrointestinal disease, and it is likely that other factors can also impact the microbiota.

Intestinal Microbiota and Disease in Horses

Recent studies have started to explore changes in the gut microbiota in response to various disease states or risk factors. Altered microbiotas have been noted in horses with nonintestinal diseases such as laminitis (Moreau et al., 2014) and metabolic syndrome (Elzinga et al., 2016). While preliminary, these findings support the notion that the microbiota may have a role in a wide-ranging list of disorders, although whether these changes are associated with the development of disease or occur because of the disease must be clarified. However, most of the attention to the microbiota and equine health relates to gastrointestinal disease, particularly colitis and colic. Study of the microbiota in horses with gastrointestinal disease using next-generation sequencing methods has been relatively limited, but some important findings have been reported.

Colitis

Alteration of the gut microbiota has long been considered an important part of the pathophysiology of at least some types of colitis, through the general assumption that disruption of the normal protective microbiota allowed opportunistic pathogens to proliferate. Whether this is an accurate description of the pathophysiology or an oversimplification of a complex issue is unclear. However, it should be of no surprise that an altered fecal microbiota is present in horses with colitis (Costa et al., 2012). One study compared the fecal microbiota of horses with acute colitis to healthy controls. Significant differences in various phyla and lower taxonomic orders, along with changes in community membership (species present) and structure (species present and their relative abundances) were reported. Furthermore, diarrheic horses had significantly lower relative abundances of some key families that have been increasingly associated with "gut health" in other species, particularly Lachnospiraceae and Ruminococcaceae. The increase in "Proteobacteria" (as a whole or specific members of that phylum) in disease is consistent with studies in other species whereby an increase in "Proteobacteria" and decrease in other major phyla, particularly Firmicutes, is an indicator of "dysbiosis" (De Minicis et al., 2014; Kaakoush et al., 2012; Suchodolski et al., 2012).

As a syndrome with multiple etiologies, not all of which are infectious, it is important to remember that the role of the microbiota in equine colitis will probably be variable. While the microbiota of horses with idiopathic colitis has been studied (Costa et al., 2012), whether similar changes occur for specific etiologies (e.g., *Salmonella*, *Clostridium difficile*) remains to be determined. The question of whether changes that are noted in horses with colitis reflect cause or effect also remains to be answered.

Study of microbiotas is also leading to broader consideration of the pathophysiology of diseases like colitis. While often thought of in the one pathogen–one disease model, where the infectious agent is the direct cause of disease, there is increasing attention paid to the role of overall microbiota modification (dysbiosis) as an inciting or potentiating cause of disease. As an example, while *Salmonella* is certainly the cause of salmonellosis, the role of the microbiota in causing, facilitating, worsening, or preventing disease is unknown. This is perhaps well exemplified by recurrent *C. difficile* infection (CDI) in humans. This potentially devastating syndrome is difficult to control with conventional antimicrobial approaches. Evaluation of the microbiota in people with recurrent CDI has demonstrated marked dysbiosis, typically with marked decreases in Firmicutes (the phylum to which *C. difficile* belongs) and increased "Proteobacteria" (Seekatz et al., 2014; Zhang et al., 2015; Shahinas et al., 2012). Fecal transplantation has emerged

as the most effective treatment, with the approach being to restore the overall microbiota, not necessarily eliminate *C. difficile* (Lee et al., 2016; Mattila et al., 2012; Kassam et al., 2013). Indeed, successful treatment does not necessarily impact the prevalence of *C. difficile* shedding, supporting the hypothesis that response to treatment is because of a "rebalancing" of the microbiota, not elimination of a single pathogen. The high prevalence of idiopathic disease in horses with colitis could represent novel or undiagnosed primary pathogens, but could more likely be the result of a dysbiosis. Therefore, it is possible that colitis should be thought of as a microbial population disorder, whether caused by a known enteropathogen or not and something that might change the mindset towards treatment and prevention.

With further study, it is possible that specific causative factors will be identified. This will be important for understanding the etiology of disease, how pathogens interact with the overall microbiota, whether disease is predominantly caused by the effects of a single pathogen versus community alteration, and, ideally, to better target treatment and prevention practices.

Colic

While colic is a nonspecific syndrome with many potential causes, the intestinal microbiota could play an inciting role through mechanisms such as excessive gas production, inflammation, and altered intestinal motility. Yet, there has been remarkably little study of the microbiota in colic. One reason may be the difficulty in differentiating cause and effect. As a sporadic disease, evaluation of feces prior to the onset of disease is challenging, and it is difficult to determine whether changes in the microbiota that are identified in a horse with colic represent changes that caused the disease or changes that occurred in response to disease (e.g., from pain, altered motility, altered food intake). One study was able to evaluate the microbiota in pregnant mares prior to the onset of colic (Weese et al., 2014). This study involved serial collection of feces from a large group of mares prior to and after foaling. While limited in scope (periparturient mares from Kentucky, USA), the ability to evaluate samples prior to and after colic provided some novel insight. Differences in the microbiota of mares that proceeded to colic compared to matched controls that did not colic were identified. This included a significant elevation in the relative abundance of "Proteobacteria" (a phylum that repeatedly is identified as associated with various disease states) and a decrease in Firmicutes in mares that had colic, along with differences in various measures of the microbial community membership (bacteria that were present) and structure (bacteria that were present and how numerous those were). Bacterial genera that tended to be associated with health (noncolic) included Firmicutes members such as Lachnospiraceae, Ruminococcaceae and other members of the Clostridiales order. While care must be taken to avoid overinterpreting the results of a single study of a specific population, the overrepresentation of "Proteobacteria" and depletion of various Firmicutes members, particularly Clostidiales, are consistent with alterations seen in various diseases in other species (Lepage et al., 2011; Suchodolski et al., 2012; McHardy et al., 2013).

While investigations are lacking, other components of the microbiota could also be of relevance. Archaea is a domain of microorganisms with properties bridging bacteria and eukaryotes. They comprise a small fraction of the microbiota when compared to bacteria, but common archaeal species in horses include methanogenic genera such as *Methanosphaera*, *Methanocorpusculum*, and *Methanobrevibacter* (Dougal et al., 2012; Fernandes et al., 2014, Lwin & Matsui, 2014). As methane producers, it is plausible (although currently completely speculative) that they could play a role in colic associated with intestinal gas production. Even less is known about the potential roles of viruses and parasites on the overall microbiota or potential influences on disease. There is increasing study of the potential benefits of some level of intestinal parasite burden in other species, through modulation of intestinal inflammation (Maizels & Yazdanbakhsh, 2003). Whether this corresponds to health effects in horses is unclear.

Effects of Antimicrobials on the Gut Microbiota

It has long been recognized that antimicrobial administration to horses can result in gastrointestinal disease, with the mechanism presumed to be alteration of the gut microbiota. It is clear that the equine gut microbiota is susceptible to alterations after exposure to antimicrobials. The nature and degree of change has not been well characterized and is likely influenced by the spectrum of activity of the drug, the route of exposure, the amount of enterohepatic recycling and a range of patient factors.

The impact of antimicrobials on the gut microbiota has been assessed in various ways. One is through reports associating antimicrobial exposure with colitis, whether through clinical treatment (Båverud et al., 1997, 1998, 2003; Wilson et al., 1996), experimental study (Yamarik et al., 2010; Gustafsson et al., 1997) or feed contamination (Keir et al., 1999). This cannot prove an impact on the microbiota but it is certainly the most logical explanation. Various antimicrobials have been associated with the induction of colitis, and it is reasonable to assume that virtually any antimicrobial can cause diarrhea. Even very low doses of antimicrobials can

cause disease, as has been demonstrated through induction of *C. difficile* infection in mares with low doses of erythromycin (Gustafsson et al., 1997). Interestingly, this phenomenon seems to be only, or predominantly, identified in Sweden, suggesting that there are regional differences in susceptibility to different antimicrobials.

Culture-based studies have been performed and while the limitations that are inherent to that approach must be considered, they have shown that at least some components of the microbiota can be altered. Administration of oxytetracycline was associated with rapid increased in coliforms, *Bacteroides* and *Streptococcus*, disappearance of *Veillonella* and increases in *Clostridium perfringens* (White & Prior, 1982). Those changes were not identified in response to trimethoprim-sulfadiazine administration. Limited change was also reported in response to either intravenous or oral trimethoprim-sulfadiazine administration in another study, with only a transient decrease in coliforms (Gustafsson et al., 1999). In contrast, a study of horses treated with trimethoprim-sulfadiazine or ceftiofur reported a profound (>99%) decrease in celluloytic bacteria after administration of either antimicrobial (Harlow et al., 2013). This change was still present 7 days after cessation of treatment. Other changes that were noted included decreases in lactobacilli and increases in *Salmonella* and *C. difficile*. Penicillin treatment has also be associated with increases in *C. difficile* shedding (Gustafsson et al., 2004).

A study combining culture and culture-independent methods reported no apparent impact of penicillin or anesthesia on the microbiota, as assessed by denaturing gradient gel electrophoresis (DGGE); a relatively insensitive method (Grønvold et al., 2010), quantitative polymerase chain reaction (PCR), detected an increase in *Bacteroides*-like, *C. perfringens*-like, and *Enterococcus* spp. in some horses, but no significant and consistent effects were observed.

At the time of writing, there was only one next-generation sequencing based study that assessed the impact of antimicrobials on the microbiota (Costa et al., 2015c). This study identified changes in various taxonomic groups (e.g., significant decrease in Verrucomicrobia after trimethoprim-sulfadiazine administration), along with alterations in the overall bacterial community structure. Trimethoprim-sulfadiazine appeared to have the most profound effects but changes were evident with the two other drugs that were studied, ceftiofur sodium and procaine penicillin. Twenty-five days after cessation of treatment, the microbiotas of treated horses had returned to a state similar to pre-treatment; however, some differences were still present. This suggests that the equine fecal microbiota rebounds fairly quickly but that there may be effects that linger for weeks, if not longer.

Modification of the Microbiota to Prevent or Treat Disease

As it is clear that alterations in the microbiota can be associated with disease, restoration of the normal microbiota is a reasonable clinical goal for prevention or treatment. This is often attempted with nontargeted approaches such as diet change, management change, or antimicrobial (e.g., metronidazole) therapy, with variable success. Certainly, these can alter the microbiota, but they do so in poorly defined and potentially unpredictable ways. These changes are not necessarily always desirable, but they sometimes result in clinical response.

A more targeted approach is the use of probiotics; live microbial supplements that, when administered in adequate numbers, confer a health benefit to the host. The concept of probiotic therapy relates directly to the microbiota, as probiotics are intended to exert beneficial effects through their growth and metabolism in the gut. While commonly used, there are very limited supporting data in horses and mixed data from humans. Most equine studies have failed to identify a beneficial effect of probiotics for outcomes such as reduction of *Salmonella* shedding, prevention of hospital-associated diarrhea, treatment of diarrhea, and prevention of diarrhea (Boyle et al., 2013; Kim et al., 2001; Parraga et al., 1997; Weese & Rousseau, 2005; Ward et al., 2004). The few studies that have reported positive effects have tended to identify limited clinical benefits, such as a difference at only one of many studied time points (Yuyama, 2004). Two randomized clinical trials in foals have identified an increased incidence of gastrointestinal disease in probiotic-treated foals compared to controls (Weese & Rousseau, 2005). This raises a few questions, perhaps the most important of which is: Is probiotic therapy ineffective in horses or have the "right" probiotics not been studied? Failure of probiotics could indeed reflect the futility of administration of proportionately minuscule doses of a small number of bacterial species into an established population of trillions of bacteria, along with challenges of surviving gastric transit. It could also be a result of inadequate bacterial selection or inadequate dosing, or inadequate study (e.g., limited statistical power, nonspecific study population) and differentiating between inefficacy of the approach versus inefficacy of studied probiotics is critical.

A potential reason for limited evidence of the efficacy of probiotics for intestinal disease is the organisms that are typically used. Commercial probiotics tend to consist of lactobacilli, bifidobacteria, and enterococci, yet these are minor components of the gut microbiota in adult horses. As members of the Clostridia class such as Lachnospiraceae, Ruminococcaceae, and Eubacteriaceae may be key determinants of gut health, disappointing

efficacy of currently available products may indicate the use of the wrong types of organisms. Poor quality control of commercial products, with frequent deficiencies in the number of viable organisms, or misidentification of contents (Weese, 2002; Weese & Martin, 2011) further compounds difficulties in clinical use and assessment of probiotics.

If disappointing results of probiotic therapy have been because of failure to use the "right" bacteria or inadequate numbers, a crude approach involves administration of the entire fecal cocktail of microorganisms. This concept, fecal microbiota transplantation (FMT), otherwise known as transfaunation or biotherapy, is a treatment that is receiving increasing attention in human and veterinary medicine. This approach has been used anecdotally in horses for years, predominantly through administration of fecal slurries by nasogastric tube to horses with chronic diarrhea. Interest has perhaps surged because of the recent interest in human medicine, where FMT has been shown to have high cure rates in humans with CDI (Lee et al., 2016; Shahinas et al., 2012; Brandt et al., 2012), and encouraging data for other disorders such as ulcerative colitis (Kunde et al., 2013; Moayyedi et al., 2015). Preliminary data from dogs and cats in a small, uncontrolled trial suggests that this might be an effective approach for chronic diarrhea (Weese et al., 2013). How well those experiences relate to potential uses in horses is unclear. While *C. difficile* is clearly an equine pathogen, the chronic recurrent form of disease that FMT is used to treat in humans does not occur in horses. Other conditions that FMT is being used for in humans do not have close equine analogs, such as ulcerative colitis or Crohn disease. Whether FMT could be useful in horses for the treatment of acute conditions such as colitis is unknown. Guidelines have been proposed for FMT in horses (Mullen et al., 2016), but they are based on anecdote and extrapolation from other species. As more information is obtained about the role of the microbiota in predisposition to colic, modification of the microbiota (by FMT, probiotics, or other approaches) might be of use; however, inadequate information is currently available.

Ultimately, a merger of the conventional approach to probiotics and FMT might occur, with identification of key components of the gut microbiota and development of "synthetic stool." This approach has been tried in preliminary studies in humans, with early success in the treatment of recurrent CDI with a cocktail of predominantly members of the Firmicutes phylum (Petrof et al., 2013).

Clinical Screening of Equine Fecal Microbiota

As the cost and throughput of sequencing have improved dramatically, it is now possible to provide an assessment of a horse's microbiota at a cost similar to a fecal culture, with a relatively short turnaround time. This leads to frequent requests for testing of healthy horses (e.g., to identify risk of disease) or those with various diseases (e.g., chronic colic, chronic diarrhea). While technological advances have been profound, understanding of the clinical relevance of any results that are obtained is still limited. While certain trends can be identified in the fecal microbiota of diseased horses, there is not yet any evidence that testing of an individual animal can be useful from a diagnostic standpoint. There is abundant inter-horse variation in the microbiota, and while, for example, a "Proteobacteria"-rich microbiota would be consistent with a state of dysbiosis at the population level, individual healthy horses can have such a microbiota and diseased horses can have microbiotas that fit within what is commonly considered normal. As knowledge improves, it is quite possible that indicators of disease or disease risk will be identified, making such testing clinically useful. Until that information is determined it is difficult to justify use of microbiota evaluation as a clinical tool.

Conclusion

Knowledge of equine intestinal microbiota has expanded greatly in recent years; however, the current grasp of its structure, function, and interaction with the rest of the horse is limited. As research advances, interesting and important new discoveries have been made. Yet, associations between the microbiota and health or disease must be interpreted for what they are: associations, not necessarily causation.

Continued research in this field should lead to a better understanding of how this complex microbial population interacts with itself and with the horse as a whole, and how these interactions shape the immune response, digestion, and other aspects of horse health. With such knowledge, measures to identify clinically relevant alterations in the microbiota and to manipulate it for the prevention or treatment of disease may be possible.

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8

Effects of Feeding on Equine Gastrointestinal Function or Physiology

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Introduction

Feeding practices have been associated with equine gastrointestinal dysfunction (Cohen et al., 1995, 1996, 1999; Hudson et al., 2001; Reeves, 1996; Tinker et al., 1997; Kaya et al., 2009). Thus, in this section, the effects of common feeding practices on equine gastrointestinal physiology are reviewed.

Feeding Grain

The need to provide enough energy and protein to maximize performance (growth, reproduction, speed, and strength), justifies adding grain to horses' diets. However, the ingestion of grain has long been recognized as a potential cause of gastrointestinal dysfunction in horses (Hintz, 1984) and has been confirmed by several epidemiologic studies (Hudson et al., 2001; Reeves, 1996; Tinker et al., 1997). Grains are rich in hydrolyzable carbohydrates (i.e., starch and sugars) (Hoffman et al., 2001) and may cause digestive problems in a gastrointestinal tract that evolved to digest plant material having a much lower content of hydrolyzable carbohydrates (Clarke et al., 1988). Enzymes secreted by the salivary glands, stomach, pancreas, and small intestine can digest hydrolyzable carbohydrates into simple carbohydrates, which are readily absorbed by the mucosa of the small intestine. When large amounts of hydrolyzable carbohydrates are ingested (i.e., starch intake exceeds 0.4% of body weight per meal), as occurs with large grain meals, the digestive capacity of the gastrointestinal tract preceding the cecum may be overwhelmed, and large amounts of the hydrolyzable carbohydrates can become available for rapid fermentation in the large intestine (Potter et al., 1992; Roberts, 1975).

Effects on the Gastrointestinal Microbiota and Intraluminal pH

The gastrointestinal tract of normal horses constitutes a unique ecosystem inhabited by a large number and variety of microorganisms (Bonhomme-Florentin, 1988; Garner et al., 1978; Gold et al., 1988; Julliand et al., 1999; Orpin, 1981). This resident microbiota has an important role in digestion and is essential for the health of the gastrointestinal tract. The environmental conditions and the availability of nutrients determine the health and balance of this microbial population (Buddington & Weiher, 1999). Experiments in horses and ponies and *ex vivo* studies have shown that feeding grain can profoundly affect the gastrointestinal microbiota and, consequently, pH and the concentration of microbial fermentation products, endotoxin, and vasoactive amines (Table 8.1). Increased production of lactic acid following acute ingestion of large amounts of hydrolyzable carbohydrates leads to a rapid decline in pH and the death of large numbers of Gram-negative bacteria (Garner et al., 1978; Goodson et al., 1988). As a result of an increased availability of lactate, the number of lactate-utilizing organisms also increases (Goodson et al., 1988). The effects of grain ingestion on these bacterial populations are proportional to the amount of grain fed (Fombelle et al., 2001; Moore et al., 1979). Abrupt ingestion of a large grain meal produces profound consequences, which tend to taper off after a few days even if the horse is maintained on the same high-grain diet (Goodson et al., 1988). This finding corroborates the clinical observation that horses that have been gradually adapted to high-grain diets may develop tolerance for considerable amounts of dietary grain that would produce signs of gastrointestinal dysfunction in nonadapted horses.

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Table 8.1 Effects of grain ingestion (acute or chronic) in the equine large intestine: changes in the microbiota, concentration of the products of microbial fermentation and endotoxin, and pH.

	Increase	Decrease
A few hours after acute ingestion of grain	Bacterial population (Fombelle et al., 2001; Kern et al., 1973; Moore & Deority 1993) Number of anaerobic bacteria (Destrez et al., 2015) Number of amylolytic bacteria (Destrez et al., 2015) Number of lactate-utilizing bacteria (Daly et al., 2012; Destrez et al., 2015) Number of *Lactobacillus* spp. (Daly et al., 2012; Garner et al., 1978; Goodson et al., 1988) Number of organisms growing in selective starch medium (Goodson et al., 1988; Julliand et al., 2001) Molar concentration of volatile fatty acids (Fombelle et al., 2001; Kern et al., 1973; Argenzio et al., 1974b; Willard et al., 1977) Molar concentration of lactate (Fombelle et al., 2001; Kern et al., 1973; Argenzio et al., 1974b; Willard et al., 1977) Concentration of endotoxin. (Moore et al., 1979) Concentration of vasoactive amines (*in vitro*) (Bayley et al., 2002)	Number of Gram-negative rods (Kern et al., 1973) Number of *Enterobacteriaceae* spp. (Garner et al., 1978; Goodson et al., 1988) Number of aerobic *Streptococcus* spp. (Garner et al., 1978; Goodson et al., 1988) Number of anaerobic *Streptococcus* spp. (Garner et al., 1978; Goodson et al., 1988) Obligate fibrolytic, acid-intolerant bacteria, Fibrobacter and Ruminococcaceae (Daly et al., 2012) Number of organisms growing in selective fiber medium (Goodson et al., 1988; Julliand et al., 2001) Number of protozoa (Goodson et al., 1988) Molar percentage of acetate (Fombelle et al., 2001; Julliand et al., 2001; Willard et al., 1977) pH (Garner et al., 1978; Julliand et al., 2001; Willard et al., 1977)
With chronic grain ingestion	Number of bacteria growing on lactate medium (Goodson et al., 1988) Digestibility of organic matter (Drogoul et al., 2001)	Digestibility of fiber (Drogoul et al., 2001)

Effects on the Mucosal Barrier and Plasma Endotoxin Concentration

Ingestion of extremely large amounts of grain can disrupt the mucosal barrier of the gastrointestinal tract. In a study of four horses with cecal fistulas, administration of 17.6 g/kg of body weight of a meal rich in hydrolyzable carbohydrates (85% corn starch and 15% wood cellulose flour) via nasogastric tube caused ultrastructural evidence of damage to the cecal epithelial lining. Mucosal damage was thought to be caused by the increase in intraluminal acidity produced by the carbohydrate overload (Krueger et al., 1986). The same model of carbohydrate overload produced clinical signs of endotoxemia (Garner et al., 1975, 1978; Moore et al., 1979) and detectable concentrations of endotoxin in the plasma (Sprouse et al., 1987), suggesting that endotoxin had reached the circulation after crossing the damaged mucosal barrier. The effects of ingestion of smaller amounts of grain on the gastrointestinal mucosal barrier and endotoxin absorption have not been investigated in the horse.

Effects on Gas Production and Accumulation in the Gastrointestinal Tract

Ingestion of large amounts of grain can result in gas accumulation within the gastrointestinal tract manifested as gastric dilation (Baker et al., 1992; Becht, 1983) or tympany of the large intestine (Baker et al., 1992; Byars, 1983). Gastrointestinal dilation with gas can have serious consequences, including abdominal discomfort, intra-abdominal hypertension (Barrett et al., 2013), gastrointestinal hypoperfusion, and respiratory distress. It has also been suggested that the reduced weight of gas distended intestinal segments can result in intestinal displacement or volvulus (Snyder et al., 1988).

Only a few studies have examined the mechanisms involved in tympany secondary to grain overload in horses. Conversely, the etiopathogenesis of bloat secondary to grain ingestion in cattle has been extensively investigated (Cheng et al., 1998; Nagaraja et al., 1998). When large amounts of soluble carbohydrates reach the rumen, rapid fermentation produces large quantities of gas (Lippke et al., 1972). In addition, ruminal microorganisms synthesize substances (e.g., mucopolysaccharides) that lead to an increase in the viscosity of the ruminal fluid and, ultimately, to formation of stable froth (Cheng & Hironaka 1973; Cheng et al., 1976). Eructation, which is the main mechanism for elimination of gas from the rumen, is inhibited by froth (Lippke et al., 1972). Thus, froth accumulates in the rumen and causes an increase in intraruminal pressure and ruminal distention (Lippke et al., 1972). Inhibition of ruminal motility as a result of luminal acidosis has also been mentioned as a factor in the pathogenesis of frothy bloat (Nagaraja et al., 1998). There are indications that individual variability and breed predisposition also play a role regarding the risk of development of bloat. Factors such as anatomic differences in the rumen, salivary production, microbiome

idiosyncrasies, and appetite may explain why some individuals are predisposed (Cheng et al., 1998).

Some of the same mechanisms responsible for frothy bloat in ruminants may apply to horses with grain overload. In a study of horses with fistulas in the right dorsal colon fed free-choice grass hay and two large grain meals (4.55 kg of "sweet feed" every 12 h), colonic contents were foamy, similar to ruminal contents of cattle with frothy bloat. Colonic ingesta of these horses had large quantities of small gas bubbles and the liquid phase (extracted by filtration) was noticeably viscous. These physical characteristics contrasted distinctly with minimal evidence of visible gas bubbles and a watery fluid phase of colonic contents when the same horses were fed only grass hay. The increased content of gas in colonic ingesta associated with grain intake was definitively documented by two objective variables: density of colonic ingesta decreased significantly (1.0 kg/L when only hay was fed to 0.7 kg/L) and volume fraction of gas in the fluid phase of colonic ingesta increased significantly (from negligible when only hay was fed to 30%) when grain was fed. Furthermore, spontaneous flow of colonic contents when the cannula was open only occurred when the horses were fed grain, suggesting that the increased gas content in ingesta associated with grain intake led to an increase in intraluminal pressure (Lima et al., 2006).

Other mechanisms described for ruminants with frothy bloat may also play a role in gastrointestinal dysfunction in horses after grain overload despite the differences in gastrointestinal physiology (e.g., horses are hindgut fermenters and do not eliminate large amounts of gastrointestinal gas by eructation). Although the equine cecum is effective at handling gas in the healthy state, excessive gas production can exceed cecal capacity for gas elimination (Cottrell et al., 1998). It is also possible that intraluminal acidosis produced by ingestion of large quantities of grain may further compromise gastrointestinal motility, as occurs in ruminants.

Effects on Gastrointestinal Transit

The results of several experiments indicate that grain ingestion delays the gastrointestinal transit of liquids and solids in horses (Figure 8.1) (Drogoul et al., 2001; Lopes et al., 2004a; Pagan et al., 1998; Yoder et al., 1997). Grain ingestion may affect gastric emptying, which is a major

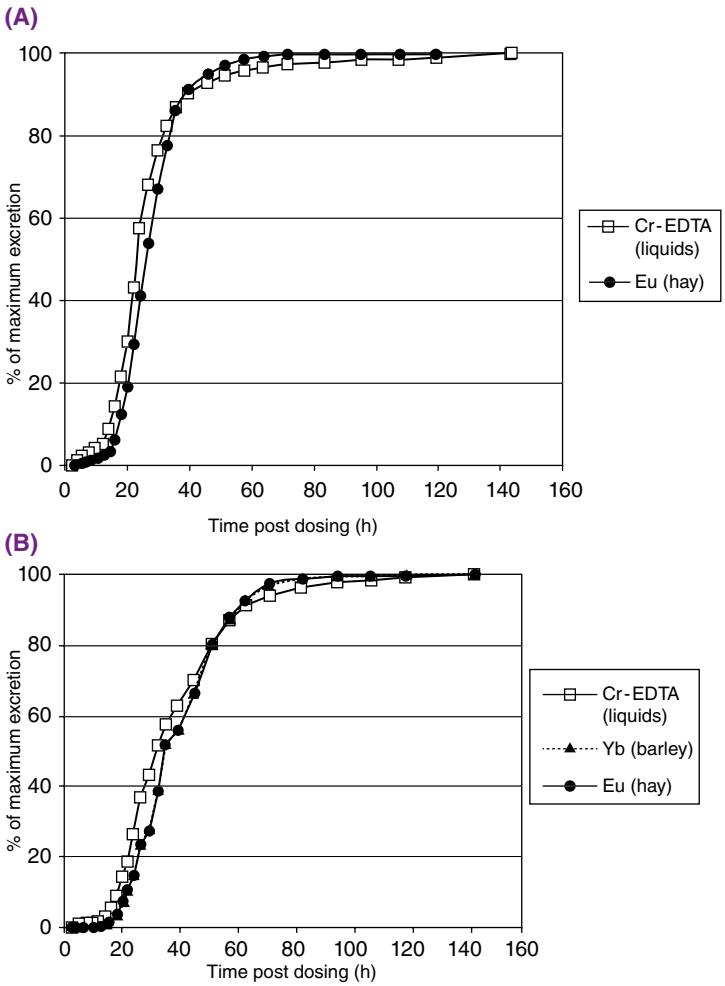

Figure 8.1 Means of cumulative excretion of markers (chromium ethylenediaminetetraacetic acid (Cr-EDTA) as a marker of the liquid phase; ytterbium (Yb) as a marker of hay; and europium (Eu) as a marker of barley) administered at time 0 to 6 ponies fed **(A)** only hay, or **(B)** a 50 : 50 hay : barley diet. The right shift of the curves observed when barley was fed indicates that transit of liquids and solids was slower. Source: Adapted from Drogoul et al., 2001. Reproduced with permission of Elsevier.

determinant of the transit of gastrointestinal contents. Gastric emptying is under the control of a negative feedback mechanism to limit the availability of nutrients for intestinal digestion and absorption. Receptors sensitive to physical (e.g., osmolality) and chemical (e.g., pH, lipids) properties of ingesta located in the duodenum trigger this feedback mechanism (Weisbrodt 2001). Compared with roughage, grain contains considerably more digestible nutrients (Hoffman et al., 2001). Thus, gastric emptying is slowed after grain ingestion to prevent the digestive and absorptive capacities of the small intestine from being overwhelmed. It has also been proposed that the slower rate of passage when horses are fed diets having a higher grain content is a consequence of a decrease in dry matter intake when compared with diets having a higher fiber content (Drogoul et al., 2001; Pagan et al., 1998; Yoder et al., 1997). Furthermore, it has been suggested that reductions in saliva production and water intake occurring when grain is fed might contribute to slower gastrointestinal transit (Pagan et al., 1998).

Effects on Water Consumption

The results of several studies document reduced consumption of water by grain-fed horses. In these studies, total daily water consumption was reduced 21–46%, while water consumption per kilogram of dry matter consumed fell 21–38% (Cymbaluk 1989; Danielsen et al., 1995; Fonnesbeck 1968; Sufit et al., 1985; Warren et al., 1999). The fact that more water is needed within the gastrointestinal tract for the flow of gastrointestinal contents when fibrous (bulkier) feed is ingested (Lopes et al., 2004a; Fonnesbeck 1968) may explain why horses eating grain appear to need less water. Ingestion of less bulky (less fibrous) food leads to reduced chewing and salivary secretion (Meyer et al., 1985). Thus, the postprandial decrease in plasma volume and increase in plasma osmolality are likely minimized when less bulky feed is ingested, and a study in ponies has demonstrated that hypovolemia and plasma hyperosmolality are the primary stimuli for water intake (Sufit et al., 1985).

Effects on Ingesta Osmolality and Ionic Composition

Ingesta osmolality and ionic composition can be affected by grain ingestion. When large amounts of highly digestible feed such as grain are digested and fermented, macromolecules are cleaved, producing large numbers of smaller molecules within the gastrointestinal lumen. Theoretically, unless products of digestion and fermentation of grain are rapidly absorbed or water is secreted into the gastrointestinal tract, ingestion of grain will result in postprandial hyperosmolality of the gastrointestinal contents. In horses, little has been objectively assessed regarding the effects of grain ingestion on the osmolality of gastrointestinal contents. In a study in ponies, hyperosmolality of the contents of the large intestine was produced by a hay-grain pelleted diet, which contrasted with the hyposmolality produced by a high-fiber low-protein diet (Argenzio et al., 1974a). In one study, however, colonic contents were consistently dehydrated after ingestion of large amounts of grain when compared with the colonic contents of the same horses fed only hay (Lopes et al., 2004). This finding suggests that products of digestion and fermentation of grain are rapidly absorbed by the gastrointestinal mucosa or utilized by colonic microbiota. If this were not the case, formation of hypertonic colonic contents would retain water within the gastrointestinal tract, making intestinal contents more watery. In the only published study on the effects of grain ingestion on the ionic composition of the gastrointestinal contents, a hay-grain pelleted diet produced postprandial changes in ionic composition of ingesta, which were not evident in ponies fed a high-fiber low-protein diet. This result is likely the consequence of dietary electrolyte composition (Argenzio & Stevens, 1975).

Effects on Ingesta and Fecal Water Content

Grain ingestion can produce dehydration of intestinal contents and feces. When ponies were fed either alfalfa only or alfalfa and grain, water content in the small colon was significantly lower when grain was fed (means 82.2% versus 77.0%, respectively); however, feeding grain did not affect water content of ingesta in the stomach, small intestine, cecum, or large colon (Hintz et al., 1971). In another study, fecal hydration was lower when a low-fiber diet was fed (mean 73.6%) in comparison with what was observed following provision of a high-fiber diet (mean 81.7%) (Warren et al., 1999). In horses with a right dorsal colon fistula, ingestion of 4.55 kg of sweet feed twice daily reduced water content of colonic ingesta (mean 86.8%), but not of feces (mean 78.9%) relative to the values measured in the same horses fed only hay (means 90.5% and 79.1%, respectively) (Figure 8.2) (Lopes et al., 2004a). These findings are in agreement with the hypothesis that ingestion of less fibrous feed requires less water to facilitate flow of contents through the gastrointestinal tract (Fonnesbeck, 1968).

Hypothetically, when intestinal contents are less hydrated when grain is fed, this would predispose to the development of large-colon impactions (Clarke et al., 1990b). This hypothesis contradicts the findings of an experiment in rabbits in which ingesta viscosity and not water content was shown to be the key factor responsible for intestinal obstruction (Morel et al., 1990). The fact that ingesta becomes foamy when grain is fed (Lopes et al., 2004a) suggests that the increased amount of gas might compensate for any trend toward an increase in

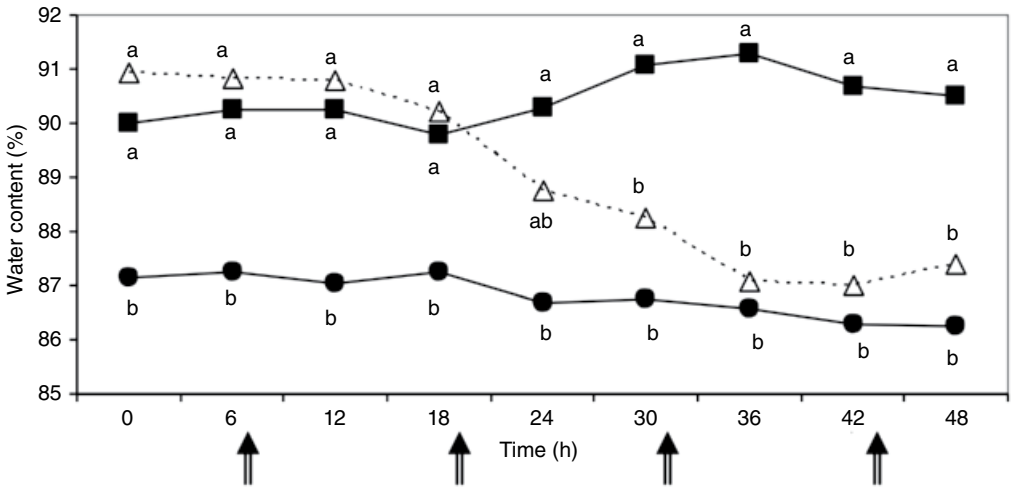

Figure 8.2 Mean percentage of water in right dorsal colon (RDC) contents obtained from six horses with fistulas in the RDC that had access to hay *ad libitum* (diet 1; closed squares), hay *ad libitum* and grain (4.55 kg) every 12 h after being adapted to hay only for at least 5 days (diet 2; open triangles), or hay *ad libitum* and grain (4.55 kg) every 12 h after being adapted to this diet for at least 5 days (diet 2; closed circles). Arrows indicate the times when horses had access to grain. Within a time point, values with different letters are significantly ($P \leq 0.05$) different. Source: Adapted from Lopes et al., 2004a. Reproduced with permission of the American Veterinary Medical Association.

ingesta viscosity produced by ingesta dehydration. Furthermore, using an ex vivo model of large colon impaction by assessing the force required to move ingesta through a pipe (inner diameter, 7 cm) attached to funnel to reduce the inner diameter by 28.6%, it was demonstrated that feeding grain significantly reduced the odds of impaction formation at the funnel (Lima et al., 2006). In support of these experimental findings anecdotal and clinical reports have linked large intestine impaction in horses to ingestion of fibrous feeds, but not to grain ingestion.

Effects on Systemic Hydration

Purportedly, the gastrointestinal tract functions as a reservoir of water and electrolytes in exercising horses. If this is true, a diet with less fiber may reduce the capacity of this water reservoir by reducing both the water content of ingesta and the volume of ingesta. Effects of grain ingestion on water and electrolyte balance have been demonstrated in horses undergoing endurance exercise, and these horses had higher plasma protein concentrations and lower plasma potassium concentrations relative to values obtained for the same horses fed only hay (Danielsen et al., 1995). Conversely, in a study comparing changes in plasma volume in horses treated with furosemide, no effect of diet (low fiber versus high fiber) could be detected (Warren et al., 1999).

Other Effects

Intragastric administration of a carbohydrate gruel (17.6 g/kg of body weight; 85% corn starch and 15% wood cellulose flour) to horses and ponies resulted in soft feces (from pasty to liquid), increased abdominal sounds, and abdominal distention (Robinson et al., 1976). Similarly, soft acidic feces, an increase in plasma lactate concentration, and clinical signs of laminitis were observed in Standardbred horses receiving high-starch pelleted feed (85% ground maize and 13% soybean meal) *ad libitum*. These changes were not evident when the antibiotic virginiamycin was added to the meal, although the horses ate less grain during the first 3 days that the antibiotic was administered. These findings were interpreted as the result of the reduced feed intake and inhibition of growth of lactate-producing bacteria by the antibiotic (Rowe et al., 1994). When horses with a right dorsal colon fistula were fed large amounts of grain using a regimen currently adopted for domestic horses (4.55 kg of sweet feed every 12 h and free-choice hay), ingesta became more homogeneous with less distinct separation between the liquid and solid phases. Furthermore, the liquid phase became more viscous when compared with colonic contents from the same horses fed only hay. It was also noticed that feces became softer (less well formed) (Lopes et al., 2004a).

It has also been demonstrated that the expression of monosaccharide transporters (SGLT1 and GLUT2) in the epithelium of the small intestine is increased in horses eating grain. These horses had epithelial monosaccharide transporters throughout the small intestine, whereas expression of the same transporters was limited to the proximal small intestine in horses maintained on grass. These findings suggest an adaptation of the small intestine occurs with ingestion of large amounts of hydrolyzable carbohydrates (Rowe et al., 1994).

Feeding Grass

Rapidly growing pasture may contain large amounts of hydrolyzable and rapidly fermentable carbohydrates (Hoffman et al., 2001). When lush grass is ingested, large amounts of these nutrients may escape digestion and absorption in the small intestine and become available for rapid fermentation by bacteria in the large intestine. Thus, ingestion of lush grass may lead to the same gastrointestinal problems caused by ingestion of grain (e.g., diarrhea, tympany, intraluminal acidosis, mucosal damage, endotoxemia). The extent to which pasture grass (and other plants) accumulates hydrolyzable and rapidly fermentable carbohydrates is significantly affected by numerous factors including seasonal and meteorological influence during growth, stage of growth, plant species, ambient temperature, and exposure to sunlight (Hoffman et al., 2001).

The gastrointestinal oligofructose overload model, originally developed for the study of pasture-associated laminitis (van Eps & Pollitt, 2006), has provided valuable insights about the potential effects of ingestion of large quantities of lush grass on the large intestine. Oligofructose overload has been shown to decrease production of volatile fatty acids, decrease pH and increase the population of *Streptococcus* spp. and the production of lactate (Milinovich et al., 2007, 2008). It has also been demonstrated that horses fed spring/summer grass, which is rich in rapidly fermentable carbohydrates (Hoffman et al., 2001), have higher concentrations of vasoactive amines in cecal contents relative to horses eating hay or winter grass (Figure 8.3) (Bailey et al., 2003a, 2003b). Vasoactive amines cause constriction of digital veins (Elliot et al., 2003) and are thought to be involved in the etiopathogenesis of pasture-associated laminitis (Elliot & Bailey, 2006).

Replacing Grain with Fat

Although provision of dietary lipid in the form of vegetable oil may decrease digestibility of fiber in the equine gastrointestinal tract (Bush et al., 2001; Jansen et al., 2000, 2001, 2002) replacing grain with vegetable oil may afford some advantages. By feeding vegetable oil to horses, it is possible to increase the energy density of the diet while minimizing consumption of hydrolyzable carbohydrates. Considering the deleterious effects of large amounts of hydrolyzable carbohydrates on the equine gastrointestinal tract, it is believed that diets rich in vegetable oil and lower in carbohydrates may prevent gastrointestinal disorders (Harris, 1998). Because of this hypothesis, the use of oil in horse feeds has gained great popularity during the last 10–15 years. Despite the lack of evidence that this approach has any practical drawbacks, further studies are needed to better assess the effects of dietary lipid on equine gastrointestinal physiology.

Feeding Mature Grass and Poor Quality Hay

Mature grass and poor quality hay are characterized by a relatively lower nutrient content and are rich in poorly fermentable fiber (Lewis, 1995). Ingestion of these bulky roughages increases gastrointestinal filling, which is evidenced by abdominal distention. This kind of feed may lead to gastrointestinal impaction, which is likely to be the result of an increased resistance to transit of rough ingesta formed by large pieces of undigested fiber. Fortunately, most horses seem to tolerate poor quality roughage and few horses fed this type of forage will

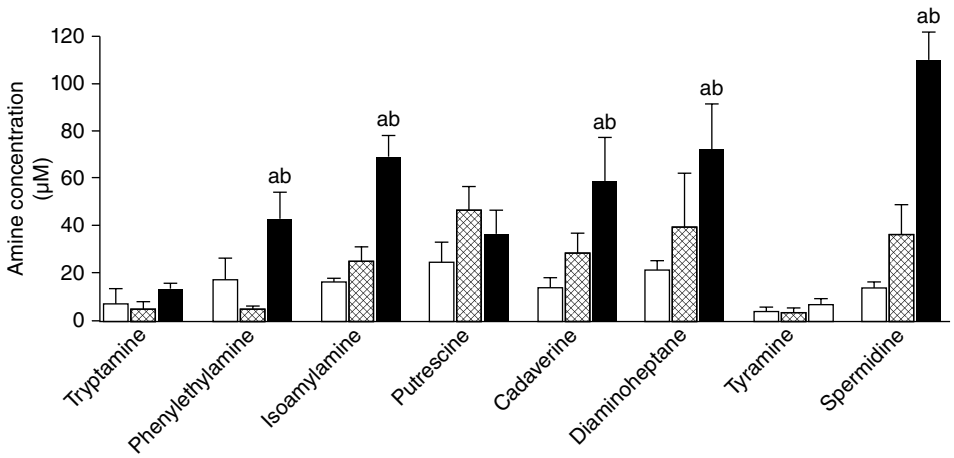

Figure 8.3 Concentration of vasoactive amines in equine cecal contents. Amine concentration (assayed for by high performance liquid chromatography, HPLC) in samples of cecal contents from horses fed on hay in winter (open columns), winter grass (hatched columns), or spring/summer grass (solid columns). Bars represent mean (SEM) values: (a) significant difference compared with hay diet; and (b) significant difference compared with winter grass diet ($P < 0.05$). Source: Bailey et al., 2003b. Reproduced with permission of Elsevier.

develop impactions. However, an abrupt change to poor quality roughage for horses adapted to good quality feed is likely to increase the risk of gastrointestinal impaction (Lowe et al., 1980; Silva, 2004).

Feeding Large Meals Intermittently and Fasting

Feeding a few large meals per day to domestic horses is a common practice because of convenience; however, this practice differs remarkably from the environment in which the horse evolved: having continuous access to roughage. Therefore, episodic feeding may predispose to gastrointestinal dysfunction (Clarke et al., 1990b). In the clinical setting, fasting horses for variable amounts of time is commonly adopted in many situations (e.g., preparation for general anesthesia and surgery, treatment of large intestinal impaction, preparation for endoscopy); however, it is important to keep in mind the side effects of feed deprivation on gastrointestinal function.

Effects on Water and Electrolyte Balance

Horses eating few large meals a day can develop postprandial plasma volume contraction, electrolyte imbalances, and hormonal changes that do not occur with a more continuous eating pattern. These effects are proportional to the amount of feed ingested and are thought to be the result of postprandial dehydration due to secretion into the alimentary tract. In one study, feeding a larger meal (2.7 kg of complete cube diet plus 5.5 kg of hay) produced more pronounced postprandial dehydration and electrolyte shifts (a 15.8% increase in hematocrit, a 12.2% increase in plasma protein concentration, and a 16.6% decrease in plasma potassium concentration), than occurred after two other daily meals (each of 1.8 kg of complete cube diet) (Kerr & Snow, 1982). Similar results were obtained in a series of experiments with ponies and horses fed a defined amount of complete pelleted feed given as a single 1 h meal/day or as 6 daily meals. The single meal per day regimen led to marked postprandial increase in hematocrit, plasma protein concentration, and plasma osmolality (as much as 9.1%, 13.2%, and 2.5%, respectively). Conversely the multiple meal per day regimen produced just mild postprandial changes in hematocrit, plasma protein concentration, and plasma osmolality (no more than 2.4%, 4.3%, and 0.7%, respectively) (Clarke et al., 1988, 1990a; Houpt et al., 1988; Youket et al., 1985). In one of these studies, it was determined that the single large meal reduced plasma volume by 15% (Figure 8.4) (Clarke et al., 1990a). In two of these studies, postprandial activation of the renin–angiotensin–aldosterone system was also demonstrated. A large meal produced an increase in plasma renin activity, which was followed by an increase in both

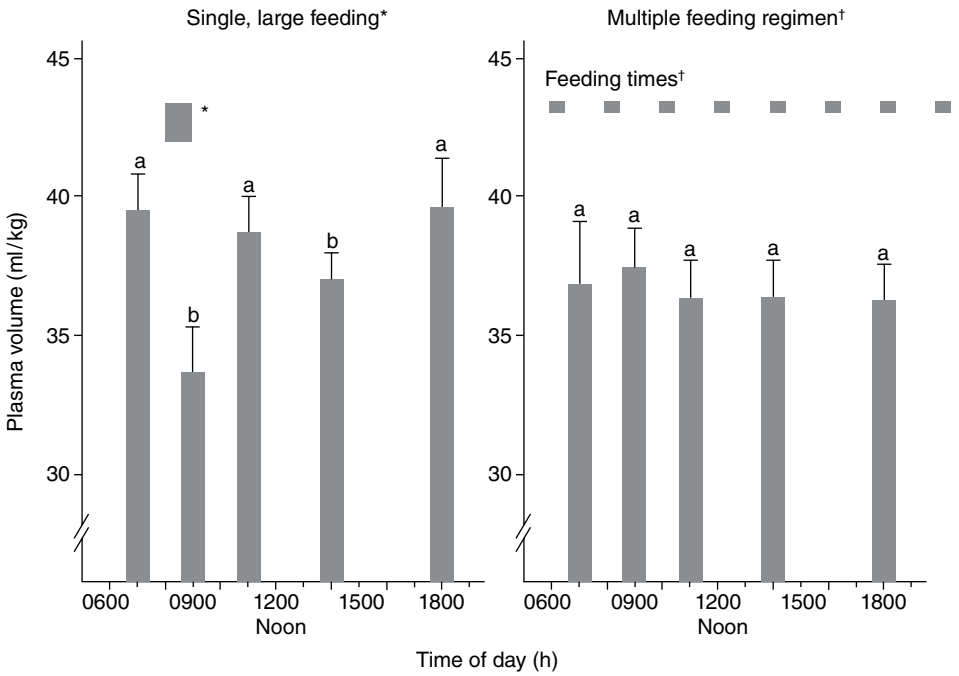

Figure 8.4 Means of plasma volume determined by dye-dilution technique in six ponies fed a single large meal and multiple smaller meals. Vertical brackets represent SEM. Means with different letters are significantly ($P \leq 0.05$) different. *Represents half the daily maintenance ration given at 0800 h. †Represents a twelfth of the daily maintenance ration given at 2 h intervals on the even-numbered hours. Source: Clarke et al., 1990a. Reproduced with permission of the American Veterinary Medical Association.

plasma aldosterone concentration and urinary excretion of potassium and a decrease in the urinary excretion of sodium (Figure 8.5) (Clarke et al., 1988, 1990a). Postprandial dehydration was also documented in athletic horses fed about 7.4 kg of grass hay and 4.1 kg of grain mix divided into two equal meals every 12 h. An immediate increase occurred in plasma protein concentration (3.0–4.7%), in plasma osmolality (1.8%), and in aldosterone concentration (up to 9%) after the large meals. These changes were not observed when the same amount of feed was divided into six equal meals every 4 h (Jansson & Dahlborn, 1999).

It has been suggested that the activation of the renin–angiotensin–aldosterone system produced by postprandial dehydration after a large meal could increase water absorption in the large intestine and lead to dehydration of intestinal content with resulting impaction of the large intestine (Clarke et al., 1990a). The fact that even with extremely artificial feeding protocols (e.g., a single 1 h meal/day) only short-term systemic dehydration (lasting less than 3 h) could be produced does not support this hypothesis. Furthermore, for a horse to eat a large meal in a short period of time as observed in these studies, it is necessary to add grain and limit the fiber content of the diet. These changes in feed composition would have additional effects on the viscosity of the intestinal contents reducing the risk of impaction formation. Although large meals and intermittent feeding could possibly lead to gastrointestinal problems such as acute gastric dilation, tympany and large colon displacements they are not likely to increase the risk of impactions of the large intestine.

Effects on Other Plasma Variables

Intermittent ingestion of feed can produce other postprandial biochemical and hormonal changes in horses, which do not occur with a more continuous eating pattern. In two studies (one with ponies and the other with horses), the effects of complete pelleted feed given as a single 1 h meal/day were compared with those of the same feed given as six daily meals per day. The single large meal produced a postprandial increase in plasma glucose (85.5%) and triiodothyronine concentrations (53.8%) (Youket et al., 1985). It is likely that these changes produced by the large meal may also affect gastrointestinal function (e.g., gastric motility and emptying). In other species, higher glucose concentration after the large meal results in higher plasma concentrations of amylin, a hormone that delays gastric emptying (Ludvik et al., 1997). In humans, higher triiodothyronine concentrations in plasma after a large meal may affect gastric motility and emptying (Gunsar et al., 2003).

Other Effects

Motility of the equine large bowel can be decreased by fasting and returns after refeeding (Alexander, 1952; Clark & Becht, 1985; Ross et al., 1990); however, only prolonged fasting seems to affect gastrointestinal transit.

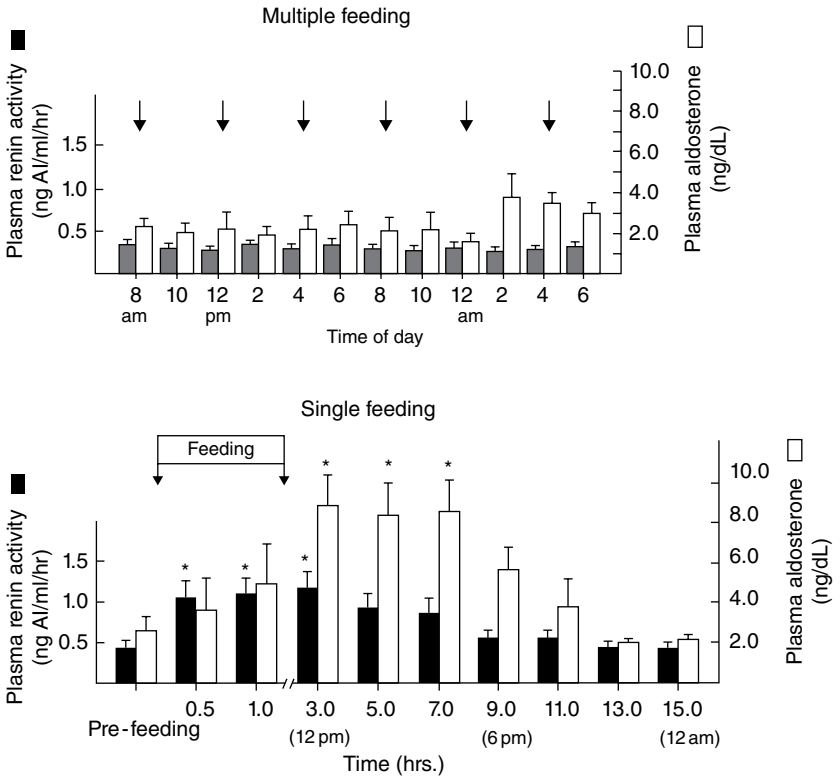

Figure 8.5 Means of plasma renin activity and aldosterone concentration in seven horses fed a single large meal (SF) and multiple smaller meals (MF). Vertical brackets represent SEM. In MF, arrows indicate the times when small, equal-portion meals were offered. In SF, actual time of day is given in parentheses below horizontal axis. *Significantly ($P \leq 0.05$) different from pre-feeding values (mean of values from 1 h before and immediately prior to feeding). Source: Adapted from Clarke et al., 1988, Figs 1 and 4. Reproduced with permission of the American Physiological Society.

In ponies, the gastrointestinal transit of the liquid phase of ingesta was not affected by feeding either a single daily meal or a smaller meal every 4 h (Houpt et al., 1988). In athletic horses, feeding about 7.4 kg of grass hay and 4.1 kg of grain mix divided into two equal meals every 12 h did not affect fecal output or fecal hydration when compared with the effects of the same amount of feed divided into six equal meals every 4 h (Jansson & Dahlborn, 1999). Conversely, in horses with a nasogastric tube, fasted and muzzled for 24 h, the gastrointestinal transit of the liquid phase of ingesta was delayed (Lopes et al., 2004a). The microbiota of the gastrointestinal tract may also be affected (reduced number and activity) by prolonged fasting because of the lack of substrate for microbial growth. Withholding food for as little as 24 h, but especially for 48 h, decreased the rate of digestion of cotton-threads inserted into the cecum and large colon of horses with surgically created fistulas (Alexander, 1952). No difference was detected in digestibility of fiber and protein in ponies allowed to consume their single daily meal in 1 h when compared with digestibility in the same ponies fed small meals every 6 h (Houpt et al., 1988).

Although relatively little is known about the effects of feeds and feeding regimens on equine gastrointestinal physiology, future research findings will make it possible to design feeding practices to maximize performance and minimize gastrointestinal problems in horses. Meanwhile, it is wise to feed horses using principles most compatible with the known features of equine gastrointestinal physiology: (i) minimize the total daily amount and the amount per meal of feeds rich in hydrolyzable and rapidly fermentable carbohydrates such as grain and lush grass; (ii) minimize the amount of low-quality roughage rich in indigestible fiber such as straw; (iii) maximize the amount of high-quality roughage such as good quality hay with adequate fiber; (iv) minimize meal size and maximize the number of meals per day; (v) make any change in feeding practices as smoothly as possible, allowing sufficient time for adjustment by the intestinal flora; and (vi) provide continuous sources of fresh water and minerals.

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9

Intestinal Motility and Transit

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Physiology of Normal Motility

Motility of the gastrointestinal (GI) tract has two major effects: to facilitate the absorption of nutrients and to maintain the aboral propagation of chyme and indigestible material. Both retrograde and normograde flow are required to optimize the absorption of nutrients. Retrograde flow most likely occurs intermittently over short distances to aid in mixing of ingesta and exposing nutrients to the mucosa for absorption. Although little work has been done in the horse to investigate the control of these mixing patterns, most likely there is feedback from both absorption of nutrients and afferent input by mucosal sensory receptors that control these mixing motor patterns in a similar fashion to other species. Since alteration of the normal aboral movement of ingesta causes immediate clinical consequences, the majority of motility investigation in the horse has centered around the control of aboral propagation of ingesta throughout the GI tract and the pathophysiology associated with delayed aboral propagation. This chapter reviews the basic mechanisms controlling normal motility patterns, reviews current thoughts as to the mechanisms underlying the pathophysiology of motility disturbances, in particular postoperative ileus, and finally reviews prokinetics that are available to the equine practitioner.

Gastrointestinal Smooth Muscle

The muscle layers in the intestinal tract responsible for gross motility are contained in the muscularis externa, which is divided into an inner circular muscle and the outer longitudinal muscle, and separated by fascia containing the myenteric plexus. Contraction of the circular muscle narrows the intestinal lumen and at the same time lengthens the segment, whereas contraction of the longitudinal muscle shortens the intestinal segment and at the same time widens the lumen. Temporal and spatial coordination of the activity of both of these muscle layers is necessary for normal progressive motility. Coordination of contractile events starts at the level of the effector cell, the myocyte. Gastrointestinal smooth muscle cells demonstrate continual oscillations in membrane potential called "slow waves" (Figure 9.1 and Figure 9.2) (El-Sharkawy et al., 1978; Szurszewski, 1981). These appear on intracellular recordings as rhythmic depolarizations which are also called electrical control activity (ECA). These slow waves or ECA develop as a result of sequential opening and closing of calcium and potassium channels, with rapid changes in intracellular and extracellular ionic composition. During the slow wave, the membrane potential becomes less negative (depolarizes). This depolarization by itself does not reach the threshold for an action potential. However, at the peak of the slow wave, the cell is at a state of increased excitability because it is closer to the threshold for an action potential. At this time it requires less excitatory input to reach its activation threshold. With further excitatory (depolarizing) stimulation, which may be neural or chemical, the slow wave rises above its threshold for activation with the opening of voltage-gated calcium channels (Figure 9.1) (Szurszewski, 1981). The increase in cytosolic calcium from both the influx of extracellular calcium and the release of intracellular stores activates the myosin and actin contractile proteins as cytosolic calcium binds to calmodulin and activates myosin kinase (Murphy, 1998). Activated myosin kinase, using energy from hydrolysis of adenosine triphosphate (ATP), catalyzes myosin cross-bridges attaching to actin filaments. The sequential attaching, releasing, and reattaching of the myosin bridge produces shortening of the muscle cell. These action potentials are manifested as electrical response activity (ERA) in intracellular recordings, with contraction occurring during this electrical activity (Figure 9.1).

The Equine Acute Abdomen, Third Edition. Edited by Anthony T. Blikslager, Nathaniel A. White II, James N. Moore, and Tim S. Mair.

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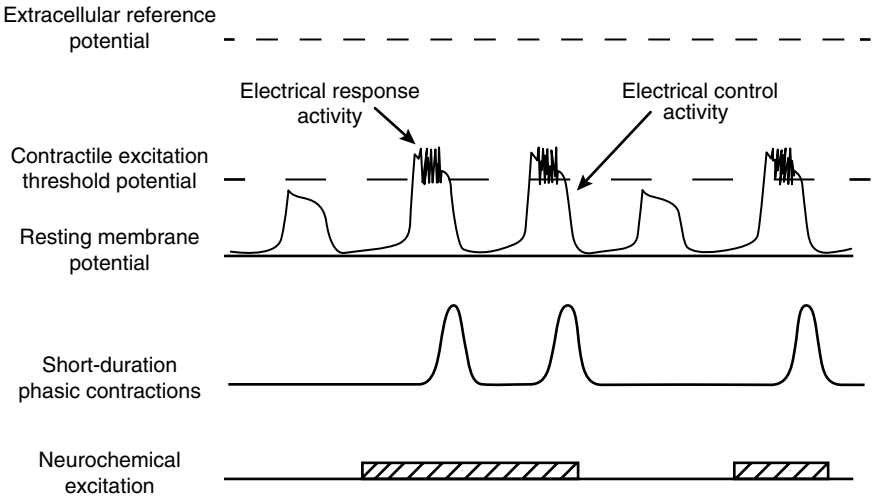


Figure 9.1 Illustration of myogenic control: type 1 for short-duration phasic contractions. The diagram illustrates the relationship of intracellular recorded myoelectrical activities and neurochemical excitation with contractions. The resting membrane potential is negative with respect to the extracellular reference potential. In the absence of neurochemical excitation, the ECA (electrical control activity) depolarizations do not exceed the contractile excitation threshold potential. Consequently, there is no ERA (electrical response activity) burst and no contraction (first and fourth ERA cycles). When neurochemical excitation occurs, ECA depolarization exceeds the excitation threshold potential, an ERA burst occurs, and the smooth muscle contracts (second, third, and fifth cycles). Source: Adapted from Sarna & Otterson, 1993.

Since action potentials and the resulting contractile activity are superimposed on the peaks of slow waves, the slow waves determine the maximal frequency of contractions. Although contractions may not occur as frequently as the slow-wave oscillations if excitatory stimulation is not sufficient to depolarize the cell to the threshold for contraction, contractions cannot occur more frequently than the frequency of the slow wave. For this reason, slow waves are also called "pacesetter potentials," "basic electrical rhythm" (BER), or "electrical control activity" (ECA) (Figure 9.1 and Figure 9.2) (Sarna et al., 1983; Sarna & Otterson, 1993).

Slow waves also determine the direction and velocity of propagation of contractions. Slow waves have characteristic frequencies depending on the region of the GI tract. The frequency of slow waves is higher in the more proximal portions of each region of the GI tract and decrease in frequency moving distally (Sarna et al., 1983; Sarna & Otterson, 1993; Szurszewski, 1969). The smooth muscle cells are connected to adjacent myocytes by specialized areas of cell-to-cell contact called gap junctions. These gap junctions are spanned by channel-forming protein molecules that allow ions to pass directly from one myocyte to the next, creating an electrically coupled syncytium (Alberts et al., 1994). In this manner, electrical activity in one cell spreads out through adjacent cells, allowing them to be excited or inhibited as a unit. Because of the electrical coupling between cells in the muscle layers, the slow waves are entrained, (i.e., the proximal slow waves that are generated at the higher frequency spread distally and so pace the distal slow waves). Since there is a short lag phase between the start of the proximal slow wave and the pacing of the distal slow wave, the slow waves appear to propagate distally. Also, because of the electrical coupling, slow waves occur almost simultaneously around the circumference of the intestinal segment. With excitation sufficient to cause an action potential, a ring of contraction forces luminal contents distally (Sarna et al., 1983; Szurszewski, 1969).

Interstitial Cells of Cajal

In recent years, the interstitial cells of Cajal (ICCs) have been shown to play a key role in the initiation of pacemaker activity (Ward et al., 2000). ICCs are highly branched cells located in the myenteric and submucosal plexuses of the enteric nervous system. They originate from the same mesenchymal precursor cell as the smooth muscle cell (Wang et al., 2003; Ward et al., 2000; Ward & Sanders, 2001b). The ICCs from the submucosal and myenteric borders surround the adjacent circular muscle cells. ICCs express c-kit, the proto-oncogene that encodes for the receptor tyrosine kinase. This finding has greatly aided in the study of ICCs by providing a method of identification by labeling either Kit receptors or c-kit mRNA (Torihashi et al., 1995). Mutant mice that do not express functional Kit proteins, and so do not have ICCs, show an absence of slow-wave activity (Ward et al., 1994). Blocking Kit function with neutralizing antibodies causes impairment in ICC development, which results in the absence of slow waves. This demonstrates that ICC pacemaker cells generate slow waves. The ICCs

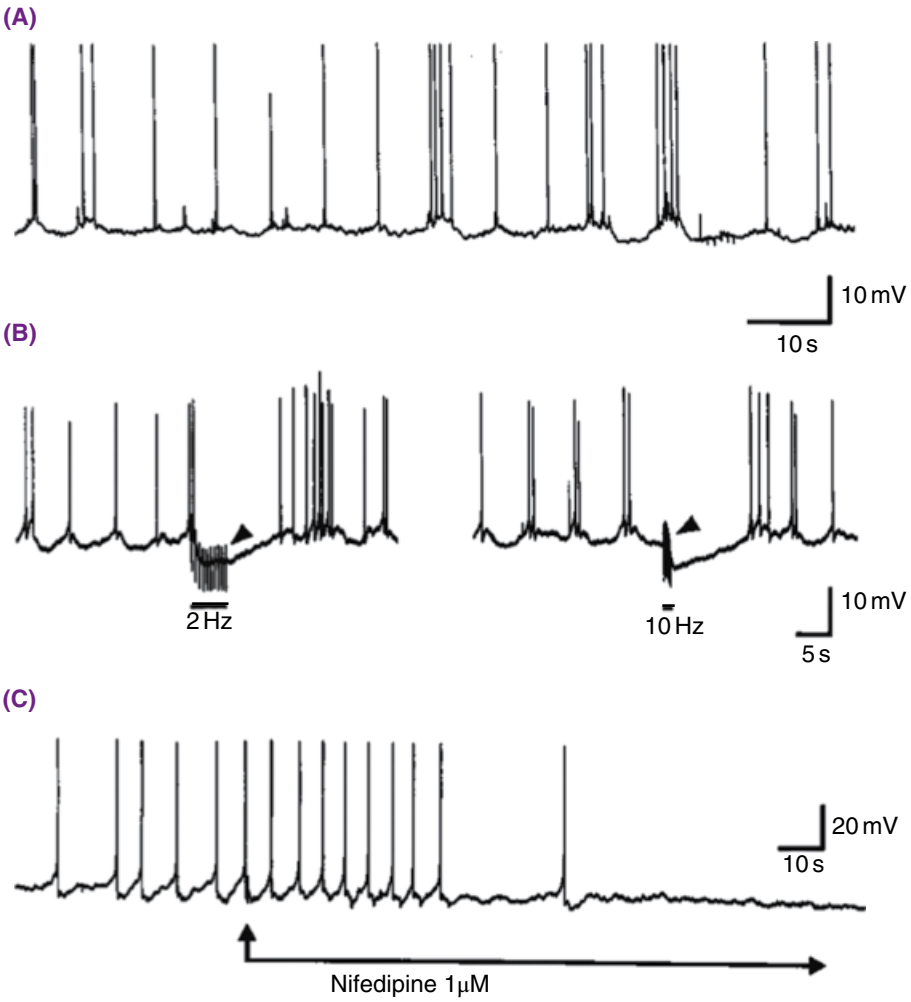


Figure 9.2 Intracellular microelectrode recording of membrane potentials associated with spontaneous myogenic activity (slow waves) in the circular muscle of jejunum in horses. All panels illustrate intracellular microelectrode recordings of membrane potentials from single circular muscle cells. **(A)** In the presence of atropine and quanethidine (2 μM each), cells had spontaneous action potentials superimposed on small-amplitude membrane potential oscillations. **(B)** Stimulation of intrinsic inhibitory neurons (2 and 10 Hz, indicated by bars) caused a transient hyperpolarization, an inhibitory junction potential (IJP), that temporarily inhibited spontaneous depolarization and action potential firing (arrowheads indicate stimulus artifacts). **(C)** Nifedipine (1 μM), a calcium channel blocker, abolished smooth muscle oscillations and action potentials. Source: Rakestraw et al., 2000. Reproduced with permission of the American Veterinary Medical Association.

are in electrical communication with smooth muscle cells through gap junctions, allowing the electrical activity to spread passively to smooth muscle cells (Ward et al., 2004). ICCs are interposed between circular smooth muscle cells and enteric motor neurons, suggesting an interaction between neural and myogenic control at the level of ICCs (Figure 9.3). ICCs amplify inhibitory nitrergic and excitatory cholinergic signals from neurons to myoctes (Wang et al., 2003; Ward et al., 2000; Ward & Sanders, 2001a). In horses, ICCs have been observed and quantitated, by using anti-c-kit antibodies, in the circular and longitudinal muscle layers, and in the myenteric plexus throughout the GI tract of normal horses (Pavone & Mandara, 2010). Abnormal function or numbers of ICCs have been linked to GI motor dysfunction in humans such as Hirschsprung disease, pyloric stenosis, chronic constipation, and pseudo-obstruction (Huizinga, 1998, 1999). In a partial obstruction model, ICC networks were disrupted orad to the obstruction, resulting in loss of slow-wave activity (Chang et al., 2001). Although several etiologies have been suggested, a reduction of ICCs has been found in horses with equine dysautonomia (grass sickness) and may contribute to the intestinal dysmotility seen with that disease (Cottrell et al., 1999; Hudson et al., 2001; McCarthy et al., 2004). Similar observations and conclusions were described by Fintl et al. (2004), who also observed a reduction in ICC densities in horses with obstructive disorders of the large colon compared with normal animals. A comparable distribution of ICCs has been observed in aged donkeys

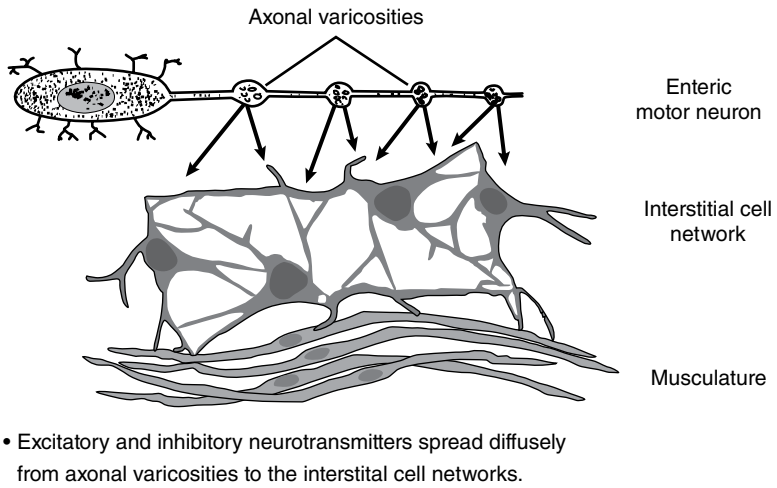


Figure 9.3 Interstitial cells of Cajal are relays for transmission from enteric motor neurons to the GI musculature. Source: American Gastroenterological Association Institute, Bethesda, MD. Reproduced with permission.

compared with horses. However, no difference in the density and distribution of ICCs in donkeys with or without impaction of the pelvic flexure were observed (Fintl et al., 2010). The extent to which abnormal function of ICCs contributes to other equine GI motility disturbances is not known.

Myoelectrical Patterns of Activity

Slow waves do not by themselves depolarize the membrane sufficiently to initiate an action potential. Additional depolarizing (excitatory) input from humoral and/or neural sources allows the membrane to reach the threshold potential necessary to generate an action potential. This depolarization results in electrical response activity or spiking activity and is associated with contractions. The stomach and small intestine cycle through three (or four) different phases of contractile activity in the fasted (interdigestive) state. Phase I, a period of quiescence or no spiking activity (NSA), is defined as the period where <5% of the slow waves (pacesetter potentials) are associated with action potentials. Phase II, a period of intermittent spiking activity (ISA), is defined as the period where action potentials and contractions are associated with between 5 and 95% of the slow waves. Phase III, a period of regular spiking activity (RSA), is defined as the period where action potentials and contractions are associated with 95–100% of slow waves (Figure 9.4). Some authors describe a phase IV, which is a short period where action potentials and contractions subside to the quiescence of phase I. This motor pattern, which involves rhythmic activity of the enteric nervous system, is called the "migrating myoelectrical complex" (MMC) (Figure 9.3) (Bueno et al., 1975; Code & Marlett, 1975; Szurszewski, 1969).

The interdigestive motility pattern usually begins in the stomach antrum as a series of contractions, migrates through the pylorus, and travels down the small intestine to the cecum.

The activity front has been described by various authors to include either phase III by itself or phases II and III (Navarre & Roussel, 1996; Roussel, 1994; Wood, 1995). It is during the activity front that coordinated contractions propel luminal contents aborally. In the horse, propulsion of ingesta has been described as occurring during phase II and III (Gerring et al., 1991; Lester et al., 1992). The activity front of the MMC traveling aborally is not a peristaltic wave. Peristaltic waves occur within the activity fronts of the MMC at the frequency of the slow waves, the pacesetter potentials. Each peristaltic wave begins orally within the activity front and migrates aborally, ending within the activity front. Some peristaltic waves end before they reach the aboral end of the activity front. Consequently, the recording of electrical and mechanical activity at the leading edge of the activity front first registers what is defined as phase II activity, where contractions are not seen to occur regularly with each slow wave. As the activity front migrates further aborally, a higher proportion of the peristaltic waves will now travel past the recording electrodes and strain gauges now within the center of the activity front until most or all of the slow waves have associated contractions, which is defined as phase III (Wood, 1995). In general, each successive peristaltic wave begins aboral to where the previous one began and ends aboral to where the previous one ended. In this way, both the activity front of the MMC and the peristaltic waves migrate down the intestinal tract. Propagation of the MMC aborally is coordinated primarily by the enteric nervous system (Sarna & Otterson, 1993). The apparent functions of the MMC are

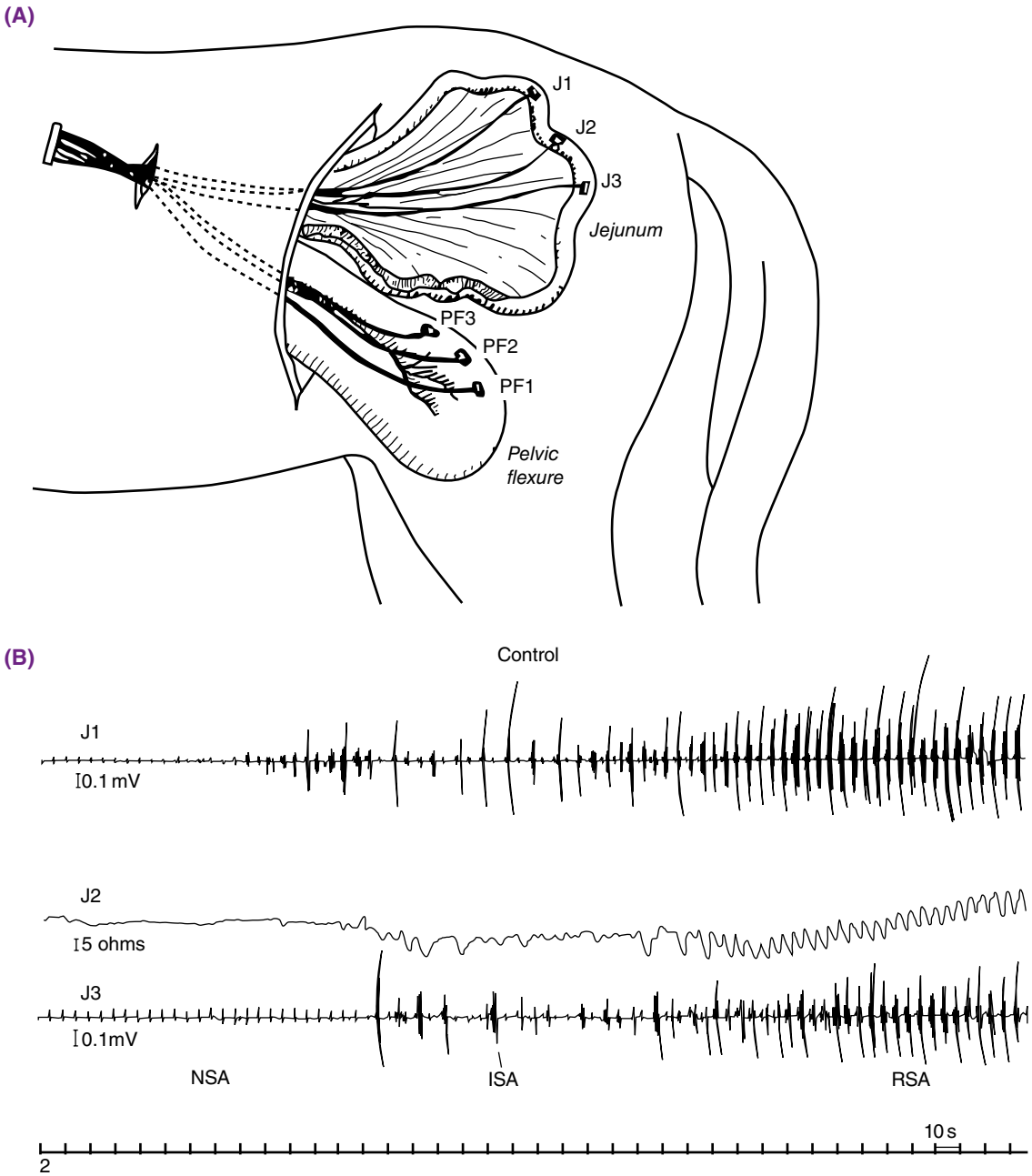


Figure 9.4 **(A)** Bipolar electrodes positioned in the jejunum and pelvic flexure. J, jejunum; PF, pelvic flexure. **(B)** Physiograph tracing of myoelectrical (J1 and J3) and mechanical (J2) activity of the jejunum. NAS, no spiking activity; ISA, intermittent spiking activity; RSA, regular spiking activity. Source: Adams et al., 1984. Reproduced with permission of the American Veterinary Medical Association.

to clear indigestible particles during the fasting state and to prevent bacterial overgrowth. Because of these functions, it has also been described as the "intestinal housekeeper" (Code & Marlett, 1975; Wood, 1995; Weisbrodt et al., 1974). In the fed state, the rhythmic pattern of the MMC is replaced with irregular spiking activity. Cholecystokinin and gastrin released in response to nutrients in the GI tract have been suggested as mediators of this change in myoelectrical activity from fasted to fed state (Mukhopadhyay et al., 1977; Weisbrodt et al., 1974).

There is a temporal association between the appearance of the MMC and plasma motilin concentrations (Itoh et al., 1978). Exogenously administered motilin induces premature gastric and duodenal activity fronts (Bueno et al., 1982). This suggests that motilin plays a role in the initiation of MMCs. This finding has stimulated attempts to develop pharmaceutical agents that act as motilin receptor agonists to initiate premature MMCs. Since the first part of the MMC that is recognizable is the activity front, premature MMCs are theoretically

associated with a return of propulsive contractile activity. As demonstrated in this example, the MMC is commonly used as a measurement to study GI motility (Figure 9.4). In general, events that interrupt or decrease the duration of the activity front (measured as phase II and/or phase III) are considered as contributing to motility disturbances, whereas events that induce premature activity fronts or increase the duration of activity fronts are considered to contribute to restoration of progressive motility patterns. The reported mean duration of the MMC in the horse is 65.5–150.0 min (Adams, 1988; Davies & Gerring, 1983; Sojka et al., 1988).

The major myoelectrical activity patterns of the equine large intestine are described as short spike bursts (SSBs) and long spike bursts (LSBs) (Fioramonti et al., 1980; Navarre & Roussel, 1996; Ruckebusch & Fioramonti, 1980). Short spike bursts, by definition, last 5 s or less. They are stationary and associated with segmental mixing. Long spike bursts last 10–20 s. They appear to be stronger contractions, may occur at sequential areas along the large intestine, and are associated with either retropulsion or propulsion. Several additional patterns have been described in the horse: a slowly migrating cluster of short and long spike bursts (SMCs), which last 4–8 min and move aborad; and a series of high-amplitude, propagated spike bursts called the colonic migrating myoelectric complex (CMMC) (Lester et al., 1992; Merritt et al., 1995). Studies of the ileo-ceco-colonic area have shown multiple contractile patterns serving different functions. In the cecum, several patterns of spike bursts were seen that directed ingesta between the cranial or caudal cecal base to the apex and back. These could be described as mixing patterns. A progressive pattern was identified that began at the cecal apex and was conducted through the cecal base and cecocolic orifice and into the right ventral colon. This appears to be coordinated with ileal contractions and continues in the colon as the CMMC (Lester et al., 1998b; Ross et al., 1990). Retropulsive and propulsive spike bursts were detected in the right ventral colon. Retropulsion is thought to prolong retention of ingesta in the cecum and colon, and so facilitate hindgut fermentation. A pacemaker in the region of the pelvic flexure is thought to coordinate retropulsion and propulsion originating at the pelvic flexure area (Sellers et al., 1982). The retropulsive spike bursts seen in the ventral colon may have originated at the pelvic flexure pacemaker. Pacemakers may also be located in the horse in the right ventral colon and the cecal apex (Ross et al., 1990).

Enteric Nervous System

The next level of control is the enteric nervous system (ENS) (Figure 9.5). The ENS has been described as the third division of the autonomic nervous system, with the parasympathetic and sympathetic being the other two divisions. The cell bodies of neurons in the ENS are located within the walls of the GI tract in either the myenteric or submucosal ganglia. The most basic reflex circuits consist of an intrinsic primary sensory afferent neuron that projects circumferentially, synapsing directly on myenteric motor neurons, which in turn synapse on muscle cells; or an intrinsic primary sensory afferent neuron that synapses on myenteric interneurons, which project orally or aborally, relaying the afferent input to myenteric motor neurons in other parts of GI tract (Figure 9.6) (Bornstein et al., 2004). The enteric neurons can be classified based on electrical activity (synaptic input and after potentials) (Hirst et al., 1974). S-neurons are neurons that have fast excitatory synaptic potentials (EPSPs) and short after-hyperpolarizations (AHPs). AH-neurons are neurons that do not show fast EPSPs but have prolonged AHPs. Another common classification scheme is based on morphology. Dogiel type I neurons are unipolar, whereas Dogiel type II neurons are multipolar. S-neurons are unipolar, and so classified as Dogiel type I. These have been shown to be motor neurons or interneurons (Figure 9.6). AH-neurons are multipolar and so classified as Dogiel type II (Bornstein et al., 1994). Intrinsic primary afferent neurons and enteric interneurons are AH/Dogiel type II neurons.

The circuitry of the ENS is responsible for many coordinated motility patterns of the GI tract. Peristaltic reflexes and other complex motor activity can occur without any extrinsic neural input (Figure 9.7). Many years ago, an enteric reflex initiated by introducing a bolus into the small intestine after severing all extrinsic neural connections was shown to be mediated by an ascending excitation (contraction of the circular muscle) and descending inhibition (relaxation of the circular muscle), with movement of the bolus aborally (Bayliss & Starling, 1899). More recent work using intracellular recordings of circular smooth muscle indicate that distention produces ascending excitation by depolarization, called excitatory junction potentials (EJPs), of orally positioned circular muscle cells, and a descending inhibition by hyperpolarization, called inhibitory junction potentials (IJPs), of the aborally positioned circular muscle cells (Bornstein et al., 2004; Smith et al., 1990, 1992). Mechanical stimulation of the mucosa, distention (or stretch), and chemical irritants have all been shown to stimulate this peristaltic motor pattern, which is under the control of the ENS (Figure 9.7). There are many more complex motor patterns mediated by the enteric circuitry but they are beyond the scope of this chapter.

Neurons are also classified chemically, depending on the type of neurotransmitter(s) that they contain. The primary neurotransmitters in the intrinsic primary afferent neurons are acetylcholine (ACh), substance P (SP), which is member of the tachykinin family of neuropeptides, and calcitonin gene-related peptide (cGRP)

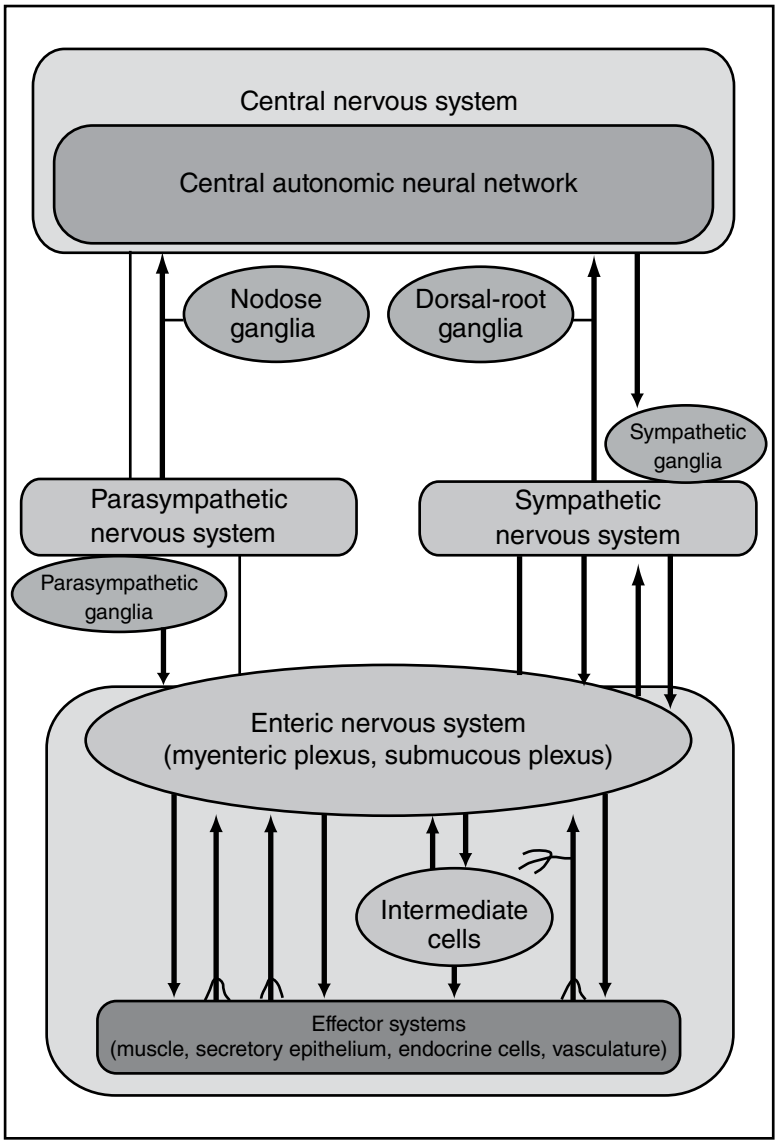


Figure 9.5 Innervation of the GI tract. The neural plexuses in the gut represent an independently functioning network known as the enteric nervous system, which is connected to the central autonomic neural network in the central nervous system by the parasympathetic and sympathetic nerves. The enteric nervous system may either influence the effector systems in the gut directly or may do so indirectly through its action on the intermediate cells, which include the endocrine cells, the interstitial cells of Cajal, and the cells of the immune system, such as mast cells. The cell bodies of the primary vagal and primary splanchnic afferent neurons are located in the nodose ganglia and dorsal-root ganglia, respectively; each carries distinct information from the gut to the central nervous system. Source: Goyal & Hirano, 1996. Reprinted with permission of the Massachusetts Medical Society.

(Bornstein et al., 2004; Grider, 1994; Smith et al., 1990, 1992). Mucosal stimulation by ingesta stimulates release of 5-hydroxytyptamine (5-HT; serotonin) from enterochromaffin cells (Grider, 2003) (Figure 9.6). This in turn activates 5-HT_4 receptors on intrinsic afferents, which then synapse on ascending and descending interneurons. The primary neurotransmitter released by enteric ascending interneurons appears to be acetylcholine acting through nicotinic receptors, although ascending interneurons are also positive for SP, enkephalins (ENKs), and calretinin immunostaining. The neurotransmitters released by enteric descending interneurons are acetylcholine and also vasoactive intestinal peptide (VIP), nitric oxide (NO), somatostatin (SOM), and 5-HT. Widespread 5-HT_4 receptor immunoreactivity has been observed in all intestinal smooth muscle layers in the horse (Prause et al., 2010). Enteric inhibitory motor neurons release NO, VIP, and ATP at the neuromuscular junction (Figure 9.6). These are responsible for the IJPs in the aboral muscle mediating descending relaxation of the bowel during a peristaltic wave (Figure 9.2A and Figure 9.8) (Grider, 2003). Other neurotransmitters found in enteric inhibitory motor neurons are neuropeptide Y (NPY), γ-aminobutyric acid (GABA), gastrin-

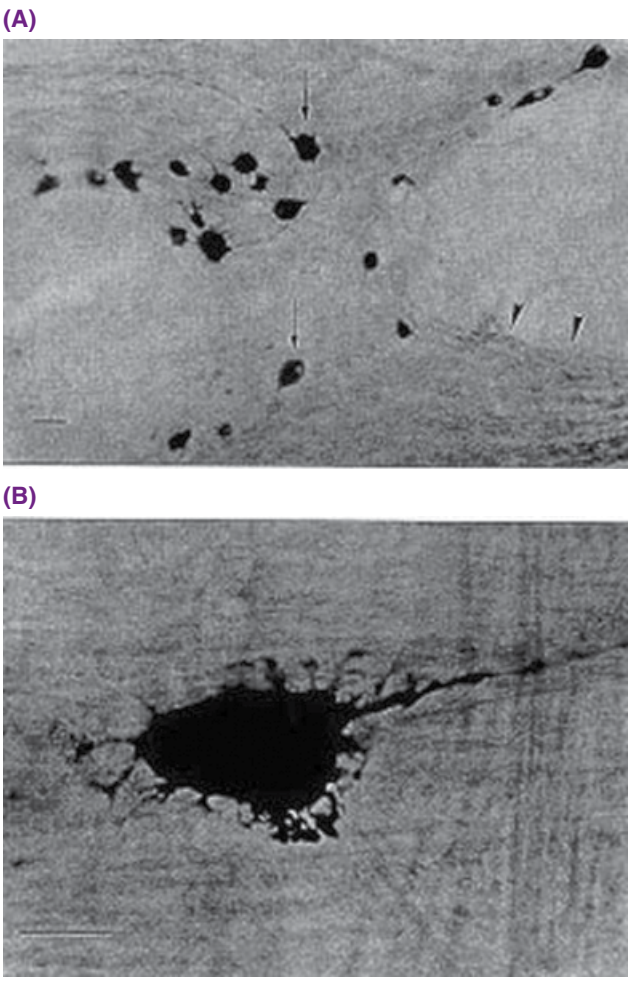


Figure 9.6 Photomicrographs illustrating histochemistry of NADPH diaphorase (NADPH-d) activity in whole mount preparations indicating nitric oxide (NO) synthase-containing neurons in the myenteric plexus. **(A)** Positively reactive cell bodies (arrows) and interganglionic fibers (arrowheads) can be identified. **(B)** Dogiel type I morphology in a positively reactive neuron. Note the numerous short dendritic processes and single axonal process. Bar = (A) 50 and (B) 30 μM. Source: Rakestraw et al., 1996. Reproduced with permission of the American Veterinary Medical Association.

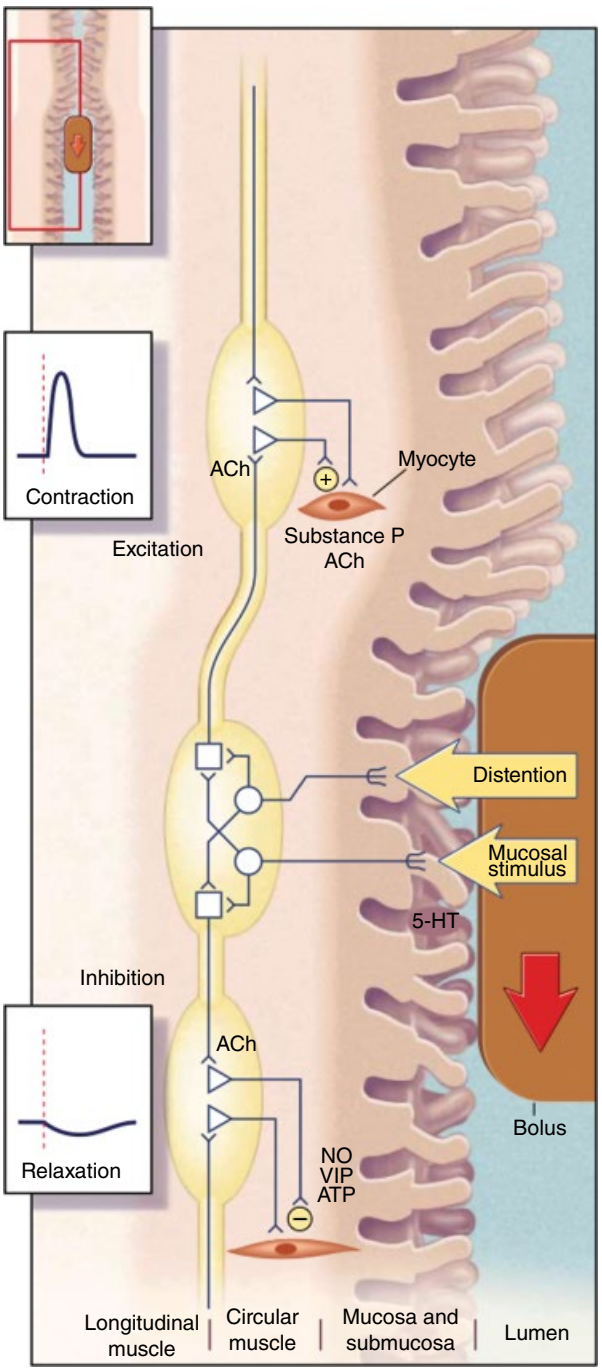


Figure 9.7 Intestinal peristaltic reflex. Peristalsis is the result of a series of local reflexes, each consisting of a contraction of intestinal muscle above an intraluminal stimulus and a relaxation of muscle below the stimulus (inset, top left). The release of 5-HT by mucosal stimulation or mechanical distention of the gut lumen (main panel) triggers activity in the intrinsic afferent neurons (circles). Above the site of the stimulus, ascending cholinergic interneurons (squares) relay this signal to excitatory motor neurons (arrowheads) containing acetylcholine (ACh) and substance P. As a result, the circular muscle above the stimulus contracts. At the same time, below the stimulus site, descending cholinergic interneurons activate inhibitory motor neurons that contain nitric oxide (NO), vasoactive intestinal polypeptide (VIP), and ATP, causing relaxation. The resultant forces propel the bolus in an antegrade direction. As the bolus moves, it triggers similar peristaltic reflexes at successive sites along the gut. Source: Goyal & Hirano, 1996. Reprinted with permission of the Massachusetts Medical Society.

releasing peptide (GRP), and pituitary cyclase-activating peptide (PACAP) (Bornstein et al., 2004; Uemura et al., 1995; Burns & Cummings, 1993; Cummings et al., 1985; Malone et al., 2000; Rakestraw et al., 1995; Sellers et al., 1985). The primary excitatory neurotransmitters in enteric excitatory motor neurons are ACh and SP, and possibly other members of the tachykinin family such as neurokinin A. At the neuromuscular junction, acetylcholine acts at muscarinic receptors on the enteric smooth muscle. ACh and SP are responsible for the EJPs in the muscle mediating ascending contraction during the peristaltic reflex (Figure 9.6). It should be noted that the majority of enteric neurotransmitters are neither adrenergic nor cholinergic. It is common in the literature to see the term nonadrenergic–noncholinergic (NANC)

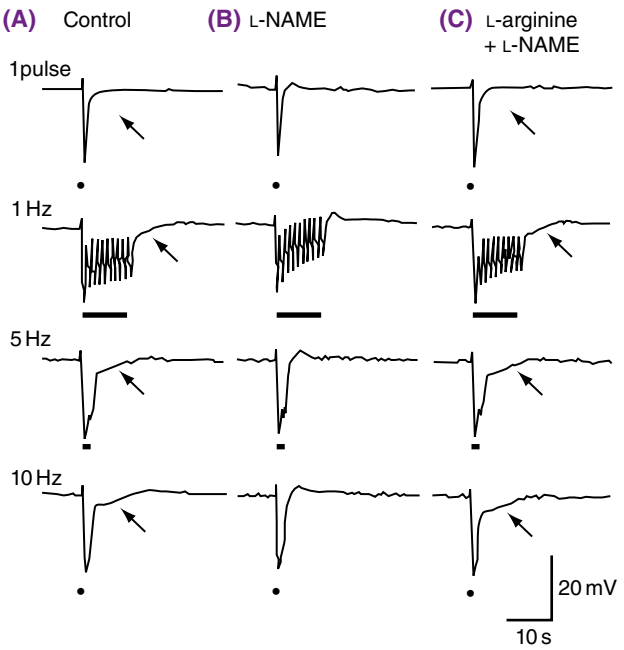


Figure 9.8 Intracellular microelectrode recording of membrane potentials in jejunal circular muscle in horses during electrical field stimulation (EFS) in absence of *N*-nitro-L-arginine methyl ester (L-NAME), an NOS blocker, or L-NAME and L-arginine. All panels are excerpts from a continuous recording from a single muscle cell, illustrating membrane potential changes resulting from stimulation of intrinsic (indicated by circles or bars). Left panels **(A)** illustrate control responses to a single pulse and trains of stimuli delivered at 1–10 Hz. The slow component of the IJP is indicated by arrows. Middle panels **(B)** illustrate responses of cells after 20 min exposure to L-NAME (200 mM). Note that treatment with L-NAME did not have a significant effect on IJP amplitude but blocked the slow component of the IJP. Right panels **(C)** illustrate the response in the presence of the nitric oxide synthase substrate L-arginine in the continued presence of L-NAME. In all traces, the upward deflections at onset of stimulus are stimulus artifacts (arrowheads at top). Source: Rakestraw et al., 2000. Reproduced with permission of the American Veterinary Medical Association.

used to describe this type of neurotransmission. Neuropeptides and NO are NANC neurotransmitters.

Although there likely are species variations, there is ample evidence that many of the substances described function as neurotransmitters in the horse. Experimental evidence supports the role of SP as an important excitatory neurotransmitter in the equine GI tract. SP-like immunostaining has been identified in the enteric ganglia and circular muscle in many regions of the equine GI tract (Burns & Cummings, 1993; Cummings et al., 1985; Malone et al., 2000; Rakestraw et al., 1995; Sellers et al., 1985). *In vitro* mechanical studies indicate that SP (and also serotonin) increases contractile activity of the circular and, to a lesser extent, longitudinal muscle of the equine jejunum and colon (Belloli et al., 1997; Malone et al., 2000; Rakestraw et al., 1996; Nieto et al., 2000). *In vivo* mechanical studies have shown that SP increases contractile activity of equine pelvic flexure (Cummings et al., 1985). In the horse, neurokinin-1 receptors have been shown to be the predominant subtype of tachykinin receptor in the smooth muscle of the pelvic flexure (Sonea et al., 1997). Neurokinin-1 receptor mRNA has been identified in small intestine and colon smooth muscle of healthy horses (Solinger & Sonea, 2008). Co-localization of SP immunostaining and choline acetyltransferase (ChAT) immunostaining in the equine myenteric plexus and circular muscle suggests that SP and ACh can be released from the same neuron (Malone et al., 2000). This relationship is likely important in their role mediating ascending contraction.

NANC inhibitory neurotransmitters have also been identified in the equine ENS. Several studies support a role for NO as an important inhibitory neurotransmitter in the equine intestine. Neurons with a Dogiel type I morphology that stain positive for NADPH diaphorase, a marker for nitric oxide synthase (NOS), have been identified in the myentric plexus and circular muscle of the equine jejunum (Figure 9.6) (Rakestraw et al., 1996). Intracellular recordings have shown that NO is responsible for a portion of the IJPs in the circular muscle of the equine jejunum (Figure 9.8) (Rakestraw et al., 2000). Another portion of the IJP is blocked by apamin, a drug that may work by blocking ATP (Rakestraw et al., 2000). *In vitro* mechanical studies have shown marked inhibition of equine jejunal and colonic circular muscle contractile activity with NO donors and reduction of inhibition with NOS antagonists (Rakestraw et al., 1996; Van Hoogmoed et al., 2000a). VIP-like immunostaining has also been demonstrated in the enteric ganglia and circular muscle throughout the equine intestinal tract (Burns & Cummings, 1993; Rakestraw et al., 1996). VIP has been shown to decrease *in vitro* contractile activity of the equine circular muscle (Rakestraw et al., 1996). These results suggest that NO, VIP, and ATP mediate inhibitory neurotransmission in the equine ENS, as occurs in other species.

Extrinsic Nervous System

Extrinsic Efferent Nerves

The next level of control is through extrinsic neural input from the sympathetic and parasympathetic divisions of the autonomic nervous system. The sympathetic division originates from thoracic and lumbar spinal cord segments T-1 through L-2 (Figure 9.9). The preganglionic efferent neuron with the cell body located within the intermediolateral horn of the spinal cord exits the spinal cord in the ventral roots and travels through the sympathetic chain, and synapses with a postganglionic neuron in one of the prevertebral ganglia (celiac, superior or inferior mesenteric ganglia) (Guyton & Hall, 1996). Acetylcholine is released and acts at nicotinic receptors on the postganglionic neuron. The postganglionic neuron travels to the GI tract and synapses with enteric neurons, releasing norepinephrine that acts at

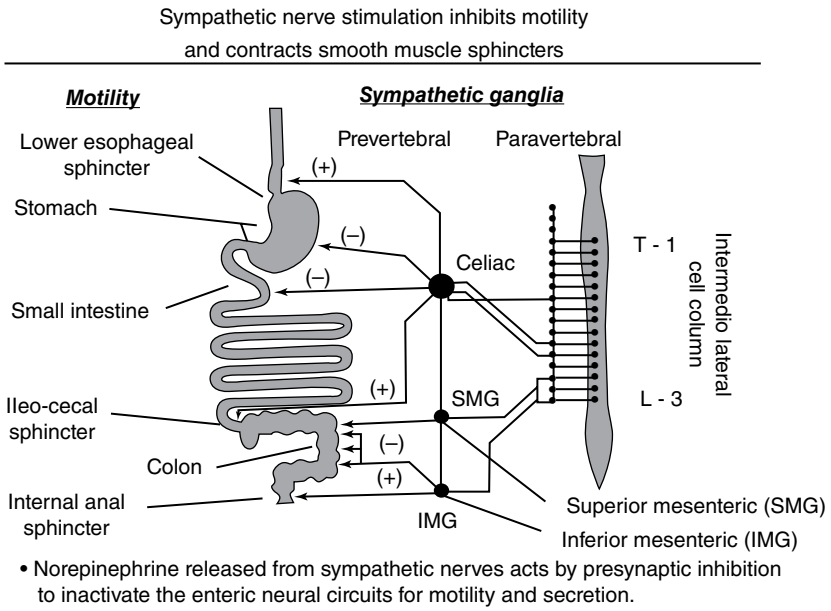


Figure 9.9 The sympathetic division of the autonomic innervation to the gut is positioned in the thoracic and lumbar regions of the spinal cord. Efferent sympathetic fibers leave the spinal cord in the ventral roots to make their first synaptic connections with the neurons in the prevertebral sympathetic ganglia located in the abdomen. The prevertebral ganglia are the celiac, the superior mesenteric, and the inferior mesenteric ganglia. Cell bodies in the prevertebral ganglia project to the digestive tract, where they synapse with neurons of the enteric nervous system in addition to innervating the blood vessels, mucosa, and specialized regions of the musculature. Source: American Gastroenterological Association Institute, Bethesda, MD. Reproduced with permission.

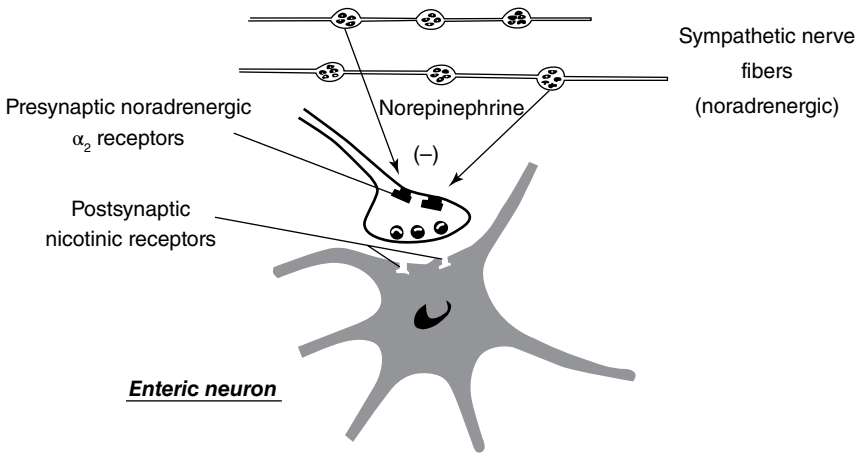


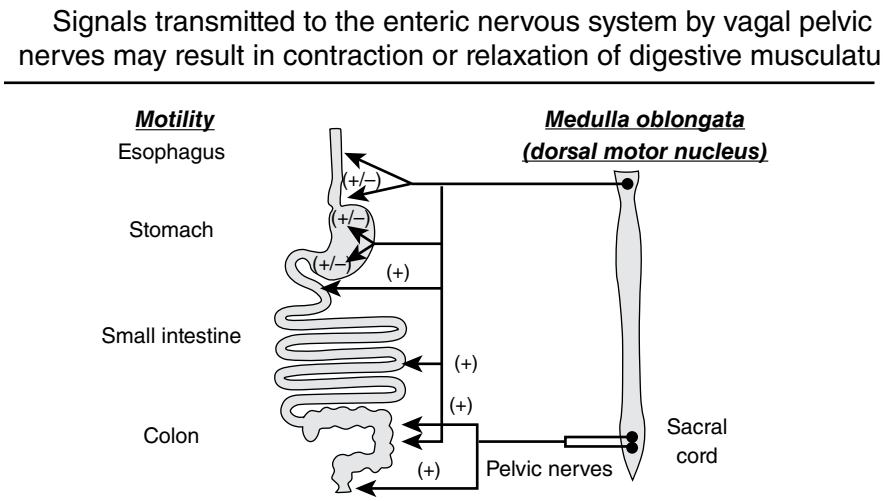
Figure 9.10 Norepinephrine released from sympathetic nerves acts by presynaptic inhibition to inactivate the enteric neural circuits. The synaptic interface between the postganglionic fibers of the sympathetic nervous system and the enteric nervous system is a presynaptic α_2-adrenoceptor. Norepinephrine released from sympathetic fibers suppresses the release of excitatory neurotransmitters at both enteric synapses and neuro-effector junctions. Source: American Gastroenterological Association Institute, Bethesda, MD. Reproduced with permission.

presynaptic α_2-adrenoceptors (Figure 9.10). The effect is to inhibit the release of excitatory neurotransmitters such as acetylcholine, at enteric synapses. In general, sympathetic stimulation depresses motility.

The parasympathetic system is divided into the cranial and sacral divisions (Figure 9.11) (Guyton & Hall, 1996). The cranial division supplies innervation from the esophagus to the proximal colon, primarily by fibers traveling in the vagus nerve. The pelvic nerve supplies innervation to the distal colon, rectal, and anal regions. The parasympathetic system is composed of a preganglionic fiber the cell body of which is in the brainstem or posteriolateral parts of the anterior columns of the spinal cord for the cranial and sacral divisions, respectively. The preganglionic fibers synapse on postganglionic neurons whose cell bodies are contained within the enteric ganglia in the wall of the GI tract. Presynaptic fibers release acetylcholine, which acts on nicotinic receptors on postganglionic neurons. The postganglionic neurons are part of the ENS since the cell body is within the intestinal wall. The postganglionic neurons are either enteric cholinergic excitatory fibers or NANC excitatory or inhibitory enteric neurons described previously. Since most extrinsic efferent nerves, both sympathetic and parasympathetic, mediate motility synapse within the enteric ganglia and not on the enteric muscle, the extrinsic neural input in general acts not by direct stimulation of muscle but through modifying and coordinating enteric neural activity.

Extrinsic Afferent (Sensory) Nerves

Subpopulations of afferent nerves have specialized receptors that are responsive to stimuli such as stretch,



• Parasympathetic innervation of small and large intestinal musculature is predominantly excitatory.

Figure 9.11 The parasympathetic division of the autonomic innervation is subdivided anatomically into the cranial and sacral divisions. This is due to the location in the brain and spinal cord of neurons that send nerve fibers to the GI tract. Fibers running from the central nervous system to the GI tract are efferent fibers. The cranial division has neuronal cell bodies in the medulla oblongata of the brain, whereas the sacral division has its cell bodies located in the sacral region of the spinal cord. Axons from cell bodies located in the medulla project in the right and left vagal nerves to the digestive tract. Axons from cell bodies in the sacral region on the spinal cord project to the large intestine in the pelvic nerves. Source: American Gastroenterological Association Institute, Bethesda, MD. Reproduced with permission.

tension, or movement (mechanoreceptors), nutrients, osmolarity, and pH (chemoreceptors), luminal temperature (thermoreceptors), and pain (nociceptors), located in the wall of the GI tract. Cholecystokinin (CCK), 5-HT, noradrenaline, opioids, bradykinin, purines, and prostaglandins are local mediators that may activate these receptors (Blackshaw & Gebhart, 2002). As previously described, one population of afferent neurons, the intrinsic primary afferent neuron, synapses either on enteric motor or enteric interneurons (Figure 9.7). In addition to these intrinsic afferents, there are two extrinsic pathways containing primary afferent neurons (Figure 9.5 and Figure 9.12). One pathway has sensory fibers running in the vagus or pelvic nerve and cell bodies in the nodose ganglia. These have been called parasympathetic afferent nerves. The other pathway, spinal sensory afferents, has fibers running in the splanchnic or mesenteric nerves and cell bodies in the dorsal root ganglia. These have been called the sympathetic afferents (Holzer, 2002). These fibers pass through the prevertebral ganglia and may send axon collaterals to synpase with sympathetic postganglionic neurons, establishing a reflex circuit at the level of the prevertebral ganglia. There are also sensory nerves (intestinofugal) with cell bodies in the myenteric ganglia whose fibers project with spinal afferents to the prevertebral ganglia, and sensory nerves with cell bodies in enteric ganglia of gastric and esophageal myenteric plexus (viscerofugal) whose fibers project in the vagal trunks to the central nervous system (CNS) (Blackshaw & Gebhart, 2002). The extrinsic afferent neurons contain SP, cGRP, neurokinin A (NKA), and other peptides that are used as neurotransmitters (Holzer, 2002; Sternini, 1992; Zittel et al., 1998).

The function of these extrinsic sensory neurons in modulating both normal and abnormal motility patterns has been elucidated with the use of capsaicin, a sensory neurotoxin that causes functional impairment of a population of sensory nerves. Systemic administration of capsaicin causes a depletion of neurotransmitters of the sensory unmyelinated C-fibers, and perineural application of high concentrations of capsaicin has the same effect on specific peripheral nerve fibers (Holzer, 1991). It should be noted that perineural application of low concentrations of capsaicin causes a transient acute stimulation as neuropeptides are released. The extrinsic afferent neurons do not appear to influence basal GI motor activity significantly, but appear to mediate a number of inhibitory motor reflexes, such as inhibition of gastric emptying in response to duodenal distention or duodenal luminal contents (Boeckxstaens et al., 1999; Holzer & Raybould, 1992). The importance of these two extrinsic sensory pathways in controlling motility is illustrated by the following study. Distention of the duodenum produces a reflex inhibition of gastric activity. Capsaicin applied to the cervical vagal trunk decreases gastric inhibition in response to low volumes of duodenal distention, but not to high volumes. However, capsaicin applied to the celiac-superior mesenteric ganglia with ablation of spinal sensory afferents attenuates the inhibitory response to all volumes of distention (Holzer & Raybould, 1992).

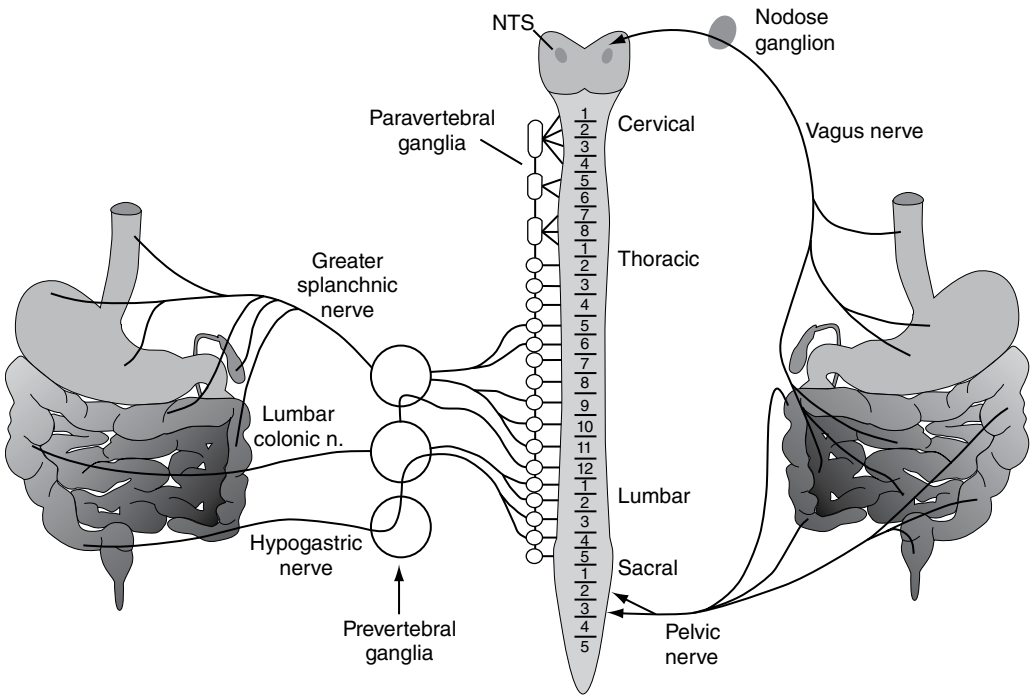


Figure 9.12 Representation of sensory innervation of the GI tract. Left: visceral afferent pathways through prevertebral and paravertebral ganglia to the spinal cord; cell bodies are located in dorsal root ganglia (not illustrated). Right: vagal and pelvic nerve afferent input through nodose and dorsal root ganglia, respectively. The innervation of the viscera as illustrated is overlapping with spinal inputs to specific, but anatomically separated spinal segment. For example, the distal colon is represented in the thoracolumbar and lumbosacral spinal segments by the least splanchnic and pelvic nerve inputs. Gastric input to the CNS is represented in the brainstem and thoracic spinal cord by vagal and splanchnic inputs. Source: Blackshaw & Gebhart, 2002. Reproduced with permission of Elsevier.

The low-volume reflex may function as a normal physiologic response coordinating the gastroduodenal motor activity involved in gastric emptying after eating through vagal afferents, while the recruitment of high-threshold mechanoreceptor endings with afferent fibers in splanchnic nerves may be important in mediating reflex inhibition of gastric emptying associated with ileus in response to potentially harmful levels of distention (Holzer & Raybould, 1992). These spinal and vagal afferents are also important in mediating sensations of fullness, satiety, nausea, and vomiting (Blackshaw & Gebhart, 2002).

Other Mediators of Motility

Opioids

Endogenous opioid peptides met-enkephalin (Met5), leu-enkephalin (Leu5), and dynorphin are present in ganglion cells of the myenteric and submucosal ganglia and in axon varicosities in both muscle layers in the small and large intestine in laboratory animals and humans (Costa et al., 1985; Polak et al., 1977). Endogenous opioids have been shown to be modulators of GI motility. Endogenous release of opioid peptides in the canine circular muscle layer suppresses or inhibits the release of inhibitory neurotransmitters and thereby increases contractile activity (Bauer & Szurszewski, 1991). Opioid peptides may act on prejunctional delta (δ)-opioid receptors to produce inhibition of NANC inhibitory neuromuscular transmission with a reduction in the amplitudes of the IJPs (Bauer & Szurszewski, 1991; Hoyle et al., 1990). During the peristaltic reflex, there is a decrease in the release of endogenous opioid peptides during the inhibitory phase of the peristaltic reflex and an increase during the excitatory phase (Grider, 2003; Grider & Makhlouf, 1987). In this way, normal levels of endogenous opioids may facilitate the ascending contraction and descending relaxation. Addition of increased levels of endogenous opioid peptides or selective opioid receptor agonists decreases the velocity of pellet movement by inhibiting the release of inhibitory neurotransmitters (Foxx-Orenstein et al., 1998). Addition of a δ-receptor antagonist increases the velocity of propulsion and has been shown to act synergistically with 5-HT. Serotonin (5-HT) acts on 5-HT_4 receptors on sensory cGRP nerve terminals, which then trigger the ascending and descending phases of the peristaltic reflex (Foxx-Orenstein et al., 1998; Grider, 2003). The opioid δ-receptor antagonist augments the peristaltic response by increasing the release of inhibitory neurotransmitters in the descending relaxation. Opioids may also act to inhibit neuronal release of excitatory neurotransmitters (Cherubini & North, 1985; Gintzler & Scalisi, 1982).

In contrast to the importance of endogenous opioids in facilitating peristaltic activity, exogenous opioids have been shown to induce nonpropulsive contractions. There are three major classes of opioid receptors, mu (μ), kappa (κ), and delta (δ), each being divided further into subtypes (Pasternak, 1993). Morphine's activation of μ_1 receptors in the brain and μ_2 receptors in the spinal cord is responsible for its analgesic effects, whereas the decrease in GI transit seen with systemic morphine administration is mediated primarily through μ_2 receptors located both centrally within the brain and peripherally in the myenteric nerve plexus (Pasternak, 1993). Although central and local opioid receptors may both contribute to postoperative ileus (POI), it is likely that GI receptors are the most important in mediating GI dysmotility (Thorn et al., 1996). Intramuscular morphine acting at peripheral receptors has been shown to enhance intrathecal morphine's delay of gastric emptying. Systemic administration of morphine has been shown to induce colonic electrical response activity (ERA), causing nonpropulsive spike bursts that interrupt normal migrating myoelectrical colonic complexes (Frantzides et al., 1992). It has been suggested that the degree of motility disturbances as a consequence of morphine use in horses is dose related. Whereas an IV dose of 0.5 mg/kg resulted in a decrease in fecal moisture content and propulsive motility for up to 6 h (Boscan et al., 2006a), a dose of 0.05–0.1 mg/kg a produced a decrease in GI motility (assessed by intestinal auscultation) for only 1–2 h (Figueiredo et al., 2012). The latter study suggested that a decrease in abdominal auscultation scores or borborygmus frequency occurs when plasma morphine concentrations are between 4 and 8 ng/mL. The use of epidural morphine (0.1 mg/kg) before laparoscopic cryptorchidectomy did not adversely affect GI transit in a randomized clinical trial study (Martin-Flores et al., 2014). However, epidural morphine (0.2 mg/kg) decreased the transit time in healthy horses (Sano et al., 2011).

Several strategies have been developed to achieve analgesia with opioid use while circumventing the motility disturbances attributed to μ-receptor agonists. κ-Opioid agonists have been identified that may provide sufficient visceral analgesia without the unwanted motility disruption of μ-agonists (Roger et al., 1994). An alternative approach being studied in humans that allows for the continued use μ-receptor agonists for pain management is the oral administration an opioid antagonist with poor GI absorption. The opioid antagonist blocks the GI actions of systemically administered opioids without interfering with the centrally mediated analgesic effects of the opioid (Taguchi et al., 2001). GI function returned earlier in postoperative patients given the oral opioid antagonist. Although these methods show promise, opioid-sparing analgesia, where nonsteroidal anti-inflammatory drugs (NSAIDs) have been used to reduce the amount of opioids required for pain management in patients, has improved overall GI motility in these patients and is one of the most effective ways to reduce POI in humans (Holte & Kehlet, 2000). In healthy horses, administration of the morphine antagonist *N*-methylnaltrexone (1 mg/kg IV q 12 h) in combination with morphine (0.5 mg/kg IV q 12 h) for 6 days partially prevented the effect of morphine on the GI tract by increasing defecation frequency, fecal weight, and fecal moisture content, and by preventing increases in transit time (Boscan et al., 2006a, 2006b).

Prostaglandins

Prostaglandins are synthesized throughout the GI tract and play a significant role in regulating GI motility. The functional role of prostaglandins in modulating motility in the normal intestine has been studied *in vitro* and *in vivo* by recording changes in contractile activity after administration of prostaglandin synthesis inhibitors such as indomethacin, and then adding selective prostaglandins and monitoring their effect on contractile activity. Drawing conclusions concerning the effect that prostaglandins have on motility is difficult since the effect of exogenous prostaglandins on motor activity varies depending on the type of prostaglandin, the dose, and the target tissue in the GI tract (Bennett et al., 1981; Burakoff et al., 1990; Sanders, 1984a, 1984b; Sanders & Szurszewski, 1981). For example, PGE_2 enhances *in vitro* contraction in longitudinal muscles but inhibits contraction in the circular muscle. PGI_2 will usually inhibit circular muscle contractions, with variable effects on longitudinal muscle. $PGF_2\alpha$ increases the contractile activity of both the circular and longitudinal muscles in the small and large intestine in most species studied (Bennett, 1976; Bennett et al., 1976, 1981; Sanders, 1984a, 1984b).

Nonselective blockage of the cyclooxygenase enzymes in the dog ileum produces an increase in both spontaneous contractile activity and responsiveness of muscles to acetylcholine stimulation mediated through an increase in slow-wave amplitude (Sanders, 1984a). In this model, both PGD_2 and $PGF_2\alpha$ were consistently shown to stimulate *in vitro* contractile activity of the ileal circular muscle. PGE_2 was found to inhibit large contractions but stimulated small contractions. Prostacyclin (PGI_2) consistently inhibited contractile activity by reducing the amplitude of the slow waves and consequently reducing the ability of the muscle to respond to excitatory stimuli. The most common prostaglandin metabolite found in the muscularis externa throughout the GI tract is 6-keto-$PGF_1\alpha$, the spontaneous breakdown product of PGI_2 (Bennett et al., 1981). Since nonselective prostaglandin blockage enhanced contractile activity, this suggests that the dominant endogenous prostaglandin effect in the canine ileum is due to inhibitory prostaglandins,

most likely PGI_2 and possibly PGE_2. In support of this, PGE_2 and PGI_2 infused into the superior mesenteric artery causes a dose-dependent inhibition of the MMC in the small intestine of dogs, whereas $PGF_2\alpha$ causes an increase in spiking activity (Thor et al., 1985). Blockage of all endogenous prostaglandins with indomethacin results in a marked increase in phase II and III of the MMC. The conclusion from these studies is that the net activity of the endogenous production of the prostaglandins appears to be a decrease in the excitability of the smooth muscle membrane resulting in inhibition of contractile activity. Other studies have contradictory findings. Prostaglandin synthesis inhibitors have been shown to decrease peristalsis in both the ileum and colon in the guinea pig (Bennett et al., 1976), whereas in the rabbit they have been shown to increase myoelectric activity in the ileum but to decrease it in the colon (Burakoff et al., 1990).

In vitro studies in the horse have been performed on the GI muscle from the large colon (Van Hoogmoed et al., 1999, 2000b). PGE_2 and $PGF_2\alpha$ enhanced contractile activity in the tenia coli and non-tenia coli longitudinal muscle whereas it decreased or had no effect on circular muscle activity. PGI_2 decreased contractile activity in the tenia colic and circular muscle whereas it had no effect on non-tenia coli longitudinal muscle. Of particular interest was the observation that *in vitro* application of NSAIDs such as phenylbutazone, flunixin meglumine, ketoprofen, and carprofen significantly decreased contractile activity regardless of location or muscle orientation (Van Hoogmoed et al., 1999, 2000b). These results suggest that in the equine large colon, the production of endogenous prostaglandins has a net excitatory effect on contractile activity. If this is true, nonselective blockade of prostaglandins may have an inhibitory effect on normal equine colonic motility. There are anecdotal data suggesting an association between the use of NSAIDs and large colon or cecal impactions (Dabareiner & White, 1995). However, *in vivo* studies on normal horses have not identified any motility disturbances when using myoelectric activity as a measurement of motility after administration of NSAIDs (Adams et al., 1984; Lester et al., 1998a; Roger & Ruckebusch, 1987). Compared with the significant inhibitory effect of prostaglandin blockade *in vitro* in colonic tissue, little effect, if any, is seen *in vitro* in small intestinal tissue. Although not examining the activity of prostaglandins specifically, *in vitro* studies have failed to demonstrate any inhibition of contractile activity during nonselective blockade of prostaglandin production when indomethacin was added to tissue baths containing equine small intestine circular or longitudinal muscle (Rakestraw et al., 1996, 2000). A more recent study found that selective α_2-agonists (xylazine, detomidine, and medetomidine) reduced spontaneous and electrically-evoked phasic contractions in equine jejunal circular smooth muscle strips (Zullian et al., 2011).

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Part II

Pathophysiology of Gastrointestinal Diseases

10

Pathophysiology of Gastric Ulcer Disease

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"Equine gastric ulcer syndrome" (EGUS) is a term which encompasses several disorders affecting the stomach. The causes of gastric ulcers are multifactorial and differ from the squamous mucosa to the glandular mucosa. Lesions in the gastric squamous mucosa (Figures 10.1 and 10.2) result primarily from excessive exposure to hydrochloric acid (HCl) (Widenhouse et al., 2002; Murray & Eichorn, 1996). This has been demonstrated by continuous or intermittent pH monitoring using pH electrodes placed in the stomach, and creating conditions that resulted in ulceration (Murray & Eichorn, 1996). One such model is the intermittent feed deprivation model, in which feed is withheld for 24 h, hay is freely available for 24 h, feed is withheld, and so on. Erosions in the gastric mucosa have been observed within 6 h of withholding feed, and histologic evidence of ulceration (loss of entire epithelium) was consistently seen after two 24 h periods of feed deprivation (Murray et al., 2001a). Other factors, including short-chain fatty acids, may contribute to damage to the gastric squamous epithelium, but HCl is the primary cause of mucosal injury.

The cause of ulcers in the gastric glandular mucosa is less well understood. Nonsteroidal anti-inflammatory drugs can cause gastric glandular mucosal ulcers in foals and horses, but the causes of spontaneous ulcers in this part of the stomach are undetermined. Excessive acid exposure does not appear to be a primary factor. In the aforementioned feed deprivation model, the investigators only rarely observed mild lesions in the glandular mucosa after four 24 h periods of feed deprivation. The prevalence of ulcers in the glandular part of the stomach differs by age and region. In foals, lesions, often severe, are observed throughout the glandular body and antrum of the stomach. In adult horses, lesions do occur in the body of the stomach, but there is a greater prevalence in the antrum (Figures 10.3 and 10.4) (Murray et al., 2001b).

Observations of lesions in the antral mucosa and histologic changes that resemble those associated with *Helicobacter pylori* infection in humans (lymphocytic/plasmacytic gastritis) have led to speculation that horses may harbor a pathogenic gastric *Helicobacter* species (Murray et al., 2003b). Studies looking for evidence of infection of equine gastric mucosa by *Helicobacter*-like organisms have yielded inconsistent results (Murray et al., 2003a; Scott et al., 2001; Husted et al., 2010; Contreras et al., 2007), and the role of these and other bacteria in equine gastric pathology remains to be determined.

There are several risk factors for gastric ulcers in horses, including feeding management and types of feeds, stall confinement, transportation, and undefined "stressors." Training has a significant impact on gastric ulceration (Murray et al., 1996), and gastric ulcers were induced even by treadmill training of research horses (Gordon et al., 2006). The prevalence and severity of gastric ulceration have been associated with the level of training (Gordon et al., 2006; Dionne et al., 2003; Vatistas et al., 1999), and in a study of Standardbred horses in training, ulcer prevalence and severity increased as the intensity of training increased (Dionne et al., 2003). The role of exercise/training in EGUS has not been clarified, but one study showed progressively increasing abdominal pressure corresponding with increased exercise intensity on a treadmill (Lorenzo-Figueras & Merritt, 2002). This was associated with compression of the stomach and exposure of the squamous epithelium to acidic gastric contents, leading to conjecture that this could contribute to the association between training and EGUS.

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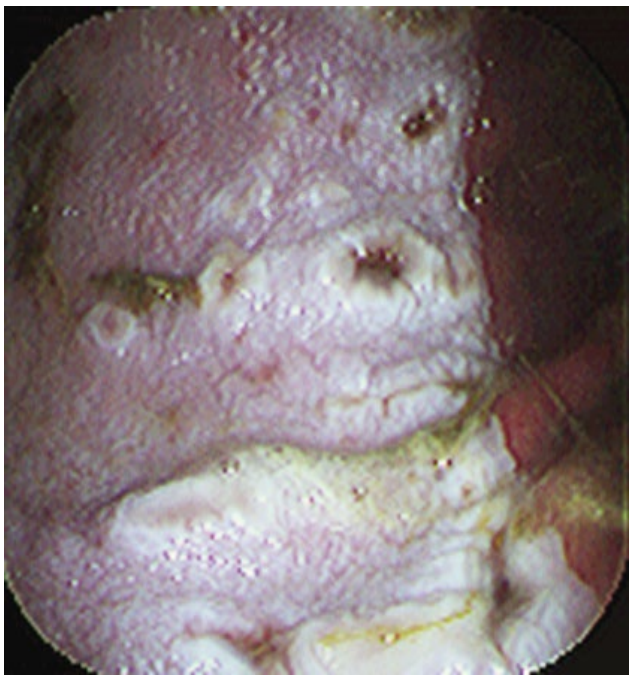

Figure 10.1 Small ulcers in the equine gastric squamous mucosa adjacent to the margo plicatus, along the right side of the stomach.

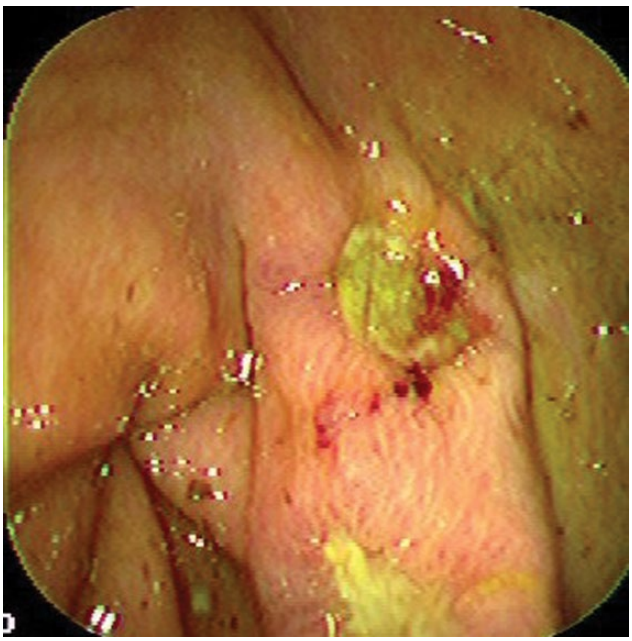

Figure 10.3 Ulcer in the mucosa of the antrum, near the pylorus.

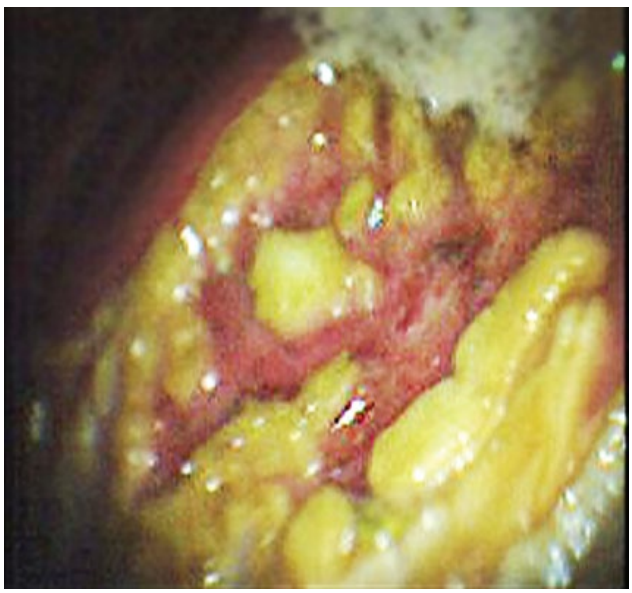

Figure 10.2 Large ulcer in the equine gastric squamous mucosa adjacent to the margo plicatus, ventral to the cardia. The adjacent mucosa is proliferative and hyperkeratotic (yellow), reflecting both healing mechanisms and continued acid injury.

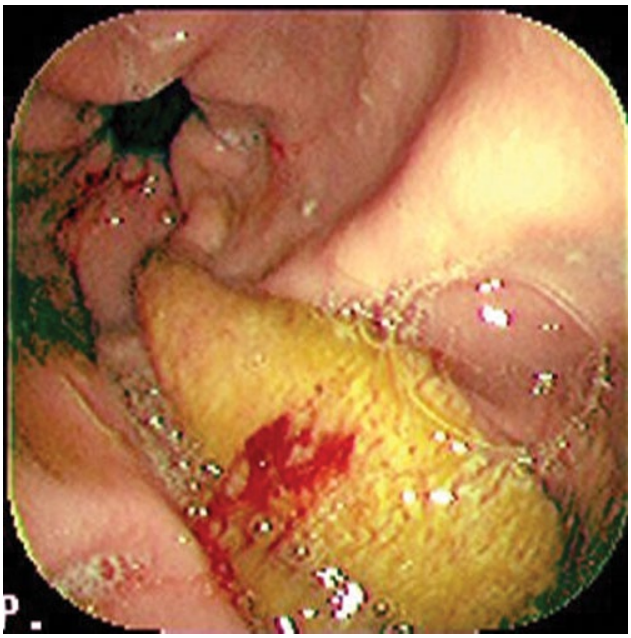

Figure 10.4 View of the antrum with thickening of a rugal fold and erosion of the mucosa with adherent exudate.

Risk factors for foals have not been well defined. Ulcers have been associated with infection with rotavirus, but it is likely that it is not a pathogen-specific association, but rather an association with enteritis and gastric changes related to delayed gastric emptying. Increased risk of ulceration of the gastric glandular mucosa has been demonstrated in foals with an illness or painful musculoskeletal condition (Furr et al., 1992). Weaning and transportation may be ulcer risk factors for foals, but this has not been documented.

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11

Pathophysiology of Gastrointestinal Obstruction and Strangulation

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Simple Obstruction

Simple obstruction of the intestinal lumen typically involves an intraluminal obstructive mass composed of ingesta or foreign material, such as bailing twine, a piece of hay net, or rubber fencing. Additionally, endogenously formed obstructive masses, specifically enteroliths, also cause simple obstruction. All of these obstructive masses block the passage of ingesta and secreted fluid, but they do not directly interrupt intestinal blood flow, at least during the early phases of obstruction. However, as simple obstructive masses persist, fluid, gas, and ingesta accumulate proximal to the mass, resulting in increased intraluminal pressure that ultimately compresses the intestinal intramural blood vessels, resulting in the onset of mural intestinal ischemia (Dabareiner et al., 1993, 2001b). Furthermore, obstructive masses may ultimately directly compress the intestinal wall surrounding them, particularly as masses are forced by propulsive intestinal motility distally into regions of the intestine having a smaller luminal diameter. For example, an enterolith formed in the distal aspect of the large colon may be small enough to reach the small colon, where it may fully occlude the lumen, and begin to induce mural pressure necrosis, leading to intestinal rupture in some cases (Hassel et al., 1999).

Pathophysiology of Increased Intraluminal Pressure

Interest in the pathophysiologic role of intestinal distension was initiated by a study indicating that the intraluminal hydrostatic pressure influenced the prognosis for survival from intestinal obstruction. Specifically, the hydrostatic pressure was markedly and significantly increased in horses with small intestinal obstruction that did not survive compared with values for horses that did survive. In that study, intraluminal pressures exceeding 15 cmH_2O correlated with a poor prognosis for survival (Allen et al., 1986). However, it was difficult to discern from that study the exact role of intraluminal distention because most of the horses that failed to survive had strangulating obstructions. Subsequently, studies have been conducted to assess the effects of intraluminal distention in the absence of overt obstruction of the vasculature. The results of initial experimental studies involving 4 h of distention at 18 cmH_2O indicated that there was no histological evidence of mucosal epithelial sloughing, as might be expected with ischemic injury (Allen et al., 1988). However, there was extensive edema in the lamina propria and villous central lacteals, and accumulation of neutrophils after reperfusion of the distended intestine (Figure 11.1). In addition, on electron microscopy, there was evidence of dilatation of paracellular spaces. The latter changes have more recently been shown to contribute to increased mucosal permeability, which may alter the fluid flux across the mucosa and result in absorption of bacterial toxins (Little et al., 2003; Blikslager et al., 2000).

More recent studies have examined the effects of small intestinal intraluminal distention and decompression on the microvasculature. For example, distention of the jejunum to an intraluminal hydrostatic pressure of 25 cmH_2O for 120 min resulted in a significant reduction in the number of perfused vessels in the seromuscular and mucosal layers, and vascular perfusion remained abnormal after decompression (Dabareiner et al., 1993). Furthermore, during distention, blood flow to the intestine was reduced by 50%, and microvascular permeability increased after decompression, suggesting that reperfusion injury was occurring in the intestine (Dabareiner et al., 2001b). Interestingly, the reperfusion injury appeared to have the greatest effect on the seromuscular layer, which had evidence of mesothelial cell loss,

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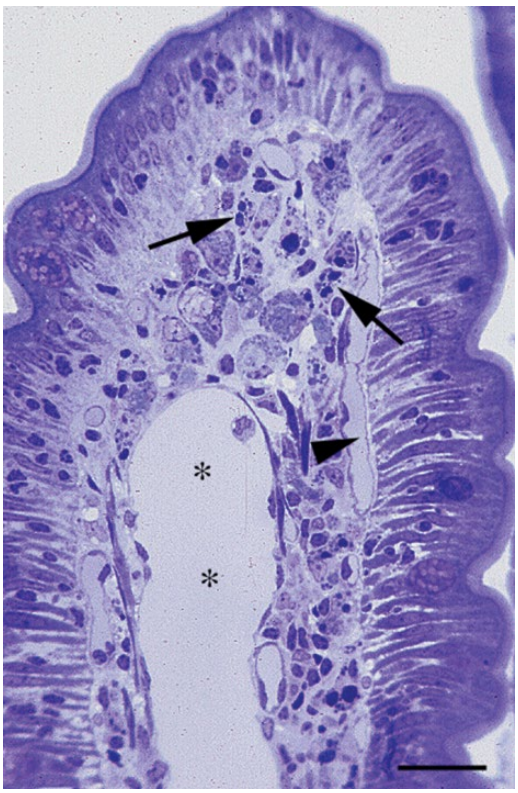

Figure 11.1 Photomicrograph of jejunal villi showing dilatation of the central lacteal (asterisks), subepithelial edema (arrowhead), and neutrophil infiltration (arrows) that occurs following reperfusion of dilated small intestine. Bar = 30 µm.

neutrophil infiltration, and edema. These types of inflammatory seromuscular lesions have also been noted in studies of the proximal resection margins of naturally occurring small intestinal strangulating obstructions (Figure 11.2), confirming that distention leads to seromuscular injury proximal to obstructive lesions, despite the fact that this intestine may appear grossly normal (Gerard et al., 1999). Experimentally, this seromuscular injury and inflammation lead to adhesion formation. For instance, foals subjected to intraluminal distention of a segment of jejunum to 25 cmH_2O for 2 h developed bowel-to-bowel and bowel-to-mesentery adhesions within 10 days after the surgical procedure (Lundin et al., 1989). Similar experiments performed using the large colon revealed that the colon is far more resistant to a comparable seromuscular injury than the small intestine (Dabareiner et al., 2001a).

Strangulating Obstruction

Strangulating obstruction results from simultaneous occlusion of the intestinal lumen and its blood supply. Thus, all of the pathophysiologic features of simple obstruction, including the effects of intraluminal distention, occur during strangulating obstruction, but the severity of injury induced by occlusion of the blood supply is more rapid in onset and of a greater magnitude that that caused by distention alone. Nonetheless, distention at the periphery of a strangulating lesion can induce injury that is difficult to detect, and therefore resection margins may not be as normal as they appear grossly (Gerard et al., 1999). The degree of injury attributable to occlusion of the blood supply is highly variable, depending upon the nature of the vascular occlusion. In most instances, the veins are occluded earlier than the arteries in the course of strangulating obstruction because of their thinner, more compliant walls and the lower hydrostatic pressure in the veins. This results in a disparity in blood flow during the early phases of strangulating

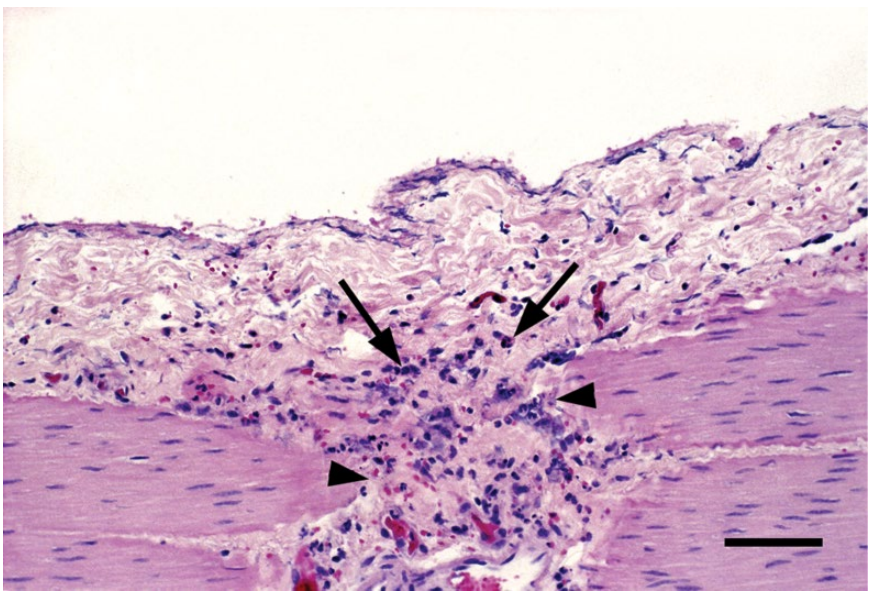

Figure 11.2 Photomicrograph of the seromuscular layer of a proximal resection margin of jejunum from a horse with strangulating obstruction of the small intestine. Although the jejunal resection margin appeared grossly normal at surgery, mesothelial cell loss and infiltration of neutrophils (arrows) is apparent. In addition, neutrophils appear to penetrate the muscular tissue layers via anatomic divisions (septa) in the outer longitudinal layer (arrowheads), which may have an effect on muscular function. Bar = 100 µm.

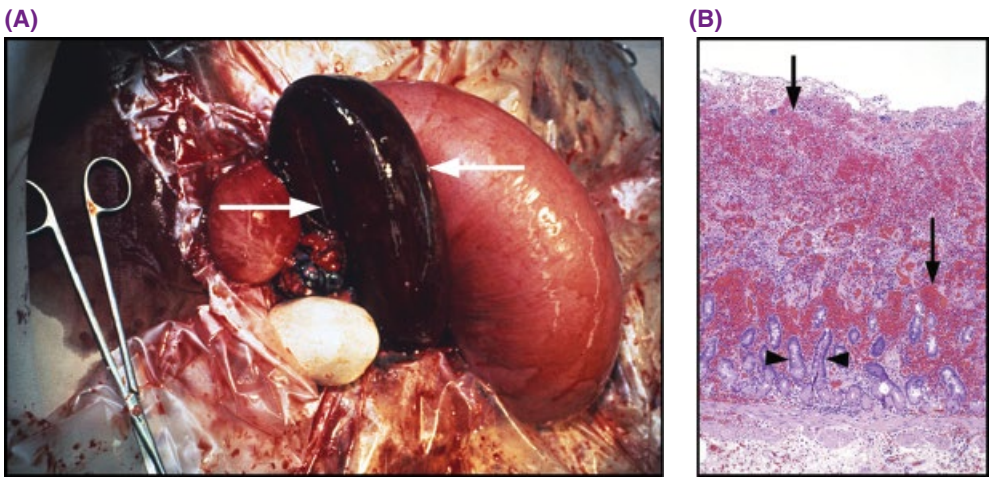

Figure 11.3 Gross and morphologic appearance of hemorrhagic strangulating obstruction. **(A)** Strangulating obstruction of the equine jejunum, in which a pedunculated lipoma has wrapped around a segment of jejunum. Note the dark appearance of the bowel (arrows) indicative of arterial flow trapped within the tissues during development of the lesion. **(B)** Photomicrograph of the mucosa from a horse with hemorrhagic strangulating obstruction. Note the extensive hemorrhage throughout the tissues (arrows), with extensive disruption of mucosal architecture. Crypts remain relatively protected deep within the mucosa (arrowheads), partly as the result of a separate blood supply to this area of the mucosa.

obstruction, with continued delivery of arterial blood into the intestinal wall, which, in the absence of patent outflow, causes a hemorrhagic lesion termed hemorrhagic strangulating obstruction. This results in ischemic injury, but also in tremendous congestion of the tissues (Figure 11.3). Such hemorrhagic congestion has two opposing effects: it disrupts the tissue architecture, including the mucosa and its epithelium, but it continues to provide oxygenated blood to the tissues during the early stages of the ischemic episode. Alternatively, the strangulation may exert enough pressure on the veins and arteries to occlude both simultaneously, resulting in so-called ischemic strangulating obstruction. This results in rapid degeneration of the mucosa (Meschter et al., 1986). For example, in experimental large colon volvulus, near-complete mucosal degeneration developed within 3 h after the vasculature was occluded (Snyder et al., 1988). Compared with hemorrhagic strangulating obstruction, intestine undergoing ischemic strangulation obstruction has a pale appearance. From a clinical standpoint, this makes it difficult to assess the degree of mucosal injury in horses with strangulating injuries, because intestine that appears nonviable (dark red) may in fact have less mucosal injury than that of ischemic strangulated intestine (Gerard et al., 1999).

Mucosal Ischemic Injury

To understand how the mucosa becomes injured during ischemia, critical anatomic features of the mucosa have to be taken into consideration. In the equine small intestine, the villus tip is the most susceptible region to ischemia, largely due to the countercurrent exchange mechanism of blood flow in the small intestinal villus (Gonzalez et al., 2015b). This countercurrent exchange mechanism is attributable to the vascular architecture, which consists of a central arteriole that courses up the core of the villus, arborizes at the tip, and is drained by venules coursing down the periphery of the villus (Dart et al., 1992). As oxygenated blood enters the central arteriole, oxygen diffuses across the wall of the arteriole across the interstitial tissues and into the peripheral venules, in which blood is flowing in the opposite direction (Figure 11.4). This short-circuits the oxygen supply, resulting in a villus tip that is relatively hypoxic even under normal conditions. Countercurrent exchange is exacerbated when the rate of the arterial blood flow is reduced, essentially providing more time for the oxygen to diffuse out of the arteriole across to the venules. When the arterial flow is reduced to a critically low level, the tip of the villus becomes hypoxic, with attendant epithelial injury (Chiu et al., 1970; Gonzalez et al., 2015b). This mechanism might explain why the small intestinal mucosa is more susceptible to ischemic injury than the colon, which lacks villi. For instance, the duration of ischemia required to produce severe morphologic damage to the equine colon is approximately 25% longer than for the small intestine (Snyder et al., 1988).

Mucosal epithelium is particularly susceptible to hypoxic injury because of the relatively high level of energy required to fuel the Na^+,K^+-ATPase that regulates epithelial ion and nutrient transport. The first biochemical event to occur during hypoxia is a loss of oxidative phosphorylation. The resulting diminished ATP concentration causes failure of the energy-dependent Na^+,K^+-ATPase, resulting in intracellular accumulation

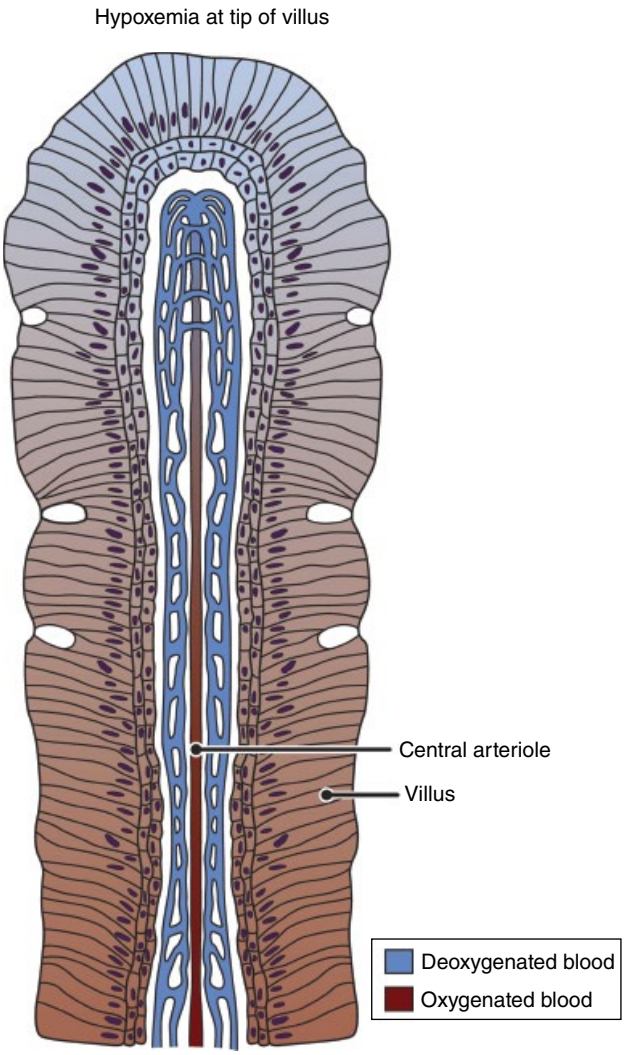

Figure 11.4 Schematic depiction of the countercurrent exchange system in small intestinal villi, during which oxygen from the central arteriole diffuses across the lamina propria to the peripheral villous venous supply, thereby depriving the villous tip of oxygen during low-flow states.

of sodium, and subsequently water. The pH of the cytosol decreases as lactic acid and inorganic phosphates accumulate from anaerobic glycolysis. The falling pH damages cell membranes, including lysosomal membranes, resulting in the release of lysosomal enzymes into the cytosol, further damaging cell membranes. Damage to the cell membranes allows the accumulation of high concentrations of calcium in the cytosol, which activates calcium-dependent degradative enzymes (McAnulty et al., 1997). These events result in cytoplasmic blebbing of the basal membrane, with subsequent detachment of cells from that membrane.

Studies on epithelial injury during ischemia suggest that epithelial cells undergo programmed cell death (apoptosis). For example, in one study in which the equine colon was subjected to 1 h of ischemia, epithelial

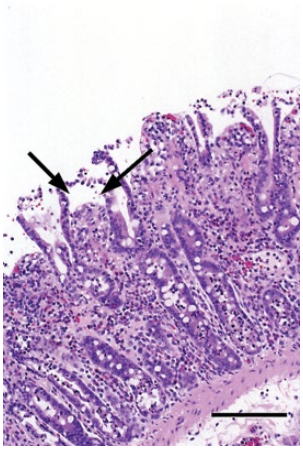

Figure 11.5 Photomicrograph of ileal mucosa subjected to 1 h of complete ischemia. Note the formation of Gruenhagen's space (arrows) with fluid trapped between an intact epithelial layer and the basement membrane. The formation of this space is exacerbated by active contraction of the villi. Bar = 100 µm.

cells had evidence of apoptosis, disintegration of microvilli, widening of interepithelial spaces and separation from the basement membrane (Grosche et al., 2011). Interestingly, epithelial injury was not worsened by reperfusion, but infiltration of inflammatory cells, including neutrophils and eosinophils, was noted (Grosche et al., 2011), and such infiltration has been associated with additional injury in equine mucosa in other studies (Moore et al., 1994b).

As epithelium separates from the underlying basement membrane in the small intestine, a fluid-filled space termed Gruenhagen's space forms at the tip of the villus (Figure 11.5) (Chiu et al., 1970). The mechanism of fluid accumulation in this space is not entirely understood, but may result from continued epithelial absorption of NaCl and water, before the cells have fully detached. The fluid accumulation likely exacerbates epithelial separation from the basement membrane. Subsequently, epithelial cells progressively slough from the tip of the villus toward the crypts, which are the last component of the intestinal mucosa to be injured (Arden et al., 1989, 1990).

The relative resistance of the crypts to injury likely relates to the vascular architecture, as the crypts have a blood supply that is separate from the vasculature involved in the villus countercurrent exchange mechanism. The early morphologic changes observed in the equine large colon during ischemia are similar to those described for the equine small intestine, with initial loss of the more superficially located surface cells, followed by cellular injury and sloughing within the crypts (Meschter et al., 1991; Snyder et al., 1988). The orderly progression of tissue injury has been used to predict accurately survival in horses with large colon volvulus. Biopsies were taken from the pelvic flexure, which has

previously been shown to reflect accurately mucosal changes along the length of the colon (Van Hoogmoed et al., 2000b), and histologically examined for the width of the crypts and intercrypt interstitial space. The latter measurements were expressed as an interstitium-to-crypt width (I : C) ratio. Nonviable colon was defined as that which had >60% loss of crypts and an I : C ratio >3. Using this methodology, survival was correctly predicted in 94% of horses (Van Hoogmoed et al., 2000a). In a more recent study, an I : C ratio of >1 and an increased colonic mucosal hemorrhage score of 3 (on a scale of 0–4, with 3 denoting clumping of red blood cells in the mucosal lamina propria) were significantly associated with nonsurvival, whereas measures of mucosal epithelial loss were not predictive of survival (Gonzalez et al., 2015a). The difference in utility of mucosal epithelial loss in the study by Gonzalez et al., as compared with the study by Van Hoogmoed et al., was attributed in part to the difficulty of obtaining accurate measurements because of poor definition between sloughing epithelium and the underlying basement membrane using routine histological evaluation of mucosal biopsies (Gonzalez et al., 2015a). Because histological evaluation of mucosal biopsies is impractical during colic surgery, efforts are under way to determine if the visible color of the colon can be correlated with the hemorrhage score, and ultimately with survival (L. M. Gonzalez et al., unpublished data). One additional finding from the study by Gonzalez et al. (2015a) is that resection of injured colon in horses with large colon volvulus did not influence survival compared with manual reduction alone, although prospective randomized controlled trials would be needed to investigate this finding fully.

Reperfusion Injury

Intestinal reperfusion injury originally was characterized in a series of basic science studies performed in feline and rodent models, during which it was shown that ischemic injury was markedly worsened by reperfusion (Granger et al., 1986; Granger, 1988; Grisham et al., 1986; Kubes et al., 1992; Nilsson et al., 1994; Schoenberg et al., 1991). The concept of further injury developing during reperfusion initially seemed counterintuitive, as reperfusion with oxygenated blood was predicted to rescue degenerating mucosa. However, it was the oxygen itself that was indirectly responsible for triggering the additional injury.

Events that culminate in reperfusion injury in the small intestine are initiated during ischemia when the enzyme xanthine dehydrogenase is converted to xanthine oxidase, and its substrate, hypoxanthine, accumulates due to adenosine triphosphate (ATP) utilization (Moore et al., 1995b; Gonzalez et al., 2015b). However, there is little xanthine oxidase activity during ischemia, because

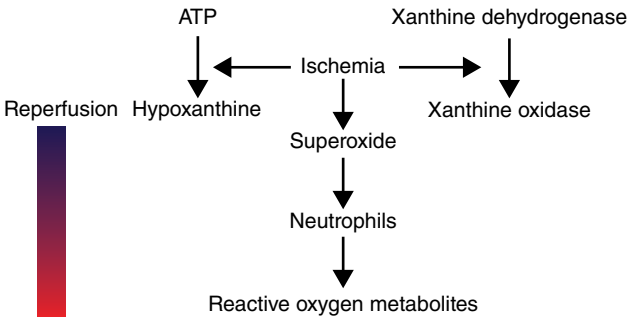

Figure 11.6 Diagram of the events that occur during ischemia-reperfusion injury, resulting in formation of reactive oxygen metabolites. As oxygenated blood is returned to tissues (depicted by the color gradient during reperfusion), reactive oxygen metabolites are generated. Neutrophils, which are attracted to the cells producing these metabolites, generate more reactive oxygen metabolites.

oxygen is required as an electron acceptor. During reperfusion, xanthine oxidase rapidly degrades hypoxanthine in the presence of oxygen, which acquires a single additional electron, producing superoxide (Figure 11.6) (Moore et al., 1995b). Superoxide contributes to oxidative tissue damage, but this reactive oxygen metabolite is relatively lipid insoluble, limiting the level of injury. However, the more important role for superoxide is in the generation of neutrophil chemoattractants (Granger, 1988; Grisham et al., 1986). Superoxide interacts with lipid membranes, triggering arachidonic acid metabolism as it seeks to couple its unpaired electron. For example, the arachidonic acid metabolite leukotriene B_4, produced by the lipoxygenase pathway, serves as a chemoattractant that also activates neutrophils. Because of the critical role of xanthine oxidase, inhibition of this enzyme in feline studies of intestinal ischemia-reperfusion injury prevented infiltration of neutrophils, and subsequent mucosal injury (Grisham et al., 1986; Nilsson et al., 1994). Subsequent studies demonstrated that reperfusion injury could be inhibited at several levels of the reperfusion cascade, including scavenging superoxide with superoxide dismutase, inhibiting neutrophil infiltration with monoclonal antibodies directed against neutrophil adhesion molecules, and scavenging neutrophil-released reactive oxygen metabolites (Grisham et al., 1986). Researchers were initially optimistic that this would provide practical therapeutic interventions, because many of the treatments tested, including the xanthine oxidase inhibitor allopurinol, could potentially be administered prior to reperfusing ischemic tissue during surgery.

Unfortunately, treatment of reperfusion injury has not proven to be highly effective at reducing the level of mucosal injury in most cases of strangulating obstruction. One important reason for this is that strangulating obstruction induces maximal mucosal injury during the

ischemic phase, as compared with studies in laboratory animals in which "low-flow" ischemia was used (Blikslager et al., 1997a). The latter involves reduction but not cessation of arterial flow, which induces relatively minor levels of injury, while priming tissues for injury during subsequent reperfusion (Kubes et al., 1992; Parks & Granger, 1986). Studies in horses using low-flow ischemia indicate that equine tissues are susceptible to reperfusion injury following this type of ischemia (Dabareiner et al., 1993, 1995; Moore et al., 1994b, 1994c). For instance, studies in equine jejunum have shown that there is increased capillary permeability associated with neutrophil infiltration during reperfusion (Dabareiner et al., 1995). Although a direct link to xanthine oxidase has not been proven, equine small intestine expresses substantial levels of xanthine dehydrogenase, which is converted to xanthine oxidase during ischemia (Prichard et al., 1991). Low-flow ischemia studies in equine colon have documented that mucosal degeneration continues during reperfusion associated with marked neutrophil infiltration, despite the fact that the equine colon does not express appreciable levels of xanthine oxidase. Alternative oxidant enzyme sources, such as aldehyde oxidase, have been offered as potential sources for the reactive oxygen metabolites (Moore et al., 1994b).

Having shown the capacity of equine tissues to develop reperfusion injury, additional studies have been performed to determine if reperfusion injury occurs in clinically applicable models of ischemia that simulate strangulating obstruction. For example, in one study assessing either arteriovenous or venous occlusion in equine jejunum, a small degree of reperfusion injury was documented after 3 h of ischemia (White et al., 1980). However, the level of ischemic injury was near maximal after 3 h, and the additional injury developed during reperfusion was not sensitive to either allopurinol, a xanthine oxidase inhibitor, or dimethyl sulfoxide (DMSO), a reactive oxygen metabolite scavenger (Horne et al., 1994). The likely cause of reperfusion injury in this instance was initiation of epithelial injury during ischemia, including initiation of apoptosis that could not be reversed during reperfusion (McAnulty et al., 1997; Grosche et al., 2011). Studies of morphologic changes occurring with total arteriovenous occlusion (including obstruction of blood flow through the bowel wall) documented initial mucosal cell loss with subsequent loss and necrosis after reperfusion. Intraluminal administration of oxygen was effective in decreasing the progressive morphologic change during the period of reperfusion (Moore et al., 1980). Studies in equine small intestine (Laws & Freeman, 1995) and studies in equine colon (Reeves et al., 1990; Grosche et al., 2011) using ischemic models relevant to strangulating obstruction have failed to detect any level of reperfusion injury. Studies of strangulating obstruction in laboratory animals have also shown that this type of ischemic insult is less likely to result in reperfusion injury (Haglund, 1994; Park et al., 1990).

There are also other species-specific factors that may affect the potential for equine tissues to develop reperfusion injury. For example, the foal appears to have very low concentrations of xanthine oxidase in the small intestine (Blikslager et al., 1997a), whereas concentrations in adult horses are much greater, particularly in the proximal small intestine (Prichard et al., 1991). In addition, horses appear to have low numbers of resident neutrophils in the intestinal mucosa (Blikslager et al., 1997a), and it is this population of neutrophils (rather than those recruited from the circulation) that appear to be most critical for induction of reperfusion injury (Kubes et al., 1992). The increases in neutrophils in both the mucosa and serosa in horses after ischemia-reperfusion suggest that neutrophils from the systemic circulation localize in the injured tissues (Dabareiner et al., 2001a).

In a review of the pathogenesis of intestinal reperfusion injury in the horse, the concept of a therapeutic window wherein treatment of reperfusion injury would be beneficial was suggested (Moore et al., 1995b). The basis for this concept is that there are certain conditions under which ischemic injury is minimal, and that tissues are severely damaged during reperfusion (Park et al., 1990). Thus, under conditions of low-flow ischemia, very little injury is evident during 3 h of ischemia, but remarkable injury occurs after 1 h of reperfusion (Granger, 1988; Grisham et al., 1986; Nilsson et al., 1994). However, a very narrow therapeutic window may exist under conditions of strangulating obstruction where severe injury occurs rapidly during ischemia, thereby limiting the prevention of further injury with treatments such as antioxidants. Nonetheless, this does not mean that treatments directed against reperfusion injury have no potential place for the treatment of horses with strangulating obstruction, particularly as new treatments become more effective. For example, multimodal therapies involving intravascular or intraluminal infusion of solutions containing antioxidants, intestinal nutrients, and vasodilators have proven very effective *in vitro* and *in vivo*, although these treatment modalities have been used predominantly in low-flow ischemia models (Table 11.1). It is also becoming clear that the consequences of reperfusion injury are more widespread, and involve tissues other than the intestinal mucosa. For instance, low-flow ischemia models have demonstrated neutrophil infiltration into the serosa (Figure 11.7) that likely contributes to important complications such as adhesions (Lundin et al., 1989; Nieto et al., 2002).

Table 11.1 Partial listing of therapeutics that have been used experimentally for the treatment of ischemia-reperfusion injury in horses.

Therapeutic	Segment of intestine	Type of ischemia	Time of ischemia-reperfusion	Effect of treatment on mucosa	Ref.
DMSO	Jejunum	Arterial occlusion	1 h/1 h	None	Arden et al., 1989, 1990
Superoxide dismutase	Jejunum	Anoxia (*in vitro*)	15 min/15 min	Reduced injury	Johnston et al., 1991
Allopurinol DMSO Intraluminal O_2 insufflation	Jejunum	Venous obstruction Ateriovenous obstruction	3 h/1 h	None (treatments evaluated separately)	Horne et al., 1994
U-74389G (21-aminosteroid)	Jejunum	Arteriovenous obstruction Low flow	2 h/2 h 2 h/2 h	None None	Vatistas et al., 1993, 1996
Carolina rinse[a)]	Jejunum	Low flow Low flow/no flow Distention/decompression	1 h/1 h 2 h/10 days 1 h/1 h	Reduced microvascular injury Decreased serosal fibroplasia None	Young et al., 2002 Dabareiner et al., 2003
Custom solution[b)]	Jejunum	Low flow (*in vitro*)	40 min/60 min	Reduced injury	Van Hoogmoed et al., 2001, 2002
Lidocaine	Jejunum	Strangulating obstruction	2 h/18 h	Reduced injury	Cook et al., 2008
DMSO	Large colon	Venous obstruction Ateriovenous obstruction	1 h/1 h	None	Reeves et al., 1990
U-74389G (21-aminosteroid)	Large colon	Arteriovenous obstruction	2 h/2 h	Prevented reductions in mucosal surface area	Vatistas et al., 1993
WEB 2086 (PAF[c)] antagonist)	Large colon	Strangulating obstruction (720° volvulus)	3 h/3–5 h	None	Wilson et al., 1994
DMSO Allopurinol U-74389G (21-aminosteroid) Manganese chloride	Large colon	Low flow	3 h/3 h	None (all treatments evaluated separately)	Moore et al., 1995a
High molecular weight dextran macromolecules	Large colon	Low flow	3 h/3 h	None	Moore et al., 1996, 1998
L691880 (PAF[c)] antagonist)	Large colon	Low-flow	3 h/3 h	None	Moore et al., 1998

a) Carolina rinse solution contained allopurinol, deferoxamine, glutathione, glucose, fructose, glycine, nicarpidine, and adenosine.
b) Custom solution contained allopurinol, deferoxamine, DMSO, glutamine, dextrose, PGE1, and adenosine.
c) Platelet activating factor.

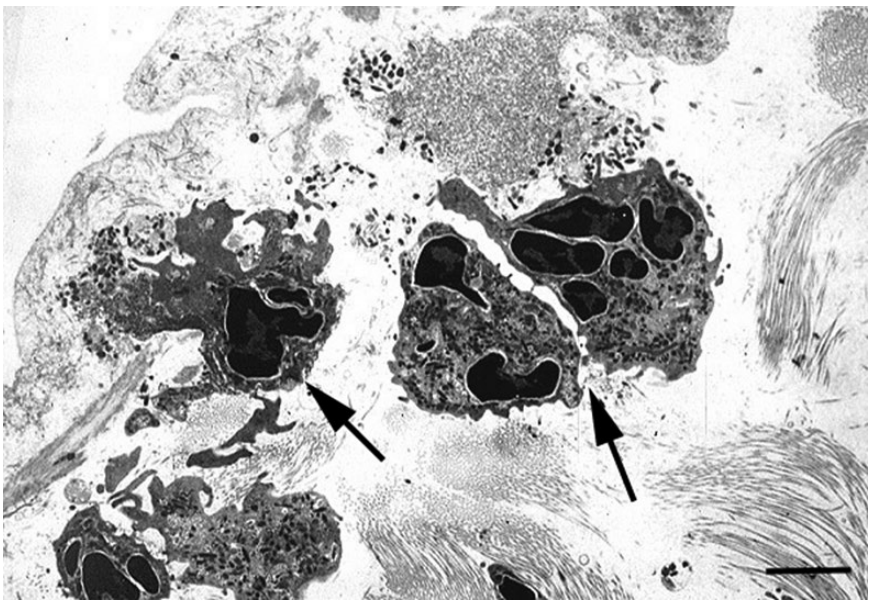

Figure 11.7 Transmission electron micrograph of neutrophil infiltration into the serosa of intestine injured by ischemia-reperfusion. Neutrophils (arrows) are actively degranulating, contributing to serosal injury. Note the lack of mesothelial cells on the edge of the serosa. Bar = 5 µm.

This neutrophil infiltration appears to be relevant to strangulating obstruction, because similar neutrophil infiltrates were noted in the resection margins of strangulated small intestine (Gerard et al., 1999). Thus, although antioxidant-based therapies may be unable to reduce mucosal injury owing to its rapid onset during ischemia, both immediate and subsequent treatments may be able to reduce neutrophil infiltration in other layers of the intestine. In addition, once strangulated intestine has been reperfused, even if there is no reperfusion injury to the mucosa during the early phases of reperfusion, there may be injury to the mucosa associated with inflammation that develops during mucosal wound healing. For example, in a study using a porcine model of strangulating obstruction, there was no evidence of neutrophil infiltration or further mucosal injury during 1–3 h of reperfusion after a 1 h period of ischemia, but there was significant neutrophil infiltration between 4 and 18 h after reperfusion (Gayle et al., 2002). These neutrophils collected beneath repairing epithelium, and rendered this repairing mucosa more permeable to macromolecules. Interestingly, this injury was inhibited by treatment at the time of reperfusion with superoxide dismutase [complexed with poly(ethylene glycol) to prolong its half-life], or with a monoclonal antibody directed against critical neutrophil adhesion molecules (CD11/CD18) (Gayle et al., 2002). Neutrophil infiltration of the mucosa was also reported in the horse during reperfusion after low-flow ischemia (Figure 11.8) (Dabareiner et al., 2005). Interestingly, manipulation of the equine colon in the absence of ischemia, including manual evacuation of the colon via an enterotomy, also resulted in accumulation of neutrophils in all layers of the colon

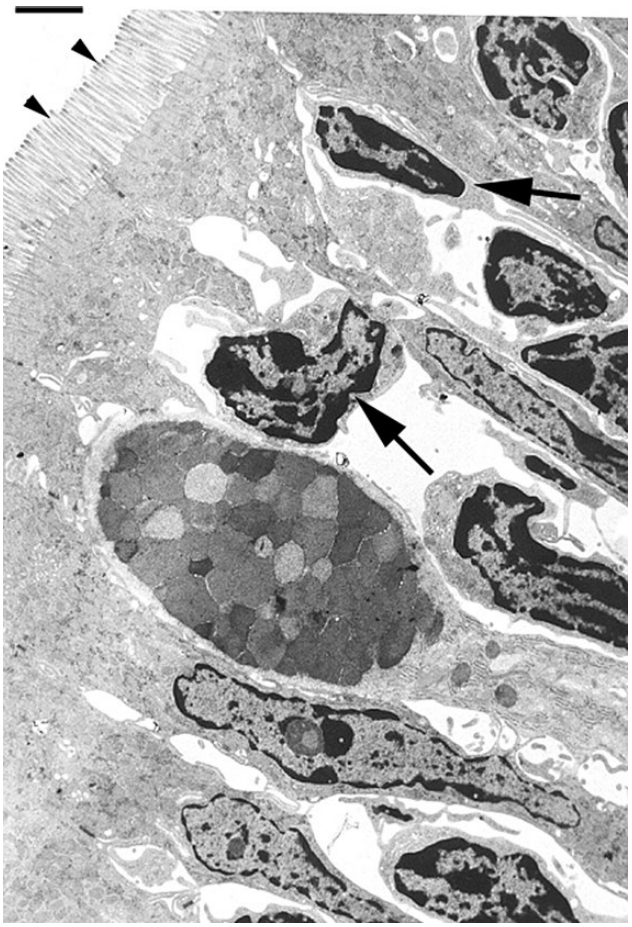

Figure 11.8 Photomicrograph of neutrophil infiltration into mucosal epithelium following ischemia-reperfusion of equine jejunum. The microvillus brush border of mucosal epithelium is marked with arrowheads. Neutrophils (arrows) physically separate epithelial cells as the infiltrate the mucosa and ultimately traverse the epithelium into the intestinal lumen. Bar = 5µm.

(Hopster-Iversen et al., 2011), suggesting that studies assessing ischemia-reperfusion injury may be partially inducing neutrophil accumulation during surgical preparation of the bowel.

Intestinal Reparative Mechanisms

Mucosal Barrier Function

Before detailing mechanisms by which intestinal mucosa is repaired, it is important to understand regulation of mucosal integrity under physiologic conditions, otherwise commonly referred to as mucosal barrier function. Intestinal barrier function is vital because it prevents bacteria and associated toxins from gaining access to subepithelial tissues and the circulation. However, the mucosa has two conflicting functions: it must serve as a protective barrier while continuing to absorb solutes necessary to maintain the host. This conflict is most notable at the intercellular (paracellular) space, which allows passage of select solutes and water but which does not admit large molecules, including bacterial toxins (Shen et al., 2011; Turner & Turner, 2010) (see Chapters 4 and 5). The paracellular space is almost exclusively regulated by tight junctions, which are the interepithelial junctions at the apical-most aspect of the paracellular space (Marchiando et al., 2010). Although these tight junctions were originally viewed as inert cellular adhesion sites, it has become clear in recent years that tight-junction permeability is dependent on tissue-specific molecular structure, and is regulated by a complex array of intracellular proteins and the cytoskeleton (Van Itallie & Anderson, 2014). Tight junctions consist of a group of transmembrane proteins that interdigitate from adjacent cells, including occludin and a group of tissue-specific proteins called claudins (Van Itallie & Anderson, 2013). These transmembrane proteins interact with the cytoskeleton via a series of tight-junction plaque proteins, including zonula occludens (ZO)-1, ZO-2, and ZO-3 (Van Itallie & Anderson, 2014). In general, the relative contractile state of the actin cytoskeleton determines the degree to which tight junctions are open or closed, and this in turn is dependent on the activation of plaque proteins and a range of intracellular signaling molecules (Mitic et al., 2000). Tight-junction function also is dependent upon the anatomical location. For example, tight junctions in the crypts leak more than those in the surface epithelium because of fewer and less organized tight-junction strands (Tice et al., 1979). Conversely, surface epithelium has a greater number of well-organized tight-junction strands that result in epithelium with a relatively high resistance (Marchiando et al., 2010). This correlates well with the absorptive function of epithelium located on the mucosal surface and the secretory function of crypt epithelium. The structure of tight junctions also varies with the segment of intestine. For instance, tight junctions in the ileum have more strands than those in the jejunum, which is reflected by a higher transepithelial resistance in the ileum (Marcial et al., 1984).

Aside from interepithelial tight junctions, the other components of the mucosal barrier are the apical epithelial membrane and an adherent layer of mucus. The apical membrane is far less permeable than adjacent tight junctions in the small intestine, which has a relatively "leaky" barrier. Conversely, colonic mucosa is far less permeable than the small intestine, largely because colonic tight junctions are less permeable to ions and macromolecules than tight junctions in the small intestine (Madara & Marcial, 1984). Because of the relative impermeability of the apical epithelial membrane, an array of distinct protein transporters is present that selectively allow entry of specific ions, nutrients, and water. Although the apical epithelial membrane provides a stringent barrier against potentially harmful luminal contents, including bacteria and their toxins, some pathogenic bacteria have developed specific mechanisms for penetrating the apical membrane. For example, *Salmonella typhimurium* can penetrate the apical membrane using a type III secretion apparatus, which allows the insertion of bacterial proteins into the host cell (Sears, 2000).

Mucus, secreted by goblet cells, adheres to the microvilli on the apical epithelial membrane, forming the so-called unstirred water layer. The most critical barrier-forming component of mucus is mucin, glycoproteins that provide the viscoelastic properties required to maintain a continuous protective layer over the mucosa during intestinal motility and secretion. This mucus protective layer prevents bacterial organisms from adhering to the apical epithelial membrane as a result of its physical properties, including electrical charge (Allen et al., 1993). The importance of this component of the barrier is highlighted by studies showing that pathogenic bacteria adhere to and invade intestinal epithelium in the absence of the unstirred water layer (Dial et al., 2002). Perhaps the most relevant cause of diminished mucus barrier function is surgical stress, although the reasons for reduced mucus formation after abdominal surgery are not clear. Interestingly, the mucus layer can be reconstituted in surgical patients by administration of exogenous gel-forming compounds such as high molecular weight poly(ethylene glycol) (Wu et al., 2004).

Villus Contraction and Restitution

In the small intestine, villi contract during injury (Figure 11.5) and during the reparative phase after injury in order to reduce the size of the epithelial defect. Villus

contraction that commences during injury is mediated by enteric nerves, and the contractile element is a series of myofibroblasts situated immediately beneath the epithelial basement membrane (Moore et al., 1989). Once the injurious event has subsided, such as correction of a strangulating lesion, villus contraction continues to a lesser extent, as a result of prostaglandin-mediated contraction of smooth muscle cells that line the central villus lacteal (Erickson et al., 1990). The initial phase of contraction that occurs during injury is very important for mucosal repair; inhibition of this process by blocking enteric nerve conduction delays repair of the mucosal defect (Moore et al., 1989). However, the subsequent phase of villus contraction that continues during early mucosal repair under the influence of prostaglandins appears to have little effect on the speed of mucosal recovery. For example, treatment of acutely injured small intestine with a non-elective cyclooxygenase (COX) inhibitor prevented ongoing villus contraction, but this had no discernible effect on mucosal repair (Gookin et al., 2002).

As villi contract, assuming that there is an intact basement membrane, epithelial cells from the margins of the wound migrate in a centripetal direction to resurface toward the tip of the villus, a process called restitution (Moore et al., 1989). Restitution also occurs in denuded colonic mucosa, except that it may proceed more rapidly because of the lack of villi (Argenzio et al., 1988). Epithelial restitution is solely a migratory event that does not depend on the provision of new enterocytes by proliferation. Cellular migration is initiated by extension of cellular lamellipodia that receive signals from the basement membrane via cell-surface integrins (Figure 11.9). Intracellular signaling converges on the actin cytoskeleton, which is responsible for movement of lamellipodia. Specific components of the basement membrane appear to be critical to the migratory process. For example, application of antibodies to collagen types III and IV, which are important components of the intestinal mucosal basement membrane, impedes epithelial restitution (Moore et al., 1992, 1994a). Other elements of the basement membrane, including proteoglycans, hyaluronic acid, and noncollagenous proteins such as fibronectin and laminin, may also provide important signals (McCormack et al., 1992). These subepithelial matrix components that facilitate restitution may form the basis for clinical treatments designed to speed the repair process, analogous to administration of matrix components to horses with articular cartilage damage.

The process of restitution is dependent on a group of compounds called polyamines (Rao et al., 2012; McCormack et al., 1994; Wang & Johnson, 1992). The rate-limiting enzyme in the formation of the polyamines spermine, spermidine, and putrescine is ornithine decarboxylase (Johnson et al., 1989). Polyamines are constructed of long carbon chains, which are heavily protonated under physiologic conditions. The mechanism by which polyamines stimulate epithelial

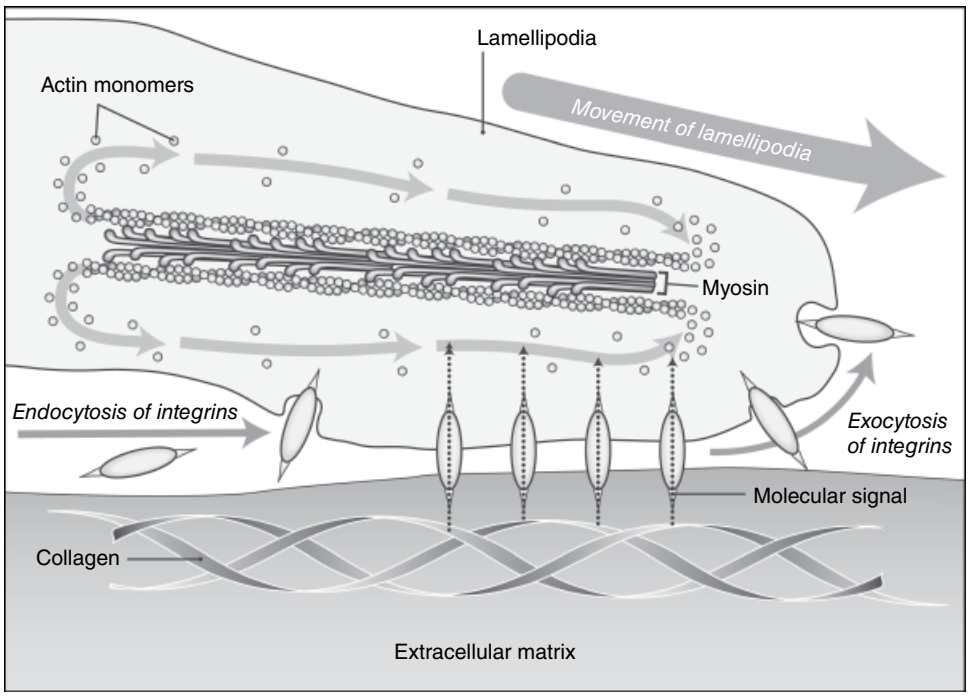

Figure 11.9 Diagram of the cellular events that occur during epithelial restitution. Note the extension of a lamellipodia across denuded basement membrane, driven "tread-milling" of the actin–myosin cytoskeleton. The signal that drives this tread-milling process is derived from basement membrane components, which convey information via integrins to the cell. Source: Adapted from Blikslager et al., 2007.

restitution is not clear, although it may relate to their physical structure. Polyamines are relatively long carbon-chain molecules that are heavily protonated because of their amine groups and may, therefore, facilitate restructuring of extracellular matrix in order to facilitate cellular crawling. For example, physical extension of lamellipodia is significantly reduced in rodent IEC-6 intestinal epithelial cells depleted of polyamines (McCormack et al., 1994).

Other important mediators of restitution include growth factors, which are locally produced peptides that interact with specific cell-surface markers to induce a cellular response. The most important of these growth factors in early mucosal repair events is transforming growth factor-beta (TGF-β), which is produced by gastrointestinal epithelium, and is a potent stimulus of epithelial restitution and modulator of the extracellular matrix (Podolsky, 1999). Other growth factors with potent effects on restitution include epidermal growth factor (EGF), which is produced by the salivary glands and duodenal Brunner's glands, and the related TGF-α, produced by small intestinal enterocytes. These growth factors share approximately 30% of their amino acid structure, bind to the same receptor on the basolateral surface of enterocytes, and are not related to TGF-β (Barnard et al., 1995). The physiologic role of EGF is difficult to discern because it is present in the intestinal lumen, with no apparent access to its basally located receptor (Playford & Wright, 1996). However, it has been proposed that EGF acts as a "surveillance agent" that gains access to its receptor during epithelial injury (when the EGF receptor would likely be exposed) to stimulate proliferation (Playford & Wright, 1996). TGF-α presumably has a similar role, but it is present in greater concentrations in the small intestine, where it is produced by differentiated villus enterocytes. The mature peptide is cleaved from the extracellular component of the transmembrane TGF-α precursor and released into the lumen (Barnard et al., 1995).

Another group of pro-reparative peptides that are locally produced within the gastrointestinal tract are the trefoil peptides. Under physiologic conditions, trefoil peptides are secreted by mucus-producing cells at distinct anatomic sites. For example, the trefoil peptide pS2 is produced by gastric epithelium whereas intestinal trefoil peptide is produced by small and large intestinal mucosa (Blikslager et al., 2007). However, any of the trefoil peptides may be up-regulated within repairing epithelium regardless of anatomic site (Podolsky, 1999). Trefoil peptides are the most potent stimulants of epithelial migration *in vitro*, and their effects are independent of growth factors (Goke et al., 1996). The importance of trefoil peptides to the mucosal repair response *in vivo* is illustrated by gene knockout studies, in which mice deficient in intestinal trefoil peptide have a dramatically reduced ability to repair injured intestine (Mashimo et al., 1996). The mechanisms whereby trefoil peptides stimulate epithelial migration are yet to be fully characterized, but appear to involve translocation of the adherens junction protein E-cadherin, thereby allowing cells to become untethered from neighboring cells (Podolsky, 1999).

Tight-junction Closure

Although epithelial restitution results in gross closure of previously denuded regions of gastrointestinal mucosa, closure of interepithelial spaces is ultimately required to restore normal epithelial barrier resistance (Figure 11.10) (Blikslager et al., 1999b, 2000, 2007). Since the tight junction is principally responsible for regulating the permeability of the interepithelial space, repair and closure of this structure are critical to restore intestinal barrier function. This tight-junction closure appears to be mediated by prostaglandins, particularly PGE_2 (Blikslager et al., 1997b, 2001). Therefore, administration of nonselective COX inhibitors retards the recovery of intestinal barrier function, not as a result of inhibition of villous contraction or restitution, but as a result of delaying recovery of normal levels of paracellular permeability (Blikslager et al., 2007). This may have particular relevance to horses with colic, which are routinely treated with the nonselective COX inhibitor flunixin meglumine. For instance, in two preclinical trials in which horses were subjected to 2 h of complete jejunal ischemia,

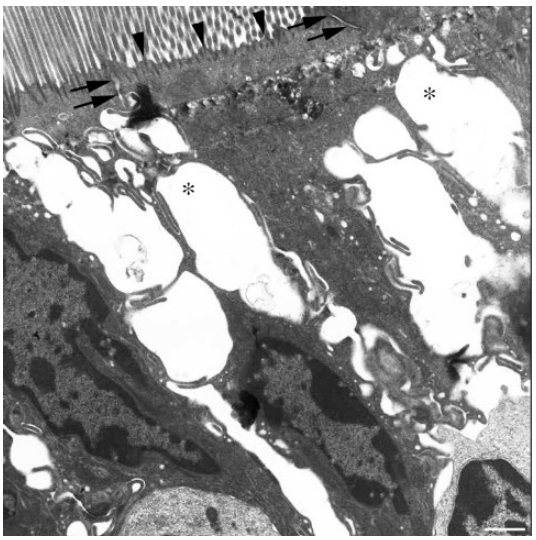

Figure 11.10 Electron micrograph of the mucosal epithelium showing the apical membrane (arrowheads) with its microvilli, interepithelial tight junctions (arrows), and paracellular spaces (asterisks). This section of jejunum has been subjected to ischemia-reperfusion, and is restituting. However, the paracellular spaces and tight junctions show evidence of dilatation (asterisks). Closure of the tight junctions will result in restoration of normal paracellular apposition, and recovery of mucosal barrier function. Bar = 3 μm.

postoperative treatment with flunixin meglumine retarded the recovery of mucosal barrier function for at least 18 h, resulting in increased permeability to endotoxins (Little et al., 2007; Cook et al., 2009).

As an alternative to nonselective COX inhibitors, there has been recent interest in a group of nonsteroidal anti-inflammatory drugs (NSAIDs) that target pro-inflammatory COX-2, but not COX-1, which is presumed to be important for physiologic functions such as mucosal repair (Cook & Blikslager, 2015). Use of either meloxicam or firocoxib, NSAIDs that are more selective for COX-2, in the same preclinical trials involving 2 h of ischemia and an 18 h recovery period, resulted in complete recovery of mucosal barrier function and significantly less permeability to endotoxins than in horses treated with flunixin meglumine (Little et al., 2007; Cook et al., 2009). However, a randomized clinical trial comparing the use of flunixin meglumine with that of meloxicam in horses with small intestinal strangulating obstruction showed that horses treated with meloxicam had significantly more signs of colic in the postoperative period, and there was no apparent difference in measures of endotoxemia (Naylor et al., 2014). Nonetheless, there was a trend toward greater survival in the meloxicam-treated group. Additional investigations are currently under way to compare firocoxib, which is more selective for COX-2 than meloxicam, with flunixin meglumine in a blinded randomized multi-institutional clinical trial in the United States (A. T. Blikslager et al., unpublished data).

Mucosal Proliferation

Once the epithelial barrier has been restored, normal mucosal architecture must be reestablished to allow the return of normal gut absorptive and digestive functions. The flattened villus epithelium that characterizes restitution is replaced by newly proliferated crypt epithelium. Under normal circumstances, new enterocytes are formed by division of stem cells within the stem-cell niche at the base of the crypts. Newly divided enterocytes migrate from the crypt onto the villus (Clevers, 2013). During migration, enterocytes differentiate and acquire specific absorptive and digestive functions. Fully differentiated enterocytes reside on the upper third of the villus for 2–3 days, and are then sloughed into the intestinal lumen (Jankowski et al., 1994). This process is accelerated during mucosal repair, which requires increased rates of proliferation. Increased proliferation may be stimulated within 12–18 h by a variety of locally available gut-derived factors, including luminal nutrients, polyamines, and growth factors (Blikslager et al., 2007). The return of the normal leaf-like shape of the villus occurs subsequent to the appearance of normal columnar epithelium (Blikslager et al., 1999a).

Factors involved in regulating and stimulating epithelial proliferation include polyamines, growth factors, and luminal nutrients. Polyamines are produced by fully differentiated enterocytes at the villus tip, and may reach the crypt either within sloughed luminal epithelium or via the local villus circulation in order to stimulate crypt cell proliferation (Wang & Johnson, 1992). After intestinal injury, polyamines appear to stimulate enhanced proliferation of crypt cells by increasing the expression of protooncogenes, which control the cell cycle (Wang & Johnson, 1994). The mechanism whereby polyamines influence gene expression likely relates to the cationic nature of these compounds, which may influence the tertiary structure of negatively charged DNA and RNA (Wang & Johnson, 1992). Of the growth factors that stimulate restitution, EGF and TGF-α also stimulate proliferation, whereas TGF-β has an inhibitory effect on proliferation.

Normal intestinal nutrients also have potent effects on epithelial proliferation, suggesting that early refeeding of patients with intestinal injury likely stimulates mucosal recovery. The principal metabolic fuel of small intestinal enterocytes is glutamine, whereas for colonocytes it is butyrate. However, studies suggest that glutamine and butyrate have more specific proliferative actions aside from their role as nutrients. For example, in the piglet IPEC-J2 enterocyte cell line, glutamine enhances gene transcription by increasing mitogen-activated protein kinase activity (Rhoads et al., 2000). Similarly, butyrate stimulates mucosal growth after colonic infusion in the rat (Kripke et al., 1989). Owing to its growth-promoting actions, glutamine prevents intestinal mucosal atrophy and dysfunction that accompany starvation (Inoue et al., 1993; Platell et al., 1993) and long-term total parental nutrition (Platell et al., 1993). Intestinal nutrients may also synergize with other proliferative agents. For example, administration of glutamine and TGF-α to porcine ileum that had been subjected to 2 h of ischemia resulted in a synergistic increase in mitogen-activated protein kinase activity, enterocyte proliferation, and villous surface area (Blikslager et al., 1999a). Although there has been a concern that such early return of normal surface area may result in dysfunctional mucosal digestive and absorptive function because the new epithelium is immature, nutrients and growth factors also appear to promote early differentiation. In the case of glutamine and TGF-α restoration of postischemic small intestine, rapid recovery of digestive enzymes was also documented (Ahdieh et al., 1998).

Serosal Reparative Responses

Although a lot of attention has been directed toward mechanisms of mucosal restoration, repair of injured serosal surfaces is also a critical event, particularly

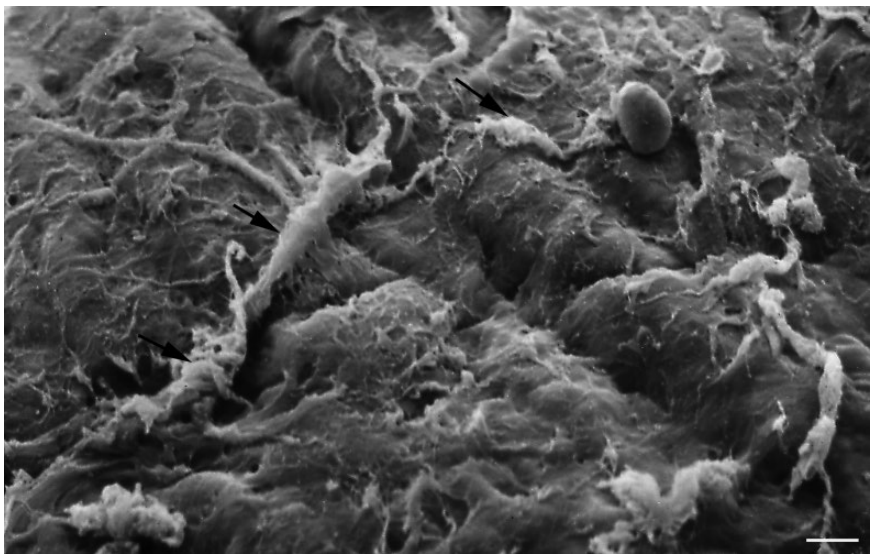

Figure 11.11 Scanning electron micrograph of the serosa following ischemia-reperfusion injury. Note deposition of fibrin (arrows) that may ultimately lead to the formation of fibrous adhesions. Bar = 4 μm.

considering the important role of adhesions in postoperative morbidity and mortality. Prior studies indicate that distention/decompression or ischemia-reperfusion resulting from vascular occlusion lead to loss of serosal mesothelial cells and infiltration of neutrophils (Figure 11.7) (Dabareiner et al., 2001a). The altered microvascular permeability and neutrophilic infiltrate results in deposition of a fibrinous exudate (Figure 11.11) that is invaded by fibroblasts. Depending on the extent of injury, the healing response creates a fibrous scar, which may result in adhesion formation when inflamed, and fibrinous serosal surfaces become adhered. Therefore, a number of studies have been directed toward serosal reparative responses in order to reduce the incidence of adhesions. For example, by reducing the neutrophilic infiltrate immediately after injury, the extent of adhesion formation is significantly reduced. This has been proven in experimental studies in which serosal injury was induced by distention/decompression, and treatment with Carolina rinse solution significantly reduced serosal fibroplasia (Dabareiner et al., 2003). Furthermore, application of a variety of topical agents to a site at increased risk for adhesions, such as an anastomosis, can also modulate the degree of adhesion formation. For instance, application of a hyaluronate solution to the serosal surface of a jejunal end-to-end anastomosis significantly reduced adhesion formation, presumably because of decreased deposition of fibrin (Eggleston et al., 2004). In a clinical study examining the effects of administration of the serosal barrier-forming agent carboxymethylcellulose solution at the time of surgery, horses with small intestinal obstructions that received this solution were significantly more likely to survive, possibly as a result of recued adhesions (Fogle et al., 2008).

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12

Pathophysiology of Pain

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Introduction

Pain is defined as a "sensory and emotional experience associated with actual or potential tissue damage" (IASP Task Force on Taxonomy, 1994) that is consciously perceived after a noxious stimulus. The term "noxious" derives from the Latin *nocere*, meaning "to harm," and refers to any potentially harmful stimulus. When a noxious stimulus is applied to peripheral tissues, processes collectively referred to as nociception are initiated. The final step of the nociceptive pathway is entry of a signal into the thalamus and cerebral cortex, where it is consciously perceived as pain (Flecknell & Waterman-Pearson, 2000; Hellyer et al., 2007).

Why Does Pain Exist? Is Pain Good or bad?

The main purposes of nociception and the initial sharp pain are to initiate responses that will help the individual escape the noxious insult and form memories that will help avoid similar situations in the future. The resulting pain also may initiate changes in metabolism designed to ensure that the individual will rest and that energy and amino acids are available for tissue healing to occur.

Manifestations of Abdominal Pain

Horses express abdominal pain in a characteristic manner, which classically includes pawing, sweating, and rolling. However, horses also may exhibit more subtle, less easily detected signs of pain. Research has identified specific behaviors and physiologic parameters associated with painful conditions in horses [reviewed by Ashley et al. (2005)]. Most of these investigations on the recognition and quantification of pain in horses have been performed on hospitalized horses. However, assessment of pain begins in the horse's home environment, where early intervention and a positive outcome from a colic episode depend on the presence of observant caretakers. Caretakers may contact the veterinarian with complaints such as feeding problems, behavioral issues, muscle tension, or poor performance, all of which may be early indicators of abdominal pain (McDonnell, 2005).

Pain elicits physiologic and behavioral responses. The majority of the physiologic changes associated with pain are mediated by the sympathetic nervous system and the hypothalamic pituitary–adrenal axis. These responses include increases in circulating levels of catecholamines, adrenaline, and noradrenaline, and also autonomic changes, such as an increased heart rate, increased respiratory rate, peripheral vasoconstriction, and transitional changes in breathing. Although these physiologic changes are measurable and elicited as a response to pain, they are also affected by other stressors and hence are not pain specific (Serrie & Servière, 2014). The immediate response to threat or nociception is withdrawal and vigorous activity to escape the potentially harmful event and prevent further tissue damage (Schaible & Richter, 2004). Additional responses are initiated to protect the injured or inflamed area and to allow for convalescence (Bateson, 1991; Dunckley et al., 2005). Because behavior reflects the severity of the pain experienced, behavioral measures are suitable for pain evaluation. Protecting the injured or inflamed area may be manifested as attention toward the painful area or by changes in social behavior, such as isolation from other group members (Anil et al., 2005) or a decreased interest

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in human interaction (Pritchett et al., 2003; Bussières et al., 2008). Above all, changes in posture to help protect a painful area and avoiding or reducing stimulation of hyperalgesic tissue (Molony & Kent, 1997) may be reflected in muscle tension. As a result, postural changes are included in several scales used to evaluate pain in horses (Pritchett et al., 2003; Bussières et al., 2008; Graubner et al., 2011) and humans (Walsh et al., 2014).

Physiologic Parameters Suitable for Pain Evaluation

Physiologic parameters are often not well correlated with the severity of pain. In a few studies, serum cortisol levels have significantly correlated with pain (Raekallio et al., 1997; Pritchett et al., 2003; Sellon et al., 2004; Bussières et al., 2008). β-Endorphins have been positively correlated with pain in horses after arthroscopic surgery (Raekallio et al., 1997), whereas no correlation has been detected between serum amyloid A levels and pain (Pader et al., 2011). Colic and other moderate to severe diseases may affect heart rate (Pritchett et al., 2003; Bussières et al., 2008; Lindegaard et al., 2009), respiratory rate (Bussières et al., 2008), and blood pressure measured noninvasively (Gleerup et al., 2015). However, these parameters also may be altered due to endotoxemia, cardiovascular compromise, and/or hypovolemia. Bleeding, drug treatment, and/or anesthesia may additionally influence heart rate, respiratory rate, blood pressure, and circulating concentrations of cortisol and catecholamines. The stress experienced by the animal during hospitalization or in response to the measurement of physiologic parameters may influence these parameters, and the test results may not be available in time for decision making and treatment. The inclusion of physiologic parameters in the evaluation of pain is theoretically well founded, but has had limited success in quantifying pain (Gleerup & Lindegaard, 2016). Despite their lack of pain specificity, physiologic parameters should be evaluated when possible, as they may indicate other things; for example, heart rate may indicate the severity of colic (Mair & Smith, 2005b; Jennings et al., 2014b) and may be related to postoperative survival (Mair & Smith, 2005a; McConachie et al., 2016). Pupil dilation may also be used as a measure of pain, although this is challenging to measure accurately in animals (Holton et al., 1998).

Pain Behavior

Behavioral parameters are most useful for pain evaluation in horses [for a review, see Gleerup & Lindegaard (2016)]. Pain, regardless of the type, elicits some general changes in behavior, and may be accompanied by disease-specific pain behavior and possibly changes in some physiologic parameters. Poor performance and unwillingness to work may be pain related and can progress to aggression when pain is not diagnosed and treated promptly (McDonnell, 2005). Therefore, pain should always be considered as a possible cause when a horse's attitude changes. For example, aggressive prefeeding behavior and increased pawing in anticipation of feed may be indicative of equine gastric ulcer syndrome. In those situations, gastric pain worsens in anticipation of feed and is soothed when the horse is fed, because secretion of saliva changes the pH in the stomach (Andrews et al., 2005; Malmkvist et al., 2012). Horses are usually sincere in their behavior, meaning that if a certain behavior is induced by a painful condition, the horse's behavior returns to normal when the pain is eliminated (Cook, 2003; McDonnell, 2005). However, negative associations do seem to be stronger than positive associations in horses, which may explain why horses with abdominal or other pain react very strongly to saddle fitting or riding (Fureix et al., 2010). Another known pain-related behavior is self-mutilation, which is a behavioral response to intense or chronic unrelieved pain from the limbs, the gastrointestinal (GI) tract, urogenital organs, and so on (McDonnell, 2008). Consequently, pain should always be ruled out as the primary cause of behavioral changes such as aggression and/or poor performance.

General responses to pain may include restlessness or depression with decreased physical activity, decreased appetite, and a diminished interest in socialization (Raekallio et al., 1997; Price et al., 2003; Pritchett et al., 2003). Horses in pain tend to stand in a resting position with their head lowered (Figure 12.1), and may have a reduced foraging time and a reduced feed intake (Raekallio et al., 1997; Pritchett et al., 2003; Lindegaard et al., 2010). Horses in pain often show no interest in their surroundings and tend to spend more time in the back of the stall (Jones et al., 2007). When looking at more specific pain behavior, orthopedic pain is characterized by decreased weight bearing (Jones et al., 2007; Bussières et al., 2008; Lindegaard et al., 2010), and colic pain is often displayed by pawing, flank watching, and rolling (Mair & Smith, 2005a; Graubner et al., 2011; Sutton et al., 2012).

The Equine Pain Face

The most recent advance in the recognition of subtle behavioral changes associated with pain in horses is the investigation of the facial expressions of pain. The equine pain face was described for horses subjected to acute somatic pain and it consists of six features (Gleerup et al., 2015):

1) increased distance between the base of the ears and a changed movement pattern of the ears;
2) tension in the muscles surrounding the eyes (musculus levator anguli oculi medialis);
3) changed quality of the glance (withdrawn during painful events);

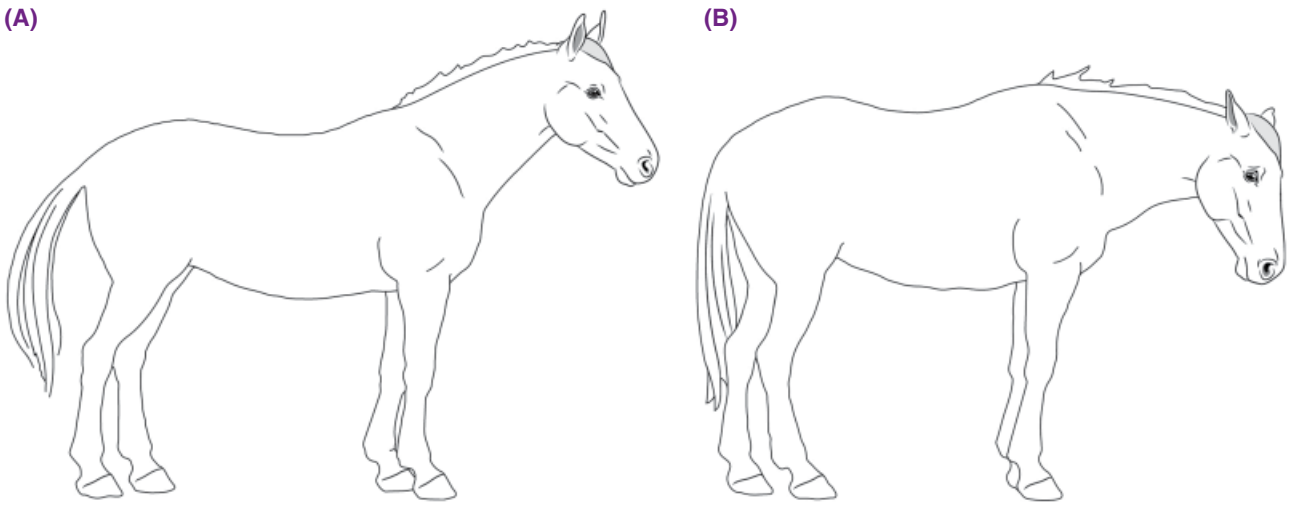

Figure 12.1 Equine posture and facial expression of pain. **(B)** The typical posture of a horse in pain, with a lowered head and a "pain face," compared with **(A)** the nonpainful horse. Source: Courtesy of the Swedish Agricultural University.

4) changed shape of the nostrils (dilated mediolaterally to an edged square-like shape);
5) tension in the lips and chin;
6) increased tension of the muscles visible on the lateral aspect of the head (especially musculus zygomaticus and the musculus caninus).

In a recent study, Dalla Costa et al. (2014) characterized the pain face of horses undergoing routine castration and developed the Horse Grimace Scale, consisting of six features in three levels. The two descriptions of the facial expressions of pain in the horse are very similar. The latter includes changes due to surgical stress response and starvation, whereas the former describes only the facial expression of induced pain. In a recent paper, visibility of the sclera is also included in the pain face of horses (Van Loon & Van Dierendonck, 2015). Many clinicians use facial cues subconsciously and unsystematically, but this recent research makes it possible to use these important features in a more standardized manner.

Clinical Assessment of Pain

A simple approach to pain evaluation includes touching or pressing a potentially painful area while evaluating the reaction of the horse. This parameter has been incorporated into some of the more comprehensive pain scales in both small and large animals (Holton et al., 2001; Bussières et al., 2008; Graubner et al., 2011; Van Loon & Van Dierendonck, 2015). However, a painful reaction elicited by palpation does not necessarily correlate with the level of pain experienced when the area is not touched. Furthermore, the response may be difficult to interpret in horses with referred pain (Christoffersen et al., 2007). Palpation of the painful area may provide important information, but may also be stressful and painful to the horse if carried out repeatedly in an effort to monitor the progression of pain. Moreover, this method is not useful for all pain types; it is also not adequate for a complete pain evaluation. Instead, it is useful to evaluate pain frequently and systematically to recognize worsening of painful events and the effect of analgesic treatments. The pain expression varies considerably among horses, depending on the breed, age, and personality of the horse (Ijichi et al., 2014), but the quality of the pain expression differs significantly before and after surgery. These differences are described later in relation to the *goals of treatment of abdominal pain*.

When choosing a pain evaluation scheme for use in a clinic, it is important to use one that is only as detailed as necessary. In other words, whereas a research study may require the collection of detailed information on many parameters, a pain evaluation scheme that facilitates optimal treatment of horses in a clinic likely will require fewer parameters. It is important that pain evaluations are thorough but not too time consuming, as colic pain often fluctuates, making repeated measures valuable to decision making and the treatment outcome. In a critical care colic patient, it may be helpful to record a pain score every time the heart rate is measured (Figure 12.2). Some very comprehensive pain evaluation schemes have been developed specifically to evaluate abdominal pain (Graubner et al., 2011; Sutton et al., 2013; Van Loon & Van Dierendonck, 2015), but an orthopedic pain scale has also proven useful in evaluating abdominal pain (Van Loon & Van Dierendonck, 2015).

Behavioral indicators of colic pain described in the various studies include the following:

- decreased appetite
- decreased activity/exploring or restlessness
- less time spend in front of the box-stall

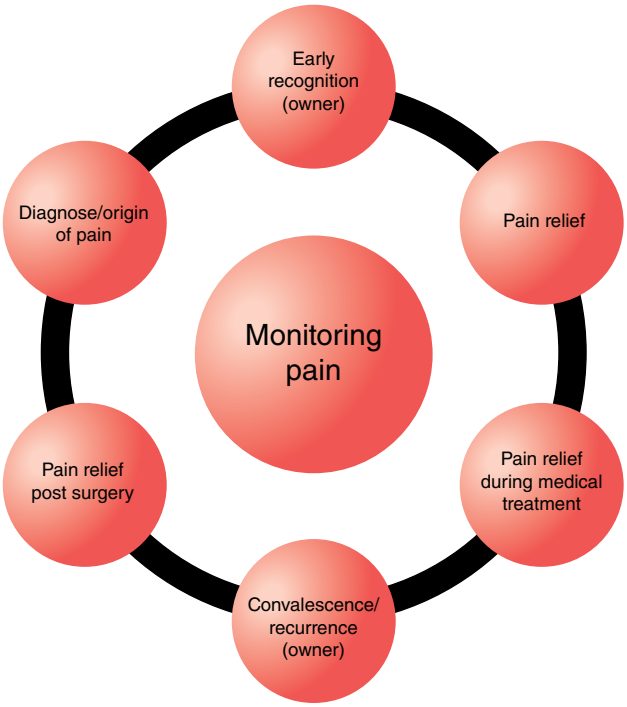

Figure 12.2 The relationship of monitoring pain with expected outcomes. Monitoring pain is a continuous task, especially when working with abdominal pain, as it is very inconsistent. Monitoring pain is therefore valuable in all the phases of the treatment of a colic horse. The horse owner/caretaker has the great responsibility of detecting early signs of pain while the clinician has the obligation to monitor pain continuously so as to be able to adjust analgesic treatment and decisions on the need for surgery. Source: Courtesy of the Swedish Agricultural University.

- decreased social interaction
- pain face
- abnormal posture
- lowered head
- reaction to palpation of painful area
- attempts to lie down
- flank watching
- pawing
- tail swishing
- stretching
- kicking at the abdomen
- rolling
- sweating
- sternal recumbency/lateral recumbency
- head movements, repeated
- flehmen, yawning, tooth grinding, mouth playing/lip curling, pain sounds
- shivering
- depression.

An easily manageable, clinically applicable pain scoring system, based on research findings, that is suitable for various pain types has recently been published (Gleerup & Lindegaard, 2016) (Table 12.1). This pain evaluation system, which can be completed in approximately 2 min, is based on the concept that the frequency of pain evaluations may be more important than meticulousness, especially when the horse is not yet stable.

The advantage of such a systematic pain evaluation system is that it is reliable among observers, a fact that is crucial in clinics providing 24 h care. Use of a system such as this makes it possible to evaluate changes in a horse's status at different times of the day and the effect of treatments.

General Anatomy and Function of the Nociceptive System

This section summarizes the different types of pain and the anatomy of the nervous system responsible for handling the nociceptive signal. The nociceptive system consists of peripheral free nerve endings, afferent nerves, the dorsal horn of the spinal cord, the spinal cord, and pain-specific centers of the brain.

Nociceptors and Transduction

Nociceptors are specialized organelles of the primary afferent nerve fibers that react only to noxious stimuli. Nociceptors are present in nerves in the skin, subcutis, periosteum, muscles, tendons, synovial linings, subchondral bone, serosal surfaces, the walls of hollow viscera, pulp cavity of the teeth, and the cornea. No nociceptors are present in the parenchyma of the liver, lungs, kidneys, or brain. Nociceptors consist of different types of receptors (transducer proteins). Nociceptors can be subdivided into different categories depending on the receptors that exist and the stimuli to which they react. Nociceptors can be activated by a noxious thermal, mechanical, chemical, and/or electrical stimulus. For example, the TRPV1 receptor is activated by chemical or noxious heat (>43 °C), the TRPM8 receptor by noxious cold, and the IB4 receptor by low pH. There are also specific receptors for prostaglandins, neuronal growth factor (NGF), 5-hydroxytryptamine (5-HT; serotonin), histamine, glutamate, and other neurotransmitters (Woolf & Ma, 2007; Basbaum et al., 2009).

The first step of the nociceptive process is *transduction*, whereby the mechanical or chemical stimulus is converted into an electrical signal. The receptors mentioned are mainly ion channels that open when activated, resulting in an influx of sodium or calcium ions. This influx leads to the depolarization of the cell membrane and generation of an action potential, which is transmitted along the primary afferent nerve (first-order neuron) to the central nervous system (CNS) (Woolf & Ma, 2007; Basbaum et al., 2009) (Figure 12.3).

Table 12.1 The equine pain scale. Source: Gleerup & Lindegaard, 2016.

	Score				
Behavior category	**0**	**1**	**2**	**3**	**4**
Pain face	No pain face		Pain face present	Intense pain face	
Gross pain behavior[a)]	None		Occasional		Continuous
Activity	Exploring, attention toward surroundings or resting	No movement		Restless	Depressed
Location in the stall	At the door watching the environment	Standing in the middle, facing the door	Standing in the middle facing the sides	Standing in the middle facing back or standing in the back	
Posture/weight bearing	Normal posture and normal weight bearing	Foot intermittently off the ground/occasional weight shift	Pinched (groove between abdominal muscles visible)	Continuously taking foot off the ground and trying to replace it	No weight bearing. Abnormal weight distribution
Head position	Foraging, below withers or high	Level of withers	Below withers		
Attention toward the painful area	Does not pay attention to painful area		Brief attention to painful area (e.g., flank watching)		Biting, nudging, or looking at painful area (e.g., flank watching)
Interactive behavior	Looks at observer or moves to observer when approached	Looks at observer but does not move	Does not look at observer or moves away and avoids contact	Does not move, not reacting/introverted	
Response to food	Takes food with no hesitation	Looks at food		No response to food	

a) Gross pain behavior includes all readily visible behaviors, such as excessive head movements (vertically/laterally), flehmen, kicking, pawing, rolling, tail swishing, mouth playing, stretching.

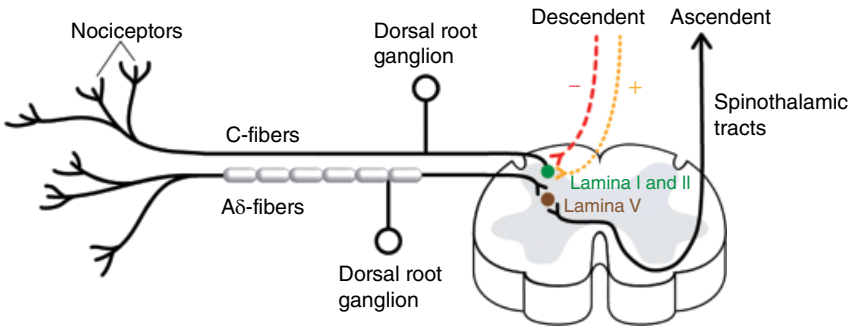

Figure 12.3 Schematic depiction of a peripheral nerve fiber. When a noxious stimulus activates peripheral nociceptors, the signal travels via peripheral Aδ and C fibers to the dorsal horn of the spinal cord, where the signal is transmitted through the CNS via the spinothalamic tract. The cell bodies of the peripheral nerves are located in the dorsal root ganglion just outside the CNS. Source: Courtesy of Stiftelsen Svensk Djursjukvård.

Peripheral Nerves and Transmission

Primary afferent nerves are Aβ, Aδ, or C fibers, depending on their anatomic and physical properties and mode of action. Aβ nerve fibers are thick, myelinated fibers with free nerve endings mainly responsible for the transmission of innocuous mechanoreception (touch) and thermal (heat and cold) information within the non-noxious range. Aδ fibers are responsible for the first, acute, sharp pain immediately following nociceptive stimulation. Somatic Aδ fibers can be mechanical, cold or heat specific, or polymodal, reacting to both mechanical and heat stimuli. Aδ fibers can be further subdivided into Aδ type 1 and Aδ type 2 based on their respective receptors. Aδ type 1 fibers are responsible for primary hyperalgesia associated with peripheral sensitization, generally have a very high threshold, and conduct the electrical signal at a high conduction velocity (50 m/s). Aδ type 2 fibers conduct the signal significantly more slowly (15 m/s) and are responsible for transmission and perception of the acute sharp "first" pain. However, the majority of all nociceptors are located on C fibers, which are unmyelinated nerve fibers with a low conduction velocity (1 m/s). C fibers can be either specific for a certain type of stimulus or polymodal if they can be activated by different types of stimuli. The majority of visceral C fibers are polymodal, responding to mechanical, chemical, and heat stimuli. C fibers are responsible for a dull, burning, and longer lasting "second" pain (Mense, 2009; Djouhri & Lawson, 2004; Dubin & Patapoutian, 2010; Lawson, 2002).

Both Aδ and C fibers can also have "silent nociceptors." This subgroup of nerve fibers has very high threshold receptors that are not activated under normal circumstances, but can be activated by inflammation or other types of sensitization, and therefore may have a significant influence on the pain process in trauma and chronic inflammation.

Coupling of the Signal in the Spinal Cord and Further Ascending Transmission

The cell bodies of the primary afferent fibers are located in the dorsal root ganglion just outside the spinal cord (Figure 12.3). The primary afferent nerves then enter the CNS in the dorsal horn of the spinal cord. The signal is transmitted in the *first synapse* to the ascending nerves of the medulla (second-order neurons) and propagated to higher levels of the CNS (Basbaum et al., 2009). Transmission of the signal is primarily conducted by excitatory neurotransmitters, including glutamate [activates α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors] and substance P [neurokinin-1 (NK-1) receptors]. The signal is modulated by descending serotonin and norepinephrine neurons from the brain, inhibitory γ-aminobutyric acid (GABA) interneurons, and also the endogenous opioid and cannabinoid systems.

Neurons of the gray matter of the spinal cord are arranged in anatomically and physiologically well-defined laminae (Figure 12.4). The Aδ and C fibers terminate in the superficial laminae I, II, and V, whereas the Aβ fibers terminate in laminae III and IV. The so-called high-threshold neurons, specific for high-intensity painful stimuli, are located in laminae I and II. Wide dynamic range neurons that react to a wide range of stimuli from pain to low-intensity physiologic inputs are in laminae IV and V. Input from viscera and other deep tissue structures terminate in the deep laminae IX and X that also receive input from cells of the more superficial laminae. The fact that input from the viscera terminates in deep layers of the spinal cord that receive information from other layers and that viscera generally spread their input over more than one segment of the spinal cord may contribute to the poor localization of visceral and deep somatic pain, and also the phenomenon of referred pain (see later) (Basbaum et al., 2009; Schmidt et al., 2009; Millan, 1999; Lawson, 2002; Dubin & Patapoutian, 2010).

The Nociceptive Signal's Entry into the Brain and the Conscious Perception of Pain

From the dorsal horn of the spinal cord, the majority of nerve fibers cross the midline and then ascend in the contralateral spinothalamic, spinomesencephalic, and spinoreticular tracts to the brainstem, thalamus, and eventually the cerebral cortex. The processing of pain signals in the brain occurs in both the thalamus and in centers in the primary and secondary sensory cortex.

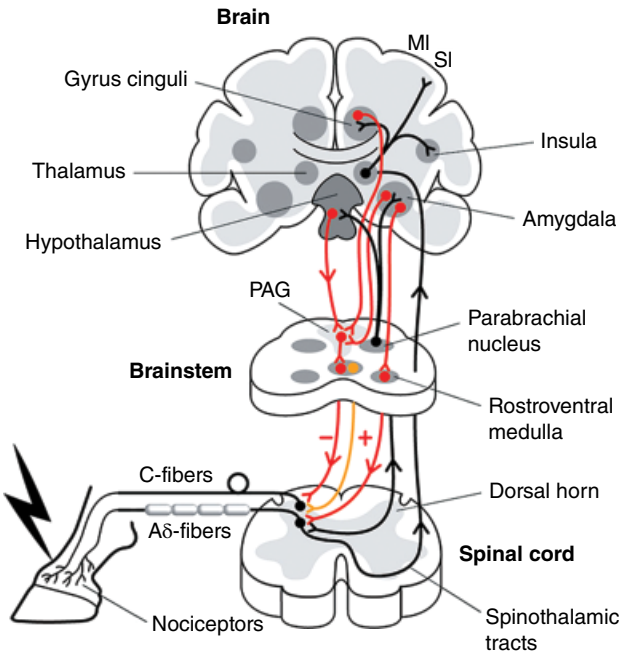

Figure 12.4 Schematic depiction of the nociceptive system. After the nociceptive signal enters into the spinal cord the signal ascends (black lines) via the spinothalamic tract to the brain. The first relay stations are amygdala and hypothalamus, where the signal is modulated before further transmission to the primary sensory cortex (S1) and primary motor cortex (M1), where the signal is now perceived consciously as pain. The red lines illustrate inhibitory (–) and facilitating (+) ascending and descending mechanisms of the CNS. PAG, periaqueductal gray matter. Source: Courtesy of Stiftelsen Svensk Djursjukvård.

The thalamus and sensory cortex have some similar characteristics and properties; both have a sort of map of the body that helps localize the origin of the input (*somatotopy* and *viscerotopy*), and both possess high-threshold and wide dynamic range neurons with different responses to the input. Under normal circumstances, the areas where receptors are located are very specific. However, during and after increased or longer lasting input (high-intensity noxious insult or chronic inflammation), these areas may expand and some neurons, particularly wide dynamic range neurons, may even change modality, which means that they may respond to another type of input. This is known as neuronal plasticity and leads to an increased pain perception, termed sensitization (Dubin & Patapoutian, 2010; Latremoliere & Woolf, 2009; Apkarian et al., 2005).

Modulation of the Nociceptive Signal

Although the majority of information in the nociceptive system is ascending from the periphery to the cerebral cortex, significant crosstalk and descending inhibitory and excitatory modulation occur. Modulation can be divided into three categories; descending modulation, ascending modulation, and segmental inhibition (Dubin & Patapoutian, 2010; Latremoliere & Woolf, 2009). Descending modulation occurs at the first synapse in the dorsal horn of the spinal cord and is mainly regulated by areas of the hypothalamus, the periaqueductal gray matter of the brainstem, the rostroventral medulla, the mesencephalon, and the locus coeruleus. These areas have neurons that project back to the dorsal horn of the spinal cord and exert their effects via various neurotransmitters, including 5-HT and norepinephrine. The complexity of the interactions between these different centers, and whether this leads to inhibition or stimulation of the nociceptive signal, are beyond the scope of this chapter. However, an important example of the potential clinical relevance of these mechanisms occurs in the rostroventral medulla. This area has both "on" and "off" neurons and, depending on which are activated, modulation can lead to either increased pain or analgesia. Based on information from humans, pain can be influenced by pain itself, attention to other input, hypnosis, and suggestion, leading to either reduced or increased pain perception. This may explain why the attention received from nurses, visits from the owner/caretaker, or tender, loving care might lead to reduced pain behavior in hospitalized horses, even those with moderate to severe pain (Ossipov et al., 2010; Gamsa, 1994).

The endogenous opioid and cannabinoid systems are also significant components of the descending inhibitory systems. Enkephalins, dynorphins, and endorphins have all been detected in the CNS, where they can exert significant analgesic effects. Importantly, opioid receptors are present in both the CNS and the peripheral nervous system. When an opioid receptor is activated, sodium efflux occurs, which inhibits depolarization and hence no action potential can be initiated. During inflammation, significant increases in the number of opioid receptors may occur in both central and peripheral nerves. This further influences the nociceptive signal and, ultimately, the level of perceived pain. Ascending regulation of the nociceptive signal might also take place. However, the complex mechanisms responsible for this phenomenon are less well understood.

Segmental inhibition is an important modulatory mechanism and is based on the "gate control theory" of Melzack & Wall (1965). This theory suggests that the nociceptive activity of the dorsal horn is gated by inhibitory interneurons. The simple implication of this theory is that stimulation of any non-nociceptive fibers will activate these inhibitory interneurons, thereby inhibiting nociceptive activity. During activity of nociceptive nerve fibers, this mechanism will inhibit the inhibitory interneurons and lead to an increased nociceptive activity. This mechanism may explain the well-established observation that gentle squeezing or rubbing a painful area has an analgesic effect, as this

will activate the non-nociceptive nerve fibers and hence the inhibitory interneurons (Apkarian et al., 2005; Ossipov et al., 2010).

Various Types of Pain

Pain can be categorized in many ways. The most traditional categorization is by temporal association – acute or chronic. However, another physiologically and clinically more relevant terminology would classify pain as either adaptive or maladaptive (Woolf, 2004). Whereas adaptive pain includes all the "healthy" responses to tissue damage that will ensure withdrawal, future avoidance, and healing, maladaptive or chronic pain lasts beyond healing and has no physiologic function (Molony & Kent, 1997). Physiologically, pain can also be divided into nociceptive and neuropathic pain (IASP Task Force on Taxonomy, 1994). Nociceptive pain is pain perception caused by tissue injury that has activated peripheral nociceptors, ultimately leading to the effects as described previously for adaptive/acute pain. However, as described later in this chapter, the nociceptive system may be altered during intense, repeated, or long-lasting stimulation. In some situations, the somatosensory nervous system may be damaged, leading to neuropathic pain.

Somatic, Deep Somatic, and Visceral Pain

Pain can also be categorized by anatomic origin – somatic, deep somatic, or visceral pain. There are some features of the pathophysiology of the different pain categories that might help the clinician understand the pain, clinical signs, and implications regarding therapies and response to treatment.

Acute pain is the "first" pain, which leads to withdrawal to reduce tissue damage and to establish a memory to secure future avoidance of a similar situation. In many situations, the nociceptive input will be short lasting and self-limiting and ceases when the stimulus is removed. If the noxious insult leads to tissue damage, neuroplastic changes will occur within minutes to hours. This includes all "standard" aspects of inflammation: *calor*, *rubor*, *tumor*, and ultimately *dolor* (and potentially *functio laesa*) (Basbaum et al., 2009; Woolf, 2004). The basis for this is the initial degranulation of mast cells (PGE2 and histamine) and release of cytokines (NGF, TNF-α, IL-1, and IL-6) by macrophages, which will immediately sensitize the nociceptor and its receptors. The resulting nociceptive signal will elicit a reflex mechanism originating in the dorsal root ganglion and the spinal cord, resulting in increased production of substance P and calcitonin gene-related peptide (CGRP), which undergo retrograde transport to the periphery, further stimulating inflammation and increasing the sensitivity of the peripheral nociceptor. This is a cycle that is initially part of "adaptive pain," as the goal is the debridement and repair of the damaged tissues, and is hence beneficial for maintaining body homeostasis (Hellyer et al., 2007).

Chronic pain is sometimes defined as pain lasting more than 3, 6, or 12 months, and usually implies that the pain outlasts healing of the damage caused by the initial insult. Because the pain might be long lasting if the insult continues or if healing takes a long time, "adaptive pain" or "maladaptive pain" are more appropriate terms (Woolf, 2004; Molony & Kent, 1997).

Determination of the Origin of the Pain, Segmentation of the Spinal Cord – "Dermatomes"

Somatic nerves generally innervate a distinct area and the information originating from this area is transmitted to a segment of the spinal cord where it travels in the spinocervicothalamic tract before entering specific areas of the thalamus and cerebral cortex. On the spinal cord level, each spinal nerve takes information from one specific area of the skin and body, called a "dermatome." Collectively, these distinct features of the somatic nociceptive system give the brain its ability to determine very accurately the origin of the input and hence a high degree of *somatotopy* (Basbaum et al., 2009; Manni & Petrosini, 2004).

For visceral nerves, the path from the periphery to the cerebral cortex differs significantly from that in the somatic system. First, most organs or even portions of an organ project their afferent fibers to more than one segment of the spinal cord. Second, each segment of the spinal cord receives input from more than one organ or more than one portion of an organ. Third, afferent input from viscera diverges and spreads cranially, caudally, and bilaterally before it travels via the spinoreticular tract to the thalamus and cerebral cortex. Fourth, visceral input accounts for only 10–15% of the total peripheral input to the spinal cord, which results in a nociceptive system that is mainly accustomed to somatic and not visceral input. The end result is a diffuse system that makes it difficult for the brain to determine the precise origin of the visceral afferent input. In other words, the visceral system has a poor degree of localization or *viscerotopy*. These characteristics partly explain the phenomenon of so-called referred pain, mainly associated with visceral pain.

Visceral Pain

Visceral pain originates from an internal organ in the thorax, abdomen, or pelvis. In horses with colic, the most frequent sources of pain are the intestines (small and large). However, the peritoneum, pleura, stomach, renal pelvis, ureter, and bladder are also recognized sources of abdominal or pelvic pain in the horse. Abdominal pain is a common reason for veterinary

consultation and is now recognized as the most common reason for people to seek medical attention (Arendt-Nielsen et al., 2004; Cervero & Laird, 1999). Traditionally, visceral pain has been understood and managed via direct extrapolation from the concepts of somatic pain processing. However, an increasing awareness has emerged that visceral pain should be distinguished from somatic pain (Cervero, 2009). Important differences between visceral and somatic pain, and clinical implications of these differences, are discussed in the following.

Dual Innervation of Viscera

The viscera have a dual innervation, comprised of an enteric and a vagal/pelvic afferent population with complementary roles in gut signaling (Cervero, 2014). An enteric network of 10^8 neurons is located in the wall of the esophagus, stomach, small intestine, and proximal part of the colon. This network is the largest collection of neurons outside the brain, and continuously regulates motility, local blood flow, growth, absorption, and the immune function of the gut. Vagal afferent fibers, originating in the nodose ganglion, innervate the GI tract from the esophagus to the proximal parts of the colon and project centrally to the nucleus of the solitary tract (Figure 12.5). The distal parts of the colon and rectum are innervated by pelvic nerve afferent fibers originating in the lumbosacral dorsal root ganglia, and projecting centrally to the sacral spinal cord. The entire GI tract is further innervated by afferent fibers of the splanchnic nerves projecting from T5 to L2 segments of the spinal cord, which are called sympathetic afferents owing to their anatomic association with sympathetic nerves.

The brain is in direct bidirectional contact with the viscera through the vagal nerve; this is called the brain–gut axis. For example, if the brain experiences stress, the gut may become overstimulated, with diarrhea as a consequence (Knowles & Aziz, 2009). If the gut is exposed to toxic feed or excessive gas, the painful intestinal cramping will induce brain memory and future aversion. Vagal afferents do not project painful stimuli, but have a profound influence on immunity and pain modulation, as described later (Blackshaw & Gebhart, 2002; Pavlov & Tracey, 2012).

Visceral Nociceptors Are Distinctive

The visceral afferent system may convey both nonpainful signals (e.g., satiety, passage of gas) and painful signals (e.g., inflammation, ischemia, extensive distention)

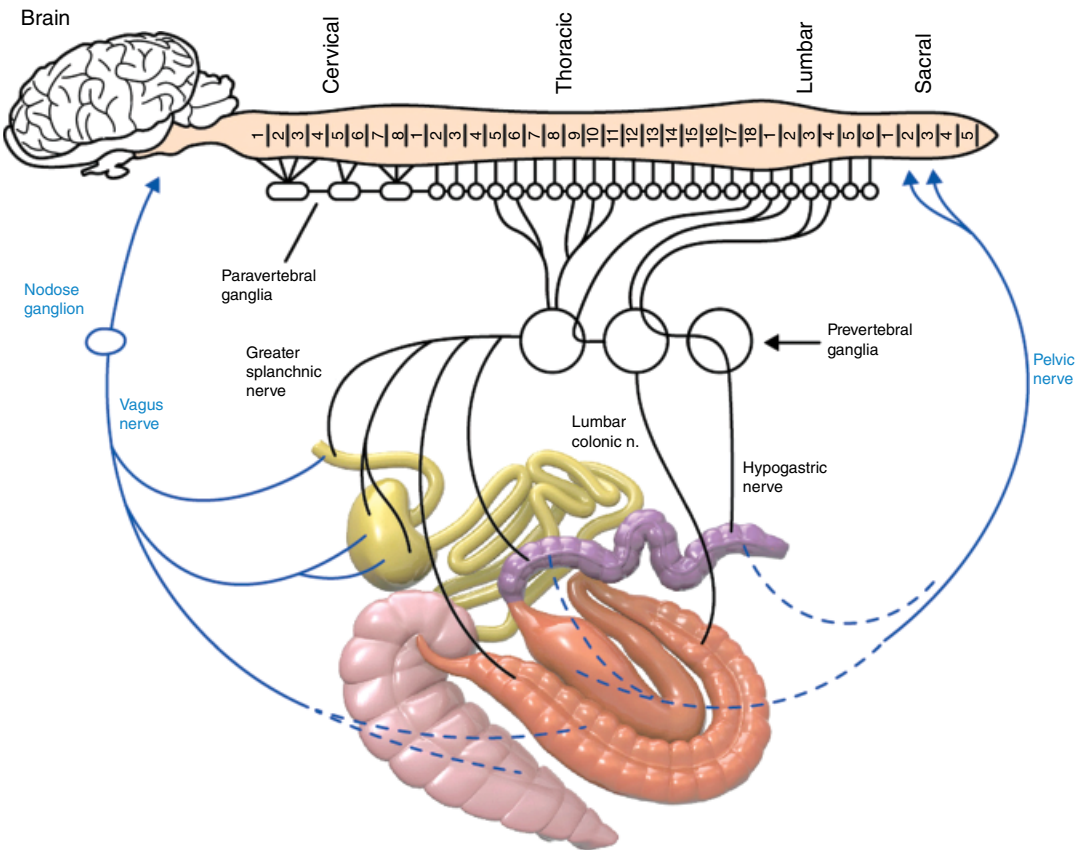

Figure 12.5 Dual innervation of viscera. Schematic illustration of the afferent pathways in the equine GI tract (hypothetical, based on knowledge in humans). Source: Courtesy of the Swedish Agricultural University.

(Christianson et al., 2009; Robinson & Gebhart, 2008). The visceral nociceptive properties are not yet fully understood in either humans or horses, but it is generally agreed that adequate stimuli for production of visceral pain include ischemia, distention of hollow organs or organ capsules, traction of the mesentery, endogenous chemicals such as inflammatory products, and acidosis. This is in contrast to other traumatic insults, such as cutting and burning, which do not produce pain unless hypersensitivity is present. Visceral afferents are mostly connected to free nerve endings. Visceral and nonvisceral afferents communicate different types of information and conscious experiences generated by the visceral sensory system cannot be initiated by nonvisceral afferents.

Characteristics of Visceral Pain

Visceral pain has five pathophysiologic and clinical features that distinguish it from somatic pain (Giamberardino, 2003; Sikandar & Dickenson, 2012). First, some viscera, for example lung, liver, and kidney parenchyma, lack an afferent innervation or contain receptors that do not evoke conscious perception of pain. In contrast, the capsules of these organs contain nociceptors that are sensitive to distention and inflammation. Because visceral pain cannot be evoked from all viscera and because pain is not always linked to visible visceral injury, it has been speculated that some viscera lack afferent innervation. This is not true; however, many organs are only innervated by receptors that do not evoke conscious perception (Ness & Gebhart, 1990).

Second, visceral pain is poorly localized. As a result, the third characteristic of visceral pain is that it may be felt at sites distant from the damaged tissue. These two features of visceral pain are key elements in the theoretical background for convergence – referred pain, which is discussed later.

The fourth clinical characteristic of visceral pain, namely that pain may exist in the absence of identifiable visceral lesions, is called functional pain. Functional visceral pain has not yet been described in horses; however, the lack of a diagnosis for many horses with abdominal pain indicates that functional visceral pain may also be present in horses. In addition, the correlation between intensity of pain, for example in some horses with colitis or gastric ulcerations, and the severity of the tissue damage may be surprisingly poor (Murray, 2002). Experimental animal studies in which visceral pain was caused by distention of the colon or bladder revealed that significant pain and/or discomfort soon follow an unpleasant feeling of fullness without the presence of lesions in the viscus.

Finally, the fifth clinical feature of visceral pain is a strong association with autonomic and emotional responses, which in humans induces pallor, sweating, nausea, vomiting, and changes in heart rate and blood pressure (Cervero, 2014). Urinary bladder distention is also commonly observed in some horses with ileus, and in rodents this is associated with pseudoaffective reflexes, including a visceromotor response that induces contractions of the hind limbs and abdominal musculature (Greenwood-Van Meerveld et al., 2015). Many of the signs observed in colic horses may thus be ascribed to visceral pain, which may also resemble the clinical signs of shock.

Sensitization of the Nociceptive System

Pain itself may modify the function of the nervous system, resulting in a magnified pain sensation even with low nociceptive input. These neuroplastic changes are due to the inherent "positive" feedback mechanism of the inflammatory reaction and of the nociceptive signal created by the initial tissue damage. Sensitization starts as peripheral or primary sensitization and develops into a central or secondary sensitization depending on the intensity and duration of the nociceptive input. Both somatic and visceral nociception may contribute to the development of sensitization.

Peripheral Sensitization

Primary sensitization may develop as a result of a succession of events causing continuous activation of peripheral nociceptors, resulting in a state of hypersensitivity/hyperalgesia or allodynia (pain sensation arising from a nonpainful stimulus such as touch) (Figure 12.6). This state is due to an exaggerated local inflammatory response associated with the release of IL-1, IL-6, NGF, TNF-α, histamine, serotonin, and PGE2. This results in sensitization and activation of peripheral nociceptors, which continues as long as the inflammation is active, and may persist throughout the healing process. This leads to an increased response by the receptors, a lower nociceptive threshold, and a heightened response to all stimuli. The increased receptor response and sensitization result in increased production of receptors (TRPV-1 and sodium channels) and peptides (CGRP and substance P) in the dorsal root ganglion. These are transported retrograde from axon to cell body, resulting in an additional increase in sensitivity. The accumulated effect of sensitization eventually may lead to a phenotypical shift in the nociceptors from A type to C type, which likely is responsible for allodynia. Most importantly, peripheral sensitization also is the cause of the swelling, hyperemia, and hypersensitivity immediately surrounding the injured area, but not extending into noninjured areas (Basbaum et al., 2009; Stein et al., 2009).

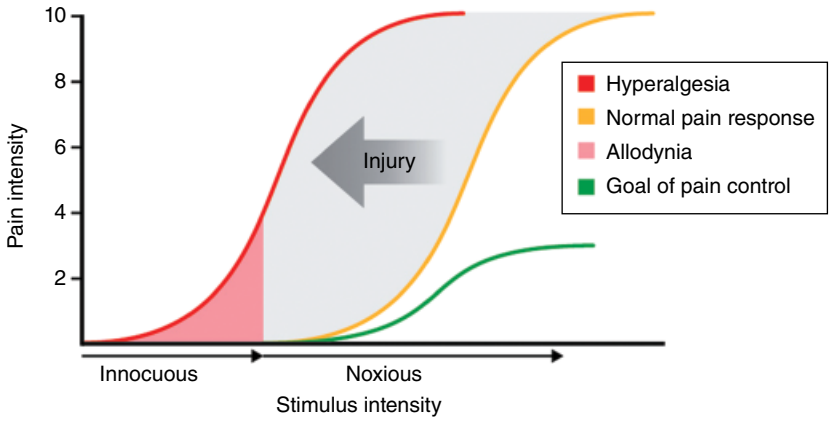

Figure 12.6 Illustration of pain intensity as a function of stimulus intensity. The middle, yellow curve shows the physiologic condition where non-noxious stimuli do not elicit a pain experience and noxious stimuli of increasing intensity lead to an increased pain experience. The left, red curve illustrates the situation during sensitization; non-noxious stimuli lead to a perception of pain (allodynia) and noxious stimuli lead to a higher degree of experienced pain than expected. The right, green curve illustrates the ideal situation after application of analgesia; noxious stimuli are not experienced as painful as generally expected. Source: Courtesy of Stiftelsen Svensk Djursjukvård.

Central Sensitization

Sensitization, hyperalgesia, and potentially allodynia of the surrounding, noninjured areas occur as the result of a plethora of complex changes in the spinal cord known collectively as central sensitization. In brief, central sensitization is the spinal cord's reaction to and further development of peripheral sensitization. This phenomenon develops with continuous input from the afferent nerves and recruitment of silent nociceptors, which further increase the sensitivity of the spinal cord. This in turn leads to continuous activation of the *N*-methyl-D-aspartate (NMDA) receptor system, and upregulation of a local inflammatory response in the spinal cord. These changes increase the excitability of the second-order neurons, which eventually fire without input. The end result is development of a vicious cycle. The local spinal cord inflammation and sensitization also lead to activation of neighboring neurons and production of nociceptors and inflammatory mediators, which are transported retrograde to the periphery. The collective result of central sensitization is a self-activating spinal cord with peripheral input and creation of a peripheral area of sensitization or secondary hyperalgesia. In contrast to the injured area involved in peripheral sensitization, the surrounding area of secondary hyperalgesia is not inflamed per se, but remains hypersensitive with hyperalgesia and allodynia (Basbaum et al., 2009; Latremoliere & Woolf, 2009; Woolf, 2011).

The clinical consequence of peripheral sensitization is the development of a painful area immediately surrounding the injured area, more or less as expected. Unexpectedly, central sensitization will result in a much larger area of hypersensitivity surrounding the injured tissue. This can lead to unanticipated responses in the form of exaggerated reactions during clinical examination procedures, palpation, or bandage changes.

Convergence – Referred Pain

Owing to the complex nature of the nervous system and the subtle nature of some signs of pain, veterinarians might sometimes misinterpret various types of abdominal pain as arising from a somatic structure and vice versa. For example, some horses with rhabdomyolysis might be diagnosed as having laminitis or abdominal pain. Furthermore, one veterinarian may interpret hypersensitivity over the flanks or problems with tightening the girth as behavioral problems, whereas another might interpret these findings as abnormalities involving the skin or muscle, when in fact those signs may be the result of pain arising from the GI or urogenital systems – so-called referred pain (Giamberardino, 1999, 2003). Although the situations described above have a completely different underlying nature, they illustrate the potential difficulties associated with clinical diagnostics and decision making. The background for each is described in the following.

Pain That Might Erroneously Be Interpreted as Abdominal Pain

As already mentioned, rhabdomyolysis likely is the best-known situation in which severe somatic pain might be interpreted as colic. Horses with rhabdomyolysis often begin to sweat profusely, their heart and respiratory rates increase, and they may paw the ground and try to lie down. Because GI motility might be reduced owing

to generalized pain, the initial clinical examination might indicate colic. However, the major difference between colic and rhabdomyolysis is that the large muscles of the hindlimbs will be firm or very hard when palpated in horses with rhabdomyolysis. A diagnosis based on this clinical finding will be confirmed by combining a thorough anamnesis with results obtained by blood biochemistry. Other examples of somatic pain that might erroneously be interpreted as abdominal pain are thoracic pain associated with fractured ribs or punctured pleura, and lumbosacral and pelvic pain from fractures or subluxations. These horses might present with increased heart and respiratory rates, sweating, pain behavior, reluctance to move, and no gastrointestinal borborygmi. Without a more thorough anamnesis and clinical examination, the veterinarian might misinterpret these findings as colic. However, these patients will rarely try to lie down and get up again and they will not kick at their abdomen as occurs in horses with abdominal pain. Hence it is important for veterinarians always to take a complete anamnesis and combine this with a systematic registration of the clinical signs and a thorough clinical examination to avoid making an erroneous diagnosis.

Referred Pain

Referred pain, or nociceptive convergence, is a well-recognized phenomenon in people that was described more than a century ago (Head, 1893). Although referred pain has been intensively studied in humans and laboratory animals over the past three decades (Arendt-Nielsen et al., 2008; Giamberardino, 1999), much remains unknown about the underlying pathophysiology. In popular terms, referred pain means that pain arising in a visceral organ may be perceived as originating from a somatic structure (viscero-somatic convergence). In humans, the best-known example of viscero-somatic convergence is myocardial infarction (heart attack), where the nociceptive signal originating from the myocardium and coronary arteries is perceived as radiating pain from the left shoulder area and arm, the chest, the back, and even the lower jaw. Although this phenomenon is well described in humans, it has only been sporadically reported in veterinary medicine and has been studied minimally, if at all, in a systematic way. Based on results obtained from research performed using laboratory animals and their correlation with clinical observations in humans, it seems reasonable to assume that similar processes and pain states exist in most species, including the horse.

Theoretical Background of Referred Pain

Referred pain can be categorized as viscero-somatic, viscero-visceral, somato-somatic, and even somato-visceral convergence, where viscero-somatic refers to a state in which the pathology, and hence the noxious insult, exist in a visceral structure but the pain is perceived as originating from a somatic structure. There are several theories behind the phenomenon of referred pain, the convergence theory being the most widely accepted. A simplistic explanation of this theory is based on the description of general pain physiology and the specific physiology of visceral pain. As already described, despite the large surface area of the visceral organs, the visceral input to the spinal cord accounts for a maximum of 10–15% of the total input. In addition, this input converges bilaterally, cranially, and caudally and up to 75% of the neurons of the spinal cord receive input from the viscera. In combination, these characteristics of the visceral nociceptive system lead to a very diffuse system with a poor ability of the thalamus and the cerebral cortex to localize the origin of the signal. Since the entire nociceptive system is much more attuned to receiving and processing input from the somatic system, the convergence theory hypothesizes that nociceptive visceral input might mistakenly be attributed to a somatic structure terminating its first-order neuron within the same spinal segment as the visceral organ. This explains the pain in the left arm in the case of human myocardial infarction (Head, 1893; Arendt-Nielsen et al., 2008; Giamberardino, 1999).

Referred Visceral Pain

Visceral pain is even more interesting and complex. Studies in both humans and laboratory animals have shown that not only pain but also neurogenic inflammation can occur at the reference area (Wesselmann & Lai, 1997). This can be seen as central sensitization of the "referred" set of neurons, which is attributable to its close anatomic positioning in the spinal cord. In the case of referred pain, peripheral sensitization occurs after central sensitization. This is because central sensitization increases the central production of inflammatory mediators (including CGRP, substance P, and others), which are transported retrograde along the first-order neuron and released at the periphery, where they lead to a local inflammatory response. This has been shown in studies in rats in which urogenital inflammation was initiated by injection of dental cementum unilaterally into the uterine tube. Initially, this caused local inflammation that led to central sensitization and ultimately to hyperalgesia and local inflammation over the lower back and flank dermatomes, which share the same spinal segments as the input from the uterine tube. This study creates a very solid "proof of principle" of the entire phenomenon of referred pain and inflammation. The literature has many other examples of referred pain, most often viscero-somatic convergence but also somato-somatic convergence and other combinations.

In human medicine, the phenomenon is widely recognized, and there are maps of the human body depicting specific areas of referred pain from specific visceral organs (Giamberardino, 1999, 2003; Sikandar & Dickenson, 2012; Arendt-Nielsen et al., 2008).

Referred Pain in the Horse

There are only a few well-documented reports of potential referred pain in equine medicine. One is a case series of 14 mares exhibiting poor performance and adverse behavior and increased hypersensitivity of the flanks, hindquarters, and lumbosacral pain (Christoffersen et al., 2007) (Figure 12.7). All mares were diagnosed with poor perineal conformation, leading to vaginitis, cervicitis, or metritis, or a combination thereof, and this visceral inflammation led to referred pain of the flanks and lower back. All 14 mares underwent vulvoplastic surgery (Caslick's procedure), and in 12 mares the clinical symptoms and poor performance were either eliminated or significantly improved after 6 months.

Another case description included a 6-year-old Warmblood gelding with poor performance and similar symptoms to those described in the previous case (Lindegaard et al., 2009). The gelding was increasingly unwilling to be ridden, had hyperalgesia/hypersensitivity of the flanks, and demonstrated bucking behavior when ridden. The horse had undergone a full clinical and orthopedic examination (including radiographs) by several veterinarians. The horse was finally referred for urethral obstruction, which was resolved relatively easily. However, a larger urolith of the bladder was revealed at rectal palpation and the bladder was noted to be severely inflamed when inspected by endoscopy. The urolith was surgically removed and the horse was subjected to standard postoperative care. The riding problems, poor performance, and hyperalgesia of the flanks had completely resolved at follow-up after 6 and 9 months.

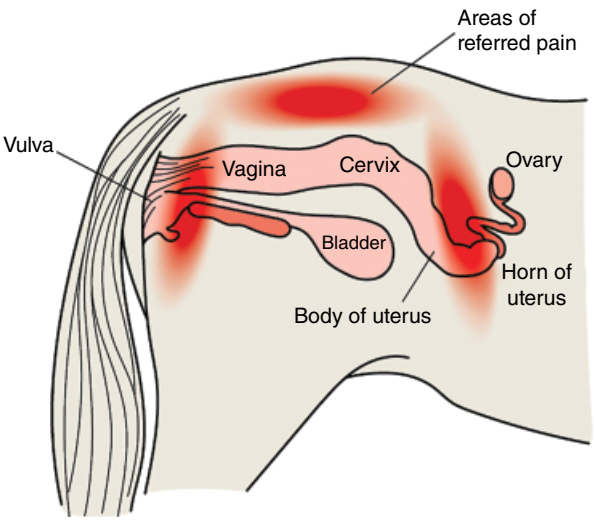

Figure 12.7 Referred pain in the horse with uterine inflammation. When chronic inflammation of the urogenital system occurs, referred pain may be clinically observed as hyperalgesia of the red-colored areas. Source: Courtesy of Stiftelsen Svensk Djursjukvård.

Although both of these examples are case based and do not provide evidence that the performance and behavioral problems were caused by referred pain originating from visceral inflammation, we believe that with increased awareness, more cases will emerge and corroborate the parallels with viscero-somatic convergence in humans and laboratory rodents.

In addition, it is likely that there are other diseases or syndromes of the equine viscera that present as poor performance, hyperalgesia/hypersensitivity of specific areas of the body, and/or other adverse behavior. Such examples could include gastric ulceration syndrome, in which sensitivity to tightening the girth and/or poor performance might be the prevailing clinical signs. Inflammatory bowel disease and urogenital inflammation with or without urolithiasis and nephrolithiasis are also commonly associated with visceral sensitization in humans, and their equine parallels remain to be described.

In summary, viscero-somatic convergence should be considered in difficult cases of hypersensitivity, hyperalgesia, poor performance, or otherwise adverse behavior for which no standard orthopedic or medical diagnosis can be established by means of standard investigations.

Consequences of Pain

Tissue injury activates the orchestration of interrelated nervous, endocrine, and immune processes, with pain, stress, and inflammation as the prominent biological responses, known as the endocrine–metabolic stress response (EMSR) shown in Figure 12.8 (Chapman et al., 2008). Clinical and preclinical evidence compiled over the prior two decades has shown the complex and potent effects of stress on pain processing (Jennings et al., 2014a; Butler & Finn, 2009). Stress is an adaptive biological response to homeostatic threats, and it is characterized by a series of typical hormonal and metabolic responses (Chrousos & Gold, 1992). The stress response results from activation of the hypothalamic–pituitary–adrenal (HPA) axis, which transforms afferent sensory input to the CNS into a physiologic response. During stress, attention is enhanced and the brain focuses on perceived threats. Increasing levels of corticotropin-releasing factor in the hypothalamus, amygdala, and locus coeruleus contribute to the development of such behavior as hyperresponsiveness, agitation, and aggression in the stressed horse (Muir, 2015). Furthermore, the pituitary gland secretes a number of hormones, including adrenocorticotropic

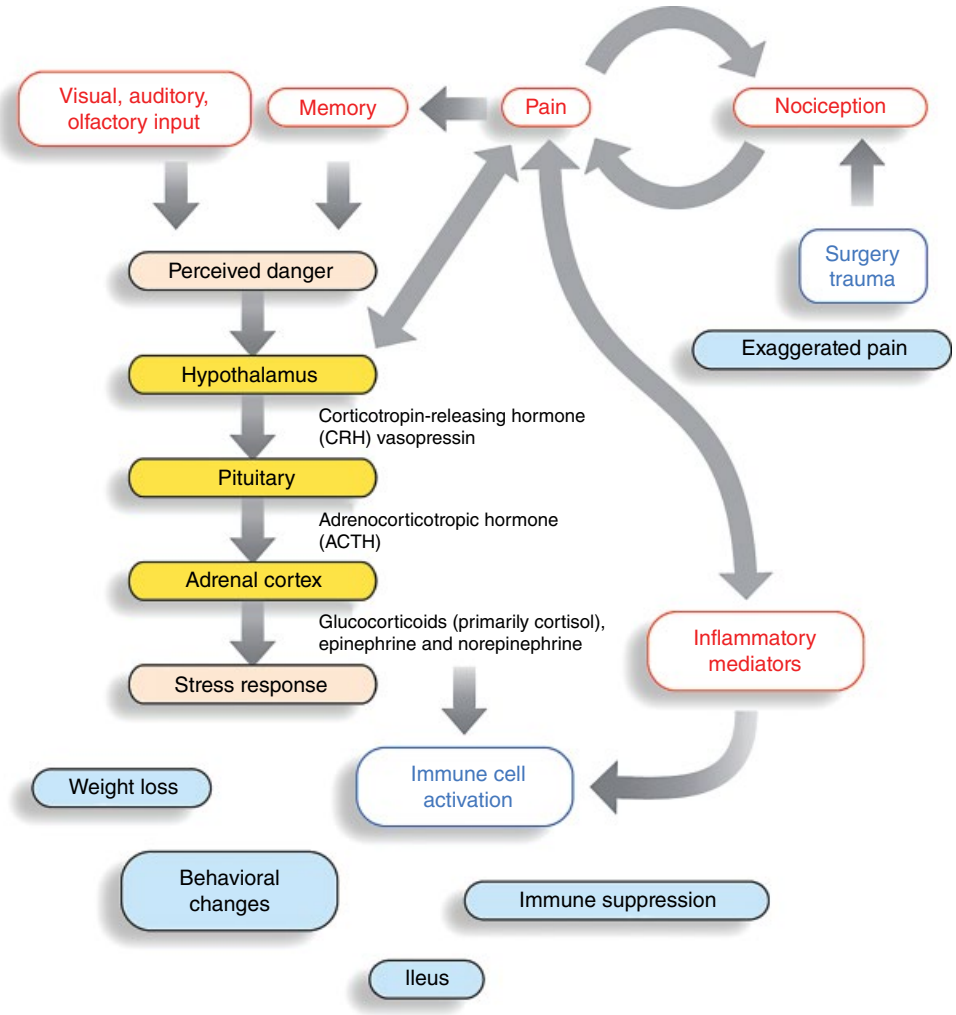

Figure 12.8 Illustration of the possible interactions between stress, pain, and inflammation that may lead to weight loss, behavioral changes, ileus, and immune suppression. Source: Courtesy of the Swedish Agricultural University.

hormone (ACTH), melanocortin, prolactin, vasopressin, thyroid-stimulating hormone, and growth hormone, resulting in organ-specific production, particularly of glucocorticoids from the adrenal gland and noradrenaline via activation of the sympathetic nervous system (Rivier & Rivest, 1991; Tsigos & Chrousos, 2002). This results in altered hemodynamic responses, including increased cardiac output and heart rate, and also an increased respiratory rate. Blood flow is redirected to provide the greatest perfusion to vital organs, coagulation is increased, metabolism and caloric requirements are increased, and catabolism is instituted to fuel the stimulated brain, heart, and muscles (Rivier & Rivest, 1991; Tsigos & Chrousos, 2002; Giannoudis et al., 2006; Kehlet & Dahl, 2003; Verbrugghe et al., 2012).

Stress is induced by factors such as tissue injury, including trauma, surgery, and severe disease, and by unpleasant sensory and emotional experiences, particularly pain, anxiety, and fear, in addition to visual and auditory input. Adverse memories may also contribute (Jennings et al., 2014a; Butler & Finn, 2009; Chrousos & Gold, 1992; Muir, 2015). Stressors commonly encountered by the colic horse include pain, fear, and severe disease with tissue destruction, trauma, shock, and unpleasant memories. Stress responses are described in horses with colic (Mair et al., 2014; Hinchcliff et al., 2005), after anesthesia (Taylor, 1991), during and after surgery (Jacobsen et al., 2009; Pollock et al., 2005), in association with inflammation (Mills et al., 1997), after transportation (Fazio et al., 2008), with cross-tying during transportation (Stull & Rodiek, 2002), and after social separation (Harewood & McGowan, 2005). Although the ethics of an optimal pain treatment plan are obvious, few studies have documented the benefits of reducing stress by improved analgesic management on mortality and morbidity in horses.

A hallmark of visceral pain in humans is its association with experiences of other emotions, including fear and nausea. These emotions are unknown in horses and are thought to be related to the autonomic component of visceral pain, resulting in pallor, sweating, nausea, and changes in heart rate and blood pressure. These autonomic responses are potent stressors and are observed frequently in the horse with colic. Other stressors, such as the introduction of a gastric tube, would be of short duration and support only a brief and acute "fight–flight" response without inducing an EMSR. Stressors such as anesthesia, surgery, starvation, or a new environment perceived as hostile may induce clinically significant EMSR. Depending on the duration and intensity of the EMSR, immune function may be depressed (Giannoudis et al., 2006; Kehlet & Dahl, 2003; Verbrugghe et al., 2012; Mair et al., 2014), leading to delayed wound healing (Mair et al., 2014; Hinchcliff et al., 2005; Taylor, 1991) and prolonged convalescence. Numerous studies have documented that measures to reduce stress also reduce postoperative complications and the use of analgesics in humans (Jacobsen et al., 2009).

It should also be noted, however, that an innocuous stressor, such as the replacement of a clogged intravenous catheter, cumulatively adds to the development of a maladaptive stress response in a horse in pain with ongoing immunosuppression. Additionally, earlier negative experiences are important. In humans, the expectation of pain during changing of a bandage significantly increased the level of pain (Woo, 2015). Even the mildest EMSR is associated with a certain biological cost and it is therefore valid to question whether this response contributes to survival in modern surgery and medicine (Rivier & Rivest, 1991; Kehlet, 1997).

Stress-induced Hypoalgesia and Hyperalgesia

Mechanisms that inhibit and facilitate pain are balanced in healthy individuals, but this balance can be disturbed during stress. Stress may reduce or exacerbate the pain state (Jennings et al., 2014a). Severe stress, induced by anxiety, fear, or pain, can induce episodes of stress-induced analgesia (Butler & Finn, 2009). The phenomenon is known to occur in war situations, in which soldiers suffering from battle wounds experienced little or no pain even when the injuries should be considered as very painful. Neurobiologically, stress-induced hypoalgesia is ascribed to a combination of the activation of strong descending opioid and nonopioid inhibitory medullar pathways from the periaqueductal gray. Stress-induced analgesia is generally of short duration and the pain will shortly recur.

It may be more clinically relevant that stress can induce hyperalgesia (Jennings et al., 2014a; Muir, 2015; Nyland et al., 2015). In particular, repeated or chronic exposure to stressors may induce the less well-understood phenomenon of stress-induced hyperalgesia (SIH) in humans (Crettaz et al., 2013). Likewise, stress exacerbates existing pain associated with chronic pain disorders (Jennings et al., 2014a). The mechanisms are thought to be initiated by decreased GABA release or GABA receptor activation at the spinal level, which eventually produces peripheral allodynia. In this and probably in other ways, stress contributes to the development of central sensitization and chronic pain states. Stressors such as negative reinforcement and chronic restraint induce aversive behaviors and hyperalgesia in a variety of animal species, including horses (Muir, 2015). The presence of stress may thus alter the experience of pain and amplify pain pathology and the severity of pain-related mortality and morbidity.

Immunologic Interaction with the Nervous System in Pain

Injury initiates an inflammatory response that is clinically noted based on five cardinal signs: pain, redness, heat, swelling, and decreased function of the tissue. Whereas pain is processed in the peripheral and central nervous systems, the remaining cardinal signs are triggered by the activation of the innate immune system, including activation of Toll-like receptors. By binding to microorganisms and pathogen-associated molecules such as endotoxins, damage-associated molecules such as actin cytoskeletal elements, or heat-shock proteins from damaged cells, these receptors can induce the cellular production of immunologic messengers. The acute-phase response involves both local and systemic components and comprises a complex web of numerous cell types and organs producing and reacting to a multitude of cytokines and other mediators (Baumann & Gauldie, 1994). The biological function of this acute-phase response is to contain pathogens, clear damaged cells, and initiate repair. In the horse, serum amyloid A, haptoglobin, and fibrinogen are well-known acute-phase proteins (Jacobsen & Andersen, 2007; Jacobsen et al., 2009). Colic is associated with an acute-phase response, manifested by increases in acute-phase proteins, and which affects disease duration and pathology (Pihl et al., 2013, 2015).

The role of the innate immune system in the activation of pain pathways is less well investigated. Activated immune cells, such as mast cells, macrophages, and neutrophils interact directly with nociceptors and neurons through the release of soluble mediators that contribute to nociceptor sensitization. It is also known that neutrophil migration is associated with inflammatory pain and that nerve terminals influence neutrophil recruitment through release of vasoactive neuropeptides such as substance P and CGRP, in a process of neurogenic inflammation that spreads to other neurons (Ren & Dubner, 2010). Complement components are also important in

the innate immune system and may have a direct effect on C fibers, also leading to neurogenic inflammation in order to facilitate further neutrophil influx and hypersensitivity. Recent research has shown that a continuous afferent input, especially from viscera and deep tissues, involves glial cells. Glia-derived mediators may contribute to the transition to chronic pain and to the development of neuropathic pain.

At the same time, factors that promote healing, reduce inflammation, and reduce pain may be released. A large number of anti-inflammatory cytokines are produced in response to experimental endotoxin administration in horses (Vinther et al., 2015), and it is known that endomorphins are expressed in T cells, macrophages, and fibroblasts from synovial tissues of patients with osteoarthritis (Rittner et al., 2002). Also, a neural mechanism was described by which efferent vagus nerve-mediated cholinergic signaling was shown to control immune function and pro-inflammatory responses via a pro-inflammatory reflex (Pavlov & Tracey, 2012). Large gaps still exist in our knowledge of the way in which immune cells, the nervous system, and glial cells interact to influence pain pathways, but research is intensive in this field. Owing to complex interactions, the consequences of pain are intimately connected to the consequences of inflammation and stress. An effective pain treatment regimen should therefore also consider stress and immune function.

Implications of Pain Physiology for the Principles and Goals of Treatment of Abdominal Pain

In contrast to physiology and pathophysiology, where there seem to be only minor differences between species, the treatment of abdominal pain in horses may have a different goal and definitely a different perspective compared with humans. The reasons for this include the use of the horse and hence the goal of the treatment, recognition of chronic abdominal pain, diagnostic capabilities in the horse, availability of drugs, and the distinct pharmacodynamics and pharmacokinetics in horses. In addition, there are frequently economic limitations in horses. This section focuses on some specific considerations of analgesia and pain, inflammation, sensitization, and stress, and also important considerations regarding pain and pain management research. Specific classes of drugs, treatment regimens, and dosages are discussed in detail in Chapter 27.

Goal of Analgesic Management of Abdominal Pain in Horses

From an animal welfare perspective, the primary goal of analgesic treatment is to keep the horse free of pain. Nevertheless, for horses with acute abdominal pain, the strategy and goal of pain management may differ, based on the working diagnosis (medical versus surgical colic), general and circulatory status of the horse, and the owner's economic situation or commitment. Of course, the ultimate analgesic therapy is to treat and cure the underlying disease. However, this is not always immediately achievable so that the immediate effort is focused on alleviating pain, which serves several different purposes – providing safety for the clinician undertaking continued examination and treatment, reducing the risk of self-mutilation during the course of severe colic, simply providing analgesic relief during the course of further treatment, and trying to avoid inflammation and sensitization.

Avoiding Inflammation and Stress

As described earlier in this chapter, pain and inflammation are often tightly coupled, just as stress is an unavoidable factor. Consequently, it is always important to consider pain management of the acute colic horse from more than just the perspective of keeping the horse calm and safe for further examination and treatment. This includes considering the inflammatory mechanisms included in the disease process and associated with the pain. This means that various combinations of spasmolytics, nonsteroidal anti-inflammatory drugs (NSAIDs), local analgesics, and opioids can be used as multimodal pain control to achieve the stated goals: (1) spasmolytics will decrease intestinal spasm and thus pain for a short period; (2) NSAIDs will decrease inflammation and diminish further damage; (3) local analgesics might serve both of these purposes; and (4) opioids will be analgesic for severe pain. For a comprehensive review, see Robertson & Sanchez (2010). Pain relief in the acute colic horse can effectively be achieved by decreasing the intra-abdominal pressure by decompression of the stomach by nasogastric intubation and/or decompression of the cecum by trocarization. This will also reduce further inflammation resulting from the development of abdominal compartment syndrome, and may potentially save the life of the horse by avoiding GI rupture.

Pain After Colic Surgery

The steps for managing acute colic pain are relatively well known and mutually agreed upon. However, when it comes to the management of postsurgical colic, opinions often differ. This may be due to different philosophies of intensive care and hence a different focus when it comes to this particular type of pain. In any case, the clinician should always consider the pathophysiologic processes involved in the pain process and the clinical picture of the equine patient. Following colic surgery, some horses may be misinterpreted as being free of pain due to the calm, secluded behavior compared with the pain behavior

displayed prior to surgery. Horses rarely display "real" colic behavior after surgery, after which pain primarily originates from a combination of inflammation and peripheral sensitization of the abdominal incision. This type of pain does not cause the horse to kick at its abdomen or continually lie down and get up. The horse usually prefers to stand as quietly as possible and avoid palpation or manipulation of the wound area. Depending on the initial surgical problem, pain from the wound will be combined with various degrees of pain from inflammation of the peritoneum and/or the intestine. This might add further to the emotional component of the pain and hence the withdrawn, asocial behavior often observed. It must be emphasized that it is the authors' opinion that horses should return to "normal equine behavior" relatively soon after surgery. In other words, the horse should be managed in such a way that it returns to normal facial expressions, normal social behavior, and normal appetite within 12–24 h after surgery (Gleerup & Lindegaard, 2016).

Managing pain after colic surgery will depend on both medical and nonmedical management. Horses that have undergone colic surgery are at risk of being stressed. The complete scenario includes initial colic pain, restraint of the horse for examination, and transport to an unfamiliar place, where the horse is again restrained, then anesthetized and recovered in unfamiliar surroundings. After surgery, the horse is placed in an unfamiliar environment, with unknown caretakers and probably starved, while having additional pain from an abdominal wound. This amount of stress modulates the pain perception and adds further to the perceived pain. Therefore, it is also extremely important to take care of the horse psychologically. This might include frequent contact and grooming, preferably by the same handler, short periods of hand-walking, short periods of grazing (if possible), and visits from the owner or a familiar caretaker. Medically, pain originating from the wound should be treated with a combination of NSAIDs, constant-rate infusion (CRI) of local analgesics, and systemically administered opioids such as morphine.

Under some circumstances, there might also be GI distention due to postoperative ileus, which adds further visceral input and can potentially trigger colic behavior and increased heart rate and respiratory rate. This more recognizable colic behavior generally responds to gastric decompression and, if it does not, continued or recurrent intestinal pathology and/or mechanical obstruction of an anastomosis should be considered and investigated.

Evidence Behind Pain Management in Equine Colic

Many clinicians will object to postoperative treatment with opioids owing to their potential for decreasing GI motility. This is a valid argument and this side effect has been documented in many studies. Nevertheless, the majority of studies, if not all, investigating the effect of opioids on equine GI motility have been conducted in healthy individuals without pain, inflammation, or stress; for a comprehensive review, see Clutton (2010). In human medicine, it is well documented that the three main reasons for postoperative ileus after major surgery are pain, inflammation, and stress (Holte & Kehlet, 2000). This has not been investigated fully in horses, but the similarities between other aspects of pain and inflammation suggest that this also might be similar in horses. Sellon et al. (2004) showed that CRI of butorphanol increased the GI transit time slightly in postoperative colic horses. Furthermore, this study elegantly showed that compared with the saline-treated control group, horses treated with CRI butorphanol recovered significantly faster, had significantly lower plasma cortisol levels, lost significantly less body weight, and had significantly lower pain scores (both groups were treated with flunixin meglumine at 1.1 mg/kg q 12 h).

One of the reasons for an improved outcome after continuous treatment with opioids is the direct analgesic effect, but in addition to the analgesic and/or anti-inflammatory effect, the opioids also reduce stress (as measured by significantly lowered plasma cortisol levels; Figure 12.8). Another very plausible effect of opioids is that the reduced degree of pain and inflammation leads to a decreased emotional component of the pain and hence to a reduced sympathetic tone. The intimate association between pain, inflammation, and stress and the influence that these phenomena have on GI function explains the outcome of the study by Sellon et al. (2004) – analgesia and potentially an anti-inflammatory effect lead to a decreased emotional component and stress level, which explains the lower pain scores and lower plasma cortisol levels. This in turn increases appetite, so the horse does not enter a catabolic state in order to produce substrates for healing, and this explains the reduced weight loss. As in experimental studies with opioids, time to first fecal output was increased slightly, but this in no way affected the outcome in these clinical cases with inflammatory pain. Combined with data from human medicine, these considerations support a stronger focus on improved pain and stress management in horses subjected to colic or other major surgery.

Conclusion

Pain physiology is complex, and specific knowledge regarding all aspects might not be relevant for the detection, evaluation, understanding, and treatment of abdominal pain in horses. However, the authors believe that the management and treatment of equine colic pain may sometimes benefit from an increased focus on the pathophysiologic aspects of nociception, pain,

sensitization, inflammation, and stress. This should not be seen as moving the focus from the classical thorough clinical examination centered on establishing a clinical diagnosis, but as an addition to this approach to assist the clinician in determining the reasons for colic pain. For optimal management of pain and stress associated with medical and surgical colic, the following points are essential to consider:

- Pain assessment should be carried out systematically and at frequent intervals.
- Pain is closely associated with inflammation.
- The nociceptive system has the ability to modify pain processing into exaggerated pain states.
- Visceral pain is diffuse and difficult to localize.
- Visceral pain may be referred to other anatomic sites, potentially confusing the clinician.
- Pain might be closely associated with the endocrine metabolic stress response.
- Untreated pain may lead to weight loss, behavioral changes, and immune suppression.
- Management of pain should be initiated early and effectively.

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13

Pathophysiology and Treatment of Postoperative Ileus

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Neurogenic Theory

Numerous theories have been proposed to define factors that may contribute to postoperative ileus (POI). The central nervous system (CNS), enteric nervous system (ENS), and humoral factors most likely all contribute to ileus to some extent. Surgical manipulation with activation of the sympathetic nervous system has long been recognized as one potential mechanism mediating POI. This may be explained by the neurogenic theory of ileus, which states that POI is mediated by mechanoceptor or nocioceptor stimulation of extrinsic afferent neurons, which then activate either a peripheral or central inhibitory efferent neural pathway, decreasing gastrointestinal (GI) progressive motility. One peripheral inhibitory reflex has been shown to be mediated by calcitonin gene-related peptide (cGRP) in spinal afferents acting at prevertebral ganglia. Immunoneutralization of cGRP, a neurotransmitter located in afferent intrinsic and extrinsic neurons, peripheral ganglia, and the CNS, will partially reverse abdominal surgery-induced ileus (Zittel et al., 1998). It has been proposed that surgical manipulation may stimulate the release of cGRP, which enhances nociception, possibly through potentiating substance P (SP) release, with activation of the spinal afferent pathway with neurons synapsing on sympathetic postganglionic efferent nerves, resulting in reflex inhibition of motility (Geppetti et al., 1991; Sternini et al., 1987; Zittel et al., 1994, 1998). This is supported by partial reversal of surgically induced ileus in the response to functional ablation of the spinal afferent pathway with capsaicin applied to the celiac/superior mesenteric ganglia (Zittel et al., 1994).

Surgical manipulation of the intestine has also been shown to be associated with a transient increase in norepinephrine (Furness & Costa, 1974; Smith et al., 1977). The increase in norepinephrine seen after abdominal surgery may be neurogenically mediated through afferent activation of the sympathetic postganglionic efferent nerves. In addition to the previously described peripheral extrinsic afferent pathway, there is also support for a mechanism in which a spinal afferent pathway activated by abdominal surgery sends sensory information for further processing to the CNS. Abdominal surgery and other stress-related events have been shown to neurally mediate the release of corticotropin-releasing factor (CRF) from the paraventricular nucleus of the hypothalamus and the dorsal vagal complex. The CRF functions as a central neurotransmitter that mediates the efferent limb of a GI inhibitory reflex pathway, with spinal sensory afferents synapsing with ascending neurons in the spinal cord (Barquist et al., 1996; Martinez et al., 1997; Sheldon et al., 1990). It is possible that CRF may activate the sympathetic efferent pathways with release of norepinephrine, which depresses GI motility by presynaptic inhibition of acetylcholine release from cholinergic motor neurons (Barquist et al., 1996; Dubois et al., 1973; Furness & Costa, 1974; Glise et al., 1980; Livingston & Passaro, 1990; Sheldon et al., 1990). In addition to activating sympathetic inhibitory pathways, CRF can also act centrally to inhibit vagally (parasympathetic) stimulated gastric motility (Hernandez et al., 1993).

Based on neurogenic pathophysiology, therapies have attempted to block the efferent inhibitory pathways with sympatholytics, or to potentiate the efferent excitatory pathways with cholinomimetic agents. These have met with limited success for several reasons. First, nonadrenergic noncholinergic (NANC) inhibitory neurotransmitters, such as nitric oxide (NO) and vasoactive intestinal peptide (VIP), are most likely involved in POI in addition to norepinephrine. Blocking sympathetic adrenergic pathways will inhibit the ileus induced by laparotomy without bowel manipulation but will only partially

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reverse more intense ileus induced by laparotomy and bowel manipulation (De Winter et al., 1997). Adding a nitric oxide synthase (NOS) inhibitor completely reverses the additional inhibition induced by mechanical stimulation of bowel. The increased release of NO in response to manipulation is likely produced by constitutive NOS, and released from enteric neurons through an inhibitory vagal neural pathway and not produced by inducible NOS as discussed later in the inflammatory model (De Winter et al., 1997). VIP has also been shown to contribute to inhibition of motility induced by manipulation (De Winter et al., 1998). Since NO and VIP have been shown to be important inhibitory neurotransmitters in the GI tract of many species, the poor results in clinical patients with therapies focused on pharmacologic manipulation of the adrenergic and cholinergic pathways might be explained by failure to block this additional inhibitory NANC reflex mediated by NO and/or VIP (Boeckxstaens et al., 2000; De Winter et al., 1998). Unfortunately, pharmacologically decreasing inhibitory neural input and expecting a progressive motility pattern to return are too simplistic when dealing with the required coordination of excitatory and inhibitory activity necessary for aboral propulsion of ingesta. The complexity of interactions is illustrated by the fact that simultaneous blockade of both NO and VIP abolishes the beneficial effect of individual blockade of NO or VIP (De Winter et al., 1998). This suggests that inhibition of one of the neurotransmitters is required to maintain the descending relaxation required for propulsion.

Inflammatory Model

The neurogenic theory appears to explain the acute phase of ileus seen after surgery. A large body of evidence has accumulated to suggest that more prolonged motility disorders, such as POI and ileus associated with enteritis/colitis or septicemia, may be mediated by an inflammatory infiltrate into the intestinal wall (Eskandari et al., 1999; Kalff et al., 1998, 1999; Schwarz et al., 2002). These causes of ileus are more clinically relevant than the acute phase of ileus, especially with respect to possible therapeutic intervention. Intestinal manipulation, lipopolysaccharide (LPS) administration, and ischemia-reperfusion injury have all been shown produce significant decreases in *in vitro* contractile activity of jejunal smooth muscle (Eskandari et al., 1999; Kalff et al., 1998). This reduction in motility is temporally associated with an influx of inflammatory cells into the muscularis externa (circular and longitudinal layers). The activation and recruitment of inflammatory cells may be stimulated by bacterial products, complement, and cytokines. LPS exposure and intestinal manipulation have been shown to increase mucosal permeability, leading to increased bacterial translocation and transference of bacterial products (Schwarz et al., 2002). The leukocyte influx, primarily neutrophils and monocytes, peaks at 24 h, but may last for 7 days or longer. A cause and effect relationship between the leukocyte infiltrate and motility disruption is supported by the observation that blocking the influx of leukocytes into the muscularis externa by antiadhesion antibodies eliminates the depressed motility (Kalff et al., 1999). The infiltration of leukocytes may also result from activation of nerve fibers in the bowel wall with release of proinflammatory mediators such as SP or cGRP, which may mediate neurogenic inflammation and/or the additional release of proinflammatory mediators (Sharkey, 1992).

Several mediators have been demonstrated to be involved in the inflammation-associated impairment of motility. The influx and activation of inflammatory cells leads to the up-regulation of inducible nitric oxide synthase (iNOS), with the subsequent production of large quantities of NO (Eskandari et al., 1999; Kalff et al., 1999). As stated previously, NO has been shown to be a potent inhibitory regulator of GI activity in the horse and many other species (Billiar, 1995; Rakestraw et al., 1996; Stark et al., 1991). When the effects of iNOS are eliminated, either by use of a selective iNOS inhibitor or by running the experiments in iNOS knockout (iNOS KO) mice, the impairment of contractile activity by surgical manipulation is improved (iNOS inhibition) or eliminated (iNOS KO) (Kalff et al., 2000). In the iNOS KO experiments, the inflammatory infiltrate was also significantly reduced. These findings support the role of NO as one mediator in the pathogenesis of ileus, functioning both to inhibit smooth muscle contractility directly and to play a signaling role potentiating the inflammatory response that causes ileus by recruiting more inflammatory cells into the muscularis externa (Kalff et al., 2000).

Another likely mediator involved in postoperative ileus is cycloxygenase-2 (COX-2) and its prostanoid products. COX-2 is an inducible enzyme that can be stimulated by LPS, growth factors, and proinflammatory cytokines (Dubois et al., 1998; Josephs et al., 1999). It is released from inflammatory cells and also endothelial cells, neuronal cells, and vascular smooth muscle (Dubois et al., 1998). Surgical manipulation with subsequent leukocyte infiltration produces an up-regulation of COX-2 with an increased production of prostaglandins coming from inflammatory cells and from myenteric neurons within the muscularis externa (Josephs et al., 1999; Schwarz et al., 2001). A concomitant depression of *in vitro* jejunal contractility and *in vivo* intestinal transit is seen, both of which can be alleviated by blocking COX-2 with a selective antagonist. Leukocyte recruitment into the muscularis is also prevented with selective COX-2 antagonism. This demonstrates a role for COX-2 and prostanoid production in POI and also a potential role in other motility disorders where inflammation is involved.

It is known that manipulation of one area of the GI tract can influence motility in adjacent areas that have not been manipulated. In fact, early motility work in the horse described the pathogenesis of POI as lack of gastroduodenal coordination after manipulation of a more distal segment of small intestine (Gerring & Hunt, 1986). Neurogenic theories with activation of afferent extrinsic neurons mediating efferent inhibition may account for this component of POI. In a study in which both inflammatory and neurogenic pathways were involved in POI (De Jonge et al., 2003), the infiltration of leukocytes into the small intestine after surgical manipulation was shown to activate an orad inhibitory neural pathway, which in turn mediated a sustained decrease in gastric motility via spinal afferents activating sympathetic efferent inhibitory fibers. Adrenergic blocking agents normalized the delay in gastric emptying (the neurogenic component), but did not reverse the delay in transit in the small intestine (the inflammatory component). Another study demonstrated that surgical manipulation of the bowel produces a "pan-enteric" inflammatory and dysmotility response (Schwarz et al., 2004). In addition to depressed contractile activity in the rat jejunum after surgical manipulation, the motility of both the stomach and colon is also disrupted. The molecular basis of this "pan-enteric" response is thought to be mediated through activation of the proinflammatory cytokines such as nuclear factor interleukin-6 (NF-IL-6) and nuclear factor kappa B (NF-κB), which in turn induce tumor necrosis factor alpha (TNF-α), iNOS, and COX-2. These mediators of ileus are significantly elevated in the unmanipulated stomach and colon and also in the manipulated small intestine (Schwarz et al., 2004). Mechanical manipulation of equine jejunum for 30 min resulted in local inflammatory reactions characterized predominantly by infiltration of neutrophils (Hopster-Iversen et al., 2014). Jejunal samples collected at the time of surgery of clinical cases and samples collected 18 h after surgical manipulation or experimental ischemia found neutrophilic inflammation through all intestinal layers (Little et al., 2005). The elevated level of neutrophilic inflammation was mirrored by an increased number of calprotectin-positive cells, indicating leukocyte activation. At present, the extent to which these inflammatory mechanisms contribute to ileus in the horse is unknown.

Diagnosis and Treatment of Postoperative Ileus in the Horse

Incidence and Risk Factors for Postoperative Ileus

Ileus, the functional obstruction of aboral GI transit, is one of the most commonly encountered complications of equine GI surgery. In horses, POI occurs predominantly after correction of lesions involving the small intestine. POI may also be seen after correction of ascending colon lesions, primarily large colon volvulus. Traumatic handling of the intestine, intestinal distention, resection, and anastomosis, and intestinal ischemia may contribute to ileus in these cases. Other conditions that have been associated with ileus are anterior enteritis, peritonitis, electrolyte imbalances, endotoxemia, and anesthesia. Almost all of these proposed conditions contributing to sustained ileus may be explained by the previously described inflammatory model of POI.

Risk factors for POI identified in one equine retrospective study were age >10 years, Arabian breed, packed-cell volume (PCV) >45%, high serum concentrations of protein and albumin, anesthesia >2.5 h, surgery >2 h, resection and anastomosis, and lesions in the small intestine (Roussel et al., 2001). Performing a pelvic flexure enterotomy decreased the risk of POI in this study. In another report, PCV >48%, high heart rate, elevated serum glucose, small intestine lesion, and ischemic small intestine were identified as risk factors (Blikslager et al., 1994). Similarly to those studies, more recent investigations found an association between POI and high heart rate, high PCV, the presence of >8 L of reflux at admission, increased duration of anesthesia, and the performance of a small intestinal resection (Torfs et al., 2009; Cohen et al., 2004).

The incidence of POI in horses undergoing surgical treatment of colic has been reported to be 18.4–21% (Blikslager et al., 1994; Roussel et al., 2001; Cohen et al., 2004). There is a significant reduction in survival (59–87%) for horses that developed POI compared with survival (93–94%) in horses that did not develop POI (Blikslager et al., 1994; Roussel et al., 2001; Cohen et al., 2004). This is a significant improvement over a previous report, in which 86% of horses with POI did not survive (Hunt et al., 1986). Although management of POI cases has improved, POI is still associated with 38–60% of all postoperative deaths after surgical intervention for conditions causing colic (Blikslager et al., 1994; Roussel et al., 2001; Cohen et al., 2004).

Diagnosis

Disruption of propulsive motility results in the sequestration of fluid, gas, and ingesta in the dysfunctional segment of the GI and in the intestine proximal to that segment. This distention occurs primarily in the stomach and small intestine, but can also occur in the large intestine, especially with colitis, endotoxemia, or ischemia following a large colon volvulus. The first signs associated with ileus are depression and anorexia. As the intestine distends, the horse demonstrates increasing signs of colic, such as pawing, flank watching, lying down, and rolling (Adams, 1988; Becht & Richardson,

1981; Gerring, 1992) (see Chapter 20). Borborygmi are usually decreased or absent. The heart rate is elevated at first owing to the pain associated with the distention. The mucous membranes become discolored and the capillary refill time is prolonged. Hemoconcentration is reflected by increases in the PCV and total protein concentration. Decreases in plasma chloride and potassium are the most common electrolyte abnormalities seen, although sodium may also be low (Adams, 1988; Becht & Richardson, 1981; Gerring, 1992). As the severity of the intestinal distention increases, abdominal distention may become grossly visible. Rectal examination and ultrasonography will aid in determining if the small or large intestine is involved (see Chapter 23). In foals, both abdominal radiography and ultrasonography can be helpful in assessing the cause of intestinal distention (see Chapter 32). Nasogastric decompression often results in the retrieval of 3–10 L of fluid (Figure 13.1). The response to nasogastric decompression provides an important clue that the underlying problem is the result of loss of function. After decompression, the horse should show some improvement, such as decreased pain and decreased heart rate. If no alleviation of signs is observed, careful thought should be given as to the likelihood that the problem may be a mechanical obstruction and not a functional ileus.

Figure 13.1 Nasogastric intubation of a horse presented for colic after performing in a show. On presentation, heart and respiratory rate were elevated at 92/min and 42/min, respectively, and the patient was clinically dehydrated (PCV 64% and total protein 9.1 g/dL). Large amounts of spontaneous red gastric reflux were obtained through the tube for several days. Positive levels of oleander glycosides were detected in serum and gastric reflux. Serum troponin levels were elevated at 0.16 ng/mL(reference range, 0.01–0.07 ng/mL).

Supportive Therapy

Although a variety of prokinetic agents have been administered in an attempt to improve GI motility in horses with ileus, the lack of consensus as to which one, if any, is effective attests to their therapeutic limitations. Consequently, the hallmark of treatment remains supportive therapy. Included in this supportive therapy are fluid, acid–base, and electrolyte replacement, which are important in any horse with colic. Antibiotics are also indicated if there is compromised intestine or the possibility of bacterial contamination. Nasogastric intubation and decompression remain the primary method to treat POI in the horse. Questions remain regarding when to place the tube, if the tube should be kept in place, and when to start feeding. A study in normal horses indicated that leaving a nasogastric tube in place for 18 h has little impact on gastric emptying (Lammers et al., 2005). However, another study using the same methodology showed that leaving the nasogastric tube in place for 72 h produced a delay in gastric emptying of fluids (Cruz et al., 2006). The clinical significance of this finding in horses after surgery involving the GI tract is unknown. In humans, eliminating or decreasing routine nasogastric intubation (Cheatham et al., 1995) with early return to enteral feeding has been shown to be safe and may reduce POI (Hartsell et al., 1997; Ortiz et al., 1996). However, these retrospective studies involved human patients with colonic problems and not ileus associated with small intestinal motility disturbances Management of pain and inflammation is also important in the treatment of affected horses (see Chapter 27).

Anti-inflammatory Therapy

Intestinal distention, ischemia, and trauma occurring during decompression and/or resection and anastomosis induce inflammation of the bowel wall, with an increase in the production of inflammatory mediators such as prostaglandins PGI_2, PGE_1, and PGE_2 and TNF. Endotoxemia associated with necrotic intestine or systemic infection can also stimulate production of these inflammatory mediators. Infusions of endotoxin, PGE_2, and TNF have been shown to disrupt normal motility patterns in horses (Eades & Moore, 1993; Hunt & Gerring, 1985; King & Gerring, 1989; Valk et al., 1998b). Phenylbutazone and flunixin meglumine have been

shown to attenuate significantly this disruption of gastric, small intestinal, and large colonic motility in the horse (King & Gerring, 1989; Valk et al., 1998b). The analgesic effect of these agents should also decrease stimulation of sympathetic inhibitory reflexes. Based on these observations, nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended for the prevention and treatment of motility disorders associated with GI inflammation such as POI, anterior enteritis, and colitis. Although some work has indicated that selective COX-2 inhibitors are effective in reducing surgically-induced ileus in laboratory animals (Schwarz et al., 2001), in an experimental distention/surgical manipulation model in the horse, selective COX-2 inhibition was not beneficial in attenuating the *in vitro* depression of jejunal contractions, whereas nonselective COX inhibition was able to attenuate the depressed contractile activity (P. C. Rakestraw, unreported data). Other drugs, such as polymixin B, dimethyl sulfoxide, and hyperimmune plasma, potentially may help if they can decrease the inflammatory response to endotoxemia.

Analgesia

In addition to NSAIDs, adrenergic agonists and opioids are the two classes of drugs commonly used in horses to control pain associated with colic. Xylazine and detomidine are α_2-adrenergic agonists that may inhibit presynaptic acetylcholine release in the myenteric plexus or may directly inhibit smooth muscle, thereby decreasing motility (Hsu, 1982). In the horse, xylazine and detomidine have been shown to decrease motility as measured by myoelectrical activity of the distal jejunum, pelvic flexure, cecum and right ventral colon, and cecal emptying based on radiolabeled markers (Adams et al., 1984; Clark et al., 1988; Lester et al., 1998a; Roger & Ruckebusch, 1987; Rutkowski et al., 1989). However, the results of another study suggest that although xylazine resets the duodenal migrating motor complex (MMC) in the horse, it does not seriously disrupt GI motility (Merritt et al., 1989b). Although β-adrenergic receptors are present on circular and longitudinal smooth muscle in the horse and β-adrenergic agonists cause inhibition of contractile activity (Belloli et al., 1997), their role in motility disturbances has not been demonstrated in the horse (Gerring & Hunt, 1986). However drugs administered for reasons other than pain management which act at β-adrenergic receptors such as dobutamine, a β_1-agonist, and terbutaline, a β_2-agonist, may depress motility. In an attempt to reduce side effects of detomidine without decreasing the sedative effect, a peripherally acting α_2-adrenoceptor antagonist (MK-467) with poor penetration into the CNS was used in healthy horses (Vainionpaa et al., 2013). The combination prevented induced bradycardia and intestinal hypomotility without affecting the quality of detomidine-induced sedation, but the duration of the sedation was reduced. In addition, MK-467 is still not commercially available.

Opioid agonists should be avoided if possible in horses with ileus as they depress motility in most species studied (Frantzides et al., 1992; Pasternak, 1993; Roger et al., 1985, 1994). Opioids slow small intestinal transit, increase the duration of POI, and may increase the chances of impaction colic by slowing progressive motility (Davies & Gerring, 1983; Holte & Kehlet, 2000; Roger & Ruckebusch, 1987). In ponies, morphine and fentanyl, both of which are mu-receptor agonists, have been shown to depresses colonic motor activity (Roger et al., 1994; Roger & Ruckebusch, 1987). Naloxone, an opioid antagonist, has been suggested by some investigators to be a potentially beneficial drugs in treating equine motility disorders (Ruckebusch & Roger, 1988), and there has been some evidence that naloxone enhances progressive motility in the horse. However, naloxone has also been shown to cause diarrhea and colic in the horse (Kamerling et al., 1990). Butorphanol tartrate, an opioid agonist/antagonist, is a strong analgesic and mild sedative used in horses with colic (Robertson & Muir, 1983). Butorphanol (and also meperidine and pentazocine) was shown to inhibit myoelectric activity in the equine jejunum whereas they had no effect on the pelvic flexure activity in one study (Sojka et al., 1988). Butorphanol also prolonged xylazine-induced inhibition of myoelectrical activity of the equine cecum and right ventral colon (Rutkowski et al., 1989). However, in another study, butorphanol was shown to reset the antroduodenal MMC without causing undesirable effects on antroduodenal motility (Merritt et al., 1989a). Continuous-rate infusion of butorphanol (13 μg/kg/h) for 24 h after celiotomy decreased plasma cortisol concentrations and improved the recovery characteristics; however, treated horses had a delay in first passage of feces compared with controls (Sellon et al., 2004). In addition, continuous-rate infusion for 96 h of butorphanol alone or in combination with lidocaine, or lidocaine plus ketamine, caused a delay in GI transit in healthy horses (Elfenbein et al., 2014).

Ketamine, a noncompetitive *N*-methyl-D-aspartate receptor antagonist, has antinociceptive properties at subanesthetic doses when used as a continuous-rate infusion. In addition to analgesic properties, ketamine also has anti-inflammatory properties *in vitro* and *in vivo*. However, ketamine (0.55 mg/kg IV over 15 min followed by 1.2 mg/kg/h) caused a delay in transit of feces and decreased fecal weight in healthy horses (Elfenbein et al., 2011).

Prokinetics

It should be evident from the given description of the physiology of normal motility that many different factors must be precisely coordinated in order to

produce progressive motility patterns. It is logical to assume that during ileus in the horse and other species, an imbalance in the factors that control excitation and inhibition of GI tract smooth muscle contributes to the ileus. Historically, pharmacologic modulation of intestinal muscular activity in the horse has been directed either at increasing excitatory cholinergic activity with the administration of parasympathomimetic agents such as bethanechol or neostigmine, or at blocking inhibitory sympathetic hyperactivity with α-adrenergic blockers such as yohimbine and acepromazine (Gerring, 1991; Gerring & Hunt, 1986). A major portion of the support for the drugs discussed in the following subsections comes from experimental models evaluating the efficacy of the various pharmaceutical agents in changing motility patterns in normal horses or changing motility patterns in an acute abrasion model where there is a transient ileus induced by rubbing the small intestine (Gerring, 1991; Gerring & Hunt, 1986). Both models have made significant contributions to our understanding of POI. However, the perceived limited efficacy of prokinetics may be due to the inability of these studies to reproduce accurately what occurs during clinically relevant ileus in the horse.

Bethanechol

Bethanechol hydrochloride is a muscarinic cholinergic agonist that stimulates acetylcholine receptors (M_2 receptors) on GI smooth muscle, causing them to contract (Reynolds & Putnam, 1992). Support for the use of bethanechol in the treatment of motility disorders in the horse is predicated on observations that in normal horses bethanechol increases the rate of gastric and cecal emptying as measured with radiolabeled isotopes, and it induces premature MMC phase III-like activity in the ileum (Lester et al., 1998a). In an equine POI model, bethanechol (0.025 mg/kg SC at 2 and 5 h postoperatively) shortened intestinal transit measured by passage of beads, and reduced the time until normal activity levels returned throughout the GI tract when administered in combination with the α-adrenergic receptor blocker yohimbine (Gerring & Hunt, 1986). However, bethanechol was not as effective as metoclopramide in restoring coordinated gastroduodenal motility patterns. Although its efficacy in treating motility dysfunction in the horse and other species has been questioned (Gerring & Hunt, 1986; Reynolds & Putnam, 1992), its prokinetic effects in normal horses and the clinical impression of its benefit in treating horses with ileus provide some support for its use in the treatment of certain GI motility dysfunctions such as POI and gastric and cecal impactions. The recommended dose is 0.025 mg/kg IV or SQ q 4–6 h. The most common side effect of the drug is salivation, with abdominal cramping and diarrhea occurring less frequently.

Neostigmine

Neostigmine methylsulfate is a cholinesterase inhibitor that prolongs the activity of acetylcholine at the synaptic junction. In studies on normal horses, the effects of neostigmine (0.022 mg/kg IV) varied depending on the portion of the GI tract examined (Adams et al., 1984; Adams & MacHarg, 1985; Lester et al., 1998a). Neostigmine, at 0.022 mg/kg SC on four occasions at 30 min intervals, was shown to delay gastric emptying and decrease propulsive motility in the jejunum but increased propulsive motility at the pelvic flexure (Adams et al., 1984; Adams & MacHarg, 1985). These results suggest that the drug would not be appropriate for gastric and small intestinal problems, but may be beneficial for large intestine motility dysfunction. However, neostigmine increased the amplitude of rhythmic contractions in both resting and distended jejunum in anesthetized ponies in one study (Parks et al., 1989), induced premature phase III-like activity in the ileum, and increased the rate of cecal emptying in another study (Lester et al., 1998a), and induced a dose-dependent increase in contractile amplitude in jejunum and pelvic flexure muscle strips (Nieto et al., 2013b). In addition, a recent study using a continuous-rate infusion (0.008 mg/kg/h) of neostigmine for 5.5 h detected increased fecal production and urination frequency, but not a decrease in gastric emptying (Nieto et al., 2013b). There has been no consensus as to the recommended use of this drug for the treatment of equine motility disorders. It is rarely used as a prokinetic in humans (Reynolds & Putnam, 1992). There is anecdotal support that neostigmine can reduce the severity of POI in horses, particularly if the large colon is involved. However, its use for impaction colic or in cases with excess GI distention has not been recommended owing to the apparent force of drug-induced contractions (Lester et al., 1998a). The dose used clinically is 0.0044 mg/kg (2 mg per adult horse) SC or IM, repeated after 20–60 min. If there is no response and the horse is not exhibiting any side effects, the dose can be increased in 2 mg increments to a total of 10 mg per treatment. The most common side effect is abdominal pain. If neostigmine is used in patients with ileus, continuous-rate infusion seems to be preferable since it reduced the severity and occurrence of abdominal pain and it does not seem to delay gastric emptying (Nieto et al., 2013b).

Acepromazine and Yohimbine

Both of these drugs are α-adrenergic antagonists. As described in the neurogenic theory of POI, afferent stimulation during surgery activates inhibitory sympathetic efferent pathways. Norepinephrine released by postsynaptic sympathetic neurons at the enteric ganglia inhibits the release of the excitatory neurotransmitter acetylcholine by stimulating α_2-receptors located presynaptically

on cholinergic neurons. Increased circulating concentrations of catecholamines, which can persist for the duration of the ileus, have been associated with increased synthesis of norepinephrine in the bowel wall in humans after laparotomy (Furness & Costa, 1974; Livingston & Passaro, 1990; Davies & Gerring, 1983). Acetylpromazine maleate facilitates small intestinal transit in normal ponies (Davies & Gerring, 1983). Based on clinical impression, acepromazine administered at 0.01 mg/kg IM q 4 h is thought to reduce the severity of POI in horses with small intestinal lesions. Because acepromazine is a nonselective α-adrenergic blocker that can produce hypotension through α_1-receptor antagonism, horses should be well hydrated before the drug is administered.

Yohimbine hydrochloride (Yobine®) is a competitive antagonist that is selective for α_2-adrenergic receptors. When administered at 0.15 mg/kg IV at 1, 4, 7, and 10 h postoperatively, it reduced the severity of experimentally induced POI, especially when combined with bethanechol. Yohimbine administered at 75 µg/kg was demonstrated to attenuate some of the negative effects that endotoxin has on propulsive motility (Eades & Moore, 1993). Since yohimbine is a selective α_2-antagonist, it should not produce the hypotensive response seen with acepromazine.

Metoclopramide

Metoclopramide (Reglan®) is a substituted benzamide whose primary prokinetic activity is through dopamine receptor antagonism. Metoclopramide produces additional prokinetic activity by augmenting the release of acetylcholine from intrinsic cholinergic neurons by acting at 5-HT receptors and through adrenergic blockade (Fernandez & Massingham, 1985; Gerring & Hunt, 1986; Megens et al., 1991; Reynolds & Putnam, 1992). Metoclopramide has been shown to stimulate *in vitro* contractile activity of circular muscle from the stomach and small intestine in the horse (Nieto et al., 2000a). In a POI model in horses, metoclopramide was more effective in restoring GI coordination, a measurement of motility strongly correlated with return of normal transit, than adrenergic antagonists or cholinergic agonists used individually or in combination (Gerring & Hunt, 1986). This provided strong evidence that POI in this model was due to a disruption of gastroduodenal coordination that was mediated through dopamine hyperactivity. Although the functional role of dopamine in GI disorders is controversial, metoclopramide does improve motility in humans regardless of its mechanism of action. In horses, the drug has been administered at a dosage of 0.25 mg/kg, diluted in 500 mL of saline, infused over 30–60 min. In a retrospective study, metoclopramide administered as a continuous infusion (0.04 mg/kg/h) decreased the total volume, duration, and rate of gastric reflux when used prophylactically after small intestine resection and anastomosis (Dart et al., 1996). Metoclopramide administered at a dose as low as 0.1 mg/kg may cause extrapyramidal side effects such as excitement, restlessness, and sweating, and also abdominal cramping. For this reason, a slow or continuous infusion is recommended (Dart et al., 1996).

Domperidone

Domperidone is also a dopamine receptor antagonist with affinity for dopaminergic type 2 receptors; however, in contrast to metoclopramide, it does not cross the blood–brain barrier (Reddymasu et al., 2007). In humans, domperidone has been used as an antiemetic and to treat dyspepsia, gastroparesis, and gastroesophageal reflux disease. Administration of domperidone (0.2 mg/kg IV) in horses with experimentally induced POI was effective in restoring the electrical and mechanical activity of the stomach, jejunum, ileum, and colon, coordination of activity cycles between the stomach and small intestine, and stomach-to-anus transit time (Gerring & King, 1989). However, the IV formulation of domperidone was withdrawn from the market in the 1980s following human deaths as a result of cardiac arrhythmias (Anon, 2012). In horses, oral domperidone (1.1 mg/kg) has been used to treat fescue toxicosis and to increase milk production in mares (Chavatte-Palmer et al., 2002; Redmond et al., 1994). A recent study in clinically healthy horses showed that oral domperidone at 5 mg/kg, but not at 1.1 mg/kg, accelerates gastric emptying of fluids evaluated by the acetaminophen absorption test (Nieto et al., 2013a). However, the use of oral prokinetics may not be applicable in horses with ileus because the presence of gastric reflux will interfere with this route of administration.

Cisapride

Cisapride (Propulsid®), a more recently developed substituted benzamide, was one of the most effective and popular prokinetics in human medicine (Reynolds & Putnam, 1992). It functions as an indirect cholinergic stimulant by selectively enhancing the release of acetylcholine from postganglionic neurons in the myenteric plexus. Unlike metoclopramide, cisapride's main prokinetic activity appears to be mediated through 5-HT_4 receptor agonism and 5-HT_3 antagonism rather than dopamine antagonism (Barone et al., 1994). In the horse, cisapride has been shown to act partly through a noncholinergic effect mediated by 5-HT_2 receptors (Nieto et al., 2000b). In experimental studies and in clinical trials in humans, cisapride's prokinetic effects were consistently equal or superior to those of metoclopramide and domperidone, a dopamine antagonist used as a prokinetic in humans (Orihata & Sarna, 1994; Reynolds & Putnam, 1992; Wiseman & Faulds, 1994). In normal horses, cisapride augments the amplitude of gastric

contractions, stimulates jejunal activity coordinated with gastric contractions, enhances contractile activity of the large and small colon, and stimulates coordinated activity in the ileocecocolonic junction (Gerring et al., 1991; Ruckebusch & Roger, 1988; Sasaki & Yoshihara, 2000). In clinical trials, cisapride has been shown to be effective in preventing POI in horses (Gerring et al., 1991). There are conflicting reports on its efficacy for correcting motility dysfunction caused by endotoxemia. One study reported no benefit, but another study suggested that cisapride could attenuate the motility dysfunction induced by endotoxemia (King & Gerring, 1992; Valk et al., 1998a). Unfortunately, the drug is now difficult to obtain owing to its cardiotoxic effects (Rampe et al., 1997). A report has shown that levosulpride, a substituted benzamide with dopamine (D_2) receptor antagonist activity in addition to 5-HT_4 agonist and 5-HT_3 antagonist activity, is as effective as cisapride in treating dysmotility in humans (Mearin et al., 2004).

Tegaserod

Tegaserod (Zelnorm®) is a partial 5-HT_4 agonist that is highly effective in humans with constipation, predominantly irritable bowel disease. *In vitro*, tegaserod increases intestinal smooth muscle contraction of the ileum and pelvic flexure (Delco et al., 2007; Weiss et al., 2002). *In vivo*, tegaserod accelerates the GI transit time and increases the frequency of defecation and score of intestinal sounds in healthy horses (Lippold et al., 2004). Plasma therapeutic concentrations of tegaserod were achieved following oral administration of a single dose of 0.27 mg/kg. However, in 2007, the US Federal Drug Administration required Novartis to suspend marketing and selling Zelnorm because of the increased risk of heart attacks, strokes, and unstable angina in treated patients. It is likely that drugs being tested or developed that have 5-HT_4 agonist and/or 5-HT_3 antagonist activity, such as levosulpride, and prucalopride, will take the place of cisapride or tegaserod in the near future (Pandolfino et al., 2000).

Mosapride

Mosapride is a selective 5-HT_4 agonist used clinically in the treatment of humans with GI motility dysfunctions (Curran & Robinson, 2008). In healthy horses, mosapride promoted motility in the small intestine and cecum (Sasaki et al., 2005) and may facilitate gastric emptying (Okamura et al., 2008). In addition, using electrointestinography to measure intestinal motility, oral mosapride (1.5 mg/kg q 24 h) increased small intestinal motility after jejunocecostomy compared with control animals (Okamura et al., 2009a). However, its use in clinical cases of POI may be limited as it is not available in the United States, there is only an oral formulation, and in humans administration is recommended at 8 h intervals.

Erythromycin

Erythromycin is a macrolide antibiotic with recognized GI side effects. Erythromycin is a motilin agonist that influences motility partly by acting on motilin receptors on GI smooth muscles. Motilin is a hormone that is released by enterochromaffin cells and that stimulates contractile activity in the stomach and small intestine. Motilin infusion in the horse causes strong contractions in the proximal jejunum *in vivo* (Sasaki & Yoshihara, 1999). Erythromycin also appears to act on enteric cholinergic neurons through motilin receptors and/or 5-HT_3 receptors to stimulate the release of acetylcholine (Ohtawa et al., 1993; Parkman et al., 1995; Reynolds & Putnam, 1992). Erythromycin initiates phase III of the MMC (Peeters, 1993). When it is administered at subtherapeutic antimicrobial concentrations, it has been shown to stimulate gastric emptying, antroduodenal coordination, and phase III activity in the duodenum in humans and laboratory animals (Peeters, 1993). In the horse, erythromycin was effective in stimulating gastric and cecal emptying and inducing phase III activity in the small intestinal (Lester et al., 1998b; Ringger et al., 1996). The recommended dose is 0.5–1.0 mg/kg in 1 L of saline infused over 60 min q 6 h. Erythromycin can down-regulate motilin receptors, which may explain why the prokinetic effect diminishes with repeated treatment. At the recommended dose, which is below the effective antimicrobial dose, antibiotic-related diarrhea should not be observed. However, there have been reports of severe colitis associated with its use, making some clinicians reluctant to use it. Although it has been a commonly used drug to treat gastroparesis in humans, some of the therapeutic benefits that were anticipated in the human field have failed to materialize.

Lidocaine

Intravenous lidocaine shortens the duration of paralytic ileus in the colon in humans after abdominal surgery (Rimback et al., 1990). A survey found that lidocaine is the most commonly use prokinetic after equine intestinal surgery (Van Hoogmoed et al., 2004). Lidocaine hydrochloride may act by (1) reducing the concentration of circulating catecholamines by suppressing the sympathoadrenal response, (2) suppressing the activity of the primary afferent neurons involved in reflex inhibition of gut motility, (3) stimulating smooth muscle directly, and (4) decreasing the inflammation in the bowel wall through inhibition of prostaglandin synthesis, inhibition of granulocyte migration and their release of lysosomal enzymes, and inhibition of free radical production (Malone et al., 1998; Wallin et al., 1987; Wood, 1972). *In vitro*, lidocaine produces an increase in contractility of circular and longitudinal smooth muscle from the small intestine of healthy horses (Nieto et al., 2000a; Tappenbeck et al., 2013) In a model of ischemia-reperfusion, *in vitro* administration of lidocaine stimulated more pronounce

contractility in injured than in control tissue (Guschlbauer et al., 2010). In addition, treatment with systemic lidocaine ameliorated the inhibitory effects of flunixin meglumine on the recovery of the mucosal barrier from ischemic injury (Cook et al., 2008). *In vivo* administration of lidocaine to healthy horses shortened the duration of phase III of the MMC (Milligan et al., 2007), had no effect on gastric emptying, small intestinal, and cecal motility (Okamura et al., 2009b), and increased the transit time of feces (Rusiecki et al., 2008). However, a study using a similar methodology found no effect of lidocaine on the transit time of feces (Elfenbein et al., 2014). In clinical trials in horses, lidocaine appeared to be effective in decreasing the duration of reflux in horses with POI and in horses with duodenitis-proximal jejunitis, reducing the incidence of POI, shortening hospitalization time, and enhancing short-term survival (Malone et al., 1998, 2006; Torfs et al., 2009). The recommended protocol requires an initial loading bolus of 1.3 mg/kg IV administered slowly over 5 min followed by 0.05 mg/kg/min in saline or lactated Ringer solution every 24 h. Side effects include muscle fasciculation, trembling, and ataxia. Muscle fasciculation has been reported in 18% of clinical cases (Malone et al., 2006). Lidocaine is metabolized by the liver to monoethylglycine xylidide and glycine xylidide and further eliminated by biliary and renal excretion. The concentration of lidocaine metabolites increased progressively after prolonged IV infusion of lidocaine in horses after colic surgery (De Solis & McKenzie, 2007) but not in healthy horses (Dickey et al., 2008). When no bolus of lidocaine is used, serum lidocaine reaches a steady state by 3 h (Dickey et al., 2008); therefore, when managing clinical cases, some clinicians prefer not to use a bolus in an attempt to prevent side effects and accumulation of lidocaine metabolites.

Conclusion

Based on the pathogenesis of POI, several areas should be targeted in treating POI in the horse. First, effective pain management with minimal use of opioid analgesics should reduce pain-induced motility depression mediated by afferent pathways while limiting the adverse affects that opioid agonists have on motility. NSAIDs should be used in preference to opioids. As stated previously, opioid-sparing analgesia in which NSAIDs have been used to reduce the amount of opioids administered has been shown to be one of the most effective ways to reduce POI in humans (Holte & Kehlet, 2000). The use of NSAIDs should have the additional benefit of decreasing the inflammatory component that contributes to POI (Kalff et al., 1998). In humans, the use of epidural local anesthetics has decreased POI. Part of this effect may be mediated by blockade of inhibitory afferent reflexes (Holte & Kehlet, 2000). Lidocaine, by blocking afferent fibers, may work in a similar manner. It currently appears to be the most frequently used drug to treat POI in horses. Choosing one of the other listed prokinetics seems to be based on the past experience of the individual clinician, attesting to the limited efficacy of available prokinetics. In humans, cisapride has received the most support based on clinical trials, although metoclopramide and erythromycin have also shown some efficacy in clinical trials (Holte & Kehlet, 2000). The limited availability of cisapride and the concern regarding erythromycin-induced diarrhea in the horse reduce the available choices for the equine clinician. A repeat laparotomy should be considered if the horse's clinical status suggests that intestinal dysfunction is due to a mechanical cause rather than a functional problem.

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14

Pathophysiology, Prevention, and Treatment of Adhesions

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Pathophysiology of Intra-abdominal Adhesions

Despite numerous research and clinical investigations, intra-abdominal adhesions continue to present clinical challenges to the equine surgeon. Depending on the location and organization of an adhesion, it may remain clinically "silent" or be the cause of serious complications. Fibrinous and omental adhesions are normal responses to peritoneal injury and inflammation and rarely cause clinical problems (Cheong et al., 2001; Ellis, 1980, 1982). Adhesions become clinically important when fibrinous adhesions mature to restrictive fibrous adhesions that compress or anatomically distort the intestine, narrowing the intestinal lumen and impeding the normal passage of ingesta (Figure 14.1). Adhesions may also lead to the development of intestinal incarceration, strangulation, or volvulus, thereby predisposing the patient to intestinal obstruction and recurrent signs of abdominal pain. Treatment of mature adhesions often is unrewarding, costly, and associated with high patient morbidity and mortality. An emphasis, therefore, should be placed on preventing adhesions rather than treating adhesions once they have formed. The primary method of minimizing the development of intra-abdominal adhesions postoperatively continues to be meticulous, atraumatic, surgical technique. However, the presence of pre-existing peritoneal inflammation and the inherently invasive nature of surgery make it difficult to prevent adhesion formation in horses. The current pharmacologic and technical advancements for adhesion prevention are directed at minimizing peritoneal trauma and inflammation, separating potentially adhesiogenic tissues during the early postoperative healing period, enhancing peritoneal fibrinolysis, and promoting intestinal motility.

Early recognition and treatment of acute abdominal pain, along with advances in anesthesia, surgery, and perioperative care have decreased the morbidity and mortality associated with surgical treatment of intestinal diseases in horses. The improved survival rate for horses undergoing exploratory celiotomy for intestinal diseases has resulted in more horse owners opting to pursue surgical treatment. Correspondingly, the clinical significance of long-term postoperative complications, such as postoperative adhesion formation, has concurrently become more apparent (Baxter, 1991; Eggleston & Mueller, 2003; Mueller, 2002).

The incidence and clinical consequences of postoperative adhesions in people are well documented. A recent prospective clinical study in human patients who had previous laparotomies demonstrated a 93% incidence of adhesion formation (Ellis et al., 1999). Furthermore, intestinal obstructions due to intra-abdominal adhesions accounted for more than 3% of all major laparotomies and more than 25% of all intestinal obstructions in people (Menzies & Ellis, 1990). The socioeconomic burden of adhesion-related intestinal obstruction in the United States is enormous, with an estimated annual healthcare expenditure of US$1.3 billion on surgical adhesiolysis and related hospital stays (Ray et al., 1998).

The specific incidence of postoperative adhesions in horses is not known, but is most likely underestimated because most adhesions are neither severe nor extensive enough to result in clinical symptoms. Additionally, many horses with postoperative pain that may be attributed to adhesion formation respond to medical management or are euthanized without a necropsy being performed. Published incidence rates of adhesions in horses have been determined primarily by findings obtained during repeat celiotomy or postmortem examination. In horses surviving surgery for small intestinal lesions, the reported incidence of adhesions that necessitate repeat celiotomy

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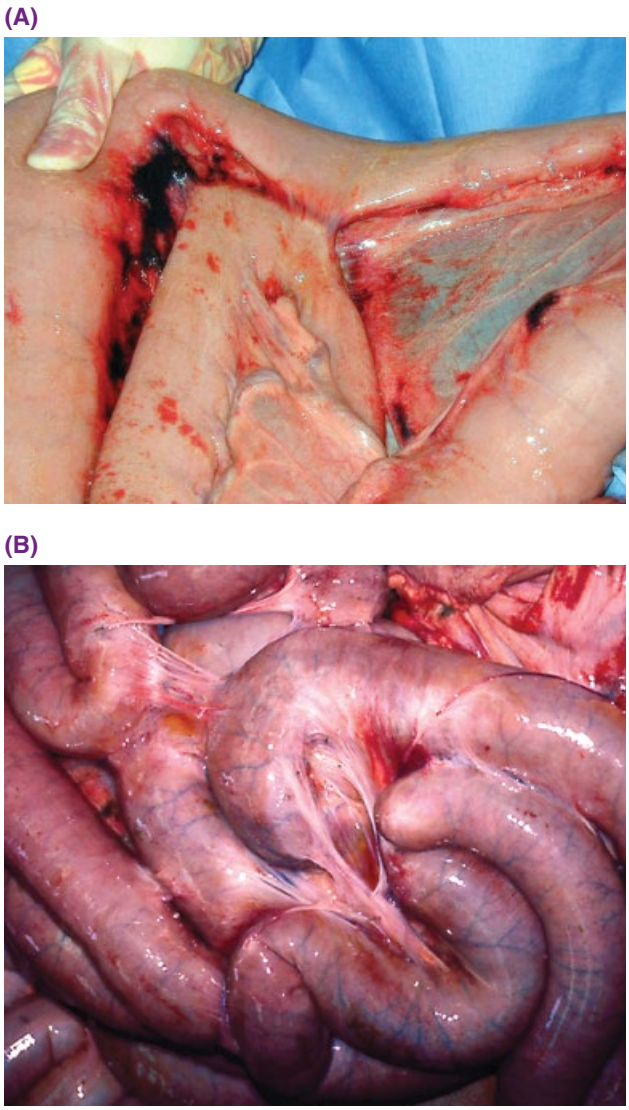

Figure 14.1 **(A)** A jejunojejunal adhesion identified during repeat celiotomy for recurrent acute abdominal pain in a horse. The adhesion caused distortion and secondary luminal obstruction of the small intestine. **(B)** Small intestinal adhesions subsequent to a volvulus in which no enterotomy was performed.

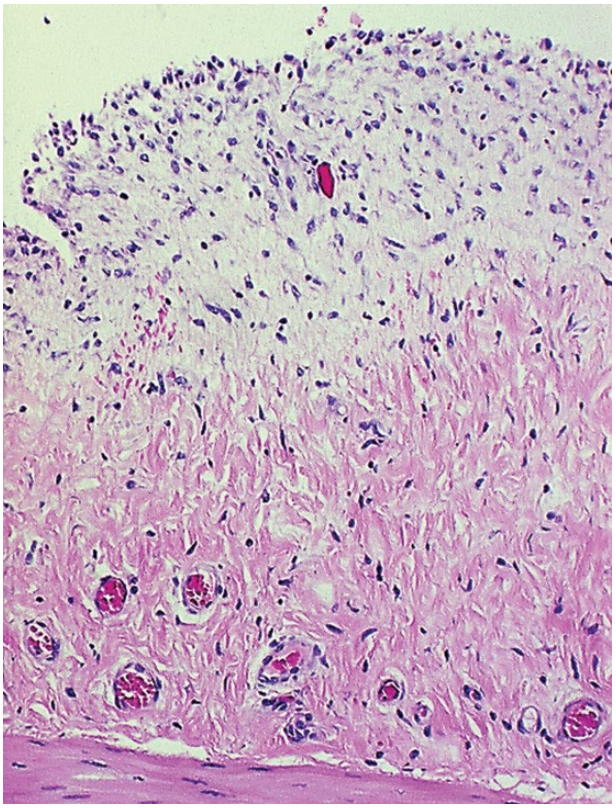

Figure 14.2 Photomicrograph of jejunal serosal adhesion resulting from experimental ischemia (2 h) and reperfusion (10 days). Fibroplasia on the surface of the original serosa has created a layer of fibroblasts without regeneration of the mesothelial surface.

or euthanasia ranges from 14 to 22% (Baxter et al., 1989; MacDonald et al., 1989; Parker et al., 1989; Phillips & Walmsley, 1993). Adhesions are the most common cause of recurrent abdominal pain in horses after small intestinal surgery and the second most common cause for repeat celiotomy in horses after abdominal surgery for any reason, with intestinal ischemic necrosis being the most common (Parker et al., 1989). When all abdominal surgeries in horses are considered, however, the incidence of postoperative adhesions has been estimated to be approximately 5% (Phillips & Walmsley, 1993).

The abdominal parietal and visceral peritoneum are composed of loose connective tissue beneath a single layer of mesothelial cells loosely interconnected by desmosomes and separated by a basement membrane (Ivarsson et al., 2001). These layers provide external support to the abdominal and intestinal musculature and maintain a lubricating layer at the serosal surface (Ellis, 1980; Lundin et al., 1989). Injury or inflammation of the peritoneal mesothelium initiates adhesion formation by stimulating procoagulant activity of the mesothelium or exposed basement membrane. This is characterized by secretion of serofibrinous exudate and deposition of fibrin (Ivarsson et al., 2001; Ellis, 1962). The result is a fibrin matrix that can form fibrinous adhesions between adjacent viscera or peritoneum within hours of injury (Holmdahl, 1997). The initial fibrin matrix provides a scaffold for vascular and cellular migration, allowing tissue repair and restoration of the inflamed serosa and mesothelium (Ellis, 1982; Holmdahl, 1997; Ellis et al., 1965). As normal peritoneal healing progresses, fibroblasts and endothelial cells migrate into the fibrin to form a layer of granulation tissue that fills the original mesothelial defect. Primordial mesenchymal cells then form fibroblasts or differentiate into mesothelial cells and cover the granulation tissue (Figure 14.2) (ArRajab et al., 1995; Felton et al., 1990).

Local peritoneal fibrinolytic activity lyses the fibrin and fibrinous adhesions within 48–72 h. Therefore, when inflammation is not excessive, adhesions are removed before they mature to fibrous tissue (Baxter, 1991; ArRajab et al., 1995; Holmdahl et al., 1997a, 1997b). However, intestinal ischemia or inflammation caused by strangulation or distention, or the incidental trauma that occurs during surgical manipulation of the bowel may depress peritoneal fibrinolytic activity, thereby, predisposing to the persistence of fibrin within the abdomen and ultimately to adhesion formation (Ellis, 1982; Baxter, 1991; Lundin et al., 1989; Holmdahl et al., 1996, 1997a, 1997b, 1998; Menzies & Ellis, 1991).

Coagulation, fibrinolysis, kinin/bradykinin, arachidonic acid metabolism, and complement activation are some of the complex biological processes that are involved in the pathogenesis of adhesion formation. The fibrinolytic system is the principal modulator of adhesion formation and is responsible for lysis of fibrin into fibrin degradation products through the action of the enzyme plasmin (Holmdahl, 1997; Holmdahl et al., 1994; Ivarsson et al., 1998b; Mayer et al., 1988). Plasmin is stored as the inactive substrate plasminogen, which is converted to the active enzyme primarily by tissue plasminogen activator (tPA), and to a lesser extent, by urokinase-type plasminogen activator (uPA). tPA is present in virtually all tissues and is responsible for 95% of plasmin generation in the human peritoneum (Holmdahl et al., 1998).

Fibrinolysis is a potent process and is tightly regulated by plasminogen activator inhibitors type 1 (PAI-1) and type 2 (PAI-2). Synthesis of these inhibitors is induced by stimuli such as trauma, infection, or endotoxin (Holmdahl, 1999; Eriksson & Risberg, 1987; Collatos et al., 1995). These inhibitors bind and form inactive complexes with tPA and uPA. Slower-acting plasma proteins, α_2-antiplasmin, α_2-macroglobulin, and α_2-antitrypsin, also are inhibitors of plasmin activity; however, their role in tissue repair and adhesions is not well delineated. A decrease in plasminogen activator activity may result from decreased concentrations of plasminogen activators, and/or increased expression of PAIs (Holmdahl, 1997; Holmdahl et al., 1994, 1996, 1997a, 1997b; Mayer et al., 1988; Ivarsson et al., 1998a). The difference between normal peritoneal healing and adhesion formation lies in the balance between fibrin deposition and degradation and, ultimately, fibrosis of the serosa. Peritoneal fibrinolytic activity has been hypothesized to play an important role in adhesion formation (Ellis, 1962; Holmdahl, 1997, 1999; Holmdahl et al., 1994, 1996; Menzies & Ellis, 1991; Ivarsson et al., 1998a). If local fibrinolysis is adequate, fibrinous adhesions are lysed and normal mesothelial restoration occurs. In contrast, if local fibrinolysis is insufficient, fibrin persists, becomes infiltrated with fibroblasts and capillaries, and permanent fibrous adhesions are formed. The precise role of peritoneal hypofibrinolysis in the pathogenesis of adhesion formation has yet to be elucidated.

Risk factors associated with postoperative adhesion formation include small intestinal disease (Baxter, 1991; Baxter et al., 1989; MacDonald et al., 1989; Phillips & Walmsley, 1993; Kuebelbeck et al., 1998), intestinal resection and anastomosis (Phillips & Walmsley, 1993; Southwood & Baxter, 1997), and abdominal surgery in foals (Lundin et al., 1989) or Miniature horses (Ragle et al., 1992). It has been the author's experience that middle to aged horses (more than 15 years of age) are less likely to develop complications related to postoperative adhesion formation than younger horses.

Prevention and Treatment of Intra-abdominal Adhesions

Diagnosis of Intra-abdominal Adhesions

The presenting clinical signs of horses with intra-abdominal adhesions are similar to those associated with acute abdominal pain secondary to small intestinal obstruction or strangulation (see Chapter 20). Consequently, a complete and thorough history, physical examination, including nasogastric intubation, transrectal examination, abdominocentesis, and laboratory examination should be performed. Information obtained from the clinical history of previous abdominal surgery or diseases causing severe intra-abdominal inflammation, such as diffuse enteritis or peritonitis, should alert the clinician to the possibility that intra-abdominal adhesions may be responsible for clinical signs of acute abdominal pain. Although not common, severe peritoneal inflammation secondary to enteritis and peritonitis may result in intra-abdominal adhesion formation and clinical symptomatology in horses or foals that have not undergone an exploratory celiotomy.

The clinical signs associated with intra-abdominal adhesions vary in relation to the degree of luminal or vascular compromise. Horses with adhesions that distort or compress the intestine without compromising vascular integrity may have clinical signs consistent with mild to moderate recurrent abdominal pain. In contrast, adhesions that result in complete luminal obstruction or secondary vascular compromise as a result of intestinal incarceration or strangulation are usually associated with clinical signs of severe, unrelenting abdominal pain. Results of cytologic examination of peritoneal fluid obtained from horses with intra-abdominal adhesions usually reflect the nature of the current disease process (obstruction or strangulation) and are not specifically indicative of adhesion formation. Transrectal examination often reveals distention of the segment of affected

intestine. Chronic, partial obstruction produces dilated, thickened intestine, proximal to the obstruction. If the adhesion is located in the caudal aspect of the abdomen, in rare instances it may be palpated by the examiner. Ultrasonography and laparoscopy are additional ancillary procedures that may be performed to support or confirm the diagnosis of intra-abdominal adhesions (see Chapter 20) (Scharneer et al., 2002; Boure et al., 2002; Chosidow et al., 2000; Rocken et al., 2001).

Current Concepts in Prevention of Adhesion Formation

An emphasis is placed on prevention of adhesion formation, because treatment of mature adhesions often is unrewarding, costly, and associated with high patient morbidity and mortality (Baxter, 1991; Mueller, 2002; Ellis et al., 1999; MacDonald et al., 1989; Ellis, 2001; Hay et al., 1998). The primary objectives in preventing adhesions are: (i) to minimize peritoneal and serosal inflammation; (ii) to maintain or enhance peritoneal fibrinolysis; (iii) to mechanically separate potentially adhesiogenic surfaces; and (iv) to stimulate adequate intestinal motility (Ellis, 1982; Baxter, 1991; Holmdahl et al., 1997a, 1997b; diZerega & Campeau, 2001; Parker et al., 1987; White, 1992).

Perioperative Pharmacologic Interventions to Prevent Adhesion Formation

Intravenous administration of broad-spectrum antimicrobials, nonsteroidal anti-inflammatory agents, and dimethyl sulfoxide (DMSO; 20 mg/kg) has been reported to minimize adhesion formation (Ellis, 1982; Baxter, 1991; Lundin et al., 1989; Southwood & Baxter, 1997; White, 1992; Dijkstra et al., 2000; Nishimura et al., 1984; Oncel et al., 2001; Sullins et al., 2004). All of these pharmacologic agents have been shown to decrease peritoneal inflammation, thereby minimizing fibrin production and subsequent adhesion formation. A routine perioperative pharmacologic regimen for a horse undergoing exploratory celiotomy includes potassium penicillin (22,000 IU/kg, IV, every 6 h), gentamicin (6.6 mg/kg, IV, every 24 h), flunixin meglumine (1.1 mg/kg, IV, every 12 h), and DMSO (100 mg/kg in 1 L 0.9% NaCl, IV, every 8 h). If a typhlotomy or small colon enterotomy is anticipated, metronidazole (20 mg/kg, PO or PR, every 6 h) is administered to provide antimicrobial activity against anaerobes. Antimicrobial administration is continued for 48–96 h postoperatively, depending on the location and severity of the initial lesion, duration of surgery, and the potential for intraoperative contamination.

Heparin, a naturally occurring proteoglycan, has been reported to decrease adhesion formation in an intestinal ischemia-reperfusion model in ponies but not in foals (Sullins et al., 2004). Heparin acts as a cofactor of antithrombin to increase the rate of antithrombin inactivation of serine protease coagulation factors. The result is decreased production of thrombin, which is responsible for the conversion of fibrinogen to fibrin, and ultimately the formation of fibrous adhesions. Heparin also enhances fibrinolysis by stimulating plasminogen activator activity. The recommended dosage and route of administration of heparin remain controversial. Systemic dosages from 20 to 100 IU/kg, IV or SQ every 6–12 h, for 48–72 h postoperatively have been used.

Fucoidans are a class of broad molecular weight, sulfated polysaccharides that are extracted from the extracellular matrix of various brown algae (Fitton, 2011; Peridan®). Fucoidan extracts have been demonstrated to possess a variety of biological properties, including antiadhesive, anticoagulative, and anti-inflammatory effects through interactions with thrombin, antithrombin, heparin cofactor II, and leukocyte membrane receptors (selectins) (Fitton, 2011). Fucoidans derived from different sources have different chemical structures and there appears to be an important relationship between structure and biological activity (Li et al., 2008; Cumashi et al., 2007). Some fucoidans induce a minimal effect on coagulation, and the extensive sulfate branching of high-molecular weight fucoidan extractions may cause them to act as a physical barrier (Yamout et al., 2007; Cashman et al., 2009a, 2009b, 2011).

Peridan® (ARC Medical Devices Inc., Vancouver, Canada) is a high-molecular weight, commercially available customized, purified fucoidan. Peridan concentrate is a nonpyrogenic, sterile, nonviscous liquid comprising 5% w/v Peridan in lactated Ringer's solution. Peridan concentrate is available in 50 mL vials (adult horse) or 5 mL vials (foal). For use in horses, the 50 mL vial is mixed into 5 L lactated Ringer's solution or Plasma-Lyte™ solutions; for use in foals, the 5 mL vial is mixed into 500 mL of either solution. The final mixture is then administered into the abdomen prior to abdominal closure.

Studies performed in laboratory animals (Cashman et al., 2009a, 2009b) and pony foals (Yamout et al., 2007) have demonstrated safety and efficacy of intraperitoneal administration of fucoidan solutions prior to abdominal closure in minimizing the number and severity of experimentally induced postoperative adhesions. Morello and colleagues also have demonstrated safety of fucoidan in a jejunojejunostomy anastomosis model in adult horses (Morello et al., 2012). There are no published clinical or experimental studies demonstrating the efficacy of fucoidans in reducing the incidence or severity of postoperative adhesion formation in adult horses. However, in a rat model, a hyaluronate-fucoidan biofilm reduced adhesion scores by 90% as compared to controls (Cashman et al., 2011). Investigating new fucuoidan films or fucoidan-Seprafilm™ combinations in horses may have potential as an affordable and efficacious preventative anti-adhesion therapy for horses.

Intraperitoneal administration of heparin has been shown to reduce adhesion prevention in laboratory animals (Diamond et al., 1991; Sahin & Saglam, 1994); however, neither experimental nor controlled clinical studies have been performed in horses. In horses at a risk of adhesion formation, the author administers 30,000 IU of heparin (Heparin Sodium™, Elkins-Sinn Inc., New Jersey, USA) diluted in 4 L of lactated Ringer's solution into the abdomen before closure of the abdominal incision. Intravenous administration of heparin sulfate (40 IU/kg, every 6 h) is continued for 48–72 h postoperatively. Systemic administration of heparin results in a transient decrease in the packed cell volume (PCV) by as much as 50% after 3–4 days of heparin therapy. This decline in PCV is due to erythrocyte agglutination and not hemorrhage or hemolysis (Mahaffey & Moore, 1986). The PCV returns to normal within 4 days after cessation of heparin therapy.

Recombinant tPA, a thrombolytic agent that binds to fibrin and activates the conversion of plasminogen to plasmin, decreases the incidence of postoperative adhesion formation in laboratory animal models (Buckenmaier et al., 2000; Evan et al., 1993; Hellebrekers et al., 2000a; Lai et al., 1998). Concentrations of 0.01–0.5 mg/mL have been used. The results of studies on the effect of recombinant tPA on the healing of anastomoses have been mixed, with some studies indicating no effect (Buckenmaier et al., 2000), and others indicating inferior anastomotic healing with intraperitoneal administration of recombinant tPA (Evan et al., 1993). The intraperitoneal use of recombinant tPA in horses may not be economically practical. However, studies demonstrating efficacy in adhesion prevention by adding lower concentrations of recombinant tPA to protective barrier solutions, such as sodium carboxymethylcellulose (Buckenmaier et al., 2000), may be of potential benefit in equine abdominal surgery.

Recent studies have elucidated beneficial effects of the class of drugs known as statins beyond their impact on serum cholesterol levels. In particular, statins have been shown to minimize the incidence and severity of intra-abdominal adhesion formation via their potent anti-inflammatory, antioxidant, and profibrinolytic properties (Haslinger et al., 2002; Lalountas et al., 2010; Van der Wal & Jeekel, 2007). Aarons et al. (2007) demonstrated that statins are effective in reducing intra-abdominal adhesions by promoting a profibrinolytic environment within the abdomen without promoting peritoneal hemorrhage. Their data provide direct evidence from both *in vivo* and *in vitro* studies that statins reduce intra-abdominal adhesion formation by modulating the peritoneal fibrinolytic environment. Statins increase tPA production and decrease PAI-1 production by human mesothelial cells (Van der Wal & Jeekel, 2007; Aarons et al., 2007). An increase in the tPA : PAI-1 ratio up-regulates and favors fibrinolysis over fibrinogenesis, thereby inhibiting adhesion formation.

The anti-adhesion properties of statins are limited to topical administration at very high doses (30 mg/kg), approximately 25-fold higher than doses typically used clinically in people. High doses of statins have been associated with various complications including rhabdomyolyis, and impaired liver and renal function (Lalountas et al., 2010). These toxic effects limit the systemic use of statins in horses. However, the potential to combine low-dose topical statin therapy with resorbable barriers substances, such as Seprafilm, may be an avenue for future research.

Postoperative ileus may increase the risk of adhesion formation by maintaining inflamed serosal surfaces in close apposition. Predisposing factors that have been implicated in the development of ileus include chronic intestinal distention, ischemia, peritonitis, excessive intestinal manipulation, electrolyte abnormalities, and sedative and anesthetic drugs (Van Hoogmoed and Snyder, 1997) (see Chapters 11 and 48). Prolonged apposition of inflamed serosal or peritoneal surfaces is likely to result in the formation of restrictive, permanent fibrous adhesions between these surfaces. In addition, intestinal distention alone results in serosal injury and ischemia, and has been demonstrated to cause adhesions in foals (Lundin et al., 1989). Various gastrointestinal prokinetic agents, such as lidocaine hydrochloride, neostigmine, metoclopramide, erythromycin, and cisapride, have been evaluated in experimental and clinical studies in horses (Van Hoogmoed & Snyder, 1997). The clinical benefit of these agents in horses after abdominal surgery remains controversial. Early return to enteral nutrition may be the most important factor in stimulating and maintaining intestinal motility postoperatively.

Intraoperative Considerations and Preventive Therapy

Minimizing peritoneal trauma and inflammation through meticulous aseptic surgical technique and removal of all potentially adhesiogenic tissues are the most important principles of adhesion prevention (Hay & Mueller, 1998). Strict adherence to Halsted's principles of surgery, including minimal and atraumatic tissue handling, meticulous hemostasis, minimizing tissue contamination from exposed bacteria-laden intestinal mucosa, minimizing exposure of foreign materials, and short surgery time are all essential to minimize the incidence of postoperative adhesion formation.

Starch powder present on commercially available surgical gloves incites peritoneal inflammation and significantly increases adhesion formation in a dose-dependent manner (Chegini & Rong, 1999; Ellis, 1990; Ignjatovic et al., 2001; Sjostein et al., 1999; van den Tol et al., 2001). Simple rinsing of gloves before surgery does not effectively remove the starch powder from the glove surface; therefore, powder-free, hydrogel-coated gloves (Biogel

Powder Free Surgical Gloves™, Regent Medical, Norcross, Georgia, USA) should be used when performing intra-abdominal surgery.

Intestinal manipulation should be as atraumatic as possible. Serosal surfaces should be kept moist with balanced electrolyte solutions to prevent direct mesothelial damage from desiccation. Protective coating solutions such as 1% sodium carboxymethylcellulose or 0.4% hyaluronate solution (see section on protective coating solutions later) should be applied to the surgeons' gloves and all serosal surfaces before and during intestinal manipulation to provide a protective lubricating barrier and minimize serosal friction, abrasion, and incidental surgical trauma (Eggleston & Mueller, 2003; Mueller, 2002; Kramer et al., 2002; Yaacobi et al., 1993). Potentially adhesiogenic tissues such as devitalized intestine, or intestine of questionable viability should be resected. Inverting or appositional anastomotic suture patterns should be used to minimize peritoneal exposure of bacteria-laden mucosa and suture, and preserve normal intestinal motility and function, thereby minimizing the incidence of adhesion formation (Dean & Robertson, 1985; Jansen et al., 1981; Pascoe & Peterson, 1989; Reinertson, 1976).

Although controversial, surgical techniques such as omentectomy have been advocated to minimize adhesion formation (Kuebelbeck et al., 1998). Omental adhesions may cause signs of abdominal pain by creating abnormal tension on the mesentery, or serving as a focus for intestinal obstruction or strangulation. Conversely, omental adhesions have also been reported to provide a vascular supply to potentially ischemic tissue, thereby, facilitating healing and potentially preventing adhesions (Ellis, 1980; Holmdahl, 1999; diZerega & Campeau, 2001). In one retrospective study in horses, omentectomy was associated with a lower incidence of clinically significant adhesions (Kuebelbeck et al., 1998). In the author's opinion, omental adhesions rarely cause clinically significant problems. The author has been successful in intentionally suturing omentum to serosal surfaces to cover potentially adhesiogenic intestinal tissues in an effort to minimize subsequent adhesion formation. If this technique is used, the possibility of future strangulations involving attached omentum must be weighed against the benefits of using a vascular omental pedicle. Removal of inflamed or damaged omentum also seems logical to prevent future adhesions, although its effect on the risk of adhesions has not been documented (Figure 14.3).

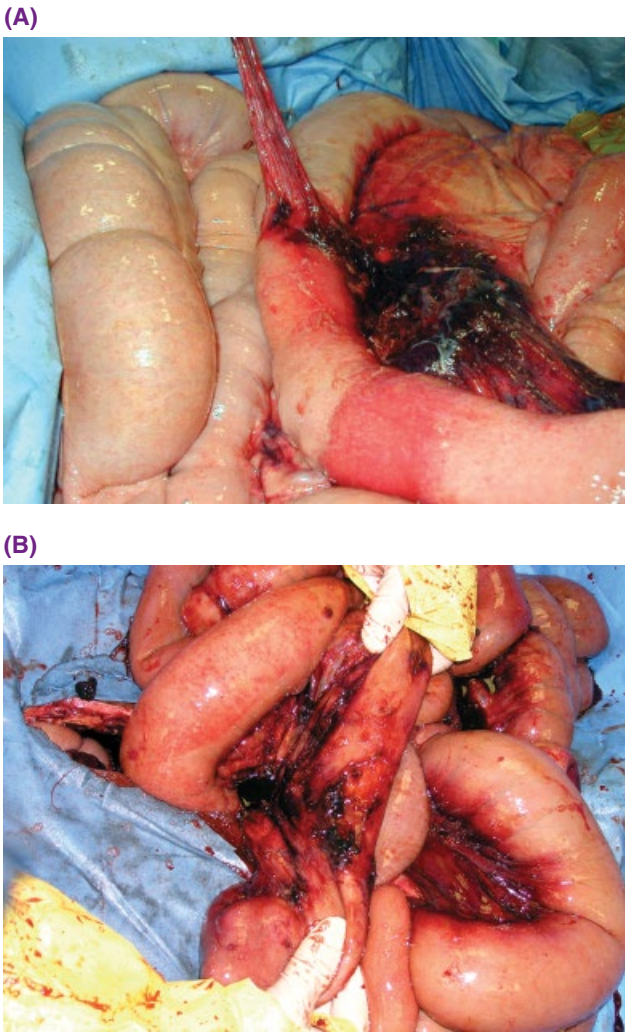

Figure 14.3 Omental fibrosis **(A)** and separation **(B)**, both of which can cause future adhesion formation and strangulation. Omentectomy is recommended when the omentum appears damaged or inflamed.

Separation of Adhesiogenic Surfaces

Intra-abdominal Lavage

Intraoperative abdominal lavage is advocated to prevent desiccation of serosal surfaces, minimize serosal trauma during intestinal manipulation, and remove blood, fibrin, and inflammatory mediators from the abdominal cavity (Southwood & Baxter, 1997; Hay & Mueller, 1998; Hague et al., 1998). Postoperative intra-abdominal lavage through an indwelling tube placed at the time of surgery has been demonstrated to reduce the incidence of adhesions in an experimental serosal abrasion model of adhesion formation (Hague et al., 1998). Ten liters of warm lactated Ringer's solution is infused into the abdomen through a 32 F fenestrated catheter (Trocar Catheter™, Deknatel Inc., Massachusetts, USA) placed in the right ventral abdomen, just cranial and lateral to the cranial extent of the celiotomy incision. The lavage fluid is then allowed to drain through a Heimlich valve (Bard-Parker Heimlich Chest Drain Valve™, Benton Dickson Co., Franklin Lakes, New Jersey, USA). The lavage procedure is performed at 12, 24, and 36 h after surgery and then the catheter is removed. Postoperative intra-abdominal

lavage is reported to decrease adhesion formation by creating a hydroflotation effect, which separates intestinal serosal surfaces, and by removing fibrin and inflammatory mediators (Hague et al., 1998). Reported complications associated with this technique include occlusion of the catheter with fibrin and localized ventral edema at the abdominal catheter placement site. The author uses postoperative abdominal lavage in horses that are at a particularly high risk of adhesion formation (severe, diffuse peritoneal inflammation and/or potential intraoperative bacterial contamination). Heparin sodium (30,000–50,000 IU/10 L lactated Ringer's solution) is routinely added to the lavage fluid.

Protective Tissue Coating Solutions

Coating tissues with protective lubricating barrier solutions during abdominal surgery minimizes adhesion formation by reducing the extent and severity of tissue damage that occurs as a consequence of surgical manipulation (Burns et al., 1995; Peck et al., 1995; Urman & Gomel, 1991a, 1991b). Precoating visceral tissues involves manual application of these solutions to the serosal surface before manipulation, and is more effective at reducing adhesion formation than intraperitoneal administration of the solutions at the end of surgery, after tissue damage has already occurred (Yaacobi et al., 1993; Burns et al., 1995; Goldberg et al., 1993). Additionally, these solutions provide a mechanical lubricating barrier between serosal and peritoneal surfaces, preventing the formation of adhesions in the early postoperative healing period (Mueller, 2002; Hay et al., 2001; Moll et al., 1991; Mueller et al., 2001a).

Protective tissue coating solutions commonly used in equine abdominal surgery are high-molecular weight viscous polymer solutions such as 1% sodium carboxymethylcellulose (SCMC) and 0.4% sodium hyaluronate solution. Of these solutions, 1% SCMC is the most popular because of its availability, ease of preparation, and relatively low cost. Administration of SCMC has been shown to prevent the reformation of adhesions after surgical lysis in laboratory animals (Yaacobi et al., 1993; Wurster, 1995). Furthermore, studies have demonstrated that intraperitoneal instillation of SCMC significantly decreases experimentally induced adhesion formation in horses (Hay et al., 2001) without adversely effecting intestinal (Mueller et al., 2000a) or abdominal wound healing (Mueller et al., 1995). Initial studies recommended administering 7 mL/kg of 1% SCMC solution (approximately 3 L/450 kg horse) into the abdomen just prior to abdominal closure (Moll et al., 1991). Based on experience and experimental studies (Holmdahl et al., 1998; Lai et al., 1998; Eggleston et al., 2001b), the author recommends using 1–2 L of 1% SCMC solution per 450 kg horse. The solution is applied to the surgeon's gloved hands and serosal surface of the intestine at the start of surgery. The solution is reapplied as necessary to keep the intestinal and peritoneal surfaces well lubricated, thereby minimizing incidental serosal trauma. The SCMC solution does not support bacterial growth (Hunt et al., 1991) and is removed from the abdomen by peritoneal macrophages within 4–7 days after administration (Burkhard et al., 1996).

A 1% w/w solution of SCMC is prepared by adding boiling, sterile water to 10 g of SCMC powder to bring the total volume to 1 L. Cold filtering of the SCMC through a 0.22 micron filter increases the viscosity of the solution, but is extremely tedious and is not routinely performed in the author's hospital. The SCMC solution is then transferred into 1 L glass bottles and autoclaved at 121 °C for 20 min. The shelf life of the solution is 60 days.

The results of a study in laboratory animals indicate that a combination of SCMC and 0.5 mg/mL of recombinant tPA is more effective at reducing postoperative adhesion formation than either agent alone (Buckenmaier et al., 2000). This combined treatment has not been evaluated in horses but may be of potential benefit in the future.

Sodium hyaluronate is a naturally occurring hydrophilic polymer that has been proven effective in reducing postoperative adhesions after abdominal (Burns et al., 1995; Urman & Gomel, 1991a, 1991b; Goldberg et al., 1993), pericardial (Mitchell et al., 1994a), and orthopedic operations (Halberg & Gerin, 1992). Sodium hyaluronate readily forms tissue protective solutions and is an excellent tissue lubricant, even at low concentrations (Burns et al., 1995; Goldberg et al., 1993; Mitchell et al., 1994b). As well as having an anti-inflammatory effect, sodium hyaluronate prevents adhesions by forming a protective lubricating barrier on the intestinal serosal surface, much like SCMC, by preventing abrasive manipulative trauma and desiccation, and by preserving the integrity of mesothelial surfaces (Burns et al., 1995; Peck et al., 1995; Urman & Gomel, 1991a, 1991b; Goldberg et al., 1993). Concentrations of 0.4% sodium hyaluronate have been shown to maximally inhibit adhesion formation (Burns et al., 1995; Peck et al., 1995). The 0.4% sodium hyaluronate solution is resorbed from the peritoneal cavity and excreted within 5 days of administration (Kramer et al., 2002; Goldberg et al., 1993).

An additional benefit of sodium hyaluronate solutions over SCMC may be chemical modulation of adhesion formation by increasing tPA concentrations at the visceral peritoneal surface and promoting mesothelial fibrinolysis (Mayer et al., 1988). This profibrinolytic effect is attributed to preservation of mesothelial cell layer integrity during intestinal manipulation, thereby, retaining local concentrations of mesothelial tPA within the visceral peritoneum. Additionally, the results of

recent *in vitro* studies indicate that sodium hyaluronate also enhances the fibrinolytic response of human mesothelial cells exposed to tumor necrosis factor-α by decreasing both the synthesis and release of PAI (Reijnen et al., 2001). Alternatively, the sodium hyaluronate solution may act as a barrier, containing profibrinolytic enzymes such as tPA, on the intestinal serosal surface, and resulting in high local concentrations of tPA (Mayer et al., 1988; Peck et al., 1995). The result is dissolution of early fibrinous adhesions before they become mature fibrous adhesions.

The results of experimental studies in horses have demonstrated that a 0.4% sodium hyaluronate solution (SepraCoat™, Genzyme, Massachusetts, USA) significantly decreases the incidence and severity of experimentally induced intra-abdominal adhesions without adversely affecting jejunal anastomotic healing (Mueller et al., 2001a). Unfortunately, cost-effective commercial preparations of sodium hyaluronate in sufficient volumes are not presently available.

Resorbable Barrier Substances

Various resorbable barrier materials have been evaluated in laboratory animal models of adhesion formation. Such materials include oxidized regenerated cellulose (Interceed TC7™) (Arora et al., 1994; Haney et al., 1995; Hellebrekers et al., 2000b), expanded polytetrafluoroethylene (Gore-Tex Surgical Membrane™) (Haney et al., 1995; Hellebrekers et al., 2000b), synthetic biodegradable polymers, fibrin glue (Tissucol™) (Hellebrekers et al., 2000b), and a bioresorbable hyaluronate-carboxymethylcellulose membrane (Seprafilm) (Hellebrekers et al., 2000b; Ghellai et al., 2000; Baptista et al., 2000; Amid, 1999; Mathias, 1999; Skinner et al., 1992).

Ideally, a barrier substance should effectively prevent adhesion formation, be highly biocompatible, be resorbable, be effective on inflamed surfaces, be applicable through a laparoscope, and cost-effective (Hellebrekers et al., 2000b). Although the ideal barrier substance does not exist, the barrier substance that has received the most attention and use in equine surgery is a bioresorbable hyaluronate-carboxymethylcellulose membrane (HA membrane; Seprafilm, Genzyme Corp., Massachusetts, USA).

The HA membrane was developed to reduce postoperative adhesion formation in people (Skinner et al., 1992; Mitchell et al., 1994b; Becker et al., 1996). In experimental models of adhesion formation in laboratory animals, the HA membrane reduced the frequency and severity of postsurgical adhesions to parietal and visceral peritoneal surfaces and the pericardium (Skinner et al., 1992; Mitchell et al., 1994b). The flexible HA membrane is applied to the serosal surface of the intestine or parietal peritoneum, forming a temporary protective barrier against serosal–serosal or serosal–peritoneal adhesion formation during early postoperative healing (Figure 14.4) (Skinner et al., 1992; Mitchell et al., 1994b; Becker et al., 1996; Mueller et al., 2000b, 2001a). After the membrane is applied to the tissue, the membrane hydrates to form a gel that adheres to tissues and most surfaces. This gel remains at the site of application for up to 7 days, separating potentially adhesiogenic surfaces, and is then cleared from the abdominal cavity within 28 days by peritoneal macrophages. In a prospective multicenter study, use of the HA membrane decreased the incidence of postoperative adhesions from 94 to 51% in people undergoing abdominal surgery for colectomy and diverting-loop ileostomy (Becker et al., 1996). Similarly, the HA membrane has been shown to significantly reduce postoperative adhesion formation in horses (Mueller et al., 2000b), with no adverse effects on intestinal or peritoneal healing (Mueller et al., 2001b).

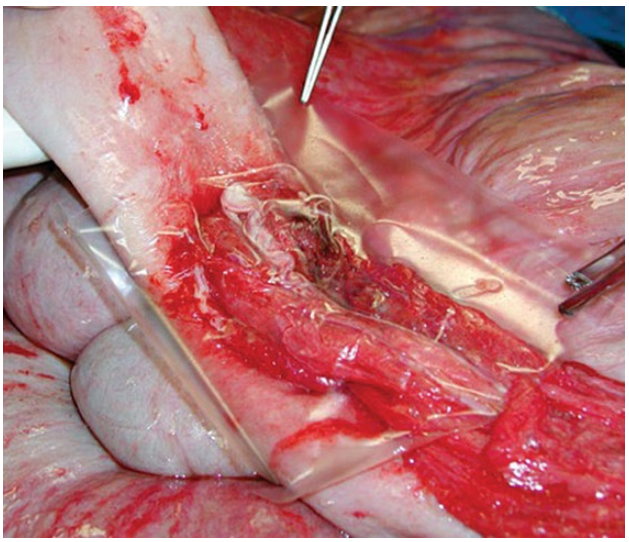

Figure 14.4 Intraoperative photograph demonstrating a hyaluronate-carboxymethylcellulose membrane covering a focal area of serosal inflammation and an omental adhesion to a segment of equine jejunum. The membrane is applied to completely cover the inflamed jejunal serosa and adjacent mesentery.

The HA membrane is used as an adjunct in abdominal surgery for reducing the incidence, extent, and severity of postoperative adhesions at the site of placement. The surgical lesion is corrected and the HA membrane is applied to potentially adhesiogenic surfaces just prior to abdominal closure (see Figure 14.4).

More recently, the HA membrane has been demonstrated to facilitate small intestinal anastomoses in horses. Use of an HA membrane in combination with a continuous single-layer appositional suture pattern results in an anastomosis with larger stomal diameters and takes less surgery time than a conventional, two-layer, inverting anastomosis (Eggleston

et al., 2001a). This technique also minimizes the incidence of perianastomotic adhesion formation (Eggleston et al., 2001a).

The author routinely uses one to two HA membranes in areas of localized serosal or peritoneal trauma that are at an increased risk of postoperative adhesion formation. Such areas would include focal areas of intestinal inflammation, segments of intestine that have vascular compromise, but deemed viable by subjective or objective measures, and focal adhesion formation in which adhesiolysis was subsequently performed. Additionally, HA membranes may be used to facilitate small intestinal and small colon anastomoses in foals and adult horses (Eggleston et al., 2001a).

Treatment of Intra-abdominal Adhesions

Treatment of horses with mature adhesions that are causing clinical problems often is unrewarding, costly, and associated with a poor prognosis for survival. In less severe cases, recurrent abdominal pain associated with postoperative adhesions may be managed successfully by feeding a low residue diet of complete pellet rations and grazing green grass. Severe restrictive adhesions that result in complete intestinal obstruction or strangulation require repeat celiotomy or euthanasia.

Surgical treatment of adhesions involves establishing a functional conduit for passage of intestinal contents and removal of any devitalized intestine. In most cases, adhesiolysis alone is associated with an unacceptable rate of repeat adhesion formation. Therefore, in such cases resection of all potentially adhesiogenic tissue should be performed. If mature, fibrous adhesions are present, an intestinal bypass is performed without adhesiolysis to minimize the formation of new adhesions. Protective lubricating solutions should be used during intestinal manipulation, and all potentially adhesiogenic tissues that must be left *in situ* should be completely covered with a resorbable barrier substance. Laparoscopic adhesiolysis has been reported in humans; however, this procedure is of limited use in horses with acute intestinal obstruction and severe intestinal distention. Successful laparoscopic adhesiolysis of focal, less severe, intestinal adhesions in foals and horses has been reported (Boure et al., 2002; Rocken et al., 2002; Bleyaert et al., 1997).

The prognosis for horses requiring repeat celiotomy due to adhesions is poor, with reported long-term survival rates ranging from 0 to 20% (Baxter, 1991; Baxter et al., 1989; Parker et al., 1989; Southwood et al., 1997). Most clinical complications in horses associated with postoperative adhesions are apparent within the first 60 days after surgery and are associated with decreased survival rates, as compared with horses in which adhesions first cause clinical problems more than 60 days after the original celiotomy (Baxter et al., 1989). In a survey of equine surgeons, 91% reported a less than 50% success rate for treating horses with adhesions that required additional celiotomies, and 25% of respondents had a less than 10% success rate in horses that required a second celiotomy (Southwood et al., 1997).

Adhesion Prevention Strategies

In the author's hospital, all horses undergoing exploratory celiotomy receive intravenous balanced isotonic fluid therapy based on their deficit and maintenance requirements (see Chapter 27), intravenous broad-spectrum antimicrobials, and flunixin meglumine (1.1 mg/kg, IV) preoperatively. One percent SCMC is applied to the surgeon's hands and serosal surfaces of the intestine at the start of surgery and during all manipulations. Horses determined to be at high risk of forming postoperative intra-abdominal adhesions, for example a horse with a rent in the mesentery incarcerating 15–20 feet of devitalized small intestine, benefit from aggressive perioperative and intraoperative anti-adhesion therapy. In these cases, additional therapies may include those targeted at correcting severe dehydration, metabolic acidosis, electrolyte abnormalities, and endotoxemia. Intraoperatively, a 1% SCMC solution is applied to the devitalized segment of intestine within the rent, via a sterile stallion catheter. This reduces the friction against the surface of the entrapped intestine and facilitates reduction of the incarceration. After completion of the resection and anastomosis, lavage of the abdominal cavity is completed with 10–20 L of warm sterile lactated Ringer's solution. Ten to 20 million units of potassium penicillin and/or 20,000–30,000 units of heparin may be added to the lavage fluid. Once lavage of the abdominal cavity is complete, SCMC is reapplied to the small intestine. The anastomosis is exteriorized, and a single HA membrane is applied to the anastomotic site. Depending on the severity of peritoneal inflammation, contamination, and overall assessment of the remaining intestine, a fenestrated abdominal drain may be placed for performing postoperative abdominal lavage. Horses undergoing surgery for small intestinal lesions are placed on a constant-rate infusion of lidocaine hydrochloride immediately after surgery. In the author's experience, delayed treatment with lidocaine, once postoperative ileus is evident, has resulted in limited success at resolving the ileus. Depending on the response to lidocaine therapy, additional prokinetic agents, such as neostigmine or erythromycin may be administered (see Chapter 48).

Conclusions

The presence of pre-existing peritoneal inflammation and the inherent invasive nature of surgery limits our potential for preventing adhesion formation in horses. The surgeon's primary defense in adhesion formation continues to be proper, meticulous, atraumatic surgical technique and removal of all potentially adhesiogenic tissues, thereby reducing peritoneal inflammation and trauma. Current methodologies of adhesion prevention are directed at minimizing peritoneal trauma and inflammation, postoperative treatment with anti-inflammatory drugs such as flunixin meglumine and DMSO enhancing peritoneal fibrinolysis, promoting intestinal motility, and separating potentially adhesiogenic tissues during early postoperative healing. No currently available treatments accomplish all of these objectives. However, through research and a more thorough understanding of the physiologic processes of adhesion formation, development of novel and innovative technologies targeted at adhesion prevention may reduce the morbidity and mortality associated with postoperative adhesions in horses.

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15

Pathophysiology of Enteritis and Colitis

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Fundamentally, the pathophysiology of enteritis and colitis is inflammatory in nature, and the clinical abnormalities that we associate with these conditions, such as enterogastric reflux and diarrhea, arise from the inflammatory processes involving the affected segment of the gastrointestinal tract. The initial stages of these conditions typically involve localized mucosal inflammation, but this frequently progresses to systemic activation of the inflammatory cascade. Many of the sequelae of these conditions, such as laminitis and multiple organ failure, are related to this systemic inflammatory response.

Inflammation

Inflammation represents the response of tissues either to injury or to the presence of microorganisms. Inflammation serves a vital role in the host's resistance to infection, as it enhances the directed movement of phagocytic cells and defensive molecules, such as immunoglobulins and complement, from the bloodstream to the site of infection or injury. Local inflammation arises as a result of several insults, including direct mucosal cellular injury by the pathogen, the elaboration of toxins that injure the mucosal cells, and the production of inflammatory mediators by the host's tissue in response to the presence of the pathogen or its toxins. Direct cellular injury requires that the pathogens gain access to the host's intestinal tissue, either from the luminal surface or by hematogenous spread. Once an organism has gained access to the host cell, it may invade the cell and establish an intracellular infection, as occurs with *Salmonella* spp. organisms. Alternatively, the organism may liberate enzymes, toxins, or other substances that damage the host cell. Injured cells release preformed mediators, such as histamine, and synthesize pro-inflammatory substances, including eicosanoids (prostaglandins, thromboxanes, leukotrienes) and the cytokines interlkeukin-1 (IL-1) and tumor necrosis factor alpha (TNF-α), and also other signaling molecules such as high-mobility group box 1 protein, that can be considered danger-associated molecular patterns (Keyel, 2014). These mediators are responsible for the initiation of a nonspecific inflammatory response.

The bacterial cellular components that are recognized by the immune system can be termed pathogen-associated molecular patterns, and include endotoxin [lipopolysaccharide (LPS)] and exotoxins from Gram-negative bacteria, and peptidoglycan, lipoteichoic acids, enterotoxins, and superantigenic exotoxins from Gram-positive bacteria (Woltmann et al., 1998; Broggi & Granucci, 2015; Moore & Vandenplas, 2014). It is important to note that whereas bacterial infection may be responsible for the initiation of an inflammatory response, the inflammatory process itself results solely from the production of endogenous mediators.

The initial changes that occur during an inflammatory response are primarily the result of local vasodilation and increased vascular permeability, due to the effects of vasoactive mediators released by injured or infected cells. These factors include histamine, serotonin, kinins, eicosanoids, platelet-activating factor (PAF), and the complement products C3a and C5a. Changes occur in the vascular endothelium under the influence of molecules arising from the injured tissue such as IL-1, TNF-α, and histamine, resulting in neutrophil diapedesis and increased vascular permeability. Upon their arrival at the site of tissue injury, neutrophils and macrophages phagocytose foreign material and injured or dead tissue cells and destroy the phagocytosed material by oxidative mechanisms (neutrophils) or by both oxidative and nonoxidative mechanisms (macrophages). In addition,

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macrophages release several factors that augment the immune response, including the pro-inflammatory cytokines IL-1, TNF-α, IL-6, IL-8, IL-12, and IL-18. These pro-inflammatory cytokines signal target cells, primarily neutrophils, to increase their production of secondary inflammatory mediators, including phospholipid derivatives (prostaglandins, thromboxane A_2, leukotrienes), and reactive oxygen species (O^-, O_2^-, ·OH, H_2O_2, NO, OCl^-), further enhancing the inflammatory response (Chaby, 1999). The systemic manifestations of inflammation/infection (fever, lethargy, anorexia, and cachexia) are primarily due to TNF-α and IL-1.

In moderation, the changes associated with an inflammatory response are protective, resulting in enhanced killing of microbes by antigen-specific and nonspecific mechanisms, generalized immune stimulation, and increased activity of the systems required for healing of damaged tissue. The excessive, malignant form of the inflammatory response is characterized by the systemic activity of numerous pro-inflammatory mediators, including cytokines, phospholipid derivatives, complement components, reactive oxygen species, and vasoactive gases [nitric oxide (NO); carbon monoxide (CO)] (MacKay, 2000). Although these mediators all represent components of the normal inflammatory response to a localized stimulus, the systemic activity of these pro-inflammatory mediators may result in an excessive, and often detrimental, response (see Chapter 16).

Endotoxin (LPS) is a pathogen-associated molecular pattern that is commonly involved in the inflammatory responses associated with gastrointestinal disorders in the horse, due to the involvement of Gram-negative pathogens in some of these conditions and the presence of large numbers of Gram-negative enteric organisms within the horse's bowel. These organisms represent a large pool of readily available LPS molecules that can be absorbed into the systemic circulation through the compromised intestinal mucosa. The frequent involvement of LPS in the development of the severe systemic inflammatory responses observed in horses has resulted in these responses being termed endotoxemia. Given the fact that this response can occur in the absence of LPS, it is best to describe this response as the systemic inflammatory response syndrome (SIRS) (MacKay, 2000; Moore & Vandenplas, 2014). SIRS is clinically characterized by the presence of two or more of the following abnormalities: fever, leukocytosis or leukopenia, tachycardia or tachypnea, and hypoxemia (MacKay, 2000; McKenzie & Furr, 2001; Moore & Vandenplas, 2014). The changes associated with SIRS can lead to shock, which is characterized by severe hypotension that does not improve with intravenous fluid therapy. Shock can result in hypoperfusion and multiple organ dysfunction, a progressive syndrome with initial dysfunction of the cardiovascular system, followed by involvement of the respiratory, hepatic, gastrointestinal, renal, cardiac, and neurologic systems (Bone et al., 1997; Evans & Smithies, 1999). If this process is not controlled, it can result in the development of refractory hypotension, lactic acidosis, and oliguria, and may progress to death (Bone et al., 1997). Horses that develop SIRS are at increased risk of developing laminitis, likely due to alterations in digital blood flow. There is some evidence suggesting that vasoactive agents such as endothelin-1, which are increased in association with systemic inflammation, may be associated with alterations in digital blood flow in laminitis (see Chapter 49) (Katwa et al., 1999; Katz et al., 2003; Belknap & Black, 2012; Moore & Vandenplas, 2014). Prolonged SIRS can lead to excessive activity of anti-inflammatory mediators and may result in systemic immunosuppression, which can result in the individual developing infections due to the hematogenous spread of organisms from the gastrointestinal lumen. Examples of these infections include bacterial endocarditis and fungal pneumonia (Sweeney & Habecker, 1999).

Pain

Abdominal discomfort is frequently observed in horses with enteritis or colitis, although the degree of overt abdominal pain usually subsides with appropriate supportive care in these conditions. Pain can result from the stimulation of visceral afferent neurons by local inflammatory mediators, particularly the prostanoids, produced in response to mucosal injury and inflammation. Nociceptors within the gastrointestinal mucosa detect mechanical, chemical, and thermal stimuli and relay this information to the central nervous system, with low-sensitivity fibers monitoring normal physiologic functions and high-sensitivity fibers responding only to noxious stimuli, such as severe distention (Cervero & Laird, 1999; Al-Chaer & Traub, 2002). An additional group of nociceptive fibers is composed of the "silent" fibers, the activity of which is induced only in the presence of inflammation (Cervero & Laird, 1999). These nociceptors are often stimulated by the inflammatory mediators associated with gastrointestinal inflammation, especially the prostanoids. In most cases of equine enteritis and colitis, however, the presence of bowel distention secondary to gas and/or fluid accumulation is likely the most potent stimulus for overt abdominal pain via the high-threshold nociceptors. The accumulation of gas occurs secondary to gas production arising from microbial fermentation of ingesta combined with impaired passage secondary to ileus. The accumulation of fluid occurs secondary to active fluid secretion into the gut lumen, impaired fluid absorption, and ileus. Control of abdominal discomfort is often accomplished by decompression of the stomach by nasogastric intubation in

horses with enteritis or by the passage of diarrhea in horses with colitis. The low-grade discomfort commonly present in horses with enteritis and colitis following the initial acute stages is more likely associated with stimulation of the low-sensitivity receptors and induction of the silent receptors secondary to the presence of active inflammation. Control of this type of discomfort is best achieved by administration of nonsteroidal anti-inflammatory drugs (NSAIDs) that suppress the production of the prostanoids, or by administration of other types of analgesics, such as opioids or α_2 adrenergic agents, that alter the sensitivity of the nociceptors to stimulation or influence the sensory response to nociceptor stimulation.

Ileus

Gastrointestinal ileus is defined as a decrease in propulsive bowel activity, and is commonly encountered in horses with enteritis. Ileus occurs less commonly in horses with colitis, as hypermotility is present more often than hypomotility. The presence of ileus in combination with increased secretion of fluid into the small intestinal lumen results in the reflux of large amounts of fluid from the small intestine into the stomach. Accumulation of this fluid leads to abdominal pain and may result in gastric rupture. Ileus results from interruption of the normal rhythmic contractions of the intestine that occur primarily under the control of the enteric nervous system (see Chapter 9). The activity of the enteric nervous system is modulated by the autonomic nervous system, with parasympathetic input enhancing motility and sympathetic activity suppressing motility. Additional inhibitory input is provided by nonadrenergic, noncholinergic neurotransmitters, which include vasoactive intestinal peptide, adenosine triphosphate, and NO (Lester et al., 1998). Increased sympathetic tone is thought to occur secondary to generalized sympathetic stimulation or reflexively via afferent signals from the intestine or peritoneal surface that are activated by inflammation (Doherty, 2009). This increased sympathetic tone suppresses coordinated rhythmic activity of the intestine and results in functional obstruction of the intestine.

Hypermotility

Increased propulsive activity is commonly present in horses with colitis, leading to shortened intestinal transit times and increased frequency of defecation. When combined with passive and active fluid secretion into the bowel lumen, the net result is increased fecal fluid content and output associated with increased volume and frequency of defecation. The primary stimuli for hypermotility are inflammatory in nature and consist of chemical, mechanical, and functional signals related to the injury or dysfunction of the gastrointestinal mucosa secondary to infection or irritation. The resulting increase in propulsion and decrease in transit time are primarily mediated by the enteric nervous system (Jones & Blikslager, 2002; Hansen, 2003; Bailey et al., 2013).

Hypersecretion

Increased secretion of fluid into the lumen of the bowel occurs in enteritis and colitis. This hypersecretion can result from the activity of intrinsically produced inflammatory mediators or bacterial toxins. The secretory activity of bacterial enteropathogens is traditionally ascribed to one of two mechanisms. The first is the direct injury of the enterocytes by the invasive bacteria or by means of bacterially derived cytotoxins, resulting in a loss of villous surface area for absorption and a relative increase in the surface area of the secretory crypt epithelium. The second mechanism involves activation of enterocyte cyclic adenosine monophosphate (AMP) and cyclic guanosine monophosphate (GMP) pathways, which increase loss of sodium, chloride, and water across the intestinal epithelium (Atherton et al., 2009; Hodges & Gill, 2010). This activation process can be initiated by bacterial enterotoxins, such as those produced by *Salmonella* organisms, or by inflammatory mediators synthesized within the mucosa, such as the prostanoids (Jones & Spier, 1998). The enteric nervous system is integral to the secretory response, as many of the prosecretory signals act by stimulation of the enteric nervous system rather than by direct enterocyte stimulation (Jones & Blikslager, 2002; Camilleri et al., 2012b).

Osmotic Diarrhea

The presence of incompletely digested carbohydrates can result in an increase in the osmotic pressure within the bowel lumen, leading to net fluid flow into the bowel due to increased secretion and decreased absorption (Field, 2003; Hodges & Gill, 2010). The best example of this mechanism occurs in rotaviral diarrhea in foals, in which damage to the villous tips of the small intestinal mucosal cells causes a deficiency of lactase activity that leads to an impaired ability to digest the lactose ingested in mare's milk. The osmotic activity of lactose within the small intestinal lumen interferes with the normal absorption of fluid from the intestinal lumen in the terminal small intestine (Bailey et al., 2013). Similar processes are thought to occur within the large intestine secondary to disruption of the normal fermentative processes at that site.

Decreased Absorption

The presence of inflammation within the gastrointestinal mucosa causes several changes that result in impaired absorption of fluid from the intestinal lumen (Jones & Spier, 1998). Injury to the mucosal epithelium can cause loss of the normal architecture, as occurs in the small intestine with rotavirus infections, in which the villous tips, normally absorptive in function, are atrophied, whereas the crypt cells, which are normally secretory, proliferate (Lundgren & Svensson, 2001). Disruption of the normal mechanisms that transport sodium and chloride from the lumen to the interstitium and vasculature also impairs absorption, as water normally follows these solutes along their concentration gradients (Atherton et al., 2009). Dysfunction of the intracellular tight junctions impairs the ability of the mucosal epithelium to retain the absorbed water and electrolytes, thereby decreasing their net absorption (Fink, 2003).

Endothelial Dysfunction

Injury to the intestinal mucosa can result in a relative increase in hydrostatic pressure within the vasculature, secondary to increased blood flow, potentiating the flow of fluid from the vasculature into the interstitium and thence into the intestinal lumen (Field, 2003). The loss of albumin from the vasculature secondary to endothelial injury decreases the intravascular oncotic pressure and allows fluid to leave the vasculature and enter the interstitium. This results in increases in interstitial oncotic pressure, which augments fluid flow from the vasculature to the interstitium. The flux of fluid, electrolytes, and protein into the interstitium, in combination with damage resulting from inflammation, exceeds edema safety factors and leads to the development of interstitial edema. The fluid and protein within the interstitium may then enter the intestinal lumen by way of the damaged and dysfunctional epithelium, resulting in intestinal fluid losses and protein-losing enteropathy (Camilleri et al., 2012b).

Mucosal Barrier Function

The intestinal mucosal epithelium represents a semipermeable barrier between the foreign and potentially noxious intestinal contents and the internal environment of the body (Baumgart & Dignass, 2002). This barrier is comprised of structural components, such as the mucous gel layer on the mucosal surface, the epithelium and its tight junctions, the local immune system, and the capillary endothelium (Camilleri et al., 2012a; Farhadi et al., 2003). Intestinal inflammation and injury can compromise this barrier, with the resulting increase in permeability potentially allowing for the translocation of bacteria or the absorption of pro-inflammatory factors, luminal antigens, or vasoactive factors (Farhadi et al., 2003; Elliott & Bailey, 2006). Intestinal barrier dysfunction initiates a profound immunologic response, leading to increased inflammation both locally and systemically that may have deleterious effects (Mittal & Coopersmith, 2014), potentially including laminitis (Elliott & Bailey, 2006; Milinovich et al., 2008). Restitution of the mucosal barrier can occur rapidly following resolution of the inciting factors, but this healing may be impaired by the administration of nonselective NSAIDs (Tomlinson & Blikslager, 2004; Marshall & Blikslager, 2011).

Specific Diseases

Duodenitis-proximal Jejunitis – Anterior Enteritis

Although the acute inflammatory response in the small intestine and the presence of profound hypersecretion make it likely that infectious organisms are involved in the pathogenesis of this syndrome, no definitive etiologic agents have been identified (Murray, 2002; Freeman, 2000). Historically, organisms such as *Salmonella* spp. and *Clostridium* spp. have been identified in the enterogastric reflux obtained from some horses with duodenitis-proximal jejunitis – anterior enteritis, hereafter referred to as duodenitis-proximal jejunitis (Murray, 2002). Of these potential infectious agents, *Clostridium difficile* has been most commonly implicated, with one prospective study identifying toxigenic *C. difficile* in all 10 horses affected with the syndrome, whereas these organisms were identified in only one of 16 horses with reflux due to other etiologies (Arroyo et al., 2006). There is also some suggestion that fungal toxins may be involved in the development of this condition, as the test feeding of corn containing fumonisin B_1 produced by certain strains of *Fusarium moniliforme* was associated with intestinal lesions consistent with duodenitis-proximal jejunitis; however, clinical disease was not observed in those studies (Schumacher et al., 1995; Goel et al., 1996). The mechanism by which this toxin acts is unknown, although disruption of sphingolipid metabolism has been used as a biomarker for fumonisin B_1 activity (Goel et al., 1996). With regard to predisposing factors for duodenitis-proximal jejunitis, one of the earliest reports of this condition, which the authors termed gastroduodenojejunitis, described an apparent relationship between the feeding of large amounts of concentrates and the development of the condition (Huskamp, 1985). A more recent report demonstrated that there was a significant relationship between the feeding of larger amounts of concentrates and the development of duodenitis-proximal jejunitis in

horses, and also correlations with grazing pasture and female gender (Cohen et al., 2006).

Horses with duodenitis-proximal jejunitis frequently exhibit evidence of hepatic involvement, as demonstrated by increases in the serum activities of the hepatic enzymes γ-glutamyl transferase (GGT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), and also histopathologic changes noted in the liver at postmortem (Davis et al., 2003; White et al., 1987). Hepatic involvement may occur secondary to the absorption of LPS or inflammatory mediators via the portal circulation, ascending infection via the bile duct secondary to increased intraluminal pressure, or possibly hepatic hypoxia resulting from systemic inflammation and cardiovascular shock (Davis et al., 2003). Although rarely reported, acute pancreatitis in horses has also been associated with a clinical syndrome indistinguishable from duodenitis-proximal jejunitis (Lilley & Beeman, 1981; Johnson et al., 2009; Newman, 2015; Edery et al., 2015). Some authors have questioned whether the pancreatic changes observed in these horses may merely represent secondary involvement due to ascending infection from the intestinal lumen, or whether the pancreatitis may actually play a causative role in the development of the condition (Johnson et al., 2009). Unfortunately, antemortem documentation of pancreatic dysfunction in horses is difficult, and pancreatic tissues are not consistently obtained for histologic examination on postmortem examination (Newman, 2015). For these reasons, it is possible that pancreatitis may represent an underappreciated component of duodenitis-proximal jejunitis.

Affected horses present most often with a history of mild colic followed by profound depression, large-volume enterogastric reflux (up to 15–20 L every 2 h), mild to moderate small intestinal distention on abdominal ultrasonography and/or rectal examination, low-grade fever (101.5–102.5 °F/38.6–39.2 °C), clinical dehydration, tachycardia (60–80 bpm), decreased borborygmi, and injected mucous membranes (Johnston & Morris, 1987; Freeman, 2000). Severe transmural small intestinal inflammation is associated with this syndrome, and loss of mucosal barrier function likely contributes to the severity of the systemic inflammatory responses that characterize this condition. As a result, affected horses are at increased risk for serious secondary complications, including laminitis and cardiac arrhythmias, likely because of the presence of systemic inflammation and the associated organ and tissue dysfunction (Cohen et al., 1994; Cornick & Seahorn, 1990; Freeman, 2000).

Salmonellosis

The development of salmonellosis represents the interplay of several factors, including the degree of bacterial exposure, the virulence of the *Salmonella* organisms, and the susceptibility of the host. *Salmonella* bacteria are transmitted by the fecal–oral route, and the severity of exposure is directly related to the number of bacteria ingested in contaminated feed or water, with the size of the infective dose being determined by the other factors of virulence and susceptibility. The infective dose may range from hundreds of organisms in highly susceptible individuals to millions of organisms in healthy animals (Murray, 2002). In order to establish colonization, *Salmonella* organisms must overcome an array of host protective mechanisms, which include bactericidal enzymes in the saliva, gastric acid, intestinal enzymes (proteases, lysozymes), antimicrobial peptides, complement, phagocytes, and bile salts, in addition to interference by the normal gut microbiome (Ohl & Miller, 2001). Factors that interfere with any of these protective mechanisms, such as the administration of acid-suppressive drugs or the administration of antimicrobials, will likely result in a decrease in the size of the infective dose of *Salmonella* organisms (Owen et al., 1983; Furr et al., 2012).

The virulence of any particular *Salmonella* organism is determined by its invasiveness, which depends on the attachment of the organism to the mucosal epithelium and the production of enzymes and toxins (cytotoxins, endotoxins, and enterotoxins) that damage the epithelium and/or alter epithelial permeability and facilitate bacterial entry into the mucosal cells (Murray et al., 1989). The ability of *Salmonella* organisms to cause intracellular infection allows them to evade some aspects of the immune response, such as humoral immunity and phagocytosis. Evidence exists that *Salmonella typhimurium* organisms may initially gain entry into the intestinal mucosa via mucosa-associated lymphoid tissues (Jensen et al., 1998). Host susceptibility is increased by stress, such as that associated with prolonged transport or surgery, or concurrent diseases that impair immune functions. A recent report described a mechanism whereby *Salmonella typhimurium* responds to increased host production of cortisol by increasing intracellular proliferation within infected macrophages (Verbrugghe et al., 2016). The normal ability of the enteric population of commensal bacteria to resist the proliferation of pathogenic bacteria, termed colonization resistance, is impaired in the face of antimicrobial administration or gastrointestinal dysfunction, and loss of this function increases the susceptibility of the host to *Salmonella* infection. Once colonization is established, the number of organisms shed by infected individuals can vary dramatically, with chronically infected horses passing small numbers of organisms intermittently, whereas acutely affected individuals may shed very large numbers of organisms.

After a *Salmonella* infection is established, local and systemic inflammatory responses develop in an effort to

eliminate the organism. Mucosal inflammation results in increased mucosal permeability, increased secretion of water and electrolytes, and alterations in motility due to altered enteric nervous system function. The development of this secretory response, in combination with intestinal hypermotility and decreased intestinal transit times, likely functions to decrease mucosal adherence of pathogenic organisms. Unfortunately, the loss of the normal mucosal barrier function, in combination with changes in the normal flora, increases the pathogenicity of *Salmonella* organisms. The loss of fluid, electrolytes, and protein may be severe in equine salmonellosis, requiring aggressive supportive care. Severe intestinal inflammation can occur, leading to permanent dysfunction and overwhelming systemic inflammation, resulting in the death of the affected individual.

Clostridial Enterocolitis

Clostridial enterocolitis affects both foals and adults. Improvements in our ability to detect and identify these organisms and their toxins in the feces of horses with diarrhea has increased our appreciation of the involvement of clostridial organisms in equine diarrheic syndromes. The primary pathogens of concern are *Clostridium difficile* and *Clostridium perfringens*, with *C. difficile* being more commonly implicated in equine diarrheic syndromes. These organisms are strict anaerobes with fairly wide distributions in soil. They can represent a component of the normal gastrointestinal flora of horses, as fecal shedding occurs in horses showing no clinical signs of disease. Pathogenicity depends on production of bacterial toxins, with *C. difficile* producing primarily toxins A and B, and *C. perfringens* producing as many as 17 different toxins, although four (exotoxins alpha, beta, epsilon, and iota) and enterotoxin (CPE) are the most important (Songer, 1996)The clinical signs associated with clostridial enterocolitis are not fundamentally different from those of any other equine enterocolitis, and consist of diarrhea, fever, depression, mild colic, and dehydration (Weese et al., 2006). Clostridial enterocolitis in some foals and adults is associated with hemorrhagic diarrhea, a finding that is uncommon in most other equine enterocolitis syndromes. Consequently, the presence of this abnormality should heighten the clinician's suspicions that clostridial organisms may be involved.

Clostridium difficile

C. difficile has been associated with enterocolitis in adult horses and foals in several studies, and is considered to be one of the most important causes of enterocolitis in this species (Baverud et al., 1997, 1998; Diab et al., 2013b; Jones et al., 1988; Madewell et al., 1995; Magdesian et al., 2002; Teale & Naylor, 1998; Weese et al., 1999, 2006). *C. difficile*-associated disease syndromes include enterocolitis of foals and adult horses, hemorrhagic necrotizing enteritis of foals, and nosocomial enterocolitis and antibiotic-associated diarrhea of foals and adult horses (Jones, 2000; Diab et al., 2013a). The frequent association of this organism with syndromes likely to involve disturbances in the normal enteric flora suggests that *C. difficile* is an opportunistic pathogen that is normally prevented from inducing disease by colonization resistance (Barza et al., 1987). Risk factors for *C. difficile*-associated disease syndromes include antimicrobial therapy, hospitalization, stress, nasogastric intubation, and surgical or medical treatment, although these syndromes can occur without these exposures (Baverud, 2004; Diab et al., 2013a). As this organism is not an invasive pathogen, the pathogenicity of *C. difficile* is primarily associated with its elaboration of toxin A (TcdA) and toxin B (TcdB), which exert their effects via receptor-mediated mechanisms (Pothoulakis & Lamont, 2001; Davies et al., 2011). TcdA, which is commonly referred to as enterotoxin, causes fluid secretion and inflammation (Laohachai et al., 2003). TcdB is typically termed cytotoxin, but studies suggest that it exerts a primarily enterotoxin-like effect (Pothoulakis & Lamont, 2001). The net effect of the activity of these toxins is to induce a secretory diarrhea with substantial intestinal inflammation. In addition to TcdA and TcdB, some strains of *C. difficile* can produce a binary toxin, *C. difficile* binary toxin, which consists of two independently produced components, CDTa and CDTb (Davies et al., 2011). The role of this in *C. difficile*-associated disease syndromes is currently unclear (Sun & Hirota, 2015; Arroyo et al., 2007).

Clostridium perfringens

Multiple studies have demonstrated an association between *C. perfringens* and enterocolitis in foals and adult horses (Herholz et al., 1999; East et al., 1998, 2000; Bueschel et al., 1998; Traub-Dargatz & Jones, 1993; Larsen, 1997; Netherwood et al., 1996, 1998a, 1998b; Pearson et al., 1986; Mehdizadeh Gohari et al., 2016; Uzal et al., 2012; Diab et al., 2012). This organism is a common member of the enteric flora in healthy horses, with disease being associated only with the presence of increased numbers of the organism. *C. perfringens* exerts its effects via the plethora of toxins that it produces (Uzal et al., 2014). As toxin production varies between strains of *C. perfringens*, isolates can be classified into five groups (types A–E) based on the pattern of toxin production (Uzal et al., 2014). Alpha toxin is a phospholipase produced by all strains of *C. perfringens*, and is the primary lethal toxin associated with this organism (Songer, 1996). Beta toxin is also capable of inducing mucosal necrosis and inflammation, and is

potentially lethal (Songer, 1996). Another form of cytotoxin, termed beta-2, is associated with the development of enterocolitis and typhlocolitis in horses and foals (Herholz et al., 1999; Bacciarini et al., 2003; Hazlett et al., 2011). The production of the latter toxin may be associated with exposure to subinhibitory concentrations of aminoglycoside antimicrobials (Vilei et al., 2005). Epsilon toxin is produced as an inactive prototoxin and, following protease cleavage, the molecule becomes active and increases intestinal permeability (Songer, 1996; Alves et al., 2014). Iota toxin increases vascular permeability and is potentially lethal (Songer, 1996; Alves et al., 2014). *C. perfringens* enterotoxin is produced by only 2–5% of isolates, predominantly type A, but the production of this toxin is highly correlated with the pathogenicity of isolates. This enterotoxin initially impairs fluid and electrolyte absorption, followed by increasing intestinal inflammation and injury, including villous blunting and loss of the intestinal epithelium, which lead to the development of secretory diarrhea (Songer, 1996). The presence of the enterotoxin appears to be associated with the development of diarrhea in foals and adult horses (Donaldson & Palmer, 1999; Kanoe et al., 1990; Netherwood et al., 1998b; Weese et al., 2001a, 2001b). *C. perfringens* strains producing a novel pore-forming toxin have recently been associated with necrotizing enterocolitis in neonatal foals and hemorrhagic gastroenteritis in dogs (Mehdizadeh Gohari et al., 2015, 2016).

Antimicrobial-associated Diarrhea

Antimicrobial administration can be associated with the development of colitis in horses, a condition termed antimicrobial-associated diarrhea, which can be severe and even fatal (Cohen & Woods, 1999; Atherton et al., 2009). The development of diarrhea can result simply from the disruption of the microbial flora of the intestine (McGorum & Pirie, 2009; Costa et al., 2015; Barr et al., 2013). This disruption may be sufficient to result in diarrhea, due to alterations in intestinal carbohydrate and volatile fatty acid metabolism. Alternatively, these changes in the microbial population may lessen that population's role in "colonization resistance," whereby the normal population of microorganisms impairs the normal ability of the intestinal microbiota to inhibit the proliferation of infectious organisms, such as *Salmonella*, *C. difficile*, or *C. perfringens* (McGorum & Pirie, 2009; Atherton et al., 2009). Although the administration of any antimicrobial agent can potentially be associated with the development of diarrhea, those drugs that achieve high concentrations within the intestinal lumen due to poor absorption or biliary excretion (macrolides), and those with higher efficacy against anaerobes (beta-lactams, macrolides), appear to be associated with the greatest risk of causing antimicrobial-associated diarrhea (McGorum & Pirie, 2010).

Equine Neorickettsiosis

Equine neorickettsiosis (Potomac horse fever) is an infectious colitis of horses. Although this disease was believed to represent a new entity when it was recognized in the Potomac River region in the late 1970s, there is a report from Canada of what appears to be the same clinical disease dating from 1924 (Schofield, 1925; Baird & Arroyo, 2013). The etiologic agent of this disease was originally termed *Ehrlichia risticii*, but is now named *Neorickettsia risticii*, owing to the close relationship of this organism to *Neorickettsia helminthoeca* (Pretzman et al., 1987; Wen et al., 1996; Dumler et al., 2001; Taillardat-Bisch et al., 2003). *N. risticii* is an obligate intracellular parasite, and it infects monoctyes, macrophages, intestinal epithelial cells, and colonic mast cells (Rikihisa et al., 1985). The clinical signs typically associated with equine neorickettsiosis include diarrhea, fever, depression, lethargy, anorexia, colic, dehydration, and laminitis (Ziemer et al., 1987; Dutta et al., 1988; Madigan & Pusterla, 2000; Bertin et al., 2013). Interestingly, only 60–66% of affected horses are reported to develop diarrhea (Madigan & Pusterla, 2000; Bertin et al., 2013), and the incidence of diarrhea appears clinically to be even lower among horses that have lived for long periods in endemic areas. Abortion has also been reported in association with this disease, in both experimentally induced and natural infections (Long et al., 1995a, 1995b). Clinicopathologic changes commonly associated with equine neorickettsiosis include hemoconcentration, leukopenia, neutropenia, hypoproteinemia, azotemia, hypocalcemia, hyponatremia, hyperglycemia, hypochloremia, hyperbilirubinemia, and hypoalbuminemia (Bertin et al., 2013). The reported case fatality rate of affected horses is 5–30% (Ziemer et al., 1987; Dutta et al., 1988; Palmer, 1993; Bertin et al., 2013). In a recent study, only blood hemoglobin concentration at admission was significantly associated with survival, likely as a reflection of the severity of hypovolemia (Bertin et al., 2013). That study also reported that the only treatment factor associated with survival was oxytetracycline administration (Bertin et al., 2013). Although the development of laminitis may not be an independent predictor of outcome, in some affected horses a fatal outcome may be due primarily to the development of laminitis, rather than the primary enteric disease, and laminitis has been reported to occur in some horses without the development of other clinical signs (Jones, 2015; Bertin et al., 2013).

The epidemiology of equine neorickettsiosis is interesting, as the association between the seasonal

development of this disease and exposure of affected animals to streams and rivers was well established; yet no vector associated with these water sources could be identified. The seasonality of the disease, with cases occurring only during the summer months, suggested the involvement of a vector that was only active during this time of year, which fits well with an insect vector. Much work was done to identify an arthropod vector, especially ticks, as this mode of transmission is common among other ehrlichial pathogens, but no evidence supporting this mode of transmission was found (Madigan & Pusterla, 2000; Schmidtmann et al., 1986; Barlough et al., 1996; Levine et al., 1990; Burg et al., 1990). Oral transmission was demonstrated (Palmer & Benson, 1988, 1994) and the association of this disease with natural watercourses suggested that some part of the life cycle was associated with aquatic organisms. As the close relationship between *N. risticii* and *N. helminthoeca* became clear, interest intensified in attempting to identify a trematode (fluke) vector. It has been demonstrated that several different trematodes may act as vectors for *N. risticii*, and several different species of aquatic snails appear to be intermediate hosts for these trematodes (Madigan & Pusterla, 2000; Chae et al., 2000). The definitive hosts for *N. risticii* are insectivorous birds and bats (Pusterla et al., 2013a). The route of equine exposure remained unclear until it was determined that aquatic insects (mayflies, caddisflies, damselflies, dragonflies, and stoneflies) may be infected with trematode metacercariae containing *N. risticii* DNA (Chae et al., 2000; Mott et al., 2002; Park et al., 2003). The oral transmission of equine neorickettsiosis has long been established, and the induction of the disease in horses fed infected aquatic insects (mayflies, caddisflies) was demonstrated as early as 1924 (Madigan et al., 2000; Schofield, 1925; Baird & Arroyo, 2013). Upon reaching the gastrointestinal tract, *N. risticii* is released from the trematode and then is able to infect and replicate in the colonic epithelial cells, and, after translocation across the mucosal epithelial barrier, it infects tissue macrophages, mast cells and circulating monocytes (Rikihisa et al., 1985). Infected colonic epithelial cells lose microvilli and exhibit increases in intracellular cyclic AMP, impairing water reabsorption and electrolyte transport and leading to the development of diarrhea (Rikihisa et al., 1992; Baird & Arroyo, 2013).

Larval Cyathostominosis

As control of large strongyles has improved, the small strongyles (Cyathostominae) have assumed their current role as the primary parasitic pathogen of the horse (Love et al., 1999; Lyons et al., 1999). The primary disease process associated with these parasites is related to the larval stages rather than the adult stage present within the gastrointestinal lumen. The cyathostomins have a direct life cycle, during which the adults within the lumen lay eggs that are passed in the manure, where they hatch as first-stage larvae, and after maturation to the third stage, they become infective (Lyons et al., 1999). After being ingested by a horse, the larvae enter the gastrointestinal mucosa, where they encyst and mature through the fourth to the fifth stage, which represents the adult form (Lyons et al., 1999). Disease is associated with parasite entry into and exit from the gastrointestinal mucosa, with the associated interstitial edema, along with eosinophilic and mononuclear inflammation, resulting in disruption of normal motility and, in severe cases, leading to profuse watery diarrhea and severe protein loss (Love et al., 1992, 1999; Mair et al., 2000; Uhlinger & Johnstone, 1985). Larval cyathostominosis has also been associated with weight loss, colic, fever, neutrophilic leukocytosis, hypoalbuminemia, and hyperglobulinemia (Church et al., 1986; Giles et al., 1985). The simultaneous emergence of large numbers of larvae in the late winter/early spring, or possibly after anthelmintic administration, is a poorly understood but clinically significant problem, as this may be associated with colic, diarrhea, and severe protein-losing enteropathy (Love et al., 1999). An association has been demonstrated between fenbendazole administration and the development of severe tissue inflammation in horses naturally infected with cyathostomins, whereas moxidectin therapy was not associated with severe local inflammation, perhaps owing to direct anti-inflammatory effects of macrocyclic lactones (Steinbach et al., 2006). In contrast, anthelmintic administration to infected animals does not appear to induce a significant systemic inflammatory response (Nielsen et al., 2015). Unfortunately, the difficulty in diagnosing this condition means that it is likely that many horses with cyathostominosis go undetected and untreated. Often one must assume that cyathostomins may be responsible for diarrhea and hypoproteinemia, unless another definitive diagnosis can be made. It is important to note that the presence of another etiologic agent does not preclude the presence of encysted small strongyles.

Viral Enterocolitis

Rotavirus

Rotaviral enterocolitis is the most widespread and significant form of viral enterocolitis in the equine species and is a common cause of foal diarrhea, with affected foals ranging from 2 days to 6 months of age (Cohen & Chaffin, 1995; Dwyer, 1991). Younger foals are often more severely affected than older foals, with the disorder in some older foals remaining subclinical. Rotaviruses are RNA viruses of the family Reoviridae

and are typically species specific (Lundgren & Svensson, 2001). Infection follows ingestion of the organism in feces-contaminated feed or water, with subsequent attachment to the intestinal epithelium and uptake by the epithelial cells (Lundgren & Svensson, 2001). Rotavirus is highly contagious, and outbreaks may develop rapidly after the onset of clinical disease in a single foal. Clinically normal adults and foals may shed the organism, as may clinically affected foals. The amount of virus shed often increases after exposure to a clinically affected individual. Rotaviral diarrhea often occurs in large, comingled groups of mares and foals, and affected foals are typically from 5 to 35 days of age (Conner & Darlington, 1980). Foals initially exhibit anorexia and depression, and quickly progress to acute, profuse, watery diarrhea. Affected foals may become rapidly dehydrated, and frequently develop electrolyte abnormalities and metabolic acidosis. Although the morbidity associated with rotavirus infections is high, owing to the highly contagious nature of the virus, the prognosis for survival is good.

The pathogenesis of rotaviral diarrhea is multifactorial, and this organism is frequently detected in combination with other potential gastrointestinal pathogens. Rotavirus infects the middle and upper portions of the villous epithelium of the small intestine, resulting in villous atrophy and villous blunting, with replacement of the villous epithelium with cells from the epithelial crypts (Bailey et al., 2013). Replacement of the normally absorptive villous epithelium with the secretory crypt cells appears to play a role in the impairment of intestinal absorption and increased secretion of fluid and electrolytes (Lundgren & Svensson, 2001). Interestingly, many of the small intestinal villi may be unaffected in the presence of infection, suggesting that absorption and secretion should not be severely affected and increasing the possibility that other mechanisms may be responsible for the secretory diarrhea associated with rotavirus infection (Lundgren & Svensson, 2001). Villous injury also results in decreased production of disaccharidases, particularly lactase, which may impair the digestion of lactose and contribute to the development of osmotic diarrhea. It has been demonstrated that rotaviral infection initiates a local enteric nervous system response that is responsible for as much as two-thirds of the secretory response, and this response may be initiated by a "toxin-like" protein (NSP4) produced by the virus (Lundgren et al., 2000). Other factors contributing to the development of rotaviral diarrhea may be the activity of viral enterotoxins, inhibition of sodium–glucose co-transport, dysregulation of calcium homeostasis, and activation of the enteric nervous system (Bailey et al., 2013). The resulting diarrhea is often profuse and watery, and the diarrheic phase may last from as little as 2 days to more than 1 week. Infection is ultimately self-limiting, but supportive care may be required because of substantial enteric fluid losses and associated electrolyte abnormalities.

Coronavirus

Equine coronavirus, an RNA virus of the genus *Betacoronavirus* (Zhang et al., 2007), was first associated with equine disease when it was isolated from the feces of a diarrheic foal in 1999 (Guy et al., 2000). Since that time, the virus has been associated both clinically and epidemiologically with a number of outbreaks of fever and gastrointestinal disease in adult horses in the United States, Japan, and Europe (Fielding et al., 2015; Slovis et al., 2014; Miszczak et al., 2014; Pusterla et al., 2013b; Oue et al., 2011, 2013). The virus is shed in the feces and is spread by fecal–oral transmission. The source of the virus in outbreaks has not been definitively determined, but asymptomatic horses can shed it. The clinical signs associated with this disease include fever, lethargy, and inappetance, which are common in infected animals, although some infected animals may remain clinically normal (Fielding et al., 2015; Pusterla et al., 2013b; Oue et al., 2013). Other signs may include diarrhea and/or colic and also neurologic signs, although these findings are much less common (Fielding et al., 2015; Pusterla et al., 2013b; Oue et al., 2013). The disease appears to be highly infectious and often occurs as an outbreak, with high morbidity despite efforts at quarantine. Fecal shedding of the virus in adult horses has been demonstrated to occur for up to 11 days, but there is evidence to suggest that it may occur for longer than 14 days, which may necessitate prolonged periods of quarantine for affected horses (Fielding et al., 2015). Hyperammonemic encephalopathy has been suspected as a cause of neurologic signs in association with necrotizing enterocolitis in affected horses, and this has recently been confirmed in a series of cases (Fielding et al., 2015; Giannitti et al., 2015). Although mortality rates are typically low, both the magnitude of the viral load and the development of neurologic signs have been associated with nonsurvival (Oue et al., 2013; Fielding et al., 2015; Pusterla et al., 2013b; Giannitti et al., 2015).

Protozoal Enterocolitis

The primary etiologic agent of protozoal enterocolitis in the horse is *Cryptosporidium parvum*. *C. parvum* is a fairly unique coccidial organism, which exhibits little or no host specificity, is highly resistant to antimicrobial agents, and has the potential to cause autoinfection (Tzipori & Ward, 2002). This organism has a direct life cycle, with large numbers of oocysts containing sporozoites being shed in the feces, where they represent an immediate source of infection for other animals (Lyons et al., 1991). After the oocytes have been ingested,

the sporozoites are released and invade the intestinal epithelium, where reproduction occurs (Tzipori & Ward, 2002). Autoinfection occurs when oocysts just released from the epithelium into the lumen release sporozoites that infect other intestinal epithelial cells (Lyons et al., 1991) Equine cryptosporidiosis occurs primarily in young foals, with or without immunodeficiency (Cohen & Chaffin, 1995; Grinberg et al., 2003, 2009) The normal incubation period is approximately 3–7 days, with clinical disease persisting for 5–14 days in animals with normal immune function (Cohen & Chaffin, 1995). *C. parvum* infection activates mucosal cyclooxygenase expression, resulting in increased production of prostaglandin-E_2 and -$F_2\alpha$, and appears to induce diarrhea by impairing intestinal absorption of sodium and water, and increasing chloride secretion, in conjunction with alterations in mucosal barrier function, resulting in increased permeability (Jones & Blikslager, 2002; Laurent et al., 1998; Clark, 1999). Diarrhea may also result from a combination of villous atrophy and the loss of mature enterocytes, resulting in malabsorption (Uzal & Diab, 2015). This organism is zoonotic, with cases reported among humans handling foals and calves that are shedding cryptosporidial organisms (Levine et al., 1988; Majewska et al., 1999; Galuppi et al., 2016).

Equine Proliferative Enteropathy

The causative agent of equine proliferative enteropathy, *Lawsonia intracellularis*, is an obligate intracellular organism that causes a similar syndrome in a wide range of mammalian and avian species (Smith & Lawson, 2001). Exposure alone is not sufficient to achieve infection in other species, as commensal bacteria must be present for infection to occur; the role of these bacteria in the pathogenicity of *L. intracellularis* remains unclear (McOrist et al., 1995). Infection of the enterocytes with *L. intracellularis* leads to dramatic proliferation of infected immature crypt epithelium, resulting in loss of the normal villous epithelium and gross thickening of the affected region of the small intestine (Smith & Lawson, 2001; Vannucci & Gebhart, 2014). Characteristic findings on histopathologic examination are the presence of numerous curved bacteria (*L. intracellularis*) within the apical cytoplasm of the infected cells and the relative absence of an active inflammatory response (Smith & Lawson, 2001; Ellis et al., 2011). The loss of villous architecture and proliferation of the secretory crypt epithelium are likely responsible for the loss of fluid and protein into the intestinal lumen that occurs with this disease, as little or no inflammation is present within the affected intestinal segment (McKenzie, 2009; Vannucci & Gebhart, 2014). Hypoproteinemia and hypoalbuminemia occurring secondary to this enteric protein loss, and the resulting peripheral edema, are characteristic findings in affected horses (McKenzie, 2009; Pusterla & Gebhart, 2013).

NSAID-associated Right Dorsal Colitis

NSAIDs are among the most frequently utilized drugs in equine medicine and surgery, and they are often administered at the owner's discretion with no specific dosage being prescribed. These compounds have toxic effects when used at dosages exceeding the label recommendations. Owing to their narrow therapeutic index, some cases of toxicity occur even when the recommended dosages are given. Further increasing the risk of toxicity is the common misconception that toxicity may be avoided by combining two or more NSAIDs given at appropriate dosages, despite the fact that the toxic effects of these drugs are additive (Karcher et al., 1990; Cohen, 2002; Reed et al., 2006; Keegan et al., 2008; Davis, 2017). Toxicity of NSAIDs involves both the renal system and the gastrointestinal system, and all segments of the gastrointestinal tract can be affected; however, this discussion focuses on lesions occurring in the colon. The toxic potential of these drugs arises inherently from their mechanism of action, which is the suppression of prostanoid production, although other effects, such as alteration of increased oxidant activity or alterations in volatile fatty acid concentration, also may play a role (McConnico et al., 2008; Marshall & Blikslager, 2011; Cook & Blikslager, 2015; Martinez Aranzales et al., 2015; Davis, 2017). Many of the NSAIDs traditionally administered to horses (phenylbutazone, flunixin meglumine) inhibit the activity of both inducible cyclooxygenase-2 (COX-2), which is associated with inflammation, and constitutively expressed cyclooxygenase-1 (COX-1), which is responsible for the production of the prostaglandins required for normal tissue function (Vane et al., 1998). This COX-1/COX-2 paradigm remains useful, but evidence suggests that some crossover in functionality is present, complicating efforts to develop agents with decreased toxic potential.

The maintenance of normal mucosal function and health requires the presence of certain prostaglandins, specifically prostaglandins E (PGE), F (PGF), and I (PGI). The primary function of these compounds appears to be the maintenance of normal mucosal blood flow and tight-junction functionality (Blikslager et al., 1997). Disruption of these functions results in mucosal barrier dysfunction and injury, leading to the classic signs of NSAID-associated colitis, namely secretory diarrhea with hypoproteinemia and hypoalbuminemia, in association with mucosal ulceration, neutrophilic inflammation, and colon wall edema (Bueno et al., 2000; Karcher et al., 1990; Cohen et al., 1995). These effects can occur regardless of the route of drug administration, indicating

that they do not arise solely from a topical mechanism. Impairment of mucosal blood flow and the resulting impairment of tissue integrity induced by NSAIDs are exacerbated by the presence of any type of concurrent mucosal inflammation, such as colitis, with increased tissue damage occurring as a result (Reuter et al., 1996; Whittle, 2003). Increased susceptibility to nonsteroidal toxicity has been associated with hypovolemia, decreased feed intake, the presence of pre-existing gastrointestinal disease, and critical illness (Karcher et al., 1990; Cook & Blikslager, 2015; Davis, 2017). Phenylbutazone is the NSAID that has been associated with the greatest number of reported cases, but flunixin meglumine and meloxicam have also been associated with right dorsal colitis (Bueno et al., 2000; Karcher et al., 1990; Cohen et al., 1995; Noble et al., 2012; Davis, 2017).

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16

Pathophysiology of Systemic Inflammatory Response Syndrome

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Introduction

The signs of circulatory insufficiency in horses with a variety of gastrointestinal diseases have been linked with the term *endotoxemia*. This association between translocation of bacterial endotoxins (lipopolysaccharides) from the gastrointestinal tract into the circulation, and the subsequent development of clinical signs referable to endotoxemia, initially was based on the detection of lipopolysaccharides in the circulation of approximately 30–40% of horses presented to a variety of university veterinary clinics (Fessler et al., 1989; King & Gerring, 1988; Steverink et al., 1994). The strength of this association was increased by the results of experimental studies in which the cardiovascular effects of intravenous administration of purified lipopolysaccharides were noted to be similar to the derangements in cardiovascular function encountered in horses with gastrointestinal diseases characterized by loss of integrity of the intestinal wall (Barton et al., 1998; Moore & Morris, 1992; Morris et al., 1992). However, differences between experimentally induced endotoxemia and the clinical syndrome of endotoxemia have been recognized by veterinary clinicians. For example, the profound neutropenia and febrile responses classically reported to occur after intravenous administration of purified lipopolysaccharides were absent in many horses described as being endotoxemic. During the same time frame, a similarly confusing situation existed in human medicine, especially when the terms sepsis, septic shock, and sepsis syndrome were used interchangeably. As a result of this confusion, in the early 1990s the term "systemic inflammatory response syndrome" (SIRS) was coined to account for the clinical response of human patients to a nonspecific insult (i.e., in the absence of a documented infection) (Bone et al., 1992). Whereas SIRS can be triggered by lipopolysaccharides, similar responses occur to other stimuli perceived to be dangerous by the host. Our current knowledge regarding the systemic inflammatory response to bacterial ligands provides the basis for reconsidering the widespread usage of the term endotoxemia in equine clinical practice.

Responses to Pathogen-Associated Molecular Patterns (PAMPs)

As Lewis Thomas wrote about microorganisms more than 30 years ago: "It is our response to their presence that makes the disease. Our arsenals for fighting off bacteria are so powerful … that we are more in danger of them than [of] the invaders." This observation was particularly insightful, considering what was not known at that time about the mechanisms involved in the host response to pathogens. In fact, relatively little was known until the mid- to late 1990s, when the Toll receptor protein in *Drosophila* was determined to be responsible for the fly's ability to respond to fungal elements (Lemaitre et al., 1996). Within 2 years, mammalian Toll-like receptor proteins (TLRs) were identified on the surfaces of neutrophils, monocytes, and macrophages, and our understanding of the host's responses to pathogens changed seemingly overnight (Medzhitov et al., 1997; Poltorak et al., 1998a). The Nobel Prize in medicine was subsequently awarded for this work in 2011. Currently, 13 different mammalian TLRs have been identified, with each primarily responsible for recognizing a specific PAMP on bacteria, viruses, fungi, or protozoa. It is now clear that there are many other families of receptors, in addition to TLRs, that recognize PAMPs.

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Companion website: www.wiley.com/go/blikslager/abdomen

These include Nod-like receptors, RIG-like receptors, many DNA sensors (including AIM-like receptors), peptidoglycan recognition receptor proteins (PGRPs), and caspase 11, all of which contribute to the innate immune response to pathogens (Bryant et al., 2015). Recognition of PAMPs by these receptors, collectively known as pattern recognition receptors (PRRs), leads to stimulation of intracellular signaling pathways, activation of transcription factors, the synthesis of inflammatory mediators such as cytokines, and the initiation of inflammatory cell death. The ultimate aim of these responses is to eliminate the pathogen.

While the importance of the PRRs in the host's ability to prevent the dissemination of local infections is obvious, these receptors also are involved in the systemic response to transmural movement of bacterial cell wall components, such as endotoxin, as well as to endogenous damage-associated molecule patterns (DAMPs) that are released from the host's tissues during injury. Examples of the latter type of endogenous stimulator of the innate immune response are the degradation products of heparan sulfate proteoglycans that are released *in vivo* by proteases such as elastase (Johnson et al., 2002). Endotoxin and the degradation products of heparan sulfate are recognized by the same TLR, resulting in systemic effects in the host that are indistinguishable from those initiated by lipopolysaccharides.

Because of the importance of bacteria in horses with gastrointestinal diseases and in neonatal foals with sepsis (see Chapter 31), a primary focus of this chapter will be on the manner in which the body senses and responds to Gram-negative and Gram-positive bacteria. Gram-negative bacteria generate ligands such as lipopolysaccharides, flagellin, peptidoglycan, and methylated DNA, whereas Gram-positive bacteria give rise to peptidoglycan, bacterial lipoproteins, methylated DNA, and lipoteichoic acid.

Receptors for Gram-negative Bacteria and Bacterial Ligands

Endotoxin, the bacterial ligand commonly associated with gastrointestinal diseases in adult horses and sepsis in foals, is recognized by TLR-4 in a large protein complex containing lipopolysaccharide-binding protein (LBP), CD14, and MD2 (Figure 16.1) (Bryant et al., 2015). TLR-4 is only expressed on the cell surface when it is bound to MD2; otherwise it is located within the cell in the endoplasmic reticulum. Endotoxin binds to LBP, which then binds to CD14. The role of CD14 and LBP is to increase the sensitivity of the cell to the presence of endotoxin by presenting the bound endotoxin to the

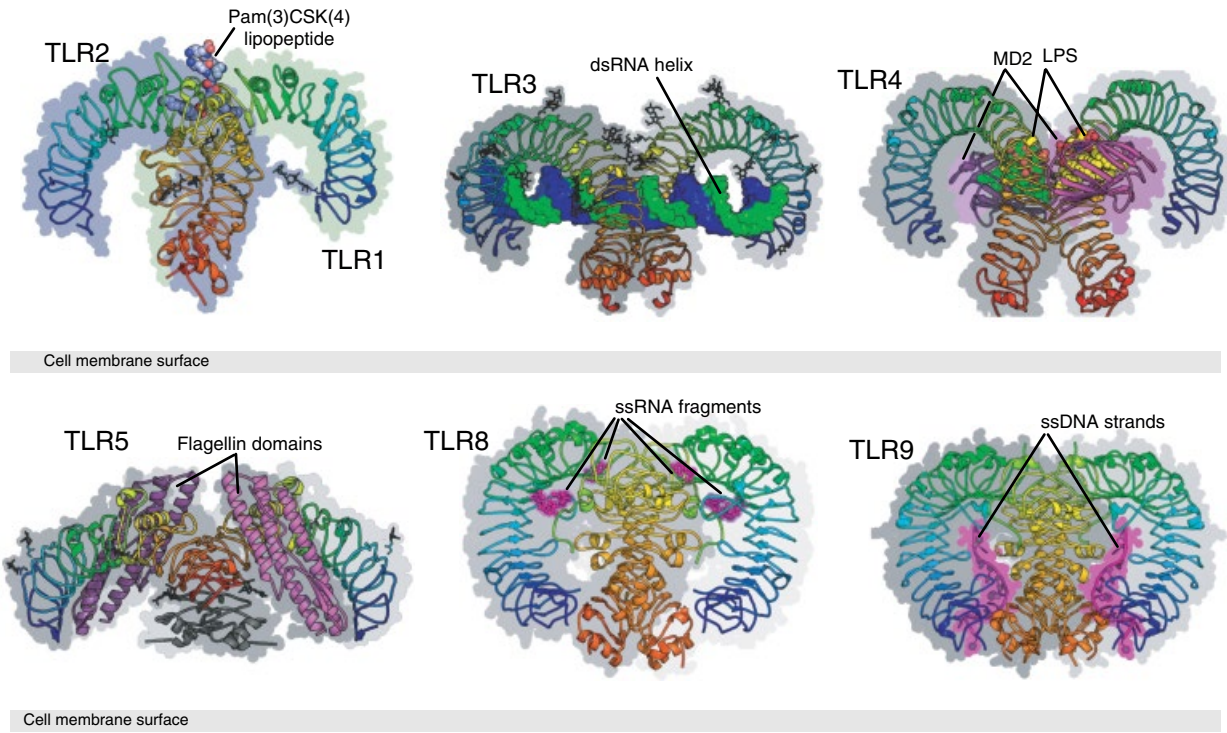

Figure 16.1 Ligand bound structures for the Toll-like receptors (TLRs). LPS, lipopolysaccharide, endotoxin; ds, double stranded; ss, single stranded.

complex consisting of TLR-4 and MD2. At this point, endotoxin binds to MD2, thereby causing a conformational change in TLR-4. This conformational change allows the receptor complex to dimerize with another complex of MD2 and TLR-4 presumably also complexes with endotoxin. Dimerization of TLR-4 initiates the intracellular signaling pathways that result in the production of pro-inflammatory mediators, such as cytokines, and inducible enzymes.

Because the cytoplasmic domain of TLR-4 is similar to the cytoplasmic domain of the interleukin-1 receptor, stimulation of TLR-4 activates many of the same intracellular signaling cascades activated by interleukin-1 through its own receptor (Figure 16.2). The finding that a single point mutation in this receptor accounts for the lack of response of the C3H/HeJ strain of mice to endotoxin highlights the importance of TLR-4 in the response to endotoxin (Poltorak et al., 1998a). Interestingly, human patients who are resistant to endotoxin also have a mutation in TLR-4 (Arbour et al., 2000), and mice and people who lack TLR-4 or whose receptors do not function normally are highly susceptible to Gram-negative bacterial infections (Agnese et al., 2002; Hoshino et al., 1999). It is important to note that there is considerable individual variation in endotoxin responsiveness among horses, and mutations in TLR-4 in horses do not always correlate with hyporesponsiveness to endotoxin (Werners et al., 2006).

One effect of activation of TLR-4 is phosphorylation of an intracellular inhibitory protein called IκB (see Figure 16.2). Phosphorylation results in degradation of this protein, and release of the associated dimeric transcription factor, nuclear factor κB (NFκB). NFκB then enters the nucleus and binds to the promoter region of genes encoding for inflammatory mediators. Although NFκB targets more than 150 genes, stimulation of TLR-4 also activates other intracellular signaling pathways, including the mitogen-activated protein kinase pathways. The end result is the synthesis and release of a variety of inflammatory mediators, some of which have been detected in the circulation of horses administered endotoxin intravenously and in horses with naturally occurring gastrointestinal diseases. Thus, as Lewis Thomas suggested, the host's responses to recognition of PAMPs by TLRs are responsible for the deleterious effects attributed to the pathogens, or in this case to lipopolysaccharides from Gram-negative bacteria.

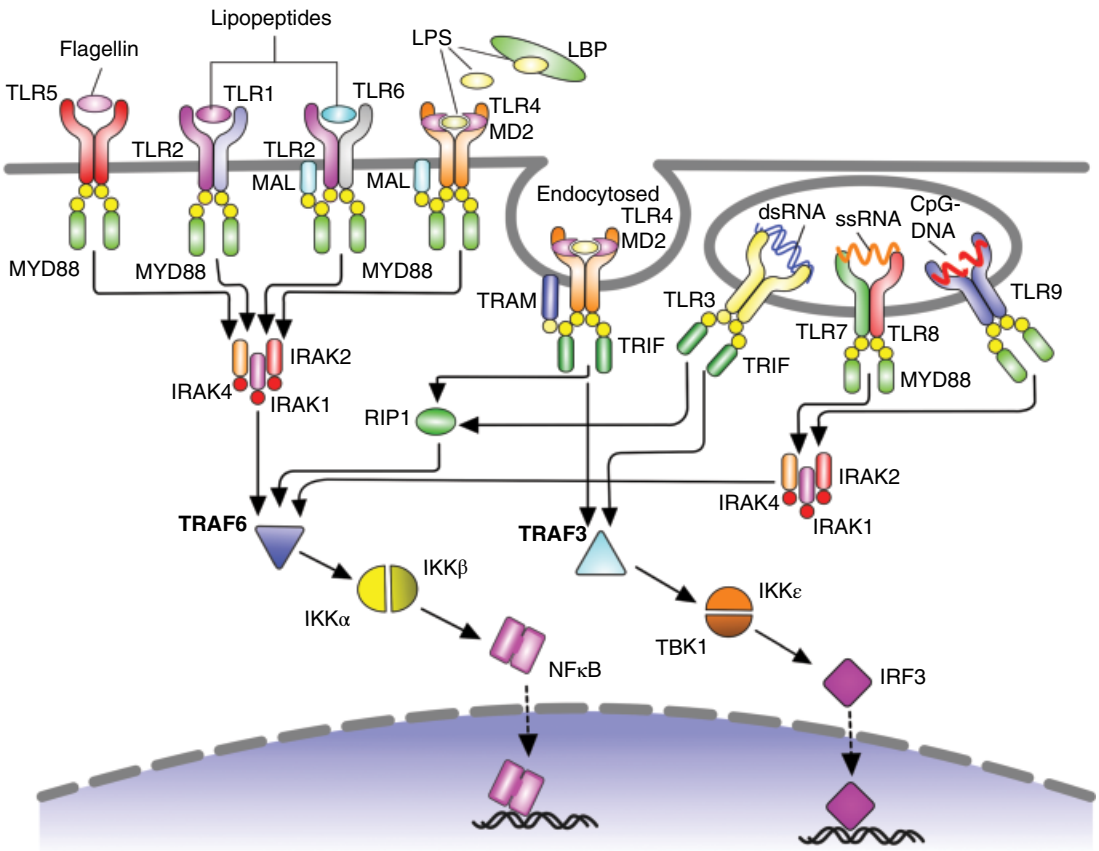

Figure 16.2 Signaling pathways activated by different ligand-bound Toll-like receptors (TLRs). LPS, lipopolysaccharide, endotoxin; ds, double stranded; ss, single stranded.

There are major mammalian species differences regarding the response of the TLR-4 protein complex to individual bacterial lipopolysaccharides. For example, lipopolysaccharides isolated from either *Salmonella enterica* serovar Typhimurium (*Salmonella* Typhimurium) or *Escherichia coli* are agonists in all species, whereas lipopolysaccharides and lipid A isolated from *Rhodobacter sphaeroides* are antagonists in humans and mice, but are agonists in horses and hamsters (Golenbock et al., 1991; Lohmann et al., 2003; Qureshi et al., 1991, Werners et al., 2006). Similarly, lipid IVa from *E. coli* is an antagonist in humans, but an agonist in the mouse and horse. The molecular basis for the species differences in the recognition of these ligands is now well understood, with key amino acid residues in MD2 (e.g., amino acids 122-132) and TLR-4 (e.g., amino acids 285-366) being important for ligand recognition (Walsh et al., 2008).

One puzzle with TLR-4 is that although an excellent receptor antagonist (eritoran) has been developed that works well in horses (Figueiredo et al., 2008), the drug failed to show improvement in clinical trials in human patients in septic shock. A potential explanation for this disappointing result was the very recent discovery of a cytosolic endotoxin receptor that is responsible for the lethal effects of this bacterial toxin in mice. In the presence of type I interferons, cytokines that are released in response to PRR activation by bacteria or viruses, caspase 11 (in mice), and caspases 4 and 5 (in humans), are up-regulated and activated to mediate the lethal endotoxin effect (Kayagaki et al., 2011). While the cytosolic receptor for endotoxin has been the subject of fevered debate, it currently is thought to be the caspases themselves (Shi et al., 2014) (Figure 16.3). Our analysis of the horse genome suggests that they have caspase 4, suggesting that this cytosolic endotoxin recognition pathway is likely to be functional in horses as well. Whether modulating caspase 4 activity ends up being an important therapeutic target for SIRS in humans or horses remains to be seen.

In contrast to TLR-4, considerably less is known about the activation of TLR-5 and its importance in clinical diseases. This TLR is expressed on the surface of epithelial cells, recognizes bacterial flagellin protein (Adamo et al., 2004; Sebastiani et al., 2000), and is an important detection mechanism for enteric infections with bacteria such as *Salmonella* Typhimurium. Flagellin activates TLR-5 on equine neutrophils to induce pro-inflammatory mediator production, but in contrast to many other mammalian species, its does not activate this receptor on equine peripheral blood monocytes where TLR-5 expression is very low (Kwon et al., 2011). Binding of flagellin to TLR-5 (see Figure 16.1) initiates receptor dimerization and activation of an immune response (see Figure 16.3). A second cytosolic flagellin receptor, NLRC4, has been identified which, in association with NAIP proteins, leads to the formation of the inflammasome

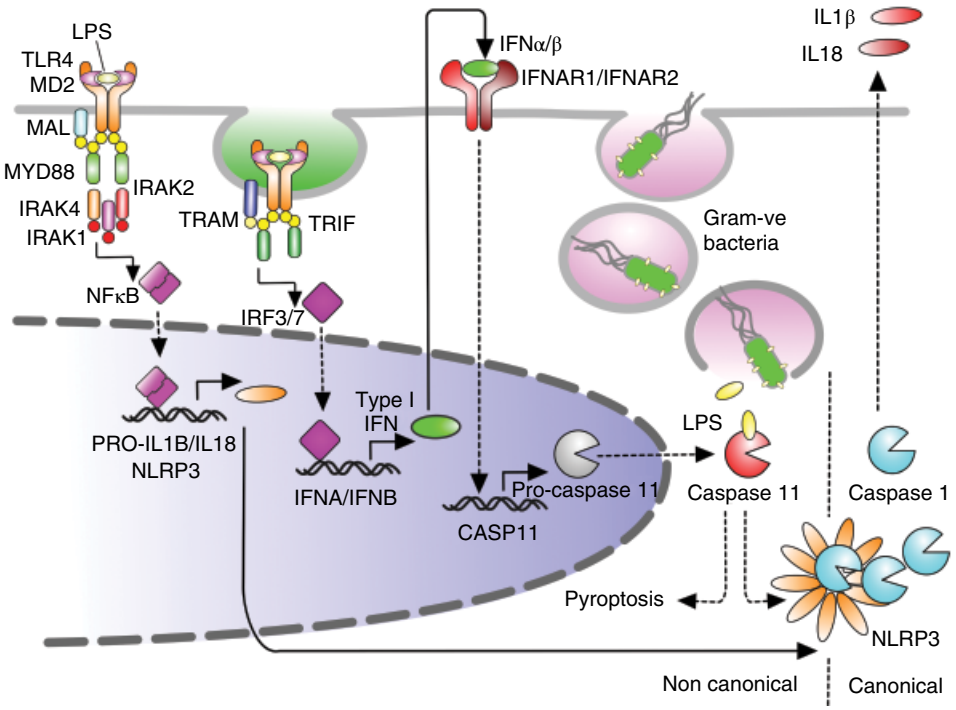

Figure 16.3 A schematic of how Toll-like receptor (TLR)-4 and the cytosolic lipopolysaccharide (LPS) receptor effector protein, caspase 11 (also known as caspase 4), might initiate signaling during the systemic inflammatory response syndrome (SIRS).

(Vance, 2015). This is a macromolecular protein complex that drives the processing of the pro-inflammatory cytokines pro-IL1β and pro-IL18 as well as initiating macrophage cell death. This cytosolic flagellin receptor is important in recognizing bacteria such as *Salmonella* in the gut and also systemically by macrophages (Vance, 2015). Our analysis suggests that NLRC4 is present in horses, but whether it is important in equine infectious or inflammatory disease remains to be determined.

Other Gram-negative bacterial ligands include methylated DNA and peptidoglycan. Bacterial DNA is recognized by TLR-9, and receptor dimerization leads to activation of intracellular signaling pathways and production of pro-inflammatory mediators. Mice lacking TLR-9, either as a single knockout or in a multiple TLR knockout, are susceptible to infection by murine cytomegalovirus, *Streptococcus pneumonia*, or *Salmonella* (Brencicova & Diebold, 2013). Human genetic data suggests that mutations in TLR-9 are associated with an altered susceptibility to bacterial infection (Brencicova & Diebold, 2013). It is currently unclear if TLR-9 is important in the development of SIRS in horses, although activation of this receptor in equine neutrophils induces pro-inflammatory responses (Liu et al., 2009). Pathogen DNA can also be recognized by many cytosolic DNA receptors, but it is currently unclear whether these PRRs make a substantial contribution to the pathogenesis of SIRS in any species.

Peptidoglycan, or its components such as muropeptides, can also be recognized by the peptidoglycan recognition receptors (PGRPs) and the Nod family of proteins. Mammalian PGRPs PGLYRP-1, PGLYRP-3, and PGLYRP-4 have bactericidal activity, while PGLYRP-2 has amidase activity. Only PGLYRP-2 among the four mammalian PGRPs has a pro-inflammatory function and PGLYRP-1 is anti-inflammatory (Boneca, 2009). The intracellular Nod family of receptors plays an important role in a number of human diseases, including Crohn disease (Nod-2) and Blau syndrome (Nod-2), and in recognizing *Shigella felxneri* (Nod-1). Nod-1 senses peptidoglycan molecules primarily from Gram-negative bacteria (MurNAc DAP tripeptide), whereas Nod-2, primarily present in cells of myeloid lineage, detects muramyl dipeptide, which is common to Gram-positive and Gram-negative bacteria (Bryant et al., 2015). The Nod-like receptors often work in conjunction with other PRRs; for example, PGLYRP-2 and Nod-2 are both required to induce arthritis in a mouse model. Other NLR proteins such as NLRP3 also recognize bacteria, but by less clearly defined mechanisms, such as possibly recognizing microbial RNA (Bryant et al., 2015). These receptors are more likely to be important in patients with sepsis, working in conjunction with TLRs and other PRRs, rather than with inflammatory responses not associated with bacterial infections.

Receptors for Gram-positive Bacteria and Bacterial Ligands

Gram-positive bacteria and their ligands, such as bacterial proteins and peptidoglycan, are detected by TLR-2 (see Figure 16.1) (Takeuchi et al., 1999). Bacterial ligands, including bacterial extracts, such as lipoarabinomannan, and other factors from *Mycobacterium tuberculous*, *M. bovis*, and *M. avium* (Bryant et al., 2015), and VapA, a protein from the equine respiratory pathogen *Rhodococcus equi*, can activate TLR-2 (Kaur et al., 2013). TLR-2 may also be one of the major receptors for lipoteichoic acid, a bacterial product associated with shock mediated by Gram-positive organisms (Bryant et al., 2015). A mutation in TLR-2 has been detected in humans who are hyposensitive to bacterial peptides and, like mice lacking TLR-2; these patients appear to be particularly sensitive to infection with Gram-positive organisms (Bryant et al., 2015). These observations suggest that TLR-2 plays a critical role in mediating host immunity to Gram-positive bacterial infections.

Functionally, TLR-2 dimerizes with other TLRs, TLR-1 (see Figure 16.1) or TLR-6 (Song & Lee, 2012). Association of the latter two receptors confers sensitivity of the receptor complex to modulin (a bacterial product secreted by *Staphylococcus epidermis*), peptidoglycan, the bacterial lipoprotein mycoplasmal macrophage-activating lipopeptide-2, zymosan, or group B streptococcus, whereas dimerization of TLR-2 and TLR-1 occurs in response to a specific mycobacterial lipoprotein (Bryant et al., 2015). Therefore, the ability of TLR-2 to dimerize with other TLR subtypes may explain how host cells respond specifically to a broad range of bacterial ligands.

Peptidoglycan breakdown products are recognized primarily by the Nod receptors (Nod-1 and Nod-2). Other NLRs, such as NLRP3, can also recognize a range of Gram-positive pathogens (Bryant et al., 2015). These receptors are all present in the equine genome. The major receptors involved in circulatory shock resulting from Gram-positive bacterial infections are most likely to be the TLR-2 heterodimers, although it is unclear to what extent other receptors may be involved. Simultaneous activation of more than one TLR, for example TLR-2 and TLR-4, results in a synergistic enhancement of the pro-inflammatory response. It is, therefore, conceivable that, in sepsis where many bacterial ligands are generated, the pronounced clinical effects may be driven by activation of more than one type of receptor.

Some host species differences between humans and horses in the response of TLR-2 heterodimers have been described (Figueiredo et al., 2009; Irvine et al., 2013), but whether this will be true for the Nod or NLR receptors in response to bacterial ligands remains to be determined.

Antagonists to TLR-2 have been developed (Bryant et al., 2015) and may well be useful in treating shock syndromes caused by Gram-positive organisms.

Systemic Inflammatory Response Syndrome

Because of the concerns regarding confusion about the classification of human patients in critical care units, the American College of Chest Physicians and the Society of Critical Care Medicine held a consensus conference in 1992 to create a common vocabulary (Bone et al., 1992). One result of this conference was a standardized series of definitions for SIRS, sepsis, severe sepsis, septic shock, bacteremia, and multiple organ dysfunction syndrome (Table 16.1).

Because the definition for SIRS is general, the syndrome is associated with a wide variety of conditions, and its incidence in hospitalized human patients is high. In fact, it has been estimated that more than 50% of patients in intensive care units and more than 80% of those in surgical intensive care units meet the criteria for SIRS (Brun-Buisson, 2000). The usefulness of the definition was evident in a study of more than 3,700 patients in whom it was determined that those meeting the criteria for SIRS had a 26% chance of developing sepsis, and those meeting more than the two required criteria were at increased risk for developing sepsis, acute renal failure, disseminated intravascular coagulation, and circulatory shock (Rangel-Frausto et al., 1995). Furthermore, approximately half of the patients that met the two required criteria on admission met an additional criterion within a week of hospitalization. Interestingly, there were only small differences in mortality rates for patients with SIRS or sepsis, either in this initial study or in a later multi-institutional study (Alberti et al., 2003).

Table 16.1 Standardized series of definitions for systemic inflammatory response syndrome (SIRS). Source: American College of Chest Physicians and the Society of Critical Care Medicine Consensus Conference, 1992.

Systemic inflammatory response syndrome	An inflammatory response to a variety of clinical insults manifested by two or more of the following: temperature >38 °C or <36 °C, heart rate >90 bpm, respiratory rate >20 breaths per minute or $PaCO_2$ < 32 mmHg, white blood cell count >12,000 or <4000, or >10% immature (band) forms
Sepsis	SIRS caused by infection
Severe sepsis	Sepsis with at least one organ dysfunction or hypoperfusion
Septic shock	Severe sepsis with hypotension that is resistant to adequate fluid resuscitation
Bacteremia	The presence of viable bacteria in the bloodstream
Multiple organ dysfunction syndrome	Impairment of two or more organ systems in an acutely ill patient in whom homeostasis cannot be maintained without therapeutic intervention

After using the classification system for a few years, some investigators noted flaws in the original definition. Specifically, the original focus on SIRS identified it as a condition characterized by the synthesis of pro-inflammatory mediators. However, the results of several clinical studies in which specific pro-inflammatory mediators were targeted were negative, suggesting either that the original definition was flawed or that using specific therapeutic approaches in patients with diseases having diverse causes may be the wrong way to proceed (Baue, 1997; Opal & Cross, 1999; Zeni et al., 1997). These concerns initiated two divergent approaches: namely, expanding the original definition to incorporate the body's anti-inflammatory response to injury, and questioning the value of grouping patients having different underlying conditions under a single heading. As an example of the first approach, the lead author on the original consensus publication altered his view of the situation to incorporate five overlapping stages representing potential progression from SIRS to multiple organ dysfunction syndrome. In this modified classification system, the stages are local response, initial systemic response, massive systemic inflammation, excessive immunosuppression, and immunologic dissonance (Bone, 1996). This classification system was based on findings that, in later stages of critical illnesses, a shift occurs in the mediators produced. The initial synthesis of pro-inflammatory mediators (e.g., tumor necrosis factor (TNF)-α and interferon-γ) subsides and the patient usually survives. If the condition does not resolve, anti-inflammatory mediators (e.g., interleukins-10 and -4) predominate, the patient's ability to ward off secondary infections is impaired, and survival rates decrease (Lederer et al., 1999). As an example of the second approach, the author of a special commentary concluded that "it has not helped to lump all those conditions together … acute appendicitis is totally different from ventilator-acquired pneumonia, even though both may be called sepsis by some" (Baue, 2003).

The use of the term SIRS in horses is now recognized as an important way to classify clinical cases, particularly with respect to developing criteria for critically ill foals. Criteria include leukocytosis, leukopenia or >10% immature band neutrophils, hyperthermia, tachycardia, and tachypnea with at least two of the criteria being present. It is now clear that nearly 30% of adult horses presenting with colic or other gastrointestinal tract disease have evidence of SIRS (Epstein et al., 2011). Foals present with

SIRS when they have bacteremia, local bacterial infections, or peripheral asphyxia syndrome (Moore & Vandenplas, 2014).

Inflammatory Mediators and their Source in the Horse

Whether an ill horse's responses are to endotoxin, other bacterial components, breakdown products of endogenous proteoglygans, or polypeptides arising from the intestine, the end results include deficits in tissue perfusion, depression, ileus, and an increased risk of complications, such as laminitis. Several mediators have been implicated in similar responses to experimental endotoxemia and some have been identified in the circulation of horses with naturally occurring gastrointestinal diseases. Attempts to link each mediator to specific clinical signs have not been possible because of simultaneous expression and systemic responses.

Mononuclear phagocytes, such as peripheral blood monocytes, peritoneal macrophages, and tissue-fixed macrophages, produce most of these mediators. The association between these cells and the host's response to PAMPs, such as those occurring in the lipid A region of endotoxins, is based on the finding that mononuclear cells normally express CD14, TLR-4, and MD2 (Poltorak et al., 1998b). The results of other studies also implicate neutrophils, and more specifically, interactions between monocytes and neutrophils in responses orchestrated via TLR-4 (Sabroe et al., 2005).

Of the numerous inflammatory mediators that have been identified, the two mediators that are most commonly monitored in studies of experimental endotoxemia in horses are TNF-α and the prostaglandins. The cytokines, such as TNF-α and the interleukins, are synthesized and released relatively early after exposure to endotoxins and exert their effects by altering the expression of other inflammatory genes, after first binding to specific receptors on target cells (Bone, 1996). Collectively, the cytokines are responsible for initiating fever, alterations in leukocyte function, activation of coagulation, and the acute phase response component of the systemic response to endotoxins (Bone, 1996; Collatos et al., 1994, 1995. Serum concentrations of TNF-α have been monitored in horses administered endotoxin under controlled experimental conditions as well as in horses with naturally occurring gastrointestinal diseases (Barton et al., 2004; Morris et al., 1991). The results of these studies document that the increase in TNF-α in response to administration of endotoxin occurs quickly, with peak serum concentrations detected in 1–2 h (Morris et al., 1991). While interest in anticytokine therapy as a way of improving patient outcome has been considerable, the results of studies utilizing this approach have been mixed at best. For example, although therapies directed against cytokines had some beneficial effects in human patients in severe septic shock, they were not effective in the majority of patients with sepsis; in fact, this form of therapy was associated with a poorer outcome in patients at low risk of death (Eichacker et al., 2002). The results of studies targeting TNF-α in horses also have yielded mixed results, with one study reporting that pre-treatment of animals with antibody directed against equine TNF-α significantly reduced the ill effects of endotoxin administration (Cargile et al., 1995), while another study reported no beneficial effects when an antibody directed against TNF-α was given after initiation of endotoxemia (Barton et al., 1998).

Much evidence has accumulated to support the concept that cyclooxygenase-derived metabolites of arachidonic acid are involved in the response of horses to experimental endotoxemia (Baskett et al., 1997; Bottoms et al., 1982; Daels et al., 1991; Semrad et al., 1987). The results of these studies indicate that the onset of endotoxemia is associated with a rapid increase in circulating concentrations of stable metabolites of prostaglandins and thromboxanes. Furthermore, studies of experimental endotoxemia have produced convincing evidence that early administration of potent nonsteroidal anti-inflammatory drugs, such as flunixin meglumine, reduces the hemodynamic and clinical responses to endotoxin as well as plasma concentrations of arachidonic acid metabolites (Baskett et al., 1997; Daels et al., 1991).

The role of eicosanoids in horses with naturally occurring gastrointestinal diseases is intriguing. When flunixin meglumine was first released for use in equine practice, its efficacy in treating horses with abdominal pain was obvious. Consequently, it became the drug of choice for most practitioners called to examine a horse with colic. Clinicians at referral institutions, however, noted that many horses were being referred after the third or fourth injection of flunixin meglumine had failed to produce the beneficial responses seen with the first or second injection. Furthermore, horses with this history had a poor prognosis for survival. These findings prompted the performance of studies designed to test the efficacy of lower doses of flunixin meglumine in experimental endotoxemia (Semrad et al., 1987; Semrad & Moore, 1987). The findings of these studies, coupled with the aforementioned beneficial effects noted for the full dose of the drug in horses with experimental endotoxemia (Baskett et al., 1997; Daels et al., 1991; Moore et al., 1986), have led to the widespread use of nonsteroidal anti-inflammatory drugs, such as flunixin meglumine, in horses with gastrointestinal diseases. Although these drugs have become a mainstay in the treatment of horses with colic, no data have been published regarding plasma concentrations of eicosanoids in horses with naturally occurring gastrointestinal diseases. Presumably,

one reason for this is that virtually all horses presented to university clinics with colic have received one of these drugs before being referred, and this form of treatment is continued in the vast majority of horses, making interpretation of plasma concentrations of eicosanoids difficult at best.

The discovery of a novel cyclooxygenase (COX-2) in 1988 that was endotoxin-inducible sparked a massive drug discovery program for COX-2 inhibitors and a reassessment of the importance of prostaglandins in shock syndromes. COX-2 is induced by endotoxin and inflammatory cytokines. The enzyme produces high levels of prostaglandins, far more than the constitutively expressed COX-1 enzyme, which is thought to be important for regulating a number of physiological states including the thromboembolic balance, the health of the gastric mucosa, and renal autoregulation. The concept emerged that inhibition of COX-2 would only block inflammatory prostaglandins whilst sparing those produced by COX-1, hence protecting the gut. Widespread administration of highly selective COX-2 inhibitors to patients, however, revealed this concept may be oversimplified. Although there was some evidence to suggest a possible reduced incidence of gastric ulceration, there also was an increase in serious cardiovascular events (myocardial infarctions and strokes thought to be due to increased levels of clotting). These side effects caused all but one COX-2 inhibitor to be withdrawn for use in humans (Mitchell & Warner, 2006). Use of COX-2 inhibitors in horses with SIRS after colic surgery may well aid mucosal repair and alleviate pain, but the potential cardiovascular consequences of these drugs in patients with a dysregulated thromboembolic balance as well as their potential effects on renal function suggest that much research is required to determine whether these drugs will be safe in endotoxemic horses (Cook & Blikslager, 2015).

Summary

Although equine practitioners have a long history with the term *endotoxemia*, it has become increasingly important to recognize that endotoxin merely serves as a potent trigger of the horse's inflammatory response, and that it is this response that ultimately makes the horse ill. Furthermore, endotoxin is but one of many pathogen-associated molecular patterns (PAMPs) that are recognized by the horse's innate immune system, and that have the capability of initiating a systemic inflammatory response. Equine clinicians should use criteria for SIRS in adult horses with gastrointestinal diseases and gather sufficient clinical data to determine whether associations can be made with the development of complications and mortality rate. Although the underlying conditions may vary considerably, at least they all involve the same body system. This is quite different from the situation in human patients and may facilitate comparisons of treatment effects in horses meeting an established set of criteria. Given our history with *endotoxemia*, it also will be interesting to determine whether an association exists between the presence of endotoxin in the circulation and fulfillment of the criteria for SIRS.

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Part III

Intestinal Parasitism

17

Intestinal Parasitism

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Principles of Intestinal Parasitism

The common parasites of the horse's intestinal tract are widespread in their host population. Most horses harboring intestinal parasite infection suffer few or no adverse effects. So what are the determinants of parasite-associated disease? The most important is infection intensity. It is intuitive that horses with small numbers of parasites are unlikely to suffer any ill effects from their parasite burdens. A logical extension of this argument is that horses with high parasite burdens are most likely to suffer parasite-associated disease. This hypothesis is supported by numerous experimental studies and field investigations in horses and other host–parasite systems (Anderson & May, 1992; Proudman et al., 1998).

A second general principle of intestinal parasitism is that not all horses are equally susceptible to infection. For reasons that are poorly understood, parasites tend to distribute in a nonrandom manner in their host population (Anderson & May, 1992). Certain individuals in the population are "predisposed" to developing high levels of infection and others are resistant to infection. This results in an asymmetric distribution: commonly 80% of the worms are present in 20% of the hosts. In other words, a few individuals harbor high numbers of parasites, but most have modest or low levels of infection. It is these heavily infected individuals that are at risk for parasite-associated disease. The concept of predisposition is further supported by observations that, after chemotherapeutic treatment of parasite infections, it is the same individuals that become heavily reinfected and harbor large worm burdens (Bensted-Smith et al., 1989).

A third issue of importance when considering intestinal parasitism is age-related susceptibility to infection. Young animals are generally more susceptible to parasitism and are more likely to develop high levels of infection. Older animals develop resistance to parasite invasion, although it is unknown whether this arises from immunity or from behavioral changes that decrease exposure to infective stages (Anderson & May, 1992).

The intestinal parasites of horses with greatest relevance to acute abdominal disease are large redworms (*Strongylus vulgaris*), small redworms (cyathostomins) and tapeworms (*Anoplocephala perfoliata*).

Strongylus vulgaris

Life Cycle

The life cycle of this parasite involves migration of third-stage larvae through the submucosa of the cecum and colon (Figure 17.1). This is followed by further migration through the small arterioles of the intestine and into the cranial mesenteric artery. At this site, damage to the arterial intima can result in thrombus formation (Figure 17.2). Both submucosal migration and cranial mesenteric arteritis have been associated with colic in experimental models of infection (Duncan & Pirie, 1975; Lester et al., 1989; Sellers et al., 1982).

Pathogenesis

Nonstrangulating infarction of cecum and colon (Figure 17.3) has been cited as the classic lesion associated with parasite-associated thromboembolic colic (Duncan & Pirie, 1975). It is proposed that emboli detach from the thrombus and are carried along the arterial tree until they become wedged in a small arteriole. This leads to physical obstruction of blood flow and to vascular spasm associated with ischemia. The net result is failure of oxygenation of tissues supplied by the arterioles and ischemic necrosis. The cecal apex, pelvic flexure, and colon are the sites most commonly involved. This lesion is rarely seen in horses at surgery or at postmortem

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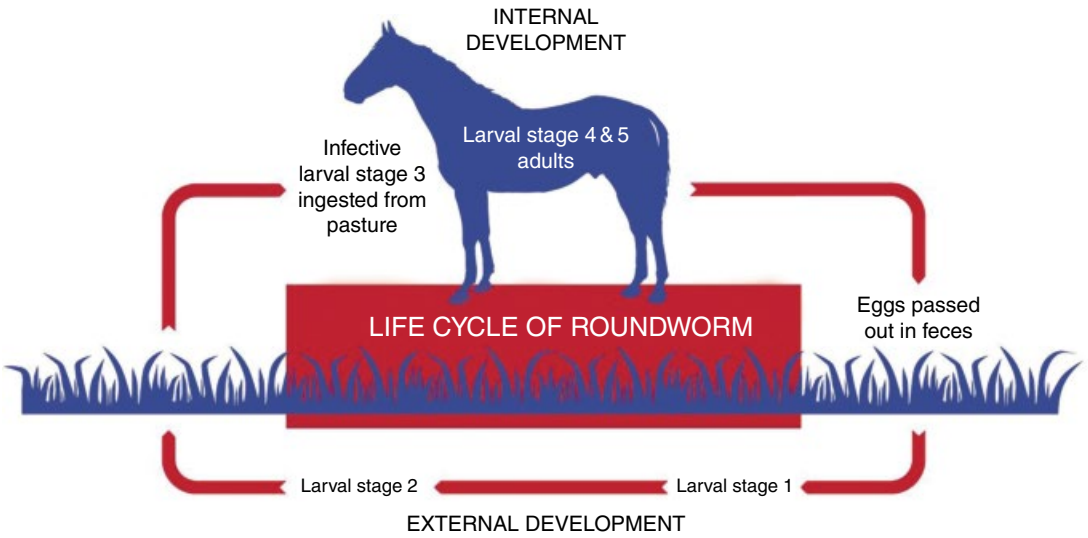

Figure 17.1 General life cycle of roundworms (strongyles). Source: Courtesy of Virbac UK.

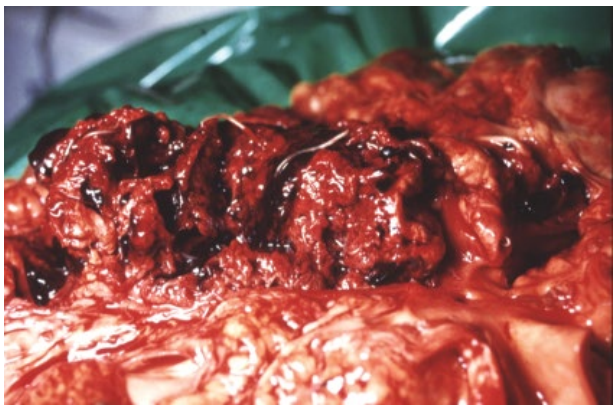

Figure 17.2 Postmortem specimen showing a large thrombus within the abdominal aorta. Note the *S. vulgaris* larvae within the thrombus.

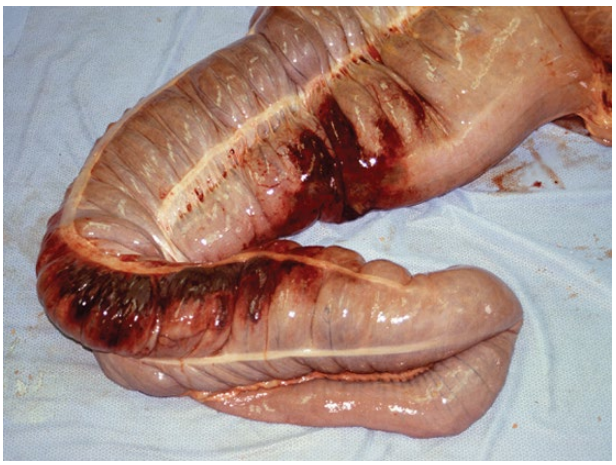

Figure 17.3 Nonstrangulating infarction of the left ventral colon.

examination (White, 1981), which may be explained by the marked decrease in prevalence of *S. vulgaris* since the introduction of modern anthelmintics (Love, 1992).

Diagnosis and Treatment

The diagnosis of *S. vulgaris*-associated colic is invariably retrospective and is often possible only after surgery or postmortem examination. Horses with nonstrangulating infarction of the cecum or colon carry a guarded prognosis, as the presence of a cranial mesenteric thrombus may lead to further thromboembolic events. Spasmodic colic episodes that resolve with medical treatment in horses with a history of poor worm control may be attributable to *S. vulgaris* infection. Fecal worm egg counts will identify strongylid eggs, but differentiation between *S. vulgaris* and cyathostomin larvae is possible only by larval culture. Knowledge of poor parasite control (monitored by periodic fecal egg count) on the farm of origin may raise the index of suspicion for this disease. Treatment of proven *S. vulgaris* infection is straightforward as the parasite is sensitive to most modern anthelmintics (Table 17.1).

Spasmodic colic episodes resulting from changes in intestinal motility can usually be managed successfully with analgesics and spasmolytic drugs. Nonstrangulating infarction results in low-grade, persistent pain and changes in peritoneal fluid consistent with infarction of intestine (see Chapters 20 and 24). Surgical resection of the affected bowel is indicated.

Cyathostomins

Life Cycle

For convenience, the many species of small strongyle parasites in the horses are considered a homogeneous group. These parasites are minimally invasive, the

Table 17.1 Anthelmintics currently used against equine intestinal helminths.

Anthelmintic	Dose	Recommended frequency of dosing	Efficacy against cyathostomes and tapeworms[a)]
Fenbendazole	7.5 mg/kg 7.5 mg/kg for 5 days	6 weeks 6–12 months	Efficacy against benzimidazole-susceptible, adult cyathostomes and "immature" stages. Ovicidal effect on nematode eggs. Five-day course effective against encysted, inhibited mucosal stages of cyathostomes. No efficacy against tapeworms
Mebendazole	5–10 mg/kg	6 weeks	Efficacy against benzimidazole-susceptible, adult cyathostomes. No efficacy against tapeworms
Oxibendazole	10 mg/kg	6–8 weeks	Efficacy against benzimidazole-susceptible, adult cyathostomes. No efficacy against tapeworms
Febantel	6 mg/kg		Efficacy against benzimidazole-susceptible, adult cyathostomes. No efficacy against tapeworms
Pyrantel embonate	19 mg/kg 38 mg/kg for tapeworms	4–6 weeks	Efficacy against adult cyathostomes. No efficacy against inhibited, encysted mucosal stages. Use antitapeworm dose every 6–12 months. No efficacy against *A. mamillana*
Ivermectin	200 µg/kg	6–8 weeks	High efficacy against adult cyathostomes, limited efficacy against encysted mucosal stages. Resistance reported in *Parascaris equorum*. No efficacy against tapeworms
Moxidectin	400 µg/kg	13 weeks	High efficacy against adult and developing encysted cyathostomes. No efficacy against tapeworms
Praziquantel	1 mg/kg	–	Efficacy against tapeworms, including *A. mamillana*. Also available as combination anthelmintic with ivermectin or with moxidectin. No efficacy against nematodes

a) Efficacy against large strongyles and *Oxyuris equi* is assumed unless stated otherwise.

infective L3 stages migrating only as far as the mucosa of the cecum and large colon. The life cycle of cyathostomins differs from the general life cycle illustrated in Figure 17.1 during the period of internal development. During larval development within the colonic mucosa, cyathostomins have the ability to go into a stage of arrested development within mucosal cysts. Such arrested encysted larvae stimulate little inflammatory response. Huge numbers of parasite larvae can inhabit the mucosa of susceptible horses (Figure 17.4). Mass emergence of these larvae as development is reactivated leads to colitis and the condition of larval cyathostominosis.

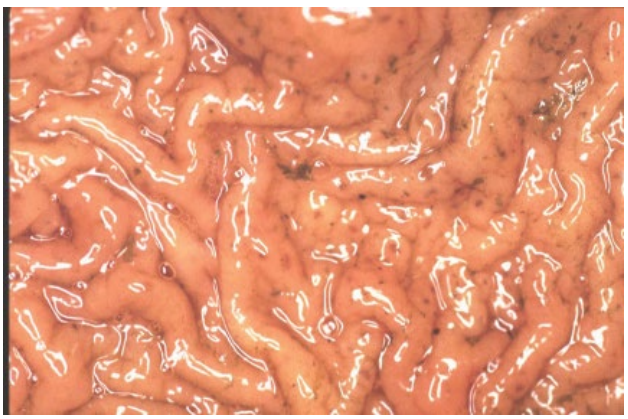

Figure 17.4 Colonic mucosa of a horse with heavy cyathostomin infection. Each black spot in the mucosa is an encysted cyathostomin parasite.

Association with Acute Abdominal Disease

Disturbance of local intestinal motility, pathology at sites of cyst reactivation, and mucosal migration are all possible mechanisms by which colic may arise. Murphy & Love (1997) observed intestinal dysfunction early in the course of experimental cyathostomin infection, suggesting a pathologic role for invading L3, not just encysted stages undergoing reactivation and emergence into the gut lumen. The role of such dysfunction in the etiology of colic is not known.

An association between cyathostomin infection and colic has been demonstrated in epidemiologic studies. Uhlinger (1990) demonstrated that the better the anthelmintic program being used in herds of horses, the lower is the incidence of colic. The only strongyle parasites harbored by the horses in this study were cyathostomes as established by larval culture. By implication, therefore, cyathostomes were associated with a significant proportion of colic cases. This observation is further supported by work that reported a reduced risk of colic in horses receiving daily pyrantel tartrate in feed (Reeves et al.,

1996) and a study that reported a decreased risk of simple colonic obstruction associated with the use of avermectin anthelmintics (Hillyer et al., 2002).

Clinical case reports have associated cyathostomin infection with nonstrangulating infarction (Mair & Pearson, 1995) and with cecocecal and cecocolic intussusception (Mair et al., 2000). In both reports the authors cited clinical and pathologic evidence suggesting an association between parasite infection and intestinal disease.

Diagnosis and Treatment

Patent infection (adult parasites producing eggs) is not difficult to detect coprologically (Figure 17.5). A fecal egg count gives an indication of luminal adult strongyle burden, although it is not possible to differentiate large strongyle (*S. vulgaris*) eggs from those of the small strongyles (cyathostomins) by microscopy alone. Fecal egg counts are quantitative but may not give an accurate estimate of total worm burden. A major limitation of this diagnostic test is the inability to detect immature, mucosal infection (Love & McKeand). Up to 95% of a horse's cyathostomin burden can be mucosal. Developing late-stage larvae may be observed by careful inspection of feces from horses with larval cyathostominosis, but this test is of limited sensitivity. The use of biochemical tests to detect markers for cyathostomin infection has been investigated and discounted. In particular, when the use of serum β-globulins was investigated, it was concluded that total serum protein and IgG(T) responses were of limited value in the diagnosis of parasitism (Herd & Kent, 1986). At present, the diagnosis of cyathostomin infection is based on history of worm control, clinical signs, fecal examination for eggs and larvae, and (after cyathostomin-associated colic) postmortem examination.

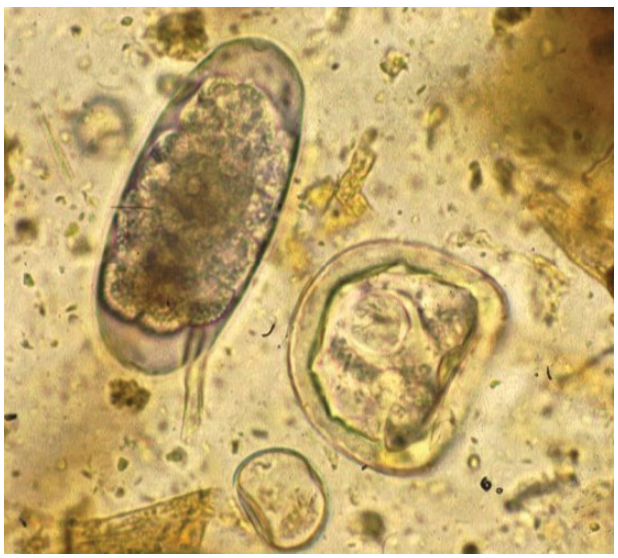

Figure 17.5 Microscopic view of a strongyle egg (left) and a tapeworm egg (right) on fecal flotation.

Treatment of cyathostomin infection is not straightforward. If encysted arrested stages are present, then some anthelmintics will lack efficacy (Table 17.1). Resistance to benzimidazoles is also widespread among the cyathostomins. The current recommendation for the treatment of encysted arrested larvae is to use fenbendazole for five consecutive days in horses with benzimidazole-susceptible infections. In the face of benzimidazole resistance (which is now widespread), moxidectin is indicated (Xiao et al., 1994). Treatment is hazardous in heavily infected horses as the use of anthelmintics is associated with the development of larval cyathostominosis (Reid et al., 1995). Preventing the accumulation of large burdens, particularly encysted arrested stages in young horses, is a safer control strategy.

Tapeworms

Life Cycle

The common tapeworm of the horse in temperate climates is *Anoplocephala perfoliata*. The life cycle of this parasite is illustrated in Figure 17.6. A fundamental difference between roundworm life cycles and that of the tapeworm is the need for an intermediate host, in this case the ground-dwelling oribatid mite. One of the implications of this indirect life cycle is that *A. perfoliata* is most prevalent in regions with a humid, warm climate, as this favors the intermediate host (Reinemeyer et al., 2003). The prevalence and clinical significance of *Anoplocephala magna* and *Anoplocephaloides mamillana* are poorly understood at present.

Association with Acute Abdominal Disease

Several studies have reported the gross and microscopic pathology associated with tapeworm infection (Beroza et al., 1983; Fogarty et al., 1994; Nilsson et al., 1995; Pearson et al., 1993). Mucosal ulceration, submucosal edema, and decreased distensibility of the ileocecal valve have all been reported. It is significant that this parasite chooses to aggregate around the ileocecal junction, and pathology is confined to this site (Figure 17.7 and Figure 17.8). Intestinal disease originating at this site has been associated with heavy tapeworm infection (e.g., ileal impaction, ileocecal and cecocecal intussusception).

Epidemiologic studies have demonstrated an association between tapeworm (*A. perfoliata*) infection and colic. In one study, both coprologic diagnosis and a novel

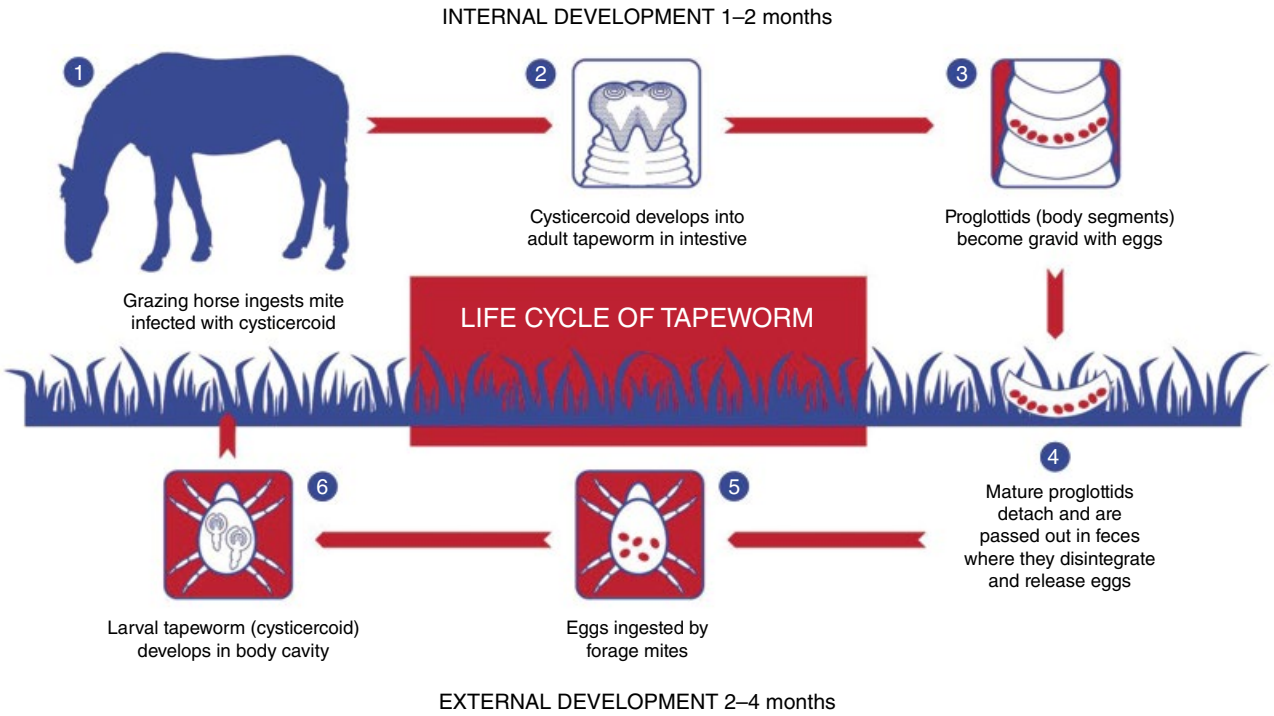

Figure 17.6 Life cycle of the equine tapeworm *Anoplocephala perfoliata*. Source: Courtesy of Virbac UK.

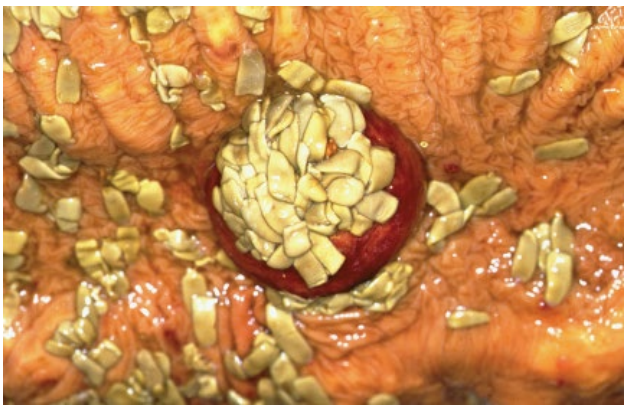

Figure 17.7 Mucosal surface of the cecum with massive edema at the site of tapeworm attachment at the ileocecal junction.

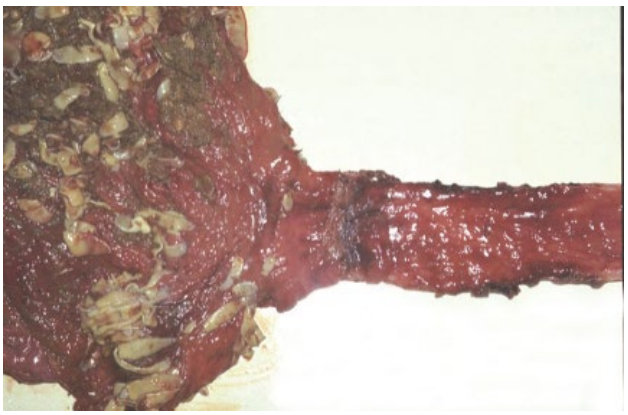

Figure 17.8 Mucosal surface of the ileocecal region of a horse with heavy tapeworm infection. Tapeworms removed from the junction revealing mucosal ulceration and edema.

serologic assay were used to demonstrate an association between the parasite and spasmodic colic and ileal impaction colic (Proudman et al., 1998). Serologic data, which correlated with infection intensity (Proudman & Trees, 1996), were used to show a dose–response relationship between tapeworms and spasmodic colic (Figure 17.9). The greater the number of tapeworms present, the higher was the risk of spasmodic colic. Slightly more than 20% of the spasmodic colic cases and over 80% of ileal impaction cases in this study were tapeworm related. A similar study focusing on ileal impaction cases in the southeastern United States confirmed an increased risk for this disease in horses that did not receive anti-tapeworm anthelmintics (Little & Blikslager, 2002).

Diagnosis and Treatment

Diagnosis of tapeworm infection is by coprologic or serologic methods. Tapeworm eggs can be detected microscopically after flotation in a high specific gravity solution (Figure 17.5). Tapeworm eggs are heavy and do not float reliably on saturated salt solution used for strongyle eggs. Coprologic identification is messy and time consuming, lacks sensitivity, and lacks correlation

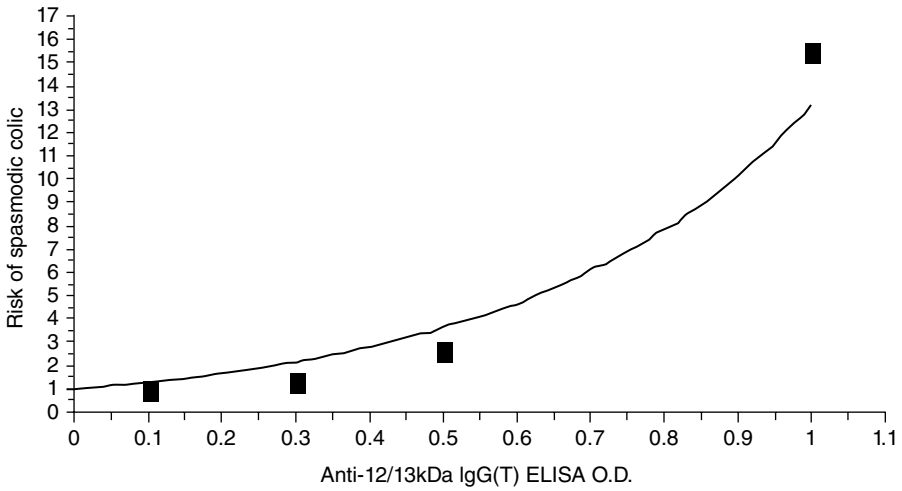

Figure 17.9 Relationship between tapeworm infection intensity (measured by ELISA) and the risk of spasmodic colic. Squares represent categorized data and the solid line represents the relationship for continuous data (conditional logistic regression model). Source: Proudman et al., 1998.

with infection intensity (Meana et al., 1998). A serologic method for tapeworm diagnosis has been described, using the IgG(T) response to tapeworm antigens (Proudman & Trees, 1996). This enzyme-linked immunosorbent assay (ELISA) test has the advantage of good correlation of test results with infection intensity, making this test useful for monitoring the risk of clinical disease in infected horses. Recently, the same IgG(T) response in saliva has been used diagnostically (Austin Davis Biologics, 2016). Although test validation has not appeared in peer-reviewed publications at the time of writing, there is no reason to suspect that it will be different from the ELISA test using serum IgG(T).

Treatment of tapeworm infection can be achieved by using anthelmintic-containing praziquantel or pyrantel (Table 17.1). Pyrantel has good efficacy against *A. perfoliata* when used at twice the nematocidal dose. It should be noted that this anthelmintic has no efficacy against *A. mamillana*; praziquantel should be used.

Parascaris equorum

This ascarid parasite of the small intestine of the horse occasionally causes acute colic in young animals. The median age of horses with ascarid-related colic was 5 months in one report (Southwood et al., 1998). Large numbers of adult parasites can occlude the lumen of the small intestine (Figure 17.10), leading to intestinal distention and obstruction of the small intestine. Surgical relief of the impaction is indicated in most cases, but a poor prognosis for such cases is reported, with long-term survival around 45% (Southwood et al., 1998). The reasons for this are unclear, but it is suggested that somatic antigens from the parasite may lead to ileus, which may compromise postoperative recovery. Affected animals that do not undergo surgical treatment are likely to develop intestinal rupture and fatal peritonitis.

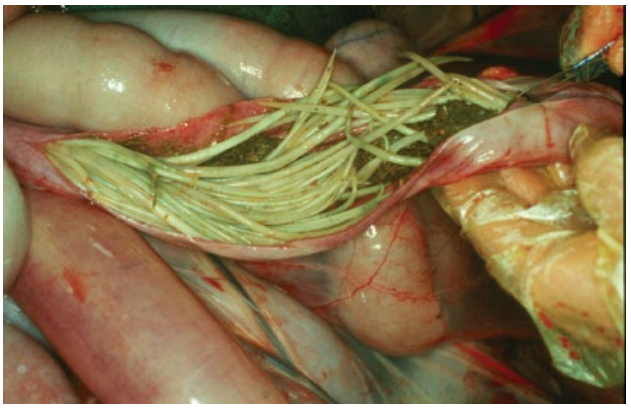

Figure 17.10 Ascarid worms in the small intestinal lumen of a young horse.

Detection of *P. equorum* infection is by coprologic means. Infected horses usually have large numbers of eggs in their feces (Figure 17.11), but correlation between egg count and infection intensity has never been quantified. A further problem with diagnosis is that many horse owners do not consider their young stock to be at risk of disease so early in life, so feces are rarely submitted for testing. Anthelmintic therapy in the presence of heavy infection is controversial. A slow kill of parasites with benzimidazoles, pyrantel, or ivermectin has been advocated to avoid release of somatic antigens (DiPietro & Todd, 1988). It should also be noted that apparent resistance of *P. equorum* to ivermectin has been reported (Boersma et al., 2002; Fogarty et al., 1994). As is so often the case, little scientific evidence is available on which to base a rational decision.

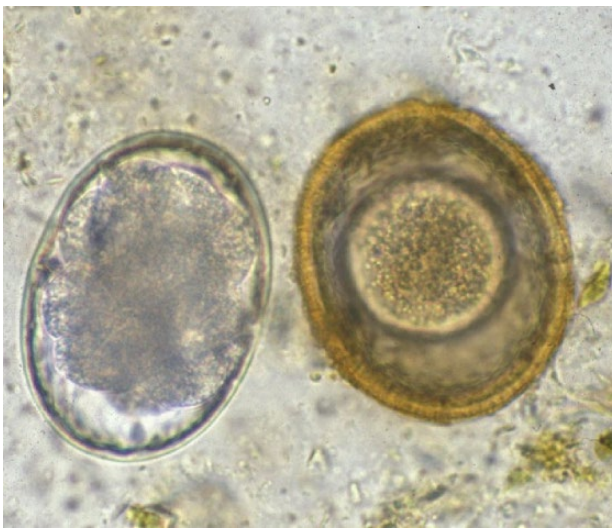

Figure 17.11 Microscopic view of a strongyle egg (left) and an ascarid egg (right).

Figure 17.12 Removal of feces from pastures is an effective worm control option. Mechanical removal is an effective option for larger horse farms.

Other Intestinal Parasites

No evidence exists to suggest that bots (*Gasterophilus intestinalis*), *Oxyuris equi*, or *Strongyloides westeri* are associated with any acute abdominal diseases. *O. equi* may be observed in the feces of horses or in intestinal contents removed from a colon enterotomy. Their presence should be regarded as a marker for poor parasite control.

Prevention

The successful prevention of all parasite-associated disease depends on the design and execution of a "custom-made" worm control program. Unfortunately, the concept of a "one-size-fits-all" approach to this problem is simplistic and does not work. Veterinarians should discuss with their clients worm control measures that are appropriate to each farm and, with the aid of diagnostic tests, design, implement, and monitor an appropriate control policy.

Managemental Control

Good pasture management is inexpensive, environmentally friendly, and a highly efficient method of preventing transmission of intestinal parasites. The collection of feces from the pasture twice weekly is optimal, but even weekly collection will significantly decrease the infectivity of pasture (Corbett et al., 2014) (Figure 17.12). Rotation of pastures, mixed-species grazing, and maintaining a low stocking density are all practices that minimize parasite spread.

Anthelmintics

Numerous anthelmintic products are readily available to help with parasite control. These are listed in Table 17.1 and the spectrum of activity of each drug is given. The different ways of using these drugs are as follows:

- *Interval treatment* involves the administration of anthelmintics to all horses on the premises at periodic intervals.
- *Strategic dosing* is the use of anthelmintics at times of the year critical to parasite transmission. The exact timing of doses varies with differing climates around the world.
- *Targeted dosing* is the use of anthelmintics on just those horses demonstrated to have significant parasite burdens by diagnostic testing.

Overdependence on anthelmintics should be avoided, as intensive use of these drugs is likely to hasten the onset of resistance within parasite populations (Matthews, 2014; Proudman & Holdstock, 2000; Sangster, 2003). Benzimidazole and pyrantel resistance have been reported in horses worldwide, and there is emerging evidence of reduced efficacy of macrocyclic lactones against cyathostomin infections (Craven et al., 1998; Matthews, 2014; Tarigo-Martinie et al., 2001). Resistance to ivermectin has been reported in *P. equorum* in the United Kingdom and North America (Boersma et al., 2002; Hearn & Peregrine, 2003; Stoneham & Coles, 2006). Currently, rotation of anthelmintics is not recommended as a strategy to avoid the creation of resistant parasites. Strategic dosing with periodic individual horse evaluation for parasites is recommended for optimal parasite control.

Diagnostic Testing

Diagnostic testing in equine intestinal parasite control has three important uses. The first is to guide the targeted use of anthelmintic drugs. Second, whatever the control program used, is to monitor effectiveness of control programs by periodic testing for strongyle eggs in the feces and for tapeworm infection (coprologic or serologic tests may be used). The third indication for diagnostic testing is the investigation of colic episodes. Veterinarians are frequently asked about the cause of a colic episode after it has resolved. Infection with adult strongyles and tapeworms can be tested easily and treated readily if found to be present.

Occasionally, veterinarians are asked to investigate the cause of a high incidence of colic in a group of horses. Evaluation of parasite status is worthwhile in such cases, but because of the nonrandom distribution of parasites in the horses, it is not satisfactory to sample a selection of affected animals – as many horses as possible should be sampled. Such investigations have been successful in identifying and preventing parasite-associated colic problems (Proudman & Holdstock, 2000).

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Part IV

Epidemiology of Colic

18

Epidemiology of Colic: Principles for Practice

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Introduction

One of the principal advancements in our understanding of the epidemiology of colic has been descriptive and analytical investigation of *specific* types of equine colic (e.g., large colon impaction, small intestinal volvulus) and their sequelae (e.g., postoperative ileus, diarrhea, and so on). As such, epidemiologic aspects of specific types of colic are described in chapters of this book pertaining to these disorders. Consequently, reviewing the epidemiology of various types of colic would be both redundant and beyond the scope of this chapter. Rather, the purpose of this chapter is to review *epidemiologic principles* that are important for understanding and interpreting information about equine colic, with an emphasis on making inferences for clinical application of epidemiologic studies.

Assessing the Accuracy of Clinical Studies of Colic

Because new information is continuously emerging, much information in textbooks (including this one) is often outdated soon after publication (if not before) (Straus et al., 2010). Consequently, we must be able to assess the accuracy of new findings as they emerge in order to be confident of their influence on our clinical decisions. The accuracy of results is reflected by the *reliability* and the *validity* of the study findings. When reading clinical studies of colic, we must be able to assess both the reliability and the validity of the reported results.

Reliability and Validity

Reliability refers to the precision of an estimate (Figure 18.1) (Fosgate & Cohen, 2008). The precision of an estimate reflects the amount of random error of the measurements. It should be noted that the instrument for taking measurements could be any device (e.g., stethoscope for heart rate), apparatus (e.g., lactometer or glucometer), or data collection procedure (e.g., a questionnaire). The more precise the instrument, the more reliable are the results. Put another way, a more precise instrument will yield the same results (or very close to the same results) when measurements are repeated. The reliability (precision) of an estimate can be improved upon by increasing the number of units (i.e., repetitions) of the experiment. For example, an estimate of the odds of postoperative ileus in horses with duration of strangulating intestinal obstruction will be more precisely estimated in a study of 200 horses than in a study of 20 horses. In the case of an estimated odds ratio or risk ratio, the precision of the estimate will most often be reflected in the 95% confidence interval calculated for the estimate: the wider the confidence interval, the less precise is the measurement. Because the number of horses included in equine clinical studies is often small, it is important to bear in mind the potential imprecision of estimated parameters from such studies.

Validity of study findings refers to the extent to which the results of a study reflect the actual parameter being estimated. For example, we might want to know how well an estimated relative risk of postoperative ileus during the 3 days following surgery in horses treated with intravenous lidocaine intra- or postoperatively reflects the true value. If the estimated relative risk is 0.8 per 3 horse-days, how close is this estimate to the true value? Whereas the principal determinant of reliability (precision) is the amount of random error, the principal determinant of validity is the occurrence of *systematic error*. Systematic error refers to lack of accuracy that results from a *consistent* error in the way the data are either collected or analyzed. Unlike random error, the effect of systematic error cannot be reduced by increasing the number of

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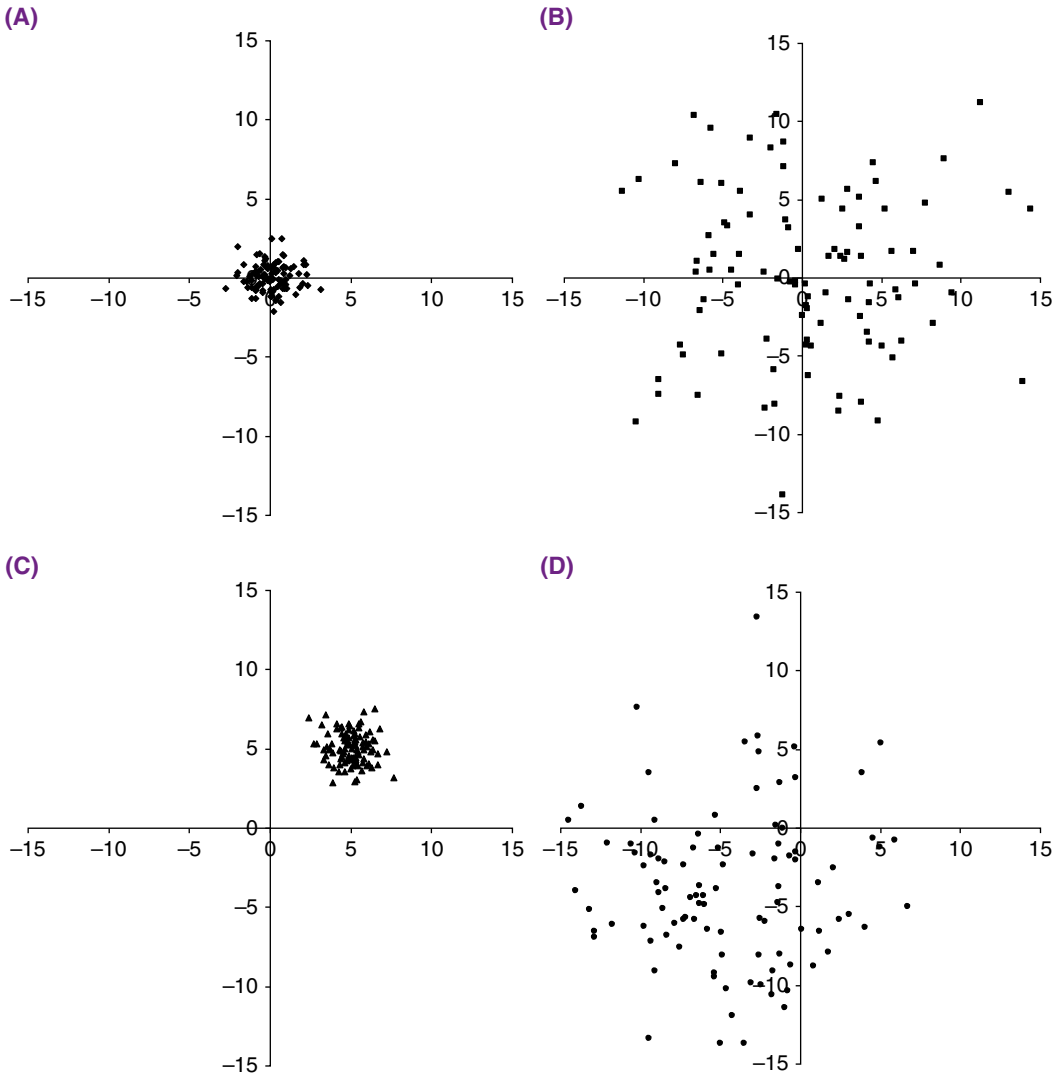

Figure 18.1 The effect of bias and precision on epidemiologic measurements. The origin (0,0) is considered to be the true (valid) value. The individual points represent values simulated from a precise and valid (unbiased) process **(A)**, an imprecise but valid process **(B)**, a precise and nonvalid (biased) process **(C)**, and an imprecise and biased system **(D)**. Source: Fosgate & Cohen, 2008; figure generated by Dr Geoffrey Fosgate.

repetitions of the experiment: for example, if a glucometer is always overestimating glucose concentration in equine blood, no matter how many times we measure glucose concentrations the measured value will not be valid. Systematic error is repeatable and consistent whereas random error is not.

Internal versus External Validity

The term *bias* is used by epidemiologists to refer to systematic error. The net effect of bias is to render the results of a study not valid. Epidemiologists commonly consider two forms of validity: internal validity and external validity. Internal validity refers to the integrity of the study design: how valid are the results of the study within the population studied? For example, consider a study of the association of postoperative diarrhea with administration of antimicrobials during the postoperative period in which the investigators observe a strong positive association between the occurrence and duration of diarrhea and antimicrobial use. Given what is known about the association of antimicrobial administration with altering the intestinal and fecal microbiota, this result is biologically plausible. Now consider that the horses that did not receive antimicrobials had forms of colic that were less severe and had fewer signs of systemic illness. Conceivably, this bias might inflate (i.e., bias upward) the observed estimate of the magnitude of the association between antimicrobial use and diarrhea, and might cause us to overestimate the risk associated with antimicrobial use. Note that bias can also either mask or diminish the magnitude of an observed association

relative to its true value (i.e., bias downward), or even change the direction of an observed association (i.e., make a harmful effect appear protective or vice versa). A study is considered internally valid when it is deemed to be free from evidence of bias that alters the validity of the results in the *observed* study population.

External validity refers to the extent to which results may be extrapolated to other populations. Results that are internally valid cannot necessarily be extrapolated to other populations. For example, a study of prognostic factors determined among horses with colic at referral centers might perform poorly when applied to a population in which the risk of death is much lower. As another example, a study of the association of amount of dietary concentrate (either the proportion of fed calories or absolute amount fed) with colic that is performed among Thoroughbred horses might not be applicable to other breeds in which the amounts and types of exercise differ from Thoroughbreds. Similarly, extrapolating results of studies of colic and feeding practices from, say, North America to Europe or Australia might not be appropriate because of regional differences in feeding practices, diet, activity level, and so on.

Forms of Bias

There are three principal forms of bias in epidemiologic and clinical studies that can result in invalid findings: selection bias, information bias, and confounding. Selection bias refers to how the horses studied were chosen for a project. There are many forms of selection bias that can occur during the design of a study, sampling horses for the study, and obtaining either the follow-up information (for cohort studies) or evaluation of exposure information (for case–control studies). A famous example of a selection bias in the design of an experiment was a reported association between coffee drinking and pancreatic cancer from a case–control study (MacMahon et al., 1981). In this study, cases were individuals who had pancreatic cancer and controls were patients from the same practices who did not have cancer. Because many of the physicians were gastroenterologists, many controls had peptic ulcer disease or other forms of disease for which their physicians recommended that they not drink coffee. Thus, the study results truly reflected lower odds of coffee consumption among controls than increased odds of cancer among people who drank more coffee (Feinstein et al., 1981). Failure either to randomly select or to use all sequential cases can cause selection bias. For example, we could obtain biased results from a study of risk factors for large colon impaction if only those cases that are managed surgically are included, or from a study of the impact of intraoperative lidocaine on postoperative ileus in horses with strangulating small intestinal lesions in which only the most severely affected horses are included. An example of bias in follow-up would be one in which horses at pasture are deemed to be at lower risk of colic because the study failed to account for mild signs of colic being less likely to be detected in horses at pasture either because of less frequent or less solicitous observation.

Information bias refers to a systematic error in the way that data are collected for a study. For example, consider an epidemiologic case–control study that shows an association between recent deworming and colic. The biological plausibility of the result supports the possible validity of the results; however, if many of the horses with colic were show horses, and if show horses were more likely to have history of vaccination and deworming recorded or recalled, then the observed association could be an artifact (i.e., not valid) of a systematic difference in information (i.e., information bias) between cases and controls. Differential health monitoring is another example of information bias: if performance horses are more likely to be monitored for signs of mild colic (or frequency of recurrent colic) than other types of horses, a systematic error in outcome assessment would exist.

The third type of bias we consider in this chapter is confounding. An epidemiologic confounder is a factor that is associated with both the outcome (i.e., disease) of interest and the exposure (i.e., characteristic) of interest, such that failure to account for the confounding factor results in an estimated association that is not valid. Consider a case–control study that identifies an association between the Thoroughbred breed and colic. Let us further consider that the study is based on a large number of horses (e.g., 2,000 horses; Table 18.1). In Table 18.1, the odds of a horse with colic being a Thoroughbred are 800:200 or 4:1, and the odds of a control horse being a Thoroughbred are 400:600 or 1:1.5. The estimated odds ratio is thus $(4/1)/(1/1.5) = (4 \times 1.5)/(1 \times 1) = 6$. Thus, relative to other breeds we estimate that the odds of colic are six-fold greater among Thoroughbreds. Our estimate is likely quite reliable (precise), because we have a larger sample size. This precision, however, does not assure us of an accurate interpretation because it does not consider potential confounding that might influence the *validity* of the association. Let us assume that previous studies have identified an association between activity level and colic. Let us also assume that activity level generally is higher for Thoroughbreds than for other breeds of horses. Activity level, however, was not considered in our results summarized in Table 18.1. To consider activity level, we stratify the data in Table 18.1 by whether the horses have a relatively high activity level (Table 18.2A) or a relatively lower activity level (Table 18.2B). In Table 18.2A, we see that there are a total of 900 horses that had a relatively high activity level and the majority of these horses (850/900 = 94%) are Thoroughbreds. The odds of a colic horse being a Thoroughbred in the high

Table 18.1 Results of a hypothetical case–control study of colic in which cases are horses with colic and controls are horses that have not had colic recently (noncolic controls). It appears that Thoroughbreds are overrepresented among the horses with colic: the odds of colic horses being Thoroughbreds (800:200 or 4:1) is higher than the odds of noncolic horses being Thoroughbreds (400:600 or 1:1.5) such that the odds ratio is 6 (4/(1/1.5) = 4 × 1.5). Note that the odds ratio for the association of breed with colic is equivalent to the odds ratio for colic with breed: the odds of Thoroughbreds having colic (800:400 or 2:1) relative to the odds of other horses having colic (200:600 or 1:3) is also 6 (2/(1/3) = 2 × 3).

Breed	Horses with colic	Noncolic control horses	Total
Thoroughbred	800 (80%)	400 (40%)	1,200
Other	200 (20%)	600 (60%)	800
Total	1,000 (100%)	1,000 (100%)	2,000

activity group is 750:100 or 7.5:1, and the odds of a noncolic control horse being a Thoroughbred are 44:6 or 7.3:1, such that the odds ratio is just a little more than 1 (7.5/7.3). Recall that an odds ratio of approximately 1 indicates that the odds of having colic are the same among Thoroughbreds and non-Thoroughbreds (or, equivalently, that the odds of being a Thoroughbred are the same for colic cases and controls). Among the 1,100 lower activity level horses, only about 14% (150/1,100) are Thoroughbreds (Table 18.2A). Among these lower activity level horses, the odds of colic horses being Thoroughbreds is 50:100 or 1:2.0, and the odds of a noncolic control horse being a Thoroughbred are 300:650 or 1:2.2, such that the odds ratio is approximately 1 (2.0/2.2). Thus, when we account for the effect of activity level, the association of Thoroughbred breed with colic has changed from an estimated six-fold greater odds of colic among Thoroughbreds relative to other horses to no association (odds ratio of approximately 1) of colic with Thoroughbred breed. In this instance, activity level appears to be acting as a confounder for the association of breed and colic. We see from Tables 18.2A and 18.2B that activity level is associated with breed: most high activity level horses are Thoroughbreds (Table 18.2A), whereas there are fewer Thoroughbreds among the lower activity level horses (Table 18.2B). Thus, an association exists between the potential confounder (namely, activity level) and the characteristic of interest (Thoroughbred breed). When we examine the data further, we observe that an association also exists between activity level and colic: the odds of high activity level among horses with colic is 850:150 or 5.7:1, and the odds of high activity level among the noncolic control horses is 50:950 or 1:19 such that the odds ratio for association is greater than 100 (5.7/(1/19) = 5.7 × 19)! Because activity level is strongly associated with colic and with breed, failing to account for the confounding effects of activity level lead us to a spurious result. Note that this is simply a hypothetical example for illustrative purposes.

Table 18.2 The same hypothetical data from Table 18.1, now stratified by those horses with a high activity level (Table 18.2A) and a low activity level (Table 18.2B). Among horses with a high activity level (18.2A), the odds ratio for the association of colic with the Thoroughbred breed is approximately 1 [(750:100)/(44:6)], indicating no association of breed with the odds of colic. Among horses with a low activity level (18.2B), the odds ratio for the association of colic with the Thoroughbred breed also is approximately 1 [(50:100)/(300:650)], again indicating the absence of an association with colic. The apparent association of colic with the Thoroughbred breed demonstrated in Table 18.1 is the result of confounding by activity level which is positively associated both with colic and with the Thoroughbred breed in this hypothetical example: when we account for the effects of activity level, the apparent association of Thoroughbred breed with colic disappears.

Table 18.2A Horses with a high activity level (n = 900).

Breed	Horses with colic	Noncolic control horses	Total
Thoroughbred	750 (88%)	44 (88%)	794
Other	100 (12%)	6 (12%)	106
Total	850 (100%)	50 (100%)	900

Table 18.2B Horses with a low activity level (n = 1100).

Breed	Horses with colic	Noncolic control horses	Total
Thoroughbred	50 (33%)	300 (32%)	350
Other	100 (67%)	650 (68%)	750
Total	150 (100%)	950 (100%)	1,100

In the example of a study of breed and colic, activity level is a confounder that led to a spurious *positive* association between breed and colic. It is important to note that confounding effects can occur in any direction: confounding effects can also mask a true association (make a truly positive or negative association appear to have an odds ratio of 1 indicating no apparent association), or make an association that is truly positive (i.e., odds ratio statistically significantly >1) appear negative (i.e., odds ratio statistically significantly <1). It is important to note that some degree of confounding likely exists in all studies because we cannot identify or collect information on all known confounding factors let alone those as yet unidentified confounding factors. This does not mean that one should adapt a nihilistic view of patient population based studies: proverbially, we do not want to toss the baby out with the bathwater. But it does require that we interpret results with caution and to wait for reproducibility of study findings by other investigators.

Interpreting Results of Colic Risk Factor Studies

Many clinically relevant epidemiologic studies of colic are those attempting to identify risk factors for development of colic, for the need to perform surgery, for complications of colic or colic surgery, and for survival from colic or colic surgery. Risk factor studies can contribute much to understanding the causes of colic and to control of colic. For example, understanding that feeding alfalfa hay increases the odds of enterolithiasis (Cohen et al., 2000; Hassel et al., 2004), in horses indicates that dietary management can be used to control the incidence of enterolithiasis. Moreover, this knowledge generated hypotheses regarding the etiopathogenesis of equine enterolithiasis that could be tested in *in vitro* and *in vivo* experiments (Hassel et al., 2009). Despite the important knowledge that can be gained from risk factor studies, there are two important limitations of risk factor studies that, in the author's experience, are often overlooked by veterinarians and which can lead to misinterpretation of study results.

Hypothesis-Generating versus Hypothesis-Testing Studies

The first of these limitations is that statistically significant findings of risk factor studies are often interpreted as stronger evidence than they truly represent. Most colic risk factor studies examine the association of colic (or a type of colic) with multiple individual factors, typically followed by a multivariable approach in which multiple risk factors are considered in a single model. The purpose of the multivariable approach is to allow us to examine the effects of any given variable (e.g., breed) adjusted for other factors in the statistical model (e.g., activity level, age, amount of concentrate fed). The problem with the multivariable model does not lie in its logic: the rationale for adjusting effects of other variables is to provide valid assessments of associations that are not confounded by other variables (e.g., the aforementioned example where, after accounting for the confounding effect of activity level, there was no association of breed with colic). Rather, the problem is that results of statistical analysis of risk factor studies are misinterpreted as though they are the result of a *hypothesis-testing* study (in which one designs a study a priori to test the association between one (or at most a few) specific hypotheses), whereas they are in fact best viewed as *hypothesis-generating* studies. For example, there is a marked difference in the interpretation of statistically significant findings of a study designed specifically to test the hypothesis that there is a positive association between the odds of duodenitis/proximal jejunitis (DPJ) and the duration of daily exposure to grazing coastal grass pasture, than for a risk factor study exploring a long list of management practices (Cohen et al., 2006) for this poorly understood disease. In the former study, the focus of testing a specific hypothesis allows us to have greater confidence in the significance of the results (even if multivariable modeling is used to account for effects of other potential confounders). The risk factor study, however, is better viewed as exploratory because we are testing many hypotheses contemporaneously and this process can result in spurious significant associations that occur due to chance alone. Thus, the probability of spurious results is greater in risk factor studies in which we are testing multiple hypotheses than in studies designed to test an individual hypothesis. Considering the previous example of the two studies of DPJ, we would give greater credence to a significant positive association between grazing coastal grass pasture and DPJ in the study that was designed specifically to test this hypothesis than to an association from the study that was designed to examine a variety of characteristics including signalment, housing practices, deworming practices, feeding practices, exercise regimen, transport, and so on. Both study designs have merit and are scientifically sound. But the interpretation of the study results is not equivalent for the two designs.

The problem of misinterpreting associations from risk factor studies is compounded by publication bias for positive results: studies reporting positive (i.e., statistically significant) associations are more likely to be accepted for publication than reports that have negative (i.e., not statistically significant) results (Egger et al., 1997). Although the perspective that most scientific results are thus false (Ioannidis, 2005) might be an overstatement, it is certainly important that results of any single study be interpreted with caution, and even greater caution is warranted for those risk factor studies that are designed to be hypothesis generating. This is especially relevant for equine medicine where findings are rarely replicated and often extrapolated, and where small-scale studies prone to unreliable results are common. Of course, the problem of reproducibility is not unique to equine medicine or to epidemiologic studies (Begley & Ellis, 2012).

Risk Factors versus Classifiers

The second problem is that some readers (and investigators) fail to distinguish between risk factors and classifiers. By a classifier, I refer to a factor or attribute that can be used to accurately classify an individual as affected with a condition or not (i.e., a diagnostic or screening test) or to accurately predict prognosis (e.g., will survive or will not survive). While most classifiers can be considered risk factors, not all risk factors can be used to accurately classify the state of individuals. In fact, most risk

Table 18.3 Proportion of horses having an increase in peritoneal fluid lactate (PFL) concentration among 94 horses referred to an equine hospital with signs of colic.

Change in PFL concentration: admission to postadmission	Horses with strangulating intestinal lesions	Horses with nonstrangulating intestinal lesions	Total
Increase	19 (73%)	33 (49%)	52
No increase	7 (27%)	35 (51%)	42
Total	26 (100%)	68 (100%)	94

Table 18.4 Proportion of horses having an increase in peritoneal fluid lactate (PFL) concentration among 81 horses referred to an equine hospital with signs of colic that had PFL concentration <4 mmol/L at admission.

Change in PFL concentration: admission to postadmission	Horses with strangulating intestinal lesions	Horses with nonstrangulating intestinal lesions	Total
Increase	18 (95%)	14 (23%)	32
No increase	1 (5%)	48 (77%)	49
Total	19 (100%)	62 (100%)	81

factors significantly associated with disease are weak or poor classifiers. The reason for this is that measures of association (odds ratios, relative risks) that are relatively large when we study risk factors for etiologic purposes (i.e., to better understand the pathogenesis or outcome of a disease) are not strong enough to accurately classify individuals. Two illustrative examples derived from the same study follow.

Our first example demonstrates the common scenario where a risk factor performs poorly as a classifier despite the fact that it is strongly and significantly associated with an outcome of interest. In a retrospective cohort study (Peloso & Cohen, 2012), it was observed that an increase in peritoneal fluid lactate concentration from the time of admission to a second sample 1–6 h after admission was strongly (estimated odds ratio of approximately 11) and highly significantly ($P < 0.001$) associated with presence of a strangulating intestinal obstructive lesion. Strangulating intestinal obstructions require surgical management. Given the magnitude and significance of the association, it is tempting to interpret these findings as meaning that one can use this test to classify horses as to whether or not they have a strangulating small intestinal lesion. That is, one might conclude that one can use the finding of an increased concentration of peritoneal fluid lactated during the first several hours of hospitalization to classify a horse with colic as to whether or not it requires surgical management. Unfortunately, this strongly associated *risk factor* is not an effective *classifier* (Table 18.3). The sensitivity is not particularly high (73%; 19/26) and the specificity is poor (51%; 35/68). Even in the population studied, if one based the decision to perform surgery on the change in the peritoneal fluid lactate concentration, one would subject more horses without strangulating intestinal obstructions (i.e., horses that did not require surgery; $n = 33$) to celiotomy than horses that had a strangulating obstruction requiring surgical intervention ($n = 19$). Furthermore, one would delay or fail to operate on more than a quarter of the horses that have strangulating lesions needing surgical management. In this example, the risk factor of interest was a binary variable (i.e., increase in lactate concentration or no increase) for simplicity of interpretation. It is important to note that results are similar in terms of the peritoneal fluid lactate being a strong risk factor but weak classifier when peritoneal fluid lactate concentration is considered as a continuous variable or when the absolute difference of the peritoneal fluid lactate concentrations (i.e., postadmission minus admission values) are examined.

The second illustration also comes from the same report. The authors observed that among horses with peritoneal fluid lactate concentrations <4 mmol/L at admission, an increase in the lactate concentration of peritoneal fluid during the period 1–6 h after admission was even more strongly (estimated odds ratio = 63) and still highly significantly associated ($P < 0.001$) with presence of a strangulating intestinal obstruction (Table 18.4). Moreover, the association appeared to be reasonably effective as a *classifier*: sensitivity of the test in this population was 95% (18/19) and specificity was 77% (48/62). Of course, even in this instance the test was far from perfect: although most positive results (i.e., increased peritoneal fluid lactate concentration in the postadmission sample relative to the admission sample) were from horses with strangulating lesions ($n = 18$), there were still almost as many horses with a positive result that had nonstrangulating lesions ($n = 14$). Nevertheless, this second example illustrates that risk factors can be useful classifiers but the association has to be very strong. This is because the strength of the association is an indication of the extent to which the distributions of the risk factor or biomarker of the two populations (i.e., diseased versus nondiseased; strangulating lesion versus nonstrangulating lesion, and so on) overlap: the less overlap, the better the ability of the factor to function as a classifier.

The principal message from these two examples from the same study is that finding a strong and highly statistically significant association between a risk factor (e.g., concentration of lactate, serum amyloid A, tumor necrosis factor-α) and a clinical outcome of interest (e.g., colic, strangulating intestinal lesion, septic peritonitis)

does *not* indicate that the parameter has clinical value to classify a horse as to the presence or absence of that outcome (Wald et al., 1999; Pepe et al., 2004; Ware, 2006). In other words, when one reads about some new biomarker that is significantly associated with a clinical condition, one should not assume the findings are evidence that this biomarker will be directly useful for accurately testing for screening or diagnostic purposes, or for accurate prognostic classification. This is because the magnitude of association (odds ratio or relative risk) of a classifier with disease has to be extremely strong in order for the factor to accurately function as a classifier. *Odds ratios and P values are poor indicators of the clinical performance of a biomarker or risk factor for diagnostic, screening, or prognostic purposes.* An example is depicted in Figure 18.2 in which the relationship of the odds ratio with the sensitivity of the test (proportion of those with the disease correctly identified by the test), assuming a specificity of 95%, a continuous variable, equal variance of affected and unaffected individuals, normal distribution, and the odds ratio being a comparison of the highest quintile of the continuous variable (i.e., risk factor) to the lowest quintile (Wald et al., 1999). We see that the odds ratios need to be well over 100 to have a sensitivity >50% with specificity of 95%. Note that this relationship applies only to the conditions and assumptions of this hypothetical example for illustration. That said, it is apparent that odds ratios well in excess of 30 are generally required for a risk factor to function accurately as a clinical test for screening, diagnostic, or prognostic purposes under almost all circumstances (Pepe et al., 2004). Please note that it is essential that the estimated odds ratio be precisely and validly estimated before it can even be considered for clinical application.

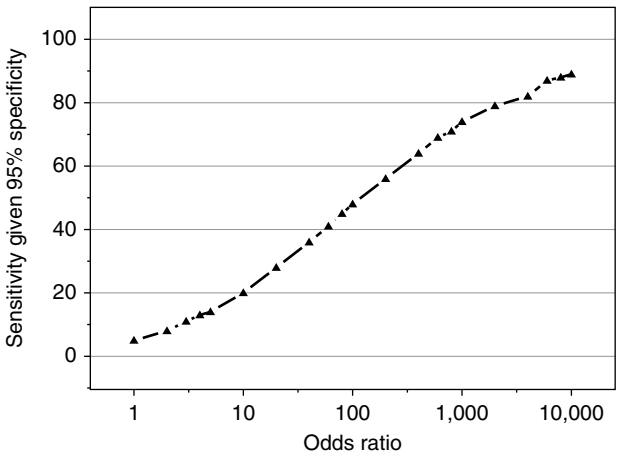

Figure 18.2 Relationship of the odds ratio to the sensitivity (true positive rate) when specificity (1 – false positive rate) is 95%. Assumptions include that there is equal variance in the continuous variable being evaluated as a classifier, and that the odds ratio is for the highest quintile (i.e., top 20% of the data) of the continuous variable relative to the lowest quintile of the data. The odds ratio is presented on logarithmic scale. This figure illustrates that very large odds ratios are needed before an apparent risk factor can be accurate for classifying individuals. Source: Adapted from Wald et al., 1999.

Summary

Readers are directed to other chapters in this book for information about the descriptive epidemiology of specific colic conditions. This chapter has reviewed selected epidemiologic principles that are clinically relevant for understanding colic. The goal of this chapter is to prepare readers to better interpret findings of epidemiologic studies of colic, including those aimed at identifying risk factors, treatments, screening and diagnostic tests, and prognosis.

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19

Epidemiology of Colic: Risk Factors

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Introduction

One of the principal advancements in our understanding of the epidemiology of colic has been descriptive and analytical investigation of *specific* types of equine colic (e.g., large colon impaction, small intestinal volvulus) and their sequelae (e.g., postoperative ileus, diarrhea, and so on). As such, epidemiologic aspects of specific types of colic are described in chapters of this book pertaining to these disorders. The purpose of this chapter is to review what is known about the incidence and risk factors for undifferentiated colic (i.e., colic as a catch-all term), because colic continues to be a common problem in the primary care/general practice setting.

Incidence of Colic

Reports of the incidence of colic are rare (Foreman & White, 1986; Uhlinger, 1990; Hillyer et al., 2001; Kaneene et al., 1997; Tinker et al., 1997a; Traub-Dargatz et al., 2001; Egenvall et al., 2008) Generally, reported risks have ranged from 0.9 to 10 episodes of colic per 100 horse-years of observation (i.e., 0.9–10 cases of colic in 100 horses observed for 1 year). The incidence of colic appears to be higher among horses that have previously experienced colic. As compared to a general risk of 0.9–10 episodes per 100 horse-years, the incidence was reported to be 50 episodes per 100 horse-years (35 episodes per 100 horse-years for veterinary-attended episodes) in a study of 127 horses that had a veterinary-diagnosed episode of colic (Scantlebury et al., 2011).

Incidence can vary significantly among farms and even within farms over time. For example, in a study of three horse farms in North Carolina, USA, the reported incidences ranged from 5 to 46 episodes per 100 horse-years (Uhlinger, 1990). The incidence of colic is likely strongly influenced by management practices that occur at the farm level. There is likely greater variability in the incidence of colic among farms than among horses. Thus, colic incidence should be considered both within and among farms (or other housing facilities such as training centers, racetracks, etc.), and estimation of the incidence of colic should consider farm-level clustering. Moreover, comparisons in incidence among regions, studies, years, and so on, should account for this farm-level clustering in reporting the incidence of colic.

Hospitalized horses can be exposed to factors that predispose to colic and should be considered to be at increased risk of colic that varies by risk factors/exposures. The incidence proportion of colic following general anesthesia for elective surgical or diagnostic procedures was reported as 8.7% (Nelson et al., 2013). The incidence proportion of colic during hospitalization was 21.4% among 337 horses hospitalized for ocular disease in Georgia (Patipa et al., 2012).

Factors that Predispose to Colic

This section attempts to summarize what is known about factors that predispose to colic as a general diagnosis (Box 19.1); in some instances, risk factors for specific forms of colic will be discussed. However, a review of factors that predispose to the wide array of specific types of colic is beyond the scope of this chapter.

Factors Related to Signalment

There is no clear evidence that any traits included in a horse's signalment predispose to colic. No breed has been unequivocally demonstrated to be at increased risk of colic. Arabians have been identified as being at increased risk of colic in a number of studies (Reeves et al., 1989, 1996; Cohen et al., 1995; Schmid et al., 2002).

The Equine Acute Abdomen, Third Edition. Edited by Anthony T. Blikslager, Nathaniel A. White II, James N. Moore, and Tim S. Mair.

Companion website: www.wiley.com/go/blikslager/abdomen

Box 19.1 Factors that predispose to colic (see text for details)

Breed	Reduced availability of potable water
Older age	Change in activity or stabling
History of previous colic	Activity level
Cribbing/crib-biting	Reduced time at pasture/increased time in box stall
Change in weather	Recent transport
Diet change	Absence of regular deworming
Feeding large amounts of concentrate	Tapeworms
Round bale hay	Absence of regular dental examinations

Other reports have suggested that Thoroughbreds and Warmbloods may be at increased risk of colic (Traub-Dargatz et al., 2001; Hudson et al., 2001; Egenvall et al., 2008). Standardbred horses have been suggested to be either at increased risk of colic (Sembrat, 1975) or decreased risk for surgical colic (Schmid et al., 2002). Differences in study design, region, and horse populations may explain the discrepancies among studies. Considering only a single factor such as breed without accounting for other factors that may be related both to breed and to colic (e.g., activity level or diet) may result in spurious associations due to confounding.

The sex of the horse has not been clearly established as a risk factor for colic. Stallions were found to be at increased risk in one study (Kaneene et al., 1997), and geldings were at increased risk for recurrent colic in another study (Cohen & Peloso, 1996). Other studies have not found any association of sex with colic (Reeves et al., 1996; Tinker et al., 1997a; Egenvall et al., 2008). Risk of colic can vary by sex for specific types of colic; for example, male horses have been identified as being at increased risk of entrapment of small intestine in the epiploic foramen (Schmid et al., 2002).

Results of the risk of colic with age have been variable among studies. Some reports indicate that horses <10 years of age are at increased risk of colic (Proudman, 1991; Tinker et al., 1997b). One report indicated that foals (horses <6 months of age) were at decreased risk (Traub-Dargatz et al., 2001). Evidence exists that risk of colic intensifies with increasing age and that the odds of colic is greater for geriatric horses (Cohen et al., 1999; Reeves et al.,1996; Kaneene et al., 1997; Egenvall et al., 2008; Malamed et al., 2010; Silva & Furr, 2013). Differences among these studies in study design, population of horses studied, and methods of data analysis likely explain these conflicting results. Moreover, the relationship of age with risk of colic appears nonlinear (Kim et al., 2003; Egenvall et al., 2008) and this complexity, though often overlooked, should be accounted for in analyses.

Factors Relating to Anamnesis

Both a history of colic and a history of surgery for colic have been demonstrated to be associated with horses being at increased risk of colic (Cohen et al., 1995; Reeves et al., 1996; Tinker et al., 1997b; Hillyer et al., 2002b). Although these are not alterable risk factors, these findings are important information for veterinarians to share with owners of horses that experience colic or undergo surgery for colic. Some common forms of colic have been demonstrated to have a high prevalence of recurrence of colic (Dabareiner & White, 1995).

Cribbing (crib-biting) has been associated with colic, recurrent colic, simple colonic obstruction or distention, epiploic foramen entrapment, and gastric ulceration (Hillyer et al., 2002b; Wilson et al., 2002; Archer et al., 2004; Malamed et al., 2010; Scantlebury et al., 2011; Escalona et al., 2014); one study indicated that crib-biting was not associated with any particular type of colic (Malamed et al., 2010). Physiologic explanations have been offered for these associations, such as prolonged intestinal transit or aerophagia leading to increased intraintestinal gas and changes in intra-abdominal pressure. It may be that cribbing is a marker for some other factor (such as being predominately stalled, lack of turn-out, and so on).

Two studies have indicated that horses are at reduced odds of colic when owners provide care for horses, relative to horses cared for by someone other than the owner (Reeves et al., 1996; Hillyer et al., 2001) This finding is plausible because owners may provide better healthcare for their horses. Alternatively, it is possible that the density of horses (i.e., number of horses per acre) or activity level is generally less for horses that are cared for by their owners relative to horses cared for by someone other than their owner. Another possible explanation for this association would be that caretakers other than owners monitor horses more closely or have greater contact with horses on a daily basis such that signs of colic are more likely to be detected by caretakers other than owners.

Many equine veterinarians and horse owners perceive that the incidence of colic is increased with certain

patterns of or changes in weather. A number of studies have failed to identify an association between weather conditions or changes in weather and colic (Foreman & White, 1986; Proudman, 1991; Moore & Dreesen, 1993). A seasonal pattern in the incidence of colic has been described by some studies (Rollins & Clement, 1979; Barth, 1982; Hillyer et al., 2001; Egenvall et al., 2008). One study documented an increased risk of colic among horses that experienced a significant change in weather conditions during the 3-day period prior to examination (Hudson et al., 2001); however, the specific climactic changes were not determined and this association could have resulted from a recall bias. Thus, epidemiologic evidence of an association between weather and colic is conflicting and likely varies by geographic region and climactic conditions (e.g., Sweden versus Texas). Moreover, the effects of climactic conditions can be co-associated with management practices, which might result in confounding or effect modification of associations with colic. This is an example of the importance of accounting for potential confounding and effect modification in epidemiologic studies.

Determining feeding history is important for the evaluation of horses with colic. Changes in the type of concentrate, type, batch, or quality of hay, or pasture grass have been associated with increased risk of colic (Proudman, 1991; Cohen et al., 1995; Reeves et al., 1996; Tinker et al., 1997b; Cohen et al., 1999; Hudson et al., 2001; Kaya et al., 2009). Horses fed relatively large amounts of concentrate also appear to be at increased risk for developing colic (Reeves et al., 1996; Tinker et al., 1997b; Hudson et al., 2001; Kaya et al., 2009). Feeding hay in round bales has been identified as a risk factor for colic (Hudson et al., 2001). Provision of fresh, potable water is important to prevent colic because decreased water consumption can contribute to risk of colic developing (Cohen et al., 1995; Reeves et al., 1996; Kaya et al., 2009).

The way horses are housed can influence the risk of colic. A number of studies have demonstrated that the amount of time horses have to graze is inversely related to the risk of colic. Studies indicate that the duration of hours stabled is associated with greater odds of colic (Cohen et al., 1995, 1999; Hillyer et al., 2002b). A number of markers for exposure to pasture grazing (e.g., number of acres used for horses, percentage time spent at pasture) have been demonstrated to increase the odds of colic (Cohen et al., 1995, 1999; Hudson et al., 2001). Risk of recurrent colic was inversely associated with time at pasture (Scantlebury et al., 2011). Although not a controlled study, Dabareiner and White (1995) documented that a large proportion of horses with large colon impaction had a history of being removed from pasture and confined to a stall prior to developing the impaction. Evidence exists that prevalence of gastric ulceration is lower among horses maintained in pastures than horses maintained in stalls (Murray & Eichorn, 1996). Clearly, grazing pasture is not without risk. Horses turned out into lush pastures are at increased risk of colic (Proudman, 1991). Some diseases such as grass sickness result directly from pasture grazing (Gilmour & Jolly, 1974). In a study of training yards in the United Kingdom, it was observed that the risk of colic was greater for premises with a larger number of horses (Hillyer et al., 2001). The reason for this association was not determined, but it is possible that access to pasture or grazing was less for horses from yards with large numbers of horses, or that the density of horses increased the risk of colic.

Changes in stabling/housing management have been associated with increased risk of colic (Cohen et al., 1995, 1999; Malamed et al., 2010). Unfortunately, these studies did not examine which specific stabling changes predisposed horses to colic. Change in stabling is often closely related to changes in level of activity and climactic conditions.

Activity level has been demonstrated to be associated with colic in a number of studies, although the specific type of activity or change in activity has varied among studies (Cohen et al., 1995; Kaneene et al., 1997; Tinker et al., 1997b; Cohen et al., 1999; Hillyer et al., 2001, 2002b). This may be partially explained by the fact that a variety of activity levels and changes in level may contribute to increased risk of colic. The incidence of colic following swimming appears to be quite low (0.08 per 100 horse-swims) (Walmsley et al., 2011).

Evidence exists that recent (within the previous 24 h) transport increases the risk of simple colonic obstruction or distention (Hillyer et al., 2002b). Although a study in Texas found no association between colic and either history of recent transport or the number of miles transported (Cohen et al., 1995), it is plausible that transport may predispose to colic when horses become dehydrated, immobile, and possibly stressed during transport.

Preventive Healthcare

Although it is intuitive that parasites that infect the gastrointestinal tract can cause colic, the results of studies of colic and parasite control programs have yielded conflicting results. Tapeworms have been associated with colic, in particular ileal impactions (Proudman & Edwards, 1993; Proudman et al., 1998). Some studies have failed to document an association between parasite control programs and colic (Cohen et al., 1995; Hillyer et al., 2001). A number of studies have documented a reduction in colic for horses receiving regularly administered anthelmintics or anthelmintics to eliminate tapeworms and strongyles (Uhlinger, 1990; Reeves et al., 1996; Proudman et al., 1998; Cohen et al., 1999; Hudson et al., 2001; L. L. Hillyer et al., 2002a). Some studies have associated increased risk of colic among horses either

receiving recent deworming (Cohen et al., 1999), increased number of dewormings (Kaneene et al., 1997), or rotation of anthelmintics (Traub-Dargatz et al., 2001).

Although these conflicting results may seem confusing, each of the results is plausible. Lack of association between colic and anthelmintic administration might occur because anthelmintics were regularly administered to most horses in these studies. An association of reduced occurrence of colic with anthelmintic administration would be expected because of intestinal pathology associated with parasite infestation. Increased risk of colic among horses receiving anthelmintics is biologically plausible because killing intraluminal parasites can trigger problems such as obstruction with ascarids in older foals or emergence of encysted small strongyles (White & Lessard, 1986; Reeves, 1992; Reid et al., 1995). Such associations, however, could also be spurious. People whose horses have colic might be more likely to recall events such as administration of an anthelmintic than owners of horses that are healthy or have a problem that they might not associate with deworming (e.g., skin laceration). Alternatively, it is possible that horses with colic received anthelmintics as a treatment for colic, such that administration of the anthelmintic was an effect rather than a cause of the disease.

Poor dentition might be expected to predispose to colic. Surprisingly, data documenting an association between dental care and reduced risk of colic are lacking. In one study, no association between frequency of dental care and colic was observed (Cohen et al., 1995); however, most horses in that study received dental care at least annually. Risk of simple colonic obstruction or distention was inversely related to the frequency of dental examination (Hillyer et al., 2002b).

Study of Colic Problems in Individuals and Herds

Epidemiology is a population-based science, and it is often considered to be a basic science of primary importance for preventive medicine and public health. Increasingly, epidemiology is recognized as a basic science of clinical medicine. Primary activities as clinical veterinarians include interpreting findings of anamnesis, physical examination, other diagnostic testing, and determining the treatment and prognosis for our patients. In doing so, we rely on epidemiologic principles (such as understanding the principles of sensitivity, specificity, and predictive values in assessing the accuracy of diagnostic tests). Moreover, we rely on information and evidence derived from epidemiologic studies. The latter is often referred to as evidence-based medicine. The primary goal of evidence-based medicine is to integrate individual clinical expertise with the best available external clinical evidence. Individual clinical expertise is considered to be the proficiency and judgment that results from practice experience. The best available external clinical evidence refers to clinically relevant findings that are primarily derived from research. Patient-centered research studies (i.e., epidemiologic studies) are considered to be the most relevant and important source of evidence (Straus et al., 2010). Although a wide range of valid and useful sources of clinical evidence exist including experiences of our teachers and coworkers, textbooks, continuing education seminars, journal articles, websites, and so on, not all these sources of information are considered to be of equal value. Controlled studies are preferable to uncontrolled studies. For example, a case–control study is generally considered superior to a case series. Furthermore, patient-centered research is preferable to studies involving experimental disease, particularly when experimental studies are conducted in species other than the horse. Thus, patient-centered epidemiologic studies provide the best source of evidence for making clinical decisions about colic. For example, our assessment of prognosis for a particular horse with colic should be based on our previous experiences with similar patients and epidemiologic studies of prognosis.

Epidemiologic principles and methods also apply to the investigation of outbreaks of colic at farms. As mentioned, the incidence of colic is probably best considered at the level of individual farms because there is considerable variability among farms in the incidence of colic and in the distribution of predisposing factors for colic. Although a review of methods for outbreak investigation is beyond the scope of this report, the topic has been reviewed well (Kane & Morley, 1999).

When initiating a study, it is important to verify the diagnosis of colic, to establish that the colic cases are similar, and to determine a case definition (Box 19.2). Case definitions should be based on clinical signs and, whenever possible, additional diagnostic information such as clinicopathologic or pathologic data. One should determine the magnitude of the problem (number of cases among horses at risk). When available, it is very helpful to have information about the cumulative incidence of colic at a farm. An apparent outbreak may represent a clustering of rare events that appear to be temporally related simply by chance. Alternatively, the frequency of colic events may be in excess for that expected at the farm.

It is helpful to consider the temporal and spatial pattern of colic episodes to determine probable sources of exposure. Investigation of outbreaks generally entails investigation to determine the characteristics that distinguish affected horses from unaffected horses. Attack rates can be determined for various exposures (number of cases of colic/number of horses exposed), along with temporal and spatial analyses. It is generally useful to collect samples of concentrates, hay, and water as soon as possible. Similarly, it is ideal to collect information about

Box 19.2 Factors to consider during a farm outbreak

1) Case definition: what form(s) of colic are observed?
   a) clinical and, when applicable, laboratory findings.
2) Determine the attack rate: number of horses affected/ number of horses at risk:
   a) is this above what might be expected?
   b) past records may be useful for comparative purposes.
3) How are the cases clustered in time and/or space?
4) Determine dietary/ feeding practices:
   a) types, sources, and amounts of concentrate and hay
   b) when possible, collect specimens of feedstuffs.
5) Examine watering practices/sources.
6) Examine characteristics of individual affected horses:
   a) compare with similar information about unaffected horses to identify incriminating factors
   b) factors should include the following:
      - age
      - breed
      - sex
      - duration of residence at farm
      - stabling (where, how long stalled, changes, etc.)
      - feeding practices (what fed, how much fed, changes, supplements, etc.)
      - source(s) of water
      - deworming practices
      - cribbing/crib-biting status
      - climactic conditions
      - activity/use of horse (including frequency, recent changes, etc.)
      - history of previous colic and colic surgery
      - recent transport
      - any other changes at the farm or in the farm environment.

exposures (e.g., pasture exposure) as close as possible to the time of the outbreak. Collecting samples and data retrospectively can result in the loss of critical sources of information.

It is important for veterinarians and farm owners to recognize that not all outbreak investigations will be rapidly or definitively resolved. It can take years of extensive and expensive investigation to solve outbreaks (consider the experiences with Legionnaires disease, or the mare reproductive loss syndrome (Cohen et al., 2003)). Despite considerable efforts, one may not be able to definitively determine the cause(s) of an outbreak. Nevertheless, investigation of farm outbreaks is often necessary and can successfully determine a cause or identify methods to prevent recurrences.

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Part V

Diagnosis of Gastrointestinal Disease

20

Diagnostic Approach to Colic

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Introduction

Colic is one of the most common emergencies faced by veterinarians. Since colic can be a life-threatening emergency, affected horses must be treated promptly for the welfare of the animal and to ease the owners' distress. Although it can be very difficult to reach a definitive diagnosis, especially during the first examination, a thorough examination should be performed in every case to determine which emergency treatments should be initiated and to decide whether the horse requires surgery or intensive care. Many horses will recover spontaneously or will respond to the first treatment. For example, a cross-sectional study of colic episodes in Thoroughbred horses at training premises revealed that 28.7% recovered spontaneously, and 63.1% recovered after medical treatment (Hillyer et al., 2001). Since some horses will require surgery, making the decision regarding the need for surgery in a timely manner will increase the chance of a successful outcome, minimize patient morbidity, and potentially decrease complications (Ragle, 1999). Early identification of critically ill horses that require surgery and rapid assessment for needed treatments are paramount for their survival (Ragle, 1999). Cardiovascular parameters indicative of responses to circulating endotoxins increase the risk for several postoperative complications after an acute abdominal crisis. Thus, early referral of colic cases before shock develops may minimize the risk of some postoperative complications (French et al., 2002).

While a horse is being examined on a farm or stable for colic, the veterinarian must decide if appropriate treatment can be completed on those premises, or if the horse needs to be transported to a hospital facility for further diagnostic procedures or treatment. Although having a definitive diagnosis simplifies the decision for surgery or referral, determining a diagnosis can be difficult when conflicting clinical signs are present. Consequently, veterinarians frequently choose to determine the category of the horse's disease on the clinical signs and physical examination findings (Moore & White, 1982).

If the horse is in severe pain and exhibiting systemic inflammatory response syndrome (SIRS) (see Chapter 16), the examination may have to be shortened to allow initiation of the emergency medical treatments needed to stabilize the horse for possible transport to a referral hospital. Even if a horse is exhibiting mild signs, a thorough examination should be performed to ensure that a more serious disease is not overlooked. This is particularly important as some horses may be stoic and, with certain advanced diseases, including strangulating obstructions of the small intestine or small colon, depression may replace pain as the primary sign. A list of disease categories that should be used when assessing horses with colic is presented in Box 20.1.

Once the category of disease has been established, the veterinarian can decide which approach to take: providing immediate treatment, transporting the horse to a referral facility, or surgery (White, 1990). If there is uncertainty about the need for surgery or the horse's condition, the horse should be referred to a hospital facility where the decision for surgery can be made by a veterinarian who makes these decisions frequently. While the improvements in survival rates after colic surgery over the past two decades may be due to advancements in all aspects of colic management, early referral of horses requiring surgery is one of the most important determinants of outcome (Freeman et al., 2014).

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Companion website: www.wiley.com/go/blikslager/abdomen

Box 20.1 Classification of disease categories causing equine colic

1) Idiopathic colic (mild abdominal pain with no distinguishing features)
2) Tympany
3) Nonstrangulating/simple intestinal obstruction
4) Strangulating intestinal obstruction
5) Nonstrangulating infarction
6) Peritonitis
7) Enteritis, enterocolitis
8) Gastric and colonic ulceration
9) Pain from another organ system (e.g., musculoskeletal, pulmonary, urogenital)

Box 20.2 Specific diseases associated with the signalment (Southwood, 2013, p. 4)

Neonate:
- Meconium retention/impaction
- Enterocolitis
- Hypoxic–ischemic syndrome
- Jejunal intussusception
- Jejunal volvulus
- Atresia coli or jejunum

Geriatric horse (older than 10 years):
- Strangulation lipoma
- Large colon impaction

Pregnant mare:
- Uterine torsion
- Large colon displacement/volvulus
- Uterine artery hemorrhage
- Parturition
- Colic associated with pregnancy

Postpartum mare:
- Large colon volvulus
- Uterine artery hemorrhage
- Strangulation in mesenteric rent
- Small colon trauma during parturition
- Uterine involution

Stallion:
- Inguinal hernia (Standardbred and some Warmbloods)

Miniature horse:
- Small colon impaction
- Small colon fecoliths
- Tricobezoar

Yearling:
- Ileocecal intussusception

Weanling:
- Ascarid impaction

Breed:
- Ileocolonicagangliosis: Overo paint foal
- Enteroliths: Arabian, Morgan, American Saddlebred and Miniature horses

Signalment

The horse's signalment may be helpful in identifying some diseases (Box 20.2). For example, a horse more than 10 years old with small intestinal distention has a high risk of having a strangulating lipoma (Freeman & Schaeffer, 2001), whereas a 2–4-month-old foal with small intestinal distention is likely to have a volvulus (Freeman, 1999). Similarly, equine neonates most commonly have meconium impaction and enteritis as a cause of colic, whereas ileocecal intussusceptions are more common in horses 6–18 months old. The horse's breed also is an important factor to consider. For example, Arabians, Arabian crosses, Morgans, American Saddlebreds (Hassel et al., 1999), and miniature breeds (Cohen et al., 2000) have an increased risk of developing enteroliths. Similarly, female ponies and American Miniature horses are more predisposed to small colon impaction than other breeds (Dart et al., 1992), and Standardbreds and some Warmblood breeds have an increased risk of inguinal/scrotal hernias (Schneider et al., 1982). Paint foals, from a dam and sire that both carry the overo lethal white syndrome gene, will be born with ileocolonicagangliosis and functional obstruction of the intestine (Lightbody, 2002).

History

It is essential that veterinarians ask owners or the employees on a farm that care for the horse direct questions to ensure that accurate information is obtained. Since some information may be withheld if there has been a mistake in the management, the veterinarian should interpret answers carefully when taking the history.

There are three general areas of the history that need to be addressed: (1) the general history of the husbandry and management, (2) any recent changes in husbandry or management, and (3) the individual history of the horse being evaluated (Box 20.3).

The general history, which concerns the conditions on the farm where the horse is kept, may already be known by the veterinarian if he/she visits the farm regularly. Each horse's environment is very important; for example, if a

Box 20.3 Historical information for the horse with colic

General historical data:

1) Habitat
2) Feed and water source
3) Daily routine
4) Horse use
5) Medical history
6) Parasite control – vaccination status
7) Dental care
8) Crib biting/windsucking
9) Mare's reproductive status: pregnant, recent foaling, nursing
10) Horse insured or not?

Recent historical data:

1) Duration of colic
2) Last time fed
3) Consumption of feed and water, composition of diet
4) Recent change in feed, water, medication, housing, bedding, travel, exercise routine, horse companions, weather, other sick horses on property

Disease-related historical data:

1) Degree and change of pain
2) Evidence of trauma to head and limbs
3) Amount of abdominal distention
4) Last defecation (amount and consistency)/last urination
5) Clinical signs seen – sweating, pawing, rolling, kicking abdomen, turning to flank, staying recumbent, rolling on back, depression, grinding teeth
6) Does walking help?
7) Medications administered and response to treatment
8) Previous colic episode or abdominal surgery

horse has been moved to a new pasture, gas production in the large intestine may have increased, resulting in tympany or displacement. Similarly, exposure to foreign objects, such as rubber or bailing twine, may indicate an obstruction in the small intestine or small colon. Horses maintained on sandy soil may ingest large quantities of sand, particularly in the summer or low-rainfall months when the pasture is short or scarce, thereby increasing their risk for sand colic. The veterinarian also should be aware that poisonous plants present on the property may be consumed as a result of overgrazing, drought, specific herbicide use, and masking of plants in hay, silage, or grain (Galey, 2015). Certain environmental conditions also may increase the concentration of toxins in plants; these conditions include soil type and content, use of herbicides (Osweiler et al., 1985), overwatering or drought, using fertilizers, and sunlight (Galey, 1994, 2015). The time of year may be important when considered in conjunction with access to certain fruits or plants. For example, intermittent signs of mild–moderate abdominal pain have been associated with ingestion of persimmons in specific geographic locations where the ripe persimmon fruit falls to the ground in the fall and is ingested (Kellam et al., 2000). In addition, certain geographic regions of the United States (e.g., California) and other parts of the world have a high prevalence of intestinal obstruction caused by enteroliths. Ileal impaction is more prevalent in horses residing in the southeastern United States (Little & Blikslager, 2002). The prevalence and severity of proximal enteritis appear to be influenced by geography, as there is an apparent lower prevalence of the disease in California than in other parts of the United States. Furthermore, a more severe form of this condition has been reported to occur in the southeastern United States than in the northeastern area (Edwards, 2000).

Since associations between the horse's environment and the number of episodes of colic have been identified, the veterinarian should determine whether the horse is housed with other horses and who is responsible for the horse's primary care. A study of colic in horses in Thoroughbred training premises in the United Kingdom determined that there was a significant association between the number of episodes of colic and the number of horses on the premises (Hillyer et al., 2001). Furthermore, when the investigators accounted for the number of horses, an increased risk of colic was associated with premises that were training establishments for flat racing. In contrast, the risk of colic was decreased when the owner was the only person caring for the horse and when a horse was housed at a combined breeding and training establishment. Information acquired in the history may not lead to the diagnosis, especially in the case of a simple obstruction or displacement, but it must be recorded, as there is the possibility that there may be a problem that affects other horses.

The horse's day-to-day routine should be recorded, particularly when it comes to feeding and housing. There is evidence that certain feeding and housing patterns are associated with an increase risk of colic. These patterns include a recent change in the batch of hay being fed, decreased exposure to pasture, a recent change in the type of grain or concentrate fed, feeding more than 2.7 kg of oats per day and feeding hay from round bales (Tinker et al., 1997). Horses stabled for 19–24 h per day are at greater risk for developing colic than horses maintained at pasture (Cohen et al., 1995, 2000; Hillyer et al., 2002; Hudson et al., 2001). Similarly, horses that spend more than 50% of their time indoors and horses fed alfalfa hay have an increased risk of enterolithiasis (Cohen et al., 2000). The feeding of Coastal Bermuda hay and the quality of this particular hay have been associated with ileal impaction (Little & Blikslager, 2002).

Any changes to the horse's routine should be recorded, including exercise, feed, travel, and medications. Significant changes in large intestinal motility patterns and parameters relating to gastrointestinal water balance occur during

transition from pasture to stabled management and are risk factors for colic (Williams et al., 2015). Any history of administration of medications such as anthelmintics, nonsteroidal anti-inflammatory drugs (NSAIDs), or antibiotics should be recorded. Although treatment with anthelmintics may reduce the overall frequency of colic episodes, recent administration of anthelmintics has been shown both to predispose some horses to colic and also to decrease the risk for colic (Cohen et al., 1999; Hudson et al., 2001). The type of anthelmintic administered is also important in horses that have not been treated with a pyrantel salt, as these drugs are efficacious against *Anoplocephala perfoliata* (tapeworms). Horses with this history may be at an increased risk for ileal impaction, especially if they also are fed Coastal Bermuda hay (Little & Blikslager, 2002). Ascarid impaction may occur in young horses after recent administration of anthelmintic medications effective against *Parascaris equorum* (roundworms) (Cribb et al., 2006).

A recent history of previous colic episodes, colic surgeries, illnesses, prolonged drug treatments, vices, and pregnancy should be noted. The specific patient history may help the veterinarian develop a list of differential diagnoses. The following lists some questions that should be asked during the examination (White, 1990):

1) When was the last defecation and what was the character of the feces?
2) Has the appetite been normal and when did the horse last eat?
3) How much water has the horse been consuming recently?
4) How severe has the pain been and has it increased, decreased, or stayed the same? Also, for how long?
5) Has the horse exhibited a specific behavior such as playing in its water or lying on its back?
6) Could the horse have ingested anything unusual, such as too much feed, chemicals, or toxic plants?
7) Has the horse been treated recently for either colic or another disease?
8) Has the horse had colic prior to this episode?
9) Has the horse had surgery for colic?
10) Does the horse have any vices such as cribbing?

This information will allow the veterinarian to judge the duration of the colic, severity, hydration, and events that may have led to the present episode. Although this information may not lead to a specific diagnosis, it can help the veterinarian decide the most appropriate treatment. For example, an acute onset of severe pain of short duration may indicate a severe lesion such as a large colon volvulus, whereas mild to moderate pain over several hours or days in a dehydrated horse may be indicative of a simple obstruction of the large colon. Descriptions of the risk factors and related historical information relating to specific diseases are provided in the chapters on the specific diseases.

Physical Examination

The majority of the decisions regarding disease severity, prognosis, and treatment are made on the basis of the horse's clinical signs. Box 20.4 outlines the steps of the examination and the order in which they are normally performed.

Pain

Horses presented to veterinary hospitals for evaluation of colic will often be restrained by the handler, which can make it difficult to assess the level of pain. This applies particularly to the hospital setting where the horses are not familiar with their surroundings and may initially be anxious and more concerned with their environment than the pain. If pain is not present, the horse should be placed unrestrained in a stall or paddock and observed. This should be done prior to administering analgesics and sedatives or at end of the examination to assess the horse's level of pain. In some cases, analgesics administered previously have yet to be metabolized and may make assessment very

Box 20.4 Sequence of the physical examination for the horse with colic

1) Pain assessment – severity; continuous, or intermittent
2) Attitude – depression, alertness, pain
3) Physical condition – body condition, distention, and colic duration
4) Temperature – hyperthermic, normal, hypothermic
5) Pulse – quality and rate
6) Jugular filling
7) Respirations – rate and effort
8) Mucous membranes – color and refill
9) Temperature of the extremities
10) Nasogastric intubation – gas, fluid reflux, color, smell, and pH
11) Auscultation – borborygmi, intensity and rate, tympany
12) Percussion – detection of gas
13) Palpation of male's testicles and scrotum
14) Rectal examination – bowel distention or displacement, peritoneal surface, mesenteric pain, masses, urogenital abnormalities
15) Abdominal ultrasound – location, motility, wall thickness and contents of the gastrointestinal tract, distended small intestine, presence of excessive peritoneal fluid, presence of sand, etc.
16) Abdominocentesis – color, turbidity, cell count, protein, presence of bacteria

difficult. For example, if the horse is still sedated, the depression and bradycardia may be the result of the drugs and not representative of the disease process.

When it is necessary to sedate a very painful or fractious horse to complete the examination, the horse should be observed for some time after the examination for recurrence of pain. Breed and age can also affect how readily a horse will demonstrate pain. For example, a very young horse may not be as stoic as a much older horse; a thoroughbred in training may exhibit severe pain when there is only a mild lesion, whereas a well-trained, experienced horse or draft breed horse may exhibit few signs with a painful strangulating lesion. Hence the observer must be careful to assess the entire horse and any subtle signs.

Horses with abdominal pain express a variety of signs, including pawing (Figure 20.1), turning the head toward the flank (Figure 20.2), kicking at the abdomen with the hind feet (Figure 20.3), crouching/attempting to lie down (Figure 20.4), repeatedly stretching as if to urinate (Figure 20.5), repeatedly backing into a corner of the stall, lying in sternal or lateral recumbency for prolonged periods of time (Figure 20.6), rolling on the ground (Figure 20.7), dropping to the ground, assuming a dog sitting position (Figure 20.8), bruxism (grinding of the teeth), dunking the nose into the water bucket and drinking excessive amounts of water, and sweating (Figure 20.9) (White, 1990). Quivering of the upper lip or demonstrating the flehmen response (Figure 20.10) can be another sign of colic.

Pain has been previously been classified into five categories based on severity: (1) no pain, (2) mild pain, (3) moderate pain, (4) severe pain, and (5) depression

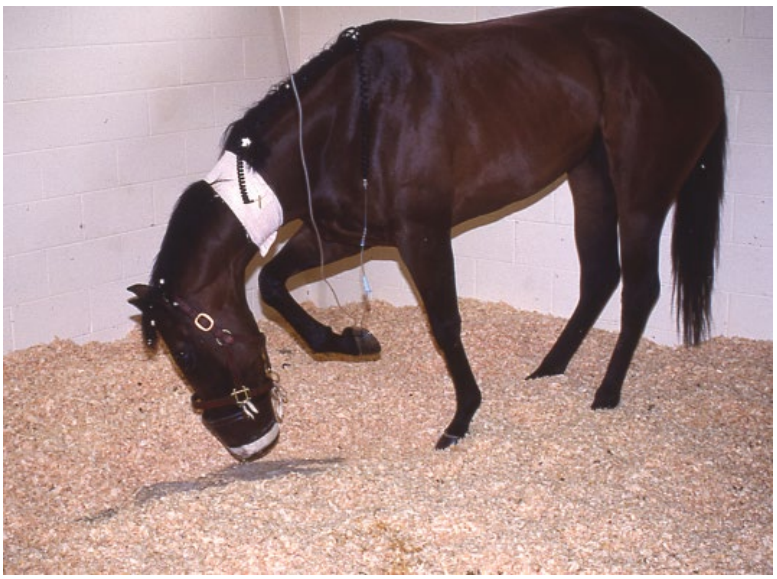


Figure 20.1 Pawing with a front foot is a common behavior in horse with colic.

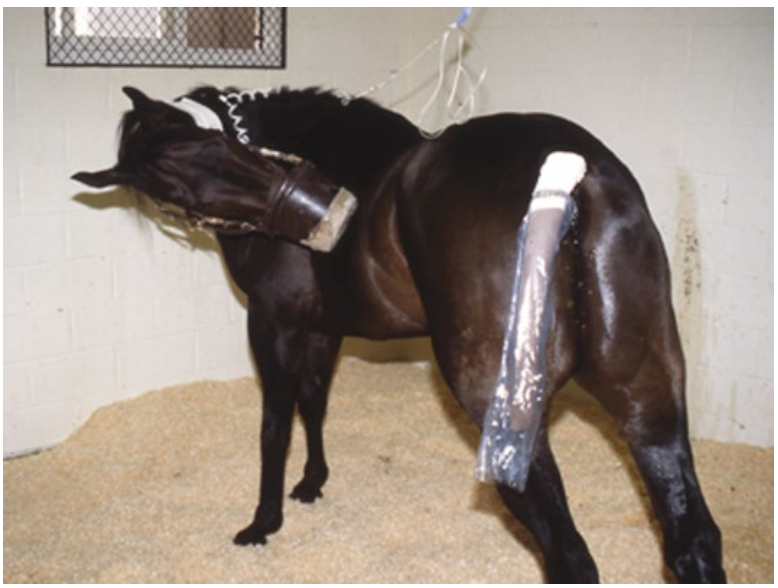


Figure 20.2 Turning the head toward the flank (flank watching) is behavior caused by pain but is not specific for a site or diagnosis.

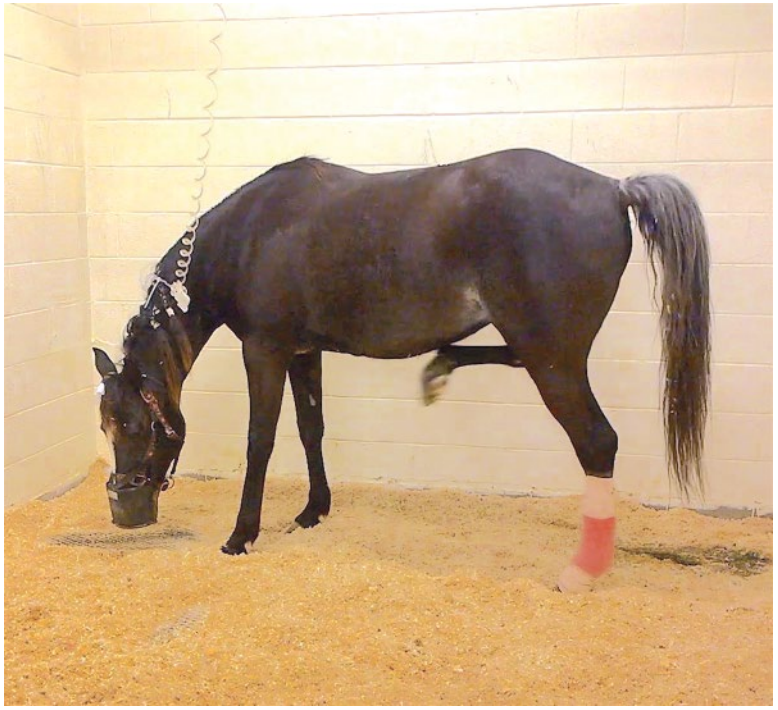


Figure 20.3 Kicking repeatedly at the abdomen is considered a sign of moderate pain.

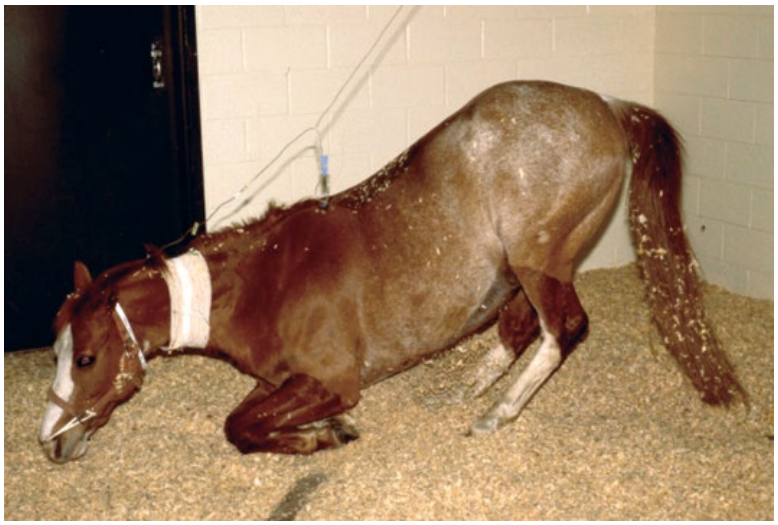


Figure 20.4 Colic causes horses to circle and crouch as if to lie down. This may be repeated several times before the horse actually lies down.

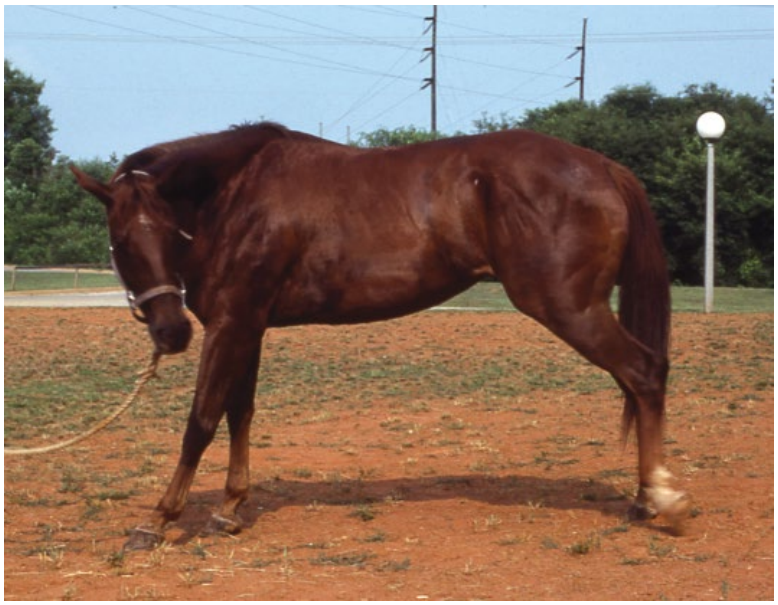


Figure 20.5 Standing in a stretched out position is frequently a sign of mild to moderate colic.

Figure 20.6 A horse with colic often stays recumbent for long periods of time. This is one of the common positional signs in a horse with colic.

Figure 20.7 Rolling from side to side is a sign of severe pain. In some cases horses will stay in dorsal recumbency for periods of time.

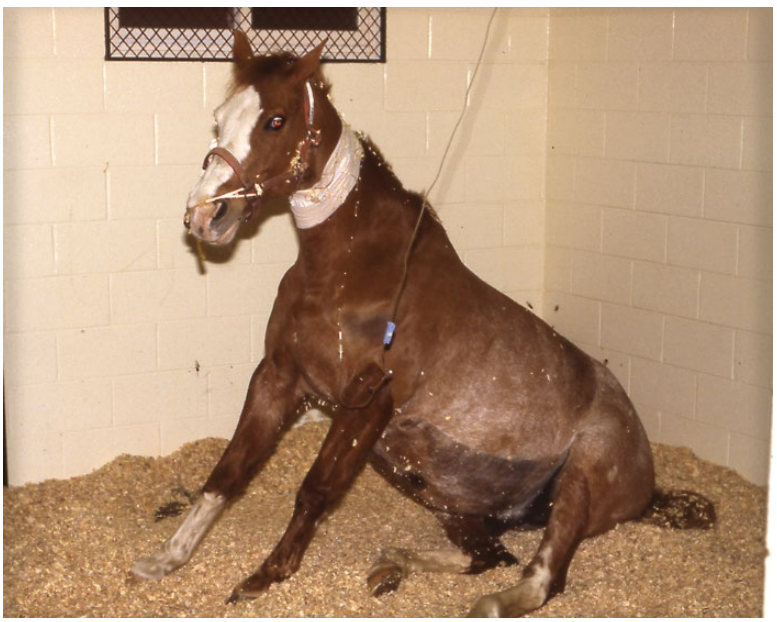


Figure 20.8 A horse rarely assumes a dog sitting position. This may help remove pressure from the diaphragm due to a distended stomach.

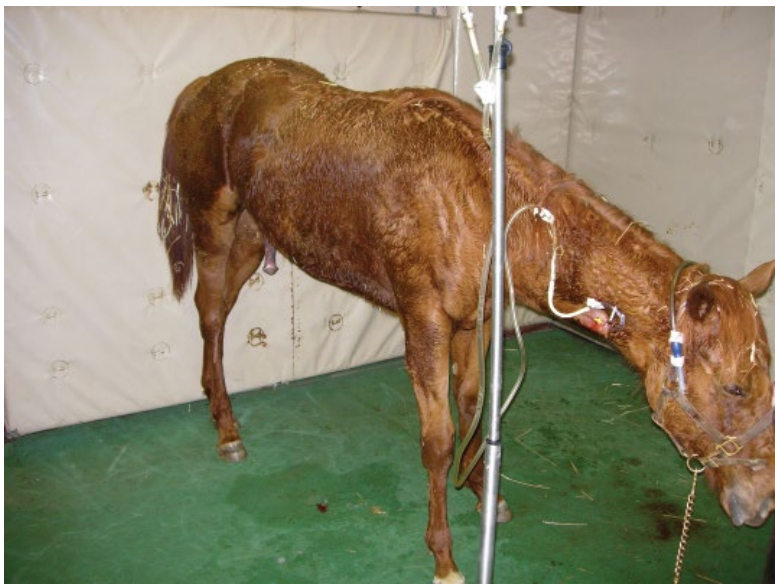


Figure 20.9 Sweating from increased activity or from a response to endotoxin suggests a serious condition.

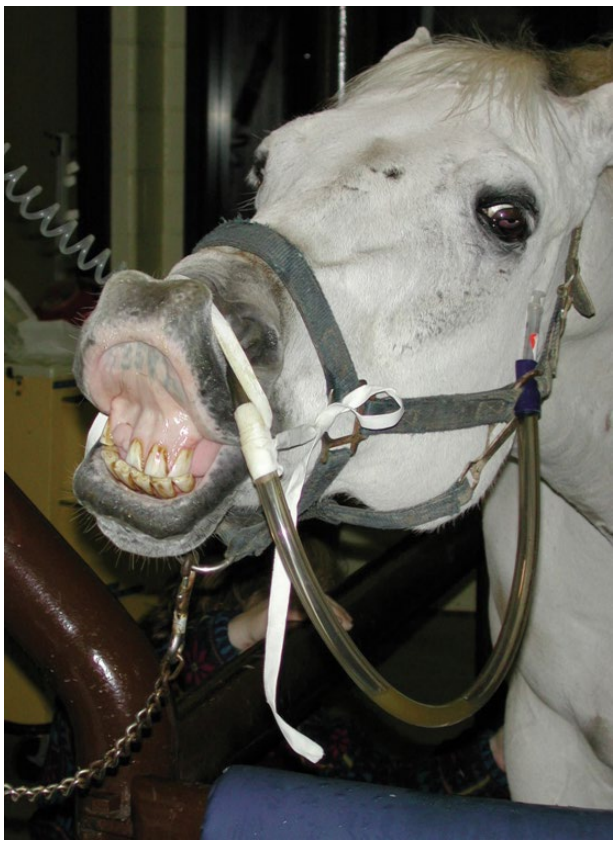


Figure 20.10 The curling of the upper lip or flehmen response can be evidence of a mild colic and may be an early sign of discomfort.

(White, 1990). Mild pain is evidenced by occasional pawing, turning to look at the flank, stretching out, bruxism, and lying down for longer than normal (White, 1990). Horses with this type of pain usually respond to analgesics for 8–12 h (Ragle, 1999) and are usually easily distracted from the pain with external stimuli such as walking. Horses with mild pain may not have signs of discomfort unless left alone in a paddock or stall. Moderate pain manifests as pawing, cramping, attempting to lie down, kicking at the abdomen, lying down, rolling, turning the head to the flank, and dog sitting (White, 1990), and is usually controlled with analgesics for 2–4 h (Ragle, 1999). It is harder to distract horses with moderate pain and analgesia is usually required. Severe pain includes sweating, dropping to the ground, violent rolling, continuous movement, or any of the previously mentioned signs (White, 1990). Horses with severe pain often are very difficult to control and the pain may only respond to analgesics for a few minutes or not at all. Depression can occur before or after an acute episode of pain, and is usually recognizable by the horse being overly quiet, not interested in food or water, the head may be hung low, and the horse may be reluctant to move, with a "tucked-up" appearance. Depression may be the first sign recognized by the owner at the beginning of a colic episode. Alternatively, the horse may be exhausted if it has been painful for a prolonged period of time before being discovered with abdominal pain. Horses in shock will often be depressed owing to acidosis. Acute rupture of the stomach or intestine can cause a dramatic shift from severe pain to depression.

Although pain scales for colic have been established, they have yet to be universally applied (Pritchett et al., 2003; Sutton et al., 2013). Head position, ear position, location, locomotion, response to horses, response to open door, response to approach, and lifting feet have been used make a pain score (Pritchett et al., 2003), and another scale was devised by assigning a numerical rating from 1 to 5 to the common clinical signs (Table 20.1)

Table 20.1 Behaviors indicating pain are scaled numerically from mild to severe. To grade the severity of pain, pick the most severe behavior manifested. Where there are two scores, choose one or the other of the scores based on the descriptions listed by the superscript.

Mild	Behavior	Mild	→	→	→	Severe
	Depression	1				
↓	Flank watching[a)]	1	2			
	Weight shifting[a)]	1	2			
↓	Pawing[a)]	–	2	3		
	Stretching[a)]	–	2	3		
↓	Kicking abdomen[a)]	–	2	3		
	Restlessness[b)]	–	2	3		
	Sternal recumbency[c)]	–	–	3	4	
↓	Attempting to lie down	–	–	–	4	
	Lateral recumbency	–	–	–	4	
↓	Rolling	–	–	–	–	5
Severe	Collapse	–	–	–	–	5

a) The lower score applies if the behavior is seen rarely or occasionally and the high score if seen frequently.
b) The lower score applies to a horse that circles, pivots around the hind end, or moves for no apparent reason. The high score applies to the horse that moves continuously and aimlessly or moves in a jerky or violent manner.
c) The lower score applies to a horse that is alert with raised head carriage and the high score if the horse's head is resting on the ground or facing the horses side (flank watching).

Source: Sutton et al., 2013, Table 6. Reproduced with permission.

(Sutton et al., 2013). Using this scale, horses that exhibited a flehmen response and assumed sternal recumbency were significantly associated with a medical treatment, and pawing, kicking at the abdomen, rolling, and dorsal recumbency were associated with surgical treatment (Sutton et al., 2013). This scale does not predict the type of disease, but may be useful when assigning pain severity.

The horse's signalment and personality are very important, as two horses with the same lesion may exhibit completely different grades of pain. For example, a horse with a low threshold for pain may be rolling and pawing continuously with a simple obstruction and mild gas distention, whereas a stoic horse may stand quietly, be inappetant, and only paw intermittently. For every disease, there is a range of pain that may be observed; all diseases can cause depression before or after a painful stage (White, 1990). Simple obstructions are usually characterized by mild to moderate intermittent pain, which is due to a combination of cyclic intestinal contractions oral to and around the obstruction and distention of the intestine with accumulated gas and fluid. Most simple large colon obstructions are not complete and some gas and fluid will pass around the obstruction. However, the horse may become more persistently or severely painful as the obstruction of the intestinal lumen becomes complete. This causes severe stretching of the intestine or mesentery. Acute severe pain is often caused by strangulation or severe tympany (White, 1990).

A horse that has mild, intermittent pain or no pain at all, but has depression, may be suffering from a primary inflammatory disorder such as peritonitis or enteritis (White, 1990). Therefore, the absence of severe pain does not indicate that the horse does not have a severe illness – for example, a very depressed, quiet horse with peritonitis, which may have a life-threatening condition.

Specific presentations of pain may be characteristic of certain diseases. For example, a neonatal foal straining to defecate or urinate will most likely have a meconium impaction or ruptured bladder (Figure 20.11), whereas a foal constantly lying on its back for long periods of time most likely has gastric ulceration (Figure 20.12) (White, 1990). A gelding straining to urinate may have a urolith. Although rare, a horse assuming a dog-sitting position may have gastric distention secondary to gastric impaction or obstruction in the small intestine (Figure 20.8) (White, 1990). Horses with sand impactions of the large colon tend to stand stretched out for minutes at a time (Figure 20.13), although this behavior also occurs with other diseases (White, 1990). Even though some behavior or body position may indicate a particular disease, this association is not always accurate.

The physical appearance of the horse may provide some clues about the severity of the condition. During violent bouts of pain, horses can traumatize themselves, resulting in contusions, abrasions, and swelling around the eyes, head, tuber coxae, and limbs (Figure 20.14). If the horse is quiet or depressed when examined, but has evidence of previous trauma and severe pain, the veterinarian should be concerned about the possibility of an advanced strangulating obstruction or rupture of either the stomach or cecum. Sweating can also be a sign of severe pain due to stimulation of the sympathetic nervous system or from endotoxic shock (Figure 20.9) (White, 1990).

A bloated appearance indicates marked distention of the cecum, large colon, or possibly the entire small intestine (Figure 20.15). Cecal distention or displacement may result in a bloated right side, whereas a left dorsal displacement of the large colon may result in a bloated left side of the abdomen. General bloating on both sides is usually indicative of severe distention of the large colon secondary to large colon volvulus or of the entire small intestine secondary to small intestinal volvulus (White, 1990). A miniature pony with generalized bloating may have a distended large colon secondary to complete obstruction of the small colon by an impaction. A wide stance with a "tucked-up" appearance may indicate

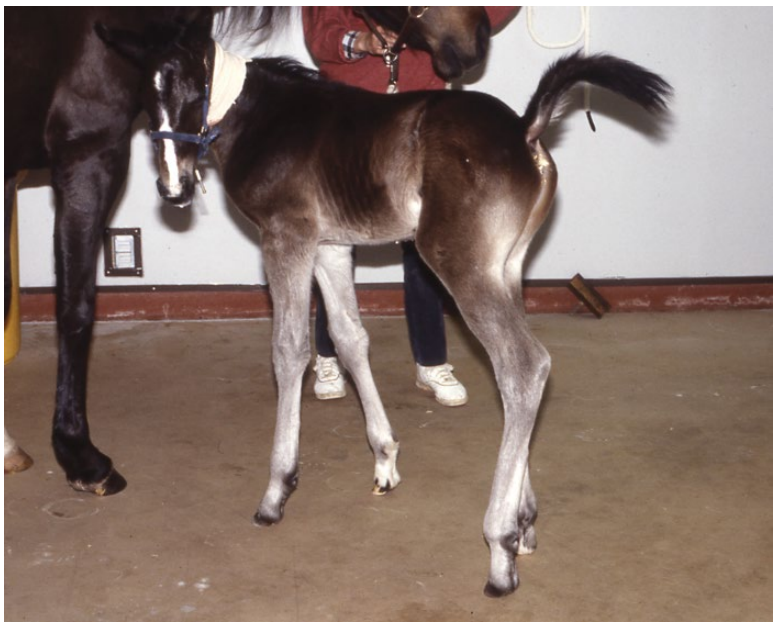


Figure 20.11 Foals with meconium impaction or a rupture bladder often strain with a raised tail.

Figure 20.12 Foals with gastric ulcers often lie in dorsal recumbency.

pleural or abdominal pain consistent with pleuritis and peritonitis (Figure 20.16). Intestinal incarcerations and subsequent strangulating obstruction through the umbilicus in a young animal or into the scrotum in an older animal can be externally visible with a very large swelling in those respective regions (see Chapter 52). Although the severity of pain is not diagnostic of specific conditions, it may narrow the differential diagnosis into a disease category (Box 20.1).

Temperature, Pulse, and Respiration

The horse's rectal temperature, pulse, and respiratory rate are helpful in determining the category or severity of the colic. The rectal temperature should be taken before the rectal examination is performed as the temperature measurement will be inaccurate once air has been drawn into the rectum. Rectal temperature usually remains normal in adult horses (99–101 °F/37.2–38.3 °C) and in foals (100–102 °F/37.8–38.9 °C) with colic. The temperature

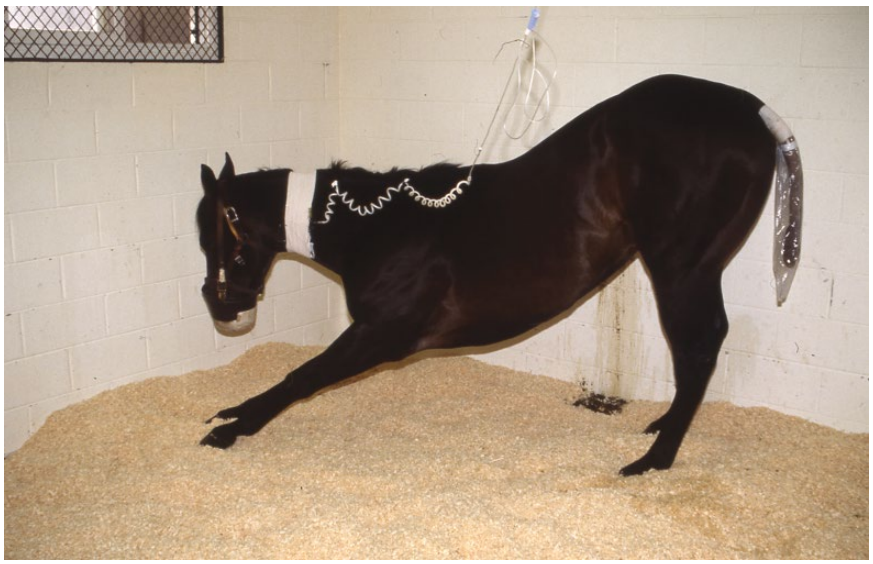


Figure 20.13 Stretching in a camped out position is a sign of colic and the horse may stay in this position for several minutes.

Figure 20.14 Abrasions on the head, limbs, and pelvis indicate previous trauma due to rolling or recumbency from severe colic. If pain is replaced by depression, gastrointestinal rupture or severely compromised intestine should be suspected.

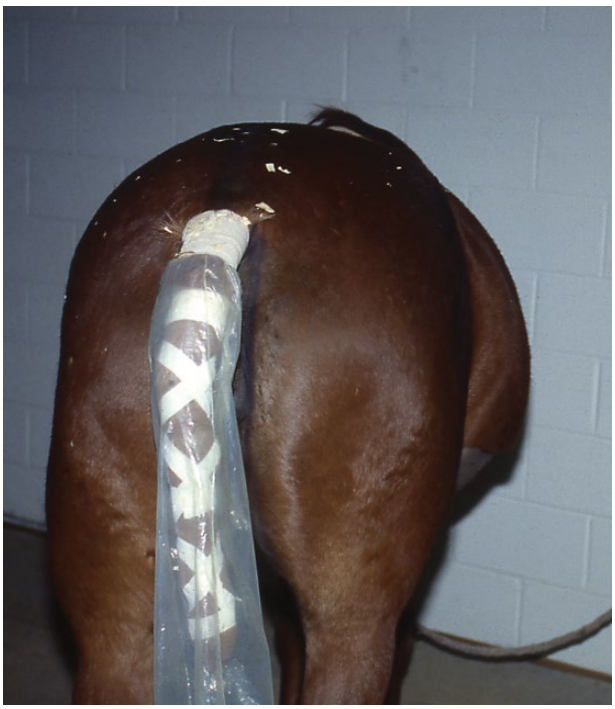


Figure 20.15 Abdominal distention frequently indicates marked intestinal distention, which can be confirmed by rectal examination or abdominal ultrasound.

may be elevated slightly (<101.5 °F/38.6 °C) in horses that have had physical exertion such as rolling or pacing due to moderate–severe pain. Generally, horses with simple obstructions or displacements of the large colon do not have an increased temperature. In some cases, the environmental temperature or the horse's hydration status, both of which interfere with heat loss, may increase the temperature more than expected (White, 1990). Infectious agents and circulating endotoxin can cause fevers, usually of 102 °F or 39 °C or higher. For example, horses with peritonitis, proximal enteritis, impending colitis, or endotoxemia often present with a fever. An increased temperature may help differentiate proximal

Figure 20.16 Abdominal splinting and walking with a stilted gait are frequently the result of peritonitis or pleuritis.

enteritis, which can be treated medically, from a strangulating lesion, such as a pedunculated lipoma, that requires surgery (see Chapter 52). In most cases, a fever will be present in horses with proximal enteritis whereas horses with a strangulating lesion usually have a normal temperature (<101.5 °F/38.6 °C). Potomac horse fever will generally cause the horse to have a high temperature (105–107 °F/40.5–41.5 °C), which normally precedes the colic signs (Palmer, 1987; Ristic et al., 1986). When severely devitalized bowel exists in a horse with a strangulating lesion, the temperature may be increased owing to the circulating endotoxin. However, this is often countered by cardiovascular compromise and reduced tissue perfusion, resulting in a normal or only slightly increased temperature.

The heart rate of normal neonatal foals varies between 100 and 120 bpm and normal adult horses have heart rates of 28–44 bpm. The heart rate of older foals and weanlings is variable, but tends to be slightly higher than that of adults until they reach approximately 6 months of age. The heart rate is an indicator of the severity of the disease and the degree of circulatory shock (Morton & Blickslager, 2002). Heart rate has been shown to be an important prognostic indicator for survival (Furr et al., 1995; Van der Linden et al., 2003) and for complications after colic surgery (French et al., 2002). However, heart rate can be unreliable and may be decreased during the onset of life-threatening conditions such as a large colon or small intestinal volvulus, or may be increased in some horses with a simple obstruction. Therefore, the heart rate must be interpreted in conjunction with the other clinical signs. Although heart rate is dependent on the level of pain and sympathetic response, the vascular volume and cardiovascular status also determine the heart rate. Cardiovascular status may be affected by hypovolemic shock or SIRS (see Chapter 16) or other conditions causing massive intestinal distention and decreased venous return. A very high heart rate should alert the veterinarian to a serious problem such as a very distended stomach that is close to rupture, or severe intestinal distention, which obstructs venous return to the heart. Commonly encountered heart rates for different categories of disease are (1) simple obstructive diseases, 40–70 bpm; (2) early strangulating lesions, 50–90 bpm; (3) late strangulating lesions, 70–120 bpm; (4) inflammatory diseases, 40–100 bpm (White, 1990). Since the heart rate is influenced by the level of pain and excitement, tachycardia cannot be relied upon as the sole indicator of disease severity (Orsini et al., 1988; White et al., 2005).

The pulse quality can be assessed by palpating the facial artery. A weak pulse may indicate low blood pressure secondary to hypovolemic shock or SIRS. An irregular heart rate or pulse may indicate a dysrhythmia caused by an electrolyte imbalance such as low ionized calcium or magnesium concentrations. Decreases in these electrolytes will usually result in tachycardia and can be a contributing cause of ileus. An electrocardiogram (ECG) may be helpful as serum concentrations of magnesium and calcium (total and ionized) correlate with abnormal PR, QRS, QT and corrected QT_c intervals (Garcia-Lopez et al., 2001). Other abnormalities such as an atrioventricular block may also be evident on the ECG. For example, a horse with a low heart rate may have a second-degree heart block secondary to administration

of α_2-agonist drugs; these effects should subside within 1–2 h of administration.

Normal respiratory rate should be 8–12 breaths per minute. The respiratory rate is consistently increased in horses with abdominal pain. The increased rate allows for more shallow breaths and thus reduced work and movement of the diaphragm and chest muscles. A similar presentation will be evident in horses with respiratory distress secondary to restriction of lung expansion, as in the case of pneumothorax or diaphragmatic hernia. In the case of diaphragmatic hernia, the horse may be in severe respiratory distress, which can be mistaken for pain. Cyanosis with a rapid respiratory rate can also occur when there is excessive pressure on the diaphragm and vena cava from large colon or cecal distention, or when endotoxemia is present with secondary pulmonary changes (White, 1990).

Metabolic acidosis, as often accompanies devitalized intestine, endotoxemia, and reduced tissue perfusion, may result in a high respiratory rate in an attempt to remove excess CO_2 to compensate for this metabolic acidosis (see Chapter 27).

Horses with colic secondary to enteritis, colitis, or peritonitis and that are febrile or endotoxemic may be at increased risk for developing laminitis. Monitoring for increasing digital pulses and hoof temperature and also for the development of lameness is recommended and preventative treatments for laminitis should be instituted as needed (see Chapter 49).

Hydration Status

The color and moistness of the oral mucous membranes are used to assess perfusion and the horse's hydration status. The conjunctiva can also be used, but may be inflamed as the result of recent trauma such as rolling, transport, or recumbency (White, 1990). The mucous membranes are usually pale pink (Figure 20.17) (Wilson & Gordon, 1987; Parry, 1987), but care must be taken in this assessment as the lighting may affect the appearance. Tungsten light may enhance a red color, whereas fluorescent light can give the mucous membranes a slight blue–gray cast compared with daylight (White, 1990). The color of mucous membranes in dehydrated horses can vary from pale pink to brick red if there is venous congestion (Figure 20.18). If the horse is endotoxemic, the membranes may have a congested appearance, with a dark-blue "toxic" line around the teeth (Figure 20.19) (Mackay, 1996). Tachycardia with pale or muddy mucous membranes may indicate internal blood loss such as with hemoabdomen.

The capillary refill time is also a good indicator of tissue perfusion and cardiovascular function. The capillary refill time is determined by pressing on the mucous membranes above the incisor teeth to cause a blanching of color and then timing how long it takes for the color to return to normal as the blood returns. The normal capillary refill time is 1–2 s. Jugular refill time is measured by holding off the vein in the lower portion of the neck. Prolonged jugular refill (>3 s) indicates hypovolemia, necessitating intravenous fluid therapy.

Skin tent is a measure of hydration status and is significantly associated with prognosis in horses with colic (Van der Linden et al., 2003). The skin on the neck or upper eyelid is pinched and the time it takes for it to return to normal is measured. With mild dehydration (5%), the skin tent is 1–3 s, mucous membranes are moist or slightly tacky, and the capillary refill time is normal; with moderate dehydration, the skin tent is 3–5 s, the mucous membranes are tacky, and the capillary refill

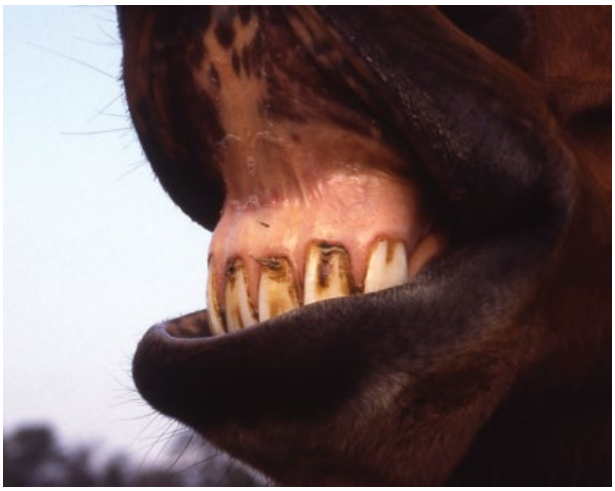


Figure 20.17 Normal membrane color can vary from pale to bright pink.

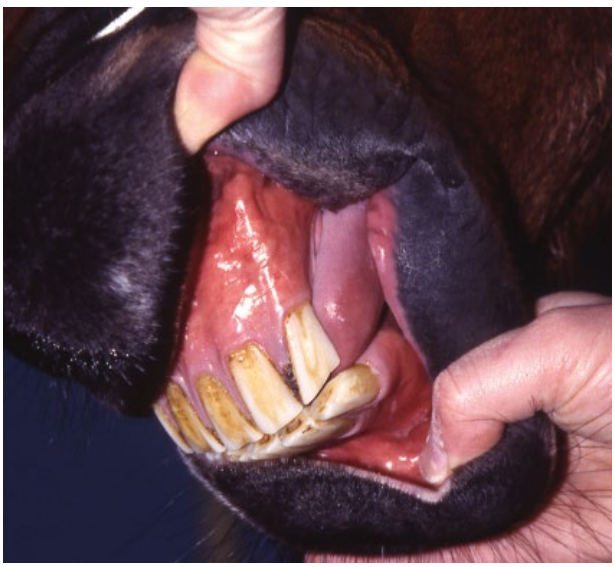


Figure 20.18 Brick-red mucous membranes are associated with the early stages of shock caused by endotoxin.

Figure 20.19 Cyanotic mucous membranes indicate poor perfusion from severe shock or lack of venous return to the heart.

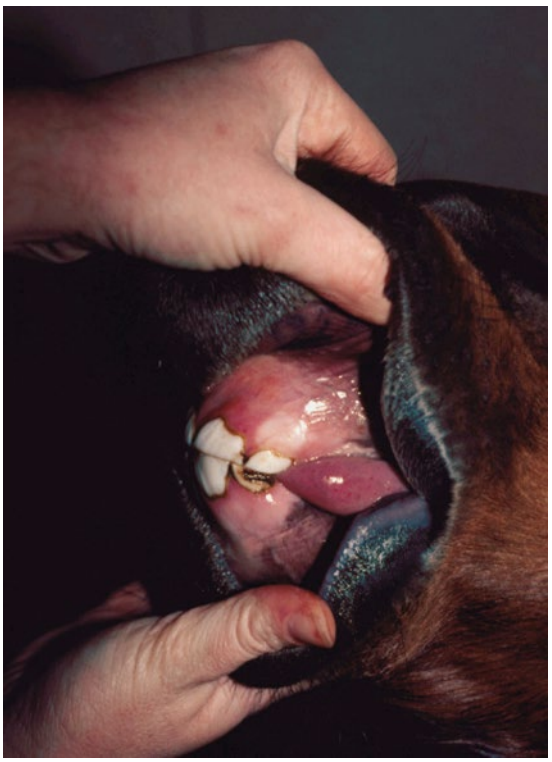


Figure 20.20 Capillary refill time is increased due to poor perfusion from hypovolemia or the later stages of endotoxemia.

time may be 2–3 s; with severe dehydration, the skin tent is ≥5 s, the mucous membranes are dry, and the capillary refill time often exceeds 4 s (Figure 20.20) (Corley, 2002). It is important to consider the amount of subcutaneous fat, as this will affect skin tent retraction. Horses with normal hydration and minimal subcutaneous fat can appear to be dehydrated based on skin tent retraction. Cold extremities, such as distal limbs, ears, and nose, may indicate poor tissue perfusion secondary to vasoconstriction and redistribution of blood to vital organs.

Deterioration of the peripheral pulse quality is consistent with hypovolemia and low cardiac output. Strong, bounding pulses may be palpated during the hyperdynamic state of shock when cardiac output is increased and peripheral vascular resistance is reduced.

The packed-cell volume (PCV) and plasma protein concentration are the most commonly used laboratory tests to evaluate hydration. Both values often increase simultaneously with a decrease in blood volume as fluid leaks into an extravascular space or is not replaced after obligatory loss in urine, feces, or respiration. Increases in PCV without a concurrent increase in the plasma protein concentration may occur with splenic contraction. A PCV exceeding 50% usually indicates dehydration (Corley, 2002). If protein loss occurs as part of the disease process, it may result in a low or normal protein concentration despite dehydration (Corley, 2002). Increased plasma protein concentrations with normal or decreased PCV may indicate an increase globulin concentration or anemia. Classifying hydration can be estimated using the values in Table 20.2.

Table 20.2 Estimate of the degree of dehydration using packed-cell volume (PCV, %) and total plasma protein (TP, g/dL).

PCV/TP	Value	Degree of hydration (%)
PCV	43–50	Slight dehydration
TP	7.0–8.0	6
PCV	50–57	Moderate dehydration
TP	8.1–9.0	8
PCV	>57	Severe dehydration
TP	>9.0	10

Nasogastric Intubation

A nasogastric tube should always be passed during every examination for abdominal pain. If the horse is mildly painful with a normal heart rate, the tube does not need to be passed immediately. However, if the horse is moderately to severely painful and is tachycardic (≥60 bpm), the tube should be passed immediately to prevent possible gastric rupture. Gas within the stomach is easily relieved with a nasogastric tube, but fluids sequestered in the stomach are more difficult to remove and usually do not flow spontaneously from the tube. A large-bore tube should be used as there are often large food particles within the fluid, which may block a small tube. For a 450 kg horse, a tube with a 1.25 cm (½ inch) inside diameter and a 1.8 cm (¾ inch) outside diameter is preferable.

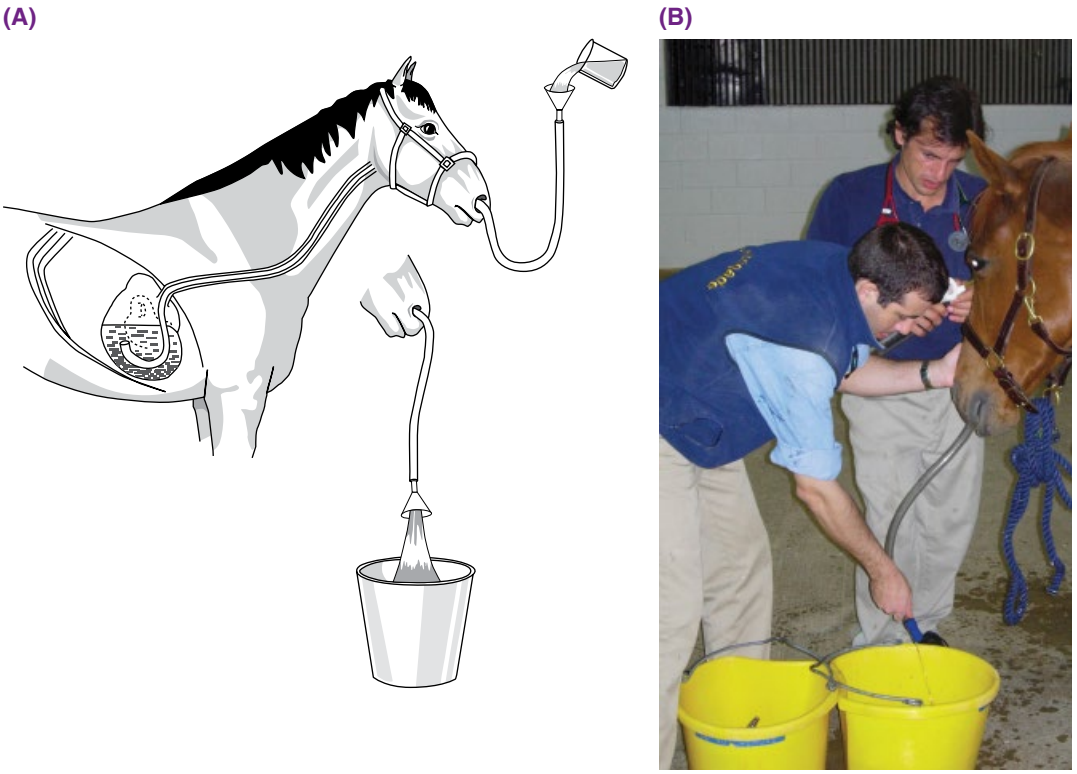


Figure 20.21 **(A)** Once a stomach tube has been placed it should be filled with water to start a siphon. **(B)** The end of the tube is lowered below the level of the stomach to drain any reflux. This should be repeated several times to make sure that as much fluid as possible is drained out of the stomach.

It is best to use a tube with a single opening at the end, as side openings may become blocked with gastric contents and are not easily cleared with retrograde flushing (Ragle, 1999). If gastric fluid does not flow freely, sufficient water (approximately 500 mL) should be used to fill the nasogastric tube via a pump or funnel. The end of the tube is first elevated and then lowered so that the end is lower than the stomach (Figure 20.21). This maneuver creates a siphon, which should allow flow of sequestered fluid.

If no fluid is retrieved immediately, attempts at creating a siphon should be repeated while the position of the tube in the stomach is changed. This should be repeated either until a fluid pocket is located or the veterinarian is convinced that there is no fluid retained in the stomach. Even with a full stomach, it can take multiple attempts (five or more) to start a siphon to locate the fluid. Suction on the end of the tube using a large-volume syringe or stomach pump in reverse may be useful, but can also cause ingesta to block the tube.

Normally, fluid from the stomach is green and sweet smelling, consists predominately of food particles, and has a pH in the range 3–6 (measured with a standard pH paper) (White, 1990). Fluid refluxed from the small intestine is yellow–brown in color from the bile and has a fetid odor due to the fatty acids produced during intestinal stasis (Figure 20.22) (White, 1990). Orange or red

Figure 20.22 Reflux due to an obstruction of the small intestines is orange tinged due to bile, with a foul odor due to fatty acid production in the stomach.

fluid may be consistent with hemorrhagic enteritis. Because small intestinal sections buffer acid, the fluid refluxed is most often neutral or slightly alkaline (pH 6–8) (White, 1990). If there is pyloric obstruction, the reflux fluid obtained may be acidic even though there are massive volumes of fluid due to the retention of acid in the stomach. The volume of fluid accumulated in the stomach is greatest with a pyloric or proximal duodenal obstruction, which may result in 40–80 L in 24 h (see Chapter 52). The volume of reflux retrieved should be recorded, particularly if reflux continues. By measuring the amount of fluid used to start a siphon and subtracting it from the amount of reflux retrieved, total fluid removed can be calculated.

Draining a large volume of fluid from the stomach indicates that there is an obstruction in the small intestine due to physical or functional obstruction, and is a sign that the horse may require surgery. Large volumes of reflux are obtained in horses with duodenitis-proximal jejunitis (anterior enteritis), which is often difficult to differentiate from a strangulating obstruction (see Chapter 52). There may also be gastric reflux with primary gastric lesion or with some diseases of the large colon, such as a large colon displacement. Gastric reflux may occur in the latter condition if the lumen of the duodenum is obstructed in the region of the duodenocolic ligament by the abnormally positioned large colon.

The passage of a nasogastric tube can save a horse's life in addition to being diagnostic for a small intestinal problem, especially when distended small intestine in the cranial abdomen is not palpable on rectal examination. Other diagnostic tests may be performed on the fluid to detect microbes (*Salmonella* spp.) by culture or for the presence of microbial toxins (*Clostridium* spp.).

In the absence of gastric reflux, administration of enteral fluids and medications, including balanced electrolytes, mineral oil, and laxatives, can be performed via the nasogastric tube, when indicated.

Abdominal Auscultation

To auscult the abdomen, the stethoscope is placed over four major sites, including the left and right lower and upper paralumbar regions (Figure 20.23). The ventral midline of the abdomen should also be ausculted, especially in regions where sand colic is prevalent. Normally, sounds will be heard on both sides of the abdomen, both high and low. The characteristic sounds of the colon mixing will be heard along either side toward the more ventral aspect of the abdomen (White, 1990). The characteristic borborygmi (i.e., fluid gurgling sounds) are produced by the interface and mixing of gas and fluid in the large colon and cecum. The small intestine can be very motile, but may not create referred sounds. Hence the borborygmi ausculted are a good indication of large bowel motility, but not always of small intestinal motility.

The amplitude of the borborygmi will vary markedly among horses (Ehrhardt & Lowe, 1987), but the frequency is more consistent, with mixing sounds normally regularly occurring 2–4 times per minute (see Chapter 9). Progressive sounds will be heard once every 2–4 min when the horse has not eaten recently. These sounds will become more intense with eating, as both their amplitude and frequency increase. This results in borborygmi that are a long progressive rush of gurgling heard on both the left side (left dorsal and ventral colon) and right side (cecum) lasting 6–10 s (Ehrhardt & Lowe, 1987; Adams, 1980). The propulsive sounds are different from the mixing sounds; they have a different cyclic pattern and intensity and are of longer duration (see Chapter 9) (Ehrhardt & Lowe, 1987; Adams, 1980). Certain motility-altering drugs, such as atropine (Ducharme & Fubini, 1983; Lester, 1990), xylazine (Rutkowski et al., 1991), romifidine (Freeman & England, 2001), detomidine (Merritt et al., 1998), and butorphanol (Rutkowski et al., 1991), will temporarily reduce or abolish these propulsive sounds (Ehrhardt & Lowe, 1987; Adams, 1980). Administration of xylazine and butorphanol can decrease gut sounds for about 1 h at standard dose rates, whereas atropine can cause long-term ileus, bowel stasis, and subsequent distention, resulting in colic (Ducharme & Fubini, 1983).

In most cases of abdominal pain, the propulsive sounds are decreased. In cases of severe intestinal disease, such as strangulated bowel, the borborygmi are absent. Even with small intestinal disease, the propulsive motility of the large colon and cecum is usually decreased or absent owing to the sympathetic response to pain and the inflammatory response affecting the entire intestine. In horses with sand accumulation, a pouring or hissing sound, almost like the sound that wind makes when blowing through a sea shell, may be ausculted along the ventral midline caudal to the xiphoid process as the colon moves (Ragle et al., 1989).

Movement of the horse may cause fluid and gas interfacing sounds of bubbling or pinging within the intestine. These sounds do not represent propulsive motility, but rather are indicative of static, distended large or small intestine. In spasmodic colic, excessive borborygmi are heard and are suspected to be due to intestinal spasms from irritation, ischemia, parasite irritation, or contraction against an impaction (White, 1990).

Borborygmi may also increase after a period of ileus, particularly after either tympany or a simple obstruction has resolved spontaneously or after treatment, a trailer ride, or walking (White, 1990). With resolution of ileus, there is an increase in borborygmi and usually no pain, but the horse may appear tired or depressed. Increased

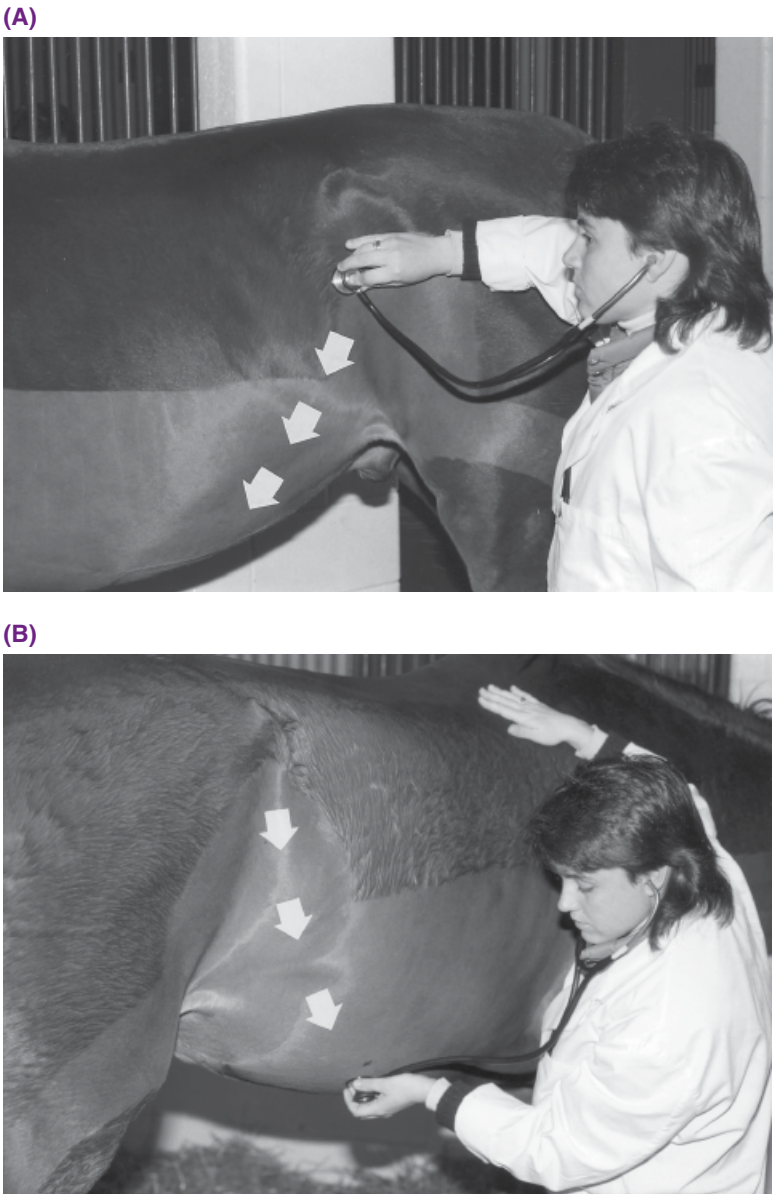


Figure 20.23 Auscultation of the abdomen is completed by moving the stethoscope down each flank to the ventral abdomen (**(A)** left side; **(B)** right side).

borborygmi can occur with hypermotility associated with impending diarrhea. In this early stage before the diarrhea has begun, the horse may be painful, and foals are especially painful with the onset of enterocolitis with the intestinal sounds of fluid sloshing with increased frequency.

Percussion

Percussion is usually performed by tapping over an area of interest while simultaneously ausculting that area (Figure 20.24). Percussion is useful in locating pockets of gas. For example, a ping in the right paralumbar fossa is indicative of a gas-distended cecum, whereas a ping in the left upper paralumbar fossa may indicate large colon distention or displacement (White, 1990). Percussion is not normally performed with a pleximeter and hammer, as these are of limited usefulness over the abdomen of the horse. It may be possible, however, to identify the margins of the spleen using these devices. The other parts of the intestinal tract vary in their fluid and gas content and thus are difficult to identify (White, 1990).

Ballottement, which is performed routinely in cattle, is rarely performed in the diagnostic workup for the equine acute abdomen; it is possible, however, to identify a fetus, a large impacted viscus, or a heavy organ as it rebounds against the abdominal wall during ballottement (Stashak, 1979). Unlike cattle, horses often do not tolerate this maneuver. Constant pressure applied to the flank or lower abdomen may be useful in differentiating visceral pain arising from the intestine from parietal pain arising from the abdominal wall or parietal peritoneum

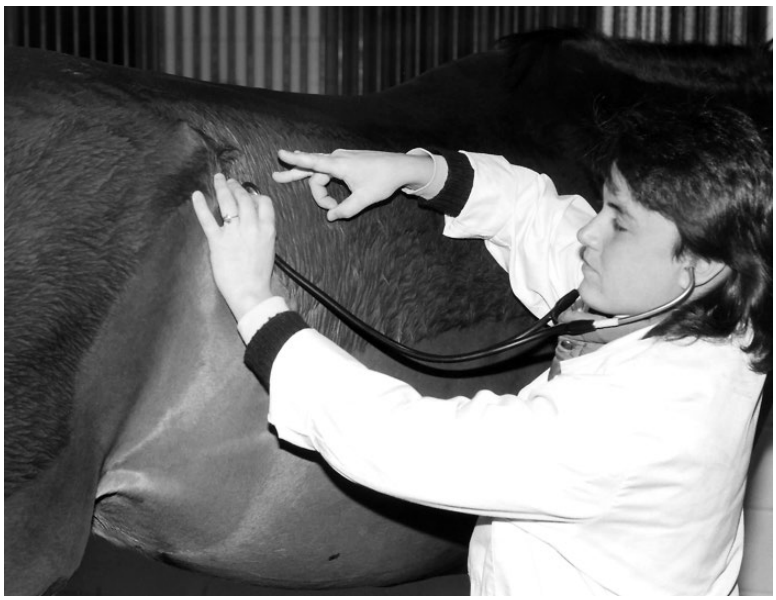


Figure 20.24 Percussion over the right flank is the area of the cecum is used to detect cecal tympany.

(Stashak, 1979). This pressure will exacerbate parietal pain, with splinting of the abdomen in horses with peritonitis, but there will be no response in horses with purely visceral pain (White, 1990).

Abdominal Palpation per Rectum

The rectal palpation is one of the most important diagnostic procedures when evaluating the acute abdomen to determine the location and severity of the condition and to help make a decision for surgery (Dabareiner & White, 1995; Kopf, 1997; Sanchez & Merritt, 2005; Kalsbeek, 1975; White et al., 2005). It may not be necessary to perform a rectal examination at the first visit for colic if the horse's physical examination parameters are within normal limits and there is no evidence of pain at the time of the examination. However, this procedure can provide vital information for the early diagnosis and treatment of intestinal conditions in horses with a history of colic. The rectal examination should always be performed when colic is observed or if pain persists, particularly if follow-up examinations are necessary.

Owing to the size and depth of the horse's abdominal cavity, only the caudal 30–40% of the horse's abdomen can be palpated (Kopf, 1997). As a result, it may not be possible to diagnose a problem definitely and some abnormalities within the abdomen may be missed. However, even determining that the findings on the rectal examination are not normal is important. A multicenter survey of 1965 colic cases from 10 equine referral centers throughout the United States determined that being able to distinguish normal from abnormal rectal findings was the most important factor in deciding the need for surgery (Reeves et al., 1991). However, the rectal examination was less important than pain and auscultation in less severe cases of colic (White et al., 2005). Rectal findings should be considered in conjunction with results of the physical examination, nasogastric intubation, abdominocentesis, and laboratory evaluations (Mueller & Moore, 2000).

The value of the rectal examination should be considered in relation to the risks involved (White, 1990). Palpation per rectum should be avoided if the horse's size, behavior, or degree of pain render the procedure unsafe for the horse, veterinarian, and others present. Adequate restraint is of paramount importance to avoid iatrogenic perforation of the rectum during the examination and to avoid injury to the veterinarian performing the procedure. If possible, the horse should be restrained in stocks. If stocks are not available, positioning the horse in a stall is preferred. A twitch should be applied to the upper lip and chemical sedation administered in the form of xylazine (0.3–0.5 mg/kg IV) or detomidine (7–10 μg/kg IV) (Mueller & Moore, 2000). Broodmares that are used to the procedure may not require sedation. Intrarectal administration of 2% lidocaine (50–60 mL, via a syringe connected to a 30 inch intravenous extension) after fecal removal will promote relaxation. Alternatively, the short-acting anticholinergic spasmolytic agent hyoscine *N*-butylbromide (Buscopan®) at 0.3 mg/kg may be used, as it is more effective than topical 2% lidocaine at reducing rectal pressure and straining (Luo et al., 2006). Rarely in a very young or fractious horse, an epidural may be required. An epidural should also be performed if the horse has a suspected rectal tear (see Chapter 57) (Mueller & Moore, 2000).

Adequate lubrication of the examiner's hand and arm with KY jelly or hydrated methylcellulose is also necessary to prevent irritation to the rectal mucosa and improve the ease of the procedure. Long plastic sleeves

are used and usually are turned inside out to avoid the glove's seam irritating the mucosa. If a rectal tear is suspected, a rubber obstetric sleeve with a surgical glove attached will provide the best sensitivity without irritating the mucosa. The rectal examination should be performed slowly, as most horses will resist the procedure if they are not accustomed to it. To begin the examination, the examiner should stand as close as possible to one side of the horse if the horse is not restrained in the stocks. The anal sphincter is usually tight and some force is required to push the hand past this constriction, which should be opened slowly and evenly with the thumb and fingers together and hand in a narrow configuration. Once the hand is passed through the sphincter, the examiner can move to the back of the horse and advance the hand slowly in to remove the feces. The feces should be examined for volume and consistency. Hard, dry fecal balls covered with mucus could indicate the presence of an impaction or lack of normal fecal transit (Figure 20.25), watery fetid feces may be indicative of colitis, parasites contained within the feces may indicate a heavy parasite burden, and sand may also be able to be seen or felt within the feces in horses with sand colic.

Once the feces have been removed, additional lubricant should be applied to the hand, which should then be advanced, fingers held together, slowly to arm's length if the rectum and small colon allow. There should never be any forceful advancement; if the small colon and rectum are tense, the arm should remain still or should be withdrawn and replaced. The examiner should never push against rectal/small colon contractions; if the intestine contracts, the examiner should remain still to allow the contraction to push the hand and arm out to the anal sphincter. If there is resistance, the hand should be withdrawn to avoid perforating the rectal mucosa and wall. Once the arm has been inserted as far as comfortably possible, the examiner should wait approximately 15–30 s while the rectum, small colon, and anal sphincter relax (White, 1990). Initial examination of the caudal abdomen with the arm inserted half way is frequently not productive, as it may result in straining and excessive peristaltic contraction of the rectum (Kopf, 1997).

Figure 20.25 Horses with increased transit time often have dehydrated feces coated with mucus.

Examination of the abdomen should be performed in a systematic manner. Although the exact sequence will vary between veterinarians, a common approach is to divide the abdomen into quadrants and then examine the abdomen in a clockwise fashion, starting from the left dorsal aspect, then proceeding to right dorsal, right ventral, and left ventral regions. This approach is thorough and avoids missing abnormalities. Dividing the abdomen into quadrants also may help the veterinarian describe structures or abnormalities palpated during the examination.

Starting in the left dorsal quadrant, the spleen is located with its smooth and sharp dorsocaudal edge palpable against the left body wall (Figure 20.26). The nephrosplenic ligament, nephrosplenic space, and the caudal pole of the left kidney can be palpated by moving the hand up from the caudal edge of the palpable spleen. Normally 3–4 fingers can be placed in the nephrosplenic space (Figure 20.26) (Mueller & Moore, 2000), but in some horses this region is difficult to reach, especially in large breeds, and it may not be possible to palpate the kidney or the nephrosplenic space. From the kidney, the hand is moved to the right and forward along midline and to the right. This allows palpation of the aorta, internal and external iliac arteries, and root of the mesentery (Figure 20.27) (Mueller & Moore, 2000). In larger horses, the root of the mesentery may not be able to be reached or just touched with the tips of the fingers (White, 1990).

While the aortic pulse is easily palpable, the pulse in the mesenteric stalk may only occasionally be palpable (Mueller & Moore, 2000). The right upper quadrant is then palpated by moving to the right. The duodenum is located dorsal to the base of the cecum, but is rarely palpable unless it is distended during a peristaltic wave or secondary to small intestinal obstruction. The hand is then moved to the base of the cecum. The ventral and medial cecal bands (tenia) are then palpated traversing in a dorsocaudal to ventrocranial direction. This palpation is facilitated by moving the hand in a lateral and caudal direction to hook the tips of the fingers into the cecal bands, which are normally relaxed and movable when gently manipulated (Figure 20.28) (Mueller & Moore, 2000). A large amount of the cecum is not palpable, but ingesta can often be palpated in the right ventral

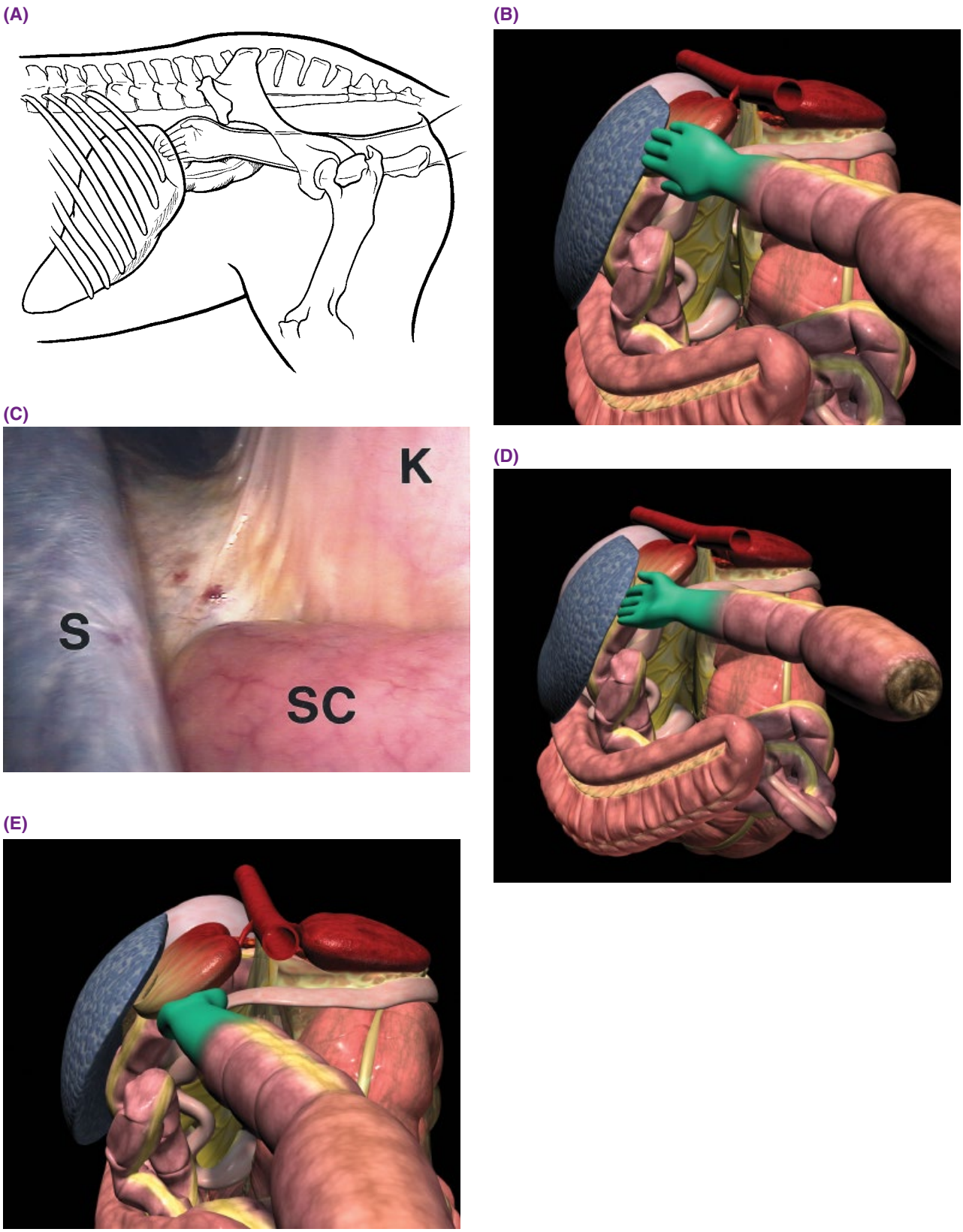


Figure 20.26 **(A)** The spleen should be identified in the left dorsal quadrant adjacent to the body wall. Source: White & Moore, 1998. Reproduced with permission of Elsevier. **(B)** The edge of the spleen can be palpated in almost all horses using the tips of the fingers. Just medial to the edge of the spleen is the nephrosplenic space. **(C)** The hand within the small colon (SC) can be positioned between the spleen (S) and the kidney (K). **(D)** Moving the hand medial from the edge of the spleen allows palpation of the nephrosplenic ligament. **(E)** Palpation of the caudal pole of the kidney. Source, (B), (D), and (E): Courtesy of The Glass Horse, Science In 3D.

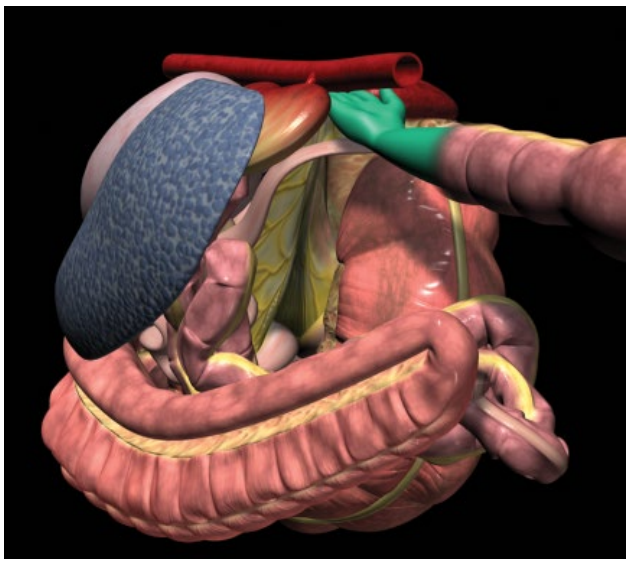
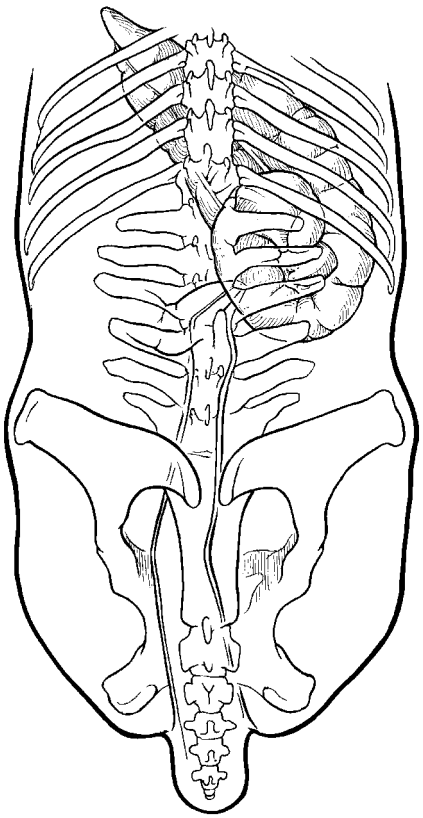


Figure 20.27 Extending the arm to the right of the left kidney and cranial to feel the aorta and mesenteric root. Source: Courtesy of The Glass Horse, Science In 3D.

(A)



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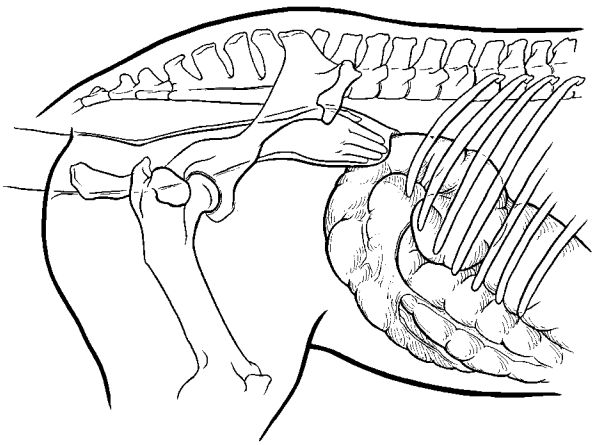

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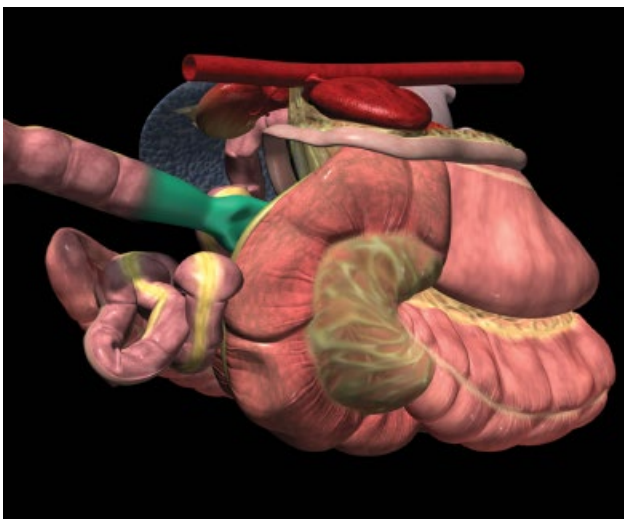

Figure 20.28 **(A, B)** The cecum is located in the right dorsal quadrant of the abdomen. Source: White & Moore, 1998. Reproduced with permission of Elsevier. **(C)** The medial and ventral tenia can often be palpated by moving the hand from cranial to caudal on the medial surface of the cecum to make these structures taut. Source: Courtesy of The Glass Horse, Science In 3D.

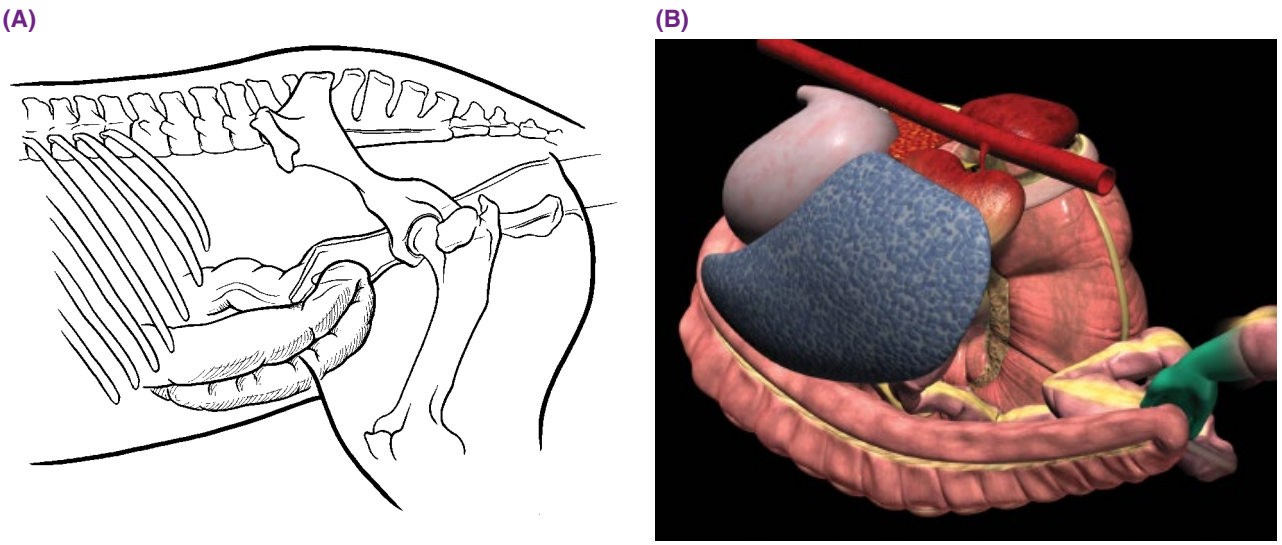

Figure 20.29 **(A)** The pelvic flexure of the large colon is normally positioned in the left ventral quadrant and is a soft structure filled with ingesta. Source: White & Moore, 1998. Reproduced with permission of Elsevier. **(B)** Because the lack of palpable tenia at the pelvic flexure the large colon is often not distinguishable from other intestine in normal horse. Source: Courtesy of The Glass Horse, Science In 3D.

quadrant and may be followed forward on the ventral midline on the floor of the abdomen (White, 1990). The examiner then moves caudally and to the left ventral quadrant where the pelvic flexure and the dorsal colon may be felt if they contain enough ingesta within the lumen (Figure 20.29). If the large colon is empty, the pelvic flexure is often out of reach and cannot be palpated. The left dorsal colon is identified by the fact it lacks palpable haustra or teniae; the only tenia is in the mesentery. In contrast, the adjacent left ventral colon has two free teniae (running cranial to caudal) and haustra (Mueller & Moore, 2000; Kopf, 1997). The small colon, usually containing formed fecal balls, can be palpated in various regions of the abdomen, but is often palpated in the left ventral quadrant (Figure 20.30) (White, 1990). The normal small intestine can sometimes be palpated if a peristaltic contraction occurs when touched, but usually cannot be identified unless it is distended.

At the completion this portion of the rectal examination, the caudal abdomen should be palpated, concentrating on the reproductive structures and pelvic rim. The urinary bladder should be palpated for thickening or calculi. In some cases, the bladder will be distended with urine, which may prevent palpation of the rest of the abdomen. In this case, the horse should be encouraged to urinate by terminating the examination and placing the horse in a stall or by catheterization of the bladder, if necessary. In the mare, the ovaries, uterus, and cervix should be palpated. Similarly, the internal inguinal rings need to be carefully palpated in stallions and geldings. The inguinal rings can be found by palpating the pelvic rim and then feeling cranial and just ventral and lateral to the cranial edge of the pelvis (Figure 20.31). In some stallions, a finger can be inserted into the inguinal ring and the ductus deferens is palpable in the caudomedial aspect of the vaginal ring. In geldings, the inguinal ring is much smaller and decreases in size with age, and the vas deferens is not usually palpable (O'Connor, 1971).

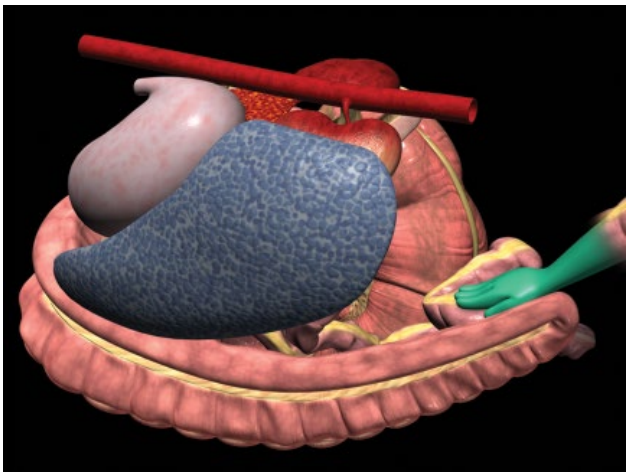

Figure 20.30 The small colon is normally found in the left abdomen and is identified by the formed fecal balls and single antimesenteric tenia. Source: Courtesy of The Glass Horse, Science In 3D.

When palpating a horse with colic, a specific diagnosis cannot always be made, but often a segment of intestine can be identified that is distended, impacted, or positioned abnormally. The diseases described in Chapters 50–57 have descriptions of rectal findings specific to each one. The typical abnormal findings are discussed here.

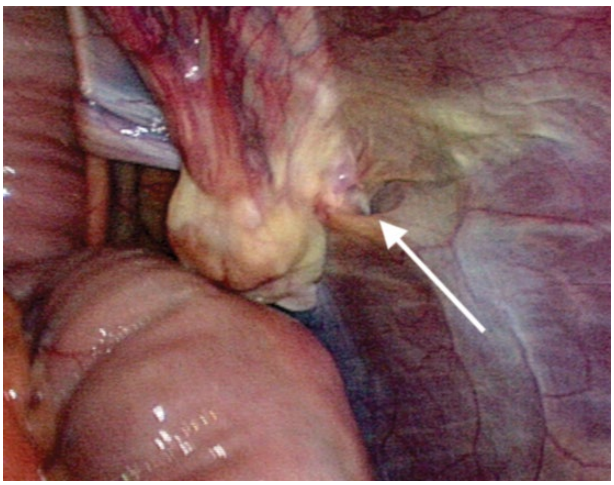

Figure 20.31 The inguinal rings are palpated to the left and right of the pelvis at the level of the floor of the pelvis. The internal ring a small slit in the peritoneum (arrow) is felt by moving the fingers over the abdominal wall as seen in this laparoscopic photograph.

Stomach and Small Intestine

Abnormalities of the stomach cannot often be palpated on rectal examination owing to the cranial position of the stomach. Distention of the stomach, as occurs with gastric impaction, may cause the spleen to be displaced caudally and away from the left abdominal wall. However, this splenic position can also be due to primary splenic enlargement. The small intestine, including the duodenum, jejunum, and ileum, cannot always be palpated in the normal horse. In horses with small intestinal obstruction or duodenitis-proximal jejunitis, a distended duodenum can be palpated as a tubular structure on midline just ventral to the aorta over the base of the cecum (Figure 20.32) (White, 1990; Huskamp, 1985; White et al., 1987). If there are no abnormalities indicating an obstruction of the stomach or small intestine but large volumes of reflux are obtained, a proximal jejunal, duodenal, or primary gastric lesion should be suspected. Obstruction in the small intestine or ileus results in a

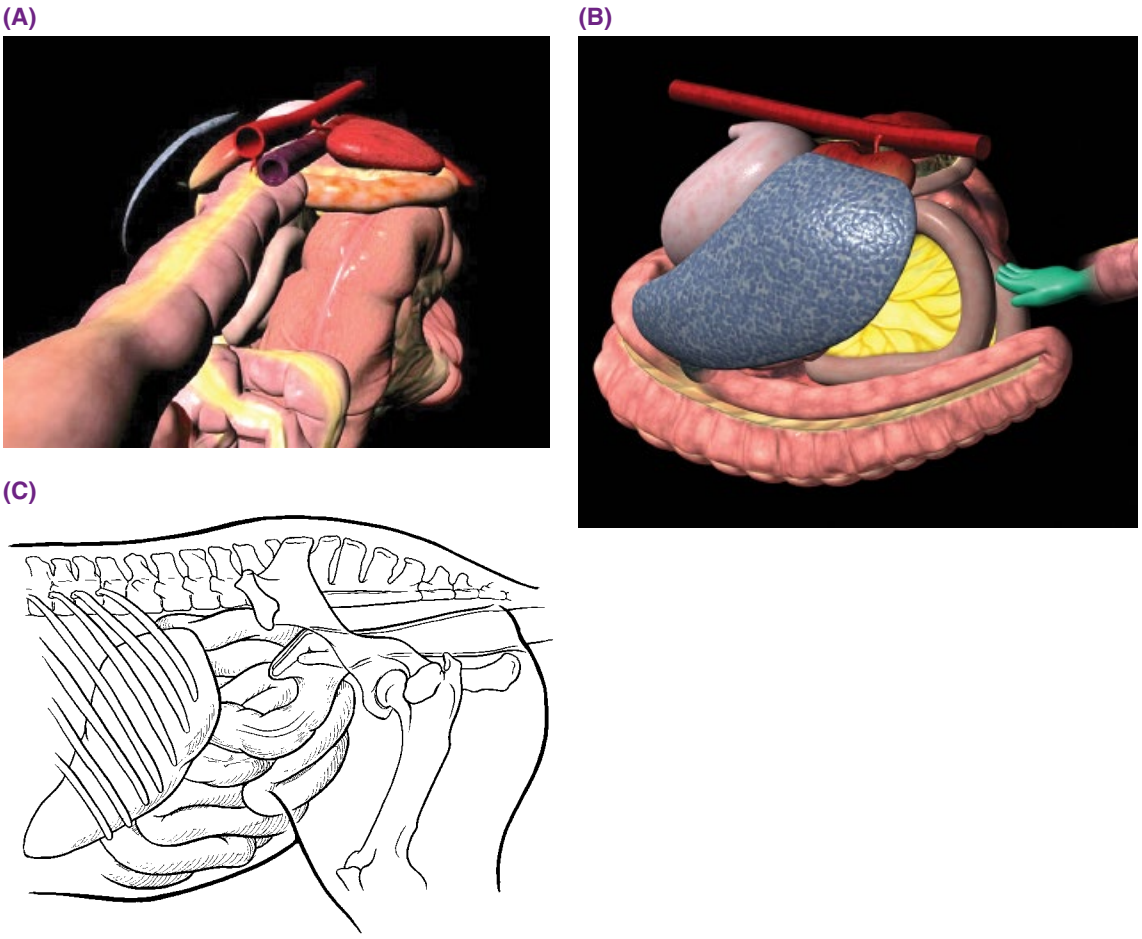

Figure 20.32 **(A)** Distended duodenum is felt at the dorsal aspect of the cecum in cases of duodenitis-proximal jejunitis. **(B)** Distended jejunum or ileum is tubular and filled with gas or fluid. The distention may be felt as one or two loops early in obstructive disease, or **(C)** may fill abdomen so the intestine is found just cranial to the pelvis. Source (A) and (B): Courtesy of The Glass Horse, Science In 3D. Source (C): White & Moore, 1998. Reproduced with permission of Elsevier.

distended small intestine, which feels like several soft to turgid tubes (Figure 20.32). The gas and fluid within the small intestine may move owing to peristaltic waves, which may be appreciated as a change in distention by the examiner (White, 1990). As the small intestine distends, the loops fold on themselves, creating alignment of the intestine, which can be found in any quadrant but often in the center of the abdomen (White, 1990). Even if only one or two small intestinal loops are palpable, there may be more present that cannot be palpated. When the small intestine is very distended, it can take up the space of almost the entire abdomen and extend into the pelvic canal. In such instances, distended small intestine will be the first structure felt during the rectal examination (Figure 20.31). The examiner should appreciate the amount of distention as this may affect the decision for surgery. If the small intestine is tightly distended, even in the case of duodenitis-proximal jejunitis, surgery may be required to decompress the small intestine.

An estimate of the intraluminal pressure may be made by estimating the tension and intestinal diameter. It is possible for distended small intestine to have an estimated diameter of 5–10 cm. The ileum can reach a very large diameter of 12–15 cm when very distended. In such instances, the distended ileum can be mistaken for the large colon, except that it has a thin mesentery (White, 1990). These measurements can be confirmed by an abdominal ultrasound examination. Pain associated with the ileal mesentery may occur in response to palpation of the normal ventral and medial cecal ligaments and has been associated with conditions such as epiploic foramen entrapment (Kopf, 1982). It is possible that this may occur with other small intestinal lesions and is therefore not a definitive test for ileal disease (White, 1990). Ileal impaction can sometimes be palpated as a dough-like mass medial to the cecum on the right side of the abdomen. When small intestine is trapped in the inguinal canal, a strand of mesentery, which is not normally attached to the inguinal ring, may be palpated; this mesentery may be very painful when traction is applied (Figure 20.33) (Kopf, 1997). Jejunojejunal intussusceptions may be distinguished by the thickened, edematous tubular structure that is created along with generalized small intestinal distention (Mueller & Moore, 2000).

When a diagnosis is not made, rectal examinations are best repeated to monitor whether the distention is increasing and is therefore indicative of a strangulating lesion rather than ileus or enteritis. Small intestinal distention will often lessen after gastric fluid is constantly removed via a nasogastric tube in horses with duodenitis-proximal jejunitis.

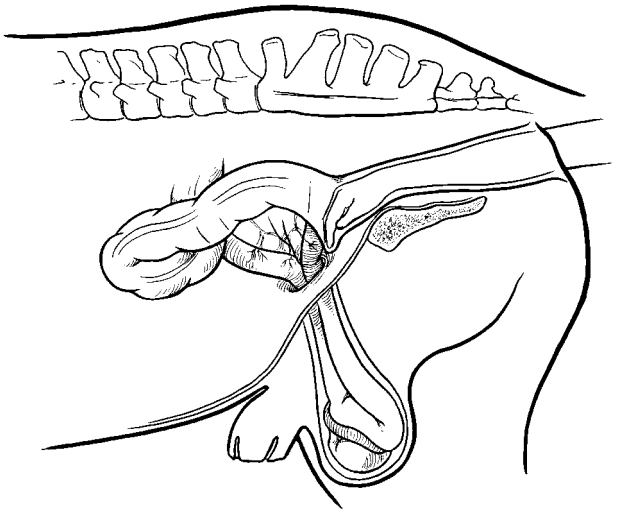

Figure 20.33 Small intestine trapped in the inguinal ring may not be distended but it may fill the ring so that the opening cannot be felt. The intestine or mesentery becomes taut and is felt to be attached at the inguinal ring. Source: White & Moore, 1998. Reproduced with permission of Elsevier.

Cecum

The cecum will become large and distended when there is a primary condition affecting the cecum or when there is obstruction of the large or small colon. When the cecum becomes distended, the teniae become taut and the cecum displaces toward midline. The ventral tenial band, which is normally vertical in orientation, can be traced from the right dorsal to the left cranioventral quadrant across the caudal abdomen (Figure 20.34) (Collatos & Romano, 1992). When the cecum is distended with gas, as occurs with primary cecal disease or large colon obstruction, the cecum is pushed back to the pelvic inlet. It will feel like a tightly distended balloon in the right dorsal quadrant, and may be difficult to differentiate from right dorsal displacement of the large colon (Mueller & Moore, 2000). However, when the cecum is full of fluid and ingesta, the weight of the cecal apex pulls it cranially and ventrally and it fills most of the right ventral quadrant. When the impaction extends above the cecocolic orifice causing complete obstruction, the cecal base fills with fluid and the cecum distends to fill both the right dorsal and ventral abdominal quadrants (Mueller & Moore, 2000). A very thickened cecum may indicate that the cecum is devitalized. A mass or edematous bowel in the right dorsal quadrant may be indicative of cecocecal or cecocolic intussusception (Martin et al., 1999).

Gas distention of the cecum may prevent complete evaluation of the abdomen. Trocarization of the cecum through the right flank while completing the examination can help evacuate the cecum and provide access to more regions of the abdomen (see Chapter 53).

Large Colon (Ascending Colon)

The large colon can move to many different positions when displaced or obstructed. The pelvic flexure is

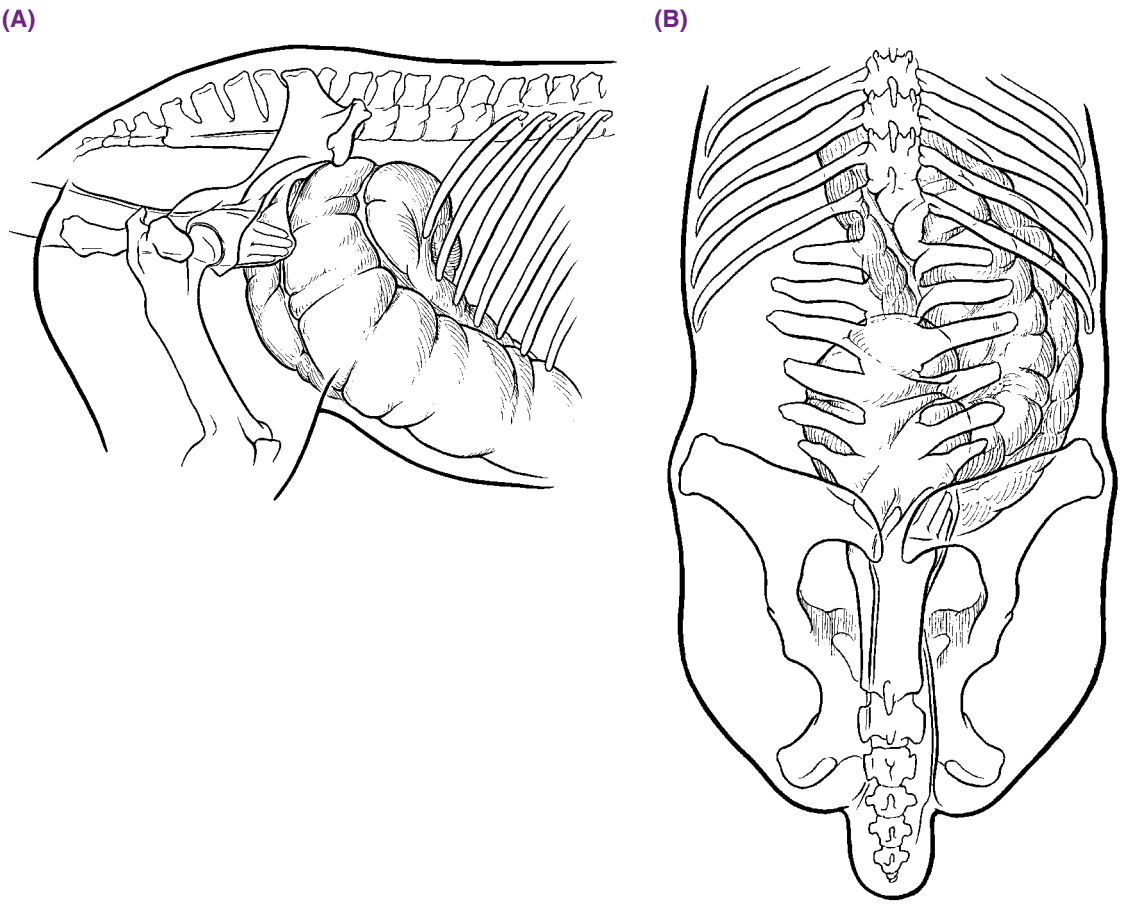

Figure 20.34 Distention of the cecum can be detected immediately upon moving past the pelvis. Characteristically the cecum is distended caudal toward the pelvis (**A** and **B**) and the ventral tenia courses from the right dorsal quadrant to the left ventral quadrant when the cecum is filled with gas and toward midline when the cecum is impacted or fluid filled. Source: White & Moore, 1998. Reproduced with permission of Elsevier.

usually palpated in the left ventral quadrant, but when it becomes impacted and enlarges it will extend to the right ventral quadrant or be palpable immediately cranial to the pelvic brim (Figure 20.35). When the large colon is severely impacted, it may fill the entire caudal abdomen with the pelvic flexure entering the pelvic inlet from the right side of the abdomen. When impactions are present, it is important to determine whether the large colon is simply impacted or displaced. A left dorsal displacement in the nephrosplenic space can be palpated before the large colon is severely distended. The displacement can be diagnosed if the large colon is found over the nephrosplenic ligament, and suspected if it is between the spleen and body wall or if the spleen is displaced medially and ventrally (Figure 20.36) (Burba & Moore, 1997). Medial displacement of the spleen alone is not diagnostic for this condition and ultrasound may be required to confirm the diagnosis. In one retrospective study, rectal examination was diagnostic of this displacement in 72% of cases (Hardy et al., 2000). However, it is not always possible to feel the position of the colon if there is a large amount of large colon distention. When very distended, the entrapped large colon may prevent palpation of the nephrosplenic space. In this case, the examiner will not be able to differentiate a gas-distended large colon from one that is dorsally displaced.

The position of the large colon in horses with right dorsal displacement will vary. In the most common presentation, the colon retroflexes and is located between the cecum and the right body wall (Mueller & Moore, 2000). The large colon and the teniae will be felt cranial to the pelvic rim coursing from the right caudal abdomen transversely toward the left cranial abdomen (Mueller & Moore, 2000). The pelvic flexure is usually out of reach within the left cranial abdomen and the colon displaces the cecum medially and cranially, which makes it difficult to palpate (Mueller & Moore, 2000). The cecum may also become distended over time.

Other displacements may result in the large colon being very distended and pushed back into the pelvic canal, with the pelvic flexure not palpable (White, 1990). With a very cranial displacement, when the pelvic flexure

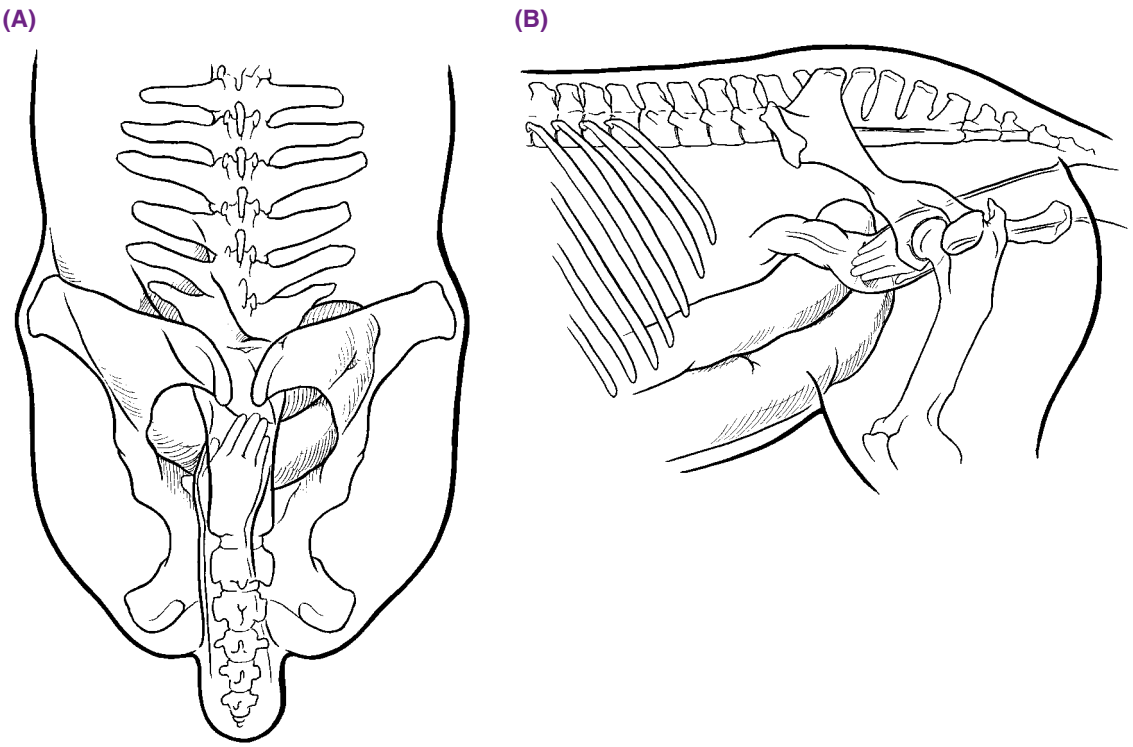

Figure 20.35 During impaction of the large colon, the pelvic flexure is enlarged and the dough-like ingesta is indentable with the fingers. When filled, the colon can be found in the ventral abdomen with the pelvic flexure on the right side **(A)** and sometimes moved into the pelvic inlet from the right side **(B)**. Source: White & Moore, 1998. Reproduced with permission of Elsevier.

is against the diaphragm, a very distended large colon may not be present at the pelvic inlet and the pelvic flexure will not be palpable.

Large colon volvulus typically results in more distention than a simple displacement. However, distention may not be severe in the early stages of a volvulus. Often the pelvic flexure is palpable on the right side, but is displaced cranially, Furthermore, the haustra of the ventral colon may be located dorsal to the dorsal colon, which indicates the presence of at least a 180° volvulus. A large amount of the cecum and large colon may be displaced cranially and not be palpable. In these cases, the horse's severe level of pain and progressive distention indicate that surgery is necessary. As the large colon fills with gas and fluid, the colonic veins become occluded, which initiates edema formation in the intestinal wall and mesentery. If the large colon volvulus progresses from 180° to 360°, the large colon will enlarge immediately and push back toward the pelvic inlet, often in a horizontal position. A volvulus of 360° or more will cause severe distention and often the colon is pushed back into the pelvic inlet. The distention may be sufficient to prevent passage of the examiner's hand past the pelvic brim (Figure 20.37). As the colon wall fills with blood and fluid, the haustra become prominent features during palpation of the colon. These horses may have decreased venous return to the heart and respiratory compromise.

Decompression of the gas-filled colon can be attempted through the abdominal wall, but there is an increased risk of bleeding if the colonic vasculature is penetrated by the trochar. Transrectal aspiration of gas is possible, but requires instrumentation that will not risk injury to the rectum or small colon (Scotti et al., 2013).

Small Colon (Descending Colon)

The small colon is usually identified in the left caudal abdomen based on the palpation of formed fecal balls, which can be present throughout its length. Fecaliths and enteroliths in the small colon may be palpable in the ventral abdominal quadrants, but will not be palpable if they are located in the proximal small colon or in the transverse colon. Enteroliths are not commonly palpable on rectal examination. However, because they can cause complete obstruction, large colon and cecal distention is common. In some cases, distention of the right dorsal colon or transverse colon may be palpable on the dorsal midline or in the right dorsal quadrant (White, 1990).

Small colon impactions create a long, thick, tubular structure with no obvious fecal balls felt on palpation. The impaction often extends forward beyond the examiner's reach. The small colon is identified by its antimesenteric and prominent mesenteric bands. In severe small colon impactions, the entire small colon may be filled with ingesta and the rectal ampulla may be pulled ventrally

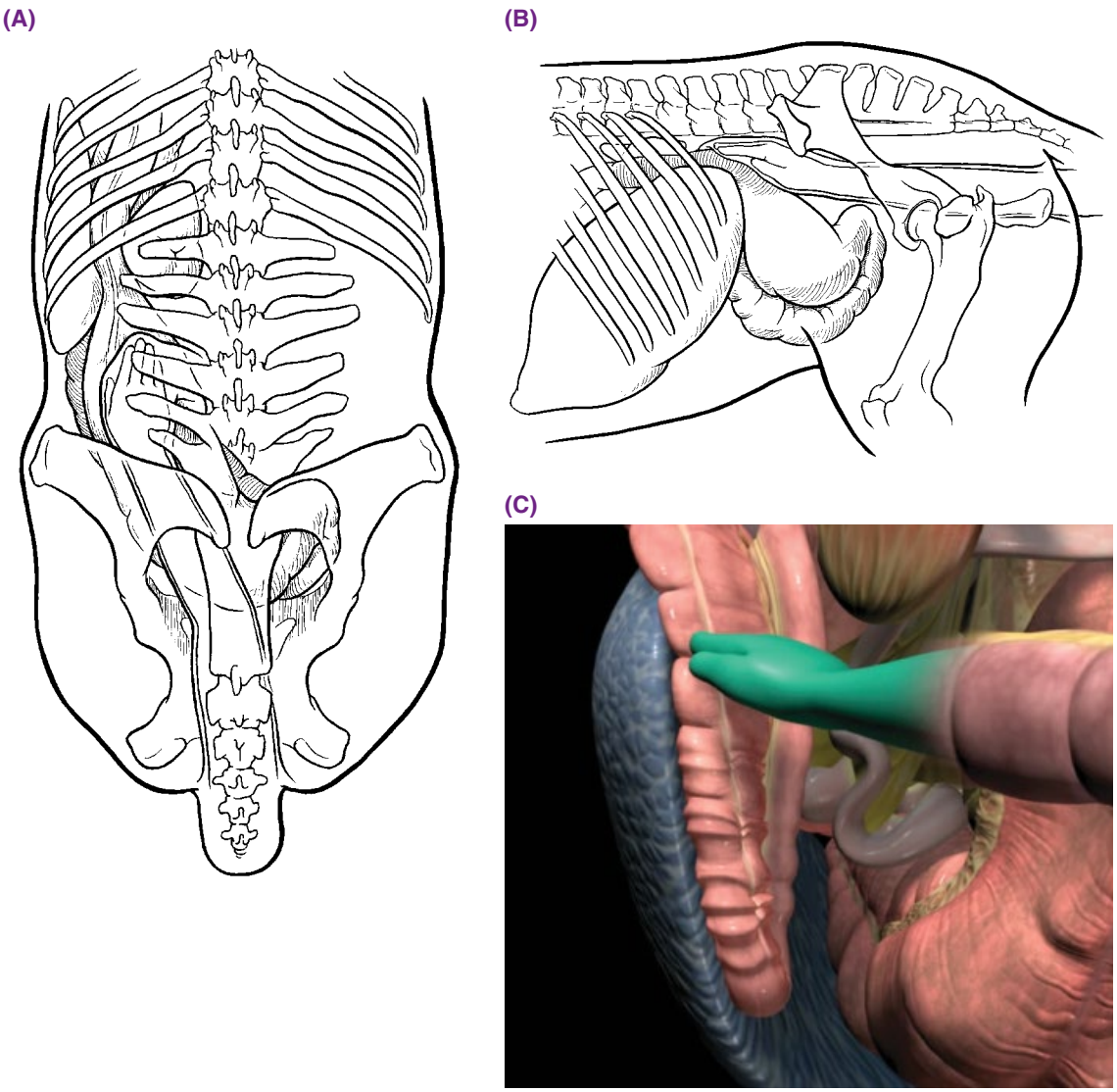

Figure 20.36 **(A, B)** During entrapment of the large colon in the nephrosplenic space, the colon can be felt between the left kidney and the spleen in the left dorsal quadrant of the abdomen. The spleen is often displaced and enlarged. Source: White & Moore, 1998. Reproduced with permission of Elsevier. **(C)** If the colon is distended it may prevent palpation of the spleen and can be followed to the region of the nephrosplenic space. Source: Courtesy of The Glass Horse, Science In 3D.

and to the left of midline by the weight of ingesta and the tension on the mesentery (Mueller & Moore, 2000). The most common lesions affecting the rectum include tears and perirectal abscesses. At the end of the rectal examination, the rectal sleeve should be examined carefully for the detection of blood consistent with rectal mucosal irritation or a possible tear.

Miscellaneous Abnormalities

Other structures that may be palpated include abscesses, adhesions, or masses (neoplastic or benign). Abscesses usually occur in the small intestinal mesentery and may be associated with adhered loops of small intestine (White, 1990). Other abdominal abscesses may be palpable in various locations and definitively diagnosed with the aid of transrectal ultrasonography. Splenomegaly may be detected by rectal palpation and is characterized by the spleen extending medially and caudally. The splenic border is rounded and the surface of the spleen may feel irregular or nodular on the surface if there is a neoplastic process present. Intestinal or omental adhesions can be difficult to palpate, but may be felt if they adhere to the inguinal rings, small colon, or abdominal wall or in the pelvic canal. Contracted small intestinal adhesions are sometimes palpable at the root of the mesentery and are thick, nodular, and hard (White, 1990). In these cases, the small intestine will be chronically distended and thickened. Adhesions of the large colon to the abdominal wall, or associated with omentum, are not usually palpable, but sometimes adhesions from an enterotomy site to

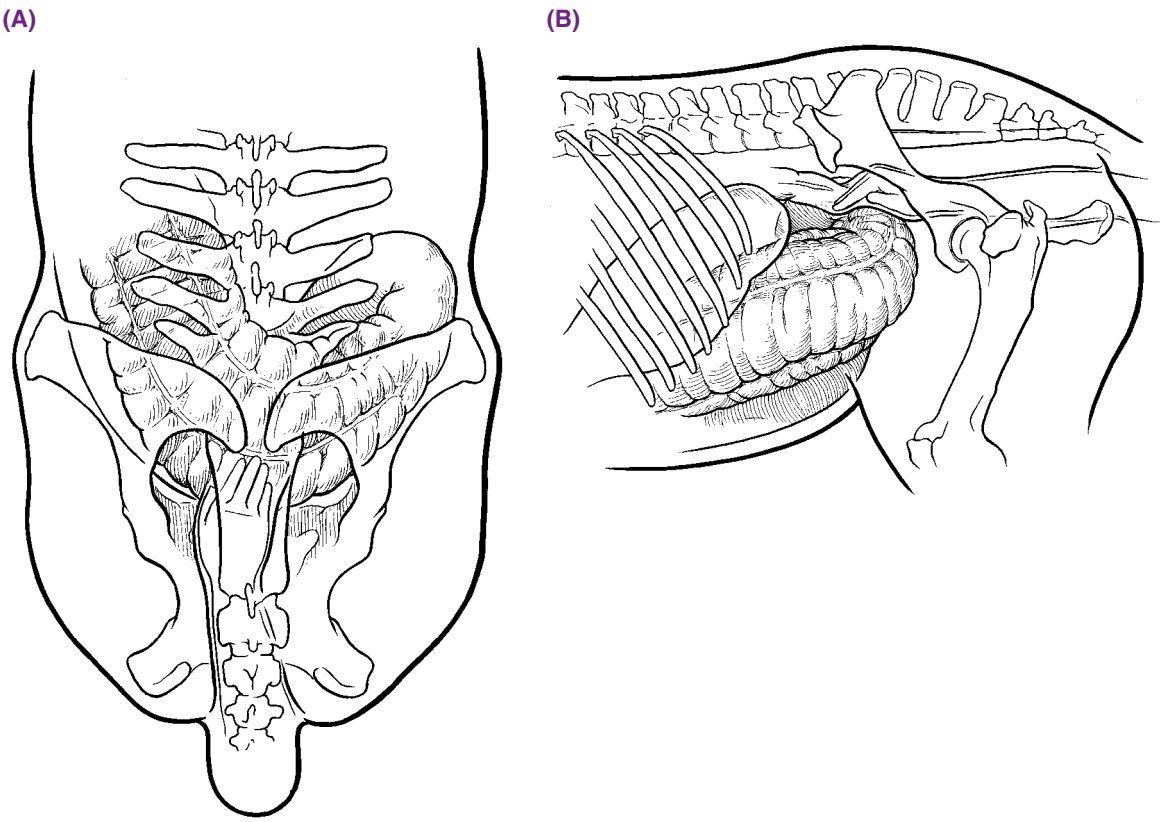

Figure 20.37 Large colon volvulus rapidly fills the abdomen and is felt as a gas and fluid-filled viscus **(A)** that is frequently positioned horizontally in the abdomen and is pushed back toward the pelvic inlet. **(B)** As the colon distends, the wall becomes thickened and creates rounded ridges on its surface Source: White & Moore, 1998. Reproduced with permission of Elsevier.

the pelvic rim will be palpable (White, 1990). Benign and malignant tumors can cause colic and neoplastic masses can sometimes be identified on rectal palpation. Most common neoplastic processes involving the abdominal cavity consist of pedunculated mesenteric lipoma, lymphoma, adenocarcinoma, and squamous cell carcinoma (Taylor et al., 2006; Santschi, 2012).

Late Gestational Mares

Rectal palpation in late gestational mares is a challenge because the gravid uterus prevents a thorough examination of the abdomen. Distended large colon and cecum can be felt around the uterus in some mares, but lesions such as small intestinal distention may not be palpable and require identification with abdominal ultrasound. Uterine torsion should be considered in the last trimester of pregnancy, and rectal palpation is essential to make the diagnosis because vaginal palpation is rarely of value. The broad ligaments will be taut as they cross the caudal abdomen below and above the cervix in mares with uterine torsion (Mueller & Moore, 2000). In most cases, the direction of the torsion can be determined by relative displacement and asymmetry of the left and right broad ligaments (Pascoe et al., 1981; Vasey, 1993). However, with chronic uterine torsions, the broad ligaments may not be palpable and rectal findings may be inconclusive (Doyle et al., 2002). Hematoma can be identified as a large, firm mass within the broad ligament to the right or left side of the uterus of colic mares with postpartum hemorrhage.

Other Findings

The examiner should pay attention to the feel of the peritoneal surface. If the intestines feel as if they are moving through fluid rather than slipping past each other, this may indicate the presence of excessive peritoneal fluid (White, 1990). Fibrin deposition will feel like roughening on the intestinal surfaces, while there will be crepitus and a rough granular feel to the intestinal surface when a component of the gastrointestinal tract has ruptured, causing fecal contamination of the abdomen. Emphysema may also be palpable after rupture of intestine. For example, crepitus may be palpated in the cecal wall or in the fibrin covering of an area of rupture in the bowel wall (White, 1990). When gas escapes into the abdomen, the viscera fill the ventral abdomen, creating an open space filled with gas in the dorsal quadrants. In certain conditions,

such as a diaphragmatic hernia, the abdomen may feel quite empty. Therefore, a negative rectal examination does not always rule out a surgical problem.

Abdominocentesis

Abdominocentesis should be performed after the rectal examination and, if equipment is available, after an ultrasound examination. If there is massive distention of the large colon due to an impaction lying against the ventral abdominal wall, abdominocentesis is performed so as not to puncture the bowel inadvertently. The same precautions should be applied to late-pregnancy mares in which the gravid uterine horn can occupy most of the ventral abdomen. Bowel containing a large amount of sand is also at risk of being penetrated. An ultrasound examination can be used to locate a pocket of abdominal fluid. If ultrasound is not available, the abdominocentesis should be performed on the ventral midline or to the right of midline to avoid puncturing the spleen. The site for abdominocentesis is the lowest, most dependent part of the ventral abdomen, which is usually at the cranial aspect of the ventral midline just caudal to the xiphoid.

Peritoneal fluid can be collected using an 18-gauge 1.5 inch needle or a teat cannula. Using a needle is the simplest method through an aseptically prepared site on ventral midline. The needle is inserted directly into the abdomen through the linea alba (Figure 20.38). If the large colon or cecum is penetrated, the needle can be pulled out enough to be redirected to another point within the abdomen. Once peritoneal fluid flows from the needle removing the contaminated fluid, the sample can be collected. Placing a second needle may be helpful to remove the vacuum in the peritoneal cavity to allow fluid to flow from the first needle. Pushing gently on the side of the horse to shift the weight of the viscera may also encourage the fluid to flow.

Enterocentesis is usually not a serious complication, except for foals in which the intestine may not seal adequately (White, 1990; Tulleners, 1983; Schumacher et al., 1985). In foals or adult horses with heavy intestine pressed against the ventral abdominal floor, a blunt-teat cannula is preferred for abdominocentesis. It may be necessary to avoid the heavy intestine by entering the abdomen at a paramedian location or at a location identified with ultrasound. The paramedian approach may increase the chance of a vessel being encountered in the rectus abdominis muscle (White, 1990). Although blunt-teat cannulas are normally safer than needles, inadvertent puncture of the large colon or cecum can result. Although these punctures normally seal by contraction and fibrin, contamination with the ingesta may make cytologic evaluation impossible.

Prior to using a teat cannula for abdominocentesis, a small, shaved site is aseptically prepared. A small bleb of local anesthetic is placed into the skin and up into the abdominal wall at the site of entry with a 23–25-gauge needle and 3 mL syringe before the final scrub. Wearing sterile gloves, the veterinarian makes a stab incision through the skin and part way through the abdominal wall with a #10 or #15 blade (Figure 20.39),

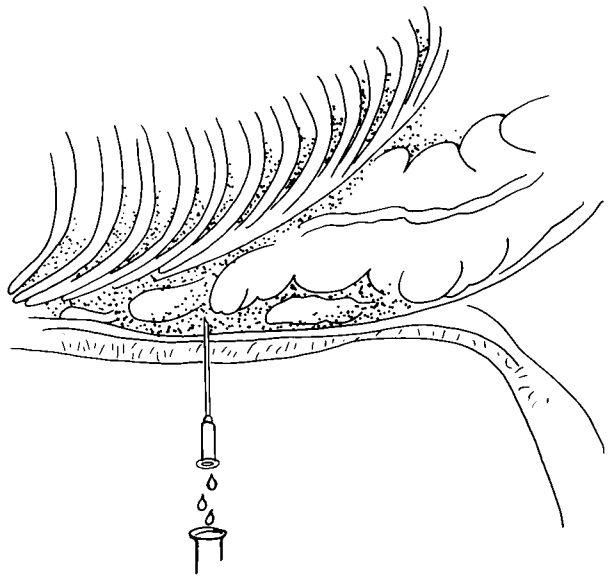

Figure 20.38 Placing an 18-gauge 1.5 inch needle through the linea alba often provides enough peritoneal fluid needed for analysis.

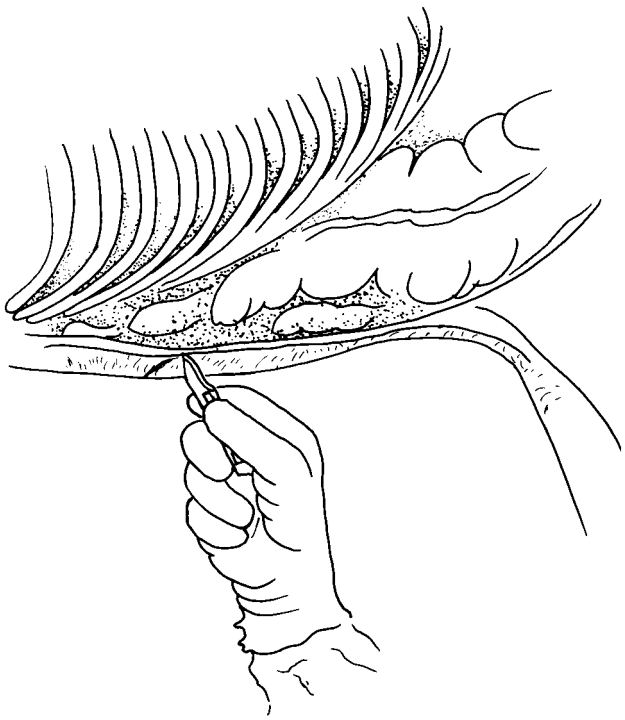

Figure 20.39 Making a small incision the skin and part way through the linea alba with a #15 scalpel blade allows a teat cannula to pushed through the linea alba and peritoneum into the abdomen.

thereby facilitating the passage of the teat cannula. The large subcutaneous vessels should be avoided to prevent sample contamination and hemorrhage. The teat cannula is pushed through the middle of a sterile gauze swab and then gently inserted into the stab incision and into the abdomen (Figure 20.40). The swab protects the sample collection tube from blood contamination from small vessels that are cut during the skin incision. The cannula is manipulated until it is felt to "pop" through the peritoneum. In some horses, there is a thick layer of retroperitoneal fat that requires the use of a canine urinary catheter to penetrate the peritoneum. Some manipulation of the teat cannula within the abdomen may be required to locate a pocket of fluid. Potential complications related to abdominocentesis include inadvertent enterocentesis, injury to the spleen, and omental herniation in foals when the teat cannula technique is used. The incidence of inadvertent enterocentesis has been reported at 2–5% (DeHeer et al., 2007) and secondary complications at 0.5% (Tulleners, 1983).

The peritoneal fluid should be collected into a potassium EDTA tube for cytology and a serum tube for bacterial culture and sensitivity, if indicated. An EDTA tube, which has been shaken out, can be used if only a few drops of peritoneal fluid are obtained. This avoids generating an abnormally high protein concentration value when using a refractometer. Once the fluid has been collected, it is observed by gross visual examination. Laboratory analysis is completed to evaluate protein concentration, white blood cell (WBC) count, cytology, and differential count and Gram stain for presence of bacteria. Normal peritoneal fluid is a clear, pale-yellow fluid (Figure 20.41) (Coffman, 1980b; Crowell et al., 1987; Nelson, 1979). The fluid will be cloudy if it contains increases in protein, WBCs or red blood cells (RBCs) (Figure 20.42). The presence of RBCs may increase the turbidity, but the fluid may not appear red until there are sufficient numbers of RBCs present. The fluid changes in color from golden to orange and then to red as the number of RBCs in the fluid increases (Figure 20.43). If the fluid is serosanguineous, it is indicative of sufficiently ischemic or infarcted bowel, which allows a large number of RBCs to leak through the capillaries (Bayly & Reed, 1980; Hunt et al., 1986; Parry, 1986; Rumbaugh et al., 1978; Wilson & Gordon, 1987). Green to reddish brown fluid with or without visible plant material is consistent with bowel rupture or enterocentesis. Whitish yellow opaque-looking fluid indicates large numbers of WBCs within the fluid, as occurs with peritonitis (White, 1990).

Although it is uncommon to retrieve whole blood during an abdominocentesis, this can occur if the spleen has been punctured, an intestinal vessel has been lacerated, or there is intra-abdominal hemorrhage from a traumatized mesenteric vessel (broodmare after foaling), or from a mass such as a neoplastic mass on the spleen. Dark blood may represent venous blood leaking into the abdomen from a mesenteric vessel draining an incarcerated loop of bowel (e.g., in the epiploic foramen or a mesenteric rent). Fat may sometimes be seen in the sample

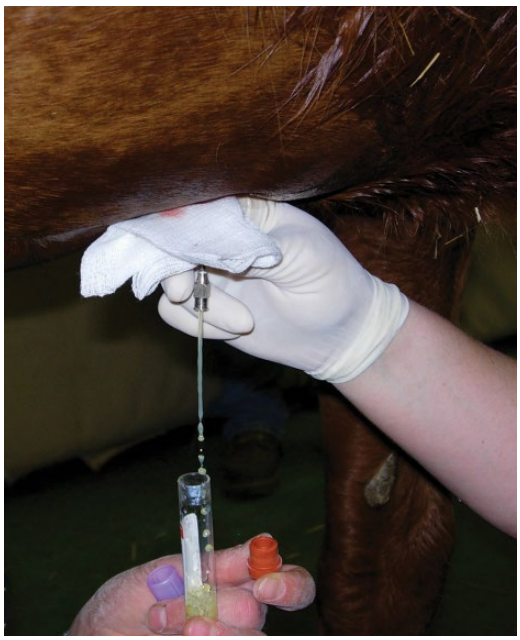

Figure 20.40 A teat cannula is pushed through a small incision using a sterile 4 × 4 inch gauze swab to prevent blood from the stab incision from contaminating the fluid sample.

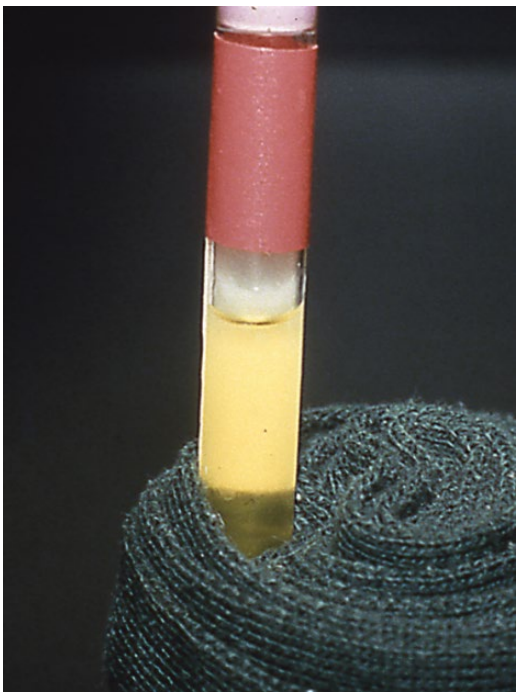

Figure 20.41 Normal color and transparency of peritoneal fluid.

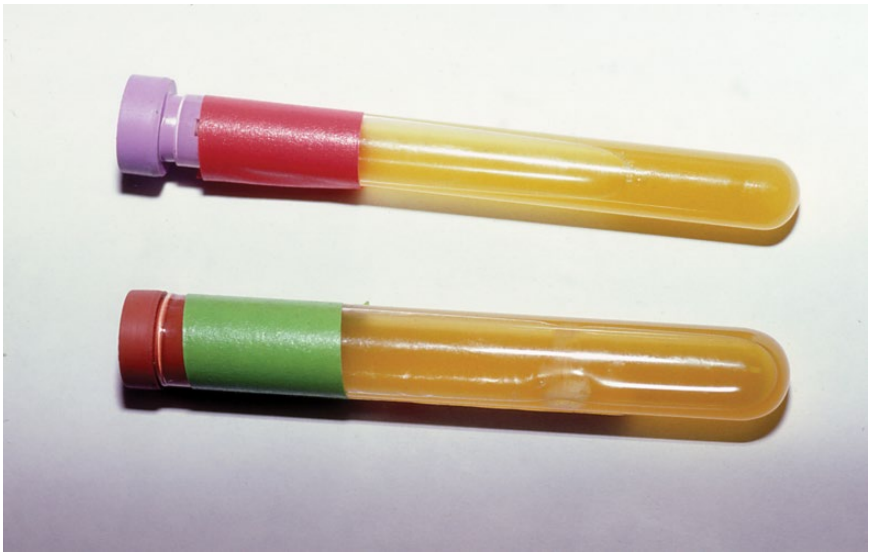

Figure 20.42 Cloudy or turbid peritoneal fluid indicates an exudate with WBCs or rarely fat or chyle.

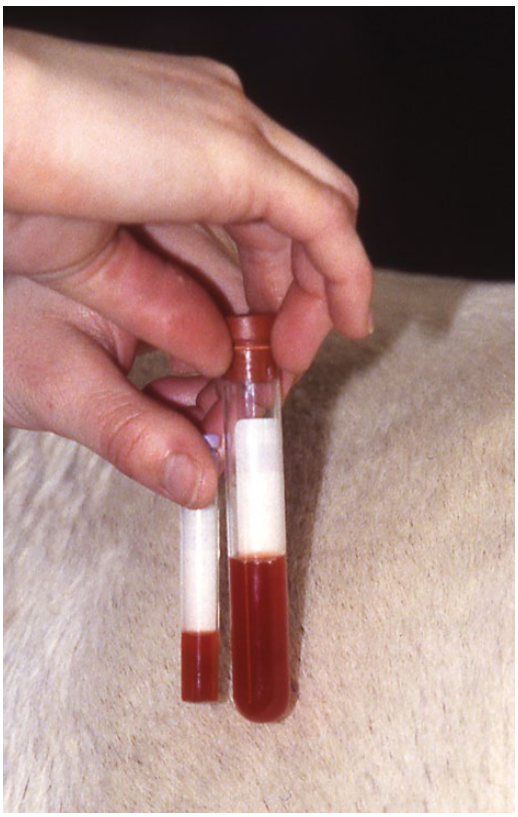

Figure 20.43 Serosanguineous fluid indicates strangulation or hemorrhage.

from retroperitoneal fat or mineral oil if there has been a rupture, such as a gastric rupture, after administration of oil (White, 1990).

If a sample appears as whole blood, a PCV should be determined. If there are low numbers of cells, the sample can be centrifuged and the layer of cells can be smeared onto a slide before staining (White, 1990). The most common stains used are Wright's stain and the Gram stain (Prasse & Duncan, 1976; Crowell et al., 1987). New methylene blue can also be used as a quick technique, but the cellular differentiation is not as good (Crowell et al., 1987). Staining allows a differential count to be calculated, the cells to be evaluated for degenerative changes, and identification of bacteria or plant material.

Reported WBC concentrations for healthy horses are 5000–10,000 cells/μL ($5.0–10.0 \times 10^9$/L) for adults and 1500 cells/μL (1.5×10^9/L) for foals (Fischer, 1997). These reported values are high for most healthy horses, which rarely have WBC concentrations exceeding 3000 cells/μL (3.0×10^9/L). The normal cell distribution reflects a 2 : 1 ratio of neutrophils to mononuclear cells (Ragle, 1999) and occasional mesothelial cells (White, 1990).

There should be no RBCs in normal peritoneal fluid. If red discoloration is seen grossly, it is the result of lysed and whole RBCs. However, small numbers of cells will not alter the color of peritoneal fluid and cannot be seen with the naked eye. In order to detect the presence of small numbers of RBCs, which may indicate questionable intestinal viability, spectrophotometric assessment of hemoglobin in the peritoneal fluid can be performed. This can aid in selecting medical versus surgical treatment and has a high sensitivity (80%) and specificity (82%) (Weimann et al., 2002). Increased hemoglobin concentrations were reported to identify whether or not horses were at a higher risk of needing surgery (Weimann et al., 2002); visual assessment had a much lower sensitivity of only 51% (Weimann et al., 2002).

The normal peritoneal protein concentration is 0.8–1.2 g/dL (8.0–12.0 g/L). Higher concentrations (>2.0 g/dL, 20.0 g/L) indicate inflammation of the intestine or the peritoneal cavity (Brownlow et al., 1981). The peritoneal fluid protein concentration can easily be measured using a handheld refractometer. Although the normal value for

peritoneal fluid protein is reported to be <2.5 g/dL (<25 g/L) with this technique (DeHeer et al., 2007), direct protein measurement more accurately reflects the response of the peritoneum to inflammation, ischemia, or intestinal distention.

In the early stages of acute obstruction or strangulation, peritoneal fluid may be normal because the intestine is not sufficiently devitalized to allow leakage of cells and protein. However, in cases of peritonitis, nonstrangulating infarction, and small intestinal enteritis, peritoneal changes frequently are present at the time that the clinical signs become apparent (White, 1990). In horses with persistent simple obstruction with intestinal distention, the protein level in the peritoneal fluid will increase, but the cell and differential counts will remain normal. If the obstruction creates enough distention to cause bowel-wall ischemia, cell concentrations in the fluid will increase. Peritoneal fluid changes associated with strangulating obstruction occur after approximately 1–2 h, depending on the type and severity of the lesion. RBC counts >20,000 cells/μL indicate a severe intestinal injury (Figure 20.44) (Hunt et al., 1986). When the bowel is devitalized, neutrophil counts increase to 5000–30,000 cells/μL ($5–30 \times 10^9$/L) and the ratio of neutrophils to mononuclear cells will increase such that neutrophils comprise 90–95% of the total white cells (Figure 20.45). As the intestine deteriorates further, the number of neutrophils may increase to 100,000–150,000 cells/μL ($100–150 \times 10^9$/L) and the cells appear degenerate (Crowell et al., 1987; Nelson, 1979). Degenerative and toxic changes to the neutrophils in response to the bacteria and toxins contaminating the abdomen include swollen nuclei, karyolysis, homogeneous pink-staining chromatin, vacuolization, and karyolysis (Figure 20.46) (Duncan et al., 1994).

Peritoneal fluid in horses with nonstrangulating infarction can appear similar to other that in conditions with increases in protein concentration and WBC counts (300,000–400,000 cells/μL; $300–400 \times 10^9$/L); these changes often are present at the time of onset of colic (White et al., 1989). If there are no RBCs but a very high WBC count, then nonstrangulating infarction or primary peritonitis should be suspected (White, 1990).

If the peritoneal fluid has the appearance of whole blood, the PCV should be measured. If the PCV is higher than it is in the circulation, the blood is likely from the spleen being punctured during abdominocentesis (White, 1990). If the hemorrhage has come from a blood vessel within the abdomen, the PCV will be the same as that of the systemic circulation and platelets will be evident. If the blood has been present for some time, erythrophagocytosis by the mononuclear cells will be seen and platelets will be absent (White, 1990).

Different ratios of components of the peritoneal fluid have been used to classify the type of disease. When the ratio of the neutrophils to the total protein is calculated

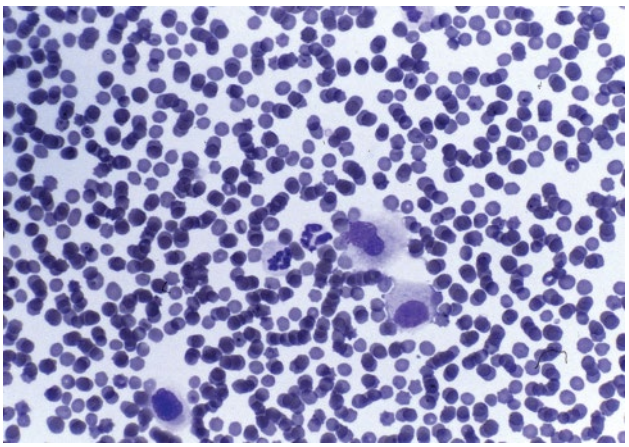

Figure 20.44 Excess RBCs are an indicator of abdominal hemorrhage.

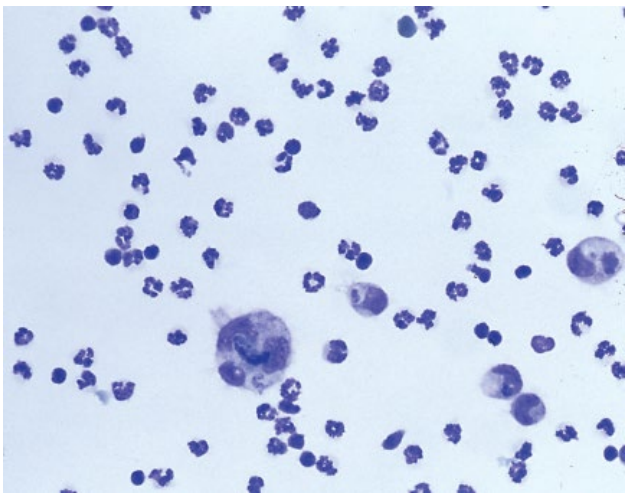

Figure 20.45 Increased numbers of neutrophils are an indicator of infection, intestinal injury such as strangulation, or intestinal leakage.

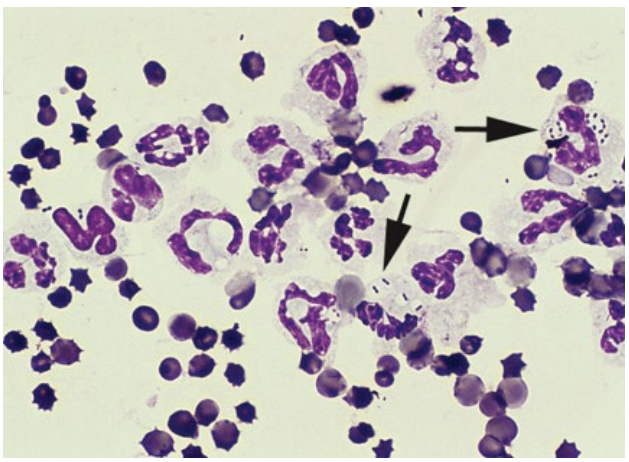

Figure 20.46 Neutrophils in peritoneal fluid that have phagocytized bacteria (arrows) and are undergoing karyolysis and karyorrhexis due to strangulated intestine.

to be <3, enteritis and simple obstruction are more likely to be present, whereas higher ratios occur with strangulated intestine. Similarly, a ratio of RBCs to total protein concentration of ≤15 has been shown to be more indicative of proximal enteritis compared with higher ratios being associated with strangulating lesions (Morris & Johnson, 1986).

Bacteria may be present in the peritoneal fluid due to leakage through deteriorating or ruptured bowel. The Gram stain will allow the identification of the type of bacteria present and will help differentiate a mixed population of bacteria, which can indicate bowel rupture (Figure 20.47). The presence of bacteria does not always indicate a poor prognosis, as horses with devitalized bowel and translocated bacteria can survive with appropriate surgical and medical treatment. However, the presence of feed material free floating in the abdomen owing to bowel rupture is associated with no chance of survival. Often bacteria will be present in only small numbers and may be phagocytized by neutrophils. Consequently, it is important that all slides be examined thoroughly (Figure 20.47) (White, 1990).

Peritoneal fluid pH and glucose concentration can be used to assist in the diagnosis of septic peritonitis (Van Hoogmoed et al., 1999). Glucose concentration differences between serum and peritoneal fluid of >50 mg/dL (>2.77 mmol/L), peritoneal fluid pH <7.3, peritoneal fluid glucose concentration <30 mg/dL (<1.67 mmol/L), and peritoneal fluid fibrinogen concentration >200 mg/dL (>2.0 g/L) are highly indicative of septic peritonitis (Van Hoogmoed et al., 1999). It is possible to find normal peritoneal fluid in horses with severe bowel disease due to fluid compartmentalization within the abdominal cavity (White, 1990). For example, horses with intussusception, incarcerated intestine within the epiploic foramen contained in the lesser omental bursa, or diaphragmatic hernia may have normal peritoneal fluid in the presence of other clinical signs of severe disease (White, 1990).

Care should be taken in interpreting the WBC counts and protein concentrations in peritoneal fluid after abdominal surgery. After a ventral celiotomy, WBC counts can be as high as 100,000–150,000 cells/μL (100–150 × 10^9/L) with protein concentrations of 3.3–6.2 g/dL (33–62 g/L). Similarly, WBC counts as high as 400,000 cells/μL (400 × 10^9/L) have been documented to occur in healthy ponies after abdominal manipulation and intestinal handling (Blackford et al., 1986; Santschi et al., 1988). Cecal trocarization also increases the WBC concentrations to 30,000–60,000 cells/μL (30–60 × 10^9/L) and the cells can be degenerate. Although some horses have a fever, most horses are usually not clinically ill after the procedure (White, 1990).

After parturition, there may be increased fluid within the abdomen but the laboratory analysis should be normal unless there is a problem with the uterus or intestines. Neoplastic cells are rarely identified in peritoneal fluid. However, when they are present, they are helpful in the definitive diagnosis of the most common abdominal tumors, gastric squamous cell carcinoma and lymphoma. The absence of these cells does not rule out neoplasia. Mesothelial cells may be seen in peritoneal fluid and may occur as sheets of cells (Figure 20.48). These are not specific for a particular problem, nor do they represent a neoplastic process.

Concentrations of creatinine phosphokinase and alkaline phosphatase in the peritoneal fluid exceed serum concentrations of these enzymes with injured intestine and can be of use in evaluating horses with chronic abdominal diseases. However, these tests are not more

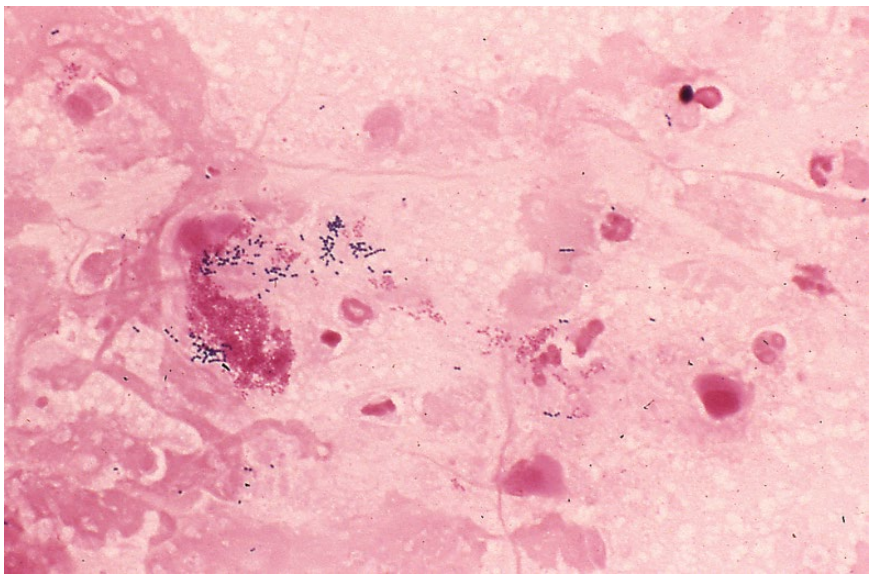

Figure 20.47 Gram stain of peritoneal fluid with Gram-positive and Gram-negative bacteria.

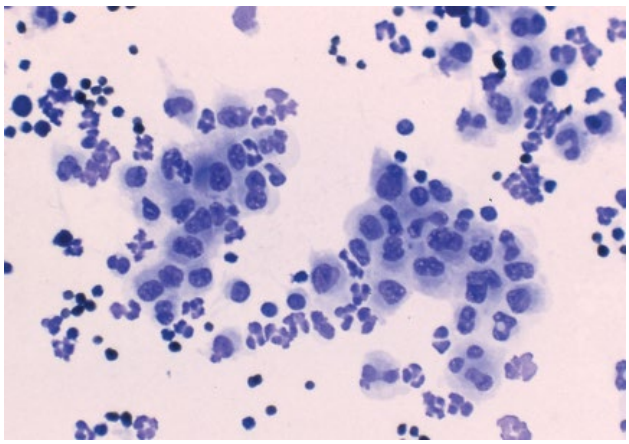

Figure 20.48 Mesothelial cells, which normally appear in clumps, have large basophilic nuclei.

sensitive than cytology (Moss et al., 1977; Nelson, 1979). Measuring the isoenzyme of alkaline phosphatase may be useful in diagnosing small intestinal disease as it is released specifically from this region of intestine (Moss et al., 1977).

Lactate is the end product of anaerobic glycolysis and has been used as a marker of ischemia in colic patients. Peritoneal fluid lactate concentrations were shown to be more sensitive than blood lactate concentrations for early detection of ischemic lesions (Delesalle et al., 2007; Latson et al., 2005). Peritoneal lactate concentrations were significantly higher in horses with strangulating than nonstrangulating lesions, with the exception of strangulating small colon obstruction (Delesalle et al., 2007; Latson et al., 2005). Lactate concentrations >4 mmol/L or increasing lactate concentrations in serial samples of peritoneal fluid from horses with blood lactate concentrations <4 mmol/L significantly increase the likelihood of a strangulating lesion (Peloso & Cohen, 2012). This test has poor sensitivity and should only be used as one of the factors when deciding about the need for surgery.

Serum creatinine concentration and serum-to-peritoneal fluid creatinine ratios are invaluable aids in the diagnosis of uroperitoneum secondary to bladder rupture in foals or adult horses (Kablack et al., 2000). D-dimer, a fibrin degradation product, is a useful indicator of fibrinolytic activity. Higher peritoneal fluid concentrations of D-dimer were correlated with greater disease severity in horses with colic in clinical studies (Delgado et al., 2009).

Hematology, Blood Gas, and Serum Biochemistry

A total WBC count and differential are helpful in classifying the type of acute abdominal disease. Most horses with acute colic have a normal leukogram or a mild neutrophilia and lymphopenia consistent with a stress leukogram. A leukocytosis may be present in horses with a mesenteric abscess (Rumbaugh et al., 1978), in some cases of peritonitis (Hanson, 1999), or duodenitis-proximal jejunitis (White et al., 1987). A leukopenia (WBC count <3000 cells/μL; $<3.0 \times 10^9$/L) usually indicates Gram-negative sepsis or endotoxemia (enteritis, colitis), salmonellosis, Potomac horse fever, or rupture bowel (Coffman, 1980a; Palmer et al., 1986; Ristic et al., 1986).

A depressed horse with a fever, distended small intestine, and leukocytosis is more likely to have enteritis, whereas strangulating lesions in the acute stages rarely change the WBC count until endotoxins cause margination of neutrophils with subsequent neutropenia. The differential WBC count may be useful in horses with Potomac horse fever in which there is often a true monocytosis (Ristic et al., 1986) or in horses with lymphosarcoma, which may result in an absolute lymphocytosis (Duncan et al., 1994).

Measuring blood gases and lactate concentration provides information about the horse's acid–base status. Venous blood gas analysis is usually adequate to assess metabolic contributions to acid–base balance, but arterial blood should be used to assess the respiratory component. Arterial blood is taken from the transverse facial or facial artery. Most horses with simple colic or simple obstruction have normal acid–base status or are slightly alkalotic. In the early stages of proximal small intestinal obstructions or large colon obstructions, horses are often alkalotic owing to fluid retention and chloride loss (White, 1990). Respiratory alkalosis due to hyperventilation may precede dehydration and shock in horses with strangulating conditions. Strangulating lesions with sequestered fluid within the intestinal tract eventually cause dehydration and endotoxemia, resulting in decreased tissue perfusion. Decreased perfusion leads to lactic acidosis and can be identified by measuring serum lactate concentration. Restoration of blood volume is critical and fluid resuscitation with polyionic fluids is recommended (Corley & Marr, 1998) (see Chapter 28). Increased blood lactate levels also correlate with decreasing percentage survival in horses with colic (Moore et al., 1976). Serial assessment of blood lactate is of greater prognostic value than a single determination, as persistently high lactate levels or an increasing trend are more indicative of a poorer prognosis than is a single value. Blood lactate concentrations >7 mmol/L had a strong association with nonsurvival in multiple studies (Delesalle et al., 2007; Hinchcliff et al., 2005; Johnston et al., 2007; Underwood et al., 2010). Care should be taken when assessing blood lactate concentrations in ponies and miniature breeds as they might present with higher concentrations than horses and might falsely be suspected of having a surgical lesion or a poorer prognosis if veterinarians are not aware of breed differences (Dunkel et al., 2013).

Similarly, anion gap is a measure of unmeasured anions, such as lactate, and has been used to predict survival in horses with colic (Bristol, 1982). The anion gap is calculated by subtracting the sum of the chloride and bicarbonate concentrations from the sodium concentration. In one study, the survival rate was 81% when the anion gap was <20 mEq/L and it was 0% when the anion gap was 25 mEq/L (Bristol, 1982). Use of anion gap does not appear accurate when dealing with conditions with altered serum chloride concentrations, such as proximal enteritis. Blood lactate and anion gap are therefore used as indicators of the prognosis rather than as a diagnostic aid (Moore et al., 1976).

Although the determination of serum electrolyte concentrations is important for developing adequate treatment and fluid resuscitation plans, rarely do these values help veterinarians make a diagnosis. Hypocalcemia, hypokalemia, and hypomagnesemia are consistent blood abnormalities reported in surgical and medical colic patients (Garcia-Lopez et al., 2001; Delesalle et al., 2002; Johansson et al., 2003; Nappert & Johnson, 2001; Navarro et al., 2005; Toribio et al., 2001). Hypokalemia and hypomagnesemia are associated with lack of gastrointestinal absorption and/or decreased intake, and one of the main causes of hypocalcemia is gastrointestinal sequestration such as gastric reflux. In an experimental study, induced endotoxemia alone caused hypokalemia, ionized hypocalcemia, and hypomagnesemia (Toribio et al., 2005). Hypomagnesemia and hypocalcemia have been shown to be common in the perioperative period, particularly in horses with strangulating lesions or ileus (Garcia-Lopez et al., 2001). Total serum magnesium and calcium concentrations are less sensitive than ionized magnesium and calcium values in detecting horses with hypomagnesemia and hypocalcemia (Garcia-Lopez et al., 2001). These electrolyte abnormalities should be corrected once treatment has been initiated and, if the hypocalcemia is severe, calcium can be administered IV during the examination. Serum calcium and magnesium are not predictors of survival, but early recognition and correction of deficiencies in these electrolytes may help reduce morbidity and mortality in horses with colic and may help restore intestinal motility (Garcia-Lopez et al., 2001).

Hypochloremia may be associated with a proximal small intestinal obstruction or gastric obstruction (Puotunen-Reinert & Huskamp, 1986; Reeves et al., 1986) and most commonly causes a metabolic alkalosis. Hypochloremia can also be seen with exhausted horse syndrome when large volumes of sweat have been lost. Marked changes in serum sodium and potassium concentrations usually occur only in cases of acute colitis, salmonellosis, or ruptured bladder. Many horses with ruptured bladder will have hyponatremia, hypochloremia, hyperkalemia, and a metabolic acidosis at the time of diagnosis (Kablack et al., 2000).

Derangements of blood glucose concentration are common in horses with acute abdominal disease. The results of clinical studies indicate that the prognosis for survival to hospital discharge worsens with severity of hyperglycemia, with concentrations exceeding 195 mg/dL (10.82 mmol/L) being associated with nonsurvival (Hassel et al., 2009; Hollis et al., 2007).

Azotemia is defined as an increase in creatinine and urea nitrogen, which often occurs in colic patients. Azotemia is categorized as prerenal if it due to a decrease in renal perfusion, such as occurs with hypovolemia, or is renal in origin resulting from damage to the nephrons, or rarely can be postrenal in patients with uroabdomen. Persistent azotemia is a negative prognostic indicator and significantly higher preoperative creatinine concentrations are noted in nonsurvivors than survivors (Groover et al., 2006; Stephen et al., 2004; Underwood et al., 2010).

Serum enzymes can change in diseases involving the liver, muscle, and kidney. Sorbitol dehydrogenase, gamma-glutamyl transferase (GGT), lactate dehydrogenase, aspartate aminotransferase, lactate dehydrogenase, and arginase can all increase with liver cell degeneration or necrosis (see Chapter 51). Obstructive liver disease, such as cholelithiasis, cause increases in bilirubin, alkaline phosphatase, and GGT (Traub et al., 1983; Bayly & Reed, 1980). Increased GGT activity was shown to occur in nearly 50% of horses with right dorsal displacement of the large colon, presumably as a result of bile duct compression (Gardner et al., 2005). GGT might also be helpful in distinguishing proximal enteritis from small intestinal strangulating obstruction, which is unlikely to cause hepatic injury. In one study in which a GGT concentration of >22 U/L (normal range 6–22 U/L) was used as a cut-off value, the positive predictive value for distinguishing proximal enteritis from small intestinal strangulating obstruction was 84% (Davis et al., 2003). A very sensitive test for obstructive disease of the liver is serum bile acids, which will have a marked elevation from a normal value of 5 μmol/L to 80–100 μmol/L.

Coagulation tests and clotting times are not commonly evaluated in horses with colic, but are indicated when horses have signs of abnormal hemostasis such as bleeding excessively from the catheter site, nasogastric tubing, or abdominocentesis site. To ensure validity, these tests are all run with controls. Disseminated intravascular coagulation (DIC) may occur with endotoxemia during the late stages of strangulation obstruction or severe peritonitis or enteritis/colitis. Clinical pathology findings indicative of DIC include thrombocytopenia, prolongation of the prothrombin and the partial thromboplastin times, elevation of fibrin degradation products, increased levels of plasma D-dimer, decreased

plasma fibrinogen level, and reduced antithrombin III levels (McClure et al., 1979; Pablo et al., 1983).

Colic in horses is associated with an elevated serum total concentration of cortisol and the degree of increase appears to relate to the severity of disease. The serum concentration of cortisol may provide additional decision-making and prognostic information in horses with colic (Mair et al., 2014).

The results of a preliminary study measuring blood concentrations of the acute-phase proteins, including serum amyloid A (SAA), haptoglobin, and ferritin, indicate a significant increase in these biomarkers with abdominal diseases (Dondi et al., 2015; Bauquier et al., 2015). SAA increases with inflammatory intestinal disease, but is not specific for strangulation (Murray & Crowell-Davis, 1985).

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21

Investigations of Chronic and Recurrent Colic

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The terms chronic *colic* and *recurrent colic* are often used interchangeably to describe repeated behaviors associated with pain. While chronic pain is defined by intermittent or constant pain during 3 days or longer (Mair & Hillyer, 1997), recurrent colic is also referred to as intermittent colic and occurs as independent colic episodes over weeks or months (Hillyer & Mair, 1997).

The causes of chronic colic include colonic impaction, colonic displacements, enteritis/colitis, peritonitis, intestinal adhesions, cecal impactions, thromboembolic disease, ileal obstruction, intussusception, enteroliths, rectal diverticulum, monensin toxicity, and tumors (Mair & Hillyer, 1997). Because some of these diseases may recur, they may also cause recurrent colic.

Recurrent or intermittent colic can be classified into three categories: primary recurrent colic, recurrent colic after surgery, and recurrence of false colic. Most often horses are presented with a history of recurrent episodes that may vary in intensity. Because a large majority of these are mild and respond to analgesics, they often go undiagnosed (Scantlebury et al., 2011).

The causes of primary recurrent colic related to the gastrointestinal tract include gastric ulcers (Murray, 1992), repeat gas colic or colon displacement (Baird et al., 1991; Farstvedt & Hendrickson, 2005), pregnancy, sand colic (Granot et al., 2008), enteroliths (Hassel et al., 1999), myenteric ganglionitis (Burns et al., 1990; Blake et al., 2012; Pavone et al., 2013), abdominal abscesses (Mair & Sherlock, 2011), choleliths (Ryu et al., 2004), enteritis (Barclay et al., 1987), muscular hypertrophy of the ileum (Chaffin et al., 1992) or cecum (Huskamp & Scheidemann, 2000), grass sickness (Newton et al., 2004), and mild or idiopathic/spasmodic colic. Although most repeat episodes of colic are mild and self-limiting, in some cases they may occur due to recurrence of large colon impaction, large colon displacement, large colon volvulus, or cecal impaction (see Chapters 54 and 55). It also is important to recognize that the small intestine can become entrapped through rents in the mesentery of the duodenum or small colon in mares after they have foaled.

Risk factors for chronic and intermittent colic related to signalment, diet, and environment include the following: previous abdominal surgery, consuming coastal grass hay, being more than 8 years of age, being of the Arabian breed, being a gelding, having a recent change in diet, and living in an environment with a high density of horses (Cohen & Peloso, 1996). Increased risk for recurrent colic in the general horse population include: dental disease, cribbing/windsucking, and weaving behavior. In contrast, there is a reduced risk for recurrent colic associated with increasing time at pasture (Scantlebury et al., 2011, 2015).

There is an increased risk of colic episodes in horses that have undergone surgery, predominately due to intestinal scarring from distention, ischemia, intestinal trauma, or contamination. Recurrent colic can result from adhesions causing obstructions and vascular occlusion. Alterations in the neurons in the myenteric plexus, including ganglionitis and the number of ganglia, have been identified in the large colon and cecum after prolonged obstruction or volvulus (Blake et al., 2012; Schusser & White, 1997; Fintl et al., 2004; Schusser et al., 2000). Similarly, alterations in the small intestinal muscle can be detected in some horses with colic (De Ceulaer et al., 2011; Mair et al., 2016). The strength of an association, if any, between changes in the enteric nervous system or smooth muscle and recurrent colic episodes after prolonged obstruction or after surgery remains to be determined.

False colic involving other organs or behaviors is a rare cause of recurrent colic. Intermittent colic and behavior similar to colic can be caused by liver disease, cholelithiasis, cardiac arrhythmias, kidney disease, urolithiasis,

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ovarian tumors, and rhabdomyolysis (see Chapter 60). Regardless, veterinarians should perform the necessary examinations needed to determine that these episodes of colic are unrelated to diseases affecting the gastrointestinal tract.

Horses with recurrent colic should be examined using the same systematic approach that would be used for an individual episode of colic (see Chapter 21). A history of previous colic should alert the examiner to the possibility of a disease similar to that associated with the prior episode, but this should not be assumed. In horses with a history of a colonic displacement or volvulus that exhibit severe colic, a repeat of the same disease should be suspected. This is particularly true in the broodmare just before or after foaling (Embertson et al., 1996). In some cases, repeat colic episodes, even if they are mild, justify exploratory surgery either using laparoscopy or by a ventral midline celiotomy. In horses that are normal at the time of surgery, exploration can reveal few if any abnormalities. However, surgery is justified in an attempt to diagnose a specific disease.

Future colic episodes may be prevented when certain diseases are identified during the exploratory surgery. These include a mesenteric rent that could be closed, muscular hypertrophy amenable to surgical bypass, and large colon volvulus that can be prevented either by colopexy or colon amputation, and left dorsal displacement that can be prevented by ablation of the nephrosplenic space (Farstvedt & Hendrickson, 2005). When mild episodes of colic recur, it is important to rule out gastric ulceration as a primary cause. If a specific diagnosis cannot be made even with surgery, the best approach is to institute a strict exercise and feeding routine, turn the horse out as frequently as possible, decrease the amount of concentrates in the diet as much as possible, provide free choice roughage and water, control parasites, provide routine dental care, and take steps to prevent the ingestion of sand. Nutritional supplements including bran mash, pre- and probiotics, and special diets have not been scientifically proven to decrease or prevent colic (Schoster et al., 2014). If used, they should be part of the daily routine and considered when formulating energy intake in the diet.

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22

Alternative Diagnostic Techniques

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Fecal Examination

Gross, cytologic, biochemical, bacteriologic, immunologic, and electron microscopic evaluations can be performed on fecal samples. The fecal contents should be examined for the presence of sand, gravel, undigested feed material, watery consistency (increased transit time), mineral oil (if administered previously), and parasites. The feces can be placed in a rectal sleeve filled with water to allow the sand to settle out. This can be a useful monitoring method to determine if sand is being passed during treatment for sand impaction.

Assessing fecal occult blood though possible, can be difficult to interpret as there may be contamination from previous rectal examinations where there has been some minor bleeding from the mucosa. It may be useful for diagnosing ulceration in the gastrointestinal tract such as right dorsal colitis, but available tests are not very sensitive or specific for digested blood. The preliminary results of a study measuring carbonic anhydrase isozymes originating from erythrocytes in feces have been published (Nishita et al., 2013). This parameter was used as a marker of occult blood in horses with intestinal tract bleeding. Cytologic examination is mainly used to evaluate the parasite burden of the animal.

Fecal culture is used primarily to detect *Salmonella* spp. Quantitative real-time polymerase chain reaction (qPCR) for the detection of pathologic agents such *Salmonella* spp. and *Lawsonia intracellularis* in feces is now often used in clinical settings (Frazer, 2008; Pusterla et al., 2010; Pusterla & Gebhart, 2013). Rectal biopsy has been used to obtain cultures for *Salmonella*, but has a limited use as biopsies taken to diagnose enterocolitis (Lindberg et al., 1996).

Transit Time

Measurement of fecal transit time may be helpful in detecting obstructions or problems with motility. The technique is not commonly used but can be helpful in the case of chronic or recurrent colic (Moore et al., 1978). Plastic beads (4 mm diameter) administered orally are retrieved in the feces at timed intervals. Beads are first observed at 14 h with all beads passing at 72 h. If the horse had an obstruction requiring surgery, the beads were retained at 36–48 h (Moore et al., 1978). Mineral oil commonly administered as a laxative will provide a crude estimate of fluid transit with oil first detected at approximately 12–18 h. Use of mineral oil does not rule out obstruction of an intestinal lumen with blockage of ingesta.

Exploratory Laparotomy

Often a definitive diagnosis is not obtained until an exploratory laparotomy is performed. This is used as both a diagnostic procedure and a treatment. Not all parts of the intestinal tract can be exteriorized for evaluation. Therefore, careful palpation is an important aspect of the surgery. Examples of chronic problems which are only diagnosed by palpation during surgery are pancreatitis, duodenal adhesions, duodenal thickening/impaction, gastric tumors, pyloric thickening, cholelith, diaphragmatic hernia, mesenteric and mesenteric artery disease, colonic foreign bodies, muscular hypertrophy of the ileum, and adhesions (see Chapter 43) (White, 1990).

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Endoscopy

Gastroscopy can be done with moderate sedation (xylazine or detomidine) in the standing horse. It can also be performed in neonates with no sedation or a low dose of xylazine (Murray & Fischer, 1996). In adult horses, feed should be withheld for 6–10 h and foals should be allowed to nurse up to 4 h prior to gastroscopy (Murray & Fischer, 1996; Jones, 2015). The diameter of the endoscopes will range from 10 to 14.5 mm with the 10 mm endoscope being able to be passed through the foal turbinates whereas the larger diameter will only pass through the turbinates of yearlings and adults. The endoscopes come in varying lengths. The 110 cm length endoscope will reach the stomach of foals up to 30–40 days of age (Jones, 2015). In weanling foals a human slim colonoscope with a diameter of 12.5 mm can be used and for most equine gastroscopy a minimum length of 200 cm is required, but at this length the antrum and pylorus cannot be adequately examined (Jones, 2015). The 200 cm endoscope will allow examination of the duodenum in foals up to 6 months of age but in most adult horses a 280–300 cm length is required to perform complete gastroscopy and duodenoscopy in adult horses (Jones, 2015). The endoscope should be carefully inserted into the ventral turbinates as the diameter is large. The endoscope is passed down the esophagus (the esophagus is examined thoroughly at the end of the examination when the endoscope is pulled out). The esophageal sphincter and entrance to the stomach is usually 170–180 cm from the nares. Some resistance may occur at this point, but it should be fairly simple to pass the endoscope into the stomach. The stomach needs to be distended by insufflation in order to evaluate the glandular and nonglandular areas of the stomach. If there is a large volume of feed material and fluid in the stomach after an adequate period of starvation (e.g., 18–24 h) gastric motility dysfunction or outflow obstruction should be suspected (Murray, 2002).

After the endoscope enters the stomach, it travels against the right side and then dorsally and is advanced to the caudal portion of the stomach where the lesser curvature and cardia can be seen (Figure 22.1) (Murray, 2002). The endoscope is then further advanced across the ventral ridge of the lesser curvature so that the antrum and pylorus can be seen (Figure 22.2). The endoscope will not be able to be advanced to the pylorus unless there are adequate gastric contractions (Figure 22.3) (Murray, 2002). The stomach and duodenum can be assessed and biopsies can be taken if necessary. Biopsies can be taken for further information if required but are not of much value from the gastric mucosa. A larger specimen can be obtained from the glandular mucosa and duodenum as the tissue can be torn with the small biopsy forceps. Gastric ulceration, gastric impaction, gastric squamous cell carcinoma, gastric outflow obstructions or abnormalities within the duodenum or duodenal papilla can be diagnosed with endoscopy (see Chapter 50).

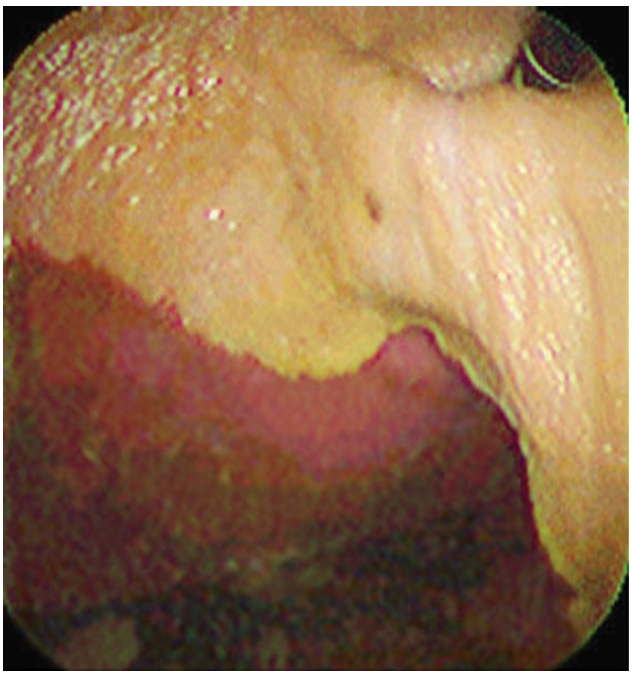

Figure 22.1 Endoscopy of the stomach. The endoscope moves along the greater curvature and allows visualization of the cardia and margo plicatus on the lesser curvature of the stomach.

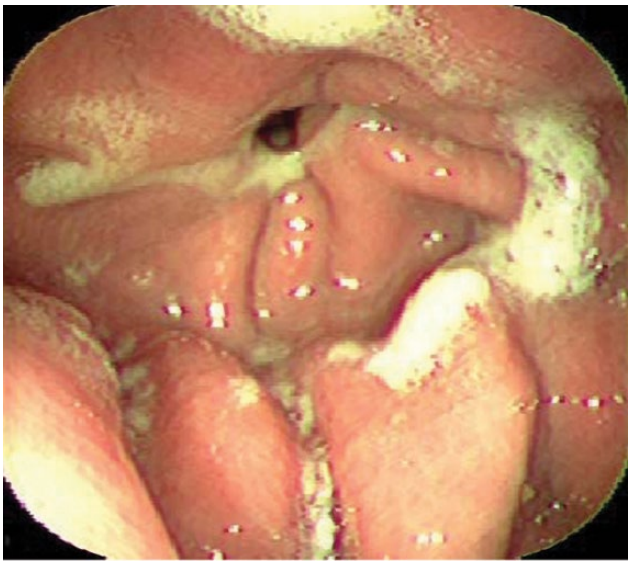

Figure 22.2 Endoscopy of the stomach antrum and entry into the pylorus.

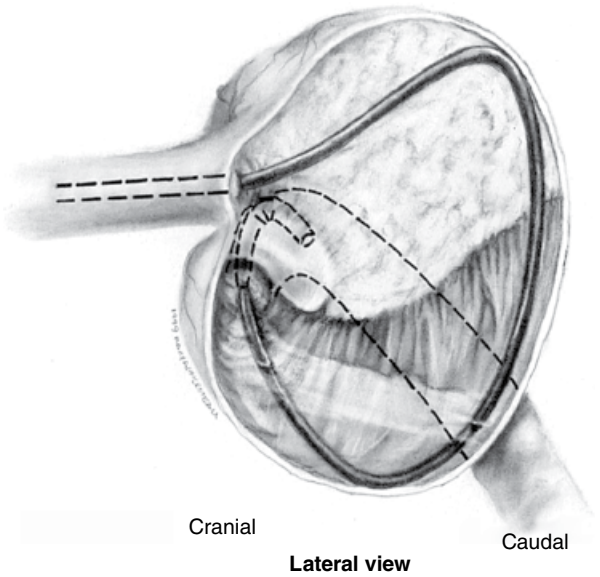

Figure 22.3 A 3 m endoscope being passed along the greater curvature of the stomach and entering the duodenum. Source: Murray, 2002. Reproduced with permission of Elsevier.

Laparoscopy

Indications for diagnostic laparoscopy include examination of horses with recurrent colic or abdominal pain which otherwise need exploratory laparotomy to make a diagnosis (Walmsley, 1999). In cases of chronic colic visualization of adhesions, serosal irritation, and abdominal masses may be helpful in making a diagnosis in the standing horse. Limitations to the examination are present in either the standing or anesthetized recumbent horse because much of the viscera remains hidden with the horse in either position.

The laparoscope used for evaluating the equine abdomen is usually a 10 mm diameter laparoscopic telescope with a lens angle of 30°. Horses undergoing laparoscopy must be held off feed for a minimum of 24 h with more reliable visualization after 36–48 h. Water should always be available free choice during the period when feed is withheld. The 30 cm 30° viewing telescope is adequate for the exploration although the longer laparoscopes help with visualization of the stomach, pelvic inlet, and duodenum. Laparoscopic portals include the paralumbar fossa proximal to the internal oblique muscle on the left and right side and via the umbilicus or linea alba when the horse is in dorsal recumbency.

Prior to proceeding with abdominal laparoscopy in a standing horse, a rectal examination should be completed to locate organs on the left (spleen and colon) and right (cecum) sides of the abdomen. Laparoscope insertion is via incision and placement of cannulas through the appropriate portal. Insufflation of CO_2 after a cannula has been passed into the abdomen is helpful to provide more visualization.

There are two main surgical approaches. The first is a standing flank approach. With this technique, the horse should be starved 1–2 days prior to surgery whenever possible (Walmsley, 1999). The horse is restrained in stocks with a continuous infusion of detomidine and butorphanol to provide analgesia and sedation. After local anesthesia at the site of the portal, the abdomen is insufflated with CO_2 gas. The laparoscope is usually first inserted into the left flank dorsal to the internal oblique muscle. The procedure can then be repeated on the right side and there will be residual gas in the abdomen which will reduce the chance of perforating the cecum (Fischer, 1989; Walmsley, 1999). The second approach is via the ventral abdomen with the horse under general anesthesia (Galuppo et al., 1996). Withholding food is even more important in these cases for an acceptable evaluation of the abdomen. The abdomen is insufflated just caudal to the umbilicus and the laparoscope placed in that position. To evaluate the caudal abdomen, the horse is tilted head down 30° described for humans as the Trendelenburg position and the reverse for evaluation of the cranial aspect. The success of this technique depends on the accessibility. It is sometimes impossible to move around a distended viscus and visibility is limited, which is why withholding feed before surgery is important. Complications of laparoscopic surgery include penetration of the spleen, right kidney, cecum and small colon, pneumoperitoneum, and decreases in cardiopulmonary indices with increased intra-abdominal pressures during general anesthesia (Donaldson et al., 1998; Shettko, 2000; Desmaizières et al., 2003; Hendrickson, 2008).

Normally the following structures can be seen with laparoscopy in the horse (Galuppo et al., 1995, 1996; Walmsley, 1999):

- From the left paralumbar fossa: the hepatic duct; left lateral and quadrate lobes of the liver; stomach; spleen; left kidney with the associated nephrosplenic ligament; segments of jejunum, descending colon, and ascending colon; left side of the male and female reproductive tracts; urinary bladder; vaginal ring; and mesorchium.
- From the right paralumbar fossa: the common hepatic duct; left lateral, quadrate, and right lobes of the liver; caudate process of the liver; stomach; duodenum; right dorsal colon, epiploic foramen; omental bursa; right kidney; base of the cecum; segments of jejunum, descending colon, and ascending colon; urinary bladder; right half of the male and female reproductive tracts; and rectum.

- From the ventral abdomen: the urinary bladder, mesorchium, and ductus deferens (left and right); left and right vaginal rings; insertion of the pre-pubic tendon; random segments of jejunum and descending colon; pelvic flexure of the ascending colon, body of the cecum, and cecocolic fold; surface of the diaphragm, falciform ligament, and round ligaments of the liver; ventral portion of the left lateral, left medial, quadrate, and right lateral lobes of the liver, spleen, right and left ventral colons; sternal flexure of the ascending colon, apex of the cecum, and stomach.

Caudal aspects of the right and left lateral caudate lobes of the liver and the pancreas can be seen through the approach viewing the epiploic foramen (Walmsley, 1999). The lateral surface of the spleen and the nephrosplenic ligament lie beneath the left laparoscopic portal in the standard paralumbar fossa location and both kidneys can be seen underneath their peritoneal coverings (Walmsley, 1999). Certain structures can be biopsied if needed such as abdominal masses, liver, spleen, mesenteric lymph nodes, kidney, or ovary (Walmsley, 1999). The intestine cannot normally be biopsied unless a portal incision is enlarged and the intestine is brought out of the incision (Walmsley, 1999).

An overall sensitivity of 75% has been recorded for diagnostic laparoscopy (Walmsley, 1999). The larger abdominal organs cannot be manipulated with either laparoscopic approach and thus lesions can be missed. Laparoscopy is not a good test for confirming the absence of disease (Galuppo et al., 1996). Certain conditions, for example duodenal adhesions, are only definitively diagnosed in most cases with laparoscopy in a standing horse antemortem (Galuppo et al., 1995). Tears in the small colon mesocolon have been identified using laparoscopy (Ragle et al., 1997). It is thus a useful technique to examine horses when the owners cannot afford an exploratory laparotomy, but the technique provides limited information. Laparoscopy can be useful for splenic conditions, diagnosing adhesions postoperatively, penetrating wounds to the abdomen, and neoplastic conditions.

Several laparoscopic procedures related to intestinal diseases causing colic include ablation of the nephrosplenic space, the epiploic foramen closure, inguinal herniorrhaphy, incisional and diaphragmatic herniorrhaphy, using mesh, rectal tear repair, and adhesiolysis (Fischer et al., 1995; Bleyaert et al., 1997; Farstvedt & Hendrickson, 2005; Epstein & Parente, 2006; Caron & Mehler, 2009; Munoz & Bussy, 2013; van Bergen et al., 2015; Stewart et al., 2014).

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23

Imaging of the Abdomen

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Ultrasonography

Ultrasonography is a safe, noninvasive, and widely available imaging modality for the diagnosis of acute and chronic gastrointestinal disorders and diseases involving the abdominal organs and urogenital tract. This chapter describes the technique of transcutaneous and transrectal ultrasonography, normal ultrasonographic findings, and features of common abdominal conditions associated with colic in adult horses.

For transcutaneous evaluation, a low-frequency (2.0–5.0 MHz) curvilinear transducer is preferable for the assessment of the abdomen because of its ability to image up to 30 cm in depth. Higher frequency transducers (5.0–13.5 MHz) allow for better image resolution of superficial structures and more accurate measurements of intestinal wall thickness. Transrectal ultrasonography can be performed with linear or microconvex linear array transducers. For better image quality, the patient's hair should be clipped using a no. 40 blade from the xiphoid process of the sternum to the pubis ventrally and bilaterally from the paralumbar fossa to the elbow, ventral to the lung fields (Reef, 1998). The skin should be thoroughly cleansed and ultrasound coupling gel applied to improve contact. Alternatively, applying large amounts of isopropyl alcohol with a spray bottle or sponge is often sufficient to eliminate the air interface between the skin and transducer to obtain a suitable image (Fontaine et al., 1999). Proper preparation for transrectal ultrasound includes adequate restraint of the patient, administration of a sedative, if needed, and use of obstetric lubricant (Freeman, 2003).

Unless the physical and rectal examination findings or clinicopathologic data direct the areas to be evaluated, the entire abdomen should be examined with the adult horse in a standing position. A protocol for fast localized abdominal sonography of adult horses (FLASH) admitted for colic was recently described and suggested that this technique can be used in an emergency setting by veterinarians lacking extensive ultrasound experience to detect major intra-abdominal abnormalities in horses with colic (Busoni et al., 2011; Naylor, 2015). This technique allows for the rapid evaluation of seven abdominal locations including the ventral abdomen, gastric window, splenorenal window, left middle third of the abdomen, duodenal window, right middle third of the abdomen, and the thoracic window.

The location, motility, contents and wall thickness of the gastrointestinal segments and appearance of the abdominal organs identifiable on abdominal ultrasound should be evaluated in horses with abdominal discomfort. The fasting state of the patient, nasogastric tube placement, prior administration of sedatives, and whether or not the evaluation is being performed post-gastroscopy or surgery can all affect the ultrasonographic findings and should be considered during their interpretation (Epstein et al., 2008; Kihurani et al., 2009; Mitchell et al., 2005).

From a transcutaneous approach, the stomach (mainly the greater curvature) is visualized from the left lateral aspect of the abdomen between the 8th to 13th intercostal spaces (Reef, 1998). The stomach is located dorsal/medial to the spleen and ventral to the lung field. The stomach should not normally be identified using the ventral window or from the right side of the abdomen in adult horses. The stomach appears as a large semicircular structure with a hyperechoic line casting a strong acoustic shadow originating from the gastric mucosal surface (Figure 23.1). The wall thickness varies with the degree of gastric distention, but is usually less than 0.75 cm (Freeman, 2003). Gastric dilatation and impaction are characterized by an enlarged stomach distended by anechoic to hypoechoic fluid secretion or hyperechoic

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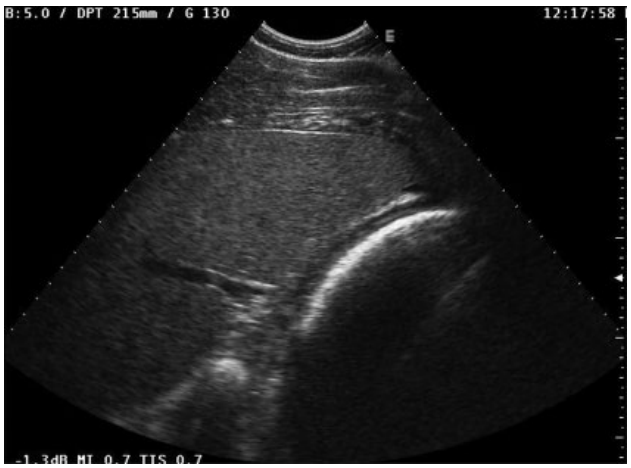

Figure 23.1 Normal gastrosplenic window. Transcutaneous image of the spleen, splenic vein, and stomach seen in the left middle third of the abdomen; dorsal is to the right of the image.

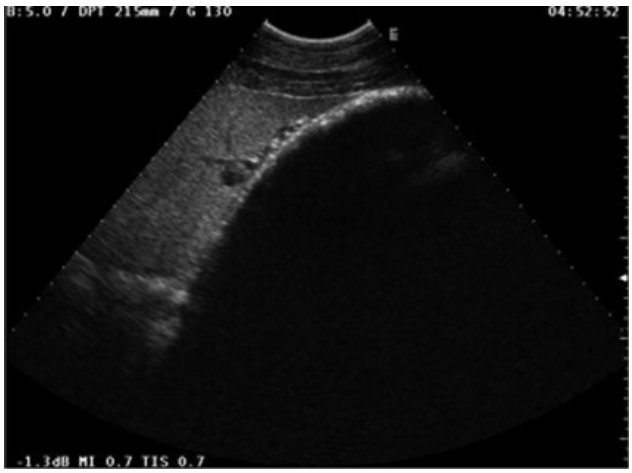

Figure 23.2 Gastric impaction. Transcutaneous image obtained from the left middle third of the abdomen; dorsal is to the right of the image. Note that with feed impaction the gastric contents appear hyperechoic along the mucosal surface and cast a dense acoustic shadow. Wall thickness is thin due to stretching of the stomach wall.

gas or feed contents (Figure 23.2) (Reef, 1998; Taylor et al., 2009). Thickening of the gastric wall can occur with neoplasia, gastritis, and severe gastric ulceration. Gastric squamous cell carcinoma usually appears as a mural mass of complex echogenicity (Figure 23.3) (Reef, 1998).

The normal small intestine appears as a small tubular structure on longitudinal view and circular loops on cross-sectional view. The contents of the small intestine vary from a hyperechoic shadowing gas echo to hypoechoic or hyperechoic fluid, mucus, or ingesta. The small intestine lacks sacculations and has frequent peristaltic contractions (6–15 contractions/min) (Freeman, 2003). The visibility of the small intestine might increase in fasted horses (Mitchell et al., 2005). The descending

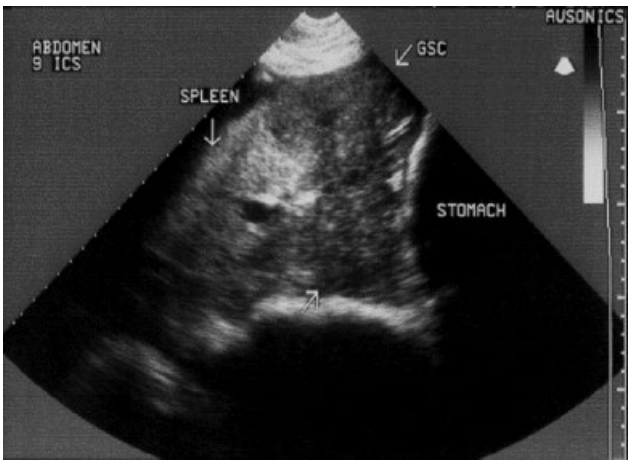

Figure 23.3 Gastric squamous cell carcinoma. Transcutaneous image obtained from the left 9th intercostal space; dorsal is to the right of the image. Note the mixed echogenic soft tissue mass originating from the stomach and extending within the splenic parenchyma.

duodenum can be identified medial to the right liver lobe and underneath the body wall below the ventral aspect of the right kidney from the right 11th to the 17th intercostal spaces (Epstein et al., 2008; Kirberger et al., 1995). The jejunum is not normally identified ventrally owing to the interposed gas-filled large colon. From the left side, the jejunum is often identified between the spleen and the stomach or ventral to the spleen (Reef, 1998). The ileum is inconsistently imaged in the ventral abdomen in adult horses. The wall thickness of the duodenum and jejunum should be less than 0.3 cm, whereas the ileal wall can measure up to 0.4–0.5 cm (Reef, 1998; Klohnen et al., 1996). Ultrasound is very useful for evaluating the small intestine, which may not be palpable on rectal examination. Distended small intestine may be identified with ultrasound before it can be appreciated by rectal examination (Scharner et al., 2002; Cavalleri et al., 2013). Small intestinal distention has been defined as a luminal diameter greater or equal to 5 cm, and increased wall thickness as greater or equal to 3 mm (Le Jeune & Whitcomb, 2014). The ultrasound findings associated with strangulating and nonstrangulating lesions can overlap, and differentiating these conditions can be challenging. In the presence of simple mechanical obstruction of the small intestine, the diameter is usually markedly increased in the prestenotic and affected segments, while the post-stenotic segment appears empty. The wall thickness is normal, but may increase with time, and peristalsis is maintained unless the condition fails to resolve (Freeman, 2003). Functional ileus is characterized by little to no motility of the affected segment. The diameter and wall thickness may be normal or increased (Reef, 1998). The diameter of the prestenotic and affected segments involved in a strangulating obstruction can

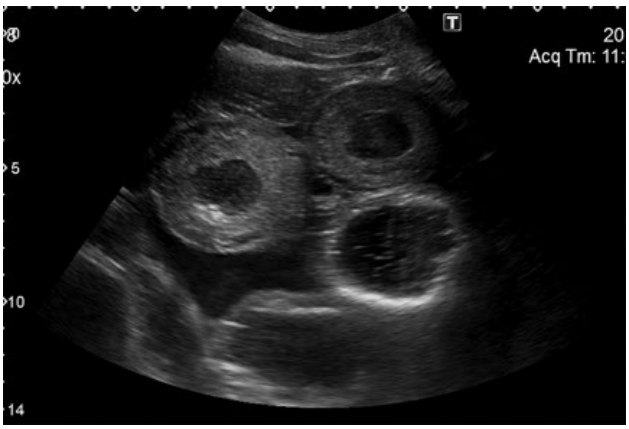

Figure 23.4 Strangulated small intestinal lesion. Transcutaneous image obtained from the ventral abdomen. Note the markedly thickened wall of the small intestinal loops imaged from a horse suffering from a strangulating lipoma. The loops were amotile in real-time imaging.

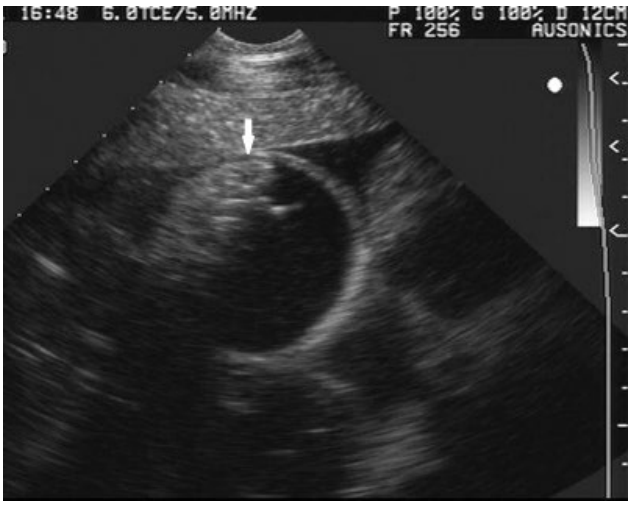

Figure 23.6 Small intestinal obstruction. Transcutaneous image obtained from the ventral abdomen. Note the sedimented ingesta (arrow) within the distended loops of small intestine.

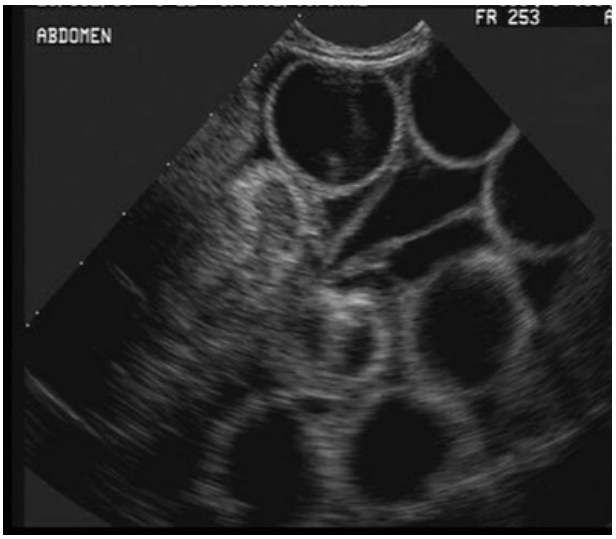

Figure 23.5 Small intestinal obstruction. Transcutaneous image obtained from the ventral abdomen. Note the severely distended loops of small intestine in a young horse with a small intestinal volvulus. The loops were amotile in real-time imaging.

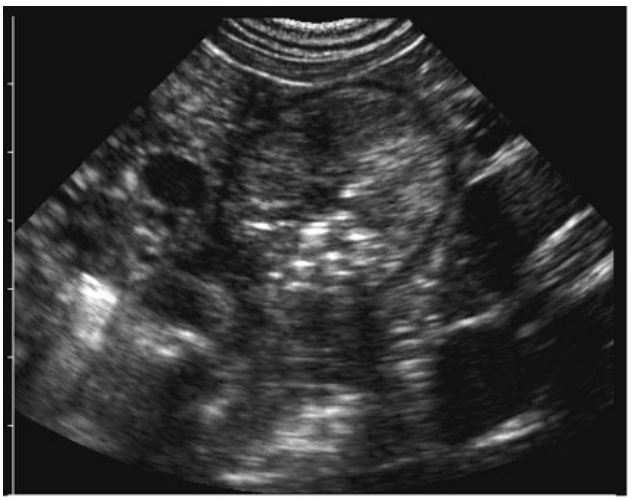

Figure 23.7 Necrotizing enteritis. Transcutaneous image obtained from the ventral abdomen. Note the severely thickened wall of the small intestinal loop seen in a transverse view. The hyperechoic reflections indicated gas within the intestinal wall.

measure 5 cm or more, particularly when the ileum is distended. The wall thickness of the strangulated segment is often increased due to mural edema and/or hemorrhage (Figure 23.4) (Freeman, 2003). The affected loops are amotile and appear turgid (Figure 23.5) and ingesta sediments ventrally in the absence of motility (Figure 23.6). With enteritis, small intestinal distention can be mild, moderate, or severe. The wall thickness of the affected segment is increased, often with evidence of mucosal irregularity, and peristaltic contractions may be increased, normal, or reduced (Reef, 1998). Necrosis can produce a gas echo in the intestinal wall and sloughing of the mucosa may be accompanied by adjacent anechoic fluid (Figure 23.7) (Fontaine et al., 1999). With any small intestinal lesion, the distended loops and often the stomach, contain anechoic to hypoechoic fluid secretion (Figures 23.8 and 23.9). In foals or young horses with ascarid impaction, the parasites may be detected within the lumen (Figure 23.10) (Fontaine et al., 1999). With epiploic foramen entrapment the edematous loops may be identified on the right side of the abdomen (Fontaine et al., 1999). Intussusceptions of the small intestine occur most commonly in foals, and appear as a target-like structure with the intussusceptum evident within the lumen of the intussuscipiens. Varying amounts of intestinal wall edema and changes in wall thickness characterize this condition (Figure 23.11) (Slack, 2013).

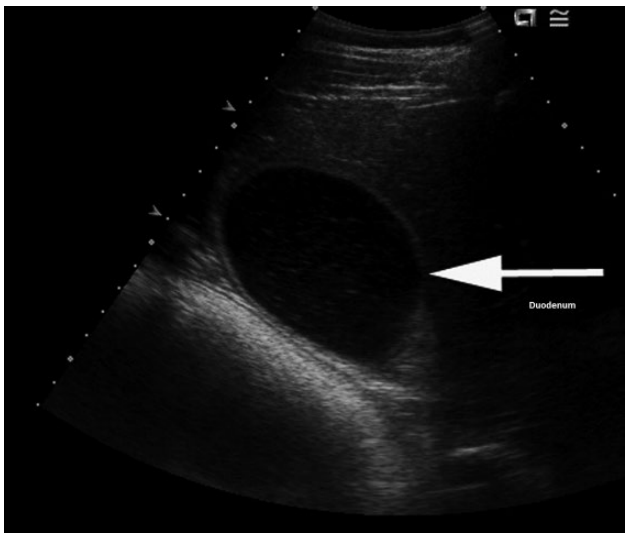

Figure 23.8 Duodenal distention. Transcutaneous image obtained from the right 11th intercostal space; dorsal is to the right of the image. Note the marked fluid distention of the descending duodenum adjacent to the right liver lobe. The duodenum was amotile in real-time imaging and the horse had significant gastric reflux secondary to the ileus.

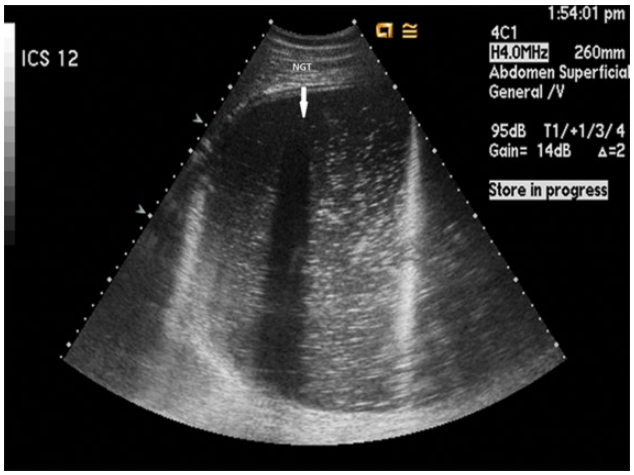

Figure 23.9 Gastric distention. Transcutaneous image obtained from the left 12th intercostal space; dorsal is to the right of the image. Note the enlarged stomach with large ventral fluid accumulation and a visible gas–fluid interface dorsally. A nasogastric tube (NGT) was in place casting a shadow in the excessive gastric fluid.

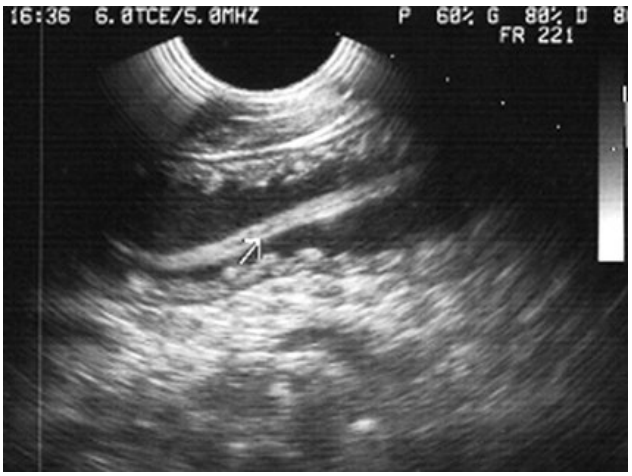

Figure 23.10 Ascarid impaction. Transcutaneous image obtained from the ventral abdomen. Note the hyperechoic linear structure consistent with an adult worm (arrow) visible within the thickened and corrugated small intestine segment imaged in a longitudinal view.

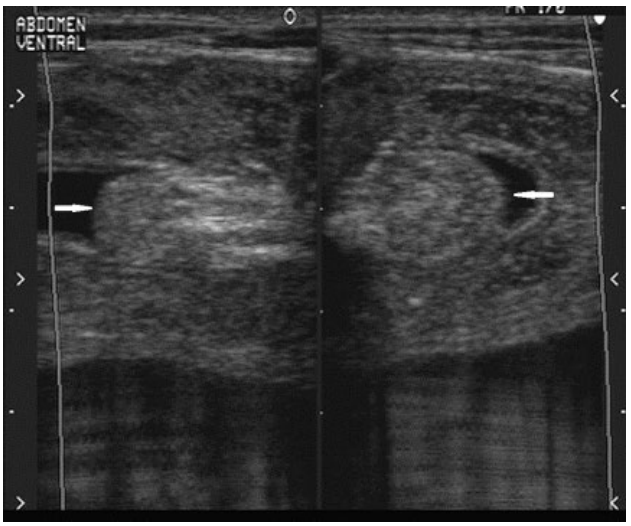

Figure 23.11 Small intestinal intussusception. Transcutaneous image obtained from the ventral abdomen. Note the typical target or bull's eye appearance created by the intussusceptum (inside) (arrows) within the severely thickened intussuscipiens (outside) imaged in a transverse image.

Fluid, fibrin, and a segment of the mesentery are often identified within the intussusception (Figure 23.12). Infiltrative bowel diseases, idiopathic muscular hypertrophy, and neoplasia are characterized by localized or diffuse echogenic thickening of the small intestinal wall.

The cecum is visualized from the upper right paralumbar fossa and flank region with its apex extending to the ventral abdomen. The cecal mesentery containing the lateral cecal vein and artery can be identified along the same path (Figure 23.13) (Vaughan et al., 2013). Segments of the large intestine are seen from the ventral abdominal region and lateral aspects of the abdomen. The small colon can be imaged from the ventral abdomen only through a distended urinary bladder, which is used as an acoustic window (Reef, 1998). The contents of the cecum and colon consist of gas or thick ingesta, which produce a semicurved hyperechoic line casting an acoustic shadow from the mucosal surface. Normal thickness of the cecal and colon wall should be less than 3–4 mm (Hendrickson et al., 2007; Reef, 1998;

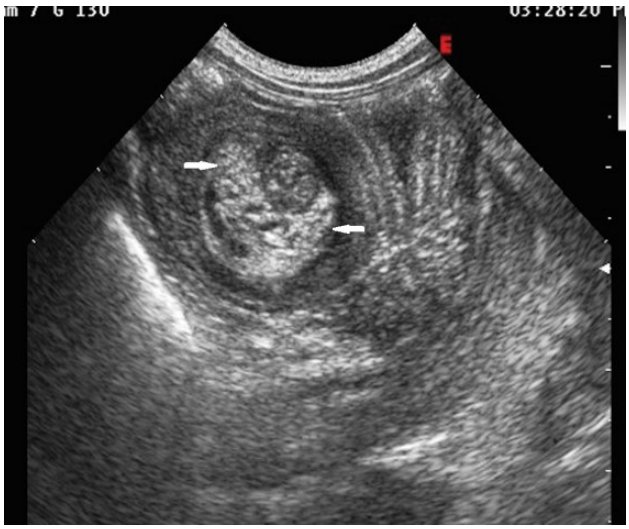

Figure 23.12 Small intestinal intussusception. Transcutaneous image obtained from the ventral abdomen. Note the mesentery (arrows) that has been dragged between the two limbs of the intussusception.

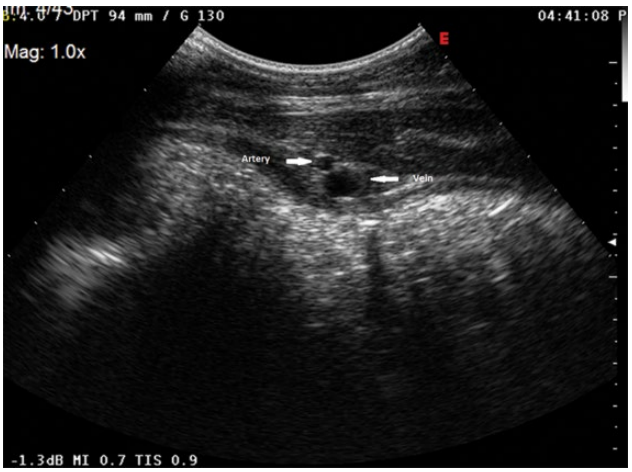

Figure 23.13 Normal cecum. Transcutaneous image obtained from the right caudal abdomen; dorsal to the right of the image. Note the normal lateral cecal artery and vein contained within the cecal mesentery.

Bithell et al., 2010; Epstein et al., 2008). Sacculations are present except for the left dorsal colon and appear as a series of rounded, hyperechoic lines (Fontaine et al., 1999). Peristaltic activity is normally subtle (2–6 contractions/min) (Freeman, 2003).

Ultrasonography has limited value in the diagnosis of tympany, spasmodic colic, and displacement and torsions of the cecum or colon (Freeman, 2003; Reef, 1998). Changes in the location, motility, and contents of the affected segment and secondary enlargement or atrophy of other abdominal structures can be indicative of gas distention or primary malposition of the cecum or colon. Ultrasound can be used in conjunction with rectal

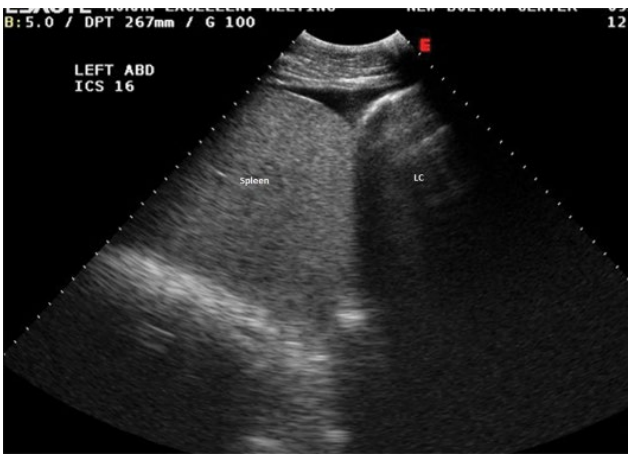

Figure 23.14 Left dorsal displacement with renosplenic entrapment. Transcutaneous image obtained from the left 13th through 16th intercostal spaces; dorsal is to the right of the image. Note the gas within the large colon creates a shadow over the dorsal aspect of the spleen preventing visualization of the left kidney.

examination to diagnose left dorsal displacement of the ascending colon over the renosplenic ligament. Characteristics of this condition include ventral displacement of the spleen and an inability to image the left kidney. The dorsal aspect of the spleen appears as a straight border due to the dorsal displacement of the large colon over the nephrosplenic ligament (Figure 23.14) (Santschi et al., 1993). This appearance is not diagnostic for renosplenic entrapment and can occur with other displacements (Hardy et al., 2000). Pneumoperitoneum may also result in gas pockets being identified dorsally in the abdomen (Fontaine et al., 1999). Cecal and large colon impactions are characterized by a round distended or flattened viscus lacking visible sacculations. In these conditions, peristalsis is absent and wall thickness is usually normal or thin. Fecal impaction appears as hyperechoic intraluminal material casting a strong acoustic shadow from the mucosal surface. Small colon impactions also have a similar appearance but are easier to detect using a transrectal ultrasound approach.

Ultrasound is a practical and reliable method for detecting the accumulation of sand in the large colon, but does not replace radiography (Korolainen & Ruohoniemi, 2002). Sand along the mucosal surface appears as pinpoint material with varying acoustic shadows in the lumen of the large colon, which often has a flattened appearance with decreased or absent motility (Figure 23.15) (Korolainen & Ruohoniemi, 2002). The ultrasound examination will reveal the length of the sand accumulations but information on their height or depth is limited.

Ultrasound findings associated with colitis and typhlitis include increased wall thickness, fluid-filled lumen, variable degrees of distention and changes in the motility

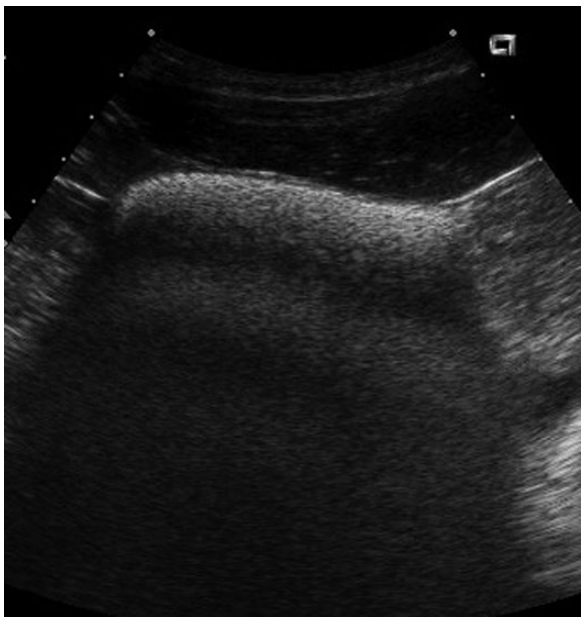

Figure 23.15 Sand impaction. Transcutaneous image obtained from the ventral abdomen. Note the echoic granular sand reflections casting an acoustic shadow and flattening of the wall of the large colon.

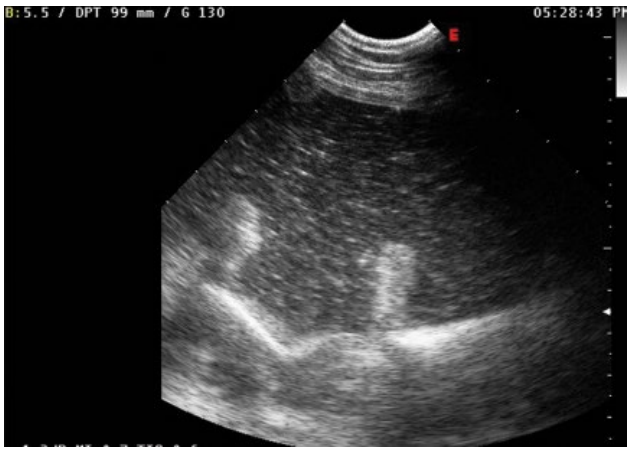

Figure 23.16 Colitis. Transcutaneous image obtained from the ventral abdomen. Note the fluid-filled distended viscus. The accumulation of fluid makes the visualization of the large colon sacculations possible.

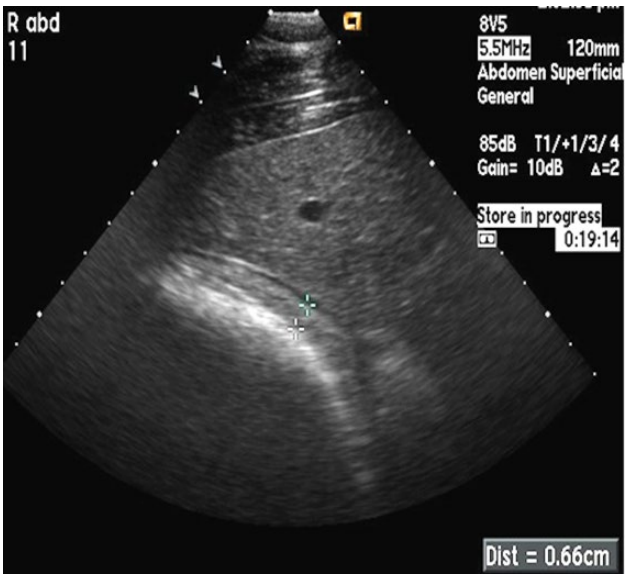

Figure 23.17 Right dorsal colitis. Transcutaneous image obtained from the right 11th intercostal space; dorsal is to the right of the image. Note the thickening and hypoechoic infiltrate of the right dorsal colon wall (between markers).

pattern (Figure 23.16) (Biscoe et al., 2011). The ultrasound appearance of intussusceptions involving the cecum or large colon has been described for cecocecal, cecocolic, colocolic, ileocecal, and ileocecolic intussusceptions (Bell & Textor, 2010; Epstein et al., 2008; Dowling & Todhunter, 1994; Ross et al., 1988; Valdez et al., 1979; Taintor et al., 2004; Valdes-Martinez et al., 2006; Lores & Ortenburger, 2008). These intussusceptions typically have a characteristic target or bull's eye sign in a cross-section view which corresponds to the intussusceptum present within the intussuscipiens and are usually larger in diameter than small intestinal intussusception (Bernard et al., 1989).

The right dorsal colon is located ventral and medial to the right liver lobe and is typically identified from the right 10th to the 14th intercostal spaces. Ultrasonographic measurement of the right dorsal colon mural thickness may be useful in the diagnosis of right dorsal colitis, with the thickness being increased in affected horses (Figure 23.17) (Jones et al., 2003). Identification of dilated colonic mesenteric vasculature coursing horizontally (Grenager & Durham, 2011; Ness et al., 2012) or vertically (Whitcomb, 2005) on the right side of the abdomen can be a predictor of right dorsal displacement of the large colon, 180° large colon volvulus, or both. The presence of hypoechoic, edematous thickening of the colonic wall and obscurity of the right liver lobe and duodenum by the displaced colon might also be detected in those cases. In one study, a colon wall thickness of ≥ 9 mm obtained from a ventral abdominal window accurately predicted the presence of a large colon volvulus (Figure 23.18) (Busoni et al., 2011).

The diaphragm and ventral thorax should be evaluated bilaterally, as diaphragmatic hernias can be diagnosed via ultrasound. Single or multiple abdominal organs or segments of the gastrointestinal tract may be herniated into the thoracic cavity, including the large and small colon, small intestine, spleen, stomach, pancreas, and liver (Figure 23.19) (Hart & Brown, 2009; Romero & Rodgerson, 2010). Findings characteristic of diaphragmatic hernia include increased thickness of the wall of the displaced intestine, accumulation of fluid or blood in

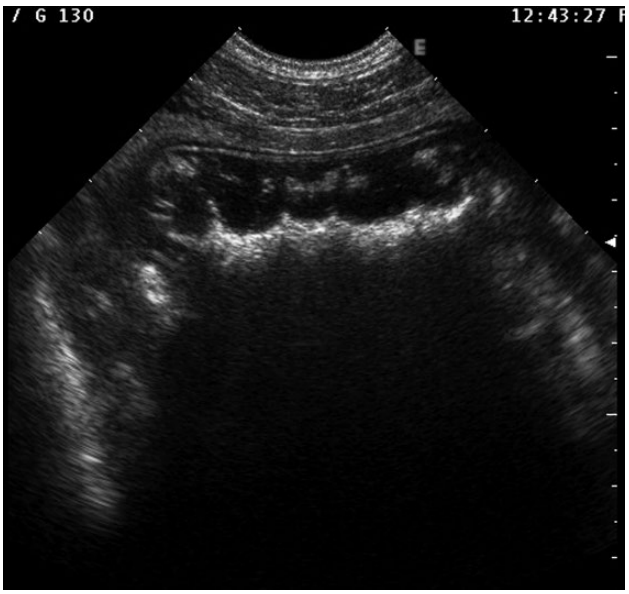

Figure 23.18 Large colon volvulus. Transcutaneous image is obtained from the ventral abdomen. Note the marked thickening and edema contained within the wall of the large colon.

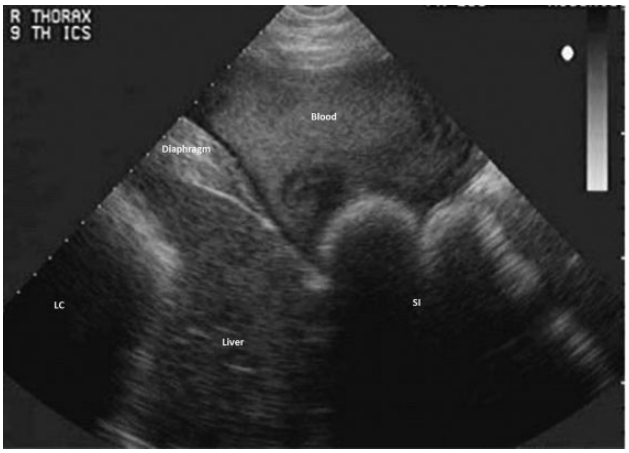

Figure 23.19 Diaphragmatic hernia. Transcutaneous image obtained from the right 9th intercostal space; dorsal is to the right of the image. Segment of the small intestine and blood is seen on the thoracic side of the diaphragm and liver and large colon on the abdominal side.

the abdomen and thorax, as well as the presence of a pneumothorax (Fontaine et al., 1999).

Characteristics of the peritoneal fluid that can be evaluated ultrasonographically include the quantity, echogenicity, motion, and the presence of solid particles or gas echoes. Care must be taken not to confuse the hypoechoic retroperitoneal fat, which contains bright sparks, with peritoneal fluid (Figure 23.20). A small volume of anechoic peritoneal fluid is normally detected between the abdominal organs and gastrointestinal tract, mainly from the ventral abdomen (Epstein et al., 2008). Strangulating lesions, inflammatory conditions, septic

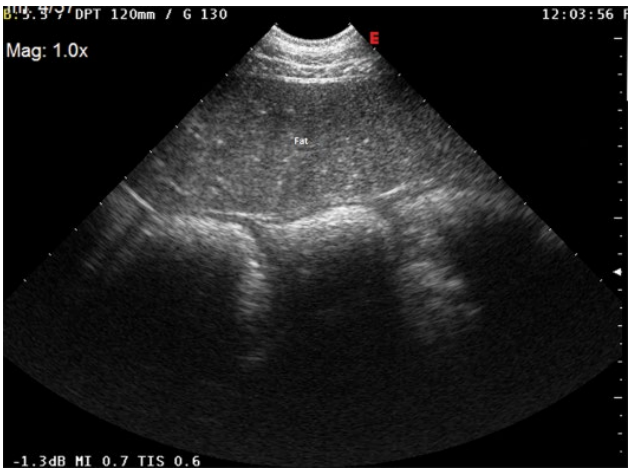

Figure 23.20 Retroperitoneal fat. Transcutaneous image obtained from the ventral abdomen of a normal horse. Note the hypoechoic and speckled appearance of a thick retroperitoneal fat layer.

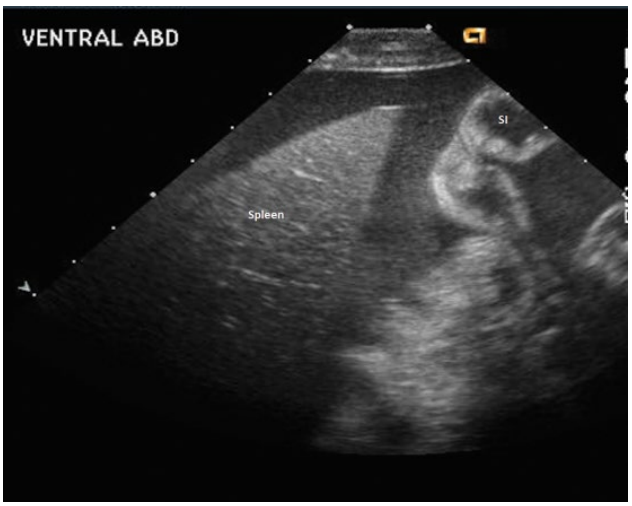

Figure 23.21 Peritonitis. Transcutaneous image obtained from the ventral abdomen. Note the tip of the spleen surrounded by hypoechoic peritoneal fluid. Loops of small intestine with thickened wall are seen floating in the peritoneal fluid.

peritonitis, hemorrhage, and neoplasia can result in an increase in volume and echogenicity of the peritoneal fluid. With peritonitis, fibrin and adhesions of the viscera and/or peritoneum can be identified. In this situation, the gastrointestinal tract is usually amotile or hypomotile, and has an increased wall thickness due to the surrounding inflammatory/infectious process (Figure 23.21). Free-flowing hyperechoic particles may include plant material or fibrin clots. Particulate matter and free gas echoes are usually present if gastrointestinal rupture has occurred (Reef, 1998). The site of rupture is often difficult to identify with ultrasound.

Hemoperitoneum initially appears as free swirling, homogeneous, hypoechoic fluid, and hypoechoic heterogeneous blood clots may subsequently develop.

The spleen will be small in horses with acute hemorrhage due to splenic contraction. The source of the hemorrhage is often difficult to identify and might involve the spleen, liver, female reproductive tract, mesenteric vessels, or be secondary to trauma or neoplasia (Figure 23.22) (Conwell et al., 2010; Dechant et al., 2006; Pusterla et al., 2005; Sertich, 2005)

Intra-abdominal abscesses are variable in appearance, as they may be poorly marginated or surrounded by a well-defined capsule (Pusterla et al., 2007; Reuss et al., 2011). The abscesses contain anechoic to hypoechoic fluids or echoic material and are sometimes multiloculated (Figure 23.23) (Reef, 1998). The presence of hyperechoic gas echoes within an abscess is consistent with anaerobic bacterial infection. Surgical incision infection can lead to peritonitis and adhesion formation.

Uroperitoneum will appear as excessive free anechoic peritoneal fluid. The rupture or tear can be located anywhere along the urinary tract. Transrectal ultrasound might be required in adult horses to identify a defect in the bladder (Fontaine et al., 1999).

Many types of intestinal tumor have been reported including gastrointestinal stromal cell tumors, leiomyomas, leiomyosarcomas, with the most common being lymphoma and adenocarcinoma (Taylor et al., 2006). Ultrasonographic appearance might vary depending on the tumor type producing annular thickening, focal or solitary masses to diffuse infiltration. Additional tumor types involving the abdominal cavity or organs might be detected during the ultrasound examination and have various appearances (Figures 23.24 and 23.25).

Transrectal evaluation of the right caudal abdomen allows identification of the base of the cecum dorsally,

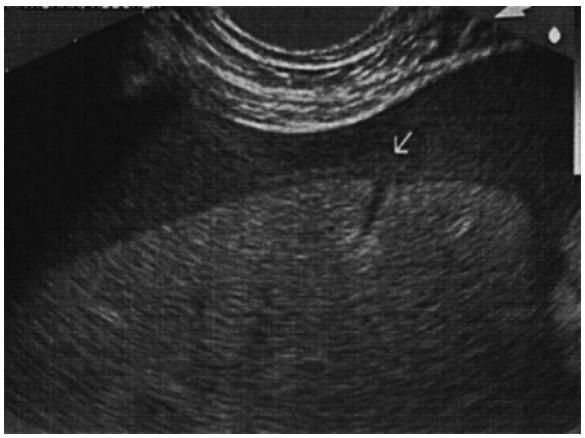

Figure 23.22 Hemoabdomen. Transcutaneous image obtained from the ventral abdomen. Note the echoic peritoneal fluid that surrounds the spleen. In real time, the fluid had a swirling appearance. Notice the splenic fracture (arrow) which was the cause of the hemoabdomen.

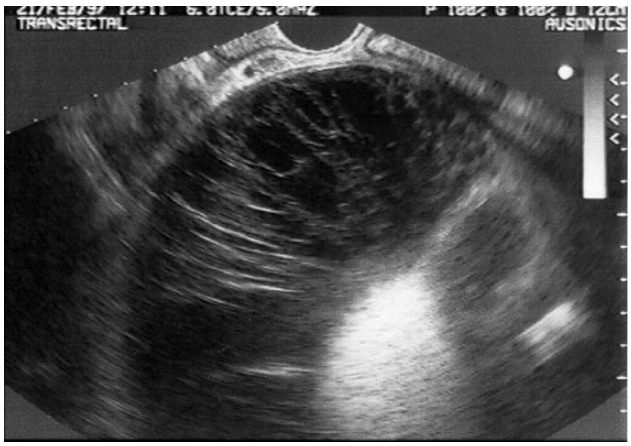

Figure 23.23 Abdominal abscess. Transrectal image of a large intra-abdominal abscess. Note the loculated appearance of the abscess containing anechoic fluid with a hyperechoic center consistent with gas.

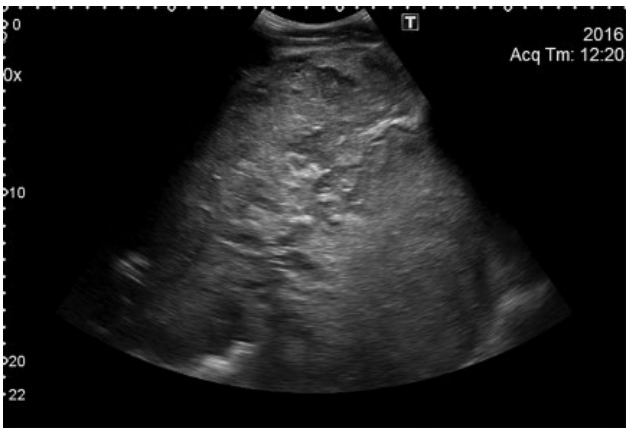

Figure 23.24 Abdominal tumor. Transcutaneous image obtained from the ventral abdomen of a horse with multicentric lymphoma. Note the large heterogeneous mass occupying most of the caudoventral abdomen. The diagnosis was confirmed at necropsy.

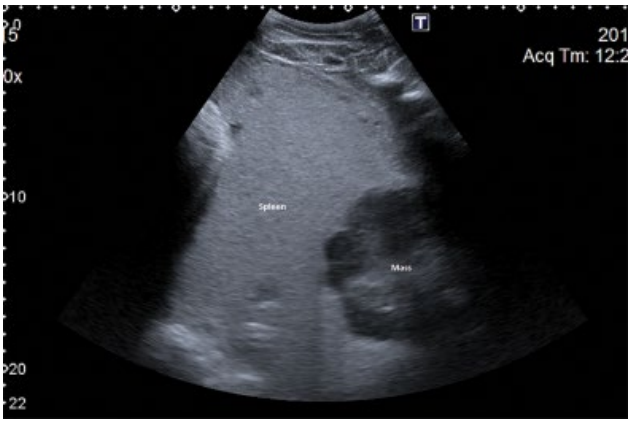

Figure 23.25 Splenic tumor. Transcutaneous image obtained from the ventral abdomen of the same horse as in Figure 23.24. Note the heterogeneous splenic mass present within the splenic parenchyma.

the right dorsal colon ventrally, and the duodenum caudal to the right kidney. The mesenteric root and small intestine are imaged in the center of abdomen. The small colon can be identified in the left caudodorsal quadrant dorsal to pelvic flexure (Reef, 1998; Schmidt, 1989).

The liver is normally imaged in the right 10th to 15th intercostal spaces (Figure 23.26) and from the left 6th to 10th intercostal spaces adjacent to the spleen in some horses (Figure 23.27) (Reef, 1998). Atrophy of the right lobe of the liver is common in older horses (Reef et al., 1990). The liver has sharp, well-demarcated margins and a homogeneous parenchyma of medium echogenicity containing a branching vascular pattern. The biliary system is not normally imaged unless it is distended (Reef et al., 1990). Acute liver diseases are characterized by an enlarged liver with rounded margins and alterations in the echogenicity of the hepatic parenchyma (Figure 23.28) (Reef, 1998). Chronic conditions are associated with increased parenchymal echogenicity, decreased liver size with loss of normal architecture and vascular markings (Freeman, 2003). Features of diseases affecting the biliary system include distention and thickening of the wall of the bile ducts. Hepatoliths are variable in echogenicity and cast variable acoustic shadows (Figure 23.29) (Reef et al., 1990). Secondary biliary distention is a common finding with hepatoliths and is characterized by a "parallel channel sign," which corresponds to a distended bile duct adjacent to portal veins. Focal lesions, such as

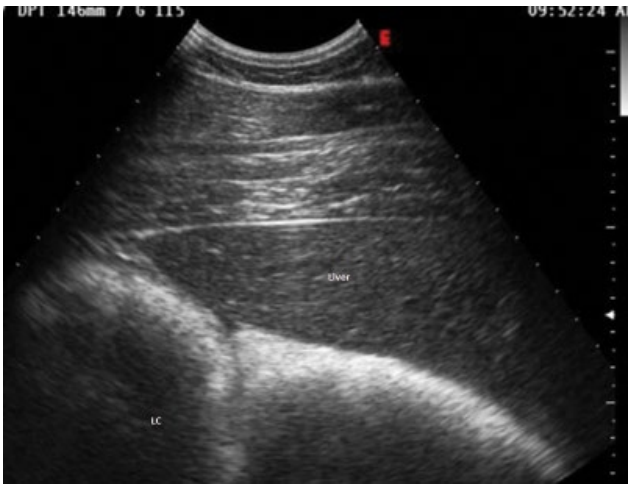

Figure 23.26 Normal right liver lobe. Transcutaneous image obtained from the right lateral side of the abdomen; dorsal is to the right of the image. The right liver lobe is seen ventral to the lung field from the right 15th to 19th intercostal space in many horses. The duodenum and right dorsal colon are visible deep to the right liver lobe. The right dorsal colon shows a characteristic large radius of curvature.

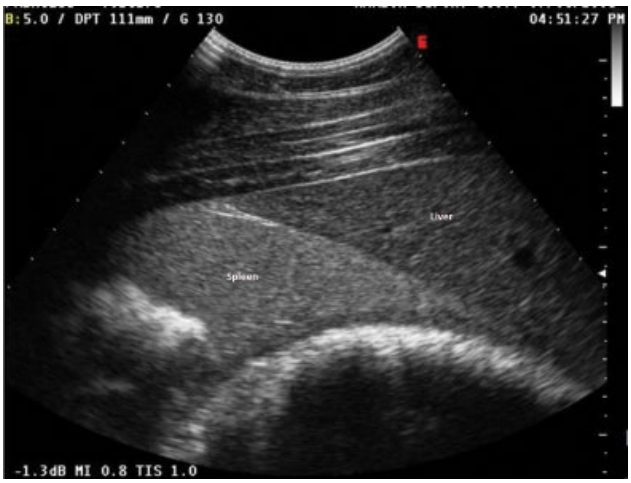

Figure 23.27 Normal left liver lobe. Transcutaneous image obtained from the left lateral side of the abdomen; dorsal is to the right of the image. The spleen and left liver lobe are seen adjacent to each other in the left cranial intercostal spaces (6th to 10th ICS).

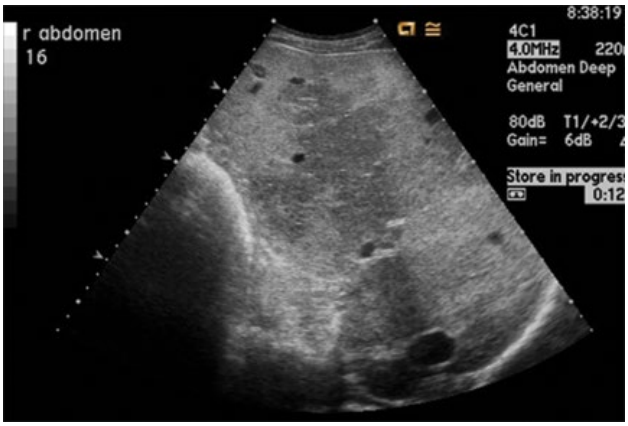

Figure 23.28 Acute hepatitis. Transcutaneous image obtained from the right 16th intercostal space; dorsal is to the right of the image. Note the enlargement of the right liver lobe. The liver parenchyma has a diffuse heterogeneous hypoechoic appearance.

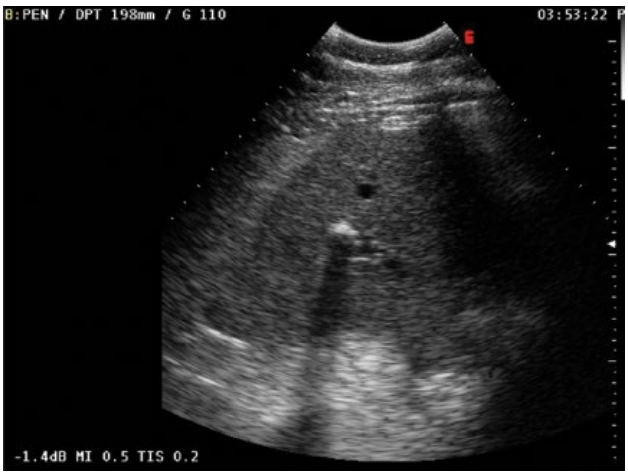

Figure 23.29 Hepatolith. Transcutaneous image of the left liver lobe; dorsal is to the right of the image. Note the relatively small hyperechoic hepatolith casting a strong acoustic shadow.

abscesses and neoplasic masses, may be single or multiple and have a hypoechoic, hyperechoic, or mixed echogenicity (Freeman, 2003). Generalized increase of the liver echogenicity occurs with diffuse neoplasia.

The spleen is visualized adjacent to the body wall from the left 8th intercostal spaces to the paralumbar fossa, extending in the ventral abdomen often to or slightly to the right of midline (Reef, 1998). The splenic parenchyma has a granular homogeneous appearance and contains a few blood vessels. The spleen is the most echogenic abdominal organ compared to the liver and kidneys (Reef, 1998). Splenic hematomas contain anechoic to hypoechoic fluid initially, then become hyperechoic and loculated as fibrinous clots form and can lead to hemoperitoneum (Freeman, 2003). Features of splenic abscesses and neoplasia are as described for the liver (Figure 23.30).

The kidneys are the least echogenic abdominal organs (Reef, 1998). The right kidney is located dorsally between the 14th and 17th intercostal spaces adjacent to the abdominal wall (Figure 23.31) (Reef, 1998). The right kidney is 13–15 cm long, 5–18 cm wide, and 5 cm thick. The left kidney can be imaged in the dorsal aspect of the 15th intercostal spaces to the paralumbar fossa medial to the spleen (Figure 23.32) (Reef, 1998). The left kidney is longer, measuring 15–18 cm with a width of 11–15 cm, and is 5–6 cm thick (Freeman, 2003).

The urinary bladder is not imaged from the ventral window, unless distended, due to the gas present within the large intestine. The ureters and urethra cannot be identified unless abnormally distended; except for the proximal portion of the right ureter (Reef, 1998). The transrectal approach is useful for the evaluation of the caudal edge of the spleen and left kidney adjacent to the left dorsal and lateral abdominal wall. The bladder appears as an oval or round structure with a hypoechoic wall cranial to the pelvic brim. The bladder contains anechoic to hyperechoic fluid depending on the degree of urine, mucus, and crystals present (Schmidt, 1989). The size, location, and wall thickness of the bladder vary upon the degree of urine distention. Normal wall thickness should measure between 0.3 and 0.6 cm (Reef, 1998). The entry points of both ureters can usually be identified in the dorsolateral aspects of the bladder wall. The pelvic urethra can often be followed caudally, mainly in males (Schmidt, 1989).

Acute renal conditions are characterized by enlarged kidneys, hypoechoic or hyperechoic parenchyma, poor

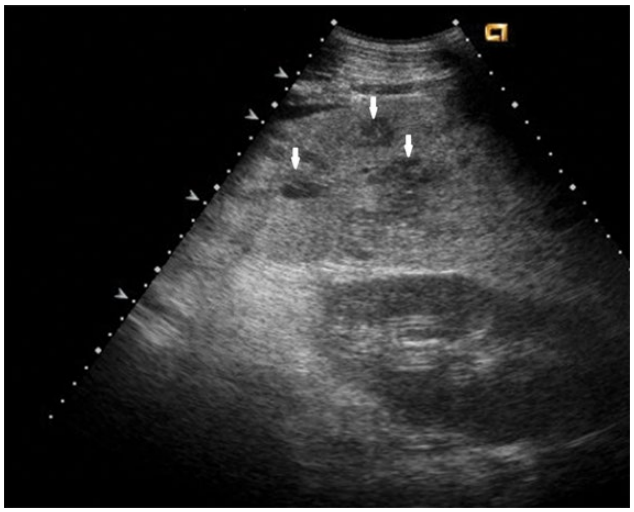

Figure 23.30 Splenic masses. Transcutaneous image obtained from the left 16th intercostal space of a horse suffering from hemangiosarcoma; dorsal to the right of the image. Note the heterogeneous appearance of the splenic parenchyma containing multiple small masses (arrows) of mixed echogenicity.

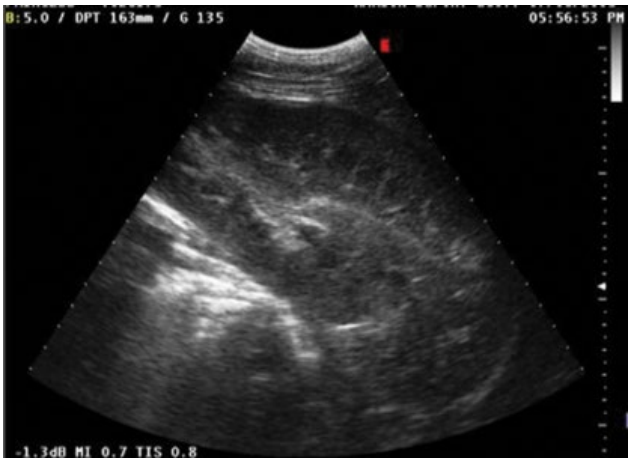

Figure 23.31 Normal right kidney. Transcutaneous image of the left lateral aspect of the abdomen; dorsal is to the right of the image. The right kidney is visualized adjacent to the body wall within the 14th to the 17th intercostal spaces.

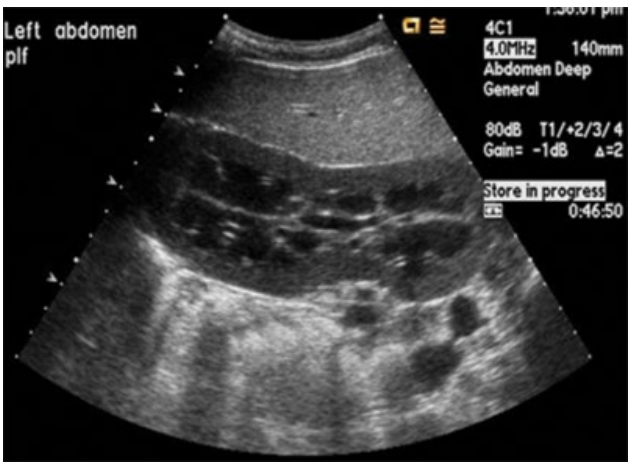

Figure 23.32 Normal left kidney. Transcutaneous image of the right lateral aspect of the abdomen; dorsal is to the right of the image. The left kidney is visualized deep to the spleen in the left paralumbar fossa region and caudal intercostal spaces (15th to 17th).

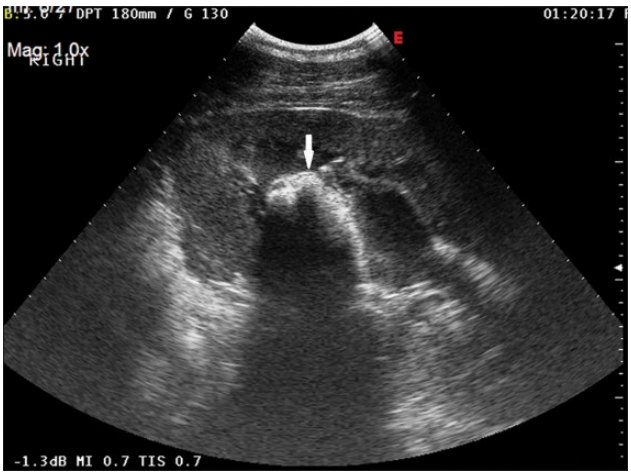

Figure 23.33 Nephrolithiasis. Transcutaneous image of the right kidney; dorsal is to the right of the image. Note the presence of a nephrolith (arrow) in the renal pelvis casting an acoustic shadow. There is evidence of mild hydronephrosis dilating the renal pelvis.

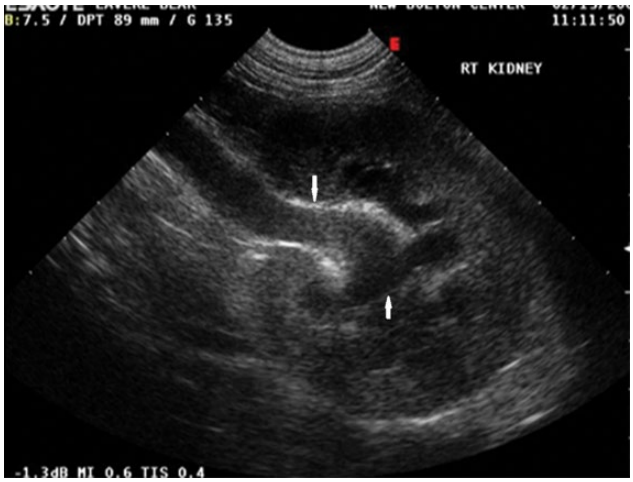

Figure 23.34 Hydronephrosis secondary to ureterolithiasis. Transcutaneous image of the right kidney; dorsal is to the right of the image. Note the severely dilated right proximal ureter (arrow) and renal pelvis (arrow). A more distal obstructive ureterolith was image transrectally (image not shown).

definition of the corticomedullary junction, and often perirenal edema (Reef, 1998). Chronic renal failure is associated with small irregular kidneys with increased echogenicity and loss of normal architecture (Freeman, 2003). Renal pelvis distention by hypoechoic fluid is usually associated with pyelonephritis. Uroliths appear as irregular, hyperechoic structures casting strong acoustic shadow and may affect the kidneys, ureters, urinary bladder, and urethra (Figure 23.33) (Reef, 1998). Obstructive uroliths can result in marked distention of the proximal urinary tract by anechoic urine (Figure 23.34). Cystitis is characterized by diffuse increased bladder wall thickness whereas neoplasia usually appears as localized thickening or discrete masses

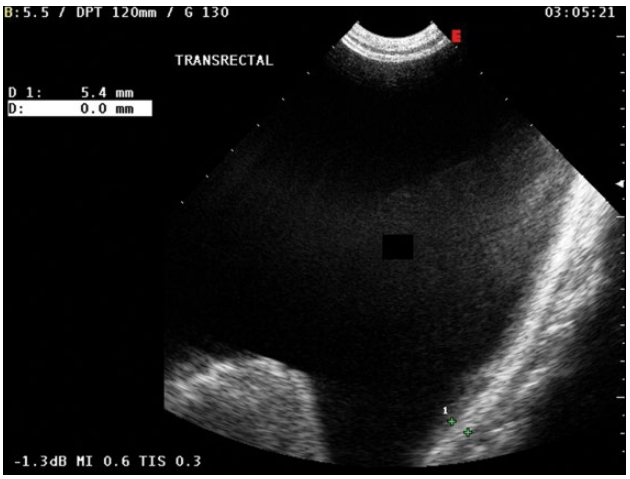

Figure 23.35 Bladder mass. Transcutaneous image of the caudoventral aspect of the abdomen of a horse suffering from a squamous cell carcinoma of the bladder. Note the mass protruding from the ventral wall into the anechoic fluid (urine) filled urinary bladder.

projecting within the lumen (Figure 23.35) (Freeman, 2003). A ruptured bladder is usually collapsed and folded on itself and contains little or no urine (Reef, 1998).

Radiography

Plain and contrast radiographs are not used commonly in the assessment of the adult horse's abdomen because of the large body size and the limited availability of equipment. Even if the equipment is available, the scattered radiation often makes it impossible to produce a high-quality image. In smaller equids, including foals, donkeys, and Miniature horses, abdominal radiography allows for a more complete evaluation of the abdomen. Thoracic radiographs can be useful for the diagnosis of diaphragmatic hernia where the small intestine, large colon, and stomach can sometimes be detected in the thoracic cavity (Figure 23.36).

Radiography is useful for identifying enteroliths and may be used as a screening test in regions where enteroliths are common (Rose et al., 1980; Lloyd et al., 1987; Murray & Green, 1992; Yarbrough et al., 1994). The technique requires X-ray machines capable of 600–900 mAs and 120 kVp (Rose & Rose, 1987). Four views are recommended. The use of computed radiography has slightly increased overall sensitivity and specificity, and of particular importance, improves the ability to detect enteroliths in the small colon (Maher et al., 2011).

Radiography of the cranioventral abdomen is a useful means for monitoring the resolution of sand accumulation and confirming the effect of medical treatment in the removal of sand (Kendall et al., 2008; Keppie et al., 2008; Ruohoniemi et al., 2001).

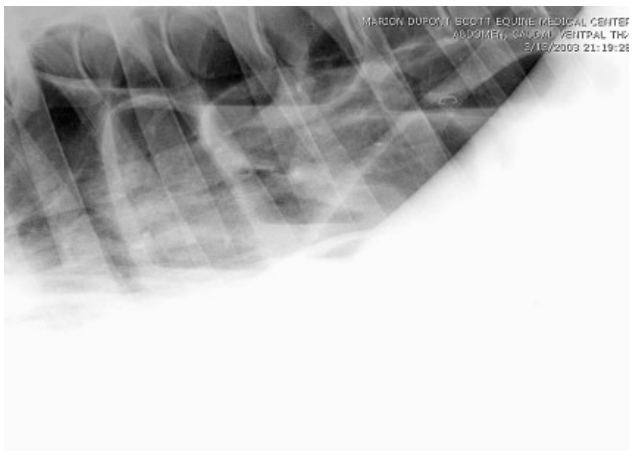

Figure 23.36 Radiograph of diaphragmatic hernia in a horse. Small intestine has filled the chest cavity.

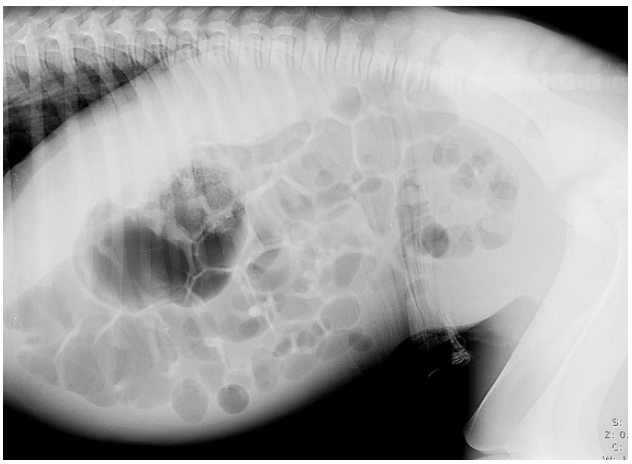

Figure 23.37 Radiograph of a foal with enteritis. The small intestine has generalized filling but is not severely distended.

Radiographs are useful for evaluating the foal's abdomen, and can help provide information about the small intestine, large colon, and bladder. The technique for the standing lateral view in foals is 20 mAs and 88 kVp for a 20 cm wide abdomen using 10:1 focused grid at 72 in focal distance (Campbell et al., 1982) or 15 mAs at 80–100 kVp with an 8:1 focused grid at 40 in both with rare earth screens (Fischer et al., 1987). Similar techniques appear satisfactory for newer digital or computed radiographs. Enteritis often appears as a slight small intestinal distention with only small amounts of gas (Figure 23.37). In contrast, obstructed small intestine will have distinct multiple loops of intestine with fluid lines and frequently indicates a strangulating lesion (Figure 23.38). Large intestinal obstruction in neonates may be due to meconium impaction or from large or small colon atresia. Atresia of the large colon can be diagnosed by the abnormal configuration of the distended colon.

Contrast radiography will help to define gastric outflow obstructions in foals and can help identify obstructions in the rectum and small colon (Zedler et al., 2009). Barium solution (2.5–5 mg/kg as a 30–40% solution) is administered via stomach tube, and gastric emptying of the barium normally occurs in 30–90 min. Barium retention indicates an outflow obstruction at the pylorus or duodenum or gastric stasis, which can be caused by gastric ulceration. In adult horses at least a liter of barium solution must be used to observe gastric emptying.

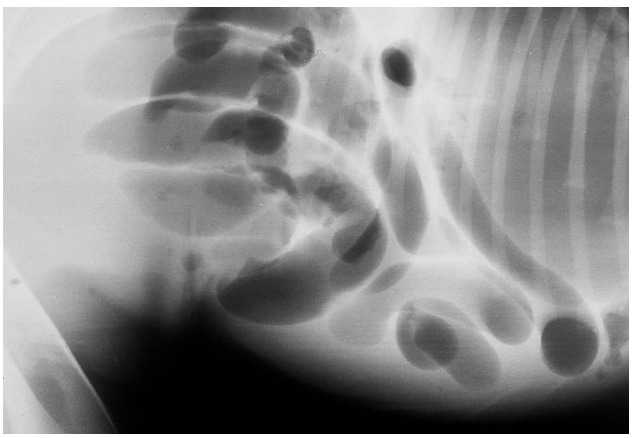

Figure 23.38 Radiograph of a foal with strangulated small intestine. The small intestine is severely distended and loop in multiple directions.

Infusion of barium in the rectum can help outline a meconium impaction in neonates. Care must be taken not to use an excess volume, which could cause rupture of the rectum or small colon.

Gastric emptying can be determined by scintigraphy using a technetium-99 m-sulfur colloid cooked in egg white administered by stomach tube or in sweet feed. Images from the left and right side are taken at 0, 15, 30, 60, 90, 120, and 150 min. Using a time versus activity curve, the gastric emptying half-time ($t_{1/2}$) can be calculated. Normal $t_{1/2}$ is 49 ± 30 min (Neuwirth, 1999).

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24

Decision for Surgery and Referral

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Determining the need for surgery in a horse with colic is often an emergency. Although the decision is best based on a diagnosis, it is not always possible for a specific diagnosis to be made. As a result, veterinarians rely on the horse's clinical signs to make the decision. The specific signs that are most helpful in indicating the need for surgery or intensive care are presented in Table 24.1. A thorough physical examination must be performed before either decision is made, as there are inherent errors associated with the use of an individual clinical sign by itself. There are circumstances when the diagnosis cannot be made and there are no definitive rectal examination findings. However, clinical signs such as unrelenting pain that does not respond to analgesics, are an indication to perform surgery as part of the diagnostic process.

Because the diseases that cause abdominal pain vary in severity and may be accompanied by a range of clinical signs, and horses may exhibit different behaviors or physiologic responses, there are no strict guidelines or list of parameters that determine the need for surgery. Therefore, every case should be judged on its own merits, based on the history and a thorough examination (see Chapter 20). In certain cases, a rapid decision can be based on a presumptive diagnosis made from the history, clinical signs, and examination findings. For example, the decision for surgery can be made immediately for a broodmare presented 5 days after foaling with an acute history of severe abdominal pain, severe large colon distention, clinical signs of endotoxemia, and a presumptive diagnosis of large colon volvulus.

Pain by itself, if persistent or recurrent, is an indication for surgery (White et al., 2005). Horses with moderate or severe pain are more likely to require surgery than horses with mild pain. Horses that have constant pain, particularly after an analgesic has been administered, are significantly more likely to need surgery. Horses that have return of pain or those that require two or more administrations of an analgesic are also more likely to need surgery (White et al 2005). The key is to monitor the horse closely, as some may show pain after administration of an analgesic, but the signs can be markedly decreased. Any recurrence should be considered a return of pain and therefore an indicator of the need for surgery. The return of pain in horses with a condition that normally would be treated medically also is important. Horses with impactions of the large colon or cecum with dry ingesta or sand may have recurrent pain, but usually can be treated medically. However, if the pain persists and there is no evidence of bowel motility after treatment, surgery is indicated. With the advent of potent analgesics, veterinarians have used the response to treatment to determine effectively which horses need surgery. If used with other physical signs, monitoring pain after treatment is highly successful in determining which horses will need surgery prior to identifying changes in other indicators.

Rectal temperature is usually not increased in horses with acute strangulation or obstruction. In contrast, horses with enteritis frequently have an increased temperature, suggesting that surgery is contraindicated (White et al., 1987).

Indicators of hydration and perfusion, such as heart rate, mucous membrane color, mucous membrane refill, packed-cell volume, and plasma protein concentration are not usually specific for diseases requiring surgery (Parry et al., 1983). In most cases, signs consistent with circulatory shock are associated with complete obstruction, strangulation, or enteritis. Consequently, changes in these indicators by themselves do not indicate a need

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Table 24.1 Indications for surgical and medical treatment of colic.

Indication	Description
Signs that indicate surgical intervention is needed[a]	
Pain	Uncontrollable and/or severe; does not completely respond to flunixin meglumine or detomidine or requires a second treatment
Gastric reflux	Alkaline yellow fluid >4 L
Rectal examination	Distended small intestine Distended and displaced large colon Distention that cannot be relieved medically Palpable foreign body or mass
Auscultation	Intestinal sounds absent
Peritoneal fluid	Increased protein concentration with red blood cells and degenerate neutrophils
Contraindications for surgical intervention[a]	
Pain	Depression or lack of pain
Temperature	>102.5 °F (39.2 °C)
Complete blood count	Neutrophilia or neutropenia (<3000/μL)
Auscultation	Progressive intestinal sounds

a) These signs are generalizations and may not fit individual cases.

for surgery. This is particularly true for heart rate. A low near-normal rate can be observed early in diseases characterized by intense pain. In these instances, the severity of pain should be considered the most important sign. Similarly, high heart rates, although associated with severe diseases and poorer survival, do not always predict the need for surgery. Diseases such as enteritis and tympany may cause high heart rates, but do not normally require surgery.

Nasogastric reflux increases the likelihood that the small intestine is obstructed and requires surgical treatment. Reflux can also be caused by ileus or duodenitis-proximal jejunitis, which can most often be treated medically. Obstructions of the colon can also lead to nasogastric reflux, but may not require surgery. Owing to the lack of sensitivity, other clinical signs should be used in conjunction with gastric reflux to make a final determination about the need for surgery. Conversely, the lack of gastric reflux does not rule out the need for surgery.

Duodenitis-proximal jejunitis, which can result in large volumes of gastric reflux, can present as a diagnostic dilemma, as affected horses are painful, have gastric reflux and distended small intestine, and the protein concentration in the peritoneal fluid is increased. Taken together, these findings are indicative of a need for surgery (White et al., 1987; Edwards, 2000). However, these horses also are febrile, have a leukocytosis, and, following gastric decompression, the pain is replaced by depression; these signs are indicative of the presence of enteritis. These findings normally indicate that surgery is not indicated. If in doubt, this type of case should have surgery to make sure that a strangulating or obstructing lesion is not present.

Horses with complete absence of borborygmi are significantly more likely to require surgery than horses with normal, decreased, or increased intestinal sounds (White et al., 2005). If borborygmi do not return after administration of an analgesic or other treatment, the likelihood that the horse will require surgery increases.

Finding an intestinal abnormality on rectal examination is not always indicative of a need for surgery. However, any abnormal distention or positioning of intestine in the absence of a diagnosis most likely requires surgical intervention. If no abdominal abnormalities are detected during the first rectal examination, repeated rectal examinations are indicated, particularly if other signs are consistent with a surgical disease (Reeves et al., 1988). Distention not felt during the initial examination may become evident in the near future.

If abnormal peritoneal fluid is obtained on abdominocentesis, intestinal lesions requiring surgery are usually present. Serosanguineous fluid with increased protein concentration is most likely to be due to strangulated intestine. If the fluid is normal but other physical signs indicate that surgery is necessary, the intestinal lesions are likely to be early in their development and have yet to result in peritoneal fluid changes. Consequently, peritoneal fluid should not be used as the only determinant for surgery, as waiting for a change could delay surgery and decrease the horse's chance of survival. An acute increase in peritoneal fluid protein concentration alone is sufficient to warrant surgery if other physical examination findings are also suggestive. If colic persists without a clear sign for surgical intervention, peritoneal fluid should be sequentially monitored for increases in lactate, protein, and cell concentrations (see Chapter 20). Peritoneal fluid concentrations of lactate exceeding 4 mmol/L and sequential increases in lactate concentration are commonly associated with strangulating lesions requiring abdominal exploration (Yamout et al., 2011; Peloso & Cohen, 2012).

Ultrasound is a valuable diagnostic tool that allows the rapid detection of intestinal injury or displacements that require surgery (Busoni et al., 2011). Ultrasound can be used to identify specific segments of the intestine and assess motility, intestinal wall thickness, visualization of vasculature, intussusception, sand accumulation, intramural hematoma, muscular hypertrophy, adhesions, diaphragmatic hernia, abdominal masses, neoplasia, choleliths, hemoperitoneum, and colon displacement or volvulus. Each of these conditions potentially requires surgical intervention (Beccati et al., 2011; Conwell et al., 2010; Dechant et al., 2008; Beckman et al., 2008; Pease et al., 2004; Slack, 2013 (see Chapter 23).

Box 24.1 Referral procedures and recommendations

1) Know the directions to and procedures of the referral hospital
2) Provide detailed history and treatment to date
3) Provide adequate analgesia for the duration of the trip
4) Place a stomach tube to allow any spontaneous gastric reflux
5) Administer treatments for shock and antibiotics, if necessary, prior to transport
6) Prepare owner for costs and need for partial prepayment of an estimate

Decision trees and predictive models have been developed to help veterinarians determine the need for surgery (Ducharme & Lowe, 1988; Pascoe et al., 1990, Reeves et al., 1991). However, these techniques lack both sufficient sensitivity and specificity and subsequently have false positives and false negatives (Thoefner et al., 2003; Ducharme et al., 1989). The statistical analysis used to generate these models is susceptible to differences in the prevalence of disease in a particular population. This renders these methods poor predictors when horses in that population rarely need surgery. These models are rarely used because the calculations require access to either a computer program or cell phone application.

When veterinarians are undecided because the horse's signs either are confusing or insufficient to support a definite decision about the need for surgery, the horse should be referred to a surgical facility for a second opinion where surgery can be completed immediately, if needed.

Frequently, physical examination findings such as heart rate and mucous membrane color and laboratory values will be normal at the onset of colic. The parts of the examination that are most helpful in the early period are observation of the horse for signs of pain, rectal examination findings, abdominal auscultation, and the response to analgesic administration (White et al., 2005). If pain is constant or returns within several hours after administration of flunixin meglumine or detomidine, the likelihood that the horse will need surgery increases substantially. In other words, normal values for heart rate, mucous membrane color, capillary refill time, and peritoneal fluid should be disregarded if pain, rectal findings, and lack of response to an analgesic indicate surgery.

Making the decision about the need for abdominal surgery for foals with colic is more difficult than for adult horses owing to an inability to perform a rectal examination. Fortunately, foals require emergency abdominal surgery far less often, and radiographs and ultrasound can help distinguish between conditions requiring surgery, obstructions and strangulating lesions, and those that can be treated medically, such as enteritis. Chronic distention of the stomach may indicate pyloric stenosis and warrant surgical exploration (see Chapter 34).

If the horse is not at a hospital where surgery or intensive care can be provided, the veterinarian must decide whether or not to refer the horse to another facility. Early referral for surgery or intensive care decreases complications and the cost of care while increasing survival (Southwood & Fehr, 2013). Delaying surgery in horses with strangulating lesions even by a few hours can dramatically decrease the prognosis. Although the owners may choose to delay referral based on the potential costs associated with either surgery or intensive care, it is important that they realize that this can adversely affect the outcome and increase the total cost once the horse is referred.

Specific recommendations for referral of horses with colic are listed in Box 24.1. Clients should be urged to preplan for the possibility of an emergency referral. Knowledge of a referral facility location, availability of transport, the cost of emergency care and what information will be required for admission should be readily available. Preselecting which horses will be referred for care helps speed the decision-making process during the emergency.

Prior to transporting the horse, it is important to initiate appropriate treatments such as antibiotics, flunixin meglumine, and intravenous fluid therapy if shock or a strangulating lesion is present. However, these should be completed rapidly so as not to delay transport of the horse to a surgical facility as soon as possible. It also is important to pass and secure a stomach tube in place for transport to allow for spontaneous reflux. Providing additional analgesics to the owner for treatment during transport may be of benefit to horses with severe colic.

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Prognosticating Equine Colic

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Prognosis for Survival

As a result of the wide variety of diseases that cause colic, determining the prognosis is challenging. With the numerous advances in critical care and surgery that have been made over the last four decades, the prognosis for most types of colic has improved. Despite these improvements, some diseases continue to have a high fatality rate, presumably due to delays in recognizing the problem and initiating veterinary care (Dukti & White, 2009). Owing to the high cost of care for some severe diseases, owners not only want an estimate of the expense associated with treatment, but also an indication of the horse's chances of survival and future use. Several models and algorithms have been developed to help evaluate risk and predict outcome that utilize clinical signs, clinical chemistry, and behavioral signs. This chapter describes the use of prognostication for horses at increased risk for a fatal outcome and the potential for return to use after a colic episode.

Signalment and History

Signalment and historical information have prognostic value for horses with colic. Several studies, including two large retrospective studies that included 774 (Proudman et al., 2006) and 300 horses (Mair & Smith, 2005a), have identified advanced age as a negative prognostic indicator for survival after colic surgery. However, there also is recent evidence from studies comparing geriatric (≥16 years of age) with nongeriatric horses undergoing colic surgery that did not show a difference in survival (Krista & Kuebelbeck, 2009; Southwood et al., 2010; Gazzerro et al., 2015). It is important to note that older horses treated medically have a higher rate of euthanasia owing owners not electing surgery (Southwood et al., 2010).

Although colic occurs in all breeds, draft horses, Thoroughbreds, and Thoroughbred cross horses are reported to be at increased risk for mortality (Proudman et al., 2006). For example, draft horses weighing >680 kg that had surgery due to colic had longer durations of anesthesia, more postoperative complications, and a higher mortality rate than lighter draft horses (weighing <680 kg) (Rothenbuhler et al., 2006). Furthermore, the short-term survival rate reported in that study was 60%, which is lower than the survival rate in many retrospective studies involving light breed horses.

Numerous studies have attempted to evaluate the association between physical examination findings and survival. Of the parameters evaluated, cardiovascular values and degree of pain have significant association with case fatality (Orsini et al., 1988; Furr et al., 1995; Parry et al., 1983; Puotunen-Reinert, 1986; Grulke et al., 2001; Proudman et al., 2006; Van der Linden et al., 2003; Ihler et al., 2004; Thoefner et al., 2001). For example, increased heart rate and packed-cell volume (PCV) were associated with decreased survival in 382 horses undergoing colic surgery for small intestinal diseases and in 275 horses requiring surgery for large intestinal disease (Proudman et al., 2005a). Furthermore, intraoperative mortality was positively associated with pain at admission and negatively associated with pain severity (Proudman et al., 2006). Similar results were reported for cardiovascular parameters (heart rate, skin tent) and pain associated with survival after surgery (Van der Linden et al., 2003; Mair & Smith, 2005a, 2005b). Increased heart rate (>80 bpm) in horses with strangulating small intestinal lesions due to pedunculated lipomas is associated with increased case fatality (Garcia-Seco et al.,

The Equine Acute Abdomen, Third Edition. Edited by Anthony T. Blikslager, Nathaniel A. White II, James N. Moore, and Tim S. Mair.

Companion website: www.wiley.com/go/blikslager/abdomen

2005). Although increases in heart rate and PCV are indicative of a reduced chance of survival, it is not possible to identify specific values that will accurately predict nonsurvival in individual horses.

Clinicopathologic Values

Numerous blood and peritoneal fluid values are used to estimate a prognosis for survival. Blood and peritoneal fluid lactate are accurate indicators of tissue perfusion, which is an estimate of the cardiovascular status of the horse (Moore et al., 1976; Genn & Hertsch, 1982; Dunkel et al., 2013; Johnston et al., 2007; Furr et al., 1995). As the concentration of lactate increases, the horse's chance of survival decreases. Blood lactate concentrations exceeding 10 mmol/L in horses undergoing surgery for colic are associated with a significant risk of death (McCoy et al., 2011). When cortisol, epinephrine, norepinephrine, lactate, electrolyte concentrations, acid–base variables, and heart rate were examined in 35 horses, higher plasma epinephrine, plasma lactate, and serum cortisol concentrations were significantly associated with fatality (Hinchcliff et al., 2005). Lactate remains the most useful prognosticator, particularly because it can be measured stall side with portable devices (Sloet van Oldruitenborgh-Oosterbaan et al., 2008; Nieto et al., 2015).

In contrast, serum electrolyte concentrations are of limited prognostic value. Horses admitted for surgical colic commonly have low serum ionized magnesium and ionized calcium concentrations before surgery (Garcia-Lopez et al., 2001). Hypocalcemia is of prognostic relevance with regard both to survival and to the probability of developing ileus during hospitalization (Delesalle et al., 2005). Furthermore, low ionized calcium and magnesium concentrations have been associated with strangulating lesions (Johansson et al., 2003). Importantly, correction of hypocalcemia has been associated with improved clinical outcome, highlighting the value of routine assessment of ionized calcium in horses with colic (Dart et al., 1992b). Although low ionized magnesium concentration is associated with postoperative ileus (Garcia-Lopez et al., 2001), there is no association between hypomagnesemia and fatality in hospitalized horses. Horses with colic that have hypomagnesemia had a lower survival rate than horses with colic and normal or hypermagnesemia (Dart et al., 1992b).

Although other electrolyte alterations occur in horses with colic and after colic surgery, none are independently linked to survival. Concentrations of sodium, chloride, and bicarbonate can be used to calculate the anion gap, which, when it exceeds 25 mEq/L, has been associated with nonsurvival in horses with abdominal pain and duodenitis-proximal enteritis (Bristol, 1982; Seahorn et al., 1992). As occurs with other clinicopathologic values, the anion gap provides a probability of survival rather that a prediction, and can be misleading if used alone.

Horses with severe hyperglycemia [blood glucose values exceeding 195 mg/dL (10.82 mmol/L)] are considered at higher risk for nonsurvival (Hollis et al., 2007; Hassel et al., 2009). Of 296 horses admitted for colic, 2.3% had glucose values below reference levels at some point during the first 48 h of hospitalization, and all of these horses had strangulating intestinal lesions (Hollis et al., 2007). In another study, a mean blood glucose concentration of 153 mg/dL (8.49 mmol/L) was reported for 228 horses with colic, whereas the mean values for horses with nonstrangulating obstruction and strangulating obstruction were 131.0 and 211.2 mg/dL (7.27 and 11.72 mmol/L), respectively. Horses that died had a mean glucose concentration of 232.2 mg/dL (12.89 mmol/L) (Hassel et al., 2009).

Other groups have evaluated the association between renal insufficiency and prognosis in horses with colic. For example, horses with colic or colitis that had increased serum creatinine that failed to normalize within 72 h of fluid therapy were three times more likely to die or be euthanized (Groover et al., 2006).

Coagulopathy

In the mid-1980s, coagulation parameters of 24 horses presented for colic were evaluated in one study; parameters included platelet count, fibrinogen, antithrombin III (AT-3), partial thromboplastin time (PTT), prothrombin time (PT), thrombin clotting time, soluble fibrin monomer, and fibrinogen degradation products (FDPs). Although all horses had at least one abnormality, those horses that failed to survive had an average of five coagulation abnormalities whereas those that survived had an average of two (Johnstone & Crane, 1986). Although evidence of hypercoagulability and fibrinolysis has not been associated with increased fatality or severity of the underlying condition, increased PAI-1 (inhibitor of fibrinolysis) has been associated with increased mortality (Prasse et al., 1993). Similarly, horses diagnosed with subclinical disseminated intravascular coagulation (DIC; defined as three or more out of six abnormal coagulation tests) were eight times more likely to die or be euthanized (Collatos et al., 1995). Furthermore, horses with large colon volvulus had abnormal results in four or more of the six coagulation tests and were significantly more likely to be euthanized (Dallup, 2001). Decreased antithrombin concentrations have been identified in horses with colic and associated with nonsurvival (Collatos et al., 1995).

Although fibrin degradation products increase in horses with colic, they increase in both survivors and nonsurvivors (Prasse et al., 1993; Collatos et al., 1995).

Although increased D-dimer concentrations were indicative of nonsurvival in a study of 105 horses with colic, (Sandholm et al., 1995) this did not prove to be true in horses with large colon volvulus in which all patients had increased concentrations and there was no association with prognosis (Dallup, 2001). Tests for coagulopathy are not frequently used unless there is evidence of excessive bleeding, decreased platelet numbers, and signs of disseminated intravascular coagulopathy.

Peritoneal Fluid

Although peritoneal fluid analysis is primarily used to determine the need for surgery, serosanguineous fluid has been linked to decreased survival in a study of 102 horses with pedunculated lipomas (Garcia-Seco et al., 2005). Interleukin-6 (IL-6) activity in peritoneal fluid exceeding 60 U/mL was associated with nonsurvival, enteritis, and strangulated intestine in 155 adult horses with colic (Barton & Collatos, 1999). IL-6 values of <24 U/mL are more useful in the prediction of survival than abnormal values in predicting fatal disease.

Increased alkaline phosphatase in peritoneal fluid is significantly associated with the severity of intestinal damage, an increased probability of the need for surgery, and a worse prognosis for survival (Saulez et al., 2004). Lactate concentration in the peritoneal fluid is a better predictor of strangulating obstruction than blood lactate (Latson et al., 2005). Increased peritoneal total protein concentration is also an indicator of increased risk of nonsurvival (White & Lessard, 1987). Although total protein is not an effective predictor when used alone, concentrations >4.5 g/dL are associated with nonsurvival.

Ultrasonographic and Histological Evaluation

Ultrasound has made it possible to evaluate intestinal wall thickness and motility in horses with colic. This is helpful in the diagnosis of large colon volvulus (Pease et al., 2004) and when monitoring intestinal well thickness postoperatively. Horses that developed multiple organ dysfunction syndrome after surgery for a large colon volvulus had significantly slower colon involution (39.7 h to wall thickness ≤5 mm) than horses that did not develop the syndrome (19.6 h) (Sheats et al., 2010). Large colon involution time was not significantly associated with survival in these 16 horses.

Biopsies obtained during colic surgery have been examined histopathologically to determine if the degree of intestinal damage was related to survival (Levi et al., 2012). Unlike scores developed using heart rate and PCV, combining the histopathologic scores of biopsies obtained from the large colon in horses with heart rate and PCV did not help to predict survival (Levi et al., 2012). This is in contrast to a larger study that determined that survival could be estimated using the ratio of the thickness of the interstitial lamina propria to the crypt, degree of loss of the superficial and glandular epithelium, and the severity of interstitial hemorrhage in large colons. Horses with interstitial-to-crypt ratios >3, 100% loss of the superficial epithelium, 50% loss of the glandular epithelium, and extensive hemorrhage did not survive. Predictions in this study had a high sensitivity and specificity (Van Hoogmoed et al., 2000).

Predictive Models

Several studies have developed mathematical models that combine a number variables together to provide the most accurate prediction for survival/nonsurvival (Orsini et al., 1988; Reeves et al., 1989; Reeves et al., 1991; Furr et al., 1995; Parry et al., 1983; Pascoe et al., 1990). In one of these studies, 1965 cases of equine colic from 10 equine referral hospitals were evaluated (Reeves et al., 1991). Data from 1336 of these horses were used for model development and the remaining 629 cases were used for validation of the model. Variables in the model included peripheral pulse (normal or weak), pulse rate, surgical or medical treatment, PCV, self-inflicted trauma (absent or present), and capillary refill time. Although this model showed a good fit with the model data set, it performed poorly on the validation set, thereby demonstrating the difficulty in standardizing predictive models (Reeves et al., 1991). Although this model was developed to be used horse side, its predictive value has never been tested because the mortality in individual practice populations is used in the model to make accurate predictions.

Examination of 32 physical examination and laboratory variables from 165 horses using logistic regression identified four significant variables (heart rate, peritoneal fluid total protein concentration, blood lactate concentration, and abnormal mucous membranes) that were used to calculate a colic severity score (Furr et al., 1995) (Table 25.1). The model is based on scores assigned each of the variables. The overall accuracy of the colic severity score was 93%, with 100% positive predictive value, 91.8% negative predictive value, and a sensitivity and specificity of 66.7% and 100%, respectively. Although these numbers seemed promising, the model has only been tested on one hospital population and should be tested in other populations before others depend on its accuracy. The model does provide a reasonable means for determining the prognosis in horses being referred for secondary care.

A gravity and shock score was developed using data obtained from 200 horses presented for surgical colic (Grulke et al., 2001). Horses were assigned to three categories of gravity score based on rectal palpation, frequency of borborygmi, abdominal distention, and severity of pain, with a gravity score of 3 representing severe distention on rectal palpation, absent borborygmi,

Table 25.1 Colic severity score. The scores matching each variable are added in each column along the bottom of the table. Survival is predicted if these scores total ≤7. Horses with a total score ≥7 are predicted to die. Source: Adapted from Furr et al., 1995. Reproduced with permission of John Wiley & Sons.

	Assigned score value				
Variable	**0**	**1**	**2**	**3**	**4**
Pulse rate (bpm)	<49	50–64	65–74	75–89	>90
Peritoneal total protein (g/dL)	<2.5		2.6–4.0	4.1–4.6	>4.7
Blood lactate concentration (mg/dL)	<49		50–70	80–90	>90
Mucous membrane appearance	Normal		CRT >3 or cyanotic		
Total					
The colic severity score equals the total of columns 0–4:					

CRT, capillary refill time.

and severe pain or depression. The horses were also categorized into four categories of shock score based on heart rate, respiratory rate, arterial blood pressure, PCV, lactate, and blood urea nitrogen. When both gravity and shock scores were equal to 3, the odds of death increased (odds ratio 7.1 and 7.2, respectively) compared with horses with scores of 1 (Grulke et al., 2001). The use of this scoring system on an independent population has not been reported. Combining the physical examination values with the cardiovascular values appears to improve the accuracy of the prognosis (Reeves et al., 1991; Grulke et al., 2001; Furr et al., 1995).

Although algorithms such as those described have increased the accuracy for predicting survival, the outcome for an individual horse with colic remains a mathematical estimate. The outcome is influenced by the population of horses being tested. In a population with a very high survival rate, these models are not as helpful as most horses survive. Nonetheless, the estimates are very helpful for categorizing the potential outcome, which can assist the veterinarian and owner in making informed decisions.

Prognosis for Specific Intestinal Diseases

Survival rates are frequently reported from hospital studies for horses undergoing surgery. Often horses discharged from the hospital are counted as short-term survivors, which does not include horses that did not survive during the treatment period or were euthanized during surgery. Therefore, the true survival rate for all horses examined and treated (including those euthanized) is often lower than the rate of survival to discharge, particularly for strangulating diseases. Euthanasia due to financial considerations also affects the reported survival rate. Some of these studies suffer from small numbers of cases and application of these results to individual cases should be used as an estimate owing to the innate variation from the time of colic onset to initiation of treatment.

Predictions for survival can be based on the segment of intestine and the disease category. Simple colic for which a diagnosis of a specific disease is not determined has a high survival rate, with one study reporting no deaths in 78 cases observed over 1 year (Tinker et al., 1997). In contrast, strangulating lesions are more fatal than simple obstructions (Dukti & White, 2009; Mair & Smith, 2005a). However, it is important to note that the duration of the particular disease and level of medical care provided affect the prognosis. Table 25.2 lists specific diseases with the short-term and, when available, long-term outcomes.

Stomach and Small Intestine

Survival from gastric rupture occurs only if the rupture happens at surgery and can be contained. Gastric impaction has a high short-term survival rate (90%) (Vainio et al., 2010). Survival rates in horses with small intestinal (75.2%) and cecal (66.7%) diseases are lower than those associated with diseases of the large colon (89%) or small colon (100%) (Mair & Smith, 2005a). Several studies have reported short-term survival for small intestinal lesions between 50 and 85% (Mair & Smith, 2005a; Freeman et al., 2000; Van den Boom & Van der Velden, 2001; Semevolos et al., 2002; Stephen et al., 2004; Archer et al., 2004; Morton & Blikslager, 2002; Fogle et al., 2008; Vatistas et al., 1996). Horses with simple small intestinal obstructions have a higher survival rate to discharge

Table 25.2 Specific disease survival based on case reports.

Disease	Survival to discharge (%)	Survival to 1 year (% of discharged)	Long-term survival (>2 years) (%)	Comments
Gastric impaction (Vainio et al., 2010)	90 ($n = 20$)	–	75	Gastroscopy diagnosis after 16 h of fasting
Small intestine surgery cases, carboxy-methylcellulose (Fogle et al., 2008)	–	Survival at 180 days Treated ~75 Untreated ~37	–	Treated horses were twice as likely to survive
Duodenitis-proximal jejunitis (Seahorn et al., 1992)	66.6 ($n = 50$)	–	–	Increased anion gap and peritoneal total protein were associated with death
Duodenitis-proximal jejunitis (Underwood et al., 2008)	87 ($n = 120$) Medical 91 Surgical 75	–	–	There was no difference in gastric reflux volume or duration between medical and surgical treatments
Small intestine, volvulus (Stephen et al., 2004)	80 ($n = 100$)	–	–	Complications occurred in 48% of survivors
Small intestine, epiploic foramen incarceration (Archer et al., 2011)	75 ($n = 126$)	50.3	34.3	Decreased survival with time. Postoperative ileus increased risk of mortality
Small intestine, gastrosplenic ligament incarceration (Bergren et al., 2015)	72.7 ($n = 22$)	–	–	84.2% of horses recovered survived to discharge
Small intestine, strangulating lipoma (Garcia-Seco et al., 2005)	75 ($n = 102$)	80	–	Higher survival rate with jejunojejunal than jejunocecal anastomosis
Small intestine anastomosis (Semevolos et al., 2002)	88 ($n = 59$)	57	–	No difference for stapled end-to-end or side-to-side
Small intestine surgery (Freeman et al., 2000)	85 ($n = 74$)	68 (39/57)	–	Long-term survival not affected by anastomosis type
Ileocecal intussusception (Ford et al., 1990)	62 ($n = 26$)	–	–	7 chronic and 19 acute cases
Mesenteric rent (Gayle et al., 2000)	47 ($n = 15$)	–	40	Small number of horses. Long-term follow-up was 5 months to 9 years
Small intestine resection (Morton & Blikslager, 2002)	76 ($n = 92$)			Variety of small intestinal diseases requiring a resection
Cecal impaction, medical and surgical (Plummer et al., 2007)	Medical 81 ($n = 54$) Surgical 95 ($n = 37$)	Medical 95 (18/19) Surgical 89 (25/28)	–	Euthanasia without treatment = 11. Cecal rupture at surgery = 11 horses
Cecal impaction (Smith et al., 2010)	65 ($n = 20$)	–	85 (11/13)	16 had cecocolic bypass; 50% of cases were secondary to previous orthopedic surgery
Cecal impaction, medical and surgical management (Aitken et al., 2015)	61 ($n = 59$ medical management) 82 ($n = 50$ surgical management)	57 (medical management) ~705 (surgical management)	–	68% had history of recent treatment or surgical procedure; 25% of 150 horses ruptured at the time of admission

(Continued)

Table 25.2 (Continued)

Disease	Survival to discharge (%)	Survival to 1 year (% of discharged)	Long-term survival (>2 years) (%)	Comments
Cecocolic intussusception (Gaughan & Hackett, 1990)	27 ($n = 11$)	–	–	Poor prognosis at surgery or due to complications
Cecocecal and cecocolic intussusception (Martin et al., 1999)	–	–	50	Loss due to rupture with leakage at surgery
Recurrent cecal impaction (Huskamp & Scheidemann, 2000)	86 ($n = 58$ treated surgically)	–	54	Outcome for cecocolic orifice enlargement surgery. Length of outcome not reported
Large colon impaction (Dabareiner & White, 1995)	94.6 ($n = 147$)	Medical 95 Surgical 57	–	Surgical survival was lower due to ruptures and compromised colon
Large colon impaction (Monreal et al., 2010)	99 ($n = 78$)	–	–	Results of enteral fluid therapy
Nephrosplenic entrapment (Hardy et al., 2000)	95 ($n = 174$)	–	–	A total of 161 horses; 8.1% had repeat entrapment; 43.4% had gastric reflux
Large colon nephrosplenic entrapment (Lindegaard et al., 2011)	91.5 ($n = 142$)	–	–	Of 114 treated conservatively 110 survived 20 of 25 treated surgically survived
Large colon volvulus resection (Ellis et al., 2008)	74 ($n = 73$)	67.8	66	3 years 63.5%
Large colon volvulus (Suthers et al., 2013)	70.7 ($n = 116$)	48.3	33.7	76.7% survived until discharge
Large colon volvulus (Hackett et al., 2015)	88 ($n = 1039$)	–	–	From 1986 to 2011. Success based on early referral and prompt surgery
Enteroliths (surgical) (Hassel et al., 1999)	96.2 ($n = 247$)	92.5	–	Excellent surgical success
Sand colic (surgical) (Granot et al., 2008)	95 ($n = 41$)	100 (35/37)	–	High survival after surgery
Sand colic (medical) (Hart et al., 2013)	90	–	–	Complications at surgery decrease survival
Small colon resection (Prange et al., 2010)	84 ($n = 43$)	93 (28/30)	–	27/43 were lipomas
Small colon (surgical) (De Bont et al., 2013)	91 ($n = 81$)	81	73	Resection associated with reduced long-term survival
Small colon impaction (Frederico et al., 2006)	Medical 91 ($n = 23$) Surgical 95 ($n = 20$)	–	–	High percentage of horses had diarrhea
Surgical colic for Miniature horses (Haupt et al., 2008)	98 ($n = 57$)	97 (39–45)	–	38 of 57 were fecoliths
Diaphragmatic hernia (Romero & Rodgerson, 2010)	23 ($n = 31$)	46 with surgery	–	No improvement on previous reports
Diaphragmatic hernia (Hart & Brown, 2009)	78 ($n = 9$ that recovered from anesthesia)	56 (5/9)	–	Of 44 horses, 26 were taken to surgery, 17 were euthanized at surgery

Table 25.2 (Continued)

Disease	Survival to discharge (%)	Survival to 1 year (% of discharged)	Long-term survival (>2 years) (%)	Comments
Peritonitis (Henderson et al., 2008)	86 ($n = 65$)	84 (32/38)	–	Poorer survival for tumors or foreign bodies
Enteroliths (Hassel et al., 1999)	96.2	92.5	–	Horses that had surgery Intestinal rupture occurred in 15% of 900 cases
Enteroliths (Pierce et al., 2010)	Small colon 88 ($n = 97$) Large colon 94 ($n = 136$)	Small colon 85 ($n = 62$) Large colon 89 ($n = 81$)	–	Complications in 27% ($n = 22$)
Foal surgery (Vatistas et al., 1996)	63 ($n = 67$)	–	57 (29/51)	Adhesions in 17% (8/51). Survival = 19% strangulating versus 69% nonstrangulating lesions
Geriatric survival (Krista & Kuebelbeck, 2009)	Geriatric 82 ($n = 34$); nongeriatric 89 ($n = 396$)	Geriatric 70 (14/20); nongeriatric 84 (108/129)	–	More geriatric horses were euthanized during surgery due to age
Geriatric survival, surgery for strangulating diseases (Southwood et al., 2010)	Small intestine geriatric 86 Small intestine mature 83 Large colon geriatric 78 Large colon mature 70	–	–	No significant differences for strangulating lesions

(Freeman et al., 2000; Underwood et al., 2008) compared with the survival rate for horses with strangulating lesions, but the short-term results vary (47–88%) (Gayle et al., 2000; Semevolos et al., 2002; Freeman & Schaeffer, 2005; Mair & Smith, 2005a; Stephen et al., 2004; Archer et al., 2011; Bergren et al., 2015). Long-term survival is consistently between 57 and 68% (Freeman et al., 2000; Freeman & Schaeffer, 2005; Semevolos et al., 2002).

Reports on long-term survival after treatment for small intestinal disease are generally similar, with short-term survival for strangulating lesions ranging from 60 to 70%. Several studies have reported similar short- and long-term survival rates, except for horses with epiploic foramen entrapment, where survival continues to decline over several years (Proudman et al., 2002, 2005b).

Cecum

Cecal impaction is the most commonly reported disease that has a lower survival to discharge rate with medical treatment compared with surgical treatment (Aitken et al., 2015). In a study of 114 horses with cecal impaction, 54 horses (81%) treated medically and 35 (95%) treated surgically were discharged from the hospital. Both studies had high rates of cecal rupture at admission or at surgery (Aitken et al., 2015; Plummer et al., 2007; Smith et al., 2010). Lack of recognition of cecal impaction prior to massive distention and subsequent rupture accounts for the lower number of horses treated or discharged after treatment. Cecal impaction due to cecal muscular hypertrophy at the base has a poor prognosis (Huskamp & Scheidemann, 2000).

Cecocolic or cecocecal intussusceptions have a low survival rate owing to challenging surgical management and the development of complications (Ford et al., 1990; Gaughan & Hackett, 1990). Of 30 horses with one of these conditions, six died or were euthanized without surgery (Martin et al., 1999). The 24 remaining horses were treated surgically and six of those were euthanized owing to peritonitis, rupture, or irreducible intussusception. Eighteen recovered from general anesthesia and 15 survived long term (Martin et al., 1999).

Large Colon

Simple obstructions of the large colon have a high survival rate (Table 25.2). Owing to their high prevalence, large colon impactions have a more favorable prognosis compared with the small intestine or cecum. Horses with large colon impactions are reported to have a survival rate of >95% if they respond to medical therapy and 58% if they require surgery (Dabareiner & White, 1995; Monreal et al., 2010). Horses undergoing surgery for sand impaction have high short- and long-term survival rates (Ragle et al., 1989; Granot et al., 2008; Hart et al., 2013). Colon displacements, such as entrapment in the

nephrosplenic space, are considered simple obstructions and have a high survival rate whether treated medically (96.5%) or surgically (80%) (Hardy et al., 2000; Lindegaard et al., 2011).

Large colon volvulus is one of the most deadly diseases causing colic, with survival rates reported to be 30–60% (Harrison, 1988; Snyder et al., 1989; Ellis et al., 2008). If caught early, however, survival to discharge after surgery can be as high as 88% (Hackett et al., 2015). Similarly, a short-term survival rate of 83% can be achieved in areas where these cases are recognized early and undergo surgery (Embertson et al., 1996). Long-term survival of horses with large colon volvulus in a 2 year study decreased from 70.7% short term to 48.3% after 1 year and 33.7% after 2 years (Suthers et al., 2013). Horses with large colon volvulus and plasma lactate concentrations <6.0 mmol/L can be predicted to survive based on a sensitivity and specificity of 84% and 83%, respectively (Johnston et al., 2007).

Determination of the viability of the large colon is most often made by clinical observation. However, many techniques have been developed in the hope of improving the accuracy of assessment. These techniques include clinical assessment, fluorescein dye, surface oximetry, Doppler ultrasonography, luminal pressure, and histopathology (Snyder et al., 1994; Van Hoogmoed et al., 2000; Brusie et al., 1989) (see Chapter 43). None of these techniques is 100% accurate at predicting survival.

A study of 900 horses with enterolithiasis determined that 15% of horses had colon rupture. However, horses undergoing surgical therapy had an excellent prognosis, with 96.2 and 92.5% short- and long-term survival, respectively (Hassel et al., 1999). Fatalities related to enteroliths are most often due to bowel leakage or rupture from pressure necrosis in the intestinal wall (Pierce et al., 2010).

Small Colon

Small colon obstructions that respond to medical therapy are reported to have survival rates of 72–100%. In contrast, horses requiring surgery have reported survival rates between 47 and 75% (Dart et al., 1992a; Ruggles & Ross, 1991; Prange et al., 2010; de Bont et al., 2013; Haupt et al., 2008). More recently, Frederico et al. (2006) reported on 44 horses with small colon impactions and determined that 21/23 (91%) of horses treated medically and 20/21 (95%) of horses treated surgically survived to discharge. Similarly, a study of four horses requiring resection and anastomosis for small colon lesions reported 100% short-term survival (Dart et al., 1992a).

Prognosis for Use

Horses surviving simple colic or other forms of medically treated colic have a high rate of return to their previous use. Other factors, such as the type of use or activity itself, are more likely to influence the long-term use of the horse. Most horses that survive colic surgery can return to their original use. In a study of 649 horses admitted with colic to one clinic, 28% were treated surgically, of which 54% survived short term, 88% were still alive after 12 months and 97% returned to the expected level of performance (Van der Linden et al., 2003). In a study of horses in sporting activities, 86.9% returned to use in any activity (Christophersen et al., 2011). For 190 patients surviving 6 months, 76% (133/195) were performing their intended use. After 1 year, 76% (145/190) were performing their intended use and 66% were performing at or above their preoperative performance (Davis et al., 2013). Similarly, 69% of Thoroughbreds returned to racing 6 months after colic surgery, whereas the reference group had a 73% return to racing (Tomlinson et al., 2013). Significantly fewer Thoroughbred foals surviving abdominal surgery raced as adults (63%) compared with unaffected siblings (82%) (Santschi et al., 2000). Considering other factors that affect performance, horses surviving surgical colic are generally able to perform as expected. Reasons for not performing associated with the disease or treatment for colic include intestinal adhesions, laminitis, and incisional hernia.

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26

Biosecurity in the Management of Equine Gastrointestinal Disease

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Biosecurity

When dealing with horses suffering from gastrointestinal disease, one must be aware of the potential involvement of infectious agents, either as primary etiologies or in the form of secondarily acquired infections. For this reason, it is critical that a proactive approach is adopted in order both to reduce the risk of infectious disease for the individual patient and to protect other animals and their human caregivers. There are numerous reports of the spread of gastrointestinal pathogens within equine facilities and hospitals, and these outbreaks can result in severe consequences for the affected animals, their owners, and the facility in which the outbreak occurred (Benedict et al., 2008; Steneroden et al., 2010; Dallap Schaer et al., 2010; Ward et al., 2005; Tillotson et al., 1997; Hartmann et al., 1996; Cummings et al., 2014). Some of these agents also have zoonotic potential, and although human infections resulting from exposure to animals suffering from these gastrointestinal pathogens are not frequently reported in the literature they do appear to be fairly common (Benedict et al., 2008). Preventing and controlling the spread of these pathogens requires a well-planned approach regardless of whether animals are being cared for in their home environment or in an equine hospital (Weese, 2014). Consideration must also be given to the risk represented by animals returning from an equine hospital to their home, as even asymptomatic animals could potentially expose naïve individuals to a nosocomial pathogen upon their return home.

The development of an infection control strategy is not inherently pathogen specific, as many control measures are universal in nature, but specific considerations may be required for agents with high contagious potential. In the context of gastrointestinal pathogens, transmission is inherently fecal–oral and by means of direct or indirect contact in most cases, and measures designed to prevent contact spread represent the cornerstone of control efforts. The greatest challenge associated with managing patients with gastrointestinal disease often lies in the assessment of the risk for disease transmission associated with the individual animal. Most often the clinician is confronted with trying to determine if their patient is likely carrying a potentially infectious agent, but there are also many situations in which the patient may not be the source of infection but is predisposed to acquiring a secondary infection. Whereas most infection control programs have historically been focused on controlling infected animals as the primary means of protecting other at-risk patients, strong consideration should be given also to actively managing the at-risk population in ways to minimize their risk of exposure.

Identifying Patients of Concern

Arguably any equid presenting with suspected gastrointestinal disease represents an at-risk patient. Patients presenting with enteritis or colitis are potentially infected with agents such as *Salmonella* spp. or *Clostridium difficile*, and although this is not always the case, these patients should be managed such that the risk of disease transmission is reduced. One widely used approach that has been used to identify patients at risk of shedding enteric pathogens has been the two out of three rule, wherein the presence of at least two of three risk factors, fever, leukopenia, and/or diarrhea, was considered an adequate indication for the initiation of barrier procedures. Unfortunately, this approach lacks sensitivity and may allow for infected individuals to be managed such that they represent an increased risk for contamination

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of the hospital or farm environment. Patients presenting with colic could be infected with infectious organisms prior to presentation, but also are likely to be at risk for healthcare-associated infections (HCAI), especially if they have undergone surgery and are receiving antimicrobial therapy. Foals presenting with gastrointestinal signs may be at increased risk for acquired infections due to impaired immune function, and may also suffer from highly infectious conditions not likely seen in adults, such as cryptosporidiosis.

Training and communication are critical to reinforce the importance of appropriate classification of patients in order to decrease the risks to the individual patient, the other patients within the facility, and the equine community outside the hospital. One complicating factor in this process is that clinicians may be reluctant to assign patients to a higher risk category owing to the inconvenience associated with having to deal with isolation or quarantine procedures, and also the increased expenses that may have to be passed on to the client. Consideration should be given to creating a biosecurity budget to cover the costs associated with surveillance, and potentially also the costs of barrier materials. This budget could be funded through a biosecurity fee charged to all patients admitted to the facility, rather than having all costs carried by the owners of affected animals. Although such charges may be questioned, it has been shown that clients and referring veterinarians understand the importance of biosecurity and accept the need for surveillance and management costs associated with this activity (Ekiri et al., 2014).

Management Protocols

Although it is common for large equine referral hospitals to have established biosecurity procedures in place, it is important that smaller facilities and ambulatory practitioners be well versed in the practices and procedures involved in infection control. Although biosecurity is a responsibility shared by all, it is beneficial to have a designated individual responsible for the implementation and maintenance of the infection control program. This designation aids in ensuring that protocols and procedures are not only followed, but also that they are frequently updated and revised in response to changing threats, both internal and external to the facility. If this responsibility is distributed too widely, there may be a loss of consistency in implementation, resulting in an increased risk of a disease outbreak.

The first step in implementation is designation of risk, most often using designations such as low, medium, and high risk. The low-risk population typically consists of the elective caseload, as these animals are generally healthy and unlikely to be carrying or shedding pathogens of concern. It is important to remember that some of these patients will undergo procedures or interventions that may create an increased risk for acquiring an HCAI, such as intravenous catheterization, antimicrobial administration, general anesthesia, and invasive procedures (endoscopy, surgery). The medium-risk population represents those animals that are clinically ill and are at an increased risk of acquiring and/or disseminating an infectious disease, but have not been proven to be infected with a pathogen of concern. This medium-risk group may also include animals that are receiving prolonged courses of antimicrobial therapy (longer than 72 h) (Aceto, 2015). The high-risk population includes those patients strongly suspected or known to be infected with a highly contagious pathogenic organism (e.g., *Salmonella* spp., *Cryptosporidium*) or with a pathogen that although perhaps not highly contagious, is associated with severe disease. An additional subset of patients are those that are known or suspected to be suffering from some degree of immune compromise, such as neonatal foals, especially those suffering from failure of passive transfer of immunity. Management of each of these groups will be different in several aspects, and it can be helpful to use some form of identification so that all caregivers are constantly aware of the individual patient's status and required management protocols. Some facilities use colored labels (green, yellow, red) on the medical record and/or stall, but this system is ineffective for those caregivers with red/green colorblindness, and use of a numbered system can avoid this concern. Any labeling system does carry the risk that visitors to the facility will be made aware that there are differences in patient status within the facility, potentially leading to questions or concerns related to the status of different patients. This is preferable, however, to labeling that includes specific information, such as naming of the pathogen of concern.

Given that the primary concern with patients suffering from gastrointestinal disease is the potential for direct or indirect contact dissemination of pathogens, the primary means of limiting spread is the implementation of barrier procedures. In most cases, patients in the low-risk group are not managed using barrier procedures, but steps should be taken to minimize the risk of exposing them to potential pathogens. Foremost among these steps is hand hygiene, but cleaning and disinfection of multiple-use medical devices (stomach tubes, speculums, thermometers, stethoscopes, etc.) or equipment (feed and water buckets, haynets, etc.) between patients is also of critical importance. These precautions are more easily performed in the hospital environment, and can be challenging to accomplish consistently in an ambulatory or field setting.

Formal barrier procedures are indicated for patients in the medium-risk group, most often consisting of disposable gloves, gowns, or coveralls, and shoe covers. In an ideal setting, this group of patients would be physically segregated from patients in the low-risk group, either in a separate area of the facility or in a dedicated isolation facility, but this is not always feasible or practical. If these medium-risk patients are housed in proximity to low = risk patients, then there should ideally be some physical separation, consisting of at least one empty stall. A concerted effort should be made to limit foot traffic into and out of the vicinity of the medium-risk patient. Although the efficacy of foot baths is open to debate, they may represent a reasonable tool to aid in trying to prevent dissemination of potential pathogens outside the immediate vicinity of the patient of concern (Stockton et al., 2006; Traverse & Aceto, 2015).

High-risk patients should ideally be placed directly in, or moved to, a dedicated isolation facility separate from the main animal housing facility. Although the additional physical barrier of distance is of obvious benefit, it is also typically easier to implement full barrier procedures within a dedicated isolation facility, as this improves compliance with isolation protocols. If an isolation facility is not available or is full, then high-risk patients are managed within the primary hospital environment. In this case, care must be taken to ensure that the environment outside a high risk patient's stall does not become contaminated, leading to dissemination, and similar precautions to those mentioned for medium-risk patients should be used (limited access, foot baths), but the area should also be disinfected several times per day to address any contamination that does occur. If a high-risk patient must be moved from the stall in order to receive care (surgery, imaging studies, etc.), then all areas through which the animal is moved and the destination area should be immediately and thoroughly disinfected prior to allowing other patients into these areas. For both medium- and high-risk patients, it is preferable to have only designated staff working with them, and if feasible the designated caregivers should not be working with patients in the low-risk group. Alternatively, caregivers should work with medium- and high-risk patients last so as to decrease the risk of contamination.

For immune compromised patients, the most common approach is the implementation of barrier procedures (gloves, gowns/coveralls, shoe covers) and segregation into a portion of the facility where the risk of exposure to patients in the medium- or high-risk groups is lowest. Limiting access to the immediate stall-side area and utilization of foot baths is also recommended. Consideration should be given to which persons should be handling and caring for these patients, as it is preferable not to have those dealing with medium- or high-risk patients also working with patients in the immune compromised group. If this is not feasible, then it makes sense to have caregivers work with the immune compromised patients before they work with low-, medium- or high-risk patients.

Barrier Procedures

The goal of barrier procedures is to prevent the transmission of a potential pathogen from one patient to another. Given that caregiver's hands represent the most likely route for this transfer, hand hygiene presents a critical opportunity to exert a profound effect with relatively little effort and expense. Unfortunately, despite its proven importance, hand hygiene is one of the areas where compliance is frequently poor (Kovacs-Litman et al., 2016). The gold standard for hand hygiene has been hand washing using antiseptic soap and fresh water, which has been shown to be very effective. Unfortunately, hand washing is typically not performed on a routine basis in the clinical setting, with forgetfulness and time constraints often being cited as the reasons for noncompliance (Anderson & Weese, 2016), and is likely performed even less often in the field owing to the lack of readily available washing facilities. Another factor that may play a role with regard to hand washing noncompliance is the development of skin drying and chapping that often occur with frequent hand washing (Kampf & Loffler, 2007). It remains clear that hand washing is indicated in any situation where gross soiling of the hands is present, but topical alcohol-based disinfectant hand rubs may represent a superior alternative when soiling is not present (Kampf et al., 2009). It has been shown that hand hygiene compliance is improved by ensuring ready access to alcohol-based hand disinfection products (Portner & Johnson, 2010). The other intervention that has been shown to be critical to improving compliance is the development and institution of protocols and routine training regarding hand hygiene (Srigley et al., 2016; Patel et al., 2016).

The most commonly used barrier procedures are gloves, gowns, and/or coveralls, and also shoe covers, although in some situations facial and hair protection is also indicated. Any barrier procedures are only as good as those individuals responsible for their implementation, and for this reason it is critical that all staff, house officers, and clinicians be appropriately trained. Errors in donning or removing any component(s) of the barriers can result in failure of containment of the pathogen of concern. At the simplest level, barrier procedures may consist only of examination gloves, which when properly applied can aid in limiting contact spread by the hands of those handling or caring for the patient. For this reason, glove use may be helpful in minimizing the risk of exposure for patients in the low-risk group. Gloves are at times seen as obviating the need for proper hand hygiene, but this is not appropriate and such assumptions may actually increase the risk of

contamination. Gloves are often contaminated owing to failure to change them between patients, or secondary to touching a contaminated piece of equipment. Contaminated gloves are also a frequent source of contamination for other items that should not be handled while gloves are being worn, such as cell phones, pens, and pagers (Girou et al., 2004; Loveday et al., 2014). For medium- and high-risk patients, gloves represent only one component of the barrier system, as contamination of caregivers' clothing and shoes represents a serious risk for dissemination of potential pathogens.

Gowns or coveralls are the two primary options for preventing soiled clothing, and coveralls are generally considered to be more effective than gowns. Gowns tend to leave the legs and back exposed, and often billow away from the body when moving or when kneeling down, predisposing to contamination. The material from which the gowns or coveralls are manufactured is also important, since fabric, paper, or spun-bonded materials are often water permeable and may allow contamination of the clothing beneath the barrier layer. For this reason, impermeable materials are preferred, especially when dealing with high-risk pathogens. Ideally any gowns or coveralls used will be disposable in order to prevent the accumulation of contaminants on the barrier garments. Owing to cost considerations, reusable, washable gowns or coveralls are often used in place of disposables, but strict procedures need to be in place to ensure that they do not become an ongoing source of contamination. A specific schedule should be in place for changing out of contaminated gowns or coveralls and replacing them with freshly cleaned items. For high-risk cases, one should consider using impermeable coveralls, or gowns paired with pants, to prevent clothing contamination, and these should be disposable. Caregivers should change out of their normal hospital attire into clean scrubs prior to working with medium- or high-risk patients, and change back into their hospital attire after working with these patients. Soiled clothing items should be handled in such a way that they do not contaminate the environment or clean clothing, and they should be laundered thoroughly to ensure that all contaminants are removed. The use of a combination of heat during the washing and drying processes, along with the use of bleach when appropriate, will help to ensure that potential pathogens are inactivated (Traverse & Aceto, 2015). When dealing with high-risk pathogens or potentially zoonotic organisms, more stringent barrier procedures may be indicated, such as face masks and hair covers.

Cleaning and Disinfection

Specific recommendations for cleaning and disinfection are beyond the scope of this chapter, given the wide variety of agents and differences in both the environments and manner in which they are used. That said, there are some broad shared concepts that are worthy of discussion. First, the ultimate efficacy of cleaning and disinfection is strongly influenced by the nature of the environment to be cleaned. If a barn with unsealed wooden walls and dirt floors needs to be cleaned and disinfected, or a grass or dirt paddock, then the best that can be accomplished is some degree of cleaning and reduction in the degree of contamination, because disinfection is impossible. For this reason, most equine hospitals house animals in stalls with sealed concrete walls and floors. An intermediate situation might be represented by a contaminated horse trailer, where aggressive cleaning and disinfection can be reasonably effective if all organic debris is removed during the cleaning process. A confounding factor in many situations is the presence of rubber matting intended to improve footing and comfort for the patient. If this material is intended to be permanent but is not fully sealed, then the area beneath the mat represents a very effective reservoir for potential pathogens. For this reason, any unsealed stall or area mats must be completely removable for the purposes of cleaning and disinfection, and cleaning must be performed between all patients.

All bedding material and waste must be removed as the first step in the cleaning process. If these materials are being removed from a medium- or high-risk patient's stall, then care should be taken to ensure that other animals are not exposed to these materials. For high-risk animals with documented infection with a highly contagious organism, such as *Salmonella*, then it is recommended that the bedding and waste be disposed of such that they cannot end up returning to the environment. The next step in the cleaning process is to wash any potentially contaminated surfaces, and it is important to ensure that the surface is not merely wetted down with water and a detergent cleaning agent. The surface should also be physically cleansed or "scrubbed" in order to dislodge fully any contaminants so that they can be removed. This represents a fairly common point of failure, as it requires substantial physical effort to ensure that all surfaces are appropriately cleaned. Although the use of pressure washers is tempting as an aid to thorough cleansing, it may result in the generation of aerosols containing the potential pathogens of concern, thereby presenting a risk to both patients and staff. Following cleansing, thorough rinsing is necessary in order to remove contaminants and residual cleaning agents prior to the application of a disinfectant. Complete removal of the cleaning agent is important, as there may be incompatibility between the cleaning and disinfecting agents used that could decrease the efficacy of the disinfection process. Surfaces should be allowed to dry prior to the application of disinfectants, or at a minimum the bulk of

the water should be removed so that the disinfectant is not diluted and rendered ineffective.

Care should be taken to ensure that the disinfectant used is active against the pathogens of concern. Quaternary ammonium compounds, although commonly used, may not be particularly effective against Gram-negative bacteria or viruses and other disinfectants may be better choices for use in equine facilities (Portner & Johnson, 2010). Chlorine compounds, most commonly hypochlorite solutions formulated from bleach, are readily available, inexpensive, and broad spectrum in activity, but are rapidly inactivated by organic matter, which means that they are useful only on well-cleaned surfaces (Dwyer, 2004; Tsujimura et al., 2015). Phenolic compounds have a broad spectrum of activity, have efficacy even in the presence of organic matter, and have residual efficacy after drying (Kinross et al., 2015). Peroxygen-based disinfectants, such as peroxymonosulfates or accelerated hydrogen peroxides, may exhibit superior efficacy (Boyce, 2016; Saklou et al., 2016). These products can be administered as mists, which allows application to all surfaces in the hospital environment, even to areas that are difficult to clean using normal methods, such as overhead duct work (Saklou et al., 2016; Traverse & Aceto, 2015).

Regardless of which disinfectant product is used, one must ensure that the proper dilution protocol is employed. Failure to use an appropriate dilution of the disinfectant will likely decrease efficacy, particularly if too low a dilution is used, and may increase the likelihood of damage to surfaces if too high a concentration is used. Metered dispensing devices for disinfectants can help to ensure that appropriate dilutions are used, and this is particularly important when large numbers of staff, perhaps with varying levels of training, are responsible for this task. If disinfectants are prepared and maintained as stock solutions, rather than being prepared immediately prior to use, then steps should be taken to ensure that the agent is still active over time, such as by testing with commercially available test strips specific to the agent used.

Surveillance Protocols

Surveillance represents a critical component of any infection control program, and takes several forms. Although microbiological surveillance of the patients and facility comes to mind first when one considers how to monitor for biosecurity concerns, it is important to remember that one must also perform medical record surveillance in order to identify patterns in the development of disease or secondary complications within the patient population (Burgess & Morley, 2015). If this task is not formally recognized and specifically assigned to someone, there is a very real risk that patterns will not be detected until an outbreak is already occurring. Formal reporting of unexpected changes in patient status to an individual tasked with collating and monitoring these reports will facilitate this early detection process. A recent report described the use of syndromic surveillance (surgical site inflammation, catheter site inflammation, gastrointestinal disorders, fever of unknown origin, etc.), which appeared to facilitate the recognition of HCAI compared with laboratory-based surveillance protocols (Ruple-Czerniak et al., 2014). Some hospitals use a system of morbidity and mortality rounds as a mechanism to involve clinicians and house officers in this process, and to enhance their awareness of these concerns.

Microbiological surveillance includes the monitoring of the hospital environment and also of patients suspected or known to be infected with pathogens of concern, and may also include monitoring of clinically normal animals. Environmental sampling consists in the collection of samples from high-traffic areas, areas with high potential for cross-contamination, and areas in which high-risk patients are housed. In most equine hospitals, the environmental monitoring program is focused on the detection of *Salmonella* spp. organisms, as these organisms historically have been responsible for most of the serious nosocomial outbreaks in this setting. Other organisms can be much harder to isolate or detect in environmental samples, but *Salmonella* spp. organisms typically serve as an excellent sentinel and facilitate the detection of high levels of environmental contamination and/or suboptimal cleaning and disinfection practices. In certain circumstances, it may be necessary to investigate other pathogens also.

Microbiological culture for *Salmonella* spp. has been the mainstay of surveillance programs as it was the only method available until the development of polymerase chain reaction (PCR)-based detection techniques. Culture will continue to remain the mainstay in the near future for several reasons, including cost, availability, and the fact that detection of viable bacteria is a more relevant measure than detection of DNA that may have come from living or dead bacteria (Alinovi et al., 2003; McKenzie & Hodgson, 2011). PCR testing does have the benefit of higher sensitivity, and newer real-time PCR techniques have improved the specificity of PCR testing (Ekiri et al., 2016). New lateral-flow immunoassays for *Salmonella* spp. organisms have excellent sensitivity and may represent a useful tool for rapid testing in the clinical setting (Burgess et al., 2015).

Patient surveillance is based primarily upon testing of fecal samples, which is logical given that fecal–oral transmission is the primary route of spread for gastrointestinal pathogens. In some cases, the testing of other samples, such as nasogastric reflux, may be indicated, but this type of sampling is focused more on clinical

management of the patient than on surveillance. The exact regimen for fecal culture may vary between institutions, but it is recommended that at least three to five samples be collected at 12–24 h intervals over a period of several days (Van Duijkeren et al., 1995; Burgess & Morley, 2014). Changes in clinical status may require that an individual be resampled, even if it was negative on previous testing. In cases where three cultures have returned negative but strong clinical suspicion remains, then consideration should be given to performing additional sampling. PCR testing may be used in conjunction with culture-based testing, and has the distinct advantage of providing more rapid results, but PCR testing is not always readily available and is more expensive. When positive test results are obtained using PCR, it is important to follow up with microbiological methods, as these allow for more detailed characterization of the organism, which is critical to continued surveillance and epidemiology. Although most of these recommendations are focused on *Salmonella* as the primary pathogen of concern, additional surveillance measures may be indicated in order to detect appropriately other pathogens of concern.

Specific Conditions

Zoonoses

Although there are not large numbers of reports regarding the transmission of zoonotic organisms from patients to caregivers or owners, the risks are very real (Morse et al., 1978; Benedict et al., 2008; Pelkonen et al., 2013). Certainly within the context of this text, one should consider *Cryptosporidium*, *Salmonella* spp., methicillin-resistant *Staphylococcus aureus* (MRSA), and *Clostridium difficile* as potential pathogens. All individuals handling or caring for animals infected with potentially zoonotic organisms should be aware of the potential for personal infection. The veterinarian has clear legal responsibilities regarding the identification and management of horses infected with zoonotic organisms and for communication of potential concerns to the staff, the patient's owner, and the public (Marsh & Babcock, 2015).

Cryptosporidiosis

Cryptosporidium infections have historically been a problem in calves but are increasingly recognized in foals suffering from diarrhea (Galuppi et al., 2015; Burton et al., 2010; Grinberg et al., 2003). Owing to the highly infectious nature of this organism, it is not uncommon to see zoonotic infections in veterinary students or others handling or caring for infected animals (Galuppi et al., 2016; Kinross et al., 2015). Control of this pathogen is complicated by its profound resistance to inactivation by disinfectant solutions, especially in situations where there is residual organic material present (Wilson & Margolin, 2003). There is evidence that some of the newer peroxygen-based disinfectants have improved efficacy against this pathogen, however (Quilez et al., 2005).

Salmonellosis

Salmonella spp. organisms have historically been responsible for outbreaks in numerous equine hospitals, and continue to be the primary microbes of concern. Although the ramifications of *Salmonella* infections are most severe in equine hospitals, community-acquired infections do occur and are often represent the original source leading to a hospital outbreak. *Salmonella* infections can be subclinical, making it impossible at the time of admission or hospitalization to identify animals that may be contaminating the environment. *Salmonella* represents an opportunistic pathogen, and hospitalized equine patients are at increased risk owing to both potentially higher levels of exposure and reduced resistance to infection (Burgess & Morley, 2015). For this reason, it is important to identify individual animals that are shedding the organism and to minimize the potential for spread to other animals within the facility. The virulence and infectivity of these organisms can vary depending upon the strain involved, as can persistence within the environment (Morley & Weese, 2015). Because environmental contamination is an inevitable consequence of managing an infected animal, the ability of *Salmonella* to persist within the environment is a major complicating factor, particularly in an outbreak situation. Very thorough cleaning and disinfection are required in order to decontaminate the environment, and this may require temporarily closing the facility to further admissions and depopulating current patients in order to allow this process to be performed appropriately.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

MRSA colonization or infection represents a serious emerging zoonotic condition, with numerous outbreaks involving equine patients and human personnel reported in equine hospitals worldwide (Carfora et al., 2016; Steinman et al., 2015; Schwaber et al., 2013; Sieber et al., 2011; Van Duijkeren et al., 2010; Cuny et al., 2006, 2008; Weese et al., 2005; Seguin et al., 1999). MRSA infections can be acquired within the hospital or the community, and the source of infection can be other equines or humans. Exposure to MRSA from infected wounds can certainly occur, but it is likely that most exposure occurs as a result of exposure to horses or humans in a subclinical carrier state involving the nasal passages. Although the potential for horse-to-human transmission is a serious concern, at present it does not appear to represent a major source of MRSA infections within the human

population (Cuny & Witte, 2016). That said, there is strong evidence that equine veterinarians are more likely than the general human population, or other veterinarians, to be carriers of MRSA organisms (Steinman et al., 2015; Kuroda et al., 2015; Schwaber et al., 2013; Jordan et al., 2011; Van Duijkeren et al., 2010) and that human carriers represent the source of MRSA in most equine outbreaks (Koop, 2016). For this reason, it is critical that surveillance following an outbreak includes not only the equine patients but also their human caregivers. Decolonization of the nasal cavity of those humans identified as carriers is recommended, but owing to the transient nature of the carrier state in horses this procedure does not appear to be required in horses (Schwaber et al., 2013; Weese & Rousseau, 2005). The use of appropriate barrier procedures, paying particular attention to meticulous hand hygiene, is critical in controlling the spread of this pathogen within the hospital.

Clostridium difficile

Clostridium difficile-associated diarrhea (CDAD) is an important clinical syndrome in adult horses and foals (Diab et al., 2013a, 2013b). The two primary risk factors for equine CDAD are considered to be antimicrobial therapy and hospitalization (Diab et al., 2013b), although one study of community-acquired CDAD in horses found that prior antimicrobial therapy was not a risk factor (Weese et al., 2006). Pathogenicity is primarily associated with the production of two major toxins, toxin A (TcdA) and toxin B (TcdB). As normal horses and foals can harbor either nontoxinogenic or toxinogenic strains of *C. difficile*, the mere presence of the organism is not diagnostically useful. Identification of either TcdA or TcdB in the feces of affected animals, in association with clinical signs consistent with CDAD, is the standard technique used for diagnosis of this condition. These tests are not routinely performed as part of the microbiological surveillance program in most equine facilities, and will have to be specifically requested by the attending clinician if CDAD is suspected. The failure to test may mean that infected animals are not identified, but routine management protocols used for medium- and high-risk patients are typically effective in containing this pathogen.

Nonspecific Conditions

Colic

Although a somewhat controversial topic, one should consider that horses suffering from colic, especially those patients undergoing colic surgery, be treated as medium-risk cases, regardless of their presenting signs. Horses suffering from colic are at increased risk of shedding potentially pathogenic organisms and for infection because they have a gastrointestinal disturbance, regardless of primary etiology. They also will likely undergo invasive procedures, such as nasogastric intubation, intravenous catheterization, and/or surgery, further increasing their risk. These patients are also suffering substantial physiologic stress, and inherently will have alterations to their normal diet.

Surgical Wound Sites

Animals that have undergone colic surgery are at substantial risk for incisional complications, and incisional infections represent a major component of these complications (Klohnen, 2009; Dukti & White, 2008). Numerous factors likely play a role in the development of incisional complications, including patient-specific factors, such as severity of illness and type of surgical lesion; surgical factors, such as the type of suture; suture pattern; requirement for enterotomy or resection/anastomosis; and postoperative incisional management (Colbath et al., 2014; Torfs et al., 2010; French et al., 2002; Wilson et al., 1995). Incisional infections certainly represent an important form of HCAI, and can have profound consequences in terms of the duration of hospitalization, expense of treatment, patient survival, and the development of complications, particularly abdominal hernias (see Chapter 48) (Davis et al., 2013; Klohnen, 2009; Kelmer, 2009; Smith et al., 2005). If incisional infection is suspected, then appropriate samples should be collected for bacterial culture and sensitivity.

Catheter-associated Complications

Horses presenting with gastrointestinal illnesses will often undergo intravenous catheterization during the course of their treatment, especially if hospitalized. Catheter-related complications, although not always definitively infectious in nature, represent a common form of HCAI in horses (Dias & De Lacerda Neto, 2013; Klohnen, 2009; Geraghty et al., 2009; Dolente et al., 2005). The most common complication is jugular vein thrombophlebitis, which is typically associated with heat, swelling, and pain in the vicinity of the catheter site and the catheterized vein, potentially accompanied by thrombus formation and vascular occlusion. Bacterial involvement may be associated with the development of systemic signs of inflammation, such as fever, leukocytosis, or leukopenia and increases in acute-phase proteins such as fibrinogen or serum amyloid A. The development of catheter-associated inflammation is a clear indication for removal of the catheter and, if infection is suspected, one should consider sterile collection of the catheter tip for bacterial culture and sensitivity testing (Geraghty et al., 2009). The collection of sterile blood samples for blood culture may also be indicated.

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Part VI

Medical Management

27

Medical Management of Gastrointestinal Diseases

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Analgesia

Relief of visceral pain in horses with colic is essential on humane grounds. It is also essential to try to minimize injury to the horse and attending personnel during evaluation and therapy. Even in mild cases, owner distress over animal pain is an important consideration. Pain is also associated with inflammation and the endocrine–metabolic stress response, so control of pain has other important influences on the response and recovery of horses following colic and colic surgery. The effect of pain on a horse's willingness to eat is well recognized (Taylor et al., 2002). Surgery or trauma leads to a substantial increase in energy requirements as a result of the stress response and the need for tissue repair; good pain relief is therefore important in postoperative patients. A detailed description of the mechanisms, effects and assessment of pain is provided in Chapter 12.

The most satisfactory method of pain relief is the correction of the underlying disease process. However, this may take time, and it is important to achieve temporary relief of pain by administration of analgesics to allow a thorough clinical examination. In many cases of colic, provision of analgesia may be the only treatment necessary, and the response to analgesic drugs can be an important determinant of the need for referral and surgery (White et al., 2005) (see Chapter 24). Analgesic drugs are also important in postoperative management. Wherever possible, it is important to select an analgesic drug that will yield the desired effect without creating complications such as inhibiting intestinal motility, predisposing to hypovolemia and shock, impeding intestinal healing after surgery or masking the signs of developing endotoxemia [systemic inflammatory response syndrome (SIRS)]. The commonly used analgesic drugs, their dosages, and their relative efficacy for the control of abdominal pain are summarized in Table 27.1.

Walking

Walking the horse with mild colic frequently appears to be beneficial, and in some cases may be the only treatment necessary. Walking appears to have an analgesic effect, in addition to stimulating intestinal motility. It also helps to prevent injury to the horse caused by falling to the ground and rolling.

Gastric Decompression

Gastric distention occurs most frequently secondary to small intestinal obstruction or small intestinal ileus. Since horses do not vomit, nasogastric intubation is necessary to determine if gastric distention is present and to provide relief (see Chapter 20). Decompression of the stomach is necessary to relieve pain and to prevent gastric rupture and death. Large volumes of reflux (10–20 L) may be obtained in some cases, and if necessary a nasogastric tube may be left in place to allow frequent (approximately every 2 h) decompression.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

The nonsteroidal anti-inflammatory drugs (NSAIDs) are a group of anti-inflammatory agents that inhibit components of the enzyme system that converts arachidonic acid into eicosanoids. The eicosanoids, including prostaglandins, leukotrienes, and thromboxanes, play a central role in the inflammatory response. Inflammation is a

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Table 27.1 Analgesic drugs and their relative efficacy for the control of abdominal pain.

Drug	Dosage	Efficacy
Dipyrone	10 mg/kg	Poor to moderate
Phenylbutazone	2.2–4.4 mg/kg	Poor to moderate
Flunixin meglumine	0.25–1.1 mg/kg	Good to excellent
Ketoprofen	1.1–2.2 mg/kg	Good
Meloxicam	0.6 mg/kg	Good
Firocoxib	0.27 then 0.09 mg/kg	Good
Xylazine hydrochloride	0.2–1.1 mg/kg	Excellent
Detomidine hydrochloride	10–40 µg/kg	Excellent
Romifidine hydrochloride	40–80 µg/kg	Excellent
Acepromazine	0.03–0.1 mg/kg	Poor
Morphine sulfate	0.15–0.66 mg/kg[a)]	Good
Pethidine	2.0 mg/kg	Poor
Butorphanol tartrate	0.02–0.075 mg/kg[b)]	Good
Buprenorphine	0.006 mg/kg	Good
Meperidine[c)]	1–2 mg/kg	Good

a) Use only with xylazine or another α_2-adrenoceptor agonist to avoid CNS excitement.
b) Doses in the upper range may cause ataxia.
c) Intravenous administration of meperidine can result in histamine release and hypotension.

succession of changes that occur in living tissue when it is injured, provided that the injury is not of such an extent that it destroys its structure and vitality (as opposed to necrosis, which is the state of irreversible arrest of function and irreparable disorganization of the structure of living tissue) (Dixon, 1967). The eicosanoids are derived from arachidonic acid, which is produced via the action of phospholipase A_2 on phospholipids in cell membranes. Once released, arachidonic acid becomes the substrate for a number of different enzyme systems. The cyclooxygenase (COX) enzymes metabolize arachidonic acid to form prostaglandins (PGs) and thromboxanes (TXs), whereas the lipoxygenases produce leukotrienes (LTs). In many tissues, PGs and TXs are produced constitutively, and these have many homeostatic roles. In the gastrointestinal tract, for example, PGs of the E series (particularly PGE_2) have a protective role in the gastric mucosa, protecting it from acids and hypertonic solutions (Guth et al., 1979). The principal reasons why NSAIDs are administered to horses are (1) to provide analgesia and (2) for their anti-inflammatory effects (Moore & Barton, 2003; Robertson & Sanchez, 2010; Muir, 2010; Cook & Blikslager, 2015). However, NSAIDs have significant side effects, primarily on the gastrointestinal mucosa (Marshall & Blikslager, 2011) and kidneys (McAllister et al., 1993).

The COX enzymes exist in at least three isoforms, known as COX-1, COX-2, and COX-3 (Vane & Botting, 1995; Cook & Blikslager, 2015). The COX-1 enzyme is produced constitutively in many tissues, and this isoform is responsible for the production of PGs involved in homeostatic functions (Mitchell et al., 1993). COX-2 production can be induced in many cells, especially those involved with the inflammatory response. In addition to their roles in inflammation, PGs have important roles in the regulation of body temperature and in mediating pain. Many of the side effects of NSAIDs (such as gastric ulceration, renal impairment, and platelet dysfunction) are believed to be due to the inhibition of the constitutively expressed COX-1 isoform. For these reasons, NSAIDs that selectively block the COX-2 isoform may offer therapeutic advantages by virtue of decreased side effects. However, this is an oversimplification, with constitutive COX-2 expression occurring in kidneys and placenta (Cook & Blikslager, 2015).

The NSAIDs are among the most frequently used drugs in horses (Kollias-Baker & Cox, 2004). They are commonly used to treat musculoskeletal inflammation and pain, colic, fever, and soft-tissue inflammation. In the treatment of pain not associated with inflammation, it has been suggested that opiates, rather than NSAIDs, may be more effective. However, recent evidence suggests that NSAIDs are effective at providing analgesia independently of their anti-inflammatory actions. In addition, there is evidence that NSAIDs and opiates may work synergistically to induce analgesia.

The principal mechanism of NSAID-induced analgesia is reduction of eicosanoid levels at sites of inflammation as a result of inhibition of COX (Vane, 1971). Eicosanoids may increase the sensation of pain by lowering the threshold for neural conduction at key sites along pain pathways (Seybold et al., 2003). Although most of the NSAIDs have relatively short half-lives, their duration of action can be very long. This may be due, in part, to their binding with very high avidity to the COX enzyme. They also tend to accumulate and persist at sites of inflammation. The most frequently recognized side effect of NSAIDs in horses is gastrointestinal ulceration, which results from the inhibition of production of cytoprotective PGs (Boothe, 1995). Ponies appear to be more susceptible to the ulcerogenic effects of NSAIDs, with signs of toxicity occurring at doses that are usually well tolerated by horses (Tobin et al., 1986). The gastric mucosa and the right dorsal colon appear to be particularly susceptible to these ulcerogenic effects of the NSAIDs (Karcher et al., 1990; Davis, 2017). Prolonged

treatment with NSAIDs and concurrent hypovolemia appear to predispose horses to ulceration of the right dorsal colon. The inhibition of protective PGs can also result in renal damage (including renal papillary necrosis and acute kidney damage), especially in horses that are geriatric, volume depleted, and hypotensive or have pre-existing renal, cardiac, or liver disease (Stillman & Schlesinger, 1990). PGs are important for the restoration of normal mucosal barrier function following injury, and flunixin meglumine inhibits the recovery of trans-epithelial barrier function in ischemia-injured jejunum (Cook et al., 2009), whereas it does not appear to affect the restoration of colonic mucosal barrier function (Matyjaszek et al., 2009).

The NSAIDs may also affect intestinal motility (Marshall & Blikslager, 2011), including inhibition of colonic motility (Van Hoogmoed et al., 1999, 2000) and inhibition of tonic ileal contractions (Menozzi et al., 2009).

The NSAIDs are classified as having nonspecific COX inhibition (e.g., phenylbutazone and flunixin meglumine) or COX-1-sparing/COX-2-selective effects (e.g., meloxicam, or coxibs, particularly firocoxib available for horses). Whilst the nonspecific COX inhibitors are most commonly used in the management of colic patients, the COX-1-sparing NSAIDs have less detrimental effects on the repair of damaged mucosa.

Aspirin

Aspirin (acetylsalicylic acid) is the oldest known NSAID. In addition to inhibiting COX, aspirin inhibits the formation and release of kinins, stabilizes lysozomes, and uncouples oxidative phosphorylation (Boothe, 1995). Aspirin has a very short half life (approximately 7 min after intravenous administration), which limits its use as an analgesic or anti-inflammatory agent. However, aspirin can be very useful as an antithrombotic agent, and at relatively small doses it can significantly prolong bleeding times. For this purpose, aspirin is usually administered orally daily or every other day at a dose rate of 17–20 mg/kg.

Phenylbutazone

Phenylbutazone is the most commonly prescribed NSAID in horses. The plasma half-life of phenylbutazone depends on the dose administered and the metabolic capacity of the animal, but is usually in the range 3–8 h. Both the parent phenylbutazone and its active metabolite, oxyphenbutazone, are highly bound to plasma proteins, and may displace other protein-bound compounds (Lees & Higgins, 1985). Therefore, phenylbutazone should be used judiciously with other highly protein-bound drugs, such as warfarin, gentamicin, and sulfonamides. Phenylbutazone can be administered intravenously or orally. In the treatment of gastrointestinal disease, it is most commonly administered intravenously. Feedstuffs, especially hay, can delay the absorption of orally administered phenylbutazone, but the bioavailability is unaffected. The use of phenylbutazone has been banned in many European countries because of concerns about its effect on human health if it enters the human food chain.

Phenylbutazone has a relatively narrow therapeutic index in horses. Although dose rates of 4.4–8.8 mg/kg (2–4 g for a 450 kg horse) are commonly used, the higher end of this dose range should be used only for short periods. The clinical signs of NSAID toxicity include depression, colic, anorexia, fever, and diarrhea (MacKay et al., 1983). Physical and clinical pathologic findings of toxicity include oral and gastrointestinal ulcers, low serum protein concentrations, renal necrosis, and neutropenia. Despite its narrow safety margin, phenylbutazone is a highly effective and commonly used NSAID in horses. The dosage should not exceed 4.4 mg/kg every 12 h.

Although the nonselective NSAIDs, such as phenylbutazone and flunixin meglumine, have the same mechanism of action in terms of inhibiting COX enzymes, their relative efficacies and dosing regimens are controversial (Cook & Blikslager, 2015). For example, flunixin meglumine is widely used as an analgesic for colic, whereas phenylbutazone is used more frequently for orthopedic pain (Clark & Clark, 1999). However, scientific evidence underlying these choices is generally lacking (Muir, 2010) and may show a higher level of complexity than is generally recognized (Cook & Blikslager, 2015). For example, in a study of gastrointestinal motility in response to low-dose endotoxin, phenylbutazone was shown to be more effective than flunixin meglumine at restoring motility, suggesting that phenylbutazone should be used for horses with colic (King & Gerring, 1989). However, flunixin meglumine was more effective at reversing the cardiovascular signs of endotoxin infusion.

Flunixin Meglumine

Flunixin meglumine is considered to be the most effective of the NSAIDs used to control visceral pain in horses, and has been shown to block the production of PGs, specifically thromboxane and prostacyclin, for 8–12 h after a single dose. Its analgesic effects are comparable to those of opioid analgesics, but it does not induce the side effects of the opioids such as central nervous system (CNS) excitation and ileus (Boothe, 1995). The duration of analgesia produced by flunixin meglumine varies from 1 h to more than 24 h depending on the cause and severity of the pain. In addition to its analgesic and anti-inflammatory effects, flunixin meglumine prevents some of the early hemodynamic effects of endotoxemia at doses lower than those used for anti-inflammatory effects (Moore et al., 1986; Templeton et al., 1987; Jackman et al., 1994).

At the recommended dose of 1.1 mg/kg, flunixin meglumine has a plasma half-life of 1.5–3 h. However, it persists in inflammatory exudates for much longer. In foals less than 1 month of age, the plasma half-life is also longer than it is in adults. The pharmacokinetics of flunixin meglumine may also be different in older horses than young adults, with a longer plasma half-life and decreased clearance (Jensen et al., 1990).

Flunixin meglumine is available in both parenteral and oral preparations. The bioavailability of the oral preparations is good. Although the parenteral preparation can be administered intramuscularly, necrotizing soft tissue infections have been reported (Kahn & Styrt 1997), so flunixin meglumine is more commonly administered intravenously. Although flunixin meglumine has a better therapeutic index than phenylbutazone, the basic side effects are similar. Gastrointestinal ulceration was produced when the drug was administered at 1.1 mg/kg three times per day for 12 days (MacAllister et al., 1993). Although flunixin meglumine is an excellent visceral analgesic and mitigates the clinical signs of endotoxemia, a major concern over its use postoperatively is that it retards the recovery of injured mucosa in the small intestine (Cook et al., 2009; Marshall et al., 2011; Cook & Blikslager, 2015).

Flunixin meglumine is typically used at 1.1 mg/kg q 12 h (twice its original labeled dosage of 1.1 mg/kg q 24 h) for analgesia (Cook & Blikslager, 2015), but studies have supported a lower dosage of 0.25 mg/kg IV q 8 h as a means of ameliorating clinical symptoms of endotoxemia while reducing potential side effects (Semrad et al., 1987).

One risk associated with the use of flunixin meglumine in treating colic of unknown cause devolves from its ability to mask clinical signs of intestinal strangulation or obstruction by reducing heart rate, relieving pain, and improving mucous membrane color. If administered to horses in which the precise cause of colic has not been ascertained, it is essential to monitor closely rectal examination findings, nasogastric reflux, peritoneal fluid, heart rate, and respiratory rate over the next few hours. The clinical evaluation of horses with colic that have already received flunixin meglumine must be adjusted as a result. Hence flunixin meglumine should be administered to control severe pain and diminish the effects of endotoxins in horses needing transport to a referral center for intensive care, closer monitoring, or surgery (i.e., in horses where the need for surgery has already been established).

Ketoprofen

Ketoprofen, like most other NSAIDs in horses, has a short plasma half-life (1–1.5 h) (Landoni & Lees, 1995). Its bioavailabilty is poor when administered orally or rectally, and it is most commonly administered intravenously. Although high doses may cause gastrointestinal and oral ulceration, the therapeutic index for ketoprofen is high, and it is considered to be less toxic than either phenylbutazone or flunixin meglumine (MacAllister et al., 1993). Ketoprofen is a very effective anti-inflammatory and analgesic agent in horses. The relative level of analgesia obtained with a full dosage of ketoprofen (2.2 mg/kg) has been assessed for equine orthopedic conditions, during which it was shown not to reduce lameness to the same extent as phenylbutazone (4.4 mg/kg) (Owens et al., 1996), and in two separate studies has been shown to be effective in alleviating abdominal pain (Betley et al., 1991; Longo et al., 1992). It also has the ability to reduce many of the early effects of endotoxins in horses (Jackman et al., 1994), and may inhibit lipoxygenase, an enzyme that is the rate-limiting step in the formation of leukotrienes (Kollias-Baker & Cox, 2004). However, experimental studies do not support this action (Owens et al., 1996).

Eltenac

Eltenac is a potent NSAID with antipyretic and antiedema properties. It has a short plasma half-life (1.7–3 h) (Dyke et al., 1998). There is limited information available concerning the efficacy of eltenac in the treatment of gastrointestinal pain, but the antiedema properties may make it useful in the postoperative colic patient. It also reduces many of the early responses to endotoxins (MacKay et al., 2000). The effects of eltenac appear to be long lasting, and a dosing interval of once every 24 h is recommended for most conditions.

Suxibuzone

Suxibuzone is a derivative of phenylbutazone. Its efficacy is similar to that of phenylbutazone, but it may be less toxic in terms of gastrointestinal ulceration (Sabate et al., 1997).

Meclofenamic Acid

Meclofenamic acid is typically administered orally to horses. It has a very slow onset of action, requiring 36–96 h of therapy before clinical effects are evident (Boothe, 1995), and it is therefore rarely used in the treatment of gastrointestinal pain.

Carprofen

Carprofen is considered to be an effective analgesic agent and weak anti-inflammatory agent (Kollias-Baker & Cox, 2004). Unlike many other NSAIDs in the horse, the half-life of carprofen is long (14–31 h) (Lees & Higgins, 1985). Carprofen is a more selective inhibitor of COX-2 than phenylbutazone and flunixin (Beretta et al., 2005), and it also appears to have a good therapeutic index in horses, possibly due to this selective inhibition of the COX-2 enzyme. The efficacy of carprofen in the treatment of gastrointestinal pain in horses has not been studied.

However, although it appears to be more efficacious as an analgesic than an anti-inflammatory agent, studies in laboratory animals have suggested that it is an effective analgesic only when the pain is associated with inflammation (Strub et al., 1992). Carprofen appears to have a greater inhibitory effect than other NSAIDs on the contractility of large colon tenia *in vitro* (van Hoogmoed et al., 1999).

Naproxen

Naproxen can be administered intravenously or orally to horses. There is little available information about its therapeutic index. Although it appears to be an effective NSAID in horses, its speed of action is very slow, often requiring several days of therapy (Plumb, 1999). This limits its use in animals with gastrointestinal pain.

Dipyrone

Dipyrone is a very weak analgesic drug that can provide only short-term relief in cases of mild abdominal pain. The drug is a relatively poor inhibitor of COX-1 and COX-2, but may select for COX-3. Dipyrone was withdrawn from the US market in the 1970s as a consequence of a rare side effect in people (agranulocytosis). However, dipyrone remains on the market in many countries as a component of an analgesic–spasmolytic combination medication (dipyrone and hyoscine *N*-butylbromide) labeled for treatment of colic. In an experimental cecal distention colic pain model in ponies, this drug combination relieved pain for at least 20 min. However, dipyrone alone was effective in only two of five ponies, whereas hyoscine *N*-butylbromide alone worked as well as the combination, suggesting relatively little analgesic efficacy of dipyrone (Roelvink et al., 1991). However, its failure to help reduce or stop pain in individual cases has been recommended as a signal that a condition exists that is more serious than a simple intestinal spasm or tympanitic colic (Maltby et al., 1977).

Etodolac

Etodolac has preferential selectivity toward COX-2. In a series of trials using a model of equine strangulating obstruction, a behavioral pain-scoring system was used to compare the analgesic effects of flunixin meglumine and a range of drugs with varying COX-2 selectivity, including etodolac. Etodolac was used at a dosage based on an initial pharmacokinetic trial (23 mg/kg IV q 12 h) (Davis et al., 2007) and found to provide the same level of analgesia as flunixin meglumine (1.1 mg/kg IV q 12 h) (Tomlinson et al., 2004). However, both drugs inhibited intestinal mucosal repair, suggesting no advantage of etodolac over flunixin. This may have been because of insufficient selectivity for COX-2 (Cook & Blikslager, 2015).

Meloxicam

Meloxicam preferentially inhibits COX-2 (Beretta et al., 2005). In a trial comparing the analgesic effects and effects on mucosal healing of flunixin meglumine and meloxicam in experimental small intestinal ischemia, meloxicam (0.6 mg/kg IV q 24 h) provided significant inhibition of behavioral signs of pain to the same extent as flunixin meglumine, but did not impede mucosal repair, whereas flunixin meglumine inhibited repair to the extent that intestinal tissues remained permeable to lipopolysaccharide (LPS) (Little et al., 2007). For this reason, meloxicam has been suggested as being a suitable choice of NSAID for use in postoperative colic patients. In a recent clinical trial comparing flunixin meglumine (1.1 mg/kg IV q 12 h) and meloxicam (0.6 mg/kg IV q 12 h) in horses with naturally occurring small intestinal strangulating obstruction, there was no significant difference between treatment groups in the level of pain judged by the clinician and the combined blinded pain score (Naylor et al., 2014). However, when a blinded observer considered overt signs of pain alone, horses administered flunixin meglumine were less painful. This study was statistically underpowered and meloxicam was used at double its recommended dosage, possibly affecting the level of selectivity of meloxicam. Additional clinical trials were recommended by the authors (Naylor et al., 2014).

Firocoxib

Firocoxib is an NSAID of the COX-2 inhibitor (coxib) class, currently approved for use in some countries in dogs and horses. In preclinical trials in horses with experimental small intestinal strangulating obstruction, firocoxib (0.09 mg/kg IV q 24 h) was compared with flunixin meglumine (1.1 mg/kg IV q 12 h) and found to provide similar levels of analgesia, but as with trials using meloxicam, intestinal LPS permeability was significantly increased in horses given flunixin meglumine (Cook et al., 2009). However, clinical trials using firocoxib in critical care patients are needed to assess fully the level of analgesia and also the prevalence of side effects compared with other NSAIDs (Cook & Blikslager, 2015). There is some question as to the relative analgesia expected with the COX-2 inhibitor firocoxib based on data that indicate that steady-state concentrations of firocoxib following an oral dose of 0.1 mg/kg q 24 h require administration for 5–7 days, associated with an elimination half-life of >24 h (Cox et al., 2013). With elimination half-lives of this length, a loading dose is often recommended to hasten the time to reach steady-state concentrations. Recent pharmacokinetic trials with oral firocoxib indicate that an initial dose of three times the labeled dose (0.3 mg/kg) followed by daily labeled doses (0.1 mg/kg) resulted in a relatively constant drug concentration in the plasma, suggesting that this would result in early and consistent onset of action in horses

(Cox et al., 2013). Firocoxib cannot be administered in an aqueous solution, including saline or heparinized saline, which are often used to flush intravenous catheters, because it precipitates. When administering the drug through an intravenous catheter, the patient's blood can be drawn back into the catheter prior to injection. When the drug mixes with the patient's blood, it can then be injected without precipitating. Alternatively, a hub on an extension set immediately adjacent to the vein can be used for injection of firocoxib.

Sedative-Tranquilizers

α_2-Adrenoceptor Agonists

The α_2-agonists exert their clinical effects by binding to α_2-adrenoceptors (Daunt & Steffey, 2002; Mason, 2004). The pharmacologic effects of the α_2-agonists used commonly in horses are similar, and differences between drugs are primarily a function of duration of effect (England & Clarke, 1996). The pharmacologic effects of these drugs include both central effects and effects on peripheral receptors in target tissues. The α_2-agonists cause sedation, with lowered head carriage, decreased locomotor activity, and decreased response to touch, sound, or visual stimulation. The degree of sedation is dose dependent; at higher doses, ataxia is produced. Medetomidine is reported to produce the greatest degree of ataxia, and romifidine causes the least degree of ataxia at similar levels of sedation when compared with xylazine or detomidine (England et al., 1991).

These agents are effective analgesics in horses with abdominal pain (Muir & Robertson, 1985; Jöchle, 1989; Chambers et al., 1993), but they have the disadvantage of decreasing gastrointestinal motility for the duration of the period of sedation. These drugs also relax smooth muscle in the distal airways. The α_2-agonists can produce hyperglycemia, sweating, mydriasis, and decreased hematocrit. The onset of action after intravenous injection is rapid for all of the agents. Their major uses in horses are for sedation, as premedication prior to general anesthesia, and for analgesia. The α_2-agonists are commonly used either alone or in combination with butorphanol. These drugs can be administered intravenously, intramuscularly, or orally; the intramuscular dose is 2–3 times the intravenous dose, and takes about 15–30 min for the peak effect. Some α_2-agonists are absorbed orally or buccally (e.g., detomidine) (effect in approximately 45 min); this drug will not be effective if swallowed owing to a first-pass hepatic effect. The effects of α_2-agonists can be reversed with yohimbine, tolazoline, atipamezole, or idazoxan.

The α_2-agonists can be combined with opioids to induce neuroleptanalgesia. They can also be combined with phenothiazines to produce synergistic or additive effects on sedation. Reliable sedation is achieved when combined with butorphanol; horses sedated with this combination are less likely to react suddenly or unexpectedly compared with sedation with α_2-agonists alone.

Epidural administration of α_2-agonists, either alone or combined with local anesthetics or opioids, can be used to provide caudal analgesia (Valverde & Gunkel, 2005).

Xylazine

The recommended dose rate of xylazine is 0.2–1.1 mg/kg IV or up to 2.2 mg/kg IM. At a dose rate of 1.1 mg/kg IV, the visceral analgesia provided by xylazine appears to be similar to that of flunixin meglumine and the opioid agonists. In a cecal distention model of colic pain, xylazine produced the most relief from abdominal discomfort compared with morphine, butorphanol, pentazocine, meperidine, dipyrone, and flunixin meglumine (Kohn & Muir, 1988). The duration of effect of xylazine is much shorter (usually 10–30 min) than that of flunixin meglumine, making xylazine more useful for controlling pain during evaluation of the cause of colic and of the need for specific therapy. However, repeated administration of xylazine may reduce visceral pain so effectively that the seriousness of abdominal pain is obscured (Kohn & Muir, 1988).

Potentially detrimental side effects of xylazine include bradycardia, decreased cardiac output, transient hypertension followed by hypotension, ileus, and decreased intestinal blood flow. These effects may restrict its use in horses in shock. In contrast to the bradycardia, hypertension, and intestinal hypotension, which last only a few minutes, the ileus and hypotension can be prolonged. A reduced dosage of 0.2–0.4 mg/kg IV can be administered in an attempt to reduce the severity and duration of the side effects. Alternatively, xylazine can be used at the lower dosage in combination with a narcotic agonist such as butorphanol.

Detomidine

The recommended dose rate of detomidine is 4–20 µg/kg IV or up to 40 µg/kg IM. The same complicating effects are likely to be present for detomidine as for xylazine; however, detomidine's duration of action is longer (60–120 min depending on the dose). Detomidine will reduce intestinal motility similarly to xylazine and can mask many of the clinical signs that clinicians use to diagnose the cause of the colic. Since detomidine is such a potent drug, any signs of colic observed within 1 h after administration are an indication that a severe disease is present, which may require surgery. Therefore, detomidine is a useful drug when used with caution and preferably at the low dose rate of 10 µg/kg IV. In a clinical trial of horses with naturally occurring colic, detomidine at 20 or 40 µg/kg was rated as highly satisfactory or satisfactory in >90% of cases (Jöchle, 1990). Detomidine can be usefully administered as a constant-rate infusion for producing steady-state sedation for standing surgeries

(in combination with local anesthesia and opioids as required); a loading dose of 7–8 μg/kg IV is followed by a 0.6 μg/kg/min constant-rate infusion.

Romifidine

Romifidine has a similar action to xylazine and detomodine, but appears to produce less ataxia. The duration of action is longer than that of either xylazine or detomidine. At a dose rate of 40–80 μg/kg IV, romifidine provides potent analgesia lasting 1–3 h. It can also be administered intramuscularly at a dose rate of 120 μg/kg (Freeman & England, 1999).

Medetomidine

Medetomidine is recommended for intravenous administration at 5 μg/kg; however, it can cause significant ataxia and is therefore more commonly used as a constant-rate infusion to produce sedation.

Phenothiazines

The phenothiazines are classified as neuroleptics, tranquilizers, or antipsychotic agents (Mason, 2004). They produce a calming effect while retaining sensitivity to noise. Ataxia is not generally seen after their use. Their mode of action involves antagonism of the neurotransmitter dopamine in the basal ganglia and limbic forebrain.

Phenothiazines do not produce analgesia, but they can potentiate the efficacy of other analgesic drugs, such as the opioids. Other effects of phenothiazines include lowering of the systolic, mean, and diastolic blood pressures. The risk of severe hypotension and collapse renders these drugs contraindicated for use in horses that are volume depleted as a result of colic or blood loss. Phenothiazines will also reduce the hematocrit and can cause penile prolapse in males. The magnitude and duration of the latter effect appear to be dose related; at a dose of 0.4 mg/kg, the penile protrusion can persist for 10 h (Ballard et al., 1982). Priapism has been reported as a long-term complication of acepromazine, and for this reason the drug is not recommended for use in breeding stallions.

Acepromazine

Acepromazine is the phenothiazine used most commonly in horses for tranquilization, premedication prior to general anesthesia, and as an analgesic (usually combined with an opioid). In view of its effects on blood pressure, acepromazine is not recommended as a routine analgesic agent in colic.

Opioid Analgesics

The analgesic and sedative effects of the opioids result from interaction with central and/or peripheral opioid receptors (Bennett & Steffey, 2002). When used in combination with acepromazine and α_2-agonists, opioids can provide very good standing restraint in the horse. Their use alone in horses has been limited owing to undesirable physiologic and behavioral side effects (Bennett & Steffey, 2002).

The analgesic effects of the opioids are mediated at both the supraspinal and spinal levels via the effects on the three different opioid receptor families (μ, κ, and σ). The μ-receptors mediate respiratory depression, supraspinal analgesia, miosis, and sedation, κ-receptors mediate spinal analgesia, miosis and sedation, and σ-receptors mediate dysphoria, hallucinations, and respiratory and vasomotor stimulation. These drugs also induce behavioral changes, which vary between different species. In horses, opioids produce CNS excitation and dysphoria. The excitement and increased locomotion seen in horses can be diminished by the concomitant administration of acepromazine or α_2-adrenoceptor agonists (Clarke & Paton, 1988). The opioids are potent respiratory depressants, but are considered safe from a cardiovascular point of view. They tend to decrease the propulsive activity of the gastrointestinal tract by inhibiting peristalsis, while increasing tone in intestinal smooth muscle. However, the gastrointestinal effects are variable depending on the segment of bowel and the opioid agent used.

Morphine

Morphine is a μ-opioid receptor agonist. It is a potent analgesic, but can cause severe excitement in horses unless used in combination with sedative drugs such as acepromazine or xylazine. Morphine also potentiates the sedative and analgesic effects of other drugs depressing CNS function (Brunson & Majors, 1987). Morphine is known to inhibit jejunal and cecocolic motility and to increase the overall muscle tone in the colon (Roger et al., 1994), and may potentially lead to ileus (Kohn & Muir, 1988; Senior et al., 2004; Boscan et al., 2006); for this reason, many clinicians believe that the use of morphine in treating horses with colic is contraindicated.

The recommended dose rate of morphine for standing restraint is 0.3–0.6 mg/kg IV in combination with acepromazine (0.05 mg/kg) or xylazine (0.5–1.0 mg/kg), detomidine (0.01–0.02 mg/kg), or romifidine (0.05–0.08 mg/kg) (Mason, 2004). Doses of 0.66 mg/kg have been shown to produce better analgesia than butorphanol for somatic pain in ponies under experimental conditions (Kalpravidh et al., 1984). Under clinical conditions, morphine exerts a calming and sedative effect when given to animals in pain (Davis & Knight, 1977). It can also be given as an epidural injection (0.1–0.2 mg/kg) (Valverde & Gunkel, 2005; Sano et al., 2011).

Meperidine (Pethidine)

Meperidine is a μ-receptor agonist with relatively few side effects and provides slight to moderate analgesia of relatively short duration in horses with abdominal pain. It has

only about 10% of the potency of morphine. The recommended dose rate of meperidine is 0.6–1.0 mg/kg IV in combination with either acepromazine (0.05 mg/kg) or xylazine (0.5–1.0 mg/kg). It can also be administered IM at a dose rate of 1–2 mg/kg. Used repeatedly, meperidine can potentiate obstructions due to impactions by reducing colon activity. It has also been shown to reduce intestinal motility in the jejunum (Sojka et al., 1988).

Methadone

Methadone is a synthetic μ-opioid receptor agonist that is three times as potent as morphine. It can be administered IV to horses at 0.1 mg/kg in combination with acepromazine (0.05 mg/kg) or xylazine (0.5–1.0 mg/kg), detomidine (0.01–0.02 mg/kg), or romifidine (0.05–0.08 mg/kg) to produce sedation that lasts for several hours.

Butorphanol

Butorphanol is a semisynthetic partial μ-opioid receptor agonist that produces the best pain relief of the drugs in this group, with the least side effects. It is approximately 25–40 times more potent and has a longer half-life than morphine in dogs and cats (Cowan et al., 1977; Robertson et al., 2005). Following IV administration in horses, plasma concentrations that are consistent with analgesia in other species persist for up to 4 h (Messenger et al., 2011). However, when assessed in a multicenter trial examining the efficacy of different analgesic drugs in horses with colic, butorphanol was not considered clinically effective (Jöchle, 1989). In addition, its effects last for only 30–90 min (Muir & Robertson, 1985). It can be used in combination with xylazine or the other α_2-adrenoceptor agonists in horses with moderate to severe abdominal pain to increase the level of analgesia. The dose is 0.01–0.05 mg/kg intravenously in combination with acepromazine (0.05 mg/kg) or xylazine (0.5–1.0 mg/kg), detomidine (0.01–0.02 mg/kg), or romifidine (0.05–0.08 mg/kg). Doses exceeding 0.2 mg/kg can cause excitement. Butorphanol reduces gastrointestinal motility and decreases defecation (Sellon et al., 2001). When combined with detomidine, butorphanol prolongs the gastric emptying time (Sutton et al., 2002). When combined with xylazine, it reduces duodenal motility for 1 h after treatment (Merritt et al., 1998) and cecal motility for 150 min (Rutkowski et al., 1991). Butorphanol is potent enough to stop colic for short periods of time when it is due to severe intestinal disease, but the pain caused by large colon volvulus or small intestinal strangulation may not be altered. When administered without xylazine or another α_2-adrenoceptor agonist, even small doses of butorphanol may occasionally cause head jerking and ataxia.

A constant-rate infusion of butorphanol (13 μg/kg/h) for 24 h after surgery has been shown to decrease plasma cortisol concentrations and improve recovery characteristics in horses following abdominal surgery (Sellon et al., 2004). However, postoperative colic patients treated in this way had reduced time to passage of first feces compared with saline-treated controls.

Fentanyl

Fentanyl is a potent synthetic μ-opioid receptor agonist. The drug was incorporated into a transdermal therapeutic system in order to provide continuous analgesia and avoid wide variations in serum drug concentrations (Scholz et al., 1996). The transdermal therapeutic system patches are designed to provide a constant and controlled release of fentanyl for 72 h and are increasingly being used for analgesia in humans, dogs, and cats with cancer or postoperative pain (Robinson et al., 1999). Limited studies suggest that fentanyl patches may also be valuable in the treatment of horses with prolonged visceral pain, especially when combined with NSAIDs (Wegner et al., 2002; Thomasy et al., 2004).

Other Analgesic Drugs

Lidocaine (Lignocaine)

Lidocaine has been used in horses with colic primarily to treat ileus (see Chapter 13), but it has also been found to be an effective analgesic. Lidocaine exerts its analgesic properties by decreasing afferent traffic through small C fibers. In addition, it has anti-inflammatory properties and decreases the influx of inflammatory cells (MacGregor et al., 1980). The plasma levels necessary for analgesia are much lower than those required to block normal peripheral nerve conduction. Lidocaine has also been shown to decrease reperfusion injury by inhibiting the release of free radicals and decreasing the migration of neutrophils at the site of injury. The prokinetic effect of lidocaine may be useful in postoperative ileus (Malone et al., 1998), and a recent survey found that lidocaine is the most commonly used prokinetic after equine intestinal surgery (Van Hoogmoed et al., 2004). In addition, treatment with systemic lidocaine appears to ameliorate the inhibitory effects of flunixin meglumine on recovery of the mucosal barrier from ischemic injury (Cook et al., 2008). An initial intravenous bolus at a dose rate of 1.3 mg/kg (administered slowly over 5 min) can be followed by a continuous intravenous infusion at a rate of 0.05 mg/kg/min (diluted in saline or lactated Ringer solution). Signs of toxicity include muscle fasciculations, ataxia, recumbency, and possible seizures; these signs are more likely to happen if the initial bolus is administered too rapidly. In clinical trials in horses, lidocaine appeared to be effective in decreasing the duration of reflux in horses with postoperative ileus and in horses with duodenitis-proximal jejunitis, reducing the incidence of postoperative ileus, shortening hospitalization

time, and enhancing short-term survival (Malone et al., 1998, 2006; Torfs et al., 2009).

Ketamine

Ketamine, a noncompetitive *N*-methyl-D-aspartate receptor antagonist commonly used for dissociative anesthesia, has antinociceptive properties when administered as a continuous-rate infusion at subanesthetic doses in both anesthetized and conscious horses (Elfenbein et al., 2011). In human and small animal intensive care units, subanesthetic doses of ketamine are commonly used for multimodal pain management, and it is believed that ketamine has few systemic adverse effects. In addition to its analgesic properties, ketamine has well-documented anti-inflammatory properties in several species. In a study of the systemic effects of a prolonged continuous-rate infusion of ketamine in healthy horses, ketamine delayed the intestinal transit time without any effects on vital parameters (Elfenbein et al., 2011). Its use in managing postoperative pain in colic patients has not yet been investigated.

Choice of Analgesics in Colic

The choice of which analgesic drug or which combination of drugs to use as the first-line treatment for an individual horse suffering from colic is usually governed by the clinician's previous experience with different drugs, the potential complications associated with different drugs, and the severity of colic pain exhibited by the horse. The response (or lack of response) of the horse to different analgesic drugs is an important factor to consider when reaching a diagnosis of the cause of colic, and in determining the need for surgical intervention (see Chapter 24). The choice of which drugs are administered, their dosages, and knowledge of their potency as analgesics and their side effects are, therefore, extremely important. In some cases the horse will already have been given an analgesic drug by the owner, which may complicate the process of making a diagnosis or assessing the need for surgical intervention.

The initial choice of analgesic drugs should be based on the clinician's provisional diagnosis of the underlying cause of the colic and the need for chemical restraint. For example, horses demonstrating signs of mild pain associated with spasmodic colic usually respond well to a spasmolytic agent or NSAID. On the other hand, a horse demonstrating violent colic behavior may require sedation and chemical restraint in order to prevent injury and to permit a thorough clinical examination. In addition, the ability of the clinician to monitor and re-examine the horse following treatment should be considered. Potent analgesic drugs and agents that may effectively mask the signs of endotoxemia that are so important in determining the necessity for surgery should be avoided in horses where the cause of colic has not been diagnosed and where close monitoring and frequent re-examinations are not possible.

Table 27.2 Selection of initial analgesic drugs.

Disease category/ severity	Drugs
Mild non-specific colic and spasmodic colic	NSAID (e.g., phenylbutazone, dipyrone, flunixin meglumine, firocoxib, meloxicam) Spasmolytic (e.g., hyoscine) Opioid (e.g., pentazocine, butorphanol)
Severe undiagnosed colic	α_2-Agonist–opioid combination NSAID (e.g., phenylbutazone, meloxicam, firocoxib) Flunixin meglumine (only if close monitoring possible)
Simple obstruction	Flunixin meglumine α_2-Agonist–opioid combination
Strangulating obstruction	Flunixin meglumine α_2-Agonist α_2-Agonist–opioid combination
Enteritis	Flunixin meglumine, meloxicam, firocoxib
Peritonitis	Flunixin meglumine, meloxicam, firocoxib

The selection of analgesics based on the severity of colic and the underlying disease classification is shown in Table 27.2.

Treatment of Intestinal Spasm and Spasmodic Colic

Increased frequency of intestinal contractions, as in spasmodic colic, or spasms occurring oral to intraluminal obstructions (such as impactions) causes pain, which can be relieved by spasmolytic drugs. Another indication for the use of spasmolytic drugs is to relax the rectum, thereby facilitating palpation of the abdomen per rectum (Murray, 2004). The most commonly used spasmolytic drugs include the cholinergic blockers atropine, hyoscine *N*-butylbromide (scopolamine), and propantheline bromide. These drugs compete with acetylcholine for the muscarinic receptors on smooth muscle cells. They cause smooth muscle relaxation and decreased intestinal motility, and are therefore contraindicated in horses that have ileus. Prolonged use can predispose to large intestinal impactions.

Atropine

Atropine is not recommended for use in horses with colic because it is a potent inhibitor of intestinal motility that can last for several hours or even days, creating

tympany and complicating the initial problem with ileus (Ducharme & Fubini, 1983; Adams et al., 1984). Even when used as a topical ocular treatment to produce mydriasis, individual horses may develop ileus and colic. However, a single subcutaneous dose of 0.02 mg/kg is considered safe in most horses. This dose may also be used in horses with a rectal tear to facilitate evacuation of the rectum (Murray, 2004).

Hyoscine *N*-Butylbromide (Scopolamine)

Hyoscine *N*-butylbromide (scopolamine) has a shorter muscarinic cholinergic blocking effect than atropine and is effective in relaxing the bowel wall. It is safe to use in conjunction with other analgesic drugs, including NSAIDs, and is available in Europe as a compound antispasmodic combined with dipyrone. Hyoscine *N*-butylbromide is administered at a dose of 0.2–0.3 mg/kg IV. The spasmolytic effect lasts only 20–30 min (Roelvink et al., 1991), and it is therefore unlikely to mask any signs associated with more serious forms of colic. Hyoscine *N*-butylbromide has an immediate, potent, short-lived inhibitory effect on the cecal and left ventral colon contractions, but a minor, longer lasting effect on duodenal contractions (Gomaa et al., 2011). In a balloon-induced model of colic in ponies, hyoscine *N*-butylbromide (0.3 mg/kg) gave more consistent analgesic effects than butorphanol tartrate (0.1 mg/kg) (Boatwright et al., 1996). The drug is commonly used for the treatment of gas colic/spasmodic colic and impactions. It also decreases rectal pressure and the number of rectal strains, and thereby improves the quality and safety of examination per rectum (Luo et al., 2006).

Administration of hyoscine *N*-butylbromide causes an increase in heart rate and blood pressure in normal horses (Morton et al., 2011). These effects should be taken into account when monitoring the response to treatment in horses with colic. Peak heart rate (86 ± 2 bpm) occurred at 5 min following administration and the effect lasted for 50 min.

Propantheline Bromide

Propantheline bromide is available as a parenteral solution for injection in some countries. Spasmodic effects are obtained at a dose rate of 0.1–0.2 mg/kg.

Treatment of Obstruction

Luminal obstruction by impacted, dehydrated intestinal contents is a common cause of colic in the horse. Such obstructions prevent the free aboral movement of ingesta, fluid, and gas. The commonest site of impaction is the large colon, specifically in the left ventral colon orad to the pelvic flexure (see Chapter 54), but impactions can also arise in the stomach (see Chapter 50), small intestine (especially the ileum) (see Chapter 52), cecum (see Chapter 53), right dorsal colon (orad to the transverse colon) (see Chapter 54), and small colon (see Chapter 55). These sites represent areas where there is transition of intestinal movement, or there is a sphincter between different segments of intestine, or regions of intestinal narrowing (White, 1997; White & Lopes, 2003). The etiology of impactions is poorly understood. Dehydration, lack of exercise, poor dentition, overfeeding, and feeding bulky indigestible fibrous food are commonly blamed, but in other cases some form of abnormality of intestinal motility may be involved.

The pathophysiologic effects of luminal obstruction by an impaction are often slow to develop and progress (compared with strangulating obstructions). In the stomach, cecum, large colon, and small colon, the obstruction is frequently incomplete, allowing fluid and gas to pass around the impaction. Pain arises from intestinal distention and intestinal spasms at the site of the impaction. Complete obstruction is more common in small intestinal impactions, but can also occur in other sites. Complete obstruction leads to more rapid distention of the bowel proximal to the obstruction, and more rapidly developing signs of colic, hypovolemia, and so on. Persistent distention of the bowel may lead to circulatory failure and ischemic damage to the bowel wall.

In most cases, the objectives of treatment of impactions are to hydrate and lubricate the impacted ingesta, thereby allowing the normal intestinal motility to move the ingesta aborally into the next intestinal segment. This can usually be achieved by enterally administered therapies, sometimes in combination with analgesic drugs, intravenous fluid therapy, and/or prokinetic drugs. However, in certain cases, especially those involving a complete intestinal obstruction, surgical treatment to prevent intestinal rupture or mural necrosis may be necessary.

Restricted Feeding

Restricted feeding is advisable in horses with impactions until such time as the impaction clears (Jennings et al., 2014). Continued feeding may allow the impaction to enlarge, thereby making it more difficult to resolve. Horses with large impactions can make a full recovery with medical therapy, even when held off feed for as long as 6 days (White & Lopes, 2003). However, there may be benefits in stimulating gastrointestinal motility by allowing horses to eat limited amounts. Very small quantities of grass or bran mashes fed frequently may be helpful in this respect, and are unlikely to be detrimental.

Walking

Walking exercise may also be helpful in managing horses with impaction colic. Walking appears to stimulate gastrointestinal motility and defecation.

Analgesic Drugs

The administration of analgesics is helpful in preserving gastrointestinal motility in addition to being required to be humane. Analgesic drugs commonly used in the treatment of impaction colic include the NSAIDs, such as phenylbutazone and flunixin meglumine. These drugs are effective analgesics while having minimal deleterious effects on intestinal motility. Flunixin meglumine at a dose rate of 0.25–0.5 mg/kg four times per day has proved to be effective in many cases (White, 1997; White & Lopes, 2003). The lowest effective dose should be used so as not to mask signs of deterioration or the need for surgery. If 0.5 mg/kg is not sufficient to relieve pain, then increasing the dose up to 1.0 mg/kg may be successful, although this dose may suppress the pain and other signs that indicate the need for surgery (White & Lopes, 2003). If pain is observed within 1 h after flunixin administration, surgery should be considered either to empty the colon or to diagnose another concurrent intestinal problem.

Although other analgesic drugs, such as α_2-adrenergic agonists, opioid analgesics, and spasmolytic drugs, can also be effective at controlling pain associated with impactions, their routine use is not recommended because of the side effects of reducing gastrointestinal motility. However, in some cases, the administration of such drugs will be required in order to achieve effective analgesia.

Laxatives/Cathartics

Laxatives are commonly used in horses with impaction colic to increase the water content and softness of ingesta, thereby facilitating intestinal transit. In severe impactions, administering oral and intravenous fluids concurrently increases the effectiveness of laxatives. These medications should never be administered orally in horses with nasogastric reflux.

Mineral Oil (Liquid Paraffin)

Mineral oil (liquid paraffin) is the most frequently used laxative in equine practice. It is a surface lubricant and is administered at a dose rate of 5–10 mL/kg once or twice per day by nasogastric tube. Its effects are considered mild, and it is safe for prolonged use. It is commonly administered with water or saline, and is considered by many clinicians as the lubricant of choice for mild colonic impactions.

Passage of the oil (as evidenced by the presence of oil on the perineum and tail) indicates a patent intestinal tract. In the normal, unobstructed intestine, oil will take approximately 12 h to reach the anus after delivery into the stomach (Schumacher et al., 1997). Identification of the oil on the perineum should not always be taken as evidence of lack of obstruction, because in some cases the oil may pass around an impaction without resolving it. Oil frequently passes around sand impactions without resolving the condition.

In most cases of impaction colic, mineral oil can be safely administered every 12 h until signs indicating resolution of the impaction are seen. These include the presence of oil on the perineum, passage of oil-coated feces, cessation of pain, and clearing of the impaction as revealed by repeated rectal examinations. Most colonic impactions resolve within 3–5 days. Administration of mineral oil reduces glucose absorption and also intestinal transit time (Rodrigues, 1998; Macoris & Gandolphi, 1998). However, chronic usage can result in a foreign body reaction in the intestinal mucosa (Stryker, 1941). Careful administration is important, as administration into the lung results in severe and potentially fatal lipid pneumonitis (Bos et al., 2002; Scarratt et al., 1998).

Other Oils

Raw linseed oil has been used as a laxative to treat impaction colic (Tillotson & Traub-Dargatz, 2003), but is not as safe as mineral oil. When administered at a dose rate of 2.5 mL/kg every 12 h, linseed oil has been shown to cause anorexia, depression, mild colic, and biochemical abnormalities consistent with intestinal inflammation (Schumacher et al., 1997). Diarrhea persisting for several days can follow its administration. If used, only raw linseed oil should be administered, since the addition of metallic salts during preparation of the oil as a wood preservative makes it highly toxic.

Castor oil is not recommended for use in horses. It can cause acute, severe colitis and diarrhea, and has been used experimentally at a dose rate of 2.5 mL/kg to induce colitis in ponies (Johnson et al., 1993).

Psyllium Hydrophilic Mucilloid

Psyllium hydrophilic mucilloid is a bulk-forming laxative, which causes the fluid and ion content of feces to increase by absorbing water. This softens the impaction and stimulates bowel activity. It has been considered to be particularly useful for treating impactions caused by ingested sand. A dose of 1 g/kg can be administered PO up to four times per day. As a long-term treatment, it may be administered daily for several weeks to help eliminate sand from the large colon. However, the efficacy of psyllium hydrophilic mucilloid in treating sand impactions has been questioned (Hammock et al., 1998). In that study, psyllium failed to increase evacuation of sand in an experimentally induced model of sand impaction. In a clinical study, horses that were refractory to treatment with psyllium were responsive to administration of magnesium sulfate and mineral oil (Ruohoniemi et al., 2001). In another study, resolution of sand impaction was improved with the combination of psyllium and

magnesium sulfate compared with either constituent alone (Niinisto et al., 2014).

Psyllium powder can be administered by nasogastric tube after mixing it with water. However, the mixture tends to form a thick gel that may not pass easily down the tube, so immediate administration as soon as the powder is mixed with water is recommended. Psyllium is also available in pelleted form, which horses generally find more palatable than a mixture of psyllium powder and other feeds.

Osmotic Laxatives

Magnesium sulfate (Epsom salt) can be used as an osmotic laxative (or "ionic cathartic") in horses. Classically, magnesium sulfate was believed to be poorly absorbed from the intestinal tract, thereby remaining in the lumen of the bowel and drawing water into the gut by virtue of its osmotic pressure. It therefore hydrates the ingesta, and facilitates passage of impactions (Lopes et al., 2002; Lopes et al., 2004). However, it has been shown that much of the magnesium is actually absorbed in the small intestine. In addition, magnesium sulfate has been shown to stimulate water secretion in the colon by a gastrocolonic reflex action immediately upon administration (Freeman et al., 1992). The precise mechanism of this action is unclear. Undiluted magnesium sulfate will cause enteritis by osmotic damage to the mucosal cells, so each dose of 0.5–1.0 g/kg should be diluted in 4 L of warm water and administered by nasogastric tube once or twice per day. Epsom salt should not be administered for longer than 3 days (once per day) because of severe enteritis and possible magnesium intoxication. Absorption of magnesium resulting in signs of toxicity was reported in two horses that had received a combination of dioctyl sodium sulfosuccinate and magnesium sulfate (Henninger & Horst, 1997). Magnesium sulfate treatment has been used for impactions of the cecum, large colon, and small colon.

Other osmotic laxatives can be used similarly. These include Glauber's salt (sodium sulfate) and table salt (sodium chloride). Studies suggest that sodium sulfate (1 g/kg) may be more efficient than magnesium sulfate in increasing the water content of colonic contents and feces. However, the use of sodium sulfate at this dose rate can result in hypernatremia, hypochloremia, and hypocalcaemia. For this reason, a lower dose rate (0.5 g/kg) with monitoring of serum electrolytes has been recommended (Lopes et al., 1999).

Dioctyl Sodium Succinate (DSS)

DSS is an anionic surface-active agent with wetting and emulsifying properties. It reduces surface tension and allows water and fat to penetrate the ingesta. A dose of 10–20 mg/kg can be administered as a 5% solution by nasogastric tube every 48 h. DSS can cause damage to the mucosa and increases fluid permeability of colon cells, which can result in mild abdominal pain and diarrhea, especially if doses higher than 20 mg/kg are used (Moffat et al., 1975; Freeman et al., 1992).

DSS is commonly mixed and administered with mineral oil. However, it has been suggested that this mixture should not be used since the surfactant effects of the DSS may reduce the droplet size of the mineral oil sufficiently to allow the oil to be absorbed.

The concurrent administration of magnesium sulfate and DSS has been associated with hypermagnesemia, flaccid paralysis, and systemic collapse in horses (Henninger & Horst, 1997), and administration of both drugs at the same time should therefore be undertaken with extreme caution. However, administration of magnesium sulfate at a low dose rate (0.5 g/kg) with sodium sulfate (0.5 g/kg) and DSS (25 mg/kg) given every 24 h has been used in the treatment of impactions (Tillotson & Traub-Dargatz, 2003). This combination of drugs allows a "full" dose of sulfate salts to be administered, but with only half of it in the form of magnesium sulfate, so that the risk of hypermagnesemia is reduced.

Enteral Fluid Therapy

Horses with gastric and intestinal impactions often benefit from orally administered fluids (Hallowell, 2008; Monreal et al., 2010; Lopes et al., 2001). In one clinical case series, enteral fluid therapy with or without intravenous fluid therapy was successful in resolving 99% of colonic impactions (Monreal et al., 2010). Enteral fluid therapy has the advantages of administering fluid directly in the gastrointestinal tract, stimulating colonic motility through the gastrocolic reflex, and decreasing the need for precise adjustment of fluid composition (Lopes et al., 2002). The fluids can be administered through a standard nasogastric tube or through an indwelling enteral feeding tube. If there is no abnormal gastric reflux and the horse tolerates the initial dose of oral fluids, up to 8 L for a 450 kg horse of either water, or isotonic or hypertonic fluids may be given to an adult horse every 30 min to 1 h. However, horses with intestinal impactions may not tolerate these fluid administration rates; a rate of 5 L/h is usually well tolerated by horses with colonic impactions. Enteral water therapy is often effective in resolving colonic impactions, although this takes on average 2.5 days, with a total water volume ranging from 85 to 208 L. Serum electrolytes should be monitored when the horse is receiving enteral water therapy, since this can result in severe hyponatremia. Granular sodium chloride, potassium chloride, and/or sodium bicarbonate may be added to the water if electrolytes are desirable. An isotonic electrolyte solution can be made by adding 5.27 g of NaCl, 0.37 g of KCl, and 3.78 g of $NaHCO_3$ to each liter of tap water (Lopes et al., 2002).

This solution results in a balanced, slightly hypotonic electrolyte solution compared with plasma (Lopes et al., 2002). Use of a balanced isotonic electrolyte solution is associated with improved fluid absorption and decreased electrolyte imbalances (Monreal et al., 1999; Sosa León et al., 1995). Frequent monitoring of serum electrolytes should be applied to determine when changes in electrolyte composition are necessary. Oral fluids are ideally administered via gravity flow rather than by pump. An indwelling enteral feeding tube is easier to manage than a nasogastric tube. Clinical monitoring of horses receiving enteral fluid therapy should also be undertaken. Although rare, ileus and gastric distention may occasionally occur in horses with impaction colic, in which case continued enteral fluid therapy is contraindicated. Any increase in pain, respiratory rate, or heart rate during therapy should be considered as a possible indication to stop the therapy. On rare occasions, gravity administration of isotonic fluids may be given per rectum. This would only be indicated for horses with colonic impactions when oral fluids cannot be given and economic considerations prevent administration of IV fluids.

Intravenous Fluid Therapy

Intravenous administration of fluids is useful in horses with impactions of long-standing (>24 h) duration, when there is evidence of hypovolemia/dehydration, or when nasogastric reflux precludes the use of enteral fluid therapy. Balanced electrolyte solutions are administered at twice the maintenance rate, 120 mL/kg/day, to restore circulating blood volume and allow secretion of fluid into the large colon in response to cathartics. Intravenous crystalloids administered at this rate, without colloids, will result in a decrease in plasma protein concentration to <4.5 g/dL (<45 g/L). The increase in hydrostatic pressure and drop in plasma oncotic pressure induced by such overhydration should cause movement of the fluids into transcellular fluid sites, such as the intestinal lumen, such that the impaction is softened. This can generally be done without harm to other body organs, assuming that there is no generalized capillary disorder, and cardiac, renal, and respiratory function is normal. When large amounts of fluids are given to horses, they should ideally be warmed to near body temperature prior to administration. The average time for resolution of impactions treated with intravenous fluids is approximately 2 days, with total fluid volumes ranging from 54 to 350 L. During this treatment, the total plasma protein concentration should be monitored (to ensure that a low concentration is maintained), and electrolytes should be monitored to ensure that deficits in plasma calcium and potassium do not arise. The commonest complication of this treatment is thrombophlebitis. Careful monitoring of the catheter site should be undertaken, and the catheter changed at the first indication of vein inflammation or thrombus formation. Overhydration of affected horses in combination with an oral cathartic such as magnesium sulfate is thought to promote rehydration of ingesta (Freeman et al., 1992; Lopes et al., 2002).

Diarrhea may occur after either enteral or intravenous fluid therapy, and also after the administration of magnesium sulfate or sodium sulfate. Diarrhea usually indicates successful hydration and movement of the impaction, but in some cases it may arise as a result of colitis. Such cases may require intensive treatment for the colitis (see Chapter 30).

Nutritional Support After Evacuation of Colon Impactions

Once the impaction has cleared, feed should be reintroduced and slowly increased over a 48 h period. Hay or grass should be provided in small quantities (0.25–0.5 kg q 3 h) (White & Lopes, 2003). This time interval allows the stomach to empty and does not overload the cecum or colon. After 12–24 h, hay or grass may be fed *ad libitum*. If colic occurs during the period of increasing food intake, then feed should be withheld and the horse examined to check that an impaction has not re-formed. Grain and concentrates should not be introduced into the diet until such time as the horse has re-established normal fecal production on a hay or grass diet. Introduction should be gradual during a 4–7 day period.

Treatment of Ileus

Ileus (adynamic ileus) is the impairment of aboral transit of intestinal contents. Postoperative ileus is the most common indication for pharmacologic manipulation of intestinal contractile activity in the horse (see Chapter 13). Traumatic handling of the intestines, intestinal distention, resection and anastomosis, and intestinal ischemia and inflammation all may contribute to the development of ileus in the postoperative period. Ileus may also occur in association with proximal duodenitis-jejunitis (anterior enteritis), colitis, and peritonitis.

An imbalance between the factors controlling excitation and inhibition of gastrointestinal smooth muscle predisposes horses to ileus. Consequently, an attempt has been made to identify prokinetic agents that potentially would restore the balance between excitatory and inhibitory control of contractility. Pharmacologic modulation aimed at increasing excitatory activity has principally involved the administration of parasympathomimetic agents that increase cholinergic transmission, such as bethanecol or neostigmine. Attempts to block inhibitory components of contractility have focused on the sympathetic system.

Metoclopramide, which among other activities has anti-dopaminergic properties, and NSAIDs have also been used in attempted treatment of ileus. The pharmacologic management of ileus is discussed in greater detail in Chapter 13.

In addition to the use of anti-inflammatory and prokinetic drugs, general supportive therapy (including fluid therapy and analgesic drug therapy) is required (see Chapter 13). Continuous or repeated gastric decompression must be provided in addition to drug therapy.

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28

Treatment of Shock

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Support of the Cardiovascular System

The cardiovascular system is key to survival of horses with acute abdominal disease. Abdominal disease can lead to profound cardiovascular changes, principally through loss of water and electrolytes from the circulation to the gastrointestinal tract and interstitial fluid, and by absorption of toxins. The principal toxin involved is endotoxin, a component of the cell wall of Gram-negative bacteria. This toxin interacts with immune-series cells to cause the synthesis and release of a cascade of soluble mediators, including the cytokines interleukin-1 (IL-1) and tumor necrosis factor alpha (TNF-α). These mediators, in turn, cause profound changes in both the contractility of the heart and the resistance of the blood vessels to blood flow. Both the effects of the toxins and loss of water from the circulation can severely reduce blood flow through the capillary beds in the organs. Toxins may also activate the coagulation system, which can result in microthrombi formation within the capillaries and further compromise blood flow. As capillary blood flow is reduced, the metabolic processes of organs are severely curtailed, which in turn leads to organ failure and ultimately death.

There are three main prongs of therapy to support of the cardiovascular system, designed to prevent the sequence of events outlined above. The first, and often the only one employed, is to replace and maintain the lost constituents from the blood (water, electrolytes, proteins) with fluid therapy. The second is to alter directly either the contractility of the heart or the resistance of blood vessels to blood flow, using vasoactive drugs, principally inotropes, vasopressors, and vasodilators. The third is the judicious use of anticoagulants to prevent intravascular coagulation.

Fluid Therapy

Fluid therapy is an essential part of managing horses with acute abdominal disease. Fluid therapy can serve one or several of the following purposes: restore circulating volume; rehydrate the tissues; correct electrolyte disturbances; correct acid–base disorders; increase plasma colloidal oncotic pressure; and rehydrate or overhydrate the gastrointestinal contents.

General Principles

Hypovolemia and Dehydration

Hypovolemia is defined as a decrease in circulating blood volume. The classic example of hypovolemia is acute arterial hemorrhage, in which the circulating volume is decreased rapidly without a change in the remainder of the extracellular fluid volume. Dehydration is defined as a loss of interstitial fluid without a change in the circulating volume. There are powerful physiologic mechanisms that protect the circulating volume during dehydration at the expense of extravascular fluid, and it is only with severe dehydration that animals also become hypovolemic.

In horses with severe gastrointestinal disease, hypovolemia and dehydration are often present together. Horses with less severe disease are frequently dehydrated but not necessarily hypovolemic. Even though they may coexist in the same horse, it is important to distinguish hypovolemia and dehydration, because their therapies are different. Hypovolemia requires emergency treatment to restore circulating volume rapidly. There is considerable evidence linking markers of hypovolemia on hospital admission with morbidity and decreased survival in equine colic (Cohen et al., 2004; Furr et al., 1995; Hackett et al., 2015). Hypovolemia is treated with rapid volume expanders, such as colloids, hypertonic saline, or large volumes of crystalloids administered

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intravenously. There is little objective evidence available regarding the treatment of hypovolemia in horses. In pediatric and adult human sepsis, previous advice was that there should be rapid administration of fluids to restore volume based on studies showing dramatically improved outcomes (Carcillo et al., 1991; Rivers et al., 2001). However, recently this advice has become more nuanced (Myburgh, 2015) owing to as yet limited studies suggesting that excessive volumes may be harmful (Maitland et al., 2011). Dehydration is treated over 12–24 h with oral or intravenous crystalloid fluids. Suggested fluids and volumes for hypovolemia are presented in the section Treatment Strategies.

Ongoing Losses

Excessive fluid losses from horses with acute abdominal disease frequently do not stop when treatment is initiated, and these must be taken into account in the fluid therapy plan. The most dramatic ongoing fluid losses are with severe diarrhea or nasogastric reflux and, in either case, they may reach 200 mL/kg/day (100 L/day for a 500 kg horse) (Rose, 1981). Even without such obvious losses, horses with primary abdominal disease may lose significant amounts of fluid through sweating, inadequate intake, or, rarely, polyuric renal failure.

Treatment for ongoing losses is aimed at replacing the amount lost to maintain hydration. This is relatively simple when the amount of fluid lost can be measured, as in the case of nasogastric reflux. Reflux is collected in a graduated bucket (Figure 28.1), and the amount collected over a 4–12 h period is compared with the amount of fluid administered. If the fluid lost exceeds the amount given, the fluid administration rates are adjusted both to replace this amount over the next 12–24 h and to account for the higher level of ongoing losses than originally estimated. If the excessive losses have resulted in hypovolemia (on the basis of clinical and laboratory evidence), this must be treated acutely.

It is much harder to estimate losses from diarrhea, sweating, and urination than from nasogastric reflux. In the case of diarrhea and urination, it is possible either to attempt to collect the feces or urine or to use absorbent bedding and measure the increase in weight. These are almost never done in clinical practice, except in the case of recumbent neonatal foals, for which feces or urine may be readily collected and weighed on incontinence pads, or urine may be collected with an indwelling Foley catheter and closed collection system (Figure 28.2). When ongoing fluid losses cannot be measured, they must be estimated. These estimates may be inaccurate and the amount of ongoing loss can change dramatically. Therefore, it is important frequently to reassess the adequacy of fluid therapy through clinical examination and relevant laboratory investigations. These are discussed later in this chapter.

Maintenance

All horses have a daily fluid requirement to replace losses from metabolic processes, sweat, urination, defecation, evaporation from the respiratory tract, and any lost salivation or lacrimation. Normally this requirement is met by a combination of drinking and the water content of feed. If a horse is deprived of feed, it will normally drink more to match these losses. For horses with reduced water intake (a frequent occurrence with abdominal disease), this maintenance requirement must

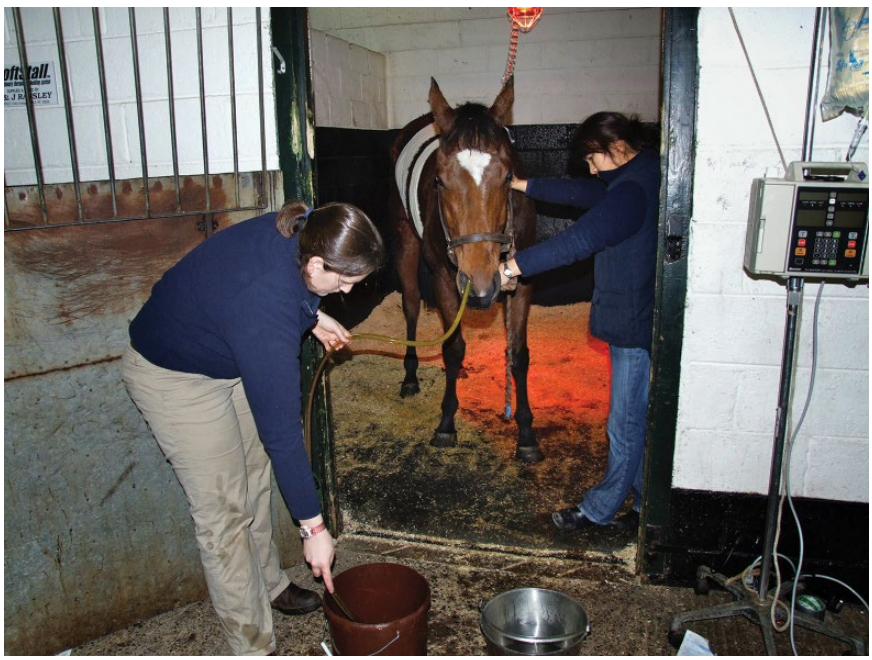

Figure 28.1 Collecting and measuring reflux in a horse after surgical treatment for colic.

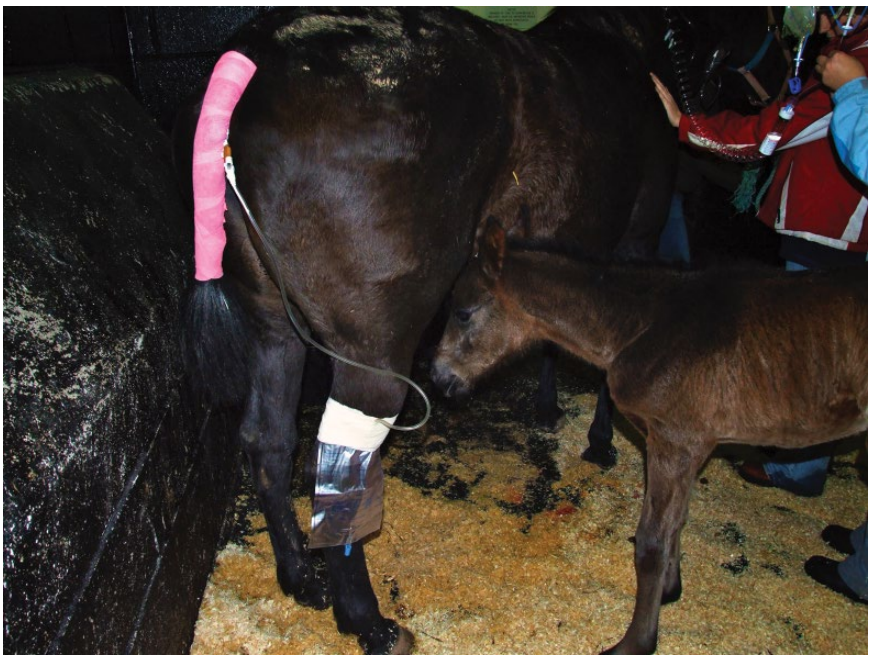

Figure 28.2 Closed urine collection system in a mare.

be met with fluids administered via a nasogastric tube or intravenously.

The exact maintenance requirement for horses is unknown, and probably varies between individuals. The mean daily water intake of normal resting adult horses is 57–64 mL/kg/day at ambient temperatures of 41–77 °F (5–25 °C) (Groenendyk et al., 1988; Tasker, 1967). It is important to note, however, that this includes the water content of feed. Horses in a pasture drink far less water, presumably because of the high water content of grass. The amount of water drunk doubled from 24 to 60 mL/kg/day in one experiment in which horses were moved from a pasture to a stable (Williams et al., 2015) The total water consumed to include that in feed was not measured in this experiment.

Although 57–64 mL/kg/day may not strictly represent the minimal fluid requirements, it is a useful guideline for the "maintenance rate" (2.5 mL/kg/h) in adult horses. Thus, a 500 kg horse requires approximately 30 L/day for maintenance, in addition to any fluids to replace ongoing losses. The maintenance requirement of neonatal foals is significantly higher and is usually estimated to be 3–5 mL/kg/h (Buchanan et al., 2005; Corley, 2004; Spurlock & Furr, 1990). In one experiment, foals showed a minor and nonsignificant increase in urine specific gravity but lost 5.5% of their body weight when infused isotonic fluids at 77 mL/kg over 24 h (Buchanan et al., 2005). It should be noted that the fluid intake of nursing foals considerably exceeds 3–5 mL/kg/h (Martin et al., 1992; Oftedal et al., 1983). It should be emphasized that it is important to take into account the fluid component of all infusions when calculating fluid rates so as to avoid inadvertent volume overload in neonatal foals receiving a number of intravenous infusions.

Oncotic Pressure and Physiologic Roles of Albumin

The net amount of fluid that leaves the circulation in the capillaries is determined by the difference in hydrostatic pressure and oncotic pressure between the fluid in the capillary and the interstitial space. Colloidal oncotic pressure refers to the osmotic pressure exerted by the molecules that do not pass freely from the vascular lumen into the interstitial space. The oncotic pressure holds water in the circulation and draws fluid back into the circulation at the end of the capillary beds (Starling, 1896). The fluid remaining outside the capillaries may be returned to the circulation via the lymphatic system but, if excessive, will result in tissue edema.

The number of particles in a solution determines its osmotic pressure. Thus, solutions containing smaller molecules can exert a higher osmotic pressure since saturated solutions will contain more molecules per unit volume. However, small molecules diffuse more easily out of the vascular space. Therefore, the net oncotic pressure exerted by a solution is a balance between the osmotic pressure exerted by that solution and the rate of diffusion of that solution out of the vascular bed. In normal plasma, most of the oncotic pressure gradient (approximately 80%) is produced by albumin. Globulins contribute the remainder of the oncotic pressure, with fibrinogen exerting little effect (<0.01% of the total) (Roberts & Bratton, 1998). The normal colloid oncotic pressure of plasma is less in neonatal foals (17–21 mmHg) than in mature Thoroughbred horses (20–22 mmHg) (Jones et al., 1997; Runk et al., 2000).

Albumin has other important physiologic functions, including binding ions, drugs, and hormones and serving

as a carrier for fatty acids and other water-insoluble compounds in the plasma (Di Masi et al., 2016). When the plasma concentration of albumin is decreased, the free (or nonbound) fraction of an albumin-binding drug will increase. However, for most drugs, plasma clearance will also increase, resulting in an unchanged free concentration of the drug, and therefore no change in drug activity (Toutain & Bousquet-Melou, 2002). Albumin also acts as a buffer in acid–base disturbances, and decreased albumin concentration contributes to a metabolic alkalosis (Corley & Marr, 1998).

Acid–Base Balance

Principles, Causes and Recognition

The most common acid–base disturbance in horses with gastrointestinal disease is metabolic acidosis, due to lactic acidosis (hypovolemia, endotoxemia), hyponatremia (colitis, peritonitis, intestinal volvulus), or hyperchloremia (occasionally seen in horses with colitis). Metabolic alkalosis, due to hypochloremia (high-volume gastric reflux or colitis) or hypoalbuminemia (severe enterocolitis, excessive fluid therapy), respiratory alkalosis (hyperventilation due to pain), and respiratory acidosis (hypoventilation due to extreme abdominal distension, central depression) can also occur (Corley & Marr, 1998).

Acid–base balance is determined by the examination of arterial pH, arterial carbon dioxide tension ($PaCO_2$) and the base excess. The pH gives the overall acid–base balance. It is calculated as the negative logarithm of the hydrogen ion concentration. A decreased pH represents an overall acidosis and an increased pH represents an overall alkalosis. The normal range is approximately 7.35–7.48 (Corley & Marr, 1998). The arterial carbon dioxide tension represents the respiratory component of the acid–base balance. Carbon dioxide combines with water to form carbonic acid, which in turn forms bicarbonate and hydrogen ions, in the following reaction:

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

If the amount of carbon dioxide increases in the blood (for example, due to compromised respiration in a horse with a diaphragmatic hernia), the equilibrium in this equation moves to the right, resulting in a higher hydrogen ion concentration, and a lower pH. This is a respiratory acidosis. If the amount of carbon dioxide decreases in the blood (for example, due to hyperventilation associated with pain), this equilibrium moves to the left, resulting in a lower hydrogen ion concentration, and a higher pH. This is a respiratory alkalosis.

Base excess represents the metabolic component of the acid–base balance. Base excess is a measure of the strong acid needed to restore the pH of whole blood to 7.4 at a pCO_2 of 40 mmHg. The base excess effectively represents a corrected value for bicarbonate. As can be seen in the equation, as the carbon dioxide tension changes, the bicarbonate concentration will change. The base excess therefore corrects the bicarbonate to remove this effect, by calculating what the bicarbonate concentration would be if the carbon dioxide tension was 40 mmHg. This removes the respiratory influence on bicarbonate, and leaves only the metabolic influence. One further calculation is performed to convert bicarbonate to base excess. The difference between the corrected bicarbonate and its normal value (usually taken to be either 24.4 or 25 mmol/L), is calculated. Therefore, a base excess of –5 mEq/L represents a corrected bicarbonate concentration of 19.4 or 20 mmol/L. A negative base excess represents a metabolic acidosis and a positive base excess a metabolic alkalosis.

There are physiologic compensatory mechanisms that attempt to return the pH toward normal. Respiratory compensation of metabolic disturbances is fairly straightforward. In metabolic acidosis, the increase in H^+ stimulates the respiratory center to increase ventilation, increasing excretion of CO_2 by the lungs, and decreasing the pCO_2 in the blood. This response is initially mediated by peripheral chemoreceptors, but the full response does not occur until there is a change in pH in the cerebrospinal fluid (CSF), which takes 14–17 h in dogs (Autran de Morais & DiBartola, 1991). The decrease in ventilation in response to a metabolic alkalosis appears to be entirely centrally mediated, and therefore only occurs after a change in pH of the CSF. The expected change in $PaCO_2$ in metabolic acidosis is a decrease of 1 mmHg for each 1 mEq/L decrease in base excess. In metabolic alkalosis, the expected increase in $PaCO_2$ is 0.6 mmHg for each 1 mEq/L increase in base excess (Schlichtig et al., 1998).

Respiratory acid–base disorders result in metabolic compensation. In acute respiratory alkalosis, sodium is exchanged for chloride by red blood cells, resulting in a mild hyperchloremia and hyponatremia. With chronicity, there is increased reabsorption of chloride and decreased reabsorption of sodium in the renal tubules. In an acute respiratory alkalosis, lactate is increased for the first 6–8 h in dogs (Autran de Morais & DiBartola, 1991). This is due to an increase in lactic acid production, particularly by red blood cells (Jones, 1987). With acute respiratory alkalosis, no change in base excess is expected. In chronic respiratory alkalosis, a decrease of 0.4 mEq/L in base excess is expected for each 1 mmHg decrease in $PaCO_2$ (Schlichtig et al., 1998). In acute respiratory acidosis, the reverse happens: the red blood cells take up chloride, and release sodium. Again, it is the kidneys that mediate the compensation in chronic respiratory acidosis; ammonium chloride is excreted, resulting in a decrease in plasma chloride but not sodium. With acute respiratory acidosis, no change in base excess is expected. In chronic respiratory acidosis, an increase of 0.4 mEq/L in base excess is expected for

each 1 mmHg increase in $PaCO_2$ (Schlichtig et al., 1998). Occasionally, both respiratory and metabolic dysfunction can contribute to the development of an acid–base disturbance, particularly an acidosis. For example, a horse with a large colon volvulus may have a metabolic acidosis because of accumulation of lactate from hypovolemia and a failing circulation. If the colon is very distended, this may interfere with the movement of the diaphragm and reduce respiration, resulting in an additional respiratory acidosis. This is termed a mixed disturbance.

Classification of acid–base disturbances is important to be able to direct treatment effectively. They are classified as acidosis or alkalosis, metabolic or respiratory, and compensated or uncompensated. The majority of acid–base disturbances can be classified by the following three steps (Table 28.1). The first step is to look at the measured pH. If the pH is below 7.40, the primary problem is likely to be an acidosis. If the pH is above 7.40, the primary problem is likely to be an alkalosis. The second step is to determine whether the $PaCO_2$ or base excess matches the pH. An increased $PaCO_2$ or negative base excess matches an acidotic pH. A decreased $PaCO_2$ or positive base excess matches an alkalotic pH. If $PaCO_2$ matches the pH, the primary problem is respiratory. If the base excess matches the pH, the primary problem is metabolic. If both match the pH, then it is a mixed respiratory and metabolic problem. The third step is to decide if there is compensation. This depends on the direction of whichever of the $PaCO_2$ or base excess that does not match the pH. If the $PaCO_2$ or base excess is within its normal range, there is almost certainly no compensation. If it is in the opposite direction to the primary problem (e.g., a decreased $PaCO_2$ for a primary metabolic acidosis), it most likely represents compensation. There are a few cases that do not fit this scheme. For example, metabolic acidosis may be primary, due to hypovolemia, and not compensatory in a horse with colitis and pain induced tachypnea.

Physiologic Role and Abnormalities of the Major Electrolytes in Plasma

Horses with acute abdominal disease can have profound changes in the plasma concentrations of the major electrolytes. Understanding the roles of these electrolytes, and the prevalence and causes of changes in their concentrations, can help prioritize therapy. Electrolyte and acid–base abnormalities are usually corrected after treatment for hypovolemia, during rehydration therapy. The choice of fluid composition for this phase of therapy is, therefore, dependent on the plasma electrolyte concentrations.

Sodium

Sodium is the major cation in plasma, and sodium and glucose concentrations are the main determinants of plasma osmolality (Brownlow & Hutchins, 1982). Changes in plasma osmolality can lead to central nervous system edema or dehydration (Buffington & Abreo, 2016; Muhsin & Mount, 2016), because the CSF equilibrates slowly with the plasma but will change rapidly if osmotic gradients are high. The plasma sodium concentration is mainly controlled by the hormone vasopressin (formerly called antidiuretic hormone). Excessive secretion of vasopressin can occur postoperatively or be due to pain (Schaer, 2008), resulting in free water retention and hyponatremia. In this case, the plasma volume may be normal. Hyperglycemia is common is postoperative colic patients, presumably as part of the physiologic response to cortisol release (Gentz & Cornblath, 1969). Glucose acts as an osmotic agent, expanding the extracellular space and, therefore, effectively diluting sodium. This effect is moderate (a decrease of 1.7 mmol/L in sodium for each increase of 100 mg/dL (5.6 mmol/L) in

Table 28.1 Scheme for classifying the majority of acid–base disturbances.

Disturbance	pH	$PaCO_2$	Base excess
Uncompensated metabolic acidosis	Decreased	Unchanged	Negative
Compensated metabolic acidosis	Decreased	Decreased	Negative
Uncompensated respiratory acidosis	Decreased	Increased	Unchanged
Compensated respiratory acidosis	Decreased	Increased	Positive
Mixed metabolic and respiratory acidosis	Decreased	Increased	Negative
Uncompensated metabolic alkalosis	Increased	Unchanged	Positive
Compensated metabolic alkalosis	Increased	Increased	Positive
Uncompensated respiratory alkalosis	Increased	Decreased	Unchanged
Compensated respiratory alkalosis	Increased	Decreased	Negative
Mixed metabolic and respiratory alkalosis	Increased	Decreased	Positive

$PaCO_2$, arterial tension of carbon dioxide.

glucose in humans (Adrogue & Madias, 2000b)), but may exacerbate other causes of decreased sodium concentration. Hyponatremia may also occur in horses with peritonitis or bowel obstructions, which can lose sodium and water into this "third space," resulting in hypovolemic hyponatremia (Buffington & Abreo, 2016). It is also possible to cause iatrogenic hyponatremia by repeated instillation of water without electrolytes into the stomach, as might be done to relieve a large colon impaction (Lopes et al., 2004).

Hypernatremia is reported to occur in 12% of postoperative colic patients (Protopapas, 2000). It results in hypertonicity, hyperosmolality, and cellular dehydration (Muhsin & Mount, 2016). Hypernatremia usually occurs as a result of to water loss, but may also result from a net gain of sodium. Diarrhea, drainage of gastric reflux, renal failure, and diuresis can all cause hypernatremia. Prolonged water restriction or excess administration of salt or sodium bicarbonate may also result in iatrogenic hypernatremia (Muhsin & Mount, 2016; Schaer, 2008).

Potassium

Potassium is primarily an intracellular ion, hence decreases in whole-body potassium may not be detected by plasma measurements (Muylle et al., 1984). Although erythrocyte potassium content has been used to estimate whole-body potassium (Muylle et al., 1984), its accuracy has not been validated. Moreover, the extracellular potassium concentration (reflected in the plasma) is critical for neuromuscular transmission and is more relevant to clinical signs than whole-body potassium stores (Rose, 1994).

Hypokalemia is common in horses after colic surgery (Protopapas, 2000), due to enhanced mineralocorticoid and glucocorticoid release and the infusion of large amounts of sodium-containing fluids, which increase distal tubular flow and renal potassium loss (Rose, 1994). Hypokalemia can also occur in colitis, after heavy sweating, and in metabolic alkalosis. In colic patients, the most relevant clinical sign of hypokalemia is reduced intestinal motility (Schaer, 2008; Gennari, 1998). However, the association between hypokalemia and ileus in the horse remains undetermined. Other clinical signs include muscle weakness, lethargy, and inability to concentrate urine (Schaer, 2008). Cardiac conduction abnormalities are rare except in severe hypokalemia and in pre-existing cardiac dysfunction (Gennari, 1998). The effect of potassium on acid–base status is small and need not be considered clinically (Corley & Marr, 1998).

Hyperkalemia has been reported to occur in association with metabolic acidosis, due to potassium exchange for hydrogen ions across cell membranes. However, this is chiefly a phenomenon of mineral (inorganic) acidosis rather than lactic acidosis (Graber, 1993; Perez et al., 1981; Trefz et al., 2013). In horses with colic, the predominant cause of acidosis is lactic acid accumulation, associated with poor tissue perfusion and hypovolemia (Nappert & Johnson, 2001). One study found a moderate inverse correlation between plasma potassium concentration and pH, but no correlation between potassium and lactate concentration, in jugular venous blood from horses undergoing surgery for treatment of abdominal diseases (C. Adams and K. T. T. Corley, unpublished observations, 2004).

Chloride

Chloride is the major anion in the extracellular fluid and is important in maintaining acid–base balance, renal tubular function, and the production of gastric acid (Maloney et al., 2002). In humans, chloride is the major determinant of metabolic acid–base status (Funk et al., 2004). High concentrations of chloride are present in the intestine, with gastric secretions being the primary source (Yunos et al., 2010). In the kidney, chloride reabsorption is heavily influenced by both plasma sodium concentration and acid–base balance. Both active and passive chloride transport mechanisms contribute to its reabsorption. Renal reabsorption of chloride is affected by several hormones, including parathyroid hormone, calcitonin, antidiuretic hormone and angiotensin II (De Morais, 1993).

Chloride ion concentration is dependent on whole-body water balance. Therefore, plasma chloride concentrations must be interpreted relative to plasma sodium ion concentrations (Corley & Marr, 1998; Yunos et al., 2010; De Morais, 1993). Large amounts of chloride can be lost from high-volume gastric reflux, or in secretory diarrhea, resulting in hypochloremia and metabolic alkalosis. There is a high prevalence (54%) of hyperchloremia in postoperative colic patients (Protopapas, 2000). Hyperchloremia can occur as a result of loss of water in excess of electrolytes, in which case it occurs in concert with hypernatremia. Hyperchloremia may also result from metabolic compensation for respiratory alkalosis and renal tubular acidosis and be due to loss of water and sodium in diarrhea (Corley & Marr, 1998; De Morais, 1993).

Calcium

Calcium is involved in excitation and contraction of cardiac muscle and the maintenance of vascular tone. It is a positive inotrope, causing an increase in smooth muscle contractility (Grubb et al., 1996; Gasthuys et al., 1991; Garcia-Lopez et al., 2001). Other functions of calcium include neuromuscular transmission, enzyme and hormone production, and coagulation (Grubb et al., 1996). It is also involved in cell messaging and receptor coupling (Zaloga et al., 1992). Calcium is primarily extracellular, with 99% located in bones and teeth. Only 1% exists in the extracellular fluid, of which roughly half is protein bound and approximately 47% ionized in the

plasma (Dart et al., 1992). Many commonly used analyzers measure total plasma calcium, which is partly dependent on the plasma albumin concentration. The equation for correcting total calcium for the measured albumin concentration is (Payne et al., 1973)

$$\text{corrected calcium}\,(\text{mg/dL}) = \text{measured calcium}\,(\text{mg/dL}) + 0.8\left[4 - \text{albumin}\,(\text{g/dL})\right]$$

Acid–base alterations affect the protein binding of calcium, with acidosis increasing ionized calcium as it is displaced from protein-bound sites by hydrogen ions (Cooper et al., 1992).

Low plasma ionized calcium concentrations are common in horses with gastrointestinal diseases requiring surgical intervention (Dart et al., 1992) and in horses with colitis. Possible causes of hypocalcemia include lactic acidosis (Cooper et al., 1992), endotoxin-induced changes in calcium homeostasis (Todd & Mollitt, 1995), loss of calcium in sweat (Taylor, 1996), and functional disturbances of the small intestine [the main site of calcium absorption in the horse (Schryver et al., 1970)]. Clinical signs of hypocalcemia reported in the horse include synchronous diaphragmatic flutter, tetany, muscle spasm, and seizures (Beyer et al., 1997). In horses after colic surgery, decreasing ionized calcium concentrations were correlated with the following changes on the electrocardiogram: increased heart rate, increased QT interval corrected for heart rate, decreased PR interval, and decreased QRS interval (Garcia-Lopez et al., 2001). Experimentally induced hypocalcemia (<3.52 mg/dL; 0.83 mmol/L) induced cardiac arrhythmias in four of seven ponies, and was fatal in two (Glazier et al., 1979). Hypocalcemia may be associated with postoperative ileus in the horse (Dart et al., 1992), but this has not been investigated.

Hypercalcemia occurs rarely in horses with acute abdominal disease unless there is concurrent chronic renal failure or neoplasia. Hypercalcemia can cause muscle weakness, depression, and seizures due to increased CSF calcium concentrations (Grubb et al., 1996). Experimentally induced hypercalcemia in ponies resulted in ventricular fibrillation or cardiac arrest at ionized calcium concentrations of 4.55–10.0 mmol/L (Glazier et al., 1979).

Magnesium

Magnesium plays a crucial role in many metabolic and cellular functions in the body, especially those involving adenosine triphosphate (ATP) and the production of energy (Page et al., 1998). It is an important coenzyme for the Na^+,K^+-ATPase pump (Tso & Barish, 1992). Abnormalities of the normal resting membrane potential can result from interference with the normal function of this pump, causing membrane destabilization and hyperexcitability. Magnesium is an essential cofactor in many enzymatic reactions in the body (Tso & Barish, 1992). Magnesium also competes directly with calcium for some of its binding sites, allowing greater binding of calcium to enzymes in hypomagnesemia. One such enzyme is phospholipase A_2; increased calcium binding results in greater activity of this enzyme, which leads to the increased formation of eicosanoids, particularly thromboxane A_2 (Gunther, 1992), which may play a role in thrombophlebitis (Morris, 1989).

In one study, 54% of horses with gastrointestinal disease had low plasma ionized magnesium concentrations (Garcia-Lopez et al., 2001). Causes of hypomagnesemia include decreased intake, gastrointestinal losses (e.g., prolonged nasogastric reflux, malabsorption), alterations in distribution (e.g., endotoxemia, parenteral nutrition administration), renal losses (e.g., prolonged administration of lactated Ringer's solution or other magnesium-free fluids, hypophosphatemia, acidemia, renal tubular acidosis) (Olerich & Rude, 1994; Salem et al., 1991), and excessive sweating (Taylor, 1996). In the horse, severe hypomagnesemia can result in ventricular arrhythmias and also muscle tremors, ataxia, seizures, and calcification of elastic tissue (Harrington, 1974). Other clinical manifestations of hypomagnesemia reported in humans include supraventricular tachycardia, atrial fibrillation, thrombosis, anemia, decreased muscle strength, increased nephrotoxicity of aminoglycoside drugs, increased pulmonary vascular resistance, and sudden death (Tso & Barish, 1992; Gunther, 1992; Salem et al., 1991; Landon & Young, 1993). Hypomagnesemia can also result in hypokalemia that is refractory to potassium supplementation (Hamill-Ruth & McGory, 1996).

Hypermagnesemia is less common than magnesium deficiency in intensive care patients. The prevalence reported in postoperative colic patients is 11–14% (Protopapas, 2000; Costa et al., 1999). Magnesium antagonizes the effects of calcium at the neuromuscular junction, and signs of hypermagnesemia include sweating, flaccid paralysis, coma, and recumbency due to a blockade of peripheral neuromuscular transmission (Bowen et al., 1970). Iatrogenic hypermagnesemia can occur in horses after administration of magnesium sulfate (Epsom salts) by nasogastric tube, for the treatment of large colon impactions. The recommended dosage of magnesium sulfate is 0.5–1.0 g/kg, and toxicity has been reported when twice the normal dosage has been administered. Any conditions that reduce renal excretion of magnesium, such as hypovolemia, or allow increased intestinal absorption of magnesium, such as delayed intestinal transit due to colic, drug therapy, or increased permeability of the intestinal wall, may allow toxicity to develop (Henninger & Horst, 1997).

Phosphate

Only 1% of total body phosphorus is present in the blood, with the majority of the remainder in the bone (Bugg & Jones, 1998). Phosphate (inorganic phosphorus) is the most abundant intracellular anion (Maloney et al., 2002). Phosphate homeostasis is controlled by parathyroid hormone, calcitonin, and vitamin D, and involves the intestine, kidneys, and bone. Absorption of phosphate from the intestine is affected by calcium, which binds to intraluminal phosphate to form insoluble complexes, thus reducing the bioavailability of both ions (Bugg & Jones, 1998). Phosphate in the body is important as an enzyme cofactor, as a buffer, and in the production of ATP for energy. It is an important part of proteins and lipids, and is also essential for normal functioning of the coagulation cascade and the immune system (Maloney et al., 2002).

The prevalence of hypophosphatemia in postoperative colic patients is 44% (Protopapas, 2000). Possible causes include withholding feed during the acute colic episode and postoperative period. Increases in circulating catecholamine and glucose concentrations, which occur after colic surgery, induce intracellular shifts of phosphate (Bugg & Jones, 1998). Extensive bowel resection can also result in hypophosphatemia, because the distal small intestine is a major site of phosphate absorption in the horse (Schryver et al., 1972). In experimental studies in rats, endotoxin administration resulted in increased renal excretion of phosphate (Mimura et al., 1997). If this response to endotoxemia also occurs in horses, it may also contribute to hypophosphatemia. The prevalence of hyperphosphatemia in horses after colic surgery is 12% (Protopapas, 2000). Large quantities of phosphate are present in intestinal tissue. Ischemic damage to the intestinal wall leads to leakage of phosphate into both the intestinal lumen and peritoneal fluid, which occurs at an early point after onset of intestinal ischemia. The phosphate in the peritoneal space may reach the systemic circulation via the portal system and lymphatics. Supporting this, the correlation between serum and peritoneal fluid phosphate concentrations was high in horses with colic (Arden & Stick, 1988).

Types of Fluid

Crystalloids

General Principles

Crystalloid solutions consist of electrolytes in water. Crystalloid solutions may be isotonic, hypertonic, or hypotonic. Isotonic solutions have approximately the same osmolality as plasma and therefore may be given rapidly, in large volumes, and into peripheral veins. Hypertonic solutions act to draw water into the extracellular fluid (ECF) from the intracellular fluid and represent a method of rapidly restoring circulating volume at the expense of tissue hydration. Hypotonic solutions are usually used only to correct plasma hypertonicity. Because true hypotonic solutions (e.g., sterile water) cause erythrolysis (Krumbhaar, 1914), they can only be given slowly via a central vein (Worthley, 1986). For this reason, isotonic solutions containing a metabolizable substrate, such as dextrose, and no electrolytes are usually used.

Crystalloid fluids pass rapidly from the circulation to the interstitial fluid. This means that their resuscitation effect may be short-lived and that they can cause edema. Only 30% of isotonic fluids and 10% of hypotonic fluids remain in the circulation after 30 min (Spalding & Goodwin, 1999). The increase in interstitial fluid may actually decrease tissue oxygen uptake in normal animals by increasing the diffusion distance between capillaries and cells (Gow et al., 1998). However, crystalloids remain the least expensive and, in many circumstances, the best fluids for administration to the horse. All fluid therapy plans involve crystalloid fluids and these are frequently the only fluids administered.

Homemade or "carboy" fluids, although considerably less expensive than fluids available commercially, have been associated with producing clinical signs of endotoxemia in normal horses (Denkhaus & Van Amstel, 1986) and a seven-fold increase in the risk of thrombophlebitis (Traub-Dargatz & Dargatz, 1994), and therefore cannot be recommended.

Balanced Electrolyte Solutions

For most situations in the field, commercial isotonic polyionic crystalloid solutions are the safest fluids with which to resuscitate hypovolemic horses. They increase plasma volume without directly causing profound electrolyte disturbances, because they contain approximately the same electrolyte concentrations as plasma. Therefore, balanced polyionic fluids are always a good choice when laboratory information is not available immediately. It also follows that polyionic crystalloid solutions are often not sufficient to correct electrolyte imbalances.

Two classes of polyionic fluids are available, those for resuscitation and those for maintenance. Maintenance fluids (Normosol-M[1], Plasma-lyte M[2], Plasmalyte-56[2], etc.) contain higher potassium (15–30 mEq/L) and lower sodium (40–60 mEq/L) and chloride (40–60 mEq/L) concentrations than resuscitation fluids (Normosol-R[1], Plasma-lyte 148[2], Isolec[3], lactated Ringer's solution[2], etc.). Currently, maintenance fluids are not available commercially in volumes exceeding 1 L, which has led to the practice of adding potassium chloride (at 10–20 mEq/L) to resuscitation formulas so that they can be used as

1 Abbott Laboratories, North Chicago, IL, USA.
2 Baxter Healthcare Corporation, Deerfield, IL, USA.
3 Ivex Division, Galen Holdings, Larne, Northern Ireland, UK.

maintenance fluids in equine medicine. Commercially available maintenance fluids should be considered as a treatment option in equine neonates.

The different alkalinizing agents (or "bicarbonate substitutes") used in resuscitation fluids are clinically relevant. The alkalinizing agent in plasma is bicarbonate. Bicarbonate-containing fluids are unstable when stored and may produce profound metabolic alkalosis. Therefore, Hartmann, an American pediatrician, replaced bicarbonate with lactate to make lactated Ringer's solution (also called Hartmann's solution). Lactate is metabolized in the liver but this process is slow enough to avoid the rapid changes in plasma pH that occur with bicarbonate. Sodium bicarbonate and sodium lactate both increase the strong ion difference resulting in a metabolic alkalosis. The cation (sodium) remains in the ECF while the anion (bicarbonate or lactate) is metabolized (Kellum, 1999). It is the speed of metabolism of the anion and the renal excretion of sodium that determines the ultimate alkalization. It may seem counterintuitive to administer lactate-containing fluids to a horse with lactic acidosis resulting from poor tissue perfusion; however clinical trials in human patients in hemorrhagic shock have shown that lactate-containing fluids do not exacerbate the lactic acidosis of hypoperfusion (Didwania et al., 1997; Lowery et al., 1971). It appears that in shock, the liver's capacity for metabolizing lactate is not overwhelmed, but instead the delivery of lactate to the liver by the circulation is impaired. Restoring the circulating volume, even with fluids containing moderate amounts of lactate, is sufficient to allow the liver to clear the circulating lactate (Lupo et al., 1990). Whereas this is true for hemorrhagic shock, uptake of lactate by the liver may be impaired in severe septicemia (Chrusch et al., 2000). In endotoxic and septic horses, and those with liver disease, lactated Ringer's solution should be used with caution. Alternative alkalinizing agents to lactate are present in some commercially available polyionic fluids (e.g., acetate and gluconate in Normosol-R). The muscles primarily metabolize acetate and a variety of tissues throughout the body metabolize gluconate. Lactated Ringer's solution contains calcium whereas Normosol-R contains magnesium. Calcium solutions should not be mixed with whole blood; blood and its products should be stored with a compound that chelates calcium ions. Similarly, calcium solutions should not be mixed with sodium bicarbonate as they react to produce calcium carbonate. Clearly, calcium solutions are contraindicated in hypercalcemia. Fluids containing magnesium can, therefore, be used in more clinical situations than those containing calcium.

Normal Saline

Isotonic (0.9%) sodium chloride is used commonly as an intravenous replacement fluid in species other than the horse. Isotonic sodium chloride has a higher ratio of chloride to sodium than plasma and therefore reduces the strong ion difference and causes a mild hyperchloremic acidosis in normal ponies (Gossett et al., 1990). This limits its utility as a resuscitation fluid in the horse, as most horses requiring fluid resuscitation already have acidosis. Furthermore, recent evidence in humans suggests that excessive chloride administration is associated with an increased incidence of acute kidney injury (Yunos et al., 2012, 2015). However, chloride may not be the only factor contributing to acute kidney injury (Yunos et al., 2015), and a recent randomized trial comparing a buffered crystalloid to saline for resuscitation of intensive care patients found no difference in the incidence of acute kidney injury (Young et al., 2015).

Isotonic sodium chloride should not be used for resuscitation of horses with acute abdominal disease unless indicated by measured electrolyte abnormalities. Sodium chloride solution has been advocated in the treatment of hyperkalemia, in order to avoid the potassium-containing polyionic fluids. However, this does not apply to the horse; in the absence of clinical signs of hyperkalemia, and with the exception of horses with hyperkalemic periodic paralysis or with a ruptured bladder, the hyperkalemia is likely to reflect acidosis and polyionic fluids are probably appropriate.

Hypertonic Saline

Hypertonic saline (2–4 mL/kg of 7–7.5% sodium chloride) has been advocated as a method of quickly restoring circulating volume in horses with severe endotoxemia (Bertone, 1989). Administration of 7% sodium chloride results in an increase in stroke volume for 60 min after the end of infusion of 5 mL/kg (Tavanaeimanesh et al., 2015). Accompanying this, there is also an increase in the ECF of four to five times the infused volume for at least 60 min (Onarheim, 1995). The hypertonic saline draws fluid into the ECF from the intracellular fluid, principally from muscle and liver cells (Onarheim, 1995), without providing significant fluid replacement. The administration of hypertonic saline should always be followed within 2.5 h of administration [the point in experimental studies when cardiac output begins to fall below baseline values (Bertone, 1989)] by the administration of large volumes of isotonic polyionic crystalloids. The volume of crystalloid fluids given should be based on the severity of clinical signs of hypovolemia and dehydration, but should be in excess of five times the volume of hypertonic saline infused. In addition to increasing ECF volume, hypertonic saline reduces the capillary endothelial swelling that may occur as part of the systemic inflammatory response syndrome and, therefore, improves tissue microcirculation and oxygen delivery (Mazzoni et al., 1990). Furthermore, in experimental hemorrhagic shock, hypertonic saline reduces neutrophil activation, resulting in reduced lung injury (Angle et al., 1998).

Administration of hypertonic saline solution, at a dose rate of 5 mL/kg immediately after administration of endotoxin to horses, attenuated the cardiovascular derangements associated with endotoxemia more effectively than an equivalent volume of isotonic saline (Bertone, 1989). Despite the positive experimental evidence for the use of hypertonic saline in endotoxemia, it should be used with caution during resuscitation in dehydrated horses. Cardiovascular improvements after the administration of hypertonic saline in 3–8% dehydrated rats were significantly reduced (Krausz et al., 1993) and resuscitation of 8–10% dehydrated rats with hypertonic saline resulted in greater renal dysfunction and decreased survival compared with lactated Ringer's solution (Malcolm et al., 1993). Despite these findings in rats, hypertonic saline was found to be a suitable resuscitation fluid for horses that had completed a 100 km endurance ride, resulting in a faster restoration of intravascular volume but more marked electrolyte deficits (Fielding & Magdesian, 2011).

Given the beneficial effects of hypertonic saline in experimental endotoxemia and sepsis, it may have a role after initial fluid resuscitation. However, this has not been evaluated clinically in horses with endotoxemia. Because of the risks associated with rapid changes in plasma osmolality (Adrogue & Madias, 2000a), 7% saline should probably not be administered to neonatal foals.

Combination of dextran 70 (a colloid) with hypertonic saline resulted in acceptable resuscitation in experimental dehydration in calf and swine models (Constable et al., 1996; McKirnan et al., 1994). However, in the horse, the administration of a highly concentrated formula of hypertonic saline–dextran 70 resulted in clinically apparent intravascular hemolysis and hemoglobinuria (Moon et al., 1991). Whether less concentrated formulas are suitable for the horse remains to be investigated. The combination of an alternative colloid, hetastarch or pentastarch (6–10 mL/kg), and hypertonic saline (4 mL/kg) may be an appropriate solution for resuscitation of horses that are both hypovolemic and dehydrated (Pantaleon et al., 2006). However, in horses with hyperdynamic shock induced by low doses of endotoxin, there is no advantage of the hypertonic saline–hetastarch solution over large-volume crystalloids (Pantaleon et al., 2006).

Sodium Bicarbonate

Sodium bicarbonate has been advocated for the correction of metabolic acidosis in horses (Divers, 1998; Johnson, 1995). However, the cause of the acidosis needs to be considered carefully prior to starting treatment. Sodium bicarbonate is indicated in acidosis due to hyponatremia or hyperchloremia (Corley & Marr, 1998), in which the sodium in the solution acts to correct the strong ion difference. An alternative to sodium bicarbonate in hyperchloremic acidosis is a polyionic solution containing a large amount of lactate (84 mEq/L) (Romão et al., 2017).

In lactic acidosis, which is far more common in the horse, treatment with sodium bicarbonate is highly controversial. It is the author's opinion that there are no grounds for administering sodium bicarbonate to horses with lactic acidosis, irrespective of the arterial (or venous) pH. This contradicts previous recommendations that it should be used when the pH decreases below 7.1 (Divers, 1998) or 7.22 (Johnson, 1995). Treatment of lactic acidosis with sodium bicarbonate is based on four suppositions: low blood pH is directly harmful, sodium bicarbonate is able to increase blood pH when infused intravenously, increasing the blood pH with sodium bicarbonate improves patient status, and any adverse effects of sodium bicarbonate are outweighed by its benefits (Forsythe & Schmidt, 2000). These suppositions are not supported by data available currently in horses, humans, and laboratory animals. For a full discussion of the issues surrounding sodium bicarbonate treatment for lactic acidosis, the reader is referred to earlier reviews (Corley, 2004; Forsythe & Schmidt, 2000).

Dextrose-containing Solutions

Dextrose (5%, D5W) and 5% glucose solutions are used to replace a deficit of pure water (without accompanying electrolyte deficits) and are effectively hypotonic because the dextrose is rapidly metabolized to carbon dioxide and water. Use of these solutions is indicated in cases where fluid loss exceeds electrolyte loss, which can occur in horses with strangulating intestinal lesions (Brownlow & Hutchins, 1982). Hypernatremia and hyperchloremia are also relatively common in neonatal foals where resuscitation formulas are used as maintenance fluids (Buchanan et al., 2003). The volume of distribution of D5W is likely to be larger than that of a balanced electrolyte solution, which could result in a diminished ability to maintain the circulating volume. Horses receiving D5W should be monitored carefully because rapid administration can lead to hyperglycemia. If the plasma glucose concentration exceeds the renal threshold (approximately 180 mg/dL or 10 mmol/L), osmotic diuresis will result, which can reduce the benefit of the fluid administration. In species other than the horse (humans and dogs), high concentrations of glucose have been shown to be detrimental in both acute renal and acute cerebral injury (Li et al., 1995; Moursi et al., 1987). It is important that 5% dextrose and glucose solutions not be considered a form of parenteral nutrition. A 1 L volume of 5% dextrose provides approximately 170 kcal (712 kJ) of energy and 1 L of 5% glucose provides approximately 190 kcal (796 kJ). In order to provide 11.5 Mcal/day, the caloric requirement of a 500 kg horse standing in a stall (Ralston, 1990) (see Chapter 39), it would be necessary to administer 60–70 L per day, which would produce

serious electrolyte abnormalities. Consequently, 50% dextrose and 50% glucose solutions may be preferable to the 5% solution. Each milliliter of 50% dextrose is equivalent to 1.7 kcal (7.1 kJ) and each milliliter of 50% glucose is equivalent to 1.9 kcal (8 kJ).

An alternative is a solution of 2.5% dextrose and 0.45% sodium chloride, which, once the dextrose has been metabolized, has an effective osmolality half that of plasma. It is retained better in the circulation (20% after 30 min compared with 10% for D5W) (Spalding & Goodwin, 1999) and can be used in the treatment of moderate plasma hypertonicity or when plasma glucose concentration is a concern. It should be noted that a rapid reduction in plasma tonicity has been associated with the development of cerebral edema, resulting in coma, seizures, and death in other species (Adrogue & Madias, 2000a). This has not been documented in the horse.

Colloids

General Principles

Colloids are solutions containing large sugar or protein molecules, in addition to the water and electrolytes that are in crystalloid solutions. All colloids, except albumin, contain a mixture of large and small protein or sugar molecules. The larger molecules allow colloid solutions to persist longer in the circulation than crystalloid solutions. The smaller molecules exert osmotic pressure to draw fluid into the circulation in a similar way to hypertonic saline. Solutions with a large number of smaller molecules allow a rapid increase in the circulating volume, greater than the actual volume infused.

The use of colloids has been advocated for the resuscitation of hypovolemic horses and for the treatment of severe hypoproteinemia (McFarlane, 1999). Colloids have two advantages over crystalloids, which makes them attractive for fluid therapy. First, because of their persistence in the circulation, a three to six times smaller volume of a colloid solution is required to produce the same resuscitative effect as a crystalloid solution. This is particularly useful in acute resuscitation of severely dehydrated horses or in the field where large amounts of crystalloids may be difficult to transport. Second, the administration of colloids can increase the colloidal oncotic pressure, in contrast to the administration of large volumes of crystalloids (Jones et al., 1997, 2001; McKenzie et al., 2016; Gratwick et al., 2017).

Colloidal oncotic pressure refers to the osmotic pressure exerted by the molecules that do not pass freely from the vascular lumen into the interstitial space. The oncotic pressure holds water in the circulation and draws fluid back into the circulation at the end of the capillary beds (Starling, 1896). The number of particles in a solution determines its osmotic pressure. Hence solutions containing smaller molecules can exert a higher osmotic pressure as saturated solutions contain a greater number of molecules per unit volume. However, small molecules diffuse more easily out of the vascular space. Therefore, the net oncotic pressure exerted by a solution is a balance between the osmotic pressure exerted by that solution and the rate of diffusion of that solution out of the vascular bed. In normal plasma, most of the oncotic pressure gradient (approximately 80%) is produced by albumin. Globulins contribute the remainder of the oncotic pressure, with fibrinogen exerting little effect (<0.01% of total) (Roberts & Bratton, 1998). The normal plasma colloid oncotic pressure of plasma is lower in neonatal foals (17–21 mmHg) than in mature Thoroughbred horses (20–22 mmHg) (Runk et al., 2000).

As already discussed briefly, the molecular weight of a colloid solution is the most important factor in determining its effectiveness. All currently available synthetic colloids are polydisperse (made up of a mixture of molecules of differing molecular weights). Albumin is a monodisperse solution, as all molecules have a molecular weight of 69 kDa. The average molecular weight refers to the average size of molecules in the solution. As a rule, the higher the average molecular weight, the longer the colloid will persist in the circulation. The chemical nature of the colloid also influences its persistence in the circulation, but generally to a lesser extent than the molecular weight. The number of molecules in the solution determines the osmotic pressure, which can be considerably greater than plasma (e.g., 342 mmHg for urea-linked gelatin). Colloids with a lower average molecular weight exert a higher osmotic pressure and expand the plasma volume more rapidly, by drawing fluid from the interstitial space into the vasculature and thus increasing the circulating volume in excess of the amount of fluid infused. However, lower molecular weight colloids are cleared faster from the circulation and may leak more readily into the interstitium.

Leakage of proteins into the interstitium is important in edema formation, a common feature in critically ill horses, particularly those with colitis. Edema impairs delivery of oxygen to the tissues, as it both compresses capillary beds and increases the diffusion distance between the capillaries and the cells. Therefore, edema may contribute significantly to morbidity and mortality. Endotoxemia and ischemia-reperfusion injury (Henninger et al., 1992; Dabareiner et al., 1995) induce capillary damage, which allows plasma albumin to leak into the interstitium. This not only reduces the oncotic pressure within the vasculature, but also allows the extravasated albumin to exert an osmotic pressure that holds fluid in the interstitial space. Large colloid molecules do not leak as readily, allowing their oncotic pressure to draw fluid back into the vasculature. Larger colloid molecules may also plug the gaps in the capillary endothelium (Zikria et al., 1989a, 1989b). Even in conditions of severe capillary leak, very large molecules are

not able to escape the vasculature unless the integrity of the capillary endothelium is totally destroyed (Conhaim et al., 1999).

All of the artificial colloid solutions available currently are removed from the circulation by the reticuloendothelial system, resulting in colloid-containing vacuoles, which may persist for years (Thompson et al., 1970; Sirtl et al., 1999). The presence of these vacuoles does not appear to interfere with the function of the reticuloendothelial system (Lenz et al., 1986).

It remains to be seen whether colloids offer any advantage in terms of clinical outcome compared with crystalloids in horses. Some of the theoretical benefits of colloids over crystalloids have not been observed in some experimental models and clinical trials. For example, increased extravascular lung water was documented in an endotoxic pig model (Baum et al., 1990) but not in a septic rat model (Rackow et al., 1989) when crystalloid and hetastarch resuscitation were compared. In preterm hypotensive human infants, treatment with 5% albumin resulted in significantly greater fluid retention than treatment with isotonic saline and the two treatments were equivalent in other respects (So et al., 1997). Three large trials of colloids versus crystalloids for resuscitation in critically ill human patients did not show any difference in mortality (Finfer et al., 2004; Annane et al., 2013; Myburgh et al., 2012). There are, to date, no large randomized trials comparing hydroxyethylstarches or gelatins with crystalloids in horses. For these reasons, the clinician should keep an open mind about the relative merits of crystalloid and colloid resuscitation in horses. One precaution when using colloids is that the plasma total solids or total protein concentration is no longer a useful guide to plasma oncotic pressure (Bumbpus et al., 1998).

Hydroxyethylstarches

Hydroxyethylstarches are modified polymers of amylopectin. Several different hydroxyethylstarch preparations are marketed around the world and they all consist of a polydisperse solution of starch molecules in which hydroxyethyl groups have been substituted for a number of the glucose subunits. The solutions differ in the number of glucose units substituted and the average molecular weight. The greater the number of glucose molecules substituted, the longer is the half-life of the solution *in vivo*. The degree of substitution is usually given as a proportion of substituted residues, which results in a number between 0 and 1, with higher numbers representing greater substitution and hence a longer half-life. The average molecular weight is also important, with lower molecular weight solutions having a greater oncotic pressure but a shorter persistence in the circulation. Often hydroxyethylstarches are described with their average molecular weight and degree of substitution in parentheses after their name. For example, hetastarch (450/0.75) has an average molecular weight of 450 kDa and a degree of substitution of 0.75.

In normal horses, hydroxyethylstarches increase the colloid oncotic pressure but cause a decrease in plasma albumin concentrations (McKenzie et al., 2016), via hemodilution with a minor component of extravasation (Zdolsek et al., 2015). If the albumin flux into the extravascular space in response to hydroxyethylstarch infusion were greater in horses with a compromised endothelial barrier, this could lead to exacerbation rather than resolution of edema by hydroxyethylstarches.

One concern with hydroxyethylstarches is the effect on kidney function. A large randomized trial of hydroxyethylstarch versus saline for resuscitation of critically ill human patients found that a greater percentage of patients receiving hydroxyethylstarch required renal replacement therapy than those receiving saline (Myburgh et al., 2012). The negative effects on kidney function appear to be more pronounced with higher molecular weight starches such as hetastarch and pentastarch than with lower molecular weight starches such as tetrastarch (Ertmer et al., 2010). It should be noted that all hydroxyethylstarches have been associated with renal injury in experimental studies, and tetrastarch was shown to cause renal injury without inflammation in laboratory rats (Schick et al., 2015). One retrospective study of dogs receiving hetastarch during intensive care found an increase in acute kidney injury compared with dogs that did not receive hetastarch (Hayes et al., 2016), whereas a retrospective study of dogs receiving tetrastarch showed no increase in plasma creatinine concentrations in the tetrastarch group (Yozova et al., 2016). An experimental study in six ponies found no changes in renal parameters after infusion of 10 mL/kg tetrastarch (Gratwick et al., 2017).

There are conflicting reports in experimental models whether resuscitation with hydroxyethylstarches attenuates intestinal injury (Lu et al., 2015) or impairs intestinal barrier integrity and metabolic function (Wong et al., 2015). Hydroxyethylstarches are eliminated by renal excretion, extravasation, and uptake by the reticuloendothelial system, and also, for a very small percentage (<1%) of molecules, by biliary excretion (Thompson et al., 1970; Lenz et al., 2000). Larger molecules are cleaved by serum α-amylase prior to elimination. Serum amylase activity is increased in horses receiving hydroxyethylstarches (Schusser et al., 2007). Enzymatic cleavage generates smaller molecules, with a higher oncotic pressure, and contributes to a long persistence of increased colloid oncotic pressure in normal animals (Jones et al., 1997). Uptake by the reticuloendothelial system can result in the presence of phagocytic cells containing starch granules in the liver, spleen, skin, small intestine, striated muscle, and lymph nodes (Sirtl et al., 1999; Lenz

et al., 1986). These deposits are dose dependent and decrease with time, but may persist for up to 4½ years after infusion of hydroxyethylstarch in humans (Sirtl et al., 1999).

Hetastarch

Hetastarch (450/0.75) is a polydisperse solution with a wide range of molecular sizes (10–3000 kDa) and a high average molecular weight and degree of substitution. Hetastarch exerts an osmotic pressure of approximately 31 mmHg in solution (Nearman & Herman, 1991) and, at a dose of 10 mL/kg, increases the plasma colloidal oncotic pressure of normal ponies from 24 to 27 mmHg (Jones et al., 1997). However, this effect of infusing hetastarch on colloid oncotic pressure is similar to infusing an equal volume of plasma (McKenzie et al., 2016). In normal dogs, hetastarch expands the plasma by 140% of the volume infused (Thompson et al., 1970). The effects on plasma volume in the normal horse are likely to be similar but have not been investigated. Hetastarch is slowly degraded in the circulation and thus has a long half-life. In normal ponies, the increase in colloidal oncotic pressure after a dose of 10 mL/kg lasts longer than 120 h (Jones et al., 1997). However, in hypoproteinemic horses and foals, the clinical effects appear to be shorter, typically lasting 24–36 h (Jones et al., 2001).

In normal ponies, hetastarch is safe but high doses (20 mL/kg) decrease circulating Von Willebrand factor, factor VIII coagulant activity, and activated partial thromboplastin time and prolong bleeding times (Jones et al., 1997). Although a dose of 10 mL/kg of hetastarch did not effect hemostasis in normal ponies (Jones et al., 1997), endotoxemia may produce coagulation derangements (Dolente et al., 2002) that might render endotoxemic horses susceptible to the development of clinically important coagulation changes at this or lower doses.

Hetastarch may decrease vascular permeability after ischemia-reperfusion injury (Zikria et al., 1989a, 1989b), which makes it a theoretically attractive solution for administration to horses prior to surgical correction of strangulating intestinal lesions. This effect on reperfusion injury is not simply a function of high molecular weight; a similar effect could not be demonstrated for a dextran solution with an average molecular weight of 250 kDa (Moore et al., 1996). There is evidence that hetastarch reduces neutrophil chemotaxis through the endothelium *in vitro* (Hofbauer et al., 1999). Hence there is a potential for hetastarch to reduce neutrophil-mediated damage in ischemia-reperfusion, endotoxemia, and other inflammatory tissue insults. However, this effect has not yet been demonstrated *in vivo*.

The rapid increase in circulating volume that occurs after administration of hypertonic saline and the increase in oncotic pressure and more prolonged effects of hetastarch may make this combination appropriate for the resuscitation of severely dehydrated horses, especially those with severe colitis. Although hetastarch (up to 10 mL/kg) and hypertonic saline (2–4 mL/kg) have been combined with apparent success in a number of clinical cases, this combination did not improve hemodynamics in an endotoxin-induced model of hyperdynamic shock in anaesthetized horses (Pantaleon, 2006). It is possible that the combination of hetastarch and hypertonic saline would be more evident in states of reduced cardiac output rather than the increased cardiac output seen in this model. If used, this combination should be followed up with crystalloid fluids.

Pentastarch Pentastarch (200/0.5) has a lower molecular weight than hetastarch and is therefore expected to produce a greater initial increase in plasma volume. The initial increase in plasma volume in human patients is reported to be 145% of the volume infused for the 10% solution and 100% of the volume infused for the 6% solution (Fresenius, 1998). The lesser degree of substitution than hetastarch is expected to lead to faster degradation by serum amylases. Pentastarch has been tested in horses (Hermann et al., 1990; Meister et al., 1992) and is approved for use in horses in Switzerland. It is available as a 6% or 10% solution in isotonic sodium chloride.

In horses presenting for surgical colic, pentastarch administration resulted in a higher cardiac output for 150 min than hypertonic saline (Hallowell & Corley, 2006). However, this does not appear to translate into any differences in outcome. In a randomized study of 100 horses presenting with a packed-cell volume (PCV) over 45%, there was no difference in long-term survival in horses receiving pentastarch or hypertonic saline for initial resuscitation (Dugdale et al., 2015).

In healthy horses, an 8 mL/kg dose of a 10% pentastarch solution resulted in a slight decrease in the thrombin time 12 h after administration, which returned to normal after 24 h. No effect on prothrombin time or partial thromboplastin time was documented (Meister et al., 1992). In healthy horses, the initial phase half-life of pentastarch is 5.6 h and the terminal phase half-life is 122 h. However, the effects on PCV, plasma total solids, and plasma viscosity appear to last only 12–24 h (Meister et al., 1992). In equine clinical cases, the half-life may be as short as 2 h (Hermann et al., 1990).

Tetrastarch Tetrastarch (130/0.4) has the lowest average molecular weight of currently marketed hydroxyethylstarches, and may have the least adverse effects on coagulation and renal function. In a study of the administration of 10 mL/kg hydroxyethylstarches to eight normal horses, tetrastarch administration resulted in an increase in colloid oncotic pressure for 8 h, compared with 1 h

with hetastarch. Both hetastarch and tetrastarch caused decreases in Von Willebrand factor, but the decrease was for a shorter period (8 h) with tetrastarch than for hetastarch. Activated partial thromboplastin time (aPTT) overall was longer in the hetastarch group than the tetrastarch group (Epstein et al., 2014). A separate study of a dose of 10 mL/kg tetrastarch in six experimental ponies found no effect on the coagulation or renal parameters measured (Gratwick et al., 2017; Viljoen et al., 2014), but at 40 mL/kg there were significant changes in the thromboelastogram (TEG) profile, although the parameters remained within the normal range (Viljoen et al., 2014).

Dextrans

Dextrans are polysaccharides composed of linear glucose residues. They are produced from a polysaccharide synthesized by the bacterium *Leuconostoc mesenteroides* grown on sucrose media. Different molecular weight dextrans are produced by acid hydrolysis of the parent molecule. Two dextran solutions are commonly marketed, dextran 40 and dextran 70; the number refers to the average molecular weights, 40 and 70 kDa, respectively. Both of these solutions are polydisperse. Dextran molecules of less than 50–55 kDa are excreted in the urine (Thompson et al., 1970). Larger molecules are extravasated and taken up by the reticuloendothelial system or excreted through the gastrointestinal tract (Nearman & Herman, 1991).

In human patients, the peak plasma volume expansion after infusion of dextran 40 is 210% of the volume infused. By 1 h after infusion, the plasma expansion is approximately 140% of the volume infused (Shoemaker, 1976). In dogs, the peak effect of dextran 70 is a 140% plasma expansion. After 1 h, the expansion effect of dextran 70 is approximately 100% of the volume infused (Thompson et al., 1970). Within 12 h, 60% of the dextran 40 and 35% of the dextran 70 have been cleared from the vascular space (Nearman & Herman, 1991). In dogs, the increase in plasma volume 24 h after dextran 70 injection is only 1.1% of the volume infused (Thompson et al., 1970).

In humans, dextran administration is associated with a decrease in factor VIII activity, decreased fibrin clot formation, and dilutional coagulopathy (Roberts & Bratton, 1998). Dextran 70 inhibits equine platelet aggregation *in vitro* (Heath et al., 1998), but other effects on hemostasis have not been investigated. Dextran 70 has been used for its presumed antithrombotic properties in horses with a clinical diagnosis of verminous aneurysm (Greatorex, 1977). Dextran 70, when combined with hypertonic saline in a very concentrated solution, resulted in a transient, severe intravascular hemolysis and hemoglobinuria in horses (Moon et al., 1991). Whether this would occur with a less concentrated solution is unlikely, but this has not been studied. Dextran 40 was reported to cause acute renal failure in 4.7% of human patients (Biesenbach et al., 1997). It is not known whether this is a risk in the horse.

Gelatins

Gelatins are produced by chemical modification of bovine collagen. Despite their bovine origin, the risk of transmission of bovine spongiform encephalopathy by these products is apparently negligible (Peano et al., 2000). Two types of gelatin are available. Urea-linked gelatin[4] is marketed as a polydisperse solution with an average molecular weight of 35 kDa and succinylated gelatin[5] is marketed as a polydisperse solution with an average molecular weight of 30 kDa. Because of their relatively small molecular size, gelatins have high osmotic pressure (342 mmHg) but are eliminated rapidly by the kidneys. The small size of the molecules in gelatin solutions also means that more of this colloid is extravasated than other colloids, leading to greater edema formation (Allison et al., 1999; Holbeck et al., 2001). The high osmotic pressure means that it is possible to cause fluid overload in normal horses with gelatin. In one study, normal ponies undergoing anesthesia were given an extremely large dose of urea-linked gelatin (average dose 48 mL/kg). This caused significant fluid overload and pulmonary edema (Taylor, 1998).

Succinylated gelatin, at a dose rate of 10 mg/kg or 20 mL/kg, significantly decreased the hematocrit and increased the colloid oncotic pressure in six normal ponies (Gratwick et al., 2017). The effect of 10 mL/kg was similar to the effects seen with 10 mL/kg of a 10% tetrastarch solution, whereas the infusion of 20 mL/kg of gelatin had the greatest effects. Neither of the doses of gelatin tested resulted in any significant changes in thromboelastography (TEG) parameters (Gratwick et al., 2017).

In human patients, allergic reactions have been reported for both gelatin preparations, with urea-linked gelatins having the higher incidence at 0.146% (Ring & Messmer, 1977). There is no evidence that urea-linked gelatin causes allergic reactions in horses (Taylor, 1998).

Plasma

Plasma has been used extensively in horses with colitis and in neonatal foals for the passive transfer of immunity. Plasma may either be purchased commercially or be collected from donors. The ideal plasma donor is a young, healthy gelding with a known, entire history that has never been administered a blood product. For blood collection from the donor, a catheter is placed in the jugular vein with the tip pointing toward the head of the animal. The use of a 10 or 12-gauge catheter speeds up

4 Haemaccel, Intervet, Cambridge, UK.
5 Gelofusine, B. Braun Medical, Sheffield, UK.

collection. A collection bag containing anticoagulant [100 mL of acid citrate dextrose for each 900 mL of whole blood collected (Collatos, 1997)] is connected to the catheter and the jugular vein occluded beneath the catheter until the bag is full. Centrifugation or plasmapheresis are the most effective methods of separating the plasma from the cells. It is possible to achieve reasonable separation of the plasma and cells by sedimentation. The bag should be placed with the administration set uppermost in an ice bucket. There is reasonable separation after 2 h, but ideally the bag should be left for 12 h, if the circumstances allow (Durham, 1996). However, if the plasma is being collected for replacement of clotting factors, no more than 6 h should elapse between collection and administration or freezing, as factors V and VIII are not stable beyond 6 h (Cotter, 1991). These clotting factors are also depleted if frozen plasma is stored for longer than 1 year. Albumin, globulin, and factors II, VII, IX, and X are stable for at least 1 year (Cotter, 1991). Horses with colitis are at high risk of coagulopathy (Dolente et al., 2002), hence fresh plasma, collected and administered within 6 h, is preferred to frozen plasma, if available.

Although classically prescribed for hypoalbuminemia, the utility of plasma for replacing protein is unclear. Approximately 80% of the colloidal oncotic pressure of plasma is provided by albumin and thus many of the reservations expressed about albumin apply to plasma. At least 6–8 L are required to treat clinically significant hypoproteinemia in adult horses, and even then the effects may be short-lived. Plasma administration does not have the advantage of the higher molecular weight colloids of potentially drawing fluid back into the circulation in damaged capillaries, but it may prevent a low plasma oncotic pressure (Collatos, 1997), leading to generalized edema. Plasma may have a role in replacing antithrombin III, protein C, and other cofactors that are depleted during the systemic inflammatory response syndrome. When used for this purpose, fresh plasma is preferable because plasma that has been frozen for longer than 1 year may no longer contain high concentrations of these proteins.

Whole Blood

Used judiciously, blood transfusion is a potentially lifesaving treatment. It should be considered in all horses with a PCV of <18% (hemoglobin concentration <6 g/dL) and is imperative in horses with a PCV of <12%. Blood transfusion is not necessary in mild anemia (PCV >24%); human patients with mild anemia who received blood transfusion therapy have a worse outcome (Hébert et al., 1999). Hemorrhage is uncommon in horses with acute abdominal disease. However, horses with hemoperitoneum may present in acute pain and may, occasionally, require transfusion. In septic shock, blood transfusion has been suggested as a method of increasing oxygen delivery to the tissues by increasing the oxygen-carrying capacity of the blood. However, in septic human patients, blood transfusion was associated with an increase in oxygen delivery but not in oxygen uptake (Lorente et al., 1993), suggesting that the increased supply of oxygen is not available to the tissues. This is supported by work in laboratory animals that suggests that tissue oxygen uptake is superior at a PCV of 20 or 30% to that at a PCV of 40%, despite the higher oxygen delivery at the higher PCV (Creteur et al., 2001). The most likely explanation for this is that the increasing PCV increases blood viscosity (Stone et al., 1968), causing blood sludging and reduced flow through the capillaries. This may be especially important in shock, where blood viscosity may be increased independently of the PCV (Andrews et al., 1990).

Blood transfusion recipients are usually cross-matched with potential donors prior to blood collection. However, the reliability of these tests in the horse is questionable (Durham, 1996; Kallfelz et al., 1978). It may be appropriate to select donors negative for the major antigens (Aa and Qa) so that cross-matching is not necessary (Durham, 1996). Several laboratories offer blood typing for horses. For neonatal isoerythrolysis, washed red blood cells from the dam are the transfusion of choice. Washing removes the plasma, which contains antierythrocyte antibodies. The red cells are washed by repeatedly separating the cells from the plasma and resuspending them in isotonic saline. Ideally, the separation of the cells from the plasma or saline should be carried out with a centrifuge or plasmaphoresis machine, but it is acceptable to allow the cells to settle, remove the plasma, and then resuspend them. Three washes are usually adequate.

In all cases, the recipient should be monitored very closely for signs of a transfusion reaction during the infusion of the initial 50 mL of blood. Signs of transfusion reactions include pyrexia, tachycardia, tachypnea, sweating, icterus, lying down, frequent defecation, proteinuria, and hemoglobinuria (Hata & Sonoda, 1974). None of these signs are invariably present, but pyrexia and sweating are frequently the most prominent signs. In one study of normal horses given repeated incompatible transfusions, icterus and proteinuria were the only clinical signs that lasted for longer than 24 h and transfusion reactions did not occur before the sixth incompatible transfusion (Hata & Sonoda, 1974). In another study, one horse died, apparently of an anaphylactic reaction, during the second transfusion (Kallfelz et al., 1978). Disease transmission is possible with blood transfusion and is a particular concern in areas where equine infectious anemia is endemic (Issel et al., 1982). All donor animals should be tested regularly for this disease.

Whole blood should be collected into bags containing acid citrate dextrose, as already described for plasma. If possible, the blood should be used immediately, but

erythrocytes may remain viable in a refrigerator for as long as 3–4 weeks (Durham, 1996).

The amount of blood needed for transfusion can be calculated using the following equation:

$$\text{amount of blood (mL)} = \frac{\text{body weight (kg)} \times (\text{desired PCV} - \text{current PCV}) \times Z}{\text{PCV of donor}}$$

where Z is blood volume of the recipient per kilogram body weight [80 mL/kg for adult horses (Durham, 1996); 150 mL/kg for a 2-day-old foal (Spensley et al., 1987; Persson & Ullberg, 1979)].

Studies of the length of survival of transfused erythrocytes in recipient horses have produced variable results. In adult horses, the half-life of ^{59}Fe-labeled donor erythrocytes was 4 days in three of six horses and <24 h in the other three recipients (Kallfelz et al., 1978). This methodology does not permit autologous transfusions as a control. In 2 to 5-day-old foals, the mean half-life of ^{50}Cr-labeled donor erythrocytes was 5.5 days compared with 11.7 days for autologous erythrocytes (Smith et al., 1992).

Blood Substitutes

Stroma-free hemoglobin preparations have been developed in response to the need for safe, infection-free, sustainable sources of blood in human medicine and to eliminate the need for cross-matching. Unfortunately, unmodified free hemoglobin has too high an affinity for oxygen, is rapidly eliminated by the kidneys, causes a substantial increase in oncotic pressure, and may cause renal injury. For this reason, research has focused on modified polymers of hemoglobin. Polymerized bovine hemoglobin has already been registered in the United States and Europe for use in dogs, where the recommended dose is 10–30 mL/kg. Successful use of this product has been reported in a foal with neonatal isoerythrolysis (Perkins & Divers, 2001) and an early version of the product was used with apparent success in an anemic Miniature horse (Maxson et al., 1993); in both cases, a compatible blood donor could not be found. Although not clinically significant in this case, the anemic mare had increased pulmonary and systemic pressures, reported side effects in humans (Fromm, 2000), after infusion of the hemoglobin product (Maxson et al., 1993). More concerning is that, in an experimental trial in ponies with normovolemic anemia, one of six ponies experienced an anaphylactic reaction (Belgrave et al., 2002).

These products are an exciting development, which may have a particular application in equine medicine owing to the difficulty of reliable cross-matching for blood transfusion. However, currently available products may not be the most optimal for use in the horse.

Oral Fluids

It is possible to treat moderately dehydrated horses effectively with oral replacement solutions (McGinness et al., 1996; Lopes, 2002). Oral fluids do not need to be sterile, can be made up on the farm, and are considerably less expensive and easier to transport than intravenous fluids. It is apparently not necessary to add glucose to oral fluids for horses, but electrolytes should be added, if feasible. Isotonic or hypotonic fluids should be administered (Sosa León et al., 1995).

Oral fluids can be a successful alternative or adjunct to intravenous fluids in many mildly dehydrated horses with large colon impactions (Lopes et al., 1999, 2004) (see Chapter 27). Unfortunately, oral fluids are insufficient for moderately to severely dehydrated horses. Rapid administration of a glucose- and glycine-containing electrolyte solution (8 L/30 min) resulted in incomplete fluid absorption in horses with castor oil-induced diarrhea (Ecke et al., 1998). The oral rehydration solutions available commercially may not be ideal for fluid replacement in horses (Ecke et al., 1998). Further research is necessary to refine oral fluid therapy for horses.

The administration of plain water is of minimal benefit in restoring plasma volume in horses exercised in hot and humid conditions (Marlin et al., 1998). However, the administration of an oral rehydration solution or an electrolyte paste together with provision of fresh drinking water may be sufficient to supplement water and electrolytes after vigorous or prolonged exercise in dehydrated horses with only mild hypovolemia (Marlin et al., 1998; Sosa León et al., 1998).

Composition and Recipes

A possible isotonic solution consists of 4.9 g/L table salt and 4.9 g/L Lite Salt[6] to produce final concentrations of 123 mmol/L sodium, 34 mmol/L potassium, and 157 mmol/L chloride (Sosa León et al., 1995). This is approximately equal to 15 mL of table salt and 15 mL of Lite Salt per 4 L of water. If using sodium chloride alone, no more than 9 g (approximately half a tablespoon or 7.5 mL) should be added per liter. A measured quantity of these fluids should be given via a nasogastric tube. The amount administered at any one time should not exceed 8–10 L for a 500 kg horse, with at least 20 min allowed to elapse between each administration. Before each dose, the stomach should be refluxed and the administration delayed if more than 2 L of fluid are recovered. Some horses will show signs of abdominal pain when large doses of oral fluids, especially if the fluids are cold, are administered.

6 Morton Salt, Chicago, IL, USA.

Electrolyte Replacement Strategies

Sodium

The fluid choice for hyponatremia depends on whether there is concurrent hypochloremia. Sodium chloride is the best choice, if the plasma chloride concentration is also low. If the chloride concentration is normal or increased, then sodium bicarbonate should be administered. If the horse is not markedly dehydrated (Malcolm et al., 1993) and the hyponatremia is severe, then hypertonic solutions may be indicated (7–7.5% sodium chloride and 5–8.4% sodium bicarbonate). In other species, rapid correction of sodium deficits has been shown to cause demyelination of the pontine and extrapontine neurons, resulting in severe neurologic dysfunction (Adrogue & Madias, 2000b). It has not been established whether this is a risk or not in the horse and, therefore, it is necessary to follow the guidelines for sodium restoration in other species. These guidelines state that sodium should be corrected at a rate of 1 mEq/L/h in acute hyponatremia and at <0.5 mEq/L/h in chronic hyponatremia, in neither case exceeding 8 mEq/L during the first 24 h (Schaer, 1999). Sodium can be replaced in oral fluids. Some horses with hyponatremia will preferentially drink electrolyte-supplemented water. The water should be isotonic or slightly hypotonic. For concurrent hyponatremia and hypochloremia, 20–30 mL of sodium chloride granules should be added per 4 L of water. For hyponatremia without hypochloremia, 10 mL of sodium bicarbonate solution should be added per 4 L. Fresh water should always be provided in addition to the electrolyte-supplemented water. These sodium-supplemented solutions may also be delivered by nasogastric tube. In foals, sodium chloride and sodium bicarbonate (one teaspoon, up to four times per day) may be administered by oral syringe. Mixing the sodium salt with yoghurt makes a paste, which foals tend to retain better when given by oral syringe.

Hypernatremia is corrected with low-sodium fluids such as 5% dextrose or 2.5% dextrose and 0.45% sodium chloride. Again, in other species, it is recommended that hypernatremia should not be corrected too rapidly: sodium should be lowered by 0.5 mEq/L/h, not to exceed 12 mEq/L in the first 24 h (Schaer, 1999).

Potassium

Treatment of hypokalemia involves potassium replacement, either intravenously or orally. Rapid administration of potassium intravenously can lead to very high circulating potassium concentrations and cardiac arrhythmias. Therefore, potassium should be infused at a maximum rate of 0.5–1 mEq/kg/h. Potassium chloride is the ideal replacement salt, especially in horses that are refluxing and are hypochloremic (Gennari, 1998). High crystalloid flow rates result in increased urine production and kalliuresis, and can make it harder to replace potassium by the intravenous route. Oral supplementation with potassium can, therefore, be more effective in horses and foals in which this route is available. The dose is 0.1–0.2 g/kg, by mouth or nasogastric tube. For foals, this is usually divided into three or four doses given at intervals of at least 4 h. Horses that are also hypomagnesemic may be refractory to potassium replacement therapy, unless the magnesium deficit is simultaneously corrected (Hamill-Ruth & McGory, 1996).

There are several treatment options for hyperkalemia. In the absence of clinical signs, polyionic fluids should be administered. Possible treatments for symptomatic or severe (>7 mEq/L) hyperkalemia include calcium gluconate (1 mL/kg intravenously over 10 min), sodium bicarbonate (1–2 mEq/L intravenously over 15 min) and 50% dextrose solution (2 mL/kg intravenously over 5 min) (Schaer, 1999).

Chloride

Treatment of hypochloremia can usually be achieved with intravenous 0.9% sodium chloride, which contains more chloride relative to sodium than plasma. In horses with high-volume gastric reflux, intravenous administration of histamine 2 receptor antagonists (e.g., cimetidine at 6.6 mg/kg intravenously, four times daily) reduces gastric hydrochloric acid secretion and may, therefore, reduce chloride loss. In humans, hydrochloric acid has been administered intravenously to treat severe hypochloremia (Kwun et al., 1983), but carries substantial risks for the patient (Rothe & Schimek, 1986).

Hyperchloremia should be treated with 5% dextrose if accompanied by hypernatremia and with sodium bicarbonate if severe and accompanied by a low or normal plasma sodium concentration (Schaer, 1999).

Calcium

Hypocalcemia is usually treated with 20, 23, or 40% calcium gluconate or calcium borogluconate solution administered intravenously. Approximately 0.2–1.0 mL/kg of the 20 or 23% solution or 0.1–0.5 mL/kg of the 40% solution will be required (Dart et al., 1992), but the amount will depend on the ongoing losses and the ionized calcium concentration should be checked frequently during therapy. Calcium solutions are irritating to the veins and should be diluted in crystalloid fluids prior to administration. Calcium solutions should not be mixed with sodium bicarbonate or whole blood. The plasma calcium concentration should be checked after 4–8 h after calcium supplementation because ongoing losses and redistribution into cells may result in further hypocalcemia. Hypocalcemia can be a sequel to magnesium deficiency and, therefore, magnesium should be supplemented in horses with refractory hypocalcemia.

Treatment for severe hypercalcemia [ionized calcium concentration exceeding 9 mg/dL (2.25 mmol/L)] should include intravenous fluids lacking calcium (sodium

chloride or Normosol-R) and intravenous administration of magnesium sulfate (see treatment of hypomagnesemia in the following section).

Magnesium

Hypomagnesemia can be treated by intravenous or oral supplementation. Intravenous administration of magnesium sulfate (at 2 mg/kg/min, not to exceed 50 mg/kg) is recommended for the treatment of ventricular arrhythmias associated with hypomagnesemia (Bonagura & Reef, 2004). Higher doses should be avoided because they cause significant muscle weakness; 140 mg/kg of magnesium sulfate administered intravenously can induce recumbency in normal horses (Bowen et al., 1970). For the treatment of hypomagnesemia in the absence of cardiac signs, 8–32 mg/kg of magnesium sulfate can be used as an initial dose in horses with normal renal function. Oral supplementation with magnesium lactate–citrate or magnesium oxide is possible, but oral administration of magnesium sulfate should be avoided owing to its laxative effects.

Treatment of iatrogenic hypermagnesemia in horses has been reported (Henninger & Horst, 1997). The horses were treated with 250 mL of 23% calcium gluconate solution, repeated after 1 h, and polyionic intravenous fluids to promote diuresis.

Phosphate

Treatment of hypophosphatemia has not been reported in the horse, and in humans there is no good evidence for commencing treatment in the absence of clinical signs. Treatment options reported in small animals include intravenous (0.01–0.03 mmol/kg/h phosphate) and oral (0.5–2 mmol/kg/day phosphate) administration of either potassium phosphate or sodium potassium phosphate (Macintire, 1997). This phosphate dose has been used with apparent clinical success by the present author in mature horses. The potential effects of potassium phosphate on the plasma potassium concentration must be considered before commencing treatment. Intravenous administration of glucose 1-phosphate (Bollaert et al., 1995) and sodium phosphate have also been reported in humans. The safety of these treatments has not been evaluated in the horse.

Hyperphosphatemia may not require treatment. It appears that increased plasma phosphate concentrations are not directly toxic (Sutters et al., 1996). The treatment recommended in small animals includes intravenous fluids to correct any acidosis and promote renal phosphorus excretion and dextrose-containing fluids to promote translocation of phosphorus into cells (Macintire, 1997).

Delivery Systems

During the early period of resuscitation of moderately to severely hypovolemic horses, it is important to use both a large-gauge catheter and a wide-bore sterile delivery system to allow rapid delivery of fluids. A 10- or 12-gauge catheter is recommended by the author for severely hypovolemic adult horses and a 12- or 14-gauge catheter for moderately hypovolemic horses. Sixteen-gauge catheters are sufficient for neonatal foals and moderately hypovolemic weanlings and Miniature horses. During total parenteral nutrition (TPN), double-lumen catheters can provide a dedicated line for the TPN and avoid the need to interrupt the TPN when administering incompatible drugs.

To place a catheter, the hair should be clipped over the vein and the area should be prepared aseptically, ideally with a chlorhexidine scrub solution (Mimoz et al., 1996). The catheter should be handled and placed wearing sterile gloves. In young and fractious horses, a bleb of local anesthetic placed subcutaneously at the catheter site makes catheterization easier. The aseptic scrub should be repeated after the local anesthetic has been deposited. A small stab incision through the skin can be helpful when using a local anesthetic or if 10-gauge or Seldinger ("over the wire") catheters are used. For fluid therapy, the catheter should be directed toward the heart. After placement, the catheter should be flushed with heparinized saline (5 U/mL) and fixed in place either with instant bonding glue (for short-term use), staples, or sutures.

In the horse, the easiest vein to catheterize is the external jugular vein. The cephalic and lateral thoracic veins may also be catheterized. These veins carry less serious consequences if they become occluded by thrombophlebitis; however, the maximum fluid rate attainable through these smaller veins (approximately 5 L/h in adult horses) is less than that attainable using the jugular vein. Furthermore, infectious thrombophlebitis may be serious at any site. If one jugular vein is thrombosed or occluded, it is inadvisable to catheterize the contralateral jugular vein and risk bilateral jugular thrombosis, which can result in life-threatening swelling of the head. Both the cephalic and the lateral thoracic vein can be technically difficult to catheterize. Good sedation or restraint is required to catheterize the cephalic vein because horse has a tendency to move during catheter placement. The cephalic and saphenous veins are relatively easily catheterized in neonatal foals. The lateral thoracic vein can be hard to identify and has a flat profile, which can make it difficult to pass a catheter into the lumen. The vein can be identified by ultrasonography and is probably best catheterized using the Seldinger ("over the wire") technique (Seldinger, 1953). In the cephalic, saphenous, and lateral thoracic veins, valves can impede the passing of a catheter stylet or wire.

A variety of fluid administration sets are available commercially. Sets that include large-bore tubing and a coil are suitable for most situations in adult horses and are recommended. Coils can also be helpful in neonatal

foals, but wide-bore tubing is unnecessary. The flow rate can be estimated by counting the number of drops per 10 s in the drip chamber or can be set by using an electronic infusion pump. In all situations, a record should be kept of the time at which the infusion was started and the infusion rate to ensure that the desired volume is being delivered in the appropriate period.

The frequency of replacement of catheters and administration sets depends on the local environmental conditions and the catheter material. Catheters made from polytetrafluoroethylene (Teflon) are associated with an increased incidence of thrombophlebitis and have a tendency to crack and kink (Spurlock et al., 1990). These catheters should not be left in place for longer than 72 h. In contrast, soft catheters made from polyurethane or silicone rubber can often be left in place safely for at least 14 days (Spurlock et al., 1990) or as long as 6 weeks when monitored properly. These catheters should only be replaced when there is a suspected problem. It is unclear how frequently administration sets should be replaced when used in a horse stall. The current US Centers for Disease Control and Prevention recommendations for human hospitals is not to replace administration sets more frequently than every 72 h, except when used to administer blood- or lipid-containing parenteral nutrition, in which case they should be changed every 24 h (O'Grady et al., 2002).

Indwelling cecal catheters have been proposed for fluid therapy in horses to avoid the expense of sterile fluids. Although it is possible to deliver fluid by this technique, the high rate of serious complications precludes the use of cecal catheters (Mealey et al., 1995). Repeated administration of oral fluids can be delivered through an indwelling nasogastric tube. The tube should be plugged with a syringe barrel between administrations to prevent excessive influx of air. Continuous enteral fluid therapy can be provided with a enteral feeding tube[7] connected to a coiled administration set designed for intravenous fluid therapy (Lopes et al., 2002).

Thrombophlebitis

Thrombophlebitis is a common complication of intravenous fluid therapy (Traub-Dargatz & Dargatz, 1994). A thrombus may cause mechanical blockage of venous drainage, resulting in local edema, and may be a nidus for infection. Edematous occlusion of the nasal passages can result from bilateral jugular vein thrombosis and can be fatal. It is therefore inadvisable to catheterize the contralateral jugular vein if one jugular vein shows signs of thrombosis. Bacterial endocarditis, particularly of the tricuspid valve, can occur as a sequel to septic thrombosis.

Thrombophlebitis can be identified by heat, swelling, or the presence of any exudate around the catheter insertion site or a palpable thrombus ("corded" feel) in the catheterized vein. Catheterized veins should be examined at least daily. Ultrasonography of the catheterized vein can help identify thrombus formation. It is prudent to continue to check the vein for 2–3 days after catheter removal because thrombophlebitis may develop or become apparent in this period.

Topical nitroglycerin ointment has been shown to be an effective treatment for thrombophlebitis in humans (Berrazueta et al., 1993). Local application of hot packs and topical application of dimethyl sulfoxide ointment are also used for treatment in the horse. Catheters should be removed aseptically from thrombosed veins and bacterial culture [preferably by the roll-plate technique (Maki et al., 1977)] and *in vitro* susceptibility testing carried out. A fine-needle aspirate of the thrombus can also be submitted for bacterial culture. Fluid-filled pockets within the thrombus can often be identified by ultrasound (Gardner et al., 1991) and should be aspirated after surgical preparation of the overlying skin. Empirical antimicrobial treatment should include an agent with a broad spectrum of activity including streptococci and staphylococci (Gardner et al., 1991) and good tissue penetration, such as doxycycline.

The risk factors for thrombophlebitis include administration of "carboy" fluids (Traub-Dargatz & Dargatz, 1994), the presence of diarrhea (Traub-Dargatz & Dargatz, 1994) or endotoxemia (Morris, 1989), polytetrafluoroethylene (Teflon) catheter material, and a long duration of catheterization (Spurlock et al., 1990). Several other risk factors for thrombophlebitis have been identified in people but not studied in horses. These include inexperienced personnel placing the catheter (Armstrong et al., 1986), administration of total parenteral nutrition (Ioannides-Demos et al., 1995), and large-bore catheters (Swanson & Aldrete, 1969).

Recognition of Hypovolemia and Dehydration

Clinical Signs

The clinical signs of hypovolemia and dehydration in the adult horse are listed in Table 28.2. Hypovolemia is defined as insufficient circulating blood volume, whereas

Table 28.2 Clinical signs of hypovolemia and dehydration in the horse.

Hypovolemia	Dehydration
Tachycardia	Prolonged skin tent
Cold extremities	Tacky mucous membranes
Tachypnea	Sunken eyes
Decreased pulse pressure	
Reduced jugular fill	

7 18 French, 100-inch nasogastric feeding tube; MILA International, Florence, KY, USA.

Table 28.3 Clinical signs associated with different degrees of dehydration in the horse[a].

Degree of dehydration	Skin tent (s)	Mucous membranes	Capillary refill time	Heart rate (pain may also increase heart rate)	Other signs
Moderate	1–3	Moist or slightly tacky	Normal (<2 s)	Normal	Decreased urine output
Marked	3–5	Tacky	Variable Often 2–3 s	40–60 bpm	Decreased arterial blood pressure
Severe	≥5	Dry	Variable Often >4 s	60 bpm or greater	Reduced jugular fill Barely detectable peripheral pulse Sunken eyes

a) Note that not all signs are consistently present in all horses.

dehydration is defined as loss of water from the tissues. It is important to distinguish between these conditions because hypovolemia requires immediate treatment but dehydration is optimally addressed over a period of 12–24 h. However, in most clinical scenarios, hypovolemia and dehydration occur concurrently.

Traditionally, clinical signs have been used to estimate percentage dehydration and formulate a fluid plan for replacement of the fluid deficit. Recent evidence from small animal medicine suggests that this method is unreliable (Hansen & DeFrancesco, 2002). In the horse, at best, clinical signs may offer an approximate guide to the severity of dehydration (Table 28.3). It should be noted that some clinical signs associated with severe dehydration are actually signs of hypovolemia. Horses that are considered to be moderately dehydrated probably require at least 50 mL/kg body weight of crystalloid fluids to replace fluid deficits. In a 500 kg horse, this would represent 25 L. The degree of dehydration is at best an approximation, and should not be relied upon to predict fluid requirements accurately. For this reason, the response to fluid therapy should always be monitored.

None of the clinical signs listed in Table 28.3 should be examined in isolation. It is important to make a judgment on the fluid status based on the whole animal. For example, in horses with colic, tachycardia may be due to hypovolemia or pain. To determine the source of the tachycardia, the accompanying clinical signs and the response to analgesics or fluid loading should be assessed.

In mature horses, tachycardia in hypovolemia is a physiologic response to maintain cardiac output in the face of reduced stroke volume. Unfortunately, this physiologic response appears not to occur in many critically ill neonatal foals (Corley, 2002a). This means that hypovolemia can be more difficult to recognize in foals and that, because of poor compensation, it is associated with far higher morbidity and mortality. Other clinical signs of hypovolemia are also inconsistently present in neonatal foals. The clinical signs of dehydration are similar in the foal to those in the mature horse. However, the skin tent may be shorter, due to increased elasticity of the skin.

Laboratory Tests

Packed-cell Volume and Total Solids Concentration

The laboratory tests used most commonly to assess hypovolemia are the PCV and the plasma total solids. Unfortunately, these tests are neither sensitive nor specific (Hansen & DeFrancesco, 2002). The PCV may be increased substantially by splenic contraction, making small increases very difficult to interpret. A PCV of over 50% usually represents hypovolemia. The plasma total solids (protein measured by refractometer) or total protein concentration (measured by a chemistry analyzer) also increases with hypovolemia. However, significant protein loss can occur in disease (particularly with colitis), resulting in a low or normal protein concentration despite hypovolemia. Further, hypergammaglobulinemia (e.g., in cyathostomosis) can increase the plasma total protein concentration in the absence of hypovolemia. The PCV and plasma total solids are most useful when greatly increased or when used serially to monitor the response to fluid therapy.

Creatinine

Plasma or serum creatinine concentrations are useful in the assessment of renal perfusion in the absence of renal dysfunction. High normal creatinine concentrations (1.5–1.8 mg/dL or 130–160 µmol/L) can be associated with subclinical hypovolemia and should be evaluated in light of the history and clinical signs. Creatinine concentrations up to 3.5 mg/dL (310 µmol/L) are common in moderate to severe hypovolemia and concentrations as high as 5.0 mg/dL (450 µmol/L) are possible with prolonged hypovolemia. In severe hypovolemia, the rate of increase of creatinine concentration is dependent on the amount of creatinine turnover in the muscles and therefore the muscle mass. In bilaterally nephrectomized ponies, creatinine was found to increase by approximately

2.3 mg/dL (200 µmol/L) per day (Tennant et al., 1981). If the creatinine concentration is higher than would be suggested by the clinical signs and other laboratory parameters and if it does not decrease appropriately with fluid therapy, renal dysfunction should be suspected. Measurement of creatinine concentrations is available on some point-of-care monitors (Radcliffe et al., 2015).

Lactate

In the nonexercising horse, increased blood lactate concentrations are sufficient evidence of a metabolic disturbance to initiate fluid therapy. They are an indication of poor tissue perfusion or increased circulating epinephrine (adrenaline) concentrations (James et al., 1999). Hypovolemia and endotoxemia are common causes of increased lactate concentrations in the horse. Endotoxemia increases tissue lactate production both through circulatory changes, which reduce blood flow to the tissues, and by inappropriate anaerobic metabolism (Fink, 1997). Whereas lactate is a good indicator of the need to start fluid therapy, continued high lactate concentrations should be assessed in the context of cardiovascular parameters such as pulse rate, urine output, and blood pressure, because decreases in plasma lactate concentration can lag behind improved cardiovascular status (James et al., 1999). High blood lactate concentrations have been associated with decreased survival and decreased return to athletic performance in equine colic (Furr et al., 1995; Hart et al., 2014) and decreased survival in neonatal foals (Borchers et al., 2012; Castagnetti et al., 2010; Corley et al., 2005). Lactate can be measured in the field using point-of-care analyzers (Radcliffe et al., 2015). An increased circulating lactate concentration should be suspected when there is a metabolic acidosis (decreased pH, negative base excess) in the absence of hyperchloremia or hyponatremia (Corley & Marr, 1998).

Urine Specific Gravity

Urine specific gravity is useful for monitoring the response to fluid therapy, and can be measured easily in the field using a refractometer. A high urine specific gravity (>1.040) indicates possible hypovolemia and normal renal concentration of urine. Isosthenuria (1.010) indicates possible renal damage or a recent high fluid load. Rising or continually high specific gravity in the face of fluid therapy may indicate that insufficient fluid is being delivered to the horse. In the neonatal foal with normal renal function, urine specific gravity may increase early in fluid deprivation, before changes in other indicators such as heart rate, PCV, central venous pressure (CVP), and arterial blood pressure. The normal urine specific gravity in the neonatal foal is 1.000–1.008.

Other Methods

Central Venous Pressure (CVP)

Cardiac filling pressures, and the changes in these pressures in response to fluid therapy, are the most accurate method of determining fluid requirements in the hospitalized animal. It is relatively easy to measure CVP in the horse. In adult horses, sterile polyethylene tubing (PE190, outside diameter 1.70 mm, at least 1.5 m long) can be passed through a 12-gauge jugular catheter into the thoracic vena cava or right atrium. In neonatal foals, the tip of a 20 cm long catheter placed half way down the jugular vein is usually intrathoracic and CVP can be measured directly from the catheter. The tubing or catheter is connected to a pressure transducer or manometer at the level of the sternal manubrium (Hall & Nigam, 1975). The normal CVP of the adult horse is between 5 and 14 mmHg (Hall & Nigam, 1975). In foals less than 14 days old, the normal CVP is 2–9 mmHg (Thomas et al., 1987). In horses with normal cardiac function, a high CVP indicates fluid overloading whereas a low CVP indicates insufficient circulating volume.

The change in CVP in response to a "fluid challenge" (bolus of fluids) (Webb, 1997) is perhaps more accurate than CVP values alone, but this awaits formal evaluation in the horse. The "fluid challenge" method of monitoring fluid therapy may prove particularly useful in animals with acute renal failure or pulmonary edema. In horses without pulmonary edema, a "fluid challenge" without measuring CVP can also be useful in the assessment of the fluid status of the horse. In horses with tachycardia, hypotension, or oliguria, the purpose of the "fluid challenge" is to determine whether additional fluids alone may reverse the abnormality or if another intervention is required. If there is no improvement by 10 min after a 10 mL/kg bolus of crystalloids or a 2–3 mL/kg bolus of colloids, it is unlikely that fluids alone will be successful. The author uses this form of "fluid challenge" routinely in hypotensive individuals prior to starting a dobutamine infusion (Corley, 2002b), as the latter drug may cause significant tachycardia in cases resuscitated with insufficient fluid (Hollenberg et al., 1999).

Treatment Strategies

The General Plan

A fluid therapy plan should be divided into three stages – initial resuscitation, rehydration, and maintenance. The focus of resuscitation is the rapid reversal of hypovolemia, rehydration aims to replace fluid losses, and the maintenance phase aims to prevent the occurrence of further fluid deficits. In severely hypovolemic horses, a transition phase, in which fluid rates are higher than those calculated for rehydration phase, may be necessary after initial resuscitation. The need for this should be assessed based on the clinical and laboratory responses

to the initial resuscitation. Although plasma electrolyte imbalances may influence the choice of fluid during initial resuscitation, their correction usually takes place during the rehydration phase.

The Horse or Foal Presenting in Acute Hypovolemia

The resuscitation phase is critical in horses with acute hypovolemia, as it aims to restore the circulating volume rapidly. However, it is important to note that aggressive resuscitation should not be used in horses with uncontrolled hemorrhage. Although uncommon in horses with acute abdominal disease, acute hypovolemia can be present in animals with an uncontrolled intra-abdominal bleed. These horses frequently, but not always, will have pale mucous membranes.

Aggressive therapy should be used when uncontrolled hemorrhage can be reasonably ruled out. There are two ways to think about the treatment of hypovolemia, both of which result in similar treatment patterns. Hypovolemic horses typically require 20–80 mL/kg of crystalloid fluids acutely.

The "shock dose" concept is borrowed from small-animal medicine. The shock dose for adults and neonatal foals is 50–80 mL/kg body weight of crystalloid fluids. Depending on the perceived degree of hypovolemia, one-quarter to half of the shock dose is given as rapidly as possible (over less than 20 min) and the horse is reassessed. If the horse requires additional fluids, another quarter of the shock dose is given and again the horse is reassessed. The final quarter of the shock dose is given only to severely hypovolemic horses.

The incremental "fluid bolus" concept is borrowed from human medicine. It is actually a much more practical method for resuscitation of neonatal foals. It assumes a similar body weight between all patients and, for this reason, it has not been adopted in small-animal medicine. The fluid bolus method is simply to give a bolus of 10 L of crystalloids to an adult horse or 1 L to a neonatal foal (i.e., approximately 20 mL/kg body weight), and then reassess. The bolus should be given over 15–20 min. Up to three further boluses may be given, reassessing the animal after each. Most hypovolemic animals require at least two boluses. In adult horses where their body weight is different from 500 kg and neonatal foals with a body weight different from 50 kg, the method needs to be adjusted so that the bolus is approximately 20 mL/kg body weight. In pony foals and very premature Thoroughbred foals, boluses of 500 mL are usually appropriate. In large draft foals, the first bolus should be 2 L.

In adult horses, the high end of the intravenous resuscitation rate (10 L over 15 min for a 500 kg horse) may be difficult to achieve. In adult horses with severe hypovolemia, both jugular veins may be catheterized with large-bore catheters (10–12-gauge), allowing approximately 35 L to be administered by gravity per hour, if a wide-bore administration set (e.g., arthroscopy tubing) is used. One of the jugular catheters should be removed immediately after the initial resuscitation phase, to reduce the risk of bilateral jugular vein thrombosis. An infusion pump may also be used to achieve high rates of fluid delivery but the high pressures may cause damage to the intima of the vein and increase the risk of thrombosis. In neonatal foals, a 16-gauge catheter will allow flow rates of up to 58 mL/kg/h for a 50 kg foal and 48 mL/kg/h for a 60 kg foal. In larger foals and for higher flow rates, a larger bore catheter should be used.

Aggressive fluid therapy should be avoided in uncontrolled hemorrhage, because it may increase bleeding. In humans and laboratory animals, aggressive fluid therapy in uncontrolled hemorrhage has been demonstrated to increase mortality (Bickell et al., 1994; Soucy et al., 1999; Burris et al., 1999). This and other evidence suggest that, if blood pressure can be measured, fluid therapy should be titrated to maintain the mean arterial pressure as close to 60 mmHg as possible, without increasing the systolic pressure over 90 mmHg. If blood pressure cannot be measured, then a fluid rate of 2–3 mL/kg/h should be used, until hemorrhage can be stopped.

After acute resuscitation, rehydration is almost always required. The rehydration phase aims to replace extravascular fluid losses. Crystalloid fluids are a logical choice for rehydration, as they readily diffuse into the interstitial fluid from the vasculature (Spalding & Goodwin, 1999; Vaupshas & Levy, 1990). Rehydration should take place over the first 12–24 h of therapy. The amount given should be based on the clinical estimate of the degree of dehydration and the response to fluid therapy.

Typically, horses with obvious clinical signs of dehydration will require 50–100 mL/kg body weight (25–50 L for a 500 kg horse) of fluid to replace their deficits. After treatment of hypovolemia, a fluid plan should be made for the first 24 h that includes fluids for rehydration, maintenance, and ongoing losses. Clinical signs are not an accurate way of estimating fluid requirements (Hansen & DeFrancesco, 2002), so frequent monitoring is required to ensure that adequate volumes of fluids are being delivered. When fluid losses have been adequately replaced, the urine specific gravity should be less than 1.020, except in horses with renal failure. Ensuring adequate fluid therapy in horses with renal failure is difficult, and is probably best achieved by measurement of the response of CVP to fluid therapy as described previously, but this is probably practical only in hospitals.

The Horse with Acute Diarrhea

Horses with acute diarrhea frequently present with marked to moderate hypovolemia. This should be treated as already described. Protein loss is very common in horses with diarrhea; therefore, colloids are often used

early in the course of treatment for colitis. In horses with profound hypovolemia, manifested by tachycardia, very high PCVs (>65%), and purple mucous membranes, the author has found that the combination of a hydroxyethylstarch (tetrastarch; 8–10 mL/kg) and hypertonic saline (2–4 mL/kg) is particularly effective for acute reversal of hypovolemia. It should be noted that hydroxyethylstarches are controversial because of adverse renal effects in human patients (Myburgh et al., 2012), and this has limited their availability in some countries. After reversal of hypovolemia, many horses with acute colitis still have significant dehydration, which must also be addressed as described.

It is extremely important to provide sufficient fluids to cover ongoing losses in horses with diarrhea. As mentioned, fluid loss may be as high as 200 mL/kg/day in horses with diarrhea (100 L/day for a 500 kg horse) (Rose, 1981). Hence a horse with severe diarrhea might require approximately 260 mL/kg/day (approximately 5.5 L/h) of crystalloid fluids to provide basal requirements and replace ongoing losses. Horses with less frequent or less watery diarrhea require less fluid. The rate should be estimated based on the volume and consistency of the diarrhea. The adequacy of the rate should then be reassessed frequently based on both clinical signs and laboratory data. Some horses with less severe diarrhea (infrequent defecation or semisolid consistency) can be effectively treated with free access to water and supplementation via nasogastric tube, as required. Electrolytes, particularly sodium, chloride, and potassium, are frequently deranged in horses with acute diarrhea.

The Horse with Ongoing Reflux

Horses with marked nasogastric reflux are also frequently hypovolemic on first veterinary attention. This hypovolemia should be treated as described earlier. Horses with nasogastric reflux are less likely to be hypoproteinemic than horses with severe colitis. Ongoing losses are also a significant issue in horses with significant nasogastric reflux. In these horses, the amount of reflux should be measured and replaced with intravenous fluids, in addition to the maintenance requirements. Again, responses to fluid therapy should be monitored frequently.

The Horse with a Large Colon Impaction

Horses with large colon impactions can frequently be treated with nasogastric fluids, without the need for intravenous fluids (Hallowell, 2008). The exception is the horse with moderate to marked hypovolemia. Part of the physiologic response to protect the circulating volume is to divert blood flow away from the gastrointestinal tract, thus reducing the capacity of the gastrointestinal tract to absorb water. In experimental models of hypovolemia in the horse, oral fluids were not sufficient to reverse hypovolemia (Ecke et al., 1998). Nasogastric fluids should also be avoided if there is palpable distended small intestine, any reflux on passage of the tube, or >2 L of reflux just prior to any scheduled nasogastric administration of fluids.

The author uses the following protocol for nasogastric fluids in the horse with a large colon impaction. After first attempting to obtain reflux, approximately 1 L of water per 100 kg body weight, containing approximately 1 g/kg of magnesium sulfate, is delivered by nasogastric tube. Additional fluids are given at 30 min intervals, after first refluxing the horse, for a further four administrations. For the second to fifth administrations, 1 L of water per 100 kg body weight, plus sodium chloride granules (7.5 mL/L) and Lite Salt granules (7.5 mL/L), is administered. The schedule of five administrations, every 30 min, can be repeated every 8 h. However, the author gives magnesium sulfate only every 24 h. If there is more than 2 L of reflux, the water is not given, and the horse is again refluxed in 30 min. If there is no reflux at this second check, the schedule of fluid administration is restarted at the point where it was interrupted. If there continues to be reflux, the horse should be thoroughly re-examined, including repeat examination per rectum, and intravenous fluids given in place of further oral therapy. A few horses show mild to moderate signs of abdominal discomfort on administration of these oral fluids. The options for these horses depend on the degree of confidence in the diagnosis. If there is total confidence that the diagnosis is a primary large colon impaction, analgesics may be administered. Alternatively, an indwelling stomach tube can be placed, and oral fluids given at approximately the same rate (2 L/kg/h) by constant-rate infusion (Lopes, 2002).

The choice of water, magnesium sulfate, and electrolytes, and not mineral oil (liquid paraffin), dioctyl sodium succinate, or intravenous fluids, is based on research suggesting that these are the most effective treatments to hydrate colonic contents (Lopes et al., 2002, 2004; Freeman et al., 1992).

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29

Diagnosis and Treatment of Peritonitis and Hemoperitoneum

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The horse's peritoneal cavity can be affected by infectious, inflammatory, neoplastic, and traumatic processes. The responses of the peritoneum to these insults are predictable, resulting in inflammation, edema, and the eventual formation of fibrous adhesions between peritoneal surfaces in an attempt to isolate and contain the pathologic process (Frode et al., 2001). This chapter first reviews the anatomy and pathophysiology of peritoneal disease and then focuses on peritonitis and hemoperitoneum.

Pathophysiology

The peritoneum is a thin, serous membrane that lines the abdominal cavity and part of the pelvic inlet and covers almost all of the abdominal viscera. In the male, the peritoneum is a closed sac, whereas in the female it has two small abdominal orifices through which the fallopian tubes communicate with the uterus. These latter orifices provide an indirect communication with the external environment (Getty, 1975). The glistening peritoneal surface is composed of a layer of mesothelial cells, which share the same embryologic origin as the endothelial cells that line blood vessels. The peritoneal surfaces are constantly moistened by peritoneal fluid, which minimizes friction during movement of the abdominal organs (Getty, 1975). The subserous surface of the peritoneum is attached to the abdominal wall and viscera. The omenta divide the peritoneal cavity into two main regions, one bounded by the greater omentum and the other by the lesser omentum. These two regions communicate via the epiploic foramen (foramen of Winslow).

The peritoneal reflections that form peritoneal ligaments, mesenteries, and omenta, coupled with the natural flow of peritoneal fluid, influence the spread of disease processes within the abdominal cavity (Healy & Reznek, 1998). The flow of peritoneal fluid is directed ventrally by gravity and cranially by the negative intra-abdominal pressure generated in that region of the abdomen by the action of the diaphragm during inspiration. Peritoneal fluid drains through stomata in the muscular portion of the diaphragm and accesses the lymphatic system via specialized openings called lacunae (Maddaus et al., 1988). The relative porosity of the diaphragm may explain the frequent clinical finding of pleural effusion in horses with inflammatory and infectious diseases involving the abdominal cavity.

The peritoneal cavity contains cells that are active in the local defensive response against bacterial invasion and in the removal of blood components when intra-abdominal hemorrhage occurs. Although mononuclear phagocytes predominate in peritoneal fluid, mesothelial cells have important roles in maintaining homeostasis by virtue of their fibrinolytic activity and ability to initiate immune responses (Broche & Tellado, 2001). The fibrinolytic function of these mesothelial cells involves the production of plasminogen activator proteins, which activate plasminogen to produce plasmin, a polypeptide responsible for breakdown of fibrin. Under normal conditions, the mesothelial cells efficiently control the coagulation cascade within the abdominal cavity. However, during intestinal diseases characterized by ischemia, infection, or inflammation, the fibrinolytic system is overwhelmed, thereby favoring the formation of intra-abdominal adhesions.

Mesothelial cells also play a central role in cell-signaling pathways and are a potent source of proinflammatory mediators, including interleukins 6 and 8, monocyte chemoattractant protein 1, macrophage inflammatory protein 1α, and tumor necrosis factor alpha (TNF-α) (Riese et al., 2002). Through the synthesis and release of these cytokines and chemokines, the mesothelial cells have a major influence on the recruitment of phagocytes and neutrophils into the peritoneal cavity. Mesothelial cells express intracellular adhesion molecule 1, vascular cell adhesion molecule 1, and platelet endothelial cell adhesion molecule 1; expression of these adhesion molecules is increased in patients with peritonitis (Sasaki,

The Equine Acute Abdomen, Third Edition. Edited by Anthony T. Blikslager, Nathaniel A. White II, James N. Moore, and Tim S. Mair.

Companion website: www.wiley.com/go/blikslager/abdomen

1999; Johkura et al., 2001). These adhesion molecules allow neutrophils to bind to peritoneal mesothelial cells, thereby facilitating emigration of the neutrophils into the peritoneal cavity. The initial infux of neutrophils is replaced by macrophages within 6–12 h affter the onset of peritonitis (Kuraoka et al., 1992).

Coupled with cellular invasion of the peritoneal cavity, complement activation also is a vital step in local peritoneal defense mechanisms (Liszewski & Atkinson, 2015; Barrington et al., 2001). Although the end result of phagocyte infiltration and complement activation is a hostile environment for invading microbes, it also can cause peritoneal damage. As an example, free radicals generated by activated neutrophils can destroy bacteria, but also may have a toxic effect on peritoneal mesothelial cells (Kinnula et al., 1995; Breborowicz et al., 1993).

In addition to the aforementioned cellular defense mechanisms, the peritoneal cavity responds to injury by gradually isolating the pathologic process through the formation of adhesions and abscesses. The omentum contributes to this localization process by adhering to inflamed tissues via a layer of fibrin. Once the omentum has localized the primary focus of contamination, it absorbs microbes and degenerated macrophages through its stomata, and accommodates neutrophils and macrophages in specialized areas called milky spots. These are perivascular lacunae in which cells of the reticuloendothelial system attempt to reabsorb debris and contaminants (Platell et al., 2000). In horses, adhesions formed in response to chronic low-grade peritonitis commonly become restrictive as they mature, resulting in obstruction of the intestine and the development of signs of colic.

Because omentectomy has been reported to decrease adhesion formation in horses, this procedure is routinely performed by some equine surgeons (Kuebelbeck et al., 1998). This is in contrast to the use of omentectomy in people and dogs. The results of a large retrospective study involving 645 human patients undergoing proctocolectomy and ileoanal anastomosis, omentectomy *increased* the incidence of postoperative sepsis and the need for a second surgery (Ambroze et al., 1991). Furthermore, in both humans and dogs, the omentum has been intentionally sutured over the incision line in an attempt to protect anastomoses and promote healing (Katsikas et al., 1977; Orsher & Rosin, 1993).

In instances in which the degree of peritoneal contamination is low and has been handled by the local inflammatory/immune response, horses may fully recover from the initial injury. If, however, the local responses were inadequate, horses may later experience signs associated with the formation of adhesions or intra-abdominal abscesses despite aggressive medical and surgical treatment (Zicker et al., 1990).

Peritonitis

Peritonitis is defined as inflammation of the peritoneum, the mesothelial cell layer that lines the abdomen and covers the abdominal viscera. Despite advances in surgical and medical treatment of equine abdominal disorders, peritonitis remains associated with a high mortality rate, ranging from 30 to 67% (Hawkins et al., 1993; Mair et al., 1990). The reported mortality rate associated with postoperative peritonitis after abdominal surgery is 56%, whereas it is 43% when abdominal surgery has not been performed (Ducharme & Hackett, 1983; Phillips & Walmsley, 1993).

Causes of peritonitis include septicemia, bacterial translocation during visceral ischemia, mechanical trauma (surgery, external injuries), chemical insults (bile, urine, pancreatic enzymes), parasitism, and miscellaneous factors (neoplasia, drug reactions, decreased immune resistance) (Hawkins, 2003; Lapointe et al., 2003; Mogg & Rutherford, 2006; Mogg et al., 2006). To provide a general framework for treatment, peritonitis can be categorized as primary, secondary, or tertiary. Primary peritonitis is a spontaneous pathologic event lacking an obvious initiating cause and is usually treated with antimicrobial agents and supportive care. In secondary peritonitis, the integrity of the gastrointestinal tract and/or the abdominal wall has been compromised, leading to contamination of an otherwise sterile peritoneal cavity. Secondary peritonitis is treated by removing the source of contamination, which usually requires surgical intervention, supportive care, and administration of antimicrobials. Tertiary peritonitis is a condition in people in which peritonitis either recurs or persists after treatment of secondary peritonitis. These cases are characterized by frequent recurrence and may need multiple surgical interventions and prolonged antimicrobial therapy (Buijk & Bruining, 2002).

The same categorization of peritonitis appears to be well suited to the horse. Primary peritonitis in the horse is usually bacterial in origin, as determined by abdominal paracentesis, and lacks evidence of intestinal or abdominal wall damage. This includes peritonitis associated with bacteremia and *Actinobacillus equuli* infection, but may also include parasitism, uroperitoneum, and hemoperitoneum as additional etiologies (Hawkins et al., 1993; Golland et al., 1994; Lapointe et al., 2003). More commonly, however, peritonitis in horses occurs secondary to a breach in the integrity of the intestine after necrosis or perforation of the bowel. Peritonitis also may be secondary to abdominal surgery as a result of leakage of an anastomosis or dehiscence of an enterotomy site (Mair et al., 1990; Mackey et al., 1987). Tertiary peritonitis in horses may characterize situations in which an exploratory celiotomy is used to treat peritoneal infection.

In these cases, an accurate diagnosis can be difficult to obtain because changes in peritoneal fluid may reflect both the underlying infectious process and the effects of the celiotomy. There is ample evidence in horses that the white blood cell count in the peritoneal fluid may be significantly increased by simple abdominal procedures and intestinal manipulation (Santschi et al., 1988; Schumacher et al., 1988).

The results of retrospective clinical studies indicate that peritonitis in horses is often idiopathic. For example, in an early retrospective study of 30 horses with peritonitis, the cause was not always identified (Dyson, 1983). In two subsequent retrospective studies, 52 and 13.4% of horses with peritonitis were diagnosed as idiopathic (Mair et al., 1990; Hawkins et al., 1993). In the latter study, peritoneal fluid cultures yielded *Escherichia coli*, *Staphylococcus epidermidis*, *Staphylococcus* spp., *Bacillus* spp., and *Streptococcus zooepidemicus* (Hawkins, 2003; Hawkins et al., 1993).

Clinical Presentation

Careful scrutiny of the horse's clinical signs can yield useful information during the diagnostic process. Common presenting clinical signs include abdominal pain, depression, anorexia, diarrhea, and tachycardia; most horses with peritonitis are febrile. The intensity and severity of symptoms depend on the underlying cause of the disease and on the magnitude of the infectious and inflammatory processes. Horses will be more severely affected by peritonitis when the normal host defense mechanisms are compromised or when the bacterial inoculum is large, or accompanied by other noxious agents such as necrotic tissue, hemoglobin, or bowel contents (Bartlett, 1995). In the latter instances, a large shift of fluid from the vasculature to the peritoneal cavity occurs, resulting in 8–10% dehydration and hypovolemic shock. This will compromise the cardiovascular system, leading to hyperemia of the mucous membranes, prolongation of the capillary refill time (>2 s), hemoconcentration [increased packed-cell volume (PCV)], and increased heart and respiratory rates. There are exceptions to this clinical presentation. In fact, in a case series of peritonitis casued by metallic foreign body penetration, fever was not present in all cases and laboratory findings were more consistent with chronic inflammation (i.e., increased PCV and total solid concentrations) (Lohmann et al., 2010). Peritonitis is often associated with endotoxemia, particularly when the abdomen is contaminated with fecal material. Abdominal infection leads to decreased gastrointestinal motility due to alterations in the coordinated propagation of the myogenic myoelectric complex (Frantzides et al., 1993). Generalized ileus will cause a reduction in fecal output and intestinal borborygmi will be decreased on abdominal auscultation.

Diagnostic Approach

A conclusive diagnosis of peritonitis can be made by documenting increases in total nucleated cell count (>5000 cells/μL) and total protein (>2.5 g/dL) in the peritoneal fluid. Abdominal paracentesis is a low-risk procedure and should be performed in all cases in which peritonitis is suspected. Although the techinque is described in Chapter 20, a few considerations deserve attention in horses with peritonitis. All efforts should be made to avoid performing an enterocentesis, which would compromise the diagnostic value of the peritoneal fluid sample. To avoid this potential complication, this author prefers to perform an ultrasound-guided abdominal paracentesis when peritonitis is suspected. Using a curvilinear 3.5 mHz ultrasound probe, the ventral abdomen can be scanned for fluid "pockets" that can be safely accessed without inadvertent penetration of the abdominal viscera. Transabdominal ultrasound is useful in determining the extent of the disease process in horses with peritonitis (Klohnen et al., 1996). In such instances, peritoneal fluid is usually turbid and hyperechoic, and peritoneal fibrin tags and thickened intestinal serosal surfaces may be identified. Both transabdominal and transrectal ultrasound examinations can be useful for verifying the presence of abdominal masses or abscesses.

Once peritoneal fluid is retrieved form the abdomen, it should be submitted for cytology and microbial culture and sensitivity. In peritonitis, the cytologic interpretation is consistent with suppurative inflammation characterized by the presence of degenerate, toxic neutrophils and intra- or extra-cellular bacteria. Retrospective case reviews indicate that Gram staining of peritoneal fluid samples revealed bacteria in only 27–32.5% of cases (Hawkins et al., 1993; Mair et al., 1990; Dyson, 1983). Regardless, peritoneal fluid samples should be cultured for aerobic and anaerobic microorganisms given that determination of antimicrobial sensitivity is critical to the selection of the appropriate antimicrobial agent(s). Commercially available 5 mL blood culture media can be used and have been reported to yield positive culture results more often than traditional culture medium devices (Montgomery et al., 1989).

Peritoneal fluid analysis may not be as valuable when evaluating horses suspected of having peritonitis after abdominal surgery as total nucleated cell count and protein concentration in peritoneal fluid increase markedly after simple abdominal procedures (Hanson et al., 1992; Santschi et al., 1988; Schumacher et al., 1988). Total nucleated cell counts may, therefore, be increased as a direct result of surgery, complicating the interpretation of the composition of a peritoneal fluid sample. Even though the presence of bacteria in peritoneal fluid samples after intestinal resection and anastomosis is a rare finding (Hanson et al., 1992), clinicians should suspect a septic process when bacteria or foreign material are

identified in a peritoneal fluid sample obtained after surgery. In such cases, assessing other peritoneal fluid parameters may be important. Reportedly, peritoneal fluid pH <7.3, glucose concentrations <30 mg/dL and fibrinogen concentrations >200 mg/dL are consistent with a diagnosis of septic peritonitis (Van Hoogmoed et al., 1999). Clinical signs such as anorexia, depression, low-grade persistent fever, and the presence of excess peritoneal fluid on transabdominal ultrasound also should alert the clinician to the possibility of postoperative peritonitis.

Other useful diagnostic tests include abdominal palpation per rectum, complete blood count, and biochemical and electrolyte profiles. On rectal examination, crepitus may be palpated in the dorsal abdomen and along with a "roughening" of the intestinal serosal surfaces covered with fibrin tags. Masses and abscesses often can be palpated near the root of the mesentery and may be confirmed by transrectal ultrasound. In most cases of peritonitis, signs of ileus include either the presence of distended jejunum or impaction of the large colon.

In horses with acute peritonitis, complete blood count results require careful interpretation. Typical findings include leukocytosis (>10,000 cells/μL) and increased fibrinogen concentration (>400 mg/dL). In peracute cases, however, leukopenia (<4000 cells/μL) may be present due to extravasation of neutrophils into the peritoneal cavity. In these peracute cases, plasma concentrations of fibrinogen and total protein may be below normal range values owing to exudation of protein into the abdomen. In contrast, plasma concentrations of fibrinogen will be increased (>500 mg/dL) in horses with chronic intra-abdominal abscessation.

Peritonitis often results in alterations in serum biochemical profiles that are consistent with azotemia. Blood urea nitrogen and serum creatinine concentrations are increased owing to movement of large volumes of fluids into the abdominal cavity, which lead to decreased glomerular filtration rate and prerenal azotemia (Hawkins, 2003). Along with dehydration, horses with peritonitis may have metabolic acidosis and electrolyte imbalances, such as decreased serum concentrations of potassium, sodium, and chloride.

General Medical Treatment

Treatment of septic peritonitis should have two immediate goals: stabilizing the horse and addressing the underlying cause. Dehydration is corrected by administering balanced polyionic fluids intravenously at twice the maintenance rate (2–4 L/h) to address the deficit. The fluid administration rate should then be slowed to the maintenance rate (1–2 L/h) until the horse is able to drink adequately. Oral fluid administration also can be performed, although this should be done with caution in horses in which the septic process has resulted in ileus. Hypertonic (7.2%) saline solution (5 mL/kg) used to correct severe dehydration and restore cardiovascular function is most efficiently used in conjunction with intravenous isotonic fluid administration at twice the maintenance rate (Seahorn & Seahorn, 2003). When necessary, concurrent electrolyte imbalances should be addressed by supplementing the intravenous fluids with potassium (20–40 mEq/L) and calcium gluconate (500 mL of a 23% solution added to 5–10 L of isotonic fluids).

When microbial culture results are available from peritoneal fluid analysis, antimicrobial therapy should be initiated based on the reported sensitivity patterns. Peritonitis in the horse is often characterized by infection with multiple organisms belonging to Enterobacteriaceae, *Streptococcus*, and *Staphylococcus* species (Hawkins et al., 1993; Mair et al., 1990). Other common bacterial species are *Rhodococcus equi* in foals and anaerobic bacteria, most notably *Bacteroides*, *Clostridium*, and *Bacillus*. In most cases, broad-spectrum antimicrobials are selected empirically prior to obtaining culture results and often involve the intravenous adminstration of an aminoglycoside and a β-lactam, which act synergistically against a wide variety of bacterial isolates. Concurrent oral or per rectum administration of metronidazole should be considered to broaden the spectrum of activity and include anaerobic microorganisms. Because the antimicrobial agent must achieve good penetration within a closed cavity such as the peritoneum, lipophilic agents, such as fluoroquinolones (e.g., enrofloxacin), may be a good choice. Furthermore, localized peritonitis originating from an intra-abdominal abscess may not respond well to hydrophilic antimicrobials (e.g., gentamicin) because of poor pentration (Kunesh, 1984; Davis, 2003).

The ease of administration of oral antimicrobials is an advantage because horses with peritonitis often require prolonged treatment. These orally administered antimicrobials include chloramphenicol, trimethoprim-sulfa (trimethoprim–sulfamethoxazole), and rifampin. Chloramphenicol has a broad spectrum of activity and good tissue penetration. It is, however, bacteriostatic and can be dangerous in immunocompromised horses. The half-life of chloramphenicol is 1.5–4 h in horses with normal renal and hepatic function, thus requiring frequent oral administration. Moreover, chloramphenicol may cause inappetence in horses after oral treatment and has been associated with aplastic anemia in people involved in its administration. Trimethoprim-sulfa is commonly used for long-term treatment after intravenous antimicrobials have been discontinued, but has been criticized because of the propensity for the development of bacterial resistance. Rifampin, with erythromycin, is the antimicrobial agent of choice for treating *Rhodococcus equi* infections in foals.

The decision to discontinue antimicrobial therapy is based on the results of serial peritoneal fluid analyses aimed at assessing total nucleated cell counts, which should decrease progressively in response to treatment. Antimicrobials should be continued, however, for several weeks after the attainment of a normal peritoneal fluid analysis.

Together with antimicrobial therapy, it is essential to administer appropriate antiinflammatory drugs, such as flunixin meglumine, to address the effects of peritoneal inflammation and endotoxemia. Additional anti-inflammatory effects can be achieved with the intravenous administration of dimethyl sulfoxide (DMSO), an oxygen free-radical scavenger, commonly used in the treatment of acute gastrointestinal conditions. In horses with signs of endotoxemia, hyperimmune plasma containing antibodies against endotoxin should be considered. In addition, large volumes of plasma may be useful to restore plasma protein concentrations in hypoproteinemic animals. Polymyxin B administration was shown to be an effective inhibitor of endotoxin-induced inflammation in healthy horses and, other than in the face of azotemia, should be considered as a valuable ancillary treatment option for endotoxemia (Parviainen et al., 2001). More in-depth discussions of endotoxemia and available treatment modalities are present in Chapters 16 and 28.

Interventional Treatment

Medical management alone can be successful in the treatment of primary peritonitis and when horses are not severely compromised by the septic process. In other cases, it may be necessary to implement more aggressive measures such as abdominal lavage with or without surgical exploration of the abdomen. Abdominal lavage is performed in conjunction with abdominal drainage in an attempt to clear the peritoneal cavity of excess fluid, bacterial contamination, cellular and organic debris, and blood by-products such as fibrin (Valdez et al., 1979). Controversy exists regarding the necessity of abdominal drainage in primary peritonitis. The argument made against the procedure is that drains may serve as an entry point for further abdominal contamination and lead to ascending infections. Drain placement in the standing horse also may result in inadvertent iatrogenic perforation of the abdominal viscera. Moreover, a study reviewing its application in clinical cases documented a high incidence of minor complications such as obstruction of the drains (26%), leakage of fluid (16%), and subcutaneous fluid accumulation around the drain (12%) (Nieto et al., 2003). Despite these complications, the veterinary literature reports that abdominal drainage and lavage in horses are successful in treating and preventing peritonitis and abdominal adhesions (Nieto et al., 2003; Valdez et al., 1979; Hawkins, 2003). Open peritoneal drainage has been evaluated experimentally in horses and has been used successfully in small animals and human patients (Staatz et al., 2002; Schein et al., 1986; Ryan et al., 1986; Chase et al., 1996). The procedure is not routinely performed in horses because it is associated with incisional infections and requires a second surgery to repair and close the abdominal wall (Chase et al., 1996).

Abdominal drains are placed with the horse standing or at the end of an exploratory celiotomy. In either case, 36–40 Fr thoracic trocar catheters (Tyco Healthcare Group, Mansfield, MA, USA) are placed percutaneously in the most ventral aspect of the abdomen. During surgery, it is important to place the catheter away from the celiotomy incision, to the right of midline and as close as possible to the diaphragm, in order to minimize possible occlusion of the drain by the omentum. In the standing horse, pharmacologic and physical restraint are needed to place abdominal drains safely. After infiltration of the rectus abdominal muscle and fascia with local anesthetic, a stab incision is made through skin, subcutaneous tissue, and external rectus sheath. The trocar and catheter can be bluntly inserted through the internal rectus sheath and peritoneum, avoiding forceful sudden penetration of the abdomen. Alternatively, the trocar can be removed and the catheter tip, held with sterile Mixter thoracic forceps, is gently guided into the abdomen. The best location for the drain can be selected or verified with transabdominal ultrasound. Once the drain is in place, the free end is occluded with a one-way valve system (Heimlich valve) and secured to the abdomen with sutures and an abdominal bandage.

The amount of fluid and the lavage solutions used to infuse into the abdomen are chosen empirically. It is important that the abdomen be lavaged with large amounts of sterile balanced polyionic solutions with a neutral pH. Lactated Ringer's or 0.9% saline solutions are not irritating and do not create an osmotic gradient that may cause significant fluid shifts into the peritoneal cavity (Parviainen et al., 2001). A volume of 20 L can be safely infused through the catheter and allowed to settle in the abdomen in order to cover as much of the serosal surfaces as possible before it is drained out. As the lavage solution distends the peritoneum, horses may experience abdominal discomfort. This can be controlled by infusing fluids gradually and by walking the horse regularly throughout the process. The addition of antiseptics in the lavage solutions is contraindicated because fluids containing povidone iodine solutions cause significant peritoneal inflammation (Schneider et al., 1988).

Solutions containing antibiotics such as potassium penicillin (5×10^6 IU per 10 L) cause only minimal irritation, although the effectiveness of this approach in treating peritonitis has not been critically studied. It is presumed that the addition of antimicrobials to lavage solutions may influence the systemic administration of

antimicrobials due to peritoneal absorption. Therefore, care should be taken when medications with similar toxicities are given parenterally and intra-abdominally. In contrast, a study evaluating the effects of peritoneal lavage, without added antimicrobials, on systemically administered gentamicin in healthy horses found no effect of lavage on the pharmacokinetics of gentamicin, indicating that no dose adjustments are needed during concurrent systemic antimicrobial therapy and abdominal lavage (Easter et al., 1997). Abdominal lavage can be carried out once or twice per day for 3–5 days and discontinued when the solution retrieved from the abdomen appears clear. Samples obtained from the lavage solution can be submitted for cytology and compared with the initial peritoneal fluid sample to evaluate the progress of the disease. However, results should be interpreted with caution as an inflammatory response is likely to occur owing to the presence of the drain and the lavage procedure.

Surgical treatment of peritonitis is always indicated when secondary peritonitis occurs after loss of integrity of the bowel wall, the abdominal wall, or both. Surgical exploration by means of an exploratory celiotomy may also be elected if the source of a primary peritonitis cannot be determined as a result of the diagnostic workup. Surgery is also indicated for the management of abdominal abscesses. The veterinary literature includes reports of three cases managed with marsupialization of the abscess to allow drainage to the exterior (Prades et al., 1989; Rigg et al., 1987).

During an exploratory celiotomy, several goals can be accomplished. The intestinal tract can be examined for puncture wounds, which can be oversewn to prevent continued contamination. Often, however, the exact source of contamination cannot be determined because small perforations may heal on their own after contamination has occurred. In cases in which peritonitis occurs after intestinal surgery, the celiotomy serves the purpose of re-examining the surgical site, which may necessitate reconstruction to prevent further leakage of intestinal contents. Traumatic disruptions of the abdominal wall can be dealt with via celiotomy by debriding and reconstructing the defect.

Abdominal lavage also can be effectively carried out via celiotomy. The most appropriate approach to a contaminated abdomen is via a ventral midline celiotomy, which allows good exposure and exteriorization of 75% of the intestinal tract (Ragle, 1999). Lavage is performed by instilling large volumes (30–40 L) of fluid into the abdominal cavity with the large colon and cecum exteriorized in order to optimize fluid distribution and retrieval. Warm balanced isotonic solutions are poured into the abdomen by an assistant and then removed using active surgical suction devices. The procedure should be continued until the fluid retrieved form the abdomen appears clear.

Laparoscopy deserves to be mentioned in the surgical management of equine peritonitis. Laparoscopy allows clinicians to inspect the abdomen either with the horse standing or under general anesthesia while avoiding the invasiveness of a celiotomy (Trostle, 2000; Fischer, 1991). Laparoscopy may be used to confirm the presence of an abdominal abscess or adhesions and to inspect the site of entry of an abdominal wound. Chapter 61 summarizes the use of laparoscopy in the diagnosis and management of abdominal wall trauma.

Complications and Prognosis

Complications are often associated with septic peritonitis and the prognosis depends on the development of secondary problems associated with the infection. Horses with septic peritonitis are prone to developing laminitis. This condition is best addressed by instituting aggressive preventative measures such as the administration of nonsteroidal anti-inflammatory drugs (NSAIDs), controlling endotoxemia, avoiding dehydration, and providing support to the hooves. Additional pharmacologic measures may be warranted and are discussed in detail in Chapter 49.

Inappetence and generalized ileus occur frequently in horses with septic peritonitis and may require careful dietary management along with gastric decompression via an indwelling tube in horses with gastric reflux. Horses may require parenteral nutrition to sustain their metabolism. Medications such as lidocaine (1.3 mg/kg bolus, followed by 0.05 mg/kg/min continuous-rate infusion) and erythromycin (1–2 mg/kg bolus every 12 h) may assist the restoration of gastrointestinal motility. A detailed description of the use of parenteral nutrition and the management of ileus can be found in Chapter 39.

The prognosis for horses with peritonitis depends on the initiating cause and on the timing of the therapeutic intervention. For example, in several individual case reports and in a review of 52 horses in which peritonitis was caused by *Actinobacillus equuli*, all horses responded rapidly to treatment with procaine penicillin, alone or in combination with gentamicin sulfate, and were discharged from the hospital. Because *Actinobacillus equuli* has been isolated from verminous aneurysms in the equine cranial mesenteric artery, treatment of affected horses with a larvicidal dose of an anthelmintic is warranted (Matthews et al., 2001; Mogg & Rutherford, 2006).

In contrast, there appear to be differences in the short- and long-term prognosis for horses with peritonitis unrelated to abdominal surgery or intestinal rupture. In fact, in a review of 65 affected horses, 86% survived to discharge, and 84% of those horses were alive at least 1 year later. Horses with the lowest survival rates had peritonitis secondary to intra-abdominal masses or urinary tract infections. Of the horses that were

discharged, 34% had complications that likely were related to peritonitis, and 13 of these were euthanized. While the underlying cause of the peritonitis was identified in only 15 cases in this study, those horses had a higher survival rate than the 50 horses for which a cause could not be identified (Henderson et al., 2008).

Treatment of horses with peritonitis should be initiated as early and aggressively as possible to avoid long-term complications such as formation of adhesions and abscesses. Horses with primary peritonitis may respond favorably to antimicrobial treatment alone, particularly if culture and sensitivity results demonstrate good sensitivity to the selected antimicrobial. Peritonitis secondary to intestinal leakage is often fatal unless spillage of fecal material is limited or immediately addressed. Tertiary peritonitis can be difficult to treat because the duration of the infection usually limits the effectiveness of the therapeutic regimen.

Hemoperitoneum

Hemoperitoneum is defined as the presence of blood within the peritoneal cavity and usually results from a traumatic event that led to disruption of visceral blood vessels. This is different from the pathologic process known as hemoabdomen, which includes bleeding within the intestinal tract (hemorrhagic enterocolitis) or other structures (hematomas of the mesentery and the broad ligament). This discussion includes common conditions leading to intra-abdominal hemorrhage, but does not cover abnormalities leading to intraluminal gastrointestinal bleeding.

The symptoms accompanying hemoperitoneum are nonspecific and often mimic those of colic, thereby rendering the diagnostic process challenging. Despite this complexity, it is important to arrive at the appropriate clinical conclusions because the therapeutic approach can be limited to confinement and observation of the horse or may involve celiotomy and blood transfusion. Collecting an accurate history is most helpful in the diagnosis of hemoperitoneum. For example, a recent history of parturition in a broodmare should lead the clinician to suspect a broad ligament hematoma (Ueno et al., 2010). Similarly, a history of blunt trauma may be associated with visceral damage leading to hemorrhage.

Etiopathogenesis

Hemoperitoneum can be caused by abdominal trauma, lesions involving the reproductive tract, loss of integrity of the intestinal vasculature, neoplasia, abdominal surgery, and medical conditions such as disseminated intravascular coagulation and liver disease. In geriatric horses, idiopathic hemoperitoneum is not uncommon. In affected horses, nonspecific clinical signs such as anorexia, depression, and general poor doing may be associated with variable amounts of intra-abdominal bleeding having no apparent cause. Hemorrhage caused by trauma can be associated with a variety of etiologies, and rupture of the spleen should be suspected in horses with abdominal hemorrhage and a recent history of being kicked by another horse. The spleen is susceptible to trauma because it is adjacent to the left abdominal wall and is only in part protected by the rib cage. Moreover, the spleen has a thin capsule that can easily rupture after blunt trauma and, by nature of its function, is engorged with a large reserve of red blood cells (Getty, 1975).

Trauma sustained during delivery of a foal usually underlies abdominal hemorrhage in the mare. Bleeding can originate from the reproductive tract due to disruption of the ovarian or uterine blood vessels or from trauma to the mesenteric vasculature. Uterine artery rupture is not uncommon in the multiparous mare and is thought to occur as the result of weakening and eventual rupture of the arterial wall due to aneurisms. Hemorrhage may be restricted to the portion of the broad ligament containing the uterine artery and may, therefore, be self-limiting; however, in some cases bleeding is profuse and fatal (Hooper et al., 1994; McCarthy et al., 1994). Other reported causes of abdominal bleeding include ovarian and abdominal neoplasia, specifically in association with granulosa theca cell tumors (Gatewood et al., 1990; Green et al., 1988; Roby et al., 1990). Mesenteric and intestinal trauma have also been reported to occur during the effort of delivery, leading to hemoperitoneum in the mare (Dart et al., 1991; Ragle et al., 1997; Zamos et al., 1993; Kobluk & Smith, 1988).

The intestinal tract is often the source of abdominal hemorrhage in horses. Strangulation obstruction of the small intestine and other intestinal segments can traumatize the mesenteric vessels, leading to localized hematoma formation or frank hemorrhage (Speirs et al., 1981; Van Hoogmoed & Snyder, 1996). Intra-abdominal abscesses have also been associated with hemoperitoneum (Rumbaugh et al., 1978). Iatrogenic abdominal bleeding can occur secondary to treatment with heparin in an effort to prevent the formation of adhesions after intestinal surgery (Edens, 1997). In addition, fatal rupture of large abdominal veins, such as the caudal vena cava or the portal vein, can occur during colic surgery following efforts to reduce an epiploic formen entrapment of the small intestine (Vachon & Fischer, 1995).

Pathophysiology

Depending upon the extent of blood loss, hemoperitoneum can occur as either an acute or a chronic clinical problem. Acute hemoperitoneum can result in hypovolemic shock and the clinical signs reflect the balance

between blood loss and physiologic compensation. In response to hemorrhage exceeding 25–30% of blood volume (blood volume equals approximately 8% of body weight in kilograms), several body systems respond to maintain homeostasis and restore normal functions. The hematologic system responds by activating the coagulation cascade and contracting the bleeding vessels through local release of thromboxane A_2. Thromboxane A_2 also is responsible for platelet aggregation, leading to clot formation at the source of bleeding. Damaged blood vessels expose subendothelial collagen, which subsequently causes fibrin deposition and stabilization of the clot (Hofmeyr & Mohlala, 2001).

The cardiovascular system initially reacts by increasing the heart rate, increasing myocardial contractility, and constricting peripheral blood vessels. This response occurs secondary to norepinephrine release and decreased baseline vagal tone, the latter of which is regulated by the baroreceptors located in the carotid sinus aortic arch, left atrium, and pulmonary vessels. The sympathetic response, triggered by hypovolemia, results in splenic contraction, which significantly increases PCV. To appreciate the magnitude of this response, one must simply recall that intravenous administration of phenylephrine causes a dose-dependent splenic contraction, as detected by ultrasonographic measurements of splenic area and thickness (Hardy et al., 1994). The cardiovascular system also responds by redistributing blood to the brain, heart, and kidneys and away from skin, muscle, and gastrointestinal tract (Hofmeyr & Mohlala, 2001). Capillary hydrostatic pressure decreases during hemorrhage, causing interstitial fluid to move into the vascular space. The combination of this latter response and the effects of splenic contraction on circulating red blood cells is a very effective means of preserving intravascular volume in the horse in the first few hours after the onset of hemorrhage (Fielding & Magdesian, 2015).

The renal system also plays an important role in response to hypovolemic shock by increasing the secretion of renin by the juxtaglomerular apparatus in the kidney. Renin promotes the formation of angiotensin I, which subsequently is converted to angiotensin II in the lungs and liver. Angiotensin II causes constriction of arteriolar smooth muscle and stimulates aldosterone secretion by the adrenal cortex. Aldosterone, in turn, is responsible for active sodium reabsorption and subsequent water conservation (Fielding & Magdesian, 2015). In response to the decrease in blood pressure that occurs during hemorrhagic shock, the neuroendocrine system causes a release of antidiuretic hormone (ADH) from the posterior pituitary gland. ADH contributes by promoting reabsorption of water and salt (NaCl) by the distal tubule, the collecting ducts, and the loop of Henle in the kidney (Fielding & Magdesian, 2015; Foreman, 1998).

When the aforementioned compensatory mechanisms result in controlling the source of bleeding, the pathophysiologic changes associated with hemoperitoneum arise from the presence of free blood in the abdomen or the formation of a hematoma. Blood spilled into the abdominal cavity has a tendency to lose clotting ability because platelets rapidly become inactive when they encounter peritoneal mesothelial cells (King, 1996; Zaramella et al., 1994). In contrast, hemorrhage occurring within a mesentery or the broad ligament will be contained in a closed space and have a tendency to clot, forming a hematoma.

In a study characterizing the site of the bleeding in 31 mares that died as the result of hematomas into the broad ligament, most of the injuries involved the uterine artery (24 of 31), with the proximal uterine artery closest to the bifurcation of the iliac artery being affected most often (Ueno et al., 2010). In most mares, the lesions occurred at bifurcations, on the lateral aspect of curvatures, and where the artery had abrupt flexures. In older and multiparous mares, there was atrophy of smooth muscle cells and fibrosis in the affected arterial wall. The authors suggested that it might be possible to monitor changes in the proximal uterine artery by transrectal echography to identify mares at risk (Ueno et al., 2010).

While ciruclating erythrocytes normally have a half-life of about 120 days and then are recycled through the spleen, erythrocytes that are free in the abdomen after acute hemorrhage are actively returned to the circulation for several days (Bojrab et al., 2014). In contrast, erythrocytes that have organized in a hematoma do not undergo lysis and maintain a normal biconcave conformation for 4–8 days in dogs (Flessner, 1999; Bojrab et al., 2014). These findings support the notion that up to two-thirds of extravasated red cells in the abdomen may be recycled back to the circulation. Consequently, free blood in the abdominal cavity should be regarded as a valuable source of red blood cells, protein, and other cellular components.

Over time, the intra-abdominal environment becomes increasingly hypoxic, which damages the erythrocytes and causes their breakdown. As a result of cellular lysis, the hemoglobin, iron, and heme are either absorbed by the peritoneal lymphatic system or digested by peritoneal macrophages (Flessner, 1999). Lymphatic absorption of protein also occurs during hemperitoneum and is an effective means of restoring lost protein to the circulation (Flessner et al., 1985). Collectively, clinical and experimental evidence suggests that drainage of the abdominal cavity after hemorrhage may not be indicated because intraperitoneal blood may serve as a reservoir of blood components which, over time, may return to the circulation.

Clinical Signs

When large amounts of blood accumulate in the abdomen, horses show varying degrees of colic-like

symptoms, which arise from the primary injury (intestinal or urogenital) in combination with the presence of free blood in the abdomen. Hemoperitoneum may also result in dyspnea as the blood that accumulates against the diaphragm limits the animal's inspiratory efforts. Consequently, it can be difficult to distinguish between colic of gastrointestinal origin and colic signs attributable to abdominal hemorrhage. Moreover, horses with hematomas within the mesentery will show signs of profound abdominal pain, most likely caused by traction on the mesenteric root. Because of unrelenting pain, these horses often undergo an exploratory celiotomy.

Blood loss exceeding 25% of blood volume will be associated with increased heart and respiratory rates, pale mucous membranes, prolonged jugular vein filling, increased capillary refill time, weakness, and depression. The PCV is not a reliable indicator of blood loss in acute hemorrhage because the cardiovascular and renal systems effectively restore 20–50% of blood volume in the first few hours (Edens, 1997). In fact, the PCV may be falsely increased owing to splenic contraction for the initial 24 h after the onset of hemorrhage. Thereafter, the PCV will progressively decline. Plasma protein concentration may be a more accurate indicator of blood loss in the first few hours after injury. Persistent anemia with a PCV of 10–12% can be tolerated without transfusion if horses are not stressed and no further decline in erythrocyte mass occurs. In these cases, it is advisable to monitor the horse carefully for onset of clinical signs consistent with hypovolemic shock. After resolution of an acute hemorrhage, the PCV will remain persistently low for up to 40 days, even if the horse is otherwise clinically normal (Radin et al., 1986).

Although some reports highlight abdominal pain (colic) and tachycardia as the most common clinical signs of hemoperitoneum, depression, tachypnea, pale mucous membranes, and prolonged capillary refill time have also been reported (Pusterla et al., 2005; Dechant et al., 2006; Conwell et al., 2010). Less commonly, horses can exhibit abdominal distention, profuse sweating, and ataxia, and may have a palpable mass within the broad ligament on rectal examination (Pusterla et al., 2005).

Diagnosis

The diagnosis of hemoperitoneum can be difficult and often is based upon the animal's history, signalment, and clinical presentation. Specifically, a horse with a history of violent trauma or a multiparous mare in the post-foaling period should be considered at risk of having a hemoperitoneum. The clinical presentation will be consistent with colic and a thorough workup should lead to the identification of free blood within the abdominal cavity. This determination can be made with an ultrasound examination and by obtaining a sample of fluid via abdominal paracentesis. Although the accuracy of abdominal paracentesis in the diagnosis of hemoperitoneum in horses has not been reported, needle aspirate of abdominal fluid is 50–62% accurate in dogs (Pusterla et al., 2005). The diagnosis of hemoperitoneum obtained via diagnostic peritoneal lavage in humans is very accurate, with values approaching 100% (Hoffmann et al., 1988). Inadvertent splenic perforation may occur during abdominal paracentesis in the horse (Tulleners, 1983). To differentiate blood of splenic origin from true abdominal hemorrhage, it may be useful to evaluate the clotting ability of the sample. Blood that has been in contact with peritoneal surfaces for more than 45 min will no longer clot because of platelet inactivation. Clotting of the sample would therefore suggest that it was obtained after perforation of the spleen or a blood vessel (McGorum et al., 1996; Matthews et al., 2002). Cytologic evaluation of a sample obtained from a horse with hemoperitoneum will often reveal erythrophagocytosis and the absence of platelets.

The diagnosis of hematomas of the broad ligament or mesentery may be made via abdominal palpation per rectum. By sweeping the abdomen ventrally and just beyond the pelvic floor, it may be possible to identify a hematoma as a large, swollen mass within the broad ligament. Mesenteric hematomas may also be palpated per rectum depending on their location and need to be differentiated from an abscess or neoplasia (Van Hoogmoed & Snyder, 1996). A follow-up transabdominal ultrasound examination may help localize and differentiate these lesions. A confirmatory diagnosis of mesenteric hematoma is often obtained via a ventral midline celiotomy.

If splenic trauma has occurred, it is important to verify whether the hematoma is located beneath the splenic capsule or is extracapsular, as the location of the hematoma may influence the therapeutic approach and the likelihood of continued bleeding. Subcapsular splenic hematomas are amenable to conservative treatment because they are self-contained, whereas hematomas accompanied by capsular tears are prone to progressive hemorrhage and necessitate splenectomy (Roy et al., 2000). Laparoscopy as been reported to aid in the diagnosis of subcapsular hematoma in a horse (Mehl et al., 1998).

Treatment

The primary therapeutic goal for horses with acute abdominal hemorrhage is to interrupt the bleeding at the source (Sugrue et al., 2004). At the same time, treatment should be aimed at stabilizing the horse with intravenous fluid administration and maximizing oxygen delivery to tissues. The latter can be achieved by delivering high-flow 100% oxygen supplementation to the horse via a tube placed in the ventral meatus of the nasal passage.

An additional important component of treatment is to reduce further stress and excitement as much as possible. Horses should be kept in a quiet environment and away from external stimuli that may cause excitement and enhance further bleeding. If possible, sedative analgesics, particularly α_2-agonists such as xylazine and detomidine, should be avoided as these drugs are associated with cardiovascular side effects that could be deleterious in a horse with active blood loss. Judicious use of acepromazine (0.02 mg/kg) may be the best option in agitated horses, although this drug should not be administered to horses with pale mucous membranes and tachycardia. Medications such as diazepam (0.1 mg/kg) and butorphanol (0.01 mg/kg) may also be beneficial. Importantly, the veterinarian should carefully weigh the risks and benefits of transporting the horse to a referral facility, as prolonged trailer rides are stressful and cause dehydration and fatigue in healthy horses and may be detrimental in horses with reduced circulating blood volumes (Friend, 2000; Stull & Rodiek, 2000).

Horses with hemoperitoneum require surgical intervention only in specific circumstances, such as to address specific conditions such as in splenic or hepatic injury and abdominal wall trauma, or in cases in which the formation of a hematoma may disturb the function of the gastrointestinal system (Kobluk & Smith, 1988; Speirs et al., 1981). In other cases, the likelihood of identifying the source of hemorrhage during a ventral midline celiotomy is low and the risks associated with anesthesia in horses with continued abdominal bleeding may be unacceptably high. For these reasons, horses with hemoperitoneum are most often treated conservatively.

Given the risks associated with surgical intervention, clinicians may choose to administer medications aimed at controlling occult abdominal hemorrhage. Aminocaproic acid (Amicar, Zanodyne Pharmaceutics, Newport, KY, USA) is a lysine analog that competitively blocks binding sites on plasminogen, the precursor of plasmin, which is a mediator of fibrinolysis. By decreasing conversion of plasminogen to plasmin, aminocaproic acid prevents breakdown of fibrinogen and fibrin, thereby promoting clot formation. In horses, aminocaproic acid can be used at a dose of 10–20 mg/kg added to the replacement fluids normally being given intravenously.

The use of formalin to control hemorrhage has been described in the horse since 1943 (Roberts, 1943). Intravenous administration of formaldehyde (either 10 mL of a 37% solution or 30–150 mL of buffered 10% formalin in 1 L of isotonic fluids) has been used to control hemorrhage in horses. Formaldehyde may induce coagulation by activating platelets or affecting endothelial function, thereby promoting primary hemostasis (Pfueller et al., 1978). However, in one study, intravenous infusions of either 0.37 or 0.74% formaldehyde did not enhance primary or secondary hemostasis. At the higher concentration, the infusion resulted in side effects such as muscle fasciculations, tachycardia, nasal and ocular discharge, and restlessness. Based on these responses, the authors concluded that formaldehyde could not be recommended as a treatment to promote hemostasis (Taylor et al., 2005). This is in contrast with anectodal information by veterinary practitioners indicating that formaldehyde administration has been beneficial in horses with uncontrolled hemorrhage.

Medical management of horses with hemoperitoneum begins with by establishing intravenous access preferably with large-bore (12-gauge) catheters placed in one or both jugular veins. Initial fluid resuscitation is achieved using a balanced isotonic crystalloid, such as lactated Ringer's solution. Controversy exists regarding the appropriate volume needed to treat active hemorrhage (Mapstone et al., 2003). If the horse is hemodynamically unstable, it is appropriate to resuscitate with large volumes of fluids. However, there is evidence that large-volume fluid replacement therapy may promote further bleeding by expanding intravascular volume and increasing blood pressure. The situation is similar in human medicine, where uncertainty exists regarding the best fluid administration protocols to use in bleeding trauma patients. These concerns support the need for randomized controlled trials to establish the most effective fluid resuscitation strategy (Kwan et al., 2001, 2003; Roberts et al., 2001).

The volume of fluid needed to maintain tissue perfusion and compensate for losses in horses can exceed the amount of blood lost by 2–5-fold because of redistribution of fluids to the extracellular space. Because the volume of the extracellular space is three times the blood volume, three times as much isotonic fluids have to be administered in order to obtain the desired volume expansion (Rose, 1981). Fluid volume depends on the degree of dehydration and hypovolemia assessed on physical examination. As a first line of treatment, horses may require large doses of fluids (50 mL/kg) administered as a bolus in the first few hours. These volumes can be achieved by using pressure bags or fluid pumps connected to large-bore intravenous catheters. Fluid rates may need continued adjustment based on the horse's cardiovascular response and changes in hematologic parameters such as PCV and plasma protein and electrolyte concentrations. Using the maintenance rate as the baseline (maintenance rate = 60 mL/kg/day in an adult horse), the rate of administration can be subsequently calculated on a 24 h requirement basis, and estimated as a volume per hour. Fluid therapy is discussed in detail in Chapter 28.

Treatment of horses with hemoperitoneum may include the use of synthetic and natural colloids and hypertonic saline solutions. Synthetic colloids (dextrans

and hetastarch) are fluids that contain high molecular weight molecules that exert an oncotic pressure. Proponents of resuscitation using colloids argue that the increased oncotic pressure produced with these substances decreases pulmonary edema. In effect, the colloids remain within the intravascular space, resulting in more efficient plasma volume expansion. In severe hemorrhagic shock, however, the permeability of capillary membranes increases, allowing colloids to enter the interstitial space, causing edema and impairing tissue oxygenation (Moore et al., 2004). Synthetic colloids have low antigenicity and are therefore rarely associated with hypersensitivity reactions. One side effect of colloids is their ability to coat platelets and as a result interfere with coagulation by decreasing platelet aggregation (Omar et al., 1999; Bakaltcheva et al., 2000). Equine plasma, a natural colloid, has several advantages over synthetic colloids because it provides a source of protein, complement, clotting factors, and antithrombin. In contrast to synthetic colloids, however, plasma may be antigenic and initiate allergic reactions.

Hypertonic crystalloid solutions (7.2% NaCl) have a powerful osmotic effect that rapidly draws fluid from the interstitium into the vasculature. This osmotic effect is temporary and proportional to the distribution constant, which depends directly on cardiac output. After the hypertonic solution has been admininstered, the redistribution of electrolytes and fluids across the extracellular space eventually restores the patient's lost plasma volume. For this reason, hypertonic saline solution is administered rapidly at a dose of 5 mL/kg and must then be followed by the administration of isotonic fluids. There is evidence that small-volume hypertonic saline treatment is as effective as administration of a large volume of crystalloids to expand the plasma volume and enhance cardiac output in hemorrhagic shock in animals (Moore, 1991). The controversy regarding its use in hemorrhagic shock arises from findings that hypertonic saline selectively increases arteriolar vasodilation, which improves capillary perfusion, but which, in turn, could lead to increased bleeding (Moore, 1991). Futhermore, clinical studies in human patients indicate that administration of hypertonic saline may be equivalent to standard isotonic crystalloid fluid administration in hypovolemic shock (Wade et al., 1997). However, there is evidence that administration of hypertonic saline markedly decreases the inflammatory response (specifically neutrophil cytotoxicity) in animal models of hemorrhagic shock, ischemia and reperfusion, and sepsis (Ciesla et al., 2000; Rotstein, 2000).

Treatment of horses with hemoperitoneum having a PCV of less than 12%, after acute blood loss, should include a whole-blood transfusion to stabilize the animal and restore intravascular volume. The most accurate parameters to use to determine when a blood transfusion is needed are obtained from assessing the overall condition of the horse. Important factors that affect the decision to administer a blood transfusion include the relatively short half-life of transfused erythrocytes and the high variability in equine blood type. Transfused allogenic erythrocytes survive approximately 4 days and are removed, after the development of surface antibodies, by circulating mononuclear phagocytes (Kallfelz et al., 1978). Because of this antigenic effect, a hypersensitivity response may be triggered if a blood transfusion is repeated after 3–4 days (Wong et al., 1986).

Prognosis and Expected Outcomes

Several recent retrospective reviews highlight the variety of clincal presentations and outcomes that can be expected in horses with a hemoperitoneum. As an example, a recent extensive review documented the rarity of hemoperitoneum after emergency colic surgery, as only 23 of 4520 horses (0.5%) developed this complication (Gray et al., 2015). Intestinal resection and anastomosis was the leading factor associated with hemoperitoneum, which was characterized the day after surgery by tachycardia, decreasing hematocrit, incisional drainage, or ultrasonographic identification of swirling, echogenic abdominal fluid. Hemoperitoneum was confirmed in 14 of the horses by examining peritoneal fluid, but the authors suggested that abdominocentesis has the potential risk of iatrogenically contaminating the intra-abdominal blood, and so preferred to use abdominal ultrasonography. Primary treatments included intravenous fluid therapy and colloids, with blood transfusion and antifibrinolytic agents being used less often. Fifteen of the 23 affected horses (65%) survived to discharge from the clinic and there was an association between survival and lactate concentration on admission and days of hospitalization (Gray et al., 2015).

Multiple studies confirm that common casuses of hemoperitoneum include splenic hematoma (Pusterla et al., 2005), trauma, neoplasia, uterine artery rupture, and injury to the mesenteric vasculature (Dechant et al., 2006; Conwell et al., 2010). In these studies, the diagnosis was made on the basis of abdominocentesis and transabdominal ultrasonography, the combination of which was very reliable in one study, allowing the diagnosis to be made in 95% of the cases. The same study confirmed that PCV at presentation was often either normal or slightly low, indicating its limited usefulness as a guide to the volume of blood loss in acute hemorrhage (Conwell et al., 2010).

In one study, 14 of 19 horses (74%) with hemoperitoneum survived and were discharged 3–15 days (median 7.0 days) after admission. Postmortem examination of the nonsurvivors revealed massive abdominal hemorrhage from splenic hematoma with capsular tear (two

horses), multicentric hemangiosarcoma with liver rupture (one horse), systemic amyloidosis with splenic hematoma and capsular tear (one horse), or bilateral ruptured ovarian hematomas (one horse). In one horse, no origin of the bleeding could be determined during postmortem examination (Pusterla et al., 2005).

In contrast, short-term survival rate was only 51% in a study of 67 horses with hemoperitoneum, with most of the nonsurvivors being euthanized within 24 h of presentation owing to the degree of hemodynamic compromise. In this study, a high respiratory rate was negatively associated with survival, and more so than heart rate, hematocrit, or rectal temperature. The authors suggested that respiratory rate may be a better indicator of cardiopulmonary status than heart rate, which reflects cardiovascular status. Respiratory rate is influenced by hypoxemia and acid–base status, and respiratory patterns may be altered by increased intra-abdominal pressure that occurs with hemoperitoneum (Dechant et al., 2006).

In a retrospective study of periparturient hemorrhage, it was determined that hemorrhage occurs in mares of any age (median age 14 years) or parity (91% were multiparous). Furthermore, the prognosis with medical treatment was good, with 84% mares surviving, and half of those for which follow-up information was available subsequently producing a foal. The mares in this study were all examined at a single referral practice, and were located within 30 miles of the clinic, which may have positively influenced the high survival rate. Also, mares with severe hemorrhage that died were not considered during this study, which also may have influenced survival rate (Arnold et al., 2008).

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Diagnosis of Enteritis and Colitis in the Horse

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Diagnosis

The definitive determination of the etiologies underlying enteritis and colitis can be challenging. For some syndromes, such as duodenitis-proximal jejunitis, no definitive etiologic agent has been identified, requiring that diagnosis be based on clinical signs and nonspecific clinicopathologic abnormalities. Additional diagnostic uncertainty regarding enteritis and colitis is due to the low sensitivity of some of the diagnostic tests available, such as fecal culture for *Salmonella* spp. In those instances in which a definitive diagnosis can be made, the results may not be available for several days, requiring that the initial decisions regarding treatment be made on an empirical basis. Despite these shortcomings, definitive diagnostic information can be of great utility in some cases in allowing more appropriate therapeutic intervention and accurate prognostication. Ultimately, obtaining a definitive diagnosis is of most importance when dealing with potentially infectious agents, in order to minimize the risk of dissemination of the disease throughout a farm or hospital population.

Specific Syndromes

Duodenitis-proximal Jejunitis (Anterior Enteritis, Proximal Enteritis) (DPJ)

Although bacterial organisms, such as *Clostridium difficile*, *Salmonella* spp., and *Clostridium perfringens*, have been identified in both the enterogastric reflux and intestinal contents obtained from some horses with DPJ, a definitive causal relationship has not been established (Murray, 2002; Freeman, 2000; Arroyo et al., 2006). The potential involvement of infectious organisms is plausible in this syndrome, given the profound acute inflammatory response observed in the small intestine in the absence of other identifiable insults and the presence of profound hypersecretion (Murray, 2002). The lack of a definitive cause, combined with the similarities in clinical presentation between DPJ and small intestinal obstruction, makes definitive diagnosis of this condition difficult and can present challenges in determining whether affected horses may have a condition that requires exploratory abdominal surgery.

The most consistent clinical findings associated with DPJ include a history of mild colic followed by profound depression, large-volume enterogastric reflux (as much as 15–20 L every 2 h), mild to moderate small intestinal distention on abdominal ultrasonography and/or rectal examination, low-grade fever (101.5–102.5 °F/38.6–39.2 °C), clinical dehydration, tachycardia (60–80 bpm), decreased borborygmi, and injected mucous membranes (Murray, 2002; Johnston & Morris, 1987; Freeman, 2000). The clinical findings associated with small intestinal obstruction may include moderate to severe colic typically persistent, minimal to moderate volume enterogastric reflux, moderate to severe small intestinal distention on abdominal ultrasonography and/or rectal examination, normal rectal temperature, moderate to severe clinical dehydration, tachycardia (may exceed 100 bpm), decreased borborygmi, and injected mucous membranes (Johnston & Morris, 1987). Differentiation between DPJ and small intestinal obstruction is important because of the risks associated with delaying surgery in horses with obstruction. Whereas distended small intestine is commonly detected in both syndromes, the degree of distention is typically more severe with obstructive disease; rectal palpation reveals multiple tightly distended, poorly compressible ("hosepipe") loops of small intestine, compared with more compressible loops of small intestine in horses with DPJ (Johnston & Morris, 1987; White et al., 1987). The results of rectal examination cannot, however, be used to differentiate the two disease processes definitively. Similarly, abdominal ultrasonography often reveals greater distention with obstructive disease (small intestinal diameters typically of 6 cm

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or greater) than with DPJ (typically 4–6 cm small intestinal diameter), but these differences are not definitive. Thickening of the small intestinal wall is not consistently observed in horses with DPJ, and some observable motility may still be present. However, the presence of small intestinal distention in combination with thickening of the small intestinal wall and a lack of small intestinal motility on abdominal ultrasonography is strongly correlated with the presence of small intestinal strangulation obstruction (Klohnen et al., 1996).

Fever has been reported in many horses with DPJ, but is not always present (Johnston & Morris, 1987). The tachycardia that occurs in DPJ is typically less pronounced than that associated with strangulating obstruction (Johnston & Morris, 1987). Peritoneal fluid analysis is not useful in differentiating obstruction from proximal enteritis, as both syndromes can be associated with serosanguineous discoloration of the abdominal fluid, and also increases in the protein concentration and white blood cell count. It has been reported that horses with DPJ typically have lower total nucleated cell counts and total protein concentrations in peritoneal fluid than do horses with strangulating obstruction, although the total protein concentration usually exceeds the normal range (Johnston & Morris, 1987; White et al., 1987). Peripheral leukocytosis has also been reported in horses with DPJ (White et al., 1987).

Ultimately, the most useful clinical parameter in differentiating small intestinal obstruction from DPJ is the persistence of substantial abdominal discomfort after gastric decompression via nasogastric intubation, as most horses with DPJ cease to have pain after gastric decompression and exhibit profound depression (White et al., 1987). The persistence of substantial discomfort is strongly suggestive of obstruction, and constitutes grounds for exploratory abdominal surgery, especially if other clinical parameters are also suggestive of obstructive disease. Surgical exploration is an important diagnostic tool, and ultimately represents the only definitive means of differentiating DPJ from small intestinal obstruction in the horse with persistent reflux and abdominal pain (Underwood et al., 2008). The literature is somewhat conflicting about the outcome of horses with DPJ that undergo surgery, as some studies have reported decreased survival for horses treated surgically compared with horses treated medically (Johnston & Morris, 1987; Underwood et al., 2008) whereas others have reported no substantial difference in outcome (Seahorn et al., 1992; Freeman, 2000). As horses affected with DPJ that ultimately require surgical exploration are typically those with prolonged reflux and/or persistent abdominal pain, it is perhaps not surprising that these horses may have poorer survival rates than less severely affected animals that respond to medical treatment. Although it has been purported that surgical decompression of the small intestine may be beneficial in shortening the time to resolution of enterogastric reflux, the results of one recent indicate that surgical intervention did not lessen either the duration or volume of reflux (Underwood et al., 2008).

Salmonellosis

Salmonella spp. organisms are reported to be the most frequently diagnosed etiologic agent in equine infectious diarrhea (Murray, 1996). Thousands of serotypes of *Salmonella* have been identified; however, the majority of equine cases of salmonellosis are associated with one of only a few serotypes, including *Salmonella enterica* subspecies *enterica* serovar *typhimurium*, serovar *enteritidis*, serovar *krefeld*, serovar *saint-paul*, serovar *anatum*, serovar *newport*, serovar *infantis*, and serovar *oranienburg* (Tillotson et al., 1997; Schott et al., 2001; Weese et al., 2001a; Van Duijkeren et al., 1994, 2002; Pare et al., 1996; Hartmann et al., 1996; Walker et al., 1991; Traub-Dargatz et al., 1990; Ikeda et al., 1986; Carter et al., 1986; Donahue, 1986; Benson et al., 1985; Hird et al., 1984; Ernst et al., 2004; Ward et al., 2005b; Dallap Schaer et al., 2010; Cummings et al., 2014; Jay-Russell et al., 2014). The most commonly implicated of these is *Salmonella enterica* subspecies *enterica* serovar *typhimurium*. Diagnostic testing for *Salmonella* organisms relies primarily on fecal culture, using selective enrichment media (selenite broth, tetrathionate broth, or Rappaport–Vassiliadis enrichment broth) to enhance the detection of *Salmonella* spp. by increasing the number of organisms, and selective isolation media (brilliant green agar, MacConkey agar, or xylose lysine deoxycholate agar) to decrease the interference of other enteric organisms in the isolation process. Suspected isolates should be cultured on lysine iron agar and triple sugar iron agar to aid in the differentiation of *Salmonella* colonies from those of other enteric bacteria. Once isolated in culture, *Salmonella* organisms should be further identified by means of standard biochemical techniques or using a biochemical identification kit (e.g., API 20E, bioMerieux, Hazelwood, MO, USA). Typically confirmed isolates are then further characterized by means of antimicrobial sensitivity testing, serotyping, and phage typing (Schott et al., 2001; Van Duijkeren et al., 2002).

When performing fecal culture, a minimum of 10 g of fecal material should be submitted (Larsen, 1997). *Salmonella* organisms are more consistently shed in formed stool than in diarrheic stool, increasing the likelihood that the organism will be isolated as the animal recovers from clinical disease. The time required to isolate and identify *Salmonella* organisms from fecal samples using culture represents one of the primary limitations of this approach, as it may require 3–4 days to obtain a definitive result on any single fecal culture. In addition, fecal culture has a low sensitivity for the

detection of *Salmonella* shedders in the equine population, although the use of multiple cultures (typically five), combined with utilization of selective media, allows for adequate sensitivity levels to be achieved (Van Duijkeren et al., 1995). Culture of rectal mucosa with fecal material substantially increases the sensitivity of culture techniques (Palmer et al., 1985). Fecal culture remains the gold standard for clinical monitoring of equine patients, despite its limitations and the development of more sensitive techniques, such as polymerase chain reaction (PCR).

PCR tests are available for the detection of *Salmonella* spp. DNA in feces. These offer a more rapid turnaround time and higher sensitivity than culture techniques, but do not allow further identification of the organisms or antibacterial susceptibility testing (Cohen et al., 1996). The PCR techniques developed for the detection of *Salmonella* DNA in equine feces have been demonstrated to be both highly sensitive and specific (Cohen et al., 1994, 1995b, 1996; Stone et al., 1994; Ewart et al., 2001; Amavisit et al., 2001; Kurowski et al., 2002; Gentry-Weeks et al., 2002; Alinovi et al., 2003; Ward et al., 2005a; Pusterla et al., 2010; Ekiri et al., 2016). The high sensitivity of these PCR techniques results from the qualitative, rather than quantitative, characteristics of many of these assays and their ability to detect even a single DNA fragment containing the targeted DNA sequence. As a result, PCR testing may result in much higher numbers of positive results than obtained with culture techniques. For example, in one study, 40% of clinical fecal samples were positive on PCR testing compared with 2% with culture (Amavisit et al., 2001). An even more dramatic example of this phenomenon was observed in a study that revealed that 17% of horses presented to the outpatient service of a veterinary teaching hospital were positive for *Salmonella* DNA on fecal PCR testing, yet none of these animals was culture positive; 65% of hospitalized horses were PCR positive, whereas only 10% were culture positive (Cohen et al., 1996). Another study found an even greater disparity between PCR and culture techniques when analyzing environmental samples, with 0.001% (1/783) of the samples being positive on culture and 14% (110/783) on PCR testing (Ewart et al., 2001). The wide disparity between the results of culture and PCR techniques likely reflects the ability of the PCR techniques to detect DNA from nonviable (dead or inactivated) organisms. This possibility was supported by a report that the use of enrichment culture techniques did not increase the detection of *Salmonella* from clinical fecal samples (Amavisit et al., 2001). On the basis of these results, it is apparent that PCR techniques may be overly sensitive for routine clinical application unless a quantitative approach is used (Ekiri et al., 2016; Burgess & Morley, 2014; McKenzie & Hodgson, 2011; Pusterla et al., 2010).

Further characterization of *Salmonella* organisms cultured from clinical cases is important epidemiologically, for both the equine population and the human population potentially exposed to these organisms. For this reason, it is important that fecal culture testing be performed in addition to PCR screening. Culture also allows for antibiogram determination, which provides insight into the strain and where it may have been acquired. Additional insight can be achieved by means of serotyping and phage typing, although these tests are not routinely performed in most clinical laboratories. Phage typing has revealed the emergence of *Salmonella enterica* subspecies *enterica* serovar *typhimurium* definitive type (DT) 104 as an increasingly common animal pathogen (Weese et al., 2001a; Van Duijkeren et al., 2002). Equine salmonellosis due to DT104 represents a serious concern, as the organism exhibits antimicrobial multiresistance and presents an increased risk of zoonosis (Weese et al., 2001a; Vo et al., 2007; Niwa et al., 2009). It has been recommended that the phage type distribution of *Salmonella* isolates should be monitored to ascertain if DT104 remains a common equine pathogen (Weese et al., 2001a; Van Duijkeren et al., 2002).

Clostridial Enterocolitis

The two primary agents of clostridial enteritis in the horse are *Clostridium difficile* and *Clostridium perfringens*. Although the detection of these organisms by means of fecal culture and their characterization with cytotoxicity assays have historically represented the gold standard for the diagnosis of clostridial enterocolitis, culture has been supplanted to some extent in the clinical setting by analysis for fecal toxin. The first reason for this transition is that culture of these clostridial organisms is challenging because of their anaerobic nature and the presence of competing species, and it can only be performed in properly equipped diagnostic laboratories (Weese et al., 2000; Marler et al., 1992). More importantly, the presence of these organisms in the feces of animals with diarrhea is not definitively diagnostic, as these organisms can also be present in low numbers in the gastrointestinal flora of healthy horses and foals. For this reason, quantitative culture is required to determine whether the number of organisms present exceeds that observed in healthy animals (Donaldson & Palmer, 1999).

The presence of certain clostridial toxins in the feces is more diagnostic than the presence of the organisms on fecal culture, because of the association between these toxins and the pathogenicity of the clostridial organisms (Weese et al., 2000). For this reason, fecal toxinalysis is considered to be of greater clinical utility than fecal culture in the detection of clostridial enterocolitis. The specific toxins of interest include *C. difficile* toxins A and B and *C. perfringens* enterotoxin, α-toxin, β-toxin, and θ-toxin (Laohachai et al., 2003). Enzyme-linked

immunosorbent assay (ELISA) tests for several of these toxins (*C. difficile* toxins A and B and *C. perfringens* enterotoxin) are commercially available (TechLab, Blacksburg, VA, USA). Although less sensitive than traditional tissue culture techniques, the ELISA toxin assays have proven to be useful in the detection of equine clostridial enterocolitis (Donaldson & Palmer, 1999; Weese et al., 2001b). The ELISA toxin assays require only 1.5–2 h to run and are easily performed in most clinical laboratories.

Additional techniques that have been utilized in the diagnosis of clostridial enterocolitis include fecal cytology, latex agglutination for *C. perfringens* enterotoxin, and PCR for *C. perfringens* toxin genotyping. Fecal cytology may be useful if large numbers of organisms are present, but lacks sensitivity and is not specific for the type of clostridial organism present (East et al., 1998). Latex agglutination testing has been demonstrated to be poorly specific for *C. perfringens* enterotoxin in foals with diarrhea (Netherwood et al., 1998a). Molecular techniques have been developed for the detection of clostridial DNA encoding for the clostridial toxins, including quantitative techniques (Netherwood et al., 1998a, 1998b; Herholz et al., 1999; Avbersek et al., 2011). Because healthy animals may carry low numbers of toxigenic and nontoxigenic *C. difficile* and/or *perfringens* organisms, the mere identification of their presence is inadequate evidence for a clinically significant infection. However, quantitative PCR techniques targeting their toxins are readily available and clinically very useful (Rodriguez et al., 2014; Magdesian & Leutenegger, 2011; Avbersek et al., 2011).

Antimicrobial-associated Diarrhea

The diagnosis of antimicrobial-associated diarrhea is typically presumptive and is based upon the demonstration of a temporal relationship between antimicrobial administration and the development of diarrhea in a horse or foal that did not previously have diarrhea (Barr et al., 2013; McGorum & Pirie, 2009). Unfortunately, this diagnosis is rarely definitive, owing to a variety of potential confounding factors that could lead to the development of diarrhea, such as transportation stress, hospitalization, changes in food intake and diet, surgery, and other medical interventions (McGorum & Pirie, 2009). Another confounding factor is the substantial overlap between antimicrobial-associated diarrhea and a number of causes of infectious diarrhea, such as *Salmonella* spp., *C. difficile*, and/or *C. perfringens*. Often when one or more of these organisms is confirmed to play a role in a given case, the diagnosis may shift from antimicrobial-associated diarrhea to a more specific one related to that agent, even though the initial inciting cause may have been antimicrobial administration. The reported prevalence of antimicrobial-associated diarrhea varies between studies, geographical regions, and antimicrobial classes, with reported ranges from 0.6 to 52% (Barr et al., 2013; Cohen & Woods, 1999; Herholz et al., 1999; McGorum & Pirie, 2009).

Equine Neorickettsiosis

Diagnosis of equine neorickettsiosis (Potomac horse fever) has depended primarily on the presence of typical clinical signs (fever, diarrhea) in combination with seasonal (summer) and geographic information (occurrence in an endemic area). Definitive diagnosis of equine monocytic ehrlichiosis requires the detection of *Neorickettsia risticii* in the blood or feces of affected individuals by means of culture, but this is not a practical diagnostic tool (Madigan & Pusterla, 2000; Mott et al., 1997). A diagnosis of equine monocytic ehrlichiosis was historically made after detection of antibodies to *N. risticii*, using a serum indirect fluorescent antibody test or ELISA test (Dutta et al., 1987; Pretzman et al., 1987; Shankarappa et al., 1989; Ristic et al., 1986). Although the ELISA tests were more sensitive than the indirect fluorescent antibody test, they are not readily available, and the latter test was more widely used. Because the latent period after infection can be as long as 14 days, seroconversion may occur prior to the development of clinical disease, limiting the diagnostic usefulness of serologic testing (Palmer et al., 1989). Although high titers (>2560) are typically associated with clinical disease, prior vaccination and the presence of high serum titers in clinically healthy animals can result in false-positive results, substantially decreasing the usefulness of a single serum titer (Madigan et al., 1995; Gibson et al., 2011). For these reasons, it has been recommended that acute and convalescent titers be determined, with either rising or falling serum titers being suggestive of infection.

PCR techniques have been developed for the identification of *N. risticii* DNA in peripheral blood or feces. Because these techniques are highly sensitive and specific, they have become the current standard for diagnosis (Biswas et al., 1991, 1994; Chaichanasiriwithaya et al., 1994; Wen et al., 1995; Mott et al., 1997; Pusterla et al., 2000). The nested PCR and real-time TaqMan PCR techniques do not appear to suffer from the excessive sensitivity that is a concern with some of the PCR tests used for other diseases, such as salmonellosis. The results with the nested PCR were well correlated with the results of standard culture techniques, and the nested PCR and TaqMan techniques were highly correlated with one another (Mott et al., 1997; Pusterla et al., 2000). PCR testing using blood and/or fecal samples is commercially available and widely used in the diagnosis of equine neorickettsiosis (Pusterla et al., 2006).

Viral Enterocolitis

The most common syndrome of viral diarrhea in equids is rotaviral diarrhea in foals. Rotavirus is detected in the

feces of foals with diarrhea in 20–77% of cases (Frederick et al., 2009; Bailey et al., 2013; Slovis et al., 2014). Equine coronavirus has been associated with clinical disease in adult horses (Fielding et al., 2015) and has been detected in the feces of diarrheic foals, but the role of this virus in foal disease is unclear at present (Traub-Dargatz et al., 1988; Guy et al., 2000; Navas de Solis & Foreman, 2010; Slovis et al., 2014). Equine adenovirus-2 has also been detected in the feces of foals with diarrhea, but the involvement of adenovirus in the development of disease is unclear, especially in immunocompetent individuals (Corrier et al., 1982; Mair et al., 1990; Browning et al., 1991). There are older reports of parvovirus-like particles identified in foals with diarrhea, but no further evidence has emerged regarding the potential pathogenic role of such organisms in foals (Baker & Ames, 1987; Biermann et al., 1989).

Rotavirus

Rotaviral diarrhea is a common syndrome in foals from 2 to 6 months of age (Cohen & Chaffin, 1995; Dwyer, 1991). The diagnosis of rotaviral diarrhea is by detection of viral particles using electron microscopy, virus isolation, ELISA, immunochromatography tests, and real-time reverse-transcriptase PCR (RT-PCR). Serology is of limited use in the diagnosis of rotaviral diarrhea, as foals commonly have detectable levels of rotaviral-specific antibodies derived from colostrum. Consequently, this test is not utilized clinically (Conner & Darlington, 1980). Electron microscopy has been the gold standard for the detection of rotaviral particles in fecal material, but it is not readily available and is of rather low sensitivity because large numbers of viral particles must be present to be identified on electron microscopy. This technique may also lack specificity, as other viral particles may appear similar to rotavirus on electron microscopy. The demonstration of viral particles is not definitive for causation, however, as healthy foals can shed the organism, especially if they have been exposed to diarrheic foals shedding large numbers of viral particles (Netherwood et al., 1996). The presence of the virus in association with clinical diarrhea in foals is, however, considered to be strong evidence of causation (Netherwood et al., 1996; Browning et al., 1991). The presence of rotaviral particles is readily ascertained with enzymatic immunoassays that detect the presence of rotaviral specific antigens (the group A VP6 antigen) in fecal samples (Rotazyme, Rotaclone). The Rotazyme test (Abbott Diagnostics, Abbott Park, IL, USA) is at least as sensitive and specific as electron microscopy in the detection of rotaviral particles (Conner et al., 1983; Ellis & Daniels, 1988). Other modalities for the detection of rotavirus include immunochromatography tests and RT-PCR, which are rapid and simple to perform and provide high sensitivity and specificity (Bailey et al., 2013; Miño et al., 2015).

Coronavirus

Although outbreaks of enteric disease associated with equine coronavirus infections appear to be uncommon, this may be due to the relatively recent appreciation of this organism's role in equine infectious disease. The clinical signs most commonly associated with this disease include fever, lethargy, and inappetance, and other less common signs may include diarrhea and/or colic in addition to neurologic signs (Fielding et al., 2015; Pusterla et al., 2013; Oue et al., 2013). The diagnosis of equine coronavirus infection has been based upon electron microscopy, immunohistochemistry, fluorescent antibody testing, virus isolation, serologic evidence, and PCR methodologies, with the last currently being most commonly used (Nemoto et al., 2015; Giannitti et al., 2015; Slovis et al., 2014; Pusterla et al., 2013; Oue et al., 2011, 2013; Guy et al., 2000; Davis et al., 2000; Durham et al., 1979).

Larval Cyathostominosis

Although the incidence of clinical disease resulting from endoparasitism has decreased with the increasingly widespread use of effective anthelmintics, gastrointestinal parasitic infestation still represents an important clinical entity. Small strongyle infestation (larval cyathostominosis) has been increasingly appreciated as a cause of diarrhea in horses, often in association with hypoproteinemia and weight loss, and *Strongyloides westerii* infestation remains an important clinical entity in foal diarrhea (Netherwood et al., 1996; Brown et al., 1997; Lyons et al., 1999, 2000). Although several techniques exist for the detection of parasite larvae or eggs in fecal material, the detection of helminthic parasitic infestation can be challenging. This difficulty arises because clinical disease resulting from endoparasitism may occur during the prepatent period, before the parasitic organisms begin to shed eggs or pass larval stages in the feces. This is especially true in the case of cyathostomins, where the reported sensitivity and specificity of fecal flotation are less than 40% for the detection of strongyle eggs, larval stages, and adult parasites, and this requires the use of additional diagnostic tools. Diagnosis of cyathostomin infection from the examination of fecal material is enhanced by the use of methods such as the Baermann technique for detection of larval stages and the modified McMaster technique for the detection of strongyle ova and larval stages (Olsen et al., 2003). Definitive diagnosis of cyathostominosis, however, requires postmortem examination of the intestine or the collection of large intestinal biopsies, as small biopsy samples may not contain a representative population of organisms. Intestinal biopsies should be examined for the presence of third- and fourth-stage larval cyathostomes, using both transillumination and peptic digestion techniques (Eysker & Klei, 1999).

Protozoal Enterocolitis

Cryptosporidium parvum has been associated with diarrhea in foals. As is the situation with rotavirus, healthy foals may also shed this organism, especially after exposure to diarrheic foals shedding large numbers of cryptosporidial organisms (Netherwood et al., 1996; Xiao & Herd, 1994). The detection of large numbers of the organism in the feces of a diarrheic foal, however, is considered to be significant and suggests a causative role for this organism. Tests that may be used to identify cryptosporidial organisms in fecal material include acid-fast staining, immunofluorescence assays, ELISA, and molecular methods (PCR) (Cole et al., 1998; Ezzaty Mirhashemi et al., 2015). The most readily performed of these is acid-fast staining, which has been reported to be more sensitive but less specific than the immunofluorescence assay (Cole et al., 1998). The Kinyoun acid-fast stain can be performed on a fecal-smear slide preparation in most clinical laboratories, and consists of a three-step process of staining, decolorizing, and counterstaining, followed by examination at 400× and 1000× magnification (Cole, 1997). Readily identifiable pale to bright pink oocysts should be detected in multiple high-power fields in order to support the clinical involvement of cryptosporidial organisms (Cole, 1997). Although the direct immunofluorescence assays are readily available, they require a fluorescence microscope for reading the stained slide, and cannot be easily performed in most clinical diagnostic laboratories, rendering these assays less useful in the clinical setting. PCR testing for *C. parvum* is readily available, often as part of a panel of tests for potential enteric pathogens, and is an excellent screening tool (Uzal & Diab, 2015; Ezzaty Mirhashemi et al., 2015; Slovis et al., 2014).

Equine Proliferative Enteropathy

The presenting signs of horses with proliferative enteropathy can include anorexia, depression, lethargy, peripheral edema, weight loss, fever, diarrhea, and colic (McKenzie, 2009; Page et al., 2014a). Clinicopathologic abnormalities at presentation can include panhypoproteinemia, hypoalbuminemia, leukocytosis, hyperfibrinogenemia, and increased hemoglobin concentration and packed-cell volume (McKenzie, 2009). Of these abnormalities, hypoalbuminemia and panhypoproteinemia are most commonly identified (Page et al., 2014b; Frazer, 2008; Lavoie et al., 2000). The antemortem detection of the causative organism, *Lawsonia intracellularis*, in horses with proliferative enteropathy was historically difficult because culture of the organism in feces requires challenging cell culture techniques (Knittel et al., 1998), and histological evaluation of biopsy specimens of the intestine may be unrewarding as the sample may have been obtained from an unaffected region of the intestine (Brees et al., 1999). Serologic testing can be used to document that exposure to this organism has occurred, and remains an important diagnostic tool (Lavoie et al., 2000). The immunoperoxidase monolayer assay is the most widely used serologic test. PCR testing provides highly specific results and can be performed on fecal material (Brees et al., 1999; Lavoie et al., 2000). Unfortunately, the sensitivity of fecal PCR testing may be relatively low and for this reason PCR testing should always be performed in concert with serologic testing in order to ensure that false-negative results are not obtained (Pusterla et al., 2009; Vannucci & Gebhart, 2014; Page et al., 2014a). This is particularly true early in the course of the condition. Additional clinical diagnostic tests may be used to aid in confirming a diagnosis of proliferative enteropathy. Ultrasonography is frequently used to evaluate the thickness of the small intestinal wall. A small intestinal wall thickness exceeding the normal value of ≤3 mm is considered strongly suggestive of proliferative enteropathy (McKenzie, 2009). This test is not always definitive, however, because although positive results are common and strongly reinforce the suspected diagnosis, false negatives do occur (Atherton & McKenzie, 2006; Frazer, 2008).

NSAID-associated Right Dorsal Colitis

The clinical presentation of horses with this condition can vary from seemingly healthy horses with soft stools to those suffering from profuse watery diarrhea with signs of endotoxemia and shock; colic may also be present (Davis, 2017; Galvin et al., 2004; Jones et al., 2003; Cohen et al., 1995a; Karcher et al., 1990). Lethargy, anorexia, and depression are common, and may be the only presenting signs (Davis, 2017). Peripheral edema is a common, but not universal, finding in this condition, because of the loss of albumin through the damaged gastrointestinal mucosa, resulting in hypoalbuminemia and hypoproteinemia (Davis, 2017; Galvin et al., 2004; Cohen et al., 1995a; Karcher et al., 1990). Diffuse gastrointestinal ulceration may be present, with the affected areas including the oral cavity, stomach, and right dorsal colon. Many affected horses present with ulceration of only the right dorsal colon, however. Young horses are most commonly affected, likely because they are more likely to be athletically active and receiving routine NSAID therapy (Cohen, 2002; Davis, 2017). Monitoring of serum total protein and albumin in animals receiving prolonged courses of NSAID treatment may allow for the early detection of right dorsal colitis, prior to the onset of outward clinical signs (Davis, 2017).

The diagnosis of this condition is basically presumptive in nature, and is based on a history of NSAID administration in combination with clinical signs suggestive of toxicity (Atherton et al., 2009). Although a history of excessive dosages of NSAIDs is strongly suggestive, toxicity can occur even with dosages within the normal

range (Cohen et al., 1995a). Hypoproteinemia due to hypoalbuminemia is the most consistent clinicopathologic abnormality, although panhypoproteinemia with hypoglobulinemia may occur in chronic or severe cases (Davis, 2017). Concurrent renal toxicity may be present, and this may result in azotemia, hyposthenuria, and proteinuria.

Definitive diagnosis of right dorsal colitis is made upon surgical exploration of the abdomen or postmortem examination, with demonstration of focal thickening and inflammation of the right dorsal colon (Karcher et al., 1990). Noninvasive diagnostic techniques include transabdominal ultrasonography and labeled white blood cell scintigraphy (Jones et al., 2003; East et al., 2000). Ultrasonographic evaluation of the right dorsal colon represents the most useful antemortem test, and is most readily performed at the level of the 11th, 12th, and 13th rib spaces on the right-hand side just below the caudoventral lung border, where the colon will be imaged deep to the liver (Jones et al., 2003). At these sites, the mural thickness of the right dorsal colon wall should be 0.36 cm (range 0.24–0.6 cm) and the ratio of the mural thickness of the right dorsal colon to the right ventral colon should be 1 (range 0.7–1.6) (Jones et al., 2003). Labeled white blood cell scintigraphic examination of horses with right dorsal colitis has revealed increased radiopharmaceutical uptake in the right dorsal colon region at 20 h after injection of the labeled white blood cells, with no uptake observed in this region in healthy horses (East et al., 2000). Fecal screening tests for hemoglobin and/or albumin exhibit poor sensitivity and specificity and their results should be interpreted carefully in light of other diagnostic information. As definitive diagnosis of right dorsal colitis is often not possible, it is important that one rule out other causes of enterocolitis before making the presumptive diagnosis of right dorsal colitis.

Treatment

The treatment of enteritis and colitis in most cases is supportive in nature, as many of these conditions have poorly defined etiologies (e.g., duodenitis-proximal enteritis–anterior enteritis) or are caused by agents that are not likely to respond to specific therapy (e.g., rotaviral diarrhea, salmonellosis). The inflammatory nature of enteritis and colitis results in similar patterns of clinical and clinicopathologic alterations in horses with these conditions and, as a result, the principles of treatment of these diseases are often similar. Substantial losses of fluid from the circulating volume usually necessitate supportive fluid therapy; accompanying losses of protein may necessitate colloid therapy also. Electrolyte derangements are often present, requiring that supplementation be provided either enterally or parenterally. Anti-inflammatory therapy is indicated in many of these conditions to address both the local and systemic components of the inflammatory response. Antimicrobial therapy is not indicated in all cases, and the exceptions will be discussed where appropriate. Disruption of normal segmental and/or progressive motility may necessitate decompression by nasogastric intubation or surgical intervention, and prokinetic therapy may be of benefit. Decreased voluntary feed intake or forced withholding of feed often necessitates nutritional support. The management of these cases can be intensive, often requiring hospitalization.

Supportive Therapies

Gastric Decompression

The potential for the accumulation of enterogastric reflux within the stomach exists in any disease process in which normal progressive gastrointestinal motility is disrupted. The inability of the horse to regurgitate makes it imperative that nasogastric decompression be performed in any equine presenting with signs suggestive of gastrointestinal distress. Although the passage of a nasogastric tube is associated with some risk of esophageal trauma, the incidence of complications is low (Hardy et al., 1992) and the risk of gastric rupture far outweighs any risks associated with intubation. As reflux may be ongoing, it is often best to leave the nasogastric tube in place to allow for frequent decompression (every 1–2 h initially). Failure to decompress the stomach adequately can result in gastric rupture. Simply having a nasogastric tube in place does not prevent this, as active decompression is required (Todhunter et al., 1986). The risk of complications associated with intubation increases with increasing duration of intubation, so it is best to remove the tube when the production of enterogastric reflux has abated (Hardy et al., 1992). Determination of the optimum time for removal of the nasogastric tube is complicated by the fact that the presence of the nasogastric tube may result in the generation of a low volume of enterogastric reflux. Therefore, the tube can usually be removed once the volume of reflux decreases to 1–2 L every 2–4 h, provided that the patient can be closely monitored for recurrence of abdominal pain (Dabareiner & White, 1992). If pain recurs, the nasogastric tube must be replaced, and the stomach should be decompressed if fluid is again present. Some horses continue to reflux for up to 7 days, necessitating repeated attempts to remove the nasogastric tube. Some horses with colitis yield moderate volumes (2–4 L) of enterogastric reflux on initial nasogastric intubation, presumably because of the presence of small intestinal ileus, but this typically resolves within the first 12 h of treatment and does not usually require prolonged nasogastric intubation.

Fluid Therapy

Horses with enteritis or colitis often present with dehydration, which occurs secondary to fluid losses in the form of diarrhea or enterogastric reflux alone or in combination with decreased voluntary fluid intake. The correction of dehydration typically requires fluid replacement therapy, as these patients are often unable to correct their fluid status by voluntary intake. The goal of fluid therapy is to improve cardiovascular function, thereby resulting in improved tissue oxygen delivery and organ function. The fluid therapy plan should address both the correction of existing deficits and the provision of fluids to replace ongoing losses and provide for basal metabolic requirements. The estimate of clinical dehydration allows for an approximate determination of an initial resuscitation volume (e.g., 5% dehydration in a 500 kg horse equals a 25 L fluid deficit), which should be corrected rapidly, usually within the first 2 h after initiating therapy. Additional information regarding an animal's hydration status can be obtained from clinicopathologic data, including hematocrit, serum total protein concentration, serum lactate concentration, serum creatinine concentration, and urine specific gravity. Unfortunately, these parameters are all susceptible to other influences that decrease their sensitivity as markers of dehydration. The hematocrit can be reduced by blood loss, blunting the expected increases associated with dehydration and hemoconcentration, and the serum total protein concentration can be decreased as a result of protein loss or increased because of chronic inflammatory disease. Serum lactate concentration may be increased because of tissue hypoperfusion associated with hypovolemia and shock, but also may be increased as a result of defects in tissue oxygen extraction (cytopathic hypoxia) despite adequate tissue perfusion (Fink, 2002). Renal insufficiency can result in increased serum creatinine concentrations without dehydration, and it may prevent appropriate increases in urine specific gravity in the presence of dehydration. Urine specific gravity will normally reflect the hydration status of the patient, but may not be appropriately increased in dehydration if renal insufficiency is present.

Intravenous Route

In most cases of enteritis and colitis, fluid replacement is best accomplished via the parenteral route, as this allows for the rapid administration of large volumes of fluid in acute situations, and also allows for correction of any electrolyte deficits. Although the use of the intravenous route for fluid delivery can be more difficult than the enteral route in the field, the availability of administration sets that allow horses to move freely within a stall greatly facilitates this process (IV 1000 Stat Large Animal IV Set, International WIN, Kennett Square, PA, USA). Intravenous fluids for replacement may be administered at rates of 10–20 mL/kg/h in the moderately dehydrated patient, but more aggressive therapy is required when the patient is in shock, with rates as high as 30–40 mL/kg/h being readily achieved using a 10- or 12-gauge intravenous catheter. Higher rates should be avoided in most cases, as they substantially increase the risk of fluid overload and pulmonary edema (Fielding, 2014). Maintenance rates of fluid administration are typically around 1–2 mL/kg/h in adult horses, but this will need to be increased to account for additional fluid losses resulting from reflux or diarrhea (Fielding, 2014).

Enteral Route

Enteral fluid therapy has been proposed for horses with colitis, as small intestinal function is usually normal in these animals (Schott, 1998; Ecke et al., 1997; Lopes et al., 2003; Nager & Wang, 2002; Rainger & Dart, 2006). The enteral route is intrinsically more physiologic, and has the additional advantages of reduced cost and simplicity (Lopes et al., 2003; Rainger & Dart, 2006). Oral rehydration solutions are widely used in the treatment of human patients with diarrhea, and the reported outcomes with oral rehydration are equivalent or superior to those reported with intravenous fluid therapy (Nager & Wang, 2002; Atherly-John et al., 2002). The enteral route of administration can be used successfully in the treatment of horses mildly afflicted with colitis. However, severely affected patients are often unable to tolerate the administration of the volumes of fluids required to correct their deficits and replace their ongoing losses, and may exhibit increased discomfort or abdominal distention or may even develop enterogastric reflux (Lopes et al., 2003; Ecke et al., 1998; Rainger & Dart, 2006).

Administration of enteral fluids is easily accomplished using a large-bore stomach tube or a smaller indwelling enteral feeding tube (18 Fr × 100 inch, MILA International, Erlanger, KY, USA). Although the administration of tap water is reasonable and well tolerated for short-term use (Lester et al., 2013), for longer term use (more than several hours) consideration should be given to using an electrolyte-containing enteral fluid solution. Enteral fluid solutions are easily prepared using tap water, and an isotonic solution can be formulated by combining 5 L of water with 1.5 tablespoons (28 g) of table salt, half a teaspoon (3 g) of Lite Salt (NaCl and KCl, Morton Salt, Chicago, IL, USA) and 1.5 tablespoons (17 g) of baking soda ($NaHCO_3$) (Lopes et al., 2003). An alternative formula consisting of 30 g of sodium chloride and 15 g of potassium chloride added to 5 L of water has also been described (Monreal et al., 1999). Enteral fluids are most often administered as repeated bolus doses of up to 8–10 L given once every 2 h, although more rapid rates of administration have been reported (Lopes et al., 2003; Ecke et al., 1998). The present author's experience suggests that these more aggressive rates of administration

can result in substantial worsening of diarrhea and abdominal discomfort. Alternatively, the enteral fluids may be administered as a continuous-rate infusion at a rate of 2–4 L/h, which seems to be better tolerated than bolus therapy by some horses (Lopes et al., 2003).

Types of Intravenous Fluids

Parenterally administered fluid solutions are generally classified into one of three types: hypotonic, isotonic, and hypertonic. The most widely used of these are the polyionic crystalloid solutions, which are classified as either replacement or maintenance solutions. Isotonic replacement fluids are the most widely used type of fluids in equine medicine, and they are most appropriate for use in rehydration, as they provide substantial amounts of sodium to aid in expansion of both the extracellular fluid volume and the intravascular volume. Examples of replacement fluids include normal (0.9%) saline, Ringer's solution, lactated Ringer's solution, Plasmalyte-A (Baxter Healthcare, Deerfield, IL, USA), and Normosol-R (Abbott Laboratories, North Chicago, IL, USA). Replacement fluid solutions are commonly used to provide maintenance fluid support after initial rehydration in horses, but they contain relatively high concentrations of sodium and chloride, with low concentrations of potassium. Most adult horses appear to be able to eliminate the excess sodium and chloride via renal excretion, but foals are less tolerant of this type of sodium load and may become hypernatremic, hyperchloremic, or edematous if replacement fluids are used for maintenance purposes. The low potassium content of the replacement solutions requires that supplemental potassium be added to the fluids in the form of potassium chloride (10–20 mEq/L) in most cases, especially in horses unable to eat because of anorexia or dietary restriction. Care must be taken to avoid delivery of excessive chloride, however, owing to concerns regarding the possible development of hyperchloremic metabolic acidosis and evidence of complications in human patients receiving intravenous fluids (Fielding, 2014). For these reasons, Normosol-R or Plasmalyte-A may represent the best choice for intravenous fluid replacement in adult horses, owing to their lower chloride contents compared with normal saline or lactated Ringer's solution (Fielding, 2014).

Maintenance fluids are isotonic or hypotonic polyionic crystalloid solutions that contain lower concentrations of sodium and chloride than replacement solutions and provide relatively more potassium. Examples of maintenance solutions include 0.45% saline with 2.5% dextrose, Plasmalyte-56 (Baxter Healthcare), and Normosol-M (Abbott Laboratories). Maintenance fluid solutions typically contain dextrose, which is used to bring the solution to an osmolality close to that of serum (250–300 mOsmol/L) as these solutions are hypotonic owing to their low concentrations of sodium and chloride. Maintenance fluids provide relatively more free water to replace the fluid volume lost as a result of insensible losses, which typically consist of water loss without concurrent electrolyte losses. Use of maintenance solutions aids in preventing the development of hypernatremia and hyperchloremia, but may be contraindicated in animals with substantial ongoing losses of electrolytes resulting from diarrhea or renal disease.

Hypertonic fluids are rarely administered as the sole fluid solution and are reserved for resuscitation of horses in life-threatening shock to provide rapid restoration of circulating blood volume and hemodynamic stabilization (Schmall et al., 1990a, 1990b; Bertone et al., 1990). Because of the relatively transient nature of the effects of hypertonic saline and the fact that the increase in circulating volume is achieved by shifting fluids from the extravascular space, hypertonic saline must be rapidly followed by the administration of isotonic solutions to maintain volume expansion. Other hypertonic solutions include sodium bicarbonate, which has been used in the treatment of acidosis associated with severe dehydration and shock. Good evidence exists, however, that this treatment is not effective at normalizing the serum pH in horses exposed to sublethal doses of endotoxin, despite increasing the serum bicarbonate concentration, and it actually results in increases in serum lactate concentration (Gossett et al., 1990). The primary uses for sodium bicarbonate solutions are in the treatment of hyponatremia without hypochloremia and hyperchloremic metabolic acidosis.

Colloids

Most horses with enteritis or colitis respond well to the administration of balanced electrolyte solutions as volume-replacement therapy, but some require the concurrent administration of colloid solutions (see Chapter 28). Colloid therapy is most helpful in two clinical situations: severe hypovolemia and hypoproteinemia. Both natural and synthetic colloid solutions are available for administration to equine patients, with the only natural colloid solutions currently available being equine plasma and whole equine blood. Although purified equine albumin has been developed, this product is not currently available. The synthetic colloids include hydroxyethylstarch solutions (hetastarch; Hespan 6% hetastarch in normal saline, Baxter Healthcare), dextrans (dextran 40, 70, and 75), gelatins (Haemaccel Veterinary Infusion Solution; 3.5% polygeline isotonic solution, Intervet UK, Milton Keynes, UK), and polymerized bovine hemoglobin [Oxyglobin; hemoglobin glutamer-200 (bovine), Biopure, Cambridge, MA, USA]. Gelatin colloids are currently not commercially available in the United States.

The most physiologically appropriate and widely used colloid for the treatment of hypoproteinemia is equine

plasma. The drawbacks associated with the use of plasma therapy include cost (a single dose of 4–8 L of plasma typically costs US$500–1000) and a relatively short duration of action, because the exogenous proteins are lost via capillaries within the gastrointestinal mucosa or the systemic circulation (Margarson & Soni, 2002). The use of hydroxyethylstarch solutions for the treatment of hypoproteinemia in horses has been reported (McFarlane, 1999) and this therapy appears to be clinically effective. Hydroxyethylstarch has the potential advantages of a longer duration of action than plasma and the reported ability to decrease the severity of capillary leak in shock and sepsis (Hoffmann et al., 2002; Jarvela et al., 2001; Cox et al., 2000). The administration of hydroxyethylstarch as a component of a small-volume resuscitation approach in endotoxemic horses did not demonstrate any hemodynamic benefit compared with crystalloid therapy (Pantaleon et al., 2006). Hydroxyethylstarch infusion has been shown to result in hemorrhagic diathesis in septic human patients, and the author has also observed this apparent effect in critically ill equine patients. The primary cause of the coagulation disorders associated with these compounds appears to be a dilutional effect on the endogenous clotting factors in critically ill patients, many of which are suffering from clotting-factor depletion secondary to consumption (Jones et al., 1997). Interestingly, similar alterations in hemostatic function have been reported in association with the administration of gelatin and dextran colloids (Glowaski et al., 2003; De Jonge & Levi, 2001). Avoidance of hemostatic dysfunction can best be achieved by limiting the total dose of hydroxyethylstarch to <10–20 mL/kg and monitoring the clotting profile of patients administered large doses of these solutions. No adverse effects of hydroxyethylstarch therapy on coagulation were detected when a dosage of 10 mL/kg was administered to horses with experimentally induced endotoxemia (Pantaleon et al., 2007). Of greater concern, however, is the evidence that the use of hydroxyethylstarches may be associated with acute kidney injury and worsened outcomes in certain subsets of human patients (Fielding, 2014). Owing to all of the concerns raised regarding these compounds, they should be used only in cases with a clear need for colloidal support.

Electrolyte Supplementation

Horses with inflammatory gastrointestinal diseases often develop hypokalemia and hypocalcemia; hypomagnesemia also may occur. Hypokalemia, which for clinical purposes can be defined as a serum potassium concentration <3.5 mEq/L (Corley, 2002), is such a common finding in horses withheld from feed that the fluids utilized for maintenance therapy should typically contain additional potassium. This is routinely accomplished by supplementation of the fluid solution, which is typically a resuscitation fluid, with 20 mEq/L of potassium chloride. When administering fluids at rates higher than maintenance, care must be taken to ensure that the rate of potassium delivery does not exceed 0.5 mEq/kg/h (Corley, 2002; Schaer, 1999).

Hypocalcemia, defined here as a serum ionized calcium concentration of <5.0 mg/dL (1.25 mmol/L), is also a common occurrence in horses with gastrointestinal disease. Intravenous supplementation with calcium gluconate solution is commonly provided to hypocalcemic horses. Adult horses typically receive 100–300 mL of a 23% calcium gluconate solution (Dart et al., 1992), although clinically some horses require as much as 500–1000 mL to correct their hypocalcemia fully.

Hypomagnesemia has been reported to occur in horses with gastrointestinal disease (Garcia-Lopez et al., 2001; Johansson et al., 2003), but routine assessment of this disorder is complicated by the fact that serum total magnesium appears to be less relevant than serum ionized magnesium, and the equipment required to assess serum ionized magnesium is not readily available (Stewart, 2011). Hypomagnesemia has been associated with the development of hypocalcemia and hypokalemia in both veterinary and human patients (Dhupa & Proulx, 1998; Stewart, 2011). In the present author's experience, supplementation with magnesium sulfate has been beneficial in aiding the correction of persistent hypocalcemia and/or hypokalemia in equine critical care patients. Intravenous supplementation with moderate dosages (4–16 mg/kg) of magnesium sulfate is well tolerated by the horse, even those with normal magnesium status, provided that renal function is normal (Corley, 2002). It has been suggested that horses receiving continuous-rate infusions of fluids may be supplemented with magnesium at the following rates: for a horse receiving 30 L of fluids per day, 25 mL of a 50% $MgSO_4$ solution can be added per 5 L bag, whereas a horse receiving 60 L per day should have 12 mL of 50% $MgSO_4$ solution added per 5 L bag (Stewart, 2011).

Anti-inflammatory Therapy

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

The NSAIDs are extremely important drugs in the management of equine gastrointestinal disorders, primarily because of their potent analgesic properties, but also because of the demonstrated ability of some of these drugs to modify the systemic inflammatory response to gastrointestinal disease. Drugs in this class include the nonselective cyclooxygenase (COX) inhibitors phenylbutazone, flunixin meglumine, and ketoprofen and the COX-2-selective drugs firocoxib and meloxicam. Of these, the most commonly used drug for the treatment of horses with gastrointestinal disease is flunixin meglumine, which is a potent visceral analgesic. This drug has a well-demonstrated ability to suppress abdominal pain in equine gastrointestinal diseases when administered at

1.1 mg/kg orally, intramuscularly, or intravenously (Clark & Clark, 1999). In addition, flunixin has been shown to suppress the systemic response to endotoxin when given as a pretreatment at doses as low as 0.25 mg/kg, thereby minimizing the severity of endotoxemia-associated hypotension, hypovolemia, hemoconcentration, pulmonary hypertension, tachypnea, tachycardia, and lactic acidosis (Bottoms et al., 1981; Moore et al., 1981; Dunkle et al., 1985; Ewert et al., 1985; Templeton et al., 1987). Additionally, flunixin meglumine and phenylbutazone have been shown to attenuate the development of ileus after onset of endotoxemia (King & Gerring, 1989). Although other NSAIDs, such as ketoprofen, have been demonstrated to have some "anti-endotoxemic" effects, flunixin meglumine remains the drug of choice in the treatment of horses with gastrointestinal disease resulting in colic and/or endotoxemia (MacKay et al., 1999; Jackman et al., 1994). Care should be taken when using the NSAIDs as the nonspecific COX inhibitors are potentially ulcerogenic and nephrotoxic in nature, owing to their interference with the maintenance of mucosal blood flow in the intestine and medullary blood flow within the kidney. The newer COX-2-selective compounds have higher safety margins and may be appropriate replacements for the more commonly used nonselective COX inhibitors. Meloxicam has been shown to be comparable to flunixin in horses recovering from colic surgery, in terms of both pain control and the development of side effects, although there was a trend toward improved survival in the meloxicam-treated group (Naylor et al., 2014). Both firocoxib and meloxicam achieve plasma concentrations that are likely to be therapeutic and appear to be safe when administered to foals (Hovanessian et al., 2014; Raidal et al., 2013).

Steroidal Anti-inflammatory Drugs

These drugs are potent anti-inflammatory compounds, and are extremely important in the management of selected equine gastrointestinal disorders. This is especially true for more chronic conditions, such as inflammatory bowel disease, which are immune mediated. The steroid anti-inflammatory drugs have not proven to be as effective as the NSAIDs in suppressing the acute systemic response to endotoxin in the horse, and are not effective analgesics, so they have a limited role in the treatment of acute gastrointestinal diseases (Ewert et al., 1985; Templeton et al., 1987; Frauenfelder et al., 1982). The literature, however, includes some mention of the use of corticosteroids in the treatment of acute equine typhlocolitis (Jones, 2003). The primary utility of this class of drugs is in the suppression of gastrointestinal inflammation, such as occurs acutely in larval cyathostominosis after the destruction of the encysted larvae within the bowel wall following anthelmintic administration, or in chronic infiltrative bowel diseases. Some work has demonstrated that these drugs exert many of their effects by mechanisms other than their well-described suppression of the pathways of arachidonic acid metabolism leading to the production of the prostanoids and leukotrienes (Auphan et al., 1995; Barnes, 1998). For example, these drugs have potent effects on the expression of genes encoding inflammatory and anti-inflammatory mediators, with overall inhibitory effects on the production of pro-inflammatory mediators and facilitating effects on the production of anti-inflammatory mediators (Ingawale et al., 2015). It has become clear that these effects are responsible for the potent, dose-dependent anti-inflammatory and immunosuppressive effects of these drugs.

Prednisone and prednisolone are commonly used in the treatment of acute and chronic gastrointestinal inflammatory conditions, although evidence exists that prednisone is poorly absorbed by the horse after oral administration (Peroni et al., 2002). Prednisolone is usually administered at dosages of 1–2 mg/kg once daily. This drug appears to be clinically effective in some cases, but the dosage may need to be increased to 4 mg/kg/day to achieve adequate immunosuppressive effects in refractory cases. One significant limitation to the use of prednisolone is cost, especially at higher dosages. Dexamethasone is often used for the treatment of inflammatory bowel disease, owing to the higher potency and lower cost of this drug on a daily basis. The dosage range of dexamethasone is 0.02–0.1 mg/kg/day, with the upper end of the range producing potent immunosuppressive effects. The possibility of the potential association of corticosteroids and laminitis must be considered, especially when corticosteroids are used in conditions that represent risk factors for laminitis or when high dosages of the more potent corticosteroids are used (Johnson et al., 2002). A recent retrospective case-controlled study of over 400 horses receiving oral prednisolone therapy found no association between steroid therapy and the development of laminitis (Jordan et al., 2017). In that study, the risk of laminitis was related primarily to a diagnosis of equine metabolic syndrome and increasing age.

Anti-endotoxin Therapies

As endotoxin plays an important role in the development of severe systemic inflammation ("clinical endotoxemia") associated with gastrointestinal disease, there has been significant interest in ways to inhibit systemic responses to endotoxin. Two basic approaches have been used in an attempt to neutralize endotoxin, the first being the administration of anti-endotoxin antibodies and the second the use of chemicals that bind endotoxin (Moore & Barton, 2003). The development of antibodies to bacterial endotoxin has been challenging because of the antigenic variation of endotoxins among species of Gram-negative bacteria. For this reason, antibodies have been targeted

against the more conserved core and lipid A regions of the endotoxin molecule (Moore & Barton, 2003). Extensive studies of anti-endotoxin antibodies were performed in humans in an effort to develop these therapies for clinical use, but the conflicting results of these studies meant that none of the products were licensed for human use (Baumgartner & Glauser, 1993). Studies regarding the efficacy of anti-endotoxin antibodies in experimental equine endotoxemia and in horses presenting with colic have also yielded conflicting data, resulting in uncertainty regarding the clinical application of this type of therapy (Morris et al., 1986; Garner et al., 1978; Spier et al., 1989). Of additional concern is a report that described worsened clinical signs of endotoxemia and increased systemic inflammation associated with the administration of anti-endotoxin antiserum in a foal model of endotoxemia (Durando et al., 1994). Serum and plasma products containing anti-endotoxin antibodies are commercially available for use in the horse and are used in some cases, but the uncertainty in the literature regarding this therapy needs to be resolved before specific recommendations can be made.

The use of the anti-endotoxin agent polymyxin B has been extensively examined in a variety of animal species and in humans, and good evidence exists that polymyxin B binds endotoxin and prevents it from initiating or potentiating the systemic inflammatory response to endotoxin. The use of polymyxin B in humans has been limited by concerns regarding the nephrotoxic potential of this compound, and this has led to the development of extracorporeal filters containing polymyxin B-immobilized fibers that are used for hemofiltration in patients with endotoxemia and sepsis, with promising clinical results (Shoji, 2003; Harm et al., 2016; Esteban et al., 2013). Polymyxin B has been examined in several equine models of endotoxemia and has been demonstrated to decrease the severity of both the clinical signs of endotoxemia and the severity of the systemic inflammatory response (Durando et al., 1994; Barton, 2000; Parviainen et al., 2001; Wong et al., 2013). Based on these reports, the current recommendations for clinical use of polymyxin B are to initiate therapy as early as possible, using a dosage of 6000–10,000 IU/kg every 8–12 h (Moore & Barton, 2003; Morresey & MacKay, 2006; Wong et al., 2013). Although no evidence of nephrotoxicity has been reported in horses or foals administered low dosages of polymyxin B, it is recommended that horses be adequately hydrated and that serum creatinine concentrations be monitored when administering this drug (Moore & Barton, 2003). Prolonged administration of polymyxin B should be avoided to minimize the risk of nephrotoxicity. Given the relatively low sensitivity of serum creatinine as a marker of nephrotoxicity, one should consider performing urinalysis on a regular basis to monitor urine specific gravity and urine sediment for casts and for the development of enzymuria.

Pentoxifylline

Pentoxifylline is a methylxanthine derivative that has been primarily used in horses owing to its rheologic effects, with the goal of improving tissue perfusion (Weiss et al., 1994, 1996; Geor et al., 1992; Bailey et al., 2010). There is some evidence to suggest that the beneficial effects of this drug on tissue perfusion may actually result from its vasodilatory effects as much as or more so than its rheologic effects (Kabbesh et al., 2012; Ruddock & Hirst, 2005). Pentoxifylline also has well-demonstrated anti-inflammatory properties that appear to be mediated by several mechanisms, including inhibition of phosphodiesterase, alteration of intracellular signaling pathways, down-regulation of pro-inflammatory cytokine production, and up-regulation of anti-inflammatory cytokine production (Coimbra et al., 2005). The anti-inflammatory effects of pentoxifylline have been demonstrated in several equine studies involving *in vitro* and *in vivo* models of endotoxemia (Milam et al., 1992; Barton & Moore, 1994; Barton et al., 1997a, 1997b; Baskett et al., 1997). Pentoxifylline has also more recently been shown to down-regulate matrix metalloproteinase activity in an equine endotoxemia model (Fugler et al., 2013). There is recent evidence that pentoxifylline may be beneficial in the treatment of neonatal sepsis, necrotizing enterocolitis, acute pancreatitis, and diabetic nephropathy in human patients (Shabaan et al., 2015; Pammi & Haque, 2015). The currently recommended oral dosage for pentoxifylline in horses is 10 mg/kg every 12 h, but there is evidence of decreasing bioavailability with repeated dosing, which may require an increase in the dosage with long-term administration (Liska et al., 2006).

Analgesic Therapy

The provision of analgesia in horses with gastrointestinal diseases is most commonly accomplished using NSAIDs, primarily flunixin meglumine, and α_2-adrenergic agents such as xylazine and detomidine. Flunixin meglumine (1.1 mg/kg IV or IM) is widely used as a visceral analgesic in horses, and it is effective, although the degree of analgesia is less than that produced by administration of the α_2-adrenergic agents (Kohn & Muir, 1988; Johnson et al., 1993). Meloxicam is a COX-2-selective NSAID that is effective as an analgesic in postoperative colic cases, although it is less effective at pain control than flunixin (Naylor et al., 2014). Detomidine (0.11–0.22 mg/kg IV or IM) and xylazine (0.5–1 mg/kg IV or IM) are potent visceral analgesics in horses and are very useful for short-term analgesia (Sanchez & Robertson, 2014). Their use is accompanied by profound sedation, which can be clinically important and beneficial, but their effects are fairly transient (Jochle et al., 1989; Sanchez & Robertson, 2014). Opioid analgesics, such as butorphanol and morphine, can be used as an alternative to, or adjunctive therapy with, NSAIDs or α_2-adrenergic agents.

Butorphanol can be administered as intermittent boluses (0.02–0.13 mg/kg IV) or as a continuous-rate infusion (initial loading dose of 18 μg/kg followed by a continuous infusion of 10–23 μg/kg/h) (Sellon et al., 2004). Morphine administration can result in central nervous system excitation, but co-administration of acepromazine appears to ameliorate this effect (Sanchez & Robertson, 2014). The recommended dosage for the intravenous administration of morphine is 0.1–0.6 mg/kg every 4–6 h (Knych et al., 2014; Sanchez & Robertson, 2014). An additional concern regarding the use of the opioids for analgesia in patients with gastrointestinal disease is the depressant effects of the opioids on gastrointestinal motility (Roger et al., 1994; Sutton et al., 2002; Doherty et al., 1999; Rutkowski et al., 1989; Sanchez, 2014). Although this may potentiate ileus in some patients, it may be of benefit in those with hypermotility, such as those with profuse diarrhea. Lidocaine is widely administered as a continuous-rate infusion to horses as a prokinetic (discussed later), but in addition to those effects this treatment has been demonstrated to have analgesic and anti-inflammatory effects (Elfenbein et al., 2014; Sanchez & Robertson, 2014; Risberg et al., 2014; Guschlbauer et al., 2011; Peiro et al., 2010; Cook et al., 2008, 2009a; Malone et al., 2006).

Prokinetics

Because of the frequent development of ileus in horses with enteritis, prokinetic drugs are often used in the treatment of these disorders. In contrast, animals with colitis rarely require prokinetic therapy. The effects of the prokinetic drugs typically derive from their ability either to increase the local activity of the enteric nervous system or to minimize the inhibitory effects of the sympathetic nervous system on the activity of the enteric nervous system. A detailed discussion of the mechanisms of these compounds is included in Chapters 9 and 13. The more commonly used drugs in animals with enteritis include the parasympathomimetic bethanechol, the benzamide metoclopramide, and the sympatholytic and local anesthetic drug lidocaine. Of these, the author most commonly uses bethanechol and lidocaine. Lidocaine administration is reported to result in suppression of the visceral afferent neurons, thereby inhibiting the reflex-mediated increased activity of the sympathetic innervation of the intestine (Rimback et al., 1990). Additional beneficial effects of lidocaine therapy may include anti-inflammatory effects and direct stimulation of intestinal smooth muscle (Das & Misra, 1992; Hyvonen & Kowolik, 1998; Nieto et al., 2000; Elfenbein et al., 2014; Sanchez & Robertson, 2014; Guschlbauer et al., 2011; Peiro et al., 2010; Cook et al., 2008, 2009a; Malone et al., 2006). Several studies of lidocaine therapy in postoperative ileus suggest that lidocaine administration, at a loading dosage of 1.3 mg/kg using 2% lidocaine solution, followed by a continuous-rate infusion of 0.05 mg/kg/min, is beneficial in decreasing intestinal inflammation and promoting a more rapid return of small intestinal function (Malone et al., 1999; Brianceau et al., 2002; Doherty, 2009; Torfs et al., 2009). Care should be taken when administering lidocaine for prolonged periods of time. Although there was no evidence of accumulation of lidocaine in healthy horses administered lidocaine as a continuous-rate infusion for 96 h, several studies have demonstrated the accumulation of lidocaine or its active metabolites in horses receiving lidocaine postoperatively (Dickey et al., 2008; Navas de Solís & McKenzie, 2007; Milligan et al., 2006).

Direct stimulation of cholinergic receptors using the cholinomimetic drug bethanechol has also been shown to enhance gastric and cecal emptying in the horse (Lester et al., 1998; Ringger et al., 1996; Gerring & Hunt, 1986). When administered at dosages of 0.018–0.024 mg/kg subcutaneously every 8 h, bethanechol appears to decrease the duration of enterogastric reflux in horses with postoperative ileus and in some horses with DPJ. Metoclopramide promotes the release of acetylcholine from postsynaptic cholinergic neurons and antagonizes dopamine and α_2-adrenoreceptors, and these effects result in increased gastric and small intestinal motility and decrease the severity of postoperative ileus (Hall & Washabau, 1997), The recommended dosage regimen for metoclopramide is a continuous-rate infusion of 0.4 mg/kg/h (Dart et al., 1996). The dopaminergic antagonist domperidone may have some beneficial prokinetic effects in horses, similar to those demonstrated in other species, but further work is required (Nieto et al., 2013).

Nutritional Support

The basic goal of nutritional supplementation is to prevent the development of a negative energy balance in patients unable to meet their nutritional needs through voluntary intake. Determining the patient's metabolic requirements is complicated by the fact that critical illness has been considered to result in an increased metabolic rate, but this effect appears to be inconsistent in human patients and has not been well documented in the horse. The presence of systemic inflammation induces protein catabolism, which, in combination with physical inactivity, leads to the loss of muscle mass regardless of the patient's overall energy balance (Reid et al., 2004; Dunkel & Wilkins, 2004; Magdesian, 2003). The degree of protein catabolism is certainly heightened, however, in the presence of a negative energy balance. In addition to protein catabolism, the presence of a negative energy balance can lead to excessive mobilization of the animal's fat stores, leading in some cases to hypertriglyceridemia. This response can be associated with additional decreases in voluntary intake of feed and secondary complications such as hepatic lipidosis and azotemia (Dunkel & McKenzie, 2003).

Horses should ideally have free-choice access to roughage and also supplemental feeding with concentrates to meet at least their maintenance metabolic energy requirements (roughly 16 Mcal for a 500 kg horse) (Magdesian, 2003). Unfortunately, equine patients with DPJ are unable to ingest feed because of the inherent small intestinal dysfunction associated with this condition. Horses suffering from colitis can often be allowed to ingest feed, provided that substantial ileus is not associated with their condition. Some horses with colitis may be anorectic because of the depression and discomfort associated with their illness, impairing their ability to meet their metabolic needs through voluntary intake. Most adult horses can reasonably be maintained without nutritional support for a few days, as they will mobilize their endogenous energy reserves (fat, muscle) to meet their metabolic needs. Some horses and ponies appear predisposed to excessive fat mobilization, however, and they should not be maintained without nutritional support because of the risks of hypertriglyceridemia and hyperlipemia.

Enteral nutritional support can be accomplished by the administration of liquid diets via repeated nasogastric intubation or an indwelling nasogastric feeding tube. Commercial liquid diet formulations are available, with products designed for either horses or humans. The use of commercial liquid-enteral diets may be associated with the development of diarrhea and laminitis in the horse, and they must be introduced slowly in order to minimize the development of gastrointestinal disturbances (Magdesian, 2003). This type of therapy is obviously not ideal for use in horses with inflammatory gastrointestinal diseases, because it may exacerbate the existing disease process due to the osmotic effects of the ingested nutrients. The alternative approach to enteral support is the feeding of slurries made according to proprietary formulations (Hallebeek & Beynen, 2001) or from commercial feedstuffs such as Equine Senior (Purina Mills, St. Louis, MO, USA) (Magdesian, 2003). Commercially formulated products for enteral feeding of horses are also available and, although expensive, these are easier to prepare and administer via nasogastric intubation (Purina Wellsolve W/G, Purina Mills, St. Louis, MO, USA). These diets must also be introduced slowly, which represents a significant limitation in acutely ill horses, as adequate energy may not be delivered in a timely manner (Geor, 2007).

More rapid delivery of nutrition can be accomplished using the parenteral route. This route is the only one available in horses with small intestinal dysfunction (see Chapter 39). Parenteral nutrition can be characterized as partial or complete, based on whether or not it meets the animal's entire nutritional needs. Total parenteral nutrition requires the use of both carbohydrate and lipid sources of energy, in combination with amino acids. Partial parenteral nutrition can be accomplished with carbohydrate or carbohydrate–amino acid solutions. Supplementation of the intravenous fluids with dextrose at a moderate rate of 5–10 kcal/kg/day (1.5–3 L of 50% dextrose per day) appears to be beneficial in clinically ill horses with decreased or absent appetite, as the dextrose minimizes the degree of fat mobilization secondary to a negative energy balance, and has been shown to correct hypertriglyceridemia (Magdesian, 2003; Dunkel & McKenzie, 2003; McKenzie, 2015).

Specific Therapies

Antimicrobial Therapy

The role of antimicrobial therapy in the treatment of equine enteritis and colitis is controversial, as for many of these conditions the etiologic agent is not definitively known or is not bacterial. Often antimicrobial therapy is used in patients with gastrointestinal disease that results in fever and leukopenia, which may indicate the presence of bacterial infection or may result from the effects of bacterial toxins such as endotoxin. There are additional concerns that severe gastrointestinal disease may be associated with impairment of the barrier function of the gastrointestinal mucosa, resulting in an increased risk of bacterial translocation and leading to localized infection or septicemia and infections distant to the intestine (pneumonia, endocarditis, meningitis, etc.). The efficacy of systemic antimicrobial therapy in the prevention of bacterial translocation in gastrointestinal disease has not been established (Koratzanis et al., 2002).

The administration of antimicrobials carries the risk of antimicrobial-associated enterocolitis in the horse, secondary to alterations in the gastrointestinal microflora. In addition, the indiscriminate use of antimicrobial drugs increases the risk of development of microbial resistance to the drugs, with ramifications both for the individual patient and for the hospital population, and also for the human population. For these reasons, the indiscriminate use of antimicrobials in equine patients should be avoided. Antimicrobial therapy is not controversial, however, in cases where the suspected etiologic agent is potentially susceptible to antimicrobials. Clostridial enterocolitis, equine monocytic ehrlichiosis, proliferative enteropathy, and possibly salmonellosis are disease processes in which antimicrobial therapy is indicated.

Specific Antimicrobials

Beta-lactams

The beta-lactams include the penicillins, synthetic penicillins, and cephalosporins. Modifications of the basic penicillin or cephalosporin molecule confer differences in antimicrobial activity, This is evident with the synthetic penicillins and third-generation cephalosporins, which have a wider Gram-negative spectrum, and may

have increased stability against beta-lactamases. The beta-lactam drugs must be present in the tissues at concentrations exceeding the minimum inhibitory concentration throughout the entire dosage interval in order to be effective, rendering them "time-dependent" antimicrobials. Penicillin G is the prototypical beta-lactam drug, and is the most widely used antimicrobial in equine medicine. Penicillin G is administered to the horse at a dosage of 20,000–60,000 IU/kg, with the procaine suspension being administered IM every 12 h and the aqueous solutions of Na and K penicillin being administered IV every 6 h. Toxicity is low for the penicillins, and is mostly due to reactions to intravenous or intra-arterial injection of the procaine form, although anaphylactic reactions have been reported (Chapman et al., 1992; Nielsen et al., 1988). Penicillins are often combined with beta-lactamase inhibitors, such as clavulanic acid, which are believed to protect the penicillin from breakdown by the beta-lactamases by serving as an alternative substrate, but may also serve to increase production of these enzymes. Ampicillin, amoxicillin, and ticarcillin are synthetic penicillins that have been used in the horse, with ampicillin being the most commonly used of the three. The primary cephalosporin administered to horses is ceftiofur, a third-generation drug. Ceftiofur is considered to have a broad spectrum, with the emphasis on Gram-negative coverage. It is usually administered at 2.2–5 mg/kg IM or IV every 12 h. There are reports of severe colitis associated with ceftiofur administration, but the incidence of this complication appears to be low when ceftiofur is used at recommended dosages (Foreman, 1998; Wilson, 2001).

Aminoglycosides

The aminoglycosides are a mainstay in the treatment of Gram-negative infections in the horse, owing to their rapid bactericidal effects, clinical efficacy, relatively low resistance rates, and synergism with beta-lactam antimicrobials. Aminoglycosides are classified as concentration-dependent antimicrobials because they exhibit peak concentration-dependent bactericidal activity and post-antibiotic effects against susceptible organisms. High peak concentrations of aminoglycosides produce more rapid and extensive bacterial killing than do lower concentrations (Craig, 1995). High peak concentrations of aminoglycosides (>8–10 times the minimum inhibitory concentration) have also been shown to decrease the emergence of resistant strains (Craig, 1995). Aminoglycosides are typically utilized in an extended-interval dosing regimen, wherein a single large bolus dose is given once every 24 h or longer. The most commonly used aminoglycoside in the adult horse is gentamicin, and the dosage for extended-interval dosing is 6.6 mg/kg IV or IM once daily (Godber et al., 1995). Although aminoglycosides are important drugs for the treatment of many equine conditions, they have a low therapeutic index, wherein little difference exists between a therapeutic and a toxic dose, and the toxic potential consists primarily of nephrotoxicity. Toxicity is minimized by the use of extended-interval dosing regimens, but can still occur in patients with decreased renal function. For this reason, therapeutic drug monitoring is recommended in critically ill equines receiving aminoglycosides, to ensure that accumulation of the drug is not occurring and to decrease the risk of toxicity. This monitoring can be performed by measuring the serum aminoglycoside concentration at 30 min and 8 h after the dose was administered (McKenzie & Furr, 2003), with the expected concentrations for gentamicin in the adult horse being 25–30 µg/mL at 30 min and <4–5 µg/mL at 8 h. Alternatively, a sample can be collected for the trough concentration at 22 h, or the concentration obtained at an earlier time point can be extrapolated to the 22 h time point, with a target trough concentration of <2 µg/mL (Bauquier et al., 2015).

Tetracyclines

Tetracyclines are bacteriostatic and broad spectrum, possessing activity against a wide variety of bacteria and protozoa, and also rickettsial organisms. These compounds are time dependent, requiring that concentrations at the site of infection remain at or above the minimum inhibitory concentration for the duration of the treatment interval. The primary indication for tetracycline therapy in equine gastrointestinal disease is for the treatment of equine monocytic ehrlichiosis; the most commonly used compounds are oxytetracycline and doxycycline. Toxicity of the tetracyclines is most often associated with disturbance of gastrointestinal flora associated with the development of colitis. Because oxytetracycline is primarily eliminated via the urinary tract, animals with renal insufficiency are at risk for toxicity from this drug (Vivrette et al., 1993). Rapid intravenous injection of oxytetracycline is associated with collapse in horses, perhaps as a result of chelation of calcium in the blood. Oxytetracycline is administered to horses at 4–8 mg/kg slowly IV once or twice daily, usually diluted in 0.5–1 L of normal saline and administered over 30 min. Doxycycline can be administered at 10 mg/kg orally twice daily, but its use has diminished owing to variable oral pharmacokinetics (Bryant et al., 2000). Minocycline is increasingly used as it is well absorbed after oral administration, well tolerated, and clinically effective at a dosage of 4 mg/kg orally twice daily (Schnabel et al., 2012).

Chloramphenicol

Chloramphenicol is highly lipophilic, is widely distributed to the tissues, and reaches high intracellular concentrations. Chloramphenicol has a wide spectrum of action, including against Gram-positive and Gram-negative

bacteria, and also rickettsia and anaerobes. The use of chloramphenicol in horses with enterocolitis is primarily directed at clostridial organisms, but some *Salmonella* isolates are also sensitive to this drug. Chloramphenicol is a time-dependent drug and, because of its short half-life in horses, it must be administered frequently to maintain adequate tissue concentrations. It is administered to horses at 50 mg/kg orally every 6 h (Gronwall et al., 1986). Chloramphenicol toxicity is rare, but when it occurs it is associated with reversible bone marrow suppression or irreversible aplastic anemia. Re-evaluation of the association between chloramphenicol administration and the development of aplastic anemia in humans has suggested that the incidence of this complication is extremely low (1 in 3 million to 1 in 20 million) (Issaragrisil, 2003; Isenberg, 2003; Wiholm et al., 1998). Despite this evidence, chloramphenicol may not be used in food animals (Fitzpatrick, 1990) and thorough client education is indicated when dispensing this drug. Clients should be advised to avoid exposure to the drug by inhalation or through contact with mucous membranes. Florfenicol is a derivative of chloramphenicol that does not appear to carry the risk of inducing aplastic anemia in humans that has been associated with chloramphenicol (Davis et al., 2009). Although the pharmacokinetics of florfenicol in horses appear to be favorable, this drug has been associated with profound disruption of the gastrointestinal flora and the development of loose feces in horses. For this reason, the use of florfenicol in horses is not recommended (Dowling, 2001; McKellar & Varga, 1996).

Fluoroquinolones

Fluoroquinolones have a relatively broad spectrum, with excellent activity against Gram-negative organisms. Fluoroquinolones are bactericidal, and achieve higher concentrations in the tissues than in the serum. The fluoroquinolones are concentration-dependent antimicrobials, having peak concentration-dependent bactericidal effects and prolonged post-antibiotic effects similar to those of aminoglycosides. As a result, the fluoroquinolones can be given at relatively high doses at a decreased frequency. Toxicity is primarily manifested through adverse effects on cartilage maturation, resulting in a contraindication to their use in growing animals (Beluche et al., 1999; Egerbacher et al., 2001). Enrofloxacin is the most commonly used fluoroquinolone in the horse in the United States, while the related compound marbofloxacin is often used in other countries. Enrofloxacin is administered at 5 mg/kg IV or 7.5 mg/kg PO once daily (Boeckh et al., 2001; Haines et al., 2000; Kaartinen et al., 1997; Giguere et al., 1996). The fluoroquinolones are primarily indicated in horses with enterocolitis caused by salmonellosis, as their high intracellular concentrations may lead to greater efficacy against this intracellular pathogen. Marbofloxacin is another fluoroquinolone approved for use in animals, and although not typically used in the United States, has favorable pharmacokinetics when administered at 2 mg/kg IV every 24 h and is used in horses and foals in other countries (Endo et al., 2015; Peyrou et al., 2004; Bousquet-Melou et al., 2002).

Metronidazole

Metronidazole demonstrates selective toxicity against anaerobic bacteria and microaerophilic organisms owing to its ability to induce an oxidative state within the normally reductive intracellular environment of these organisms. Metronidazole is administered in an inactive form but, after entering the target organism, it is reduced to reactive intermediates that interact with and damage cellular components, resulting in cytotoxicity. Metronidazole is effective against most anaerobes of veterinary importance, with the clostridial organisms being of greatest concern in enterocolitis (McGorum et al., 1998). Metronidazole is effective against most clostridial strains identified from horses with enterocolitis, but resistant strains have been reported (Jang et al., 1997). Metronidazole is typically administered at a dosage of 15 mg/kg orally every 8 h; it may also be administered per rectum or intravenously in horses with enterogastric reflux (Garber et al., 1993; Steinman et al., 2000; Britzi et al., 2010). The cost of the intravenous form is typically prohibitive in mature horses. This drug will occasionally cause inappetance at higher dosage rates, which resolves with discontinuation of therapy. Administration of metronidazole at higher dosages has been associated with hepatotoxicity and evidence of peripheral neurotoxicity, suggesting that this drug has a narrow margin of safety in horses (White et al., 1996).

Probiotics/Prebiotics

Restoration of the microbial flora of the gastrointestinal tract has been shown in many species to aid in the resolution of colitis. This is most readily accomplished by the administration of live beneficial enteric organisms. These organisms are termed probiotics, which have been defined as live microbial feed supplements that are beneficial to health (Fooks & Gibson, 2002). A broader concept is that of "biotherapeutic agents," which have been defined as living microorganisms used either to prevent or to treat diseases by interacting with the natural microecology of the host (Elmer & McFarland, 2001). Much of the research regarding probiotics has been performed in other species, and the types of organisms included in equine probiotics are generally the same as those that have been administered to humans. As a result, it is not clear that the organisms present in many equine probiotics (*Lactobacillus*, *Bifidobacterium*, *Enterococcus*) are necessarily the most relevant to the equine gastrointestinal flora. The fact that probiotics are marketed as feed supplements also means that there is no requirement

regarding the demonstration of efficacy of these products; therefore, any label claims of efficacy should be viewed with caution. This concern is reinforced by the disappointing results of the few trials that have examined the effects of probiotics in equine salmonellosis or foal diarrhea (Kim et al., 2001; Parraga et al., 1997; Schoster et al., 2015, 2016; John et al., 2015; Weese & Rousseau, 2005); Further work is clearly required to define better the types of organisms most likely to be beneficial in equine gastrointestinal disorders.

Interest in this area has focused on the administration of beneficial yeasts to horses with colitis, based on the promising reports regarding this type of therapy in humans with clostridial diarrhea (Cremonini et al., 2002; Surawicz, 2008; Czerucka et al., 2007). The organism with the most apparent promise is *Saccharomyces boulardii*, which has been demonstrated to produce a protease that exerts a proteolytic activity against the *C. difficile* toxin B molecule. *S. boulardii* also impairs the ability of *C. difficile* toxins A and B to bind to the intestinal mucosa and inhibits the pathogenic effect of both toxins on colonic epithelial cells (Czerucka & Rampal, 2002). Additional protective benefits of *S. boulardii* have been demonstrated in animal studies with *Salmonella typhimurium* and enteropathogenic *Escherichia coli*, although the mechanisms responsible for these effects are not well defined (Czerucka & Rampal, 2002). The safety profile of *S. boulardii* therapy in humans is very good, with the only concern being rare reports of *S. boulardii* fungemia in immunocompromised patients (Lherm et al., 2002; Riquelme et al., 2003). For this reason, *S. boulardii* should not be administered to equine patients with severe neutropenia. A study using 25 g of lyophilized *S. boulardii* PO every 12 h reported that the severity and duration of gastrointestinal disease were significantly decreased in horses receiving this treatment compared with placebo (Desrochers et al., 2005). A more recent study found no significant difference between *S. boulardii*-treated and untreated controls in the duration of diarrhea, normalization of clinical parameters, normalization of clinicopathologic abnormalities, or survival (Boyle et al., 2013).

An alternative means of restoring the normal gastrointestinal flora is the provision of nondigestible oligosaccharides as a "prebiotic." The concept behind prebiotics is that an insoluble fiber that selects for, and stimulates the growth of, beneficial microorganisms in the large intestine can change the microflora to a healthy composition and exert beneficial effects on the host (Bengmark & Gil, 2006). The substance most studied as a prebiotic is germinated barley feedstuff, which is generated in the brewing industry as a by-product of the brewing process. Germinated barley feedstuff has been shown to have anti-inflammatory effects in animal models of colitis, with one study reporting decreased gastrointestinal and systemic inflammation and also decreased mucosal injury in association with increased levels of the beneficial short-chain fatty acid butyrate (Kanauchi et al., 2003). A similar study demonstrated a superior effect of germinated barley feedstuff, similar to the beneficial effect associated with vancomycin or metronidazole administration, compared with a probiotic consisting of *Lactobacillus* and *C. butyricum* organisms, which had no demonstrable effect (Fukuda et al., 2002). Dried germinated barley feedstuff is widely used in dairy cattle feeds and is a component of some commercial horse feeds. Germinated barley feedstuff appears to be a safe feed supplement, although no reports are available regarding its feeding in the horse. The author has utilized fresh and frozen germinated barley feedstuff in horses with colitis at an empirical dosage rate of 0.2–0.45 kg 3–4 times daily, with variable clinical results. Further work is required to determine the efficacy of this treatment in equine enterocolitis and to identify the most appropriate dosage of germinated barley feedstuff for feeding to horses with diarrhea.

Gastrointestinal Protectants and Adsorbents

An additional means of limiting gastrointestinal inflammation is the administration by the enteral route of products that may exert anti-inflammatory effects on the mucosa or that impair the activity of the enteric pathogens or their toxins (Tillotson & Traub-Dargatz, 2003). Bismuth subsalicylate has been used as an agent to protect the gastrointestinal mucosa and decrease mucosal inflammation, but there is little evidence that it has a significant effect on secretory diarrhea in any species (Aranda-Michel & Giannella, 1999; Chowdhury et al., 2001). This compound has been reported to stimulate intestinal absorption of sodium and water and to have anti-inflammatory and antibacterial effects, including direct binding of bacterial toxins (Aranda-Michel & Giannella, 1999. Bismuth subsalicylate is widely regarded as a safe over-the-counter antidiarrheal, but there are reports of toxicity associated with overdosage in humans (Gordon et al., 1995; Vernace et al., 1994). Recommended dosages range from 0.5 to 4 mL/kg every 4–6 h (Tillotson & Traub-Dargatz, 2003).

The adsorptive substance di-tri-octahedral (DTO) smectite (Biosponge™, Platinum Performance, Los Olivos, CA, USA) is widely used in the treatment of equine colitis. This product, and the related dioctahedral smectite, have been shown to bind *C. difficile* toxins A and B, and *C. perfringens* enterotoxins *in vitro* (Martirosian et al., 1998; Weese et al., 2003; Lawler et al., 2008). Several studies in human medicine have demonstrated a benefit associated with smectite administration in the management of diarrhea (Guarino et al., 2009; Das et al., 2015). One equine study reported that outcome was substantially improved in clostridial enterocolitis

with the use of DTO smectite (Neelley & Herthel, 2000). A second equine study reported that administration of DTO smectite to colic patients with disease of the large intestine was associated with a reduction in the incidence of early postoperative diarrhea (Hassel et al., 2009). The recommended dosage of DTO smectite is 1.4 kg of powder in water via nasogastric tube, followed by 0.45 kg every 4–6 h. A paste formulation is also available.

Surgery

Abdominal exploratory surgery is not required in most cases of enteritis and colitis, but there are cases where it may be indicated. The most common indication for surgical exploration is persistent severe abdominal pain. Most horses with enteritis and colitis do not exhibit severe colic signs, and those that do show discomfort often cease to have pain after resolution of gastrointestinal distention secondary to gastric decompression (e.g., in horses with DPJ) or the onset of diarrhea. The persistence of severe pain is a strong indication that the animal may be suffering from a more severe condition that may require surgical correction. Additional diagnostic information may be provided from rectal examination and abdominal ultrasonography, as malpositioning or severe distention of the gastrointestinal viscera is suggestive of more than an inflammatory enteritis or colitis. Some reports have indicated that outcome was worsened for patients with DPJ undergoing abdominal exploratory surgery (Johnston & Morris, 1987; Underwood et al., 2008). This outcome may be related to the fact that only the more severely affected horses were likely to undergo surgery. Other studies have reported that surgical exploration is not associated with worsened outcome (Seahorn et al., 1992), and it appears clinically that some horses with DPJ may benefit from surgical decompression, with shortened duration of enterogastric reflux and discomfort, although the literature is also conflicting on this point (Underwood et al., 2008).

Specific Diseases

Duodenitis-proximal Jejunitis (Anterior Enteritis)

As no specific etiologic agent has been identified in this disease syndrome, no specific therapy can be prescribed. Aggressive supportive therapy is indicated, consisting of ongoing gastric decompression, intravenous fluids, anti-inflammatory drugs, and analgesics. The treatment of horses with DPJ is primarily medical in nature, requiring frequent (every 1–2 h) gastric decompression via an indwelling nasogastric tube in order to prevent gastric rupture and reduce the distention of the small intestine. The volume of fluid lost in the form of reflux can be large, with up to 8–16 L being lost every 2 h in severe cases, and enterogastric reflux can persist for as long as 5–7 days. Owing to these substantial fluid losses, combined with the inability to ingest water, affected horses are typically severely dehydrated and require aggressive intravenous fluid therapy in order to correct their dehydration and replace ongoing losses. The use of colloids in severely affected horses may aid in rapid volume expansion and also the retention of fluid within the vasculature. Hyponatremia, hypochloremia, hypokalemia, hypocalcemia, and acid–base disturbances may all occur in affected animals and should be addressed when formulating a plan for fluid therapy. Owing to the inability of affected animals to ingest food for prolonged periods of time, serious consideration should be given to early initiation of parenteral nutritional support in order to minimize the severity of the inevitable negative energy balance (McKenzie, 2015).

Additional therapies may include antimicrobials, prokinetic therapy, and surgical bypass procedures. The efficacy of antimicrobial therapy in this condition is unclear, as no specific bacterial pathogen has been associated with this disease syndrome. Nevertheless, many horses with DPJ receive antimicrobials because of the potential for a compromised gastrointestinal mucosal barrier and the risk of bacterial translocation from the gastrointestinal lumen to the bloodstream. Many of these patients are febrile and/or have an increased total peripheral white blood cell count; these abnormalities can represent additional indications for antimicrobial therapy. Owing to the potential involvement of *C. difficile*, treatment with intravenous penicillin or metronidazole per rectum appears reasonable (Davis & Pusterla, 2015). Prokinetic therapy is frequently utilized in cases of DPJ, although the ability of the inflamed small intestine to respond to these agents is unclear. Lidocaine is reported to be the most commonly used prokinetic in these cases (Van Hoogmoed et al., 2004). Severely affected animals that are poorly responsive to medical therapy should undergo surgical exploration to rule out strangulation obstruction or other surgical lesions. Bypass procedures can be used in DPJ to allow for the accumulated fluid to drain from the stomach and proximal small intestine into the distal small intestine or cecum; these include gastroduodenostomy and duodenocecostomy (White et al., 1987; Huskamp, 1985). If selected, the created stoma should be made by suturing the seromuscular layer so that closure by healing occurs within a few days to weeks.

Salmonellosis

The treatment of equine salmonellosis is primarily supportive. Intravenous fluid therapy is usually required because of the severe fluid losses associated with the profuse diarrhea that occurs in many of these horses. Colloid therapy may also be required for the systemic hypotension and enteric protein loss secondary to severe gastrointestinal inflammation. Anti-inflammatory therapy primarily consists of flunixin meglumine, although

the concurrent administration of polymyxin B may be of benefit because of the possibility of endotoxemia in these patients. Severely affected horses are often inappetant and require nutritional support. The use of gastrointestinal protectants is not well investigated in equine salmonellosis, and their use is not strongly indicated in these patients. Probiotic therapy has proven to have little or no efficacy in the prevention of *Salmonella* shedding in hospitalized equine patients (Kim et al., 2001; Parraga et al., 1997). Although *S. boulardii* has been reported to have beneficial effects in an animal model of salmonellosis, this has not yet been investigated in the horse (Czerucka & Rampal, 2002).

Antimicrobial therapy is controversial in equine salmonellosis, and many clinicians elect not to utilize antimicrobials in these cases because of concerns regarding lack of efficacy and the development of antimicrobial resistance. Antimicrobial resistance is common in the *Salmonella* organisms associated with enterocolitis, especially to the beta-lactams, tetracylines, trimethoprim, and sulfa drugs (Van Duijkeren et al., 2002). The intracellular localization of *Salmonella* organisms limits their susceptibility to antimicrobials that fail to penetrate the cell wall, such as the aminoglycosides. *In vivo* susceptibility is increased to those antimicrobials that are able to reach therapeutic levels intracellularly, such as the fluoroquinolones and chloramphenicol, and these drugs are widely used in humans with salmonellosis (Mandal et al., 2004). Cephalosporins are also frequently used in humans with salmonellosis, and the third-generation cephalosporin ceftiofur has been reported to be effective in the treatment of calves with salmonellosis (Fecteau et al., 2003). Many equine and domestic animal isolates are reported to be sensitive to ceftiofur and the fluoroquinolones, with slightly higher rates of resistance to chloramphenicol (Seyfarth et al., 1997; Van Duijkeren et al., 2002). In the present author's opinion, the treatment with appropriate antimicrobials of equine patients suffering from salmonellosis is reasonable, despite the concerns regarding this practice, as it may result in an improved chance of survival. Given the presence of multiresistant strains of *Salmonella*, it is important to determine the antimicrobial sensitivity pattern of any equine isolates and utilize this as a guide to ongoing therapy in the individual patient or concurrently affected individuals.

Clostridial Enterocolitis

Supportive therapy with intravenous fluids to correct fluid deficits and replace ongoing fluid losses is often required in horses with clostridial enterocolitis. Colloid therapy may also be indicated in more severely affected horses, because of the loss of plasma proteins into the gastrointestinal lumen secondary to severe intestinal inflammation. Additional supportive therapy with anti-inflammatory drugs is generally indicated, with flunixin meglumine being the most commonly utilized therapy of this type. The rationale for using anti-inflammatory drugs is to modulate intestinal inflammation and also the systemic response to possible endotoxin exposure via the inflamed gastrointestinal mucosa. Polymyxin B may also be a useful therapy in clostridial enterocolitis owing to the potential for endotoxin exposure secondary to increase intestinal permeability. DTO smectite has been demonstrated to bind clostridial toxins *in vitro*, and is reported to be effective in the treatment of equine clostridial enterocolitis (Neelley & Herthel, 2000; Hassel et al., 2009; Lawler et al., 2008; Weese et al., 2003). The use of *S. boulardii* as a probiotic appears rational because of its reported ability to interfere with the activity of the clostridial toxins and inhibit the binding of clostridial organisms to the gastrointestinal mucosa, although published reports differ with regard to the efficacy of this therapy (Desrochers et al., 2005; Boyle et al., 2013). Most horses with clostridial enterocolitis will continue to eat, and should be provided with free-choice hay, but nutritional support may be required in cases where the patient is inappetant. If required, nutritional support may best be delivered parenterally because of the risks associated with enteral feeding of liquid diets.

Specific therapy with antimicrobials is clearly indicated in horses with clostridial enterocolitis, despite the fact that this condition may arise secondary to antimicrobial therapy. Metronidazole is the most widely used antimicrobial in clostridial enterocolitis, as it is broadly effective against clostridial organisms and has few side effects in horses. Because of the possibility of metronidazole resistance (Jang et al., 1997; Magdesian, 2003), other antimicrobials should be considered as primary or adjunctive therapies in horses responding poorly to metronidazole therapy. These drugs include vancomycin and chloramphenicol, as resistance to these drugs is rarely present (Pirs et al., 2013). Vancomycin is widely used for the treatment of clostridial diarrhea in humans, but is rarely (and arguably should not be) used in the horse because of the potential for further alteration of the gastrointestinal flora and the desire to limit the development of resistant strains of bacteria, particularly with regard to organisms of concern in human health. Chloramphenicol is rarely used in horses because of concerns regarding human exposure, but has come into wider use in the past decade. The author has found it to be a useful drug in equine clostridial enterocolitis cases that are poorly responsive to metronidazole therapy. Prevention of clostridial enterocolitis is primarily by means of biosecurity and infection control, along with avoidance of unnecessary antimicrobial therapy. Certain antimicrobials, such as trimethoprim/sulfamethoxazole and ceftiofur, have been shown to cause profound alterations to the fecal microbiota that may

allow for proliferation of clostridial organisms (Costa et al., 2015; Harlow et al., 2013). At present in the United States, there is a provisionally licensed *C. perfringens* vaccine available for administration to mares on a state-by-state basis (Mehdizadeh Gohari et al., 2016; Timoney et al., 2005), and there is ongoing work related to development of *C. difficile* vaccines for use in horses and other species.

Antimicrobial-associated Diarrhea

If antimicrobial-associated diarrhea is suspected, the first intervention should be withdrawal of the offending antimicrobial, if medically appropriate, or switching to an antimicrobial that is less likely to disturb the enteric microbiota (McGorum & Pirie, 2010). If the involvement of an enteric pathogen, such as *C. difficile*, is suspected or confirmed, then appropriate antimicrobial therapy should be instituted. Beyond these interventions, treatment of affected horses is typically supportive in nature and similar to that for other types of colitis, consisting of supportive fluid therapy, potentially including colloids, and anti-inflammatory therapy as appropriate. Other potentially useful treatments include DTO smectite and probiotics, as already discussed.

Equine Neorickettsiosis

Because of the potentially fulminant nature of this disease, aggressive supportive therapy with intravenous fluids is often required. Colloids are also indicated in patients with signs of shock or enteric protein loss. Anti-inflammatory therapy typically consists of flunixin meglumine. *Neorickettsia risticii* is highly sensitive to the tetracyclines, and these drugs are the treatment of choice in this disease. The most widely utilized tetracycline for treatment of this disease is oxytetracycline, typically used at 8 mg/kg IV twice daily, and this treatment is generally efficacious (Mulville, 1991; Palmer et al., 1988, 1992). Doxycycline is reported to be the drug of choice for the treatment of ehrlichial diseases in humans and small animals (Papich, 2003). Although there are no studies reporting the efficacy of doxycycline in equine monocytic ehrlichiosis, efficacy has been demonstrated in a murine model of this disease (Rikihisa & Jiang, 1989). Although doxycycline has been used for the treatment of affected horses with anecdotally reported efficacy, concerns over its poor oral bioavailability have led to the use of minocycline instead (Winther et al., 2011). Minocycline is administered at 4 mg/kg orally twice daily (Schnabel et al., 2012). The efficacy of minocycline was also demonstrated in the murine model of this disease (Rikihisa & Jiang, 1989).

Fatal outcomes associated with this disease are often a result of secondary complications, especially laminitis, as the colitis usually resolves with tetracycline therapy. Prevention of these complications is difficult after the development of the disease. Therefore, the prevention of complications is best achieved by prevention of clinical disease. The prevention of equine neorickettsiosis is challenging, however, as the only vaccines available are killed bacterins, which do not induce a consistent or entirely protective immune response (Dutta et al., 1998). These vaccines also contain only a single strain of the organism, even though several pathogenic strains have been identified (Vemulapalli et al., 1995; Wen et al., 1995; Dutta et al., 1998). It is widely believed that vaccination, although not entirely protective (Vemulapalli et al., 1995), does lessen the severity of clinical illness associated with infection and may decrease the incidence of secondary complications such as laminitis, although one report suggests that this is not the case (Atwill & Mohammed, 1996). Vaccination in endemic areas is generally recommended, with annual boosters administered in the early spring and early to mid-summer period. The characterization of *N. risticii* antigens may allow for the development of vaccines that provide cross-strain protection (Biswas et al., 1998; Vemulapalli et al., 1998).

Viral Enterocolitis

Rotaviral enterocolitis is ultimately self-limiting in most cases, and treatment is symptomatic and supportive in nature, as there is no specific treatment targeting the etiologic agent. Intravenous fluid therapy is often indicated owing to substantial fluid losses, and balanced electrolyte replacement solutions are most effective given the frequent development of hyponatremia and hypochloremia. Enteral rest of 24–72 h duration can be useful, as the damage to the intestinal microvilli impairs the foal's ability to digest lactose in milk. Provision of enteral rest requires that the foal be provided with fluids and nutrition intravenously; this may be accomplished by separating the mare and foal by placement of a barrier within the stall or the use of a stall with a separate area provided for confining the foal. If the foal is to be left with the mare, then a muzzle must be placed on the foal to prevent nursing. The provision of fluid therapy to foals that are housed with their mares is challenging, however, but may be facilitated by using a gate or other device to separate the mare from the foal within the stall in order to prevent tangling and breakage of the fluid lines. If enteral rest is not possible, then the foal can be administered lactase enzyme orally (Lactaid, McNeil Nutritionals, McNeil-PPC, Ft. Washington, PA, USA) at the rate of 1–2 tablets (3000–6000 FCC Units lactase) every 2–6 h to aid digestion of the ingested lactose (Magdesian, 2005). There is no indication for antimicrobial therapy in this condition, and anti-inflammatory therapy is rarely needed or indicated. Control of rotaviral diarrhea outbreaks can be challenging, especially in crowded environments, owing to the highly contagious nature of the virus, its persistence in the environment,

and its resistance to disinfectants (Bailey et al., 2013). Prevention can be facilitated by the use of maternal vaccination, which has been associated with a reduction in the frequency and severity of rotaviral diarrhea on endemic farms, and a conditionally licensed commercial vaccine is available for provisional use (Equine Rotavirus Vaccine, Zoetis, Kalamazoo, MI, USA). There are no specific treatments for coronaviral infections; therefore, treatment is supportive in nature and similar to that for other causes of enterocolitis.

Intestinal Parasitism

As the primary intestinal parasites of current concern in equine enterocolitis are cyathostomes, treatment protocols should be targeted toward these organisms (Love et al., 1999). Treatment of cyathostominosis is complicated by the difficulty associated with killing of the encysted hypobiotic stages (L3, L4) of these organisms (Xiao et al., 1994). Fenbendazole (7.5 mg/kg PO once daily for 5 days) and moxidectin (0.4 mg/kg PO once) have been demonstrated to have moderate to high efficacy in the elimination of encysted cyathostomes, whereas ivermectin is ineffective (Xiao et al., 1994; Duncan et al., 1998; Corning, 2009). Although a 5 day course of fenbendazole therapy is commonly used in the treatment of equine cyathostominosis, and appears to be clinically effective, resistance to fenbendazole is increasingly common and moxidectin may have greater efficacy. The use of fenbendazole as a larvicidal therapy has also been associated with severe intestinal inflammation, whereas moxidectin treatment is associated with only mild local inflammation (Nielsen et al., 2013, 2015). Because of this possibility of increased intestinal inflammation associated with the death of encysted small strongyles after anthelmintic administration, some clinicians treat the patient concurrently with corticosteroids, using either dexamethasone or prednisolone (Church et al., 1986; Atherton et al., 2009; Kaikkonen et al., 2014). More severely affected animals may develop profuse watery diarrhea and protein-losing enteropathy, and may require intravenous fluid therapy, including colloid administration.

Protozoal Enterocolitis

The treatment of horses with cryptosporidial infections is entirely supportive as no specific therapies are available. Fortunately, this disease is ultimately self-limiting, although fatalities may occur secondary to dehydration and electrolyte derangements resulting from severe diarrhea. The profuse nature of the diarrhea in some animals may require aggressive intravenous fluid therapy, including colloid therapy. Enteral rest is typically indicated, as this may be useful in decreasing the volume of diarrhea by decreasing the osmotic load within the intestinal lumen. Nutritional support with partial parenteral nutrition is required in horses placed on enteral rest. Care should be taken in handling these horses, with strict isolation procedures maintained, as the organism is infectious and zoonotic (Konkle et al., 1997).

Equine Proliferative Enteropathy

The typical presentation of animals with equine proliferative enteropathy is one of unthriftiness, weight loss, hypoproteinemia, and peripheral edema. Diarrhea is not always present, and aggressive therapy is usually not indicated. Fluid imbalances and electrolyte disturbances may be present, but rapid administration of intravenous fluids will only cause hemodilution and exacerbation of the hypoproteinemia. The use of enteral fluids may not be appropriate, as the small intestinal dysfunction associated with this disease may impair fluid absorption. Conservative intravenous therapy is typically the most appropriate approach. The use of colloids is indicated in most cases of proliferative enteropathy to restore colloid oncotic pressure and aid in resolution of peripheral edema. Administration of hetastarch at a dosage of 5–10 mL/kg provides rapid colloidal effects and may slow the loss of plasma proteins. Equine plasma may be used as the sole colloid, at a dosage of 12–16 mL/kg, or may be used following hetastarch administration at a dosage of 8–12 mL/kg. Plasma therapy provides both albumin, for colloid effects, and globulins and other plasma constituents that may have been lost. Repeated doses of colloids may be required, as healing of the intestine may be gradual, resulting in ongoing losses of plasma protein.

Macrolides were the first drugs to be used for the treatment of horses with this disease, primarily consisting of erythromycin, often in combination with rifampin (Schumacher et al., 2000; Bihr, 2003; Lavoie et al., 2000). It is not clear that rifampin is required for the treatment of proliferative enteropathy, and macrolides used alone are clinically effective. Clarithromycin is the macrolide most commonly used (Frazer, 2008). Although no studies have reported the sensitivity of *L. intracellularis* to chloramphenicol, this drug has also been successfully used in the treatment of equine proliferative enteropathy based upon its potential intracellular penetration and broad spectrum of action (Papich, 2003; Atherton & McKenzie, 2006; Frazer, 2008). Oxytetracycline, doxycycline, and minocycline have been successfully used in the treatment of equine proliferative enteropathy, with minocycline being most commonly used (Atherton & McKenzie, 2006; Frazer, 2008). Although complete recovery can require several weeks, the prognosis for survival with appropriate treatment is considered to be favorable, except in cases presenting with evidence of systemic inflammation (fever, complete blood count abnormalities). In those cases, the prognosis may be poor (Page et al., 2012, 2014a).

Although proliferative enteropathy is sporadic in nature, farms on which it occurs often have other cases within a short period of time (Page et al., 2014a). Testing of all animals on a farm may reveal high levels of seroprevalence, up to 100%, even though relatively small numbers of the young animals that have been exposed (10–11%) may develop clinical signs of disease (Page et al., 2015). One approach to the prevention of the disease relies upon the monitoring of at-risk young animals over time and early institution of antimicrobial therapy when hypoproteinemia and/or hypoalbuminemia are detected, preferably after confirmation using serology and/or PCR testing (Page et al., 2011, 2014a). An avirulent live *L. intracellularis* vaccine developed for use in pigs has been investigated and has shown promise in both experimental models and a field trial, and extra-label use of this vaccine may be useful in reducing the incidence of proliferative enteropathy on endemic farms (Pusterla et al., 2012; Nogradi et al., 2012).

NSAID-associated Right Dorsal Colitis

As horses with NSAID-associated right dorsal colitis can present with variable degrees of severity of disease, the aggressiveness of therapy required can vary widely. The most fundamental aspect of treatment is the cessation of NSAID therapy, to avoid further toxicity. This can be a major dilemma, as the initial problem requiring NSAID treatment is often unresolved, and withdrawal of the drug may result in increased patient discomfort. The provision of analgesia by other means is strongly indicated and opioids, lidocaine, and α_2-agonists may all be useful drugs in this setting. It may be tempting to transition affected horses to specific inhibitors of COX-2, such as firocoxib, which have less toxic potential in healthy animals (Cook et al., 2009b). Owing to the potentially important role of the products of COX-2 in the healing of injured intestinal and renal tissues, it may be more prudent to forego administration of any NSAID to affected animals (Davis, 2017). Additional therapy of horses with right dorsal colitis may include intravenous fluids to correct fluid deficits and provide maintenance support, and the use of colloids to attempt to correct the profound hypoproteinemia that can occur in this condition. Sucralfate (20–40 mg/kg orally every 6–8 h) has been used clinically in an attempt to facilitate healing of the colonic mucosa, as this drug demonstrated a protective effect in an experimental model of phenylbutazone toxicity (Geor et al., 1989). The use of synthetic analogs of prostaglandin E1 (misoprostol) has also been advocated for the treatment of this condition, as it may be able to restore mucosal blood flow and aid in the healing of the ulcerated mucosa (Davis, 2017). Unfortunately, the most common side effects of this drug are colic and diarrhea, which limit its use in horses already suffering from these problems. There have been concerns regarding the safety of misoprostol in pregnant mares, but no problems were observed in an experimental trial using mid-gestation mares (Jacobson et al., 2013).

The most useful medical management in many of these cases, especially the more chronic ones, is dietary management. This consists in the avoidance of long-stem roughage that may further irritate the colonic mucosa, and its replacement with a complete pelleted diet. Supplementation of the diet with vegetable oil (corn, canola, or safflower) has been proposed as a means of providing additional calories and linoleic acid to aid in mucosal healing (Magdesian, 2003; Cargile et al., 2004). Provision of nondigestible oligosaccharides may enhance the production of beneficial short-chain fatty acids that can aid in mucosal healing, and germinated barley feedstuff or psyllium may be used to achieve this effect (Magdesian, 2003; Kanauchi et al., 2003). Because of the often unrewarding response to medical therapy, however, surgical resection of the affected region of the colon may be indicated (Simmons et al., 1990; Lane et al., 2010). With early identification and appropriate treatment, the mortality rate associated with right dorsal colitis may be as low as 20% (Davis, 2017).

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Part VII

Colic in the Foal

31

Diagnosis of Colic in the Foal

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The clinical presentation of a foal with colic, with or without abdominal distention, is fairly common in equine practice (Mackinnon et al., 2013). Accurate diagnosis is critical for successful management of these conditions, which is challenging owing to the many different conditions that can result in colic in foals (Vatistas et al., 1996; Cable et al., 1997; Mackinnon et al., 2013) (Table 31.1). Further, it requires careful observation and consideration of a number of factors that are less important in adult horses with colic, such as the fact that different conditions are more likely to occur at different ages (e.g., newborn versus neonate versus weanling). Many of the diagnostic methods applicable to the adult horse with abdominal pain are not useful in the neonate, and conversely many techniques valuable in the neonate are not used in the adult (Bernard, 2004; Cohen & Chaffin, 1995).

Particularly challenging is the determination of the need for exploratory surgery. Although the decision often rests upon finding that gastrointestinal obstruction, when an unequivocal indication for surgery is present, it is often difficult to make this determination. Further, surgical exploration of the abdomen may be indicated in foals with severe distention associated with ileus and no physical obstruction ("functional obstruction"). A consideration of the risks of surgical complications versus the risk if no surgery is performed (persistent pain, adhesion formation, or gastrointestinal vascular compromise from distention, etc.) must be carefully considered. In the author's experience, if appropriate surgical facilities and staff are available, the foal with ileus, persistent pain, and moderate to severe distention warrants surgical intervention and decompression of the bowel, and clearly appears to benefit from the procedure, even if a physical obstruction is not present. If signs suggestive of physical obstruction are present, then surgical exploration of the abdomen is immediately required. Whereas older reports suggested a fairly poor survival rate for foals that had exploratory celiotomy, more recent reports indicate a much more favorable outcome (i.e., 73% short-term survival) (Mackinnon et al., 2013). The majority of foals with colic are treated medically, however (89% in one study) (Mackinnon et al., 2013).

No specific clinical examination findings unequivocally indicate that surgical versus medical treatment alone is indicated, and the synthesis of various diagnostic procedures is important in determining the correct treatment. The signalment and history of the foal are important considerations, in addition to information gained from physical examination, clinicopathologic test results, and various imaging modalities.

Signalment and History

The potential causes of colic are strongly influenced by the foal's age. Clinical signs resulting from congenital anomalies of the gastrointestinal tract are often noted in the first hours of life, while meconium obstruction results in colic usually within the first 24 h after birth. Colic and abdominal pain resulting from uroperitoneum are typically observed at 2–4 days of life. Colic resulting from other causes, such as gastric ulceration, intussusceptions, volvulus, and large colon displacements, can occur at any age, but appear to be more common in slightly older foals. Overo American Paint-to-overo breedings may result in foals with the "lethal white syndrome" (ileocolonic aganglionosis) (Hultgren, 1982), hence white foals presenting with colic and abdominal distention should prompt a discussion about the foals' breeding. Foaling history is also important, especially for neonates (e.g., <14 days of age). A history of a dystocia or assisted delivery might make fractured ribs or other foaling injuries more likely. Determining if meconium has been passed, or an enema given, and observation of normal urination are all important historical factors that the clinician should ascertain.

The Equine Acute Abdomen, Third Edition. Edited by Anthony T. Blikslager, Nathaniel A. White II, James N. Moore, and Tim S. Mair.

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Table 31.1 Causes of colic in the neonatal foal. Source: Modified from Cudd, 1990.

Stomach	
Pyloric stricture	Gastric ulceration
Gastric perforation	Gastric abscess
Gastric ulceration	Gastric foreign body
Small intestine	
Enteritis	Duodenal stenosis/obstruction
Volvulus	Bowel incarceration (hernia, mesenteric rent)
Peritonitis	Mesodiverticular band
Adhesions	Small intestinal displacement
Intussusception	Ovarian stalk obstruction of bowel
Infarction	Necrotizing enterocolitis
Impaction (foreign bodies, trychobezoars)	
Large and small colon	
Meconium impaction	Obstruction (bezoars)
Infarction	Ileocolonic aganglionosis
Colitis	Extraluminal obstruction (adhesions)
Colonic displacements	Intraluminal obstruction
Atresia coli/recti/ani	
Other	
Peritonitis	Ascites
Hemoperitoneum	Urinary tract disruption
Ovarian artery rupture	Rectal prolapse
Ruptured spleen	Acute hepatic necrosis
Fractured ribs	Blunt abdominal trauma

Physical Examination

A complete physical examination is imperative as many conditions such as sepsis or congenital abnormalities can lead to ileus, abdominal distention, and colic. The examination should begin with observation of the foal's behavior without restraint. This allows one to assess more clearly the severity of pain, and also the nature of how the pain is expressed. For example, foals with gastric ulceration tend to lie on their back with their legs folded (Figure 31.1), whereas foals that are kicking and standing in a "hump-backed" position (hind feet moved forward) are more likely to have a caudal impaction, and foals that stretch out (hind feet moved further backward than normal) may be straining to urinate. This short period of observation also allows the clinician to assess any other signs, such as mentation abnormalities, possible seizures (which can be mistaken for colic), or musculoskeletal injuries.

Evaluation of gastrointestinal pain is more difficult in foals than mature horses. Whether foals are truly less able or willing to tolerate pain, or if there is some underlying physiologic mechanism, it is clear that foals express pain much more willingly than adults. What would seem to be minor issues can lead to vigorous expressions of pain such as kicking the abdomen, or throwing themselves down and rolling; foals are not stoic. This makes interpreting pain in the foal somewhat challenging, and different from that in the adult, although this should not be interpreted to mean that the pain is not significant or can be ignored. In foals that required surgery, pain was considered more severe and persistent than in those that did not (Mackinnon et al., 2013). Using other parameters of the physical examination, such as gastrointestinal sounds, abdominal distention, and imaging, will aid the clinician in more accurately interpreting the significance of the pain.

The initial examination should be directed at determining the nature and extent of all physiologic abnormalities, assessing gastrointestinal patency, ruling out sepsis, and determining the adequacy of passive transfer of immunoglobulins. A complete blood cell count and serum biochemistry profile should be completed on all foals with colic, and a blood culture performed on

Figure 31.1 A foal lying in a position commonly associated with gastric ulceration.

neonates (e.g., <14 days of age). Abdominal circumference, presence of ascites, cardiovascular and respiratory system function, presence of congenital defects, passage of stool, and urinary tract integrity should all be evaluated.

Vital parameters should always be determined and are key in establishing the foal's overall physiologic status. Heart rates tend to be variable in foals with colic, and are highly influenced by the foal's response to pain, and also potential comorbidities of shock, dehydration, sepsis, or diarrhea. Hence heart rate is not as valuable an aid in determining prognosis in foals as it is in adults, although persistent high heart rates are associated with more severe gastrointestinal pathologies. Increased respiratory rate is often found and may simply be a response to pain, but could also represent pneumonia, pleural effusion, or diaphragmatic hernia. Observation of respiratory movement and palpation of the ribs are indicated to determine if rib fractures are present.

As in adults, passing a nasogastric tube is important for both diagnostic and therapeutic purposes. Recovery of reflux or gas associated with a reduction in heart rate and observed pain suggests that gastric distention was contributing to the colic; this could arise from small intestinal or gastric outflow obstruction, in which case the reflux would persist. The volume of reflux that is considered excessive is difficult to define, owing to the wide range of foal sizes, but more than 250 mL of reflux in a neonate would be cause for concern. If gastric distention is present and severe, then passing a nasal gastric tube can be difficult, given the small size and soft consistency of tubes used for small foals. The author has overcome this problem by carefully using a small endoscope to enter the stomach. Recovering gastric reflux in foals is sometimes difficult, and in one study several foals had gastric distention at surgery, but only two had gastric reflux present preoperatively (Adams et al., 1988).

Abdominal circumference can be measured with a cloth tape measure (Figure 31.2). Subsequent measurements to determine if the distention is progressing need to be made in the same location as the initial measurement. If abdominal distention exists, determining if it is the result of peritoneal or gastrointestinal accumulation of fluid or gas is key to the evaluation. Ascites or uroperitoneum can readily be confirmed by ultrasonography and, coupled with abdominal radiographs, this is of great value in assessing abdominal distention.

A digital rectal examination should be performed to determine if a meconium impaction is present. This can cause signs ranging from mild colic to complete obstruction. The absence of fecal passage or the presence of clear, clean mucus on the finger after a digital examination may suggest bowel atresia. The presence of diarrhea makes a diagnosis of enteritis fairly straightforward, but foals can have severe discomfort, ileus, and abdominal distention before passing abnormal stools. About 30% of foals eventually determined to have neonatal sepsis are presented with diarrhea. In addition, diarrhea can often accompany surgical conditions of the foal (Adams et al., 1988) (Figure 31.3).

The neonate with colic should also be evaluated thoroughly for metabolic derangements such as hypoglycemia, failure of passive transfer, and electrolyte disorders. Typically, the foal with a ruptured bladder is hyponatremic and hyperkalemic. Similar electrolyte

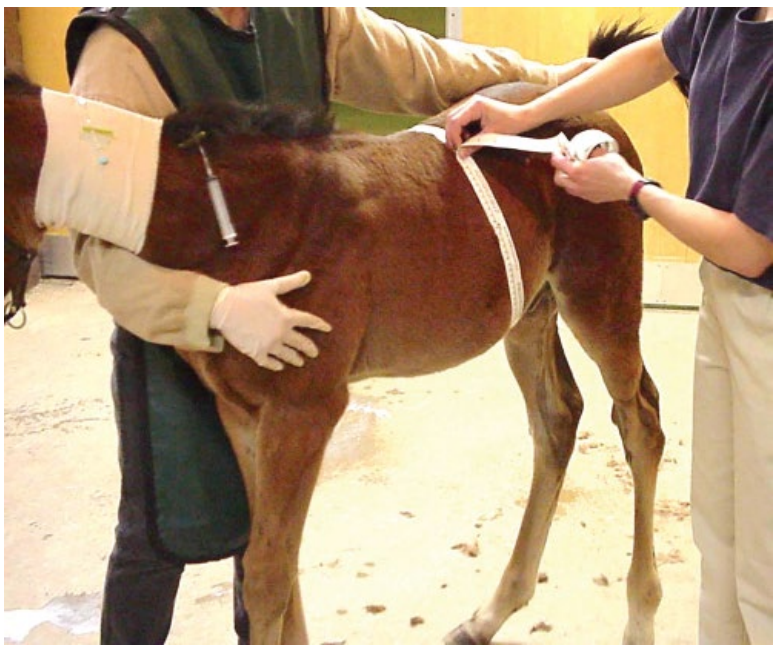

Figure 31.2 Demonstration of measurement of the abdominal circumference with a cloth tape. The hair or skin should be marked to ensure that sequential measurements are taken at the same location.

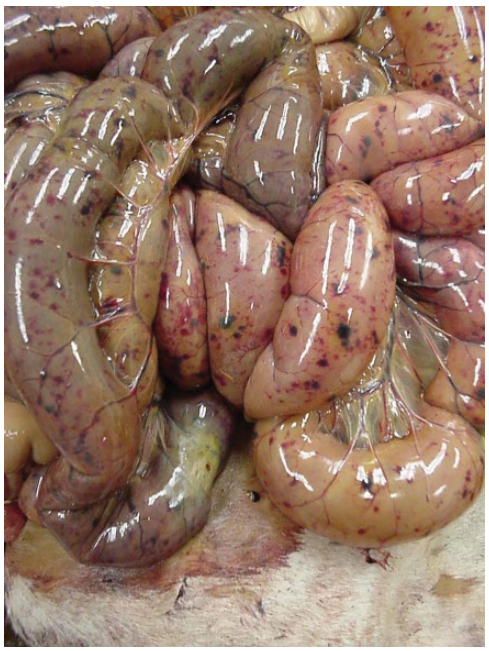

Figure 31.3 Severe diffuse enteritis in a foal.

changes can be seen in foals with septicemia, renal failure, and enteritis, necessitating additional diagnostic tests before surgical intervention is initiated. Typically, these tests include abdominal ultrasonography and abdominal fluid collection and evaluation.

Serum immunoglobulin G (IgG) concentrations should always be determined in the neonate with colic or abdominal distention to detect failure of passive transfer. Correction of this condition is critical to the overall management of such cases. Concentrations of IgG exceeding 800 mg/dL are considered normal, and several different methods, many of them stall-side, are available to determine serum IgG concentrations. It is also necessary to repeat the assessment of IgG concentration sequentially, and particularly postoperatively, as foals that are ill or nutritionally compromised, or have intestinal disease, can easily become hypoproteinemic and hypoglobulinemic. It is not uncommon in such foals that repeated treatment with plasma is necessary.

Ancillary Examination Techniques

Gastroendoscopy

Endoscopy of the proximal gastrointestinal tract is a useful technique in foals with signs of gastric or gastroduodenal ulceration (Figure 31.4). Signs such as colic, bruxism, excessive salivation, and abdominal pain should prompt gastroendoscopy. Numerous endoscopic systems are available, but in general a system with an insertion tube of 0.9 mm o.d. and 1.5 m working length is adequate to examine the esophagus, stomach, and proximal duodenum of most foals. The tissues are directly observed for ulceration.

Abdominocentesis

Abdominocentesis should be performed in the foal with caution, because enterocentesis is more likely to occur and to have more serious consequences in the neonate than in the adult horse (Tulleners, 1983). The very thin bowel wall of a neonate makes laceration by a needle possible, so if an abdominocentesis is performed, it should always be carried out with a blunt cannula. Even with a cannula, puncture of a distended bowel is possible,

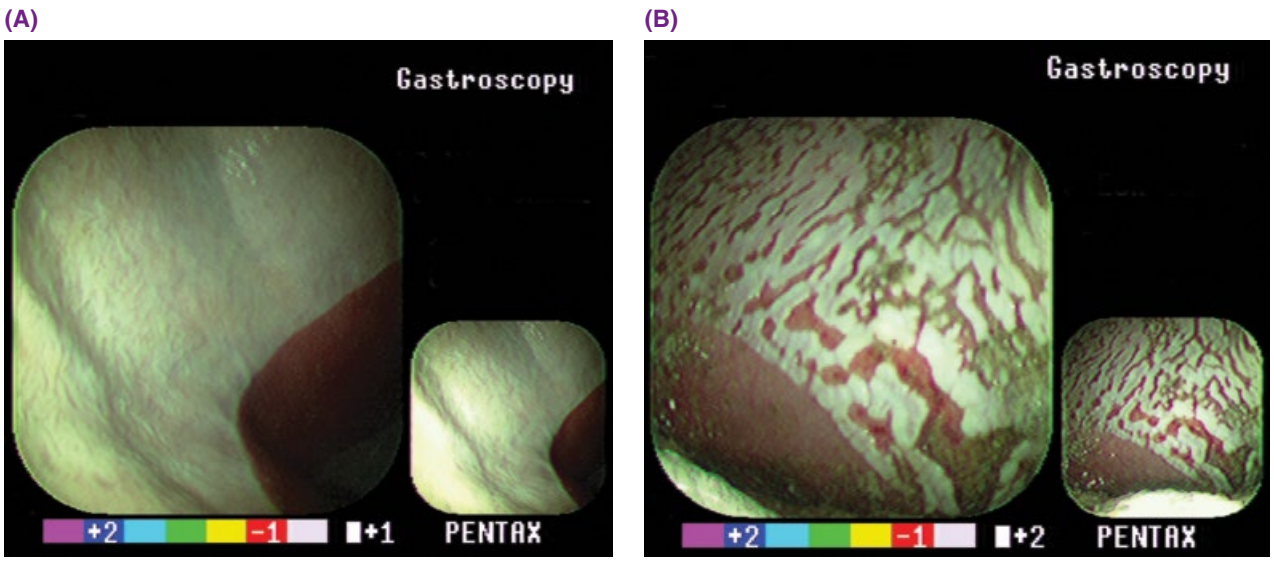

Figure 31.4 (A) Endoscopic appearance of the normal squamous and glandular linings in a neonate. The squamous lining is light pink and the glandular stomach lining is dark red. (B) A severe gastric glandular ulcer in a neonate.

but lacerations are less likely. If an enterocentesis occurs, contamination of the abdominal cavity is more likely to occur, because the very thin bowel wall of a foal does not seal after a needle puncture as readily as in adults. In addition, enterocentesis is more likely in the foal with a gas- or fluid-distended bowel. Information gained by radiography and ultrasound examination should aid the clinician in deciding if abdominocentesis is warranted. When these diagnostic aids are used, an abdominocentesis is often not necessary in order to make a decision for or against surgery. The ultrasound examination can detect large volumes of intraperitoneal fluid or localized pockets of fluid that can be retrieved, thus increasing the diagnostic yield and decreasing the risk of bowel penetration.

Analysis of abdominal fluid should include assessment of color and clarity, white blood cell count, total protein, and cytologic examination. Normal values for peritoneal fluid of the neonate are similar to those for adult horses; however, foals often have a slightly lower peritoneal fluid total protein concentration than adults owing to hypoproteinemia frequently being present in neonatal foals. Fluid that is serosanguinous uniformly throughout the collection suggests devitalized bowel. Increased intra-abdominal protein concentration and leukocyte count suggest intra-abdominal sepsis, which could be due to an abscess, umbilical remnant infection or abscessation, or generalized sepsis. In foals with abdominal distention and/or ascites, peritoneal fluid creatinine should be evaluated to determine if uroperitoneum is present. A ratio of peritoneal fluid to serum creatinine of >2 : 1 confirms uroperitoneum, which can arise from a ruptured bladder, necrotic urachus, or ruptured ureter. Blood can be recovered in cases of intra-abdominal hemorrhage or when the teat cannula punctures the spleen. In the case of bowel perforation or enterocentesis, cytologic evaluation of peritoneal fluid reveals feed material and a mixed population of bacteria, whereas intra-abdominal sepsis may result in the presence of bacteria and degenerative neutrophils.

If enterocentesis occurs during the abdominocentesis, the foal should be administered broad-spectrum antibiotics, preferably including metronidazole (10–15 mg/kg PO or IV q 6 h). Nonsteroidal anti-inflammatory drugs and heparin (40–50 IU/kg SC or IV q 6–8 h) may also be used, to help minimize the risk of intra-abdominal adhesions.

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32

Imaging of the Foal with Colic and Abdominal Distention

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Limited imaging techniques are available for the equine neonatal abdomen. However, these are important diagnostic modalities, providing important information in the overall evaluation of the foal with colic. These techniques include gastroendoscopy (discussed in detail in Chapter 22), abdominal radiography, and abdominal ultrasound (see Chapter 23). Abdominal magnetic resonance imaging (MRI) and computed tomography (CT) have been described in foals weighing up to approximately 300 lb (136 kg) (Fitz & Gerhards, 2005; Barba & Lepage, 2013), and CT has had very limited use in clinical cases (Beccati et al., 2016). However, at present, these imaging modalities have very limited applicability owing to difficulty of access to necessary equipment, particularly in an emergency situation.

Abdominal Radiography

Abdominal radiography is often very helpful in evaluating abdominal distention and colic in the neonate. Given the widespread availability of large-format digital plates and portable machines of higher power, abdominal radiography of the foal is no longer restricted to referral institutions. In one report, radiographic evaluation was proven correct in 25 of 26 cases in identifying the site of the lesion (Vatistas et al., 1996), and radiographic interpretation was correct in eight of 10 cases in another study (Adams et al., 1988). Although these are very small studies, the results are in alignment with clinical experience. Evaluating abdominal radiographs from foals requires some experience. A lateral view of the abdomen is routinely performed with the foal standing, although views of recumbent foals are often diagnostic. Usually, the abdomen can be imaged on one 14 × 17 inch cassette, and the approximate technique for the typical neonatal Thoroughbred foal is 85 kVp and 20 mAs, using a 10 : 1 focused grid and a focal film distance of 180 cm. These are guidelines only, and the technique may need to be modified based upon the specific equipment in use. The stomach is usually noted in the cranial central abdomen and is typically gas and fluid filled. Small intestinal distention with multiple erect and inverted U-shaped loops of bowel is consistent with obstructive disease (Figure 32.1), whereas ileus produces diffuse and mild small intestinal distention involving the entire length of the intestines (see Figure 23.5, Figure 23.37, and Figure 23.38 in Chapter 23). Gas shadows can be seen in the bowel wall in foals with necrotizing enterocolitis, but may be more easily observed via ultrasound. Large colon distention is often noted in foals with ileus, meconium impactions, large colon displacements (Figure 32.2), and atresia coli. Serial radiographs over time may help determine the significance of specific lesions. Abdominal CT has been used in one foal to image an intra-abdominal abscess (Barba & Lepage, 2013).

Contrast studies that can be performed to assess the gastrointestinal tract further include barium enemas and the upper gastrointestinal series (Figure 32.3). These should be performed after routine films have been taken to establish a radiographic technique. The technique should then be increased by 10% to compensate for the radiodense contrast material. To perform an upper gastrointestinal series, 5 mL/kg of barium sulfate suspension is administered by nasogastric tube after a 4 h fast. Serial radiographs are performed immediately after administration of the suspension, at 5, 15, and 30 min, and then at 2 h intervals until the contrast medium has reached the small colon. In a normal foal, contrast should be observed entering the duodenum after 15 min and the stomach should empty within 2 h. Duodenal strictures, and also generalized ileus, markedly delay gastric emptying. Radiographic findings consistent with mucosal erosion and ulceration can sometimes be identified. Filling defects of the stomach suggest gastric abscesses, foreign bodies, or masses. An upper gastrointestinal

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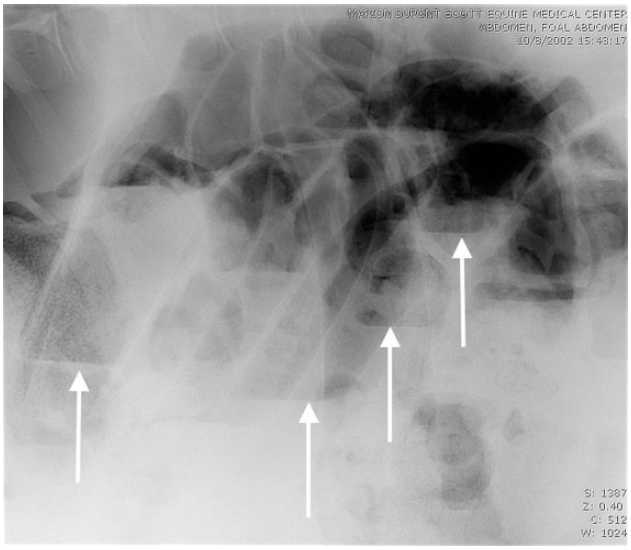

Figure 32.1 Abdominal radiographs of a foal with colic and abdominal distention demonstrating characteristic signs of small intestinal obstruction including inverted loops of distended bowel with multiple fluid lines at differing heights (arrows).

contrast study is contraindicated in the presence of severe small intestinal distention. The greatest value of this procedure lies in evaluating gastric emptying and the proximal duodenum for the presence of strictures. More distal lesions are difficult to interpret.

Barium enemas are useful to confirm an obstruction of the rectum or small colon. A well-lubricated enema tube should be passed gently into the rectum after evacuation of fecal material. Barium sulfate suspension (180 mL) is slowly infused while the anus is occluded around the tube. A radiograph of the caudal abdomen is performed immediately after instillation of the barium. Filling defects, obstructions such as meconium impactions, and atresia can be diagnosed with this method.

Ultrasonography

A 7.5 or 5 MHz scan head, preferably with a built-in standoff, is most useful for the evaluation of colic and abdominal distention in the neonate. The abdomen should be prepared by clipping the hair and applying ultrasound coupling gel, although alcohol also can be used. The examination is most productive if the foal is standing, because this allows the small intestine to drop to the ventral body wall. In a routine examination, the urachus, umbilical vein, umbilical arteries, bladder, peritoneum, and segments of the small intestine can be easily visualized via a ventral portal. Small intestinal segments can be examined and the thickness of the wall and the presence of distention identified. The normal small intestinal wall thickness should be 2–3 mm, and a bowel wall thickness >4 mm is abnormal, suggesting inflammation, cellular infiltration, or edema (Abraham et al., 2014) (Figure 32.4). The normal wall thickness of the large colon and cecum is approximately 2 mm (Abraham et al., 2014).

Suspicious areas can be compared with other segments of the bowel to determine the presence of focal thickening. Fluid filling, as is noted with diarrhea and enteritis, appears as round areas of bowel filled with composite fluid. Gas-distended bowel has a hyperechoic (echogenic) line at the surface of the bowel with little visualization within the lumen. Small focal areas of gas may sometimes be seen within the wall of the bowel in foals

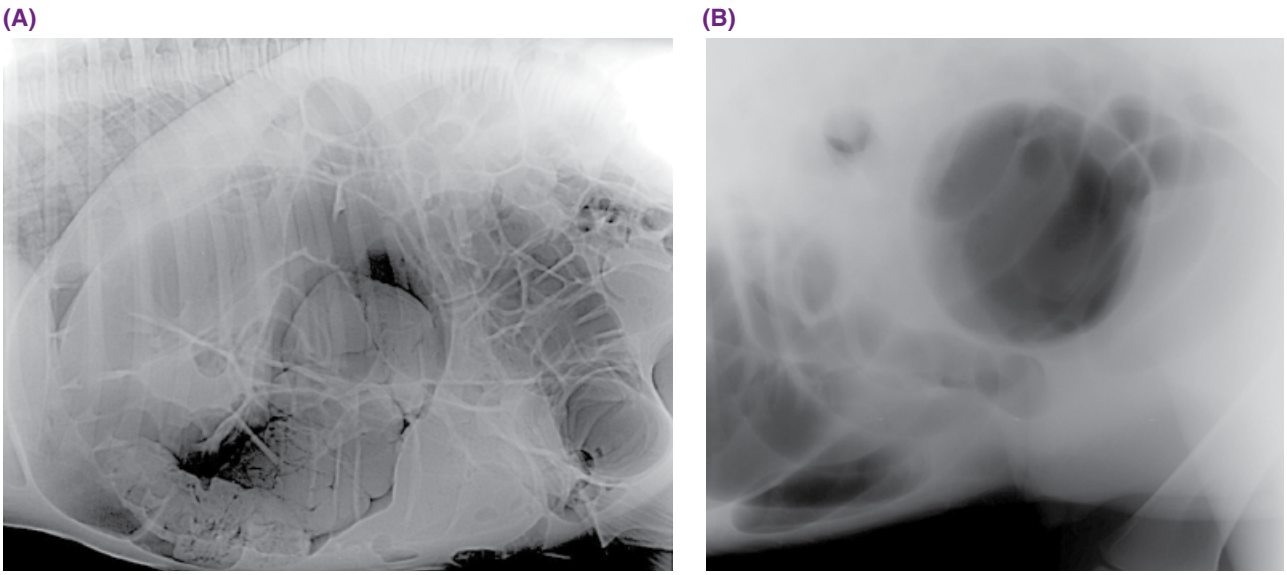

Figure 32.2 Abdominal radiographs of foals with colic and abdominal distention demonstrating characteristic signs of large colon obstruction **(A)** and large colon atresia **(B)**.

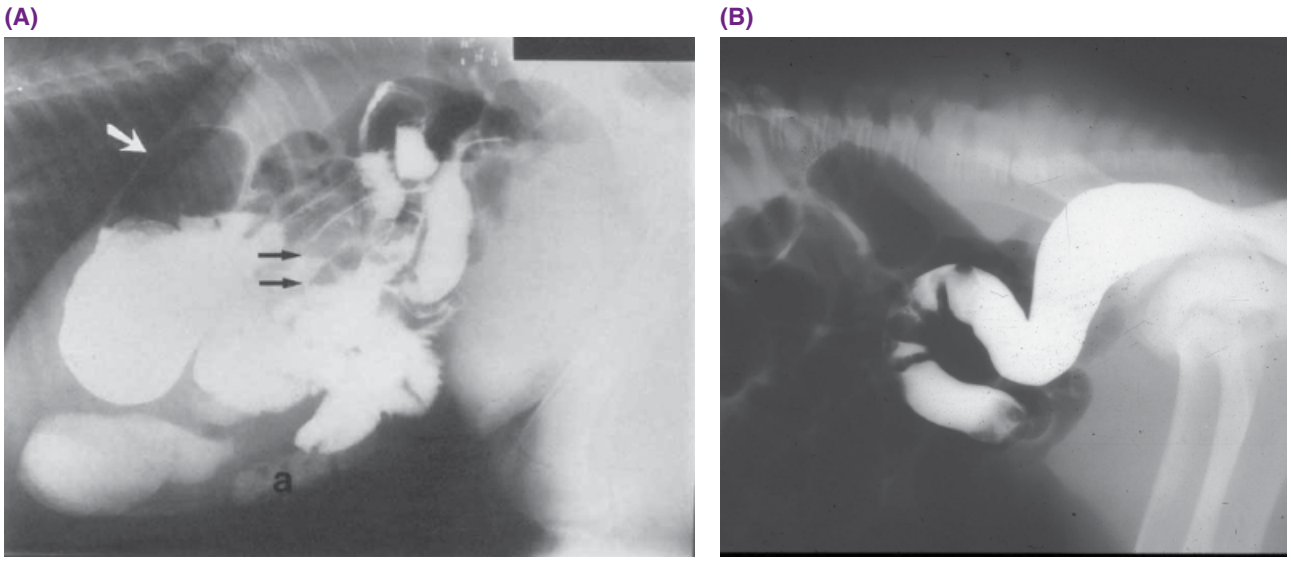

Figure 32.3 Barium contrast studies of the foal's stomach and jejunum 2 min after barium administration **(A)**, after a barium enema in a foal with colic and abdominal distention demonstrating an abrupt termination of the contrast in the small colon as a result of meconium impaction **(B)**. Source: Campbell et al., 1984. Reproduced with permission of John Wiley & Sons.

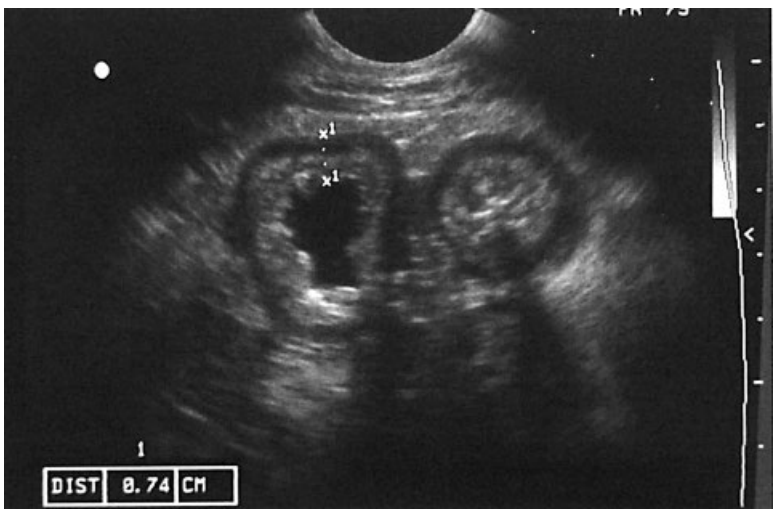

Figure 32.4 Abdominal ultrasound image from a foal with colic, demonstrating grossly thickened small intestinal wall. The thin zone of hypoechogenicity (black) around the periphery is interpreted as a zone of edema separating the muscularis from the serosa.

with necrotizing enterocolitis (see Figure 23.7 in Chapter 23). Intussusceptions have a characteristic "bulls eye" appearance with concentric rings (Figure 32.5; see also Figure 23.11 in Chapter 23). This observation may be accompanied by bowel distention in other small intestinal segments. Asymptomatic intussusceptions were see in 10 of 18 normal foals in one study (Abraham et al., 2014), so it is prudent to perform repeat examinations. Bowel motility can also be assessed using ultrasound, and observation of a lack of contractions of small intestine confirms ileus, which can be of physiologic or obstructive origin.

In addition to examination of the intestine, the urinary system can be examined ultrasonographically. The presence of excessive amounts of free fluid in the abdomen should be noted (Figure 32.6) and the urinary bladder and umbilical remnants examined to ensure that there is no urinary tract disruption. During the examination, perirenal edema or accumulation of retroperitoneal fluid may be observed arising from a ruptured ureter. If noted, this can be further evaluated by performing an intravenous pyelogram. Alternatively, ureteral rupture has been diagnosed by abdominal MRI in one in foal (Beccati et al., 2016).

Perirenal fluid should be interpreted with caution, however, as in the author's experience this is a common finding in septic foals. Subcutaneous fluid may be visualized in the ventral abdomen surrounding the umbilicus in foals with a tear of the urachus external to the abdominal wall. This finding can be further evaluated by performing a contrast cystogram to identify a torn urachus.

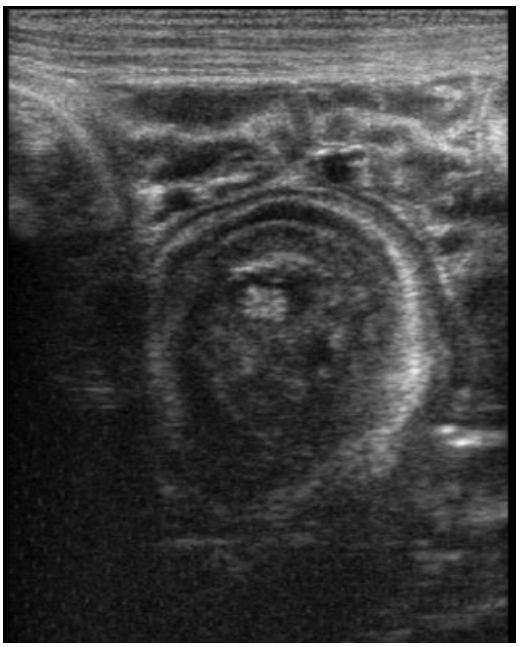

Figure 32.5 Abdominal ultrasound image from a foal with colic, demonstrating the classic "bulls eye" appearance of a small intestinal intussusception, with two concentric layers of bowel wall, one within the other. Source: Courtesy of Dr Anne Desrochers.

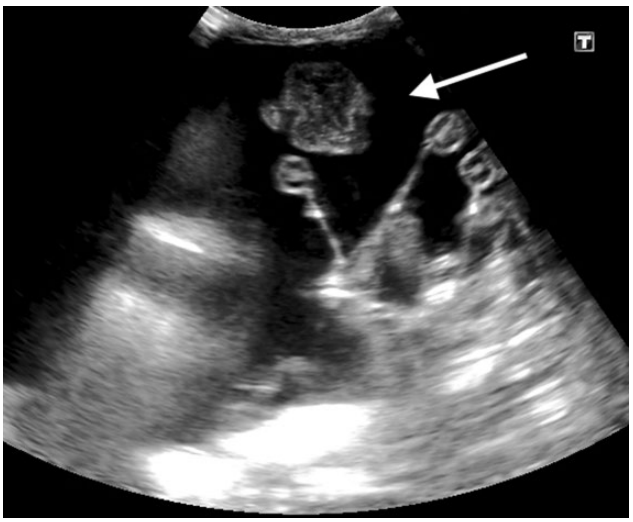

Figure 32.6 Ultrasound image obtained from a foal with abdominal distention secondary to uroperitoneum. Excess anechoic fluid can be observed in the abdomen (arrow).

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33

Medical Management of Colic in the Foal

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If physical obstruction of intestine is confirmed or suspected, immediate surgical exploration is indicated. Persistent pain and progressive distention are the most common and reliable indications for surgery in the foal, and are characterized by distended bowel on ultrasound and/or radiography. The decision for surgery should not be delayed, because the neonatal foal's condition deteriorates rapidly, and persistent distention of the bowel can lead to further metabolic compromise and intra-abdominal adhesions (see Chapter 34).

Medical management refers to any nonmanipulative treatments applied to the foal, but the term "medical management" should not be interpreted to mean that the principles of treatment differ for foals that require surgical treatment. These principles are key elements of treatment in all foals with colic or abdominal distention – surgical intervention adds specific concerns regarding intra-abdominal sepsis, wound healing, and incisional care, for example, but does not eliminate the need to employ appropriate medical management factors as described here.

Medical management of the foal with colic or abdominal distention should have the following goals:

- correction of the primary problem
- correction of metabolic or electrolyte abnormalities
- cardiovascular/circulatory support
- decompression of the bowel
- relief of pain
- treatment of endotoxemia
- resting of the bowel if intestinal distention exists.

Metabolic and electrolyte abnormalities are frequently encountered in the neonate with colic. Failure to nurse owing to pain coupled with a possible increased energy demand in a colicky foal frequently results in hypoglycemia as neonates have little glucose reserve and need to nurse frequently. Hypoglycemia complicates the assessment of colic as the foals are lethargic and quiet, and often become hypothermic. The effects of hypoglycemia on ileus, bowel healing and gastrointestinal mucosal integrity, and outcome in the foal are unknown. However, it has been documented in sick neonatal foals and foals with colic that increasing severity of hypoglycemia is associated with a poorer likelihood of survival (Hollis et al., 2008a; Mackinnon et al., 2013). Furthermore, in human adults and neonates both hyper- and hypoglycemia are associated with increased mortality and length of hospital stay (Finfer et al., 2012; Dellinger et al., 2013). These findings indicate the importance of glucose regulation and metabolism in sick foals regardless of the cause.

Hypoglycemia can be corrected with an intravenous infusion of 5–10% dextrose at a rate of 2–4 mg dextrose/kg/min. It is important to administer this solution as a constant-rate infusion rather than as a bolus, as bolus administration may lead to a rebound hypoglycemia that is more severe than the original problem; hence frequent monitoring of blood glucose is recommended. A reasonable schedule is to monitor blood glucose concentration every 6 h after beginning supplementation. The interval can be increased to every 12 h once blood glucose concentrations have stabilized. Hyperglycemia can occur in foals supplemented with dextrose, particularly if the foal is also endotoxemic. This can be treated by reducing the administration rate of the dextrose, or by administration of insulin as a constant-rate infusion (0.01–2.0 U/kg/h), beginning at the lower dose rate and titrating with the goal to maintain normoglycemia. The optimal range is not defined in foals, but maintaining the blood glucose concentration between 90 and 120 mg/dL is a reasonable goal.

In cases of colic in the foal, correction of electrolyte abnormalities, metabolic derangements, and dehydration is vital because any of these conditions can lead to or exacerbate ileus.

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Simple dehydration can be readily corrected with standard commercial polyionic replacement solutions. These solutions can be administered at 1.5 times maintenance rates (1.5 × 100–120 mL/kg/day) until the foal's hydration status is normalized. Proper hydration is determined by clinical evaluation and monitoring of packed-cell volume (PCV) and urination. The measurement of total protein concentration also can be used to monitor hydration in the foal, but one must remember that the foal's total protein concentration normally is less than that of adult horses, and is often very dynamic owing to the ingestion of (or failure to ingest) colostrum. The PCV of neonates is also lower than that of adults, and should be interpreted in this light. Once foals approach 1 month of age, these differences are no longer significant and hydration can be monitored as one would do in an adult horse. Normally hydrated neonates should urinate at least 2–4 mL/kg/h, with a specific gravity typically 1.001–1.012. If the urine volume cannot be quantified, then the foal should urinate at least twice per hour, and urine can be collected for determination of specific gravity. The volume and administration rates of intravenous solutions may need to be adjusted to correct for ongoing fluid losses from diarrhea or reflux. Consequently, assessment of hydration should be performed several times per day.

Specific electrolyte abnormalities should be corrected using the appropriate replacement solutions. Hyponatremia can be corrected using 0.9% sodium chloride (NaCl) solution or hypertonic saline (either 5 or 7.2%). To determine the effective volume to be administered, the total sodium deficit (in mEq) should first be calculated as

$$\text{sodium deficit}\left(\text{mEq/L}\right) = \left(\text{desired } Na^{+} - \text{measured } Na^{+}\right) \times \text{BW}\left(\text{kg}\right) \times 0.6$$

where BW = body weight. The appropriate volume of sodium replacement solution is then determined by dividing the calculated deficit by the concentration (mEq/mL) of the replacement solution. For example, a 50 kg foal with a serum sodium concentration of 125 mEq/mL has a calculated sodium deficit of 300 mEq (assuming a desired normal value of 135 mEq/L). To replace the deficit, one would need to administer 250 mL of 7.2% hypertonic saline (1196 mEq Na^{+}/L). This should be done over several hours to prevent excessively rapid fluctuations in serum sodium concentration, which in humans is associated with neurologic compromise. The recommendation is to correct the sodium deficit no more rapidly than at 1 mEq/L/h if the hyponatremia is acute and half that rate if the hyponatremia is chronic. Hypernatremia is corrected by providing low sodium-containing fluids, such as 5% dextrose with 0.45% sodium.

Hyperkalemia can be treated with the administration of fluids that lack potassium combined with an intravenous infusion of 5% dextrose solution (see Chapter 28). Foals are often hypokalemic, and it is reasonable practice to add potassium to intravenous fluids at a rate of 10–20 mEq/L. However, this should not be performed until urinary tract rupture has been ruled out.

Hypomagnesemia is common in horses and foals with colic, and adults with lower magnesium concentrations have a lower survival rate (Toribio et al., 2001; Garcia-Lopez et al., 2001). In a study of septic neonatal foals, however, many foals (15%) were hypomagnesemic, yet an association with increased mortality was not noted (Hurcumbe et al., 2009). Hypomagnesemia can be corrected by supplementing fluids with magnesium chloride; a dose of 50 mg/kg IV of magnesium for the first hour followed by 25 mg/kg/h has been proposed for foals with neonatal encephalopathy. Although this approach appears to be well tolerated, studies to confirm this are lacking.

Foals with hypocalcemia can be treated with supplemental intravenous calcium borogluconate 23%. Standard formulas to calculate electrolyte deficit (as described earlier) are not useful for calcium, and often underestimate the amount needed. The following equation is recommended for the calculation of calcium deficit (Toribio, 2010):

$$Ca^{2+}\text{deficit} = \left(6.5\ \text{mg/dL} - Ca^{2+}\right) \times 0.3 \times \text{BW} \times \left(10/Ca^{2+}\text{ratio}\right)$$

where the Ca^{2+} ratio is (Ca^{2+}/total calcium) and BW = body weight. A 100 kg foal with a measured ionized calcium concentration of 4.5 mg/dL and a total calcium concentration of 10 mg/dL would have a calculated calcium deficit of 1333 mg. Calcium borogluconate 23% contains 2.14 g of elemental calcium per 100 mL of solution (21.4 mg/mL); hence the foal would need to be treated with 62 mL of calcium borogluconate 23% solution. This should be administered slowly, with a recommendation not to exceed 2 mg/kg/h (Toribio, 2010). Because this equation has not been validated in neonatal foals, the foal should be monitored for cardiac irregularities during administration, particularly if there are other electrolyte abnormalities or cardiovascular problems present. Calcium should not be added to fluids containing bicarbonate, as complexes may form and precipitate.

Decompression of the bowel decreases pain and ameliorates distention-induced ileus. A nasogastric tube should be passed routinely and gastric decompression attempted. However, intestinal decompression cannot be achieved with a nasogastric tube, and neither the nature nor the amount of reflux obtained has much bearing upon the decision for or against surgery in the foal, particularly neonates (see Chapter 34). The tube should

be left in place and capped to prevent aspiration of air. Gastric decompression followed by treatment with analgesics may alleviate pain sufficiently to diminish ileus. In some neonates, it is very difficult to pass a nasogastric tube into the stomach; in these cases, the author has used a small-diameter endoscope insertion tube passed with visualization to enter the stomach. Trocharization of bowel in the neonate is almost never justified and should be performed in only the most extreme circumstances, such as agonal breathing and impending death arising secondary to extreme large colon distention. Trocharization in the foal is almost guaranteed to result in peritonitis, as the bowel wall is very thin in foals and does not seal after perforation as it does in adult horses. If distention and pain continue or progress, surgical decompression may be necessary and should not be delayed.

Although decompression of the bowel is important in controlling pain, pharmacologic pain control is also needed. Conservative doses of flunixin meglumine (Flunixamine, Zoetis) (0.25 mg/kg IV q 12 h) are often adequate for the neonate. Other nonsteroidal anti-inflammatory drugs (NSAIDs) can be used, but flunixin is probably safest in the foal. Xylazine can be utilized for short-term pain relief during the foal's initial evaluation; if evidence of pain returns within 15–20 min, this is a strong indicator of the need for surgery. Detomidine is a more potent analgesic that lasts substantially longer than xylazine, but both should be used with caution because of the potential for cardiovascular compromise. Repeated doses of either of these α_2-agonists should be carefully considered for this reason, and also because the need for repeated dosing usually suggests the need for surgical exploration. Butorphanol tartrate (0.2–0.5 mg/kg IV or IM) is an effective analgesic in foals, and can be combined with α_2-agonists. Constant-rate infusion of butorphanol and lidocaine has not been documented in the neonate and should be used with caution. However, a dose rate of 1.3 mg/kg IV of lidocaine given as a slow-loading dose, followed by 0.05 mg/kg/min, has been described by one author with the comment that it provides useful and predictable analgesia for foals with colic due to enteritis or colitis (Morresey, 2015).

The routine use of anti-ulcer medications in the neonate is somewhat controversial. In humans, the use of anti-ulcer medication is associated with an increased risk of *Clostridium difficile*-associated diarrhea (Dial et al., 2004), and also sepsis (Graham et al., 2006) and pneumonia (Laheji et al., 2004). Recent work in foals (<14 days of age) has demonstrated an increased risk of diarrhea in those treated with acid suppressive medications (H2 receptor or proton pump blockers) (Furr et al., 2012). Careful consideration of each case is necessary to determine the appropriateness of anti-ulcer prophylaxis in foals with colic. Cimetidine for intravenous treatment (6.6 mg/kg IV q 6 h) is no longer commercially available, to the author's knowledge. Ranitidine (1.5 mg/kg IV q 8 h) can also be used effectively.

Enteral feeding of foals with colic or abdominal distention is contraindicated. Nursing from the mare can be limited with a muzzle or by separating mare and foal with a partition. The foal should be supported with intravenous fluids and dextrose during this period to prevent hypoglycemia and dehydration. If the duration of enteral rest exceeds 48 h, more complete intravenous nutritional support is highly desirable. The duration of enteral rest necessarily varies with the specific inciting cause, but 24 h is the recommended minimal duration. In foals with enteritis, 3–5 days is sometimes necessary before enteral feeding can be tolerated.

Findings at surgery dictate the duration of enteral rest in foals that have had a surgical procedure performed. When oral feeding is to be reintroduced, 4 ounces (oz) of water (1 oz ≈ 28 mL), or a water and dextrose solution, should be given every 2 h. If this is tolerated, the volume can be increased with subsequent feedings until a volume of 12–16 oz of water or glucose solution is tolerated. Once this has been achieved, a 50 : 50 mixture of water and milk or a milk substitute can be given. If no intolerance is noted after several feedings, the strength of the solution can be increased to normal. Obviously, this process requires some patience, but reintroducing enteral feeding too rapidly often results in relapse of ileus and substantial setbacks in the progress of the case.

The presence of circulating endotoxin is common in horses and foals with colic and sepsis. Studies in clinical patients have reported that endotoxin can be detected in the blood of 30–40% of horses with colic (King & Gerring, 1988; Steverink et al., 1995) and 40–50% of neonatal foals with suspected sepsis (Atherton & Furr, 2006; Barton et al., 1998). Treatment of endotoxemia in the foal includes many of the same treatments as used in adult horses. Polymixin B has been demonstrated to bind endotoxin and is used in foals at a dose of 1–5000 U/kg IV two to three times per day (Moore & Barton, 2003). Higher doses (6000 U/kg) have been used experimentally with good effect and no signs of toxicity (Durando et al., 1994), although the frequent presence of renal disease in sick neonates suggests that a more conservative dose is advisable (Barton, 2000). Another important means of inactivating endotoxin pertinent to the foal is the use of plasma, in particular plasma containing anti-endotoxin antibodies. Some studies have demonstrated favorable effects when using plasma containing anti-endotoxin antibodies in foals (Garner et al., 1988; Spier et al., 1989), whereas other studies have demonstrated no effect (Morris & Whitlock, 1987). Maintaining appropriate serum total protein and correcting failure of passive transfer often require the use of plasma. The treatment of endotoxemia is discussed more completely in Chapter 28.

General high-quality nursing is important for foals with colic. Neonates should be tested for adequate passive transfer of colostral antibodies and treated as necessary, and basic hematology and clinical chemistry evaluations should be performed and abnormalities addressed. It is important to recognize that a substantial proportion (50%) of neonatal foals with diarrhea and enteritis (often associated with colic) are blood culture positive (Hollis et al., 2008b). The use of antibiotics should be determined on a case-by-case basis, but most foals, in the author's experience, have clinical and clinicopathologic abnormalities that warrant the use of antibiotics.

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34

Surgical Management of Colic in the Foal

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Introduction

The National Animal Health Monitoring System reported the incidence of colic in foals less than 6 months of age in the United States over a 12 month period between 1998 and 1999 to be 0.2 events per 100 horses (Traub-Dagartz, 2001), which is significantly less than in adults but nonetheless significant in terms of economic impact. In neonates (generally defined as foals less than 30 days old), most colic cases are due to medical conditions (MacKinnon et al., 2013). Differentiating medical from surgical colic in neonates can be difficult, as both groups exhibit comparable levels of pain and have similar clinicopathologic findings and overlapping diagnostic results (see Chapter 31). The inability to perform thorough transrectal palpation in this group is a disadvantage. Furthermore, concurrent disease processes in neonates can cause, exacerbate, or decrease signs of colic and impact the decision to pursue surgery (Bryant & Gaughan, 2005). Surgical lesions vary by age, with small intestinal volvulus being more common in neonates than older foals. Surgical lesions in older foals tend to resemble those in adult horses, although it is the authors' clinical impression that intussusceptions occur more frequently in foals. When a strangulating intestinal obstruction is suspected, early surgical intervention is crucial to increase the chance of a favorable outcome (Southwood, 2009).

Indications for Emergency Abdominal Exploration in the Foal

The clinical workup of the foal with colic is the essentially the same as performed in adults, except for limitations in performing transrectal abdominal palpation. Physical examination, including recording of vital signs and mucous membrane color/moisture, abdominal auscultation, and umbilical and scrotal palpation to rule out intestinal herniation, should be performed first (see Chapter 31). Identification of any fractured ribs is important, as these can lacerate the diaphragm and cause secondary hernias (Palmer, 2012). Digital rectal palpation and/or enema administration help distinguish a refractory meconium impaction from colonic atresia (Orsini, 1997; Bryant & Gaughan, 2005). Nasogastric tube passage should be performed to check for gastric reflux, although not all foals with small intestinal or gastric outflow obstruction will produce net reflux (Bryant & Gaughan, 2005). Transabdominal ultrasonography, abdominal radiography, and abdominocentesis are valuable in assimilating information about the etiology. In addition, serial measurement of abdominal circumference every 2–4 h can be useful in the neonate to document progressive abdominal distention (Bryant & Gaughan, 2005). Measurements should be taken just caudal to the last rib, at the level of the second lumbar vertebra.

Neonates have unique causes of colic, such as meconium impaction and congenital atresia of segments of the gastrointestinal tract, that usually are diagnosed in the first few days of life. In cases where the nature of the colic (medical versus surgical) remains unclear after the initial workup, early surgical intervention is still recommended over initially attempting medical treatment to increase the likelihood of survival (Orsini, 1997). Because of differences in presentation, clinical findings, and causes of colic between neonates and older foals, the two groups are discussed separately (see Table 34.1).

Neonates

In a retrospective study of colic in 137 neonates, the majority (86%) of cases were successfully managed medically (MacKinnon et al., 2013). The most common cause of surgical colic in neonates is small intestinal

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Table 34.1 Surgical gastrointestinal lesions in the foal by age group.

Age group	Area of gastrointestinal tract affected	Specific diseases
Neonates (<30 days)	Esophagus, stomach, duodenum	Ulceration, outflow obstruction secondary to scarification or neoplasia
	Small intestine	Volvulus
		Enteritis
		Intussusception
		Hernia – diaphragmatic, inguinal, scrotal, umbilical
		Impaction (ileal)
	Large intestine	Atresia– coli, ani
Foals (1–12 months)	Esophagus, stomach, duodenum	Ulceration, outflow obstruction secondary to scarification
	Small intestine	Intussusception – ileocecal, jejunojenunal
		Impaction (ascarids)
		Hernia – inguinal, scrotal, umbilical
		Volvulus
	Cecum	Intussusception – cecocolic
	Large intestine	Large colon displacement
		Impaction – pelvic flexure, small colon (fecolith)
		Large colon volvulus

strangulating obstruction (SISO), with small intestinal volvulus being the most common lesion. Therefore, the initial workup should be focused on ruling in/out strangulated intestine. Persistent pain, decreased or absent gastrointestinal borborygmi, abnormal oral mucous membrane color, increased capillary refill time, and increased heart rate are indicative of the need for surgery in adults with colic (Lindegaard et al., 2011) (see Chapter 24). In contrast, there was no consistent association between vital signs and the need for surgical intervention in the aforementioned study on neonatal foals. Similarly, a review of small intestinal volvulus cases showed that affected foals were normothermic and had a range of respiratory rate and mucous membrane color (Stephen et al., 2004). Progressive abdominal distention is associated with a surgical lesion, particularly small intestinal volvulus in which the root of the mesentery is involved (Adams et al., 1988; Lindegaard et al., 2011; Stephen et al., 2004).

As in adults, the patient's level of pain can be helpful in determining the need for surgery (Adams et al., 1988), but is not the only criterion that should be used (Lindegaard et al., 2011; Bryant & Gaughan, 2005). When examined individually, neonates with small intestinal strangulating obstruction were more likely to have severe, continuous pain that was less responsive to analgesia (MacKinnon et al., 2013). In that study, there was no association between specific pain signs and the need for surgery. However, foals with intestinal volvulus were equally likely to have mild, moderate, or severe pain preoperatively (Stephen et al., 2004). Similarly, foals with severe gastric ulceration, gastric outflow obstruction, or large intestinal lesions may not show significant pain (Orsini, 1997; Vatistas et al., 1996; Adams et al., 1988). Foals with concurrent diseases may develop secondary segmental ileus and/or small intestinal volvulus due to gastrointestinal inflammation, an altered eating pattern, or recumbency (Bryant & Gaughan, 2005). Furthermore, in neonates with colic, concurrent disease was reported in 63% (MacKinnon et al., 2013). Sepsis, neonatal encephalopathy, neonatal nephropathy, failure of passive transfer of maternal antibodies, and umbilical remnant infection or patent urachus were the most frequent diseases reported.

As with physical examination parameters, no consistent association has been found between clinicopathologic abnormalities and the need for surgical intervention. The only factor significantly associated with surgical intervention was a lower plasma chloride concentration that was likely due to sequestration in the upper gastrointestinal tract secondary to obstruction (MacKinnon et al., 2013). Owing to a significant overlap in plasma chloride values between medical and surgical cases, this parameter is not clinically useful.

As a result of the inability to differentiate enteritis or ileus from a strangulating obstruction on physical examination and laboratory work alone, diagnostic imaging is frequently necessary in determining the need for exploratory celiotomy. Abdominal ultrasonography is particularly useful for examining small intestinal diameter, wall thickness, and motility. Most strangulating intestine cases have mural thickening, distention, and decreased

or absent motility detected on ultrasound examination (MacKinnon et al., 2013) (see Chapter 32).

Abdominal radiography can also help rule out an obstructive lesion, although it is more helpful in determining the location versus the cause of an obstruction (Orsini, 1997). Contrast radiography can be used to rule out gastric outflow obstruction (Bryant & Gaughan, 2005). In a review of 20 colic cases in foals less than 14 days old, nine of the 10 foals that underwent surgery had abnormal preoperative abdominal radiographs (Adams et al., 1988). Unlike on ultrasonography, free peritoneal gas secondary to bowel rupture can be seen on radiographs as increased serosal detail and renal demarcation (Orsini, 1997).

Gastroscopy can also be helpful in diagnosing the severity of gastric ulceration. The authors recommend ruling out severe gastric distention on radiography or ultrasonography prior to performing gastroscopy, as air distention during the procedure may increase the risk of rupture (see Chapter 22).

Foals Aged More Than 30 days

The decision for exploratory celiotomy in older foals is less likely to be clouded by concurrent disease that is common in neonates. Similar to adults, the need for surgical intervention is often based on severity and persistence of pain. As previously described, foals with small intestinal volvulus can show a wide range of pain severity on admission (Stephen et al., 2004), so it is still important to perform abdominal imaging. Progressively increasing abdominal distention can also influence the decision to pursue surgery. In older foals, a history of decreased fecal output combined with persistent pain may indicate a large intestinal obstruction that is not responsive to medical treatment (e.g., large colon impaction, fecolith) (Nikahval et al., 2009). Foals less than 6 months old exhibited tachycardia, tachypnea, pyrexia, oral mucous membrane abnormalities, and signs of hypovolemia preoperatively due to cecal rupture (Tabar & Cruz, 2009). Those findings, however, could be found in a foal with septicemia concurrent with and/or caused by primary gastrointestinal disease. Rarely, other diseases that cause colic and require exploratory celiotomy in foals include meconium impaction, abdominal abscess (*Streptococcus* spp., *Rotococcus equi*), and adhesions. Table 34.1 gives descriptions of the more common causes of foal colic requiring surgery.

Gastric Outflow Obstruction

Gastric outflow obstruction refers to mechanical obstruction of the pylorus or proximal duodenum. The obstruction is most often caused by scar tissue and granulation tissue formation secondary to gastroduodenal ulceration. On rare occasions, neoplastic lesions (cyst, primary melanoma) have been reported to cause upper gastrointestinal obstruction in the foal (Loynacham, 2014; Caston & Fales-Willams, 2010). Gastric outflow obstruction most commonly occurs in suckling and weanling foals (Zedler et al., 2009). A bypass procedure is indicated when the affected foal fails to respond to medical therapy, including gastric decompression and antimicrobial administration. An obstruction can be diagnosed preoperatively by upper gastrointestinal contrast radiography (Orsini, 1997).

Small Intestinal Volvulus

Small intestinal volvulus has been reported as the most common cause of surgical colic in foals (Orsini, 1997). Small intestinal volvulus is more common in younger than older foals and may be associated with the transition from milk to a solid diet (Stephen et al., 2004). It also can occur secondary to a primary disease process that causes gastrointestinal inflammation or ileus, including enteritis (Southwood, 2009). The distal jejunum and ileum are most often involved (Orsini, 1997). Jejunal volvulus was the most common cause of strangulation in 67 foals under 150 days of age undergoing surgical treatment (Vatistas et al., 1996). In more recent reports of colic in neonates, nine of 11 SISO cases had small intestinal volvulus (MacKinnon et al., 2013) whereas 10 of 15 foals with small intestinal volvulus were between 2 and 4 months old (Stephen et al., 2004). One retrospective study reported small intestinal volvulus to be more common in foals between 3 and 12 months of age compared to foals younger than 3 months old (Cable et al., 1997) and less common than intussusceptions in foals 3–12 months of age and strangulating hernias in foals less than 3 months old. Whether these results reflected the overall foal population or that hospital's unique caseload was not reported.

Intussusceptions

Jejunojejunal, jejunocecal, ileocecal, cecocecal, and cecocolic intussusceptions can occur in foals of any age but have been associated with *Anoplocephala perfoliata* infestations more often in weanlings (Bryant & Gaughan, 2005). Affected foals may show signs of an acute obstruction or have mild, intermittent colic signs with anorexia and diarrhea. A characteristic bulls-eye sign may be seen on abdominal ultrasonography, but often a definitive diagnosis is only made intraoperatively.

Abdominal Hernias

Inguinal, umbilical, or diaphragmatic hernias that result in intestinal incarceration require surgical intervention. Foals with a nonreducible direct inguinal hernia will often show signs consistent with small intestinal strangulation. Surgical closure of the external inguinal ring is

recommended for inguinal hernias that do not resolve with manual reduction in the first month of life (Bryant & Gaughan, 2005). In foals with rib fractures, the integrity of the diaphragm should be assessed with ultrasonography or radiographs, to detect gastrointestinal viscera in the thorax (Bryant & Gaughan, 2005). Typically, congenital diaphragmatic defects do not cause secondary gastrointestinal hernias until 5 years of age or older (Palmer, 2012).

Large Intestinal Atresia

Atresia ani, recti, or coli is a rare but often fatal cause of colic in foals that is usually diagnosed in the first few days of life. Affected foals will not pass fecal material, even following of repeated enemas (Bryant & Gaughan, 2005). Contrast abdominal radiography following a barium enema can confirm a diagnosis of large intestinal atresia (see Chapter 32).

Intra-abdominal Adhesions

Foals are highly susceptible to intra-abdominal postoperative adhesion formation, especially following bowel injury or surgery. Intestinal vascular occlusion and/or distention to an intraluminal pressure of 25 cmH_2O for 2 h are known to cause ischemic injury (Sullins et al., 2011). Further damage to the serosa with subsequent reperfusion leads to ileus, endotoxemia, and adhesion formation (see Chapter 11). Foals can also form adhesions secondary to a medical gastrointestinal disease, such as enteritis. It is unknown why foals form adhesions more readily than adults, as the relative levels and activity of pro- and anticoagulant factors in foals and adults with colic are not significantly different (Watts et al., 2011). Adhesion formation can be subclinical or can cause recurrent abdominal pain that requires a second surgery (Bryant & Gaughan, 2005).

Techniques for Exploratory Laparotomy in the Foal

General Approach to Exploratory Celiotomy

The surgical approach to the foal's abdomen begins at the umbilicus and extends cranial for 10–15 cm through the linea alba. In foals less than 3 weeks old, umbilical stump and remnants are resected (see later). The bowel and mesentery should be handled carefully in the foal as the mesentery is more easily torn than in the adult horse.

Resection and Anastomosis

Resection and anastomoses are performed similarly in both the foal and adult (see Chapter 44). Jejunojejunostomies and jejunoileostomies are typically performed end-to-end handsewn, and jejunocecostomies and ileo- or jejunocolostomies are stapled and oversewn side-to-side. Handsewn jejunojunostomies are preferred in foals owing to the small size of the bowel lumen (Bryant & Gaughan, 2005). Similarly, stapled anastomosis is not recommended for neonates. The bowel must be handled gently and minimally to decrease the risk of postoperative adhesions. Particular attention must also be paid to the resulting lumen diameter when performing the anastomosis, as even a slight stricture of the anastomosis site will result in an overall greater reduction in total lumen diameter than in an adult.

Gastric Outflow Obstruction

The following bypass procedures have been successfully performed in foals (Zedler et al., 2009). The area of obstruction dictates which procedure is performed. If better exposure of the pylorus is required when performing a gastric bypass procedure, the ventral midline incision can be extended cranially to the xyphoid process (Orsini, 1997). The hepatoduodenal ligament can also be severed.

Gastroduodenostomy

Gastroduodenostomy (Figure 34.1) is indicated for obstructions of the pylorus and/or most proximal 1–2 cm of duodenum (Zedler et al., 2009). The surgeon must be able to align the duodenum distal to the bypass site without excessive tension in order to perform this procedure. The proximal duodenum orad to the common papilla is aligned with a less vascular region of the stomach oral to

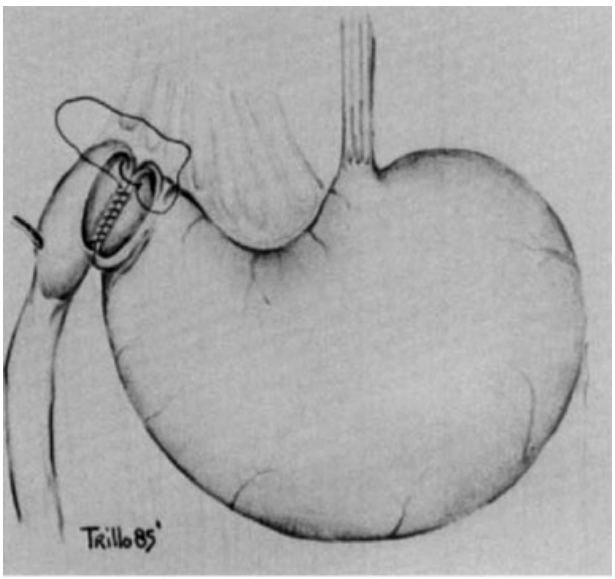

Figure 34.1 Gastroduodenostomy is used to bypass pyloric stenosis. Note the anastomosis site is oral to the entrance of the common bile duct, indicated by a black line. Source: Orsini & Donawick, 1986. Reproduced with permission of John Wiley & Sons.

the pylorus. The laparotomy site is isolated with moist sponges, and stay sutures are placed on the oral and aboral planned anastomosis sites. A 4–5 cm portion of duodenum is sutured to the stomach in a continuous Lembert pattern, then 3–4 cm full-thickness incisions are made in the opposing gastric and duodenal surfaces parallel to the first suture line. The far cut edges of the stomach and duodenum are sutured in a full-thickness, simple continuous pattern. The near cut edges are opposed in a similar fashion and oversewn in a continuous Lembert pattern. Size 2-0 absorbable suture material is used for all incisions. This creates a side-to-side anastomosis with an approximately 5 cm stoma between the stomach and duodenum.

Gastrojejunostomy With or Without Jejunojejunostomy

Gastrojejunostomy is indicated for primary duodenal obstructions or when more than the first 1–2 cm of proximal duodenum is involved in a pyloric obstruction. A 7–8 cm segment of proximal jejunum, approximately 20 cm aboral to the duodenocolic ligament, is aligned with a less vascular portion of the caudoventral stomach and secured with stay sutures. The jejunum can be aligned with the oral segment toward the left side of the abdomen or toward the right side and distal to the anastomosis (Figure 34.2 and Figure 34.3). The anastomosis is then completed in a similar fashion to the gastroduodenostomy.

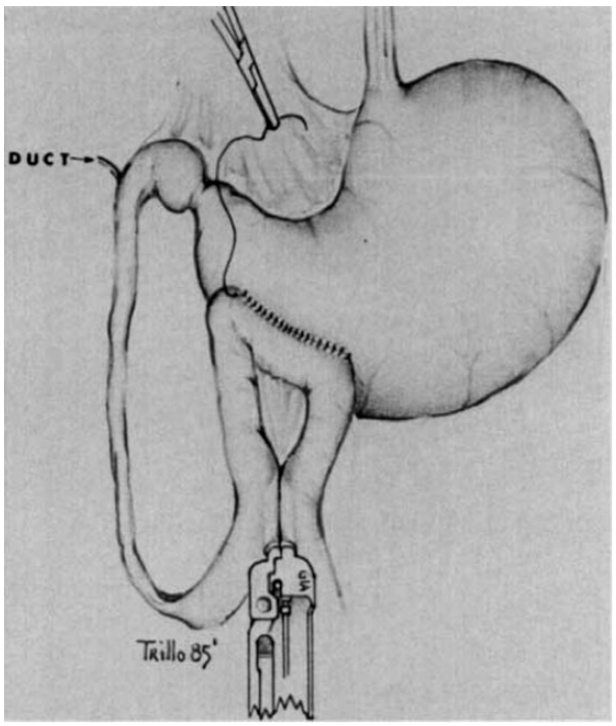

Figure 34.2 Gastrojejunostomy with jejunojejunostomy, standard technique: oral jejunal segment on the right. Source: Orsini & Donawick, 1986. Reproduced with permission of John Wiley & Sons.

Alternatively, 1 cm enterotomy portals can be made in each segment, and an ILA stapler can be inserted through the portals in the same direction as the jejunal segment and discharged (Bryant & Gaughan, 2005). The anastomosis sites are then oversewn using size 3-0 monofilament absorbable suture, and the enterotomy sites are closed routinely. The resulting stoma is 6–7 cm in length. Placing the oral segment of the jejunum on the left maintains a left-to-right flow of ingesta and is thought to decrease the likelihood of volvulus around the anastomosis site (Zedler et al., 2009). When a stapler is used, stapling in a left-to-right (oral-to-aboral) direction is also preferred to decrease the risk of stricture formation aboral to the stoma (Coleman et al., 2009). This technique must be evaluated on more cases to determine its success rate relative to the standard technique (oral segment of the jejunum on the right).

Jejunojejunostomy is often performed with the gastroduodenostomy to prevent retrograde flow of ingesta from the oral segment of jejunum into the stomach and to prevent complications with the blind loop. In a retrospective study of foals that underwent gastrojejunostomy with or without jejunojejunostomy, short-term survival was equivalent in both groups, but long-term

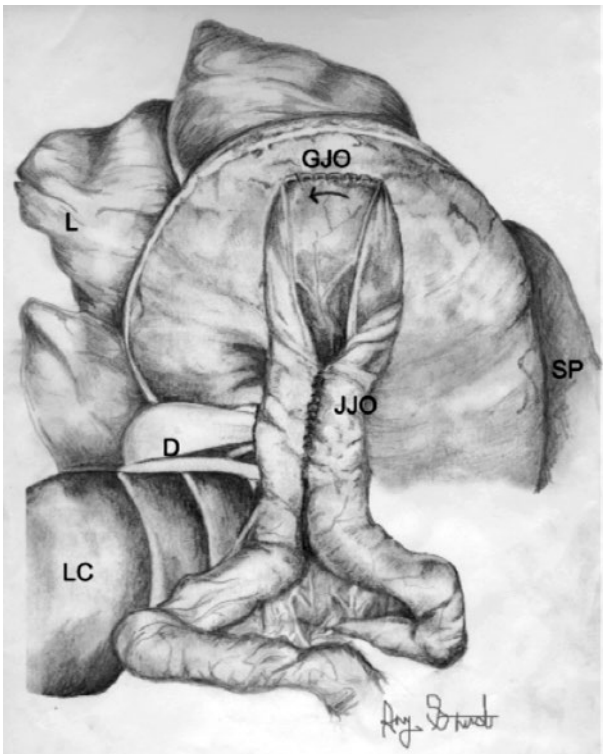

Figure 34.3 Gastrojejunostomy (GJO) with jejunojejunostomy (JJO), alternative technique. Curved arrow denotes oral to aboral direction of the jejunum. The omentum has been completely removed for illustrative purposes. D, duodenum; LC, large colon; L, liver; SP, spleen. Source: Zedler et al., 2009. Reproduced with permission of John Wiley & Sons.

survival (≥2 years postoperative) was lower in foals that did not undergo jejunojejunostomy (50% versus 63% in foals with jejunojejunostomy versus gastrojejunostomy) (Zedler et al., 2009).

Following any gastric bypass procedure, contrast radiographs should be obtained 24 h postoperatively to document a successful bypass (Bryant & Gaughan, 2005).

Partial gastrectomy has been reported in one foal with obstruction due to an abscess in the gastric antrum (Orsini & Donawick, 1986). In this case, an LDS stapler was used to divide the vascular supply to the affected pylorus and pyloric antrum. The affected stomach was transected using a TA-90 stapler, and the affected duodenum was transected. The blind end of the duodenum was then anastomosed to the stomach using a GIA stapler.

Esophagogastrotomy via a median sternotomy and diaphragmatic resection has been described in one foal with obstruction at the cardia and megaesophagus secondary to gastric ulceration (Orsini & Donawick, 1986). At the time of follow-up (20 months of age), the foal was doing well.

Umbilical Remnant Resection

Umbilical remnant resection (Bryant & Gaughan, 2005) is performed in foals less than 2–3 weeks old that are concurrently undergoing exploratory celiotomy for gastrointestinal disease. Concurrent disease processes such as patent urachus and/or umbilical remnant infection are treated during exploratory laparotomy.

Care is taken to isolate an abscessed stump from the surgical field during the approach and any open or draining urachal structures are clamped to avoid spillage. An elliptical skin incision is made around the umbilicus. The abdomen is entered cranial to the umbilical stump, taking care to avoid the underlying umbilical vein. Alternatively, an incision is made lateral to the stump. Finger dissection and palpation are used to identify the umbilical vein, urachus, and umbilical arteries. Umbilical stump is sharply dissected free. The linea alba incision may need to be continued caudal to expose the cranial bladder and urachus. The umbilical arteries are dissected free from the lateral ligaments of the bladder, taking care to preserve the lateral branches of the of the internal pudendal arteries that supply the bladder. The umbilical arteries are ligated and transected just beyond diseased tissue or at the level of the apex of the bladder if they are normal. The transition between the apex of the bladder and the urachus is usually apparent as the bladder narrows and becomes a more thin-walled urachus. Stay sutures are used to stabilize the bladder. The urachus is transected free with scissors. The bladder is closed in two inverting layers using absorbable suture material. The umbilical vein is then dissected free and ligated and transected beyond any diseased segment. The abdominal incision is closed in three layers (see later). If an infection is present, the affected components of the umbilicus should be completely removed and submitted for culture and sensitivity. If the infection extends into the liver, the remaining umbilical vein stump should be marsupialized (Bryant & Gaughan, 2005). To do this, the umbilical vein stump is redirected through a stab incision adjacent to the linea alba incision and is sutured to the skin. The stoma is left to drain and heal by second intention over 7–14 days. Prognosis for umbilical resections is good when the umbilicus is healthy or when the infection is localized. Hepatic involvement and/or concurrent sepsis in other body systems decrease prognosis.

Inguinal Hernia Repair

In foals presenting with a persistent but asymptomatic hernia, the bowel can be manually reduced into abdomen, and the external inguinal ring can be closed through an inguinal approach with or without castration (Bryant & Gaughan, 2005). In cases of intestinal strangulation, a ventral midline celiotomy is performed, and the incarcerated bowel is assessed for viability. The vaginal tunic and inguinal rings are closed, and a resection and anastomosis are performed if the involved bowel is compromised.

Diaphragmatic Hernia Repair

As in the adult, diaphragmatic hernias in the foal may be congenital or secondary to trauma. In foals, traumatic diaphragmatic hernias are more often caused by rib fractures than blunt abdominal trauma (Palmer, 2012). When a diaphragmatic hernia is diagnosed intraoperatively, the involved viscera should be removed from the thorax and assessed for viability and nonviable intestine resected (Bryant & Gaughan, 2005). Unlike in adults, diaphragmatic hernias in foals are more easily repaired by direct defect closure with absorbable or nonabsorbable suture. The few reported cases of surgically repaired diaphragmatic hernias in foals had good short- and long-term survival rates (Palmer, 2012).

Meconium Impactions

For impactions that are refractory to medical treatment, intra-abdominal manual massage of fecal material into the pelvic canal is recommended (Bryant & Gaughan, 2005). If the impaction cannot be manually reduced without rupturing the bowel, then a small colon enterotomy can be performed (see Chapter 45).

Intra-abdominal Adhesions

To prevent postoperative adhesion formation, prompt referral and treatment of any possible intestinal strangulation obstruction in a foal are recommended to minimize preoperative intestinal damage (Santschi et al., 2000). Intraoperatively, the general principles of abdominal

surgery should be strictly employed. These include removal of devitalized tissue, efficient but gentle handling of bowel, strict aseptic technique, and frequent lavage with sterile, warm, balanced electrolyte fluids (Bryant & Gaughan, 2005). Omentectomy has been reported to reduce postoperative formation of adhesions, particularly those that cause colic leading to repeat celiotomy (Kuebelbeck et al., 1998). Procedure type does not seem to affect adhesion formation. Whereas small intestinal lesions are more likely than large intestinal lesions to cause postoperative adhesions, small intestinal lesions that undergo resection and anastomosis are no more likely to form adhesions than those that do not.

Adhesions encountered intraoperatively should be gently separated. Adhesions involving the mesentery should be dissected close to the attachment of the adhesion to the mesentery to avoid creating a mesenteric rent. In humans, laparoscopic adhesion dissection after initial celiotomy is preferred over repeat celiotomy, as the former decreases adhesion reformation and new adhesion formation (Landsdowne et al., 2004). Laparoscopic dissection is typically performed 7–21 days after the first celiotomy to allow serosal healing but prevent preoperative fibrosis of existing adhesions. The improved results with laparoscopic dissection are likely due to decreased total incisional length and bowel manipulation in laparoscopic procedures. Similar results have been demonstrated in horses with experimentally induced adhesions that undergo laparoscopic adhesion dissection (Landsdowne et al., 2004). Concurrent intraperitoneal administration of 0.5% ferric hyaluronate gel is known to be more effective than laparoscopic dissection alone in decreasing adhesion formation in humans and foals. Experimentally induced adhesions in 10–15-day-old pony foals were more effectively treated with concurrent laparoscopic dissection and ferric hyaluronate administration than laparoscopic dissection alone (Landsdowne et al., 2004). The efficacy of ferric hyaluronate in foals undergoing repeat celiotomy for adhesion-induced colic is unknown. Furthermore, ferric hyaluronate administration is contraindicated in patients with septic peritonitis, as the iron potentiates bacterial growth and virulence (Landsdowne et al., 2004), and it therefore not recommended for foals with concurrent sepsis.

Postoperatively, broad-spectrum antimicrobials, nonsteroidal anti-inflammatories, and intravenous dimethyl sulfoxide have been shown to reduce experimental adhesion formation in foals (Sullins et al., 2011). Low-dose parenteral heparin administration was reported to decrease intestinal adhesions in ponies concurrently treated with flunixin (Parker et al., 1987), whereas heparin was not effective in experimental adhesions in foals (Sullins et al., 2011). The contribution of heparin versus flunixin in decreasing adhesion formation in those ponies is unknown. Intraperitoneal administration of carboxymethylcellulose (CMC) has also been recommended (MacKinnon et al., 2013). Although CMC may protect adjacent serosal surfaces, it may not counteract inflammation and adhesion formation associated with transmural intestinal damage present in strangulating lesions. In a study of foals with induced ischemic small bowel lesions, intraperitoneal CMC administration did not significantly reduce adhesion formation (Sullins et al., 2011).

Closure of the Abdomen

In foals weighing less than 200 kg, closure of the abdomen is performed in three layers; the linea alba is opposed using size 1 absorbable suture in a continuous pattern followed by closure of the subcutaneous tissue with size 2-0 absorbable suture also in a continuous pattern. The skin is opposed with either monofilament suture, stainless-steel staples, or tissue glue. In neonates, skin closure can be completed with an absorbable subcuticular suture. In larger foals, linea alba closure should be performed with larger absorbable suture (size 2). A temporary stent bandage stapled over the incision can be used for recovery from general anesthesia. An abdominal bandage is then placed to protect the incision once standing. In neonates, abdominal bandages tend not to contour to the abdomen well and are prone to slippage and capture of urine and therefore may not be beneficial. An abdominal drain may be placed in certain circumstances such as preexisting peritonitis or abdominal abscess; however, it is the authors' opinion that thorough lavage and instillation of abdominal antibiotic solutions are just as effective.

Postoperative Care

After surgery, most foals receive potassium penicillin G [20,000 IU/kg body weight (BW) IV qid], gentamicin sulfate (6.6 mg/kg BW IV sid) and flunixin meglumine (0.25–1 mg/kg BW IV bid) postoperatively for 1–3 days (or longer) depending on the condition. Antimicrobial treatment may be continued longer, particularly if there is clinical or laboratory evidence of sepsis. Balanced isotonic polyionic IV fluids are administered at maintenance or higher rates to correct dehydration. Potassium chloride (and other electrolytes) and 5% dextrose solution may be added to the IV fluids to correct electrolyte abnormalities. Gastric protectants such as omeprazole (2–4 mg/kg BW sid), cimetidine (3–6 mg/kg BW PO qid), and sucralfate (1–2 g per foal bid or tid) are often administered for 7–21 days following surgery. Nursing may or may not be permissible postsurgery, depending on the surgical lesion. Mares and foals are confined to a stall and exercised in hand 3–4 times daily for the first 2 weeks after surgery. Depending on size, foals are generally confined with the mare in a small paddock for a further 4–6 weeks.

Prognosis Following Colic Surgery in Foals

Survival

Overall survival rates for foals following colic surgery have improved in the past twen25 years but remain low (Bryant & Gaughan, 2005). Survival varies widely and is affected by several factors, including age, status on admission, intraoperative findings, specific surgical procedures performed, and postoperative adhesion formation.

Age

Foals less than 30 days of age at the time of surgery have lower short- and long-term survival rates than older foals (MacKinnon et al., 2013; Vatistas et al., 1996). The survival rates for groups of foals older than 30 days of age (e.g., weanling versus yearling) have not been described. Survival to discharge can be affected by concurrent diseases and clients not pursuing treatment owing to concerns about reduced potential for possible athletic capability (Singer & Livesey, 1997).

Physical Examination and Clinicopathologic Abnormalities

Certain preoperative physical examination parameters and clinicopathologic abnormalities have been associated with decreased survival rates. In a retrospective study of foals less than 30 days of age that underwent colic surgery, specific abnormalities were associated with decreased short-term survival (Box 34.1) (MacKinnon et al., 2013; Cable et al., 1997).

The only preoperative abnormality associated with decreased postoperative survival in both adults and neonatal foals is increased packed-cell volume (Proudman et al., 2005). Unlike foals, decreased postoperative survival in adult horses is associated with increased heart rate, decreased total protein, increased age on admission, and breed (Archer et al., 2011; Lindegaard et al., 2011; Proudman et al., 2005, 2006) (see Chapter 25). Draft and Thoroughbred or Thoroughbred cross breeds specifically have a decreased likelihood of survival compared with other breeds (Proudman et al., 2006). There is no known association between postoperative survival and breed in foals of any age group; however, Thoroughbred foals are overrepresented in the literature.

To what extent preoperative physical examination and clinicopathologic abnormalities influence short-term survival in older foals is unknown, as age groupings vary between studies. The effect of these parameters on long-term survival is also unclear, as current studies do not consistently differentiate between medical and surgical colic cases in determining long-term survival. Finally, in foals it is unknown whether the time between initial clinical signs and surgery influences survival, whereas in adult horses duration of preoperative colic signs did not influence survival (Proudman et al., 2006).

The presence of concurrent diseases in foals with abdominal discomfort is common, especially in neonates. In a review of colic in neonates, concurrent diseases were present in 64% of patients (MacKinnon et al., 2013) and included failure of passive transfer, sepsis, and neonatal encephalopathy. Concurrent diseases did not affect short-term survival, although no distinction was made between medical and surgical colic cases (MacKinnon et al., 2013). In another study of surgical colic in neonates (defined as less than 15 days old), two of 20 foals (10%) were recovered but euthanized prior to discharge due sepsis-related comorbidities (Adams et al., 1988). In the authors' experience, concurrent diseases can also influence the decision to euthanize intraoperatively and thereby decrease short-term survival.

Box 34.1 Abnormalities associated with decreased short-term survival in neonates with colic

Physical examination findings
- Severe pain
- Absent gastrointestinal borborygmi
- Abnormal oral mucous membranes
- Abdominal distention
- Hypothermia

Clinicopathologic abnormalities
- Hyperlactatemia
- Hypoglycemia
- Hemoconcentration
- Hypochloremia
- Acidemia

Lesion Location

Lesion location has been shown to influence survival rates (Table 34.2). Foals with small intestinal lesions have lower short- and long-term survival rates than those with large intestinal lesions (Vatistas et al., 1996; Singer & Livesey, 1997). This holds true even when atresia coli and meconium impaction cases are excluded. In a retrospective study of small intestinal volvulus cases, 67% of foals that underwent surgery were recovered, versus 73% of all horses (Stephen et al., 2004). Approximately 75% of foals that were recovered had postoperative complications, compared with 60% of all horses recovered. Complications included repeat colic, incisional infection, nasogastric reflux, and pyrexia. Although 20% of foals with complications died as a result of complications, the time after surgery in which these complications developed was unclear.

The reported survival rates of foals that undergo surgery for gastric outflow obstruction have improved in

Table 34.2 Survival rates for foals undergoing colic surgery by age group, lesion type, and need for resection.

	Short-term survival (to discharge) (%)	Long-term survival (6 months–2 years post-operation) (%)
Age group		
<30 days	25–75	33–75
30 days–1 year	61–85	53–69
Lesion type		
Large intestinal	–	65
Small intestinal	–	34
Strangulating	–	19
Nonstrangulating	–	69
Congenital (i.e., atresia)	0–25 (dependent on lesion)	–
Procedures		
Intestinal manipulation	–	29
Resection and anastomosis	–	79
Gastric bypass	92–100	50–69

Data from MacKinnon et al. (2013), Singer & Livesey (1997), Vatistas et al. (1996), Cable et al. (1997), Coleman et al. (2009), Estes & Lyall (1979), Zedler et al. (2009).

the last 25 years (Campbell-Thompson et al., 1986; Orsini & Donawick, 1986). Foals that undergo a gastric bypass procedure currently do better than those that require resections, provided that a ruptured viscus is not present intraoperatively (Zedler et al., 2009; Coleman et al., 2009). In a review of 16 foals that underwent gastrojejunostomy, all foals survived to discharge and 50% of foals survived 3 years postoperatively (Coleman et al., 2009). Factors that decrease long-term survival in foals treated with gastric bypass include pyloric and duodenal strictures, postoperative ileus, and the development of cholangiohepatitis secondary to obstruction of the major duodenal papilla. Early diagnosis and surgical intervention, combined with aggressive postoperative antiulcer therapy, is suggested to increase the chance of a successful outcome (Campbell-Thompson et al., 1986).

Lesion Type and Surgical Procedures

Lesion type and specific procedure(s) performed also influence outcome. Foals with strangulating lesions have lower long-term survival rates than those with nonstrangulating lesions (Vatistas et al., 1996). The exceptions to these findings are foals with ascarid impactions, which are associated with 92% fatality due to bowel rupture, peritonitis, and adhesions present at the time of surgery (Orsini, 1997; Vatistas et al., 1996). Foals that require resection and anastomosis also have lower long-term survival rates than those requiring intestinal manipulation alone (Cable et al., 1997).

The short-term survival rates of foals with strangulating lesions and those requiring resections and anastomosis have not been documented. In 102 foals less than 1 year old that underwent exploratory laparotomy, the invasiveness of the surgery did not affect short- or long-term survival (Singer & Livesey, 1997). However, this study defined invasive as including both enterotomies and resection/anastomosis, which affect outcome.

The survival rate for foals with congenital gastrointestinal abnormalities has not been described but is likely poor, as these foals are usually euthanized intraoperatively or without surgical intervention (Loynacham, 2014; Bryant & Gaughan, 2005). In a case report of four colonic atresia cases, only one foal survived (Estes & Lyall, 1979). In another review of six atresia coli cases, all foals were euthanized intraoperatively owing to failure of, or inability to perform, a colocolic anastomosis (Young et al., 1992). Foals with intestinal atresia are predisposed to having concurrent congenital abnormalities in other systems (Orsini, 1997). In Orsini's study, three of six foals with atresia coli had concurrent congenital abnormalities, including a ventricular septal defect, cerebellar dysplasia with concurrent cerebral atrophy and hydrocephalus, and a dermal hemangioma (Orsini, 1997).

Postoperative Complications

Following emergency laparotomy, peritonitis, incisional infection, septic thrombophlebitis, ileus and intra-abdominal adhesion formation cause significant morbidity and mortality in foals (Orsini, 1997). Pre-existing sepsis alone complicates recovery and can influence the decision to euthanize intraoperatively or postoperatively, even if the prognosis for gastrointestinal recovery is good. In foals that have undergone a gastric bypass procedure, persistent gastric ulceration secondary to bile reflux, poor weight gain, and obstruction of the major duodenal papilla have been reported (Coleman et al., 2009).

Adhesion Formation

Following exploratory laparotomy, intra-abdominal adhesion formation can decrease survival. The average time from surgery to adhesion formation is approximately 60 days in foals and adults (Singer & Livesey, 1997). Foals, especially neonates (less than 30 days old) are more likely to form adhesions than older foals or adults (Lundin et al., 1989). In comparing all foals with adult horses, the incidence of confirmed postoperative adhesions in foals (10%) in one study was not significantly higher than that reported in all horses (1.5–7.0%) (Singer & Livesey, 1997). However, the number of foals that formed adhesions but survived beyond the study period, or were euthanized for recurrent colic but not

necropsied, was unknown. Hence the adhesion rate in foals is likely underestimated. Another study reported that 33% of foals developed adhesions postoperatively, and that almost half (nine of 19) of those foals developed colic secondary to those adhesions (Cable et al., 1997).

Lesion location and procedure type influence the risk of adhesion formation and subsequent survival. As in adults, foals with small intestinal lesions are more likely to develop adhesions (Kuebelbeck et al., 1998), and are more than three times as likely to die from adhesion-related complications than those with large intestinal lesions (18.5% versus 5.4%) (Singer & Livesey, 1997). Furthermore, all foals that underwent small intestinal resection and anastomosis developed postoperative adhesions. In contrast, resection and anastomosis have not been associated with increased adhesion formation in adults with small intestinal lesions (Kuebelbeck et al., 1998).

Postoperative Performance

For foals that survive to maturity after surgery, the prognosis for future athletic performance depends partly on age at the time of surgery. In Thoroughbred foals that underwent colic surgery, only 47% of horses that were operated at between 2 weeks and 6 months of age raced as adults (Santschi et al., 2000). In comparison, 70–75% of horses that underwent surgery when younger than 2 weeks or older than 6 months were able to race. The number of colic surgeries performed in a foal negatively influences racing performance; only 25% of horses that underwent two or more colic surgeries as foals were able to start compared with 69% of adult horses that underwent one colic surgery (Santschi et al., 2000). However, racing career length and earnings were equivalent in horses that were able to start, regardless of whether they underwent colic surgery as foals. Lesion type also influences postoperative performance. Foals with nonstrangulating lesions were more likely to survive to discharge (96% for nonstrangulating versus 63% for strangulating) and race (78% for nonstrangulating versus 14% for strangulating) (Santschi et al., 2000). However, no information was given regarding the cause of obstruction (e.g., ascarid versus meconium), and whether that influenced postoperative performance. Furthermore, no association has been made between lesion type and earnings in foals that raced, nor is there information about the potential association of lesion location (small intestine versus large intestine), procedures performed (enterotomy versus resection), and performance. In a review of gastrojejunostomy cases, seven of the eight foals that survived to racing age underwent race training, and three of those foals raced successfully (Coleman et al., 2009).

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35

Anesthesia of Foals with Colic

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Introduction

This chapter describes the anesthetic management of foals for abdominal celiotomy. The guidelines discussed in the chapter on anesthesia for adult horses with colic (Chapter 40) are also applicable to foals, but there are some differences between foals and adults that influence the choice and administration of anesthetic agents. Specific considerations for foals are their young age, small size, and foal–mare interactions. Management of anesthesia can be separated into preparation, anesthetic protocols, monitoring and management of abnormalities, and care during recovery from anesthesia. The nature of the disease predicating the surgical procedure may pose additional problems, such as endotoxemia and sepsis resulting from an intussusception, or azotemia and metabolic acidosis resulting from a ruptured urinary bladder.

Specific Considerations

An extensive retrospective survey of equine anesthesia mortality that included 510 foals <12 months of age (excluding foals with colic), either systemically ill or healthy, determined that foals were at a greater risk of death than adult horses (Johnston et al., 2002). The highest risk for death occurred in foals <6 months of age. Increased mortality also occurred in foals anesthetized with a total inhalational anesthetic protocol where anesthesia was induced by administration of the volatile anesthetic through a mask. This may be explained by anxiety in the foal, causing the release of catecholamines and sensitization of the myocardium to arrhythmias. In addition, a higher dose of the inhalant agent will be needed to prevent the foal from responding to a surgical stimulus, as inhalation agents provide unconsciousness but little analgesia. Because inhalation agents cause dose-dependent cardiovascular depression, the higher doses needed increase the risk for death. It is important to note, however, that surveys performed a decade or more ago describing the incidence of morbidity and mortality associated with anesthesia in foals may not be representative of present-day anesthetic practice. This potential discrepancy may be due to the greater availability of monitoring equipment, the use of more favorable inhalation agents, such as sevoflurane or isoflurane, instead of halothane, and a greater understanding of the practice of balanced anesthesia.

Age

Enzymes that metabolize drugs are less active in neonatal animals for the first 3 weeks of life compared with adults (Nouws, 1992). Consequently, dosages of drugs that are metabolized for elimination used in adult horses should not be extrapolated to neonates. Glucuronidation is decreased in foals of 1 week of age compared with adults, which may result in increased efficacy of a drug if the unconjugated metabolite is also analgesic (Knych et al., 2015a, 2015b, 2016). Differences between pharmacokinetic parameters in foals and adult horses may result from differences in tissue sequestration or perfusion and are related to the decrease in the ratio of blood volume to body weight that occurs as the foal ages (Knych et al., 2016).

Small Size

Many foals are small enough to allow personnel to support them during induction of anesthesia, to lift them onto the table without resorting to hoisting, and to help them stand during recovery from anesthesia. Collectively,

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Companion website: www.wiley.com/go/blikslager/abdomen

these benefits of small size reduce the risk of injury to the animal. When the foal becomes too heavy to lift, hoisting may be necessary, which may induce some adverse effects. Significant decreases in oxygenation occurred in 223 kg 5-month-old foals after hoisting (Braun et al., 2009). Although hoisting results in decreased arterial pressure in adult horses (Braun et al., 2013), arterial pressure was unchanged when measured 5 min after hoisting in the 5-month-old foals. However, abrupt decreases in arterial pressure were observed in some foals at the start of hoisting.

Foals weighing <150 kg require the use of a smaller anesthetic delivery system and mechanical ventilator than are used for adult horses. One reason for using smaller systems is that the quantity of carbon dioxide absorbent in a large animal circle will impose unacceptable resistance to breathing for a foal. In addition, the tidal volume of a foal is disproportionate to the volume of air in the large animal circle hoses, resulting in impaired unidirectional gas flow and a slow change in the inspired anesthetic concentration. This latter effect presents a problem when the depth of anesthesia must be increased or decreased rapidly. Most commonly, inhalation anesthesia administered to foals weighing <150 kg is delivered from a circle circuit used for medium to large dogs. Pony, Miniature horse, and donkey foals may be small enough for circuits used for small dogs, such as the Universal F or Bain circuits.

Foals weighing >150 kg may be more appropriately connected to a large animal circle delivery system with the CO_2 absorber only half full with absorbent. The internal diameter of the endotracheal tube can be used as a guide to appropriate choice of delivery system. The Y-piece connector of a small animal circle is 15 mm in diameter (for a pediatric circle it is 12 mm); therefore, all foals that can accommodate an endotracheal tube with an internal diameter ≥16 mm should be connected to a large animal circle circuit to avoid resistance to breathing through a narrow orifice. Because the internal diameter of a Universal-F circuit inspiratory hose is 9 mm, only the smallest of foals should be connected to this delivery system as resistance to air flow promotes hypoventilation. Cardiac output is higher during spontaneous ventilation than during controlled ventilation (intermittent positive pressure ventilation, IPPV). Foals, because of their small size, may ventilate adequately when breathing spontaneously. In contrast, IPPV is almost always necessary in adult horses in dorsal recumbency to treat significant hypoventilation.

Endotracheal tubes manufactured specifically for foals should be used when a foal is anesthetized. Except for the smallest of foals, endotracheal tubes purchased for use in dogs are not long enough to enter the trachea sufficiently deeply to provide a secure airway. Endotracheal tubes with internal diameters of 10–20 mm and lengths of 40–57 cm should be available for foals and are supplied by several distributors, including Jorgensen Labs (Jorvet™) and Smiths Medical (Surgivet™).

A mechanical ventilator that is used for small animals or specifically manufactured for foals should be available with a bellows capacity up to 3 L. For foals large enough to be connected to the large animal circle, the ventilators on some large animal machines incorporate a bellows that can be manually reduced to a volume of 3–4 L.

Other monitoring equipment for pulse oximetry, capnography, and invasive blood pressure measurement are interchangeable among all sizes of animal. Syringe drivers and fluid pumps are useful pieces of equipment for regulating the administration of vasoactive drugs, adjunct analgesia agents, and fluids.

Foal–Mare Interaction

Foals should be prevented from nursing by applying a muzzle for 30 min before anesthesia to reduce the likelihood that milk will be regurgitated during induction of anesthesia and result in pulmonary aspiration. The muzzle should also be reapplied for a short period after anesthesia. This recommendation is based on personal observations of healthy foals that were not muzzled: milk flowing out of the foal's mouth as soon as the foal became recumbent after induction of anesthesia, and the same observation in a foal that recovered sufficiently after anesthesia to stand and nurse and then lay down to sleep, and in another foal, endoscopic observation of milk in the trachea after it had nursed soon after anesthesia.

Foals that have not been weaned may become anxious if separated from the mare. Consequently, increased circulating catecholamine concentrations may result in the need for higher doses of anesthetic agents to achieve induction of anesthesia. When the catecholamine concentrations decrease approximately 15–30 min later, the high doses of anesthetics administered will result in reductions in ventilation, cardiac output, and arterial pressure. To avoid this adverse effect, the foal should be anesthetized in the presence of the mare. The mare may also require sedation to avoid adverse behavior when returned alone to the stall. Even with sedation, when the mare is pregnant there is the possibility that separation may be followed by abortion within 24 h.

Anesthetic Management

In clinical practice, the foal's age appears to have a considerable impact on anesthetic management. Although foals are frequently classified as neonates when <1 month of age, differences in response to anesthesia are apparent within the age ranges of birth to 7 days, 1–6 weeks,

6 weeks to 3 months, and foals older than 3 months. Much of this effect may be related to the developmental age as it affects the distribution and metabolism of drugs, but also the size and the temperament of the animal. Changes in body size and mental attitude with increasing age may result in a patient being less amenable to restraint and less calm during recovery from anesthesia.

Physiologic changes occurring over the first weeks of life and subsequent months influence the response to anesthetic agents, and knowledge of these values is important to guide appropriate management.

Preparation for Anesthesia

During the initial examination process, evaluation of the patient will identify physiologic abnormalities of fluid, electrolyte, and acid–base status that are present in many foals requiring abdominal surgery. The preanesthetic examination should include a physical examination with noninvasive measurement of blood pressure, and a review of laboratory test results, with particular attention being paid to identifying evidence of central nervous system (CNS) depression, hypovolemia, hyponatremia, hyperkalemia, hypoglycemia, metabolic acidosis, and hyperlactatemia. The results of hematologic and serum biochemistry tests must be compared with normal reference ranges for foals, as these ranges may be influenced by measurement methods and the equipment employed (Barton, 2015). Correction of hypovolemia, electrolyte abnormalities, hypoglycemia, and reduction of azotemia with appropriate fluid therapy will restore abnormalities toward the normal physiologic state before anesthesia is induced and improve the foal's health status. As expected, better health status before anesthesia is correlated with a decrease in complications from anesthesia and surgery (Dugdale et al., 2016).

The packed cell volume (PCV) is higher in foals at birth than in adult horses, decreasing in the first 48 h of life and then further decreasing by 7 days. This pattern remains the same although the absolute value may vary among breeds of horses and donkeys (Aoki & Ishii, 2012; Sgorbini et al., 2012; Veronesi et al., 2014; Barton, 2015). Similarly, blood urea nitrogen, creatinine, and L-lactate concentrations are high at birth but decrease after 24 h. The value of the total serum protein concentration depends on whether or not the foal has absorbed proteins from colostrum.

Mean plasma L-lactate concentrations measured shortly after birth have been reported as 2.38 ± 1.03–5.5 ± 1.4 mmol/L (Veronesi et al., 2014). Hyperlactatemia, defined as L-lactate concentration ≥2 mmol/L, unrelated to the birthing process may reflect either the underlying disease process or the foal's inability to compensate for increased lactate production (Tennant-Brown, 2014). In view of the high lactate concentrations normally present in the first 24 h of the foal's life, the significance of hyperlactatemia measured in a neonatal foal on admission to the hospital may be better understood by comparison with a second measurement 24 h later. Under those conditions, a decrease in L-lactate concentration after medical or surgical management is indicative of a favorable prognosis. Several studies have investigated the association between lactate measurements obtained from ill foals on admission and prognosis for survival. There is no obvious lactate concentration that separates foals that survive to be discharged from the hospital from those that do not survive. However, mean lactate concentrations at admission are significantly lower in foals that survive (Corley et al., 2005; Wotman et al., 2009). Although some foals with a high lactate concentration on admission will survive, a rough guide is that L-lactate concentrations of <4.0 mmol/L are favorable and those of 6.0–8.0 mmol/L carry a worse prognosis (Corley et al., 2005; Henderson et al., 2008; Tennent-Brown, 2014; Viu et al., 2017). A correlation between high lactate concentrations and low arterial pressures was identified in foals admitted to an intensive care unit in one study (Corley et al., 2005), but not in another study until foals with hypotension but low lactate concentrations were removed from the analysis (Wotman et al., 2009). Nonetheless, arterial pressure should be measured in all foals, including those with hyperlactatemia, to identify any foals needing further cardiovascular support before anesthesia is induced. Differences in lactate concentrations between horse and pony foals warrant further investigation as significant differences were identified in a retrospective study of animals with gastrointestinal disease in which lactate concentrations in adult ponies were significantly higher on admission and in survivors compared with values for adult miniature horses (Dunkel et al., 2013).

Blood glucose concentrations are low immediately after birth but increase in the first day to values that are higher than those of their dams. Blood glucose concentrations were >100 mg/dL (>5.55 mmol/L) for the first 7 days of life in healthy donkey foals (Sgorbini et al., 2012) and approximately 135 mg/dL (7.4 mmol/L) for the first 4 weeks of life in healthy draft horse foals (Aoki & Ishii, 2012). Blood glucose concentrations should be measured in all ill foals. For example, in a multicenter study involving 515 ill neonatal foals, average age 34 h, admitted to the hospital (Hollis et al., 2008a), 34.4% were hypoglycemic and 36.5% were hyperglycemic [based on a normal reference range of 76–131 mg/dL (4.2–7.2 mmol/L)]. In that study, hypoglycemia [<76 mg/dL (<4.2 mmol/L)] was associated with sepsis and positive blood culture and a worse prognosis for survival to hospital discharge. Consequently, foals that are hypoglycemic should be treated before induction of anesthesia. This incidence of

hypoglycemia in foals is in contrast to adult horses with acute abdominal disease, which are more commonly hyperglycemic.

A large-bore (14- or 16-gauge) jugular catheter must be inserted aseptically for administration of drugs and fluid therapy. As mentioned earlier, the foal should be muzzled for 30 min before induction of anesthesia to prevent nursing and the risk of regurgitation of milk as the foal relaxes at the start of anesthesia. Weaned foals should be withheld from feed for several hours, if time is available, and debris washed from their mouths with water immediately before induction of anesthesia. The anesthesia machine, ventilator, endotracheal tubes, infusion pumps, and monitoring equipment should be assembled and connected to power sources. Anesthetic drugs and adjunct agents should be prepared before induction of anesthesia, and the components of the anesthesia equipment checklist should be verified.

Implementation of an anesthesia and surgical checklist significantly decreases the incidence of intraoperative and postoperative complications in humans (Gillespie et al., 2014) and dogs (Hofmeister et al., 2014; Bergström et al., 2016). The World Health Organization Surgical Safety Checklist (www.who.int/patientsafety/safesurgery/checklist), which is used in many hospitals, includes questions that must be answered before induction of anesthesia (e.g., Has the patient's identity been confirmed? Is the equipment ready and functioning?), before skin incision (Has antibiotic prophylaxis been administered in the last 60 min? What are the critical and nonroutine steps facing the surgeon? What are the anesthetist's specific concerns?), and before the patient leaves the operating room (What are the key concerns for recovery and management of this individual facing the anesthetist, surgeon, and nurse?). Modification of the basic checklist or expansion to address specific concerns for each hospital is recommended, and has been utilized for dogs with the encouraging result of a decrease in the incidence of complications (Hofmeister et al., 2014). The checklist should be regarded as a means to improve patient safety by involving all personnel in the animal's surgical care and promoting teamwork. Consequently, the checklist should be completed while the attentions of all personnel are engaged and should not be treated simply as a "tick box" form.

Anesthesia Protocols

Unfortunately, few studies have described the cardiopulmonary effects of anesthetic agents and their combinations in foals. Therefore, many recommendations are based on clinical experience, which may vary according to the type of hospital, equipment and anesthetic drugs available, composition of the case population, and anesthetist's training. This is very apparent in a survey performed in 2012 that gathered information on anesthetic management of horses from equine practices worldwide (Wohlfender et al., 2015). The availability of anesthetic agents in different countries, whether the drug is licensed for use in animals or in horses, and the level of training of the anesthetist varied considerably and had significant impacts on what was used. For example, methadone is administered often in Europe, but there was no veterinary preparation of the drug available in the United States. Similarly, board-certified anesthesiologists more frequently administered medetomidine and dexmedetomidine and constant-rate infusions (CRI) than non-board-certified personnel. The respondents' opinions were that the preanesthetic status of the animal and the lack of training in anesthesiology for the anesthetist were the highest risk factors for outcome from anesthesia in horses (Wohlfender et al., 2015).

Neonatal foals have high heart rates and cardiac outputs (Dunlop, 1994). Myocardial contractility and ventricular compliance are less in the newborn and the baroreceptors are immature. Therefore, bradycardia and decreased blood volume have significant adverse effects on cardiac output. The α_2-agonist sedatives cause decreased heart rates that may adversely affect cardiovascular function, especially in ill or hypovolemic foals, and should be administered cautiously in low dosage or not at all in neonatal foals. Administration of xylazine (1.1 mg/kg) IV to 10- and 28-day-old healthy foals restrained in lateral recumbency resulted in significant decreases in heart rate and mean arterial pressure (MAP) for 120 and 60 min, respectively, with some foals developing hypotension (MAP ≤65 mmHg) (Carter et al., 1990). Cardiac output was not measured in that study. Further confirmation of the adverse effect of xylazine-induced bradycardia in foals was illustrated in a more recent study. The cardiopulmonary effects of anesthesia induced with either diazepam–ketamine or xylazine–ketamine and maintained with isoflurane were investigated in healthy pony foals at 7–15 days of age for laparotomy and again ≥1 week later for laparoscopy (Kerr et al., 2009). Dose rates used in that study were diazepam 0.2 mg/kg, xylazine 0.8 mg/kg, and ketamine 2.0 mg/kg. Cardiac output, heart rate, and MAP were significantly higher when diazepam–ketamine was used in comparison with xylazine–ketamine. Most foals in both age groups that had been administered xylazine developed hypotension (MAP <60–65 mmHg).

Administration of detomidine (0.01–0.04 mg/kg) IV to foals >2 weeks of age produced the characteristic signs of sedation associated with α_2-agonists, including a dropped head, immobility, and swaying (Oijala & Katila, 1988). The effects of the drug appear to mirror the well-published effects of detomidine in adult horses, including bradycardia and second-degree atrioventricular block lasting for 60 min. Detomidine (0.02 mg/kg) provides

satisfactory sedation before induction of anesthesia with ketamine in healthy older foals, especially when butorphanol (0.02 mg/kg) is added for premedication. Medetomidine and dexmedetomidine are currently used by some anesthetists for premedication or as CRIs during anesthesia of adult horses. Studies are needed in foals to determine the pharmacodynamic effects of these drugs and to compare them with other α_2-agonists. Acepromazine should be avoided in neonatal foals owing to its propensity to potentiate low blood pressure by vasodilation.

Analgesia is commonly provided by administration of a nonsteroidal anti-inflammatory drug, an α_2-agonist in older foals, in combination with an opioid and IV infusion of lidocaine. CNS excitation and increased locomotor activity may occur after administration of some opioids to horses (Sanchez & Robertson, 2014). There is little evidence about the extent of analgesia after administration of opioids in horses or which dose rates will provide analgesia without causing CNS excitement. In equine practice, butorphanol (0.02 mg/kg) is a useful opioid to administer with a sedative to intensify the degree of sedation before or during total intravenous anesthesia (TIVA) or inhalation anesthesia in juvenile and adult horses. Butorphanol may also provide analgesia for visceral pain (Sellon et al., 2004). A study evaluating the effects of administration of butorphanol (0.05 mg/kg) IV or IM to 3 to 8-day-old Arabian-cross foals determined that sedation was induced to a variable degree among individuals, was more pronounced after IV administration, but was no longer apparent beyond 45 min after administration (Arguedas et al., 2008). A mild increase in rectal temperature, up to 0.4 °C (0.75 °F), was recorded for 1 h after IV and 3 h after IM administration. Absorption after IM administration was not complete (66% bioavailability), but was greater in the neonatal foals than had been reported previously for adult horses. Of clinical relevance, plasma butorphanol concentrations were close to those after IV administration by 6 min. An interesting effect was that the foals spent more time nursing compared with the time recorded during a saline control treatment. Another study evaluated the ability of butorphanol (0.05 and 0.10 mg/kg) IV to block behavior responses of pony foals at either 1–2 or 4–8 weeks of age to an experimental thermal stimulus attached at the withers (McGowan et al., 2013). Administration of the higher dose of butorphanol significantly increased the thermal nociceptive threshold (relevant to somatic analgesia) in both age groups.

Buprenorphine is a mu-opioid that is being studied for use in horses in drug combinations for standing restraint and analgesia. The responses of standing healthy Norwegian Fjord foals aged 2 and 11 days to electrical stimulation (train of five 1 ms pulses at 200 Hz) to the skin over a lateral palmar digital nerve were recorded before and after administration of buprenorphine (0.01 mg/kg) IM (Risberg et al., 2015). Although the foals became sedated, antinociception was observed only in the 2-day-old foals; foals in both age groups had increased locomotor activity and respiratory rates in response to the stimulus. The bioavailability after IM administration in foals is yet to be determined.

Two mu-opioids, meperidine (pethidine) and morphine, have been used in combination with a sedative for many years in horses, but have not been evaluated scientifically in foals. Meperidine has been replaced with other opioids. Although morphine (0.1 mg/kg) is used in horses, its contribution to analgesia when used at a low dose during general anesthesia has been questioned and higher doses can induce CNS excitement. Fentanyl is extensively used as a CRI in small-animal anesthesia, but in horses there appears to be a narrow window between dosages that induce CNS excitement and those that do not. Two studies described the results of administering fentanyl, either as a single IV bolus or by sequential increasing doses, to awake neonatal foals (Knych et al., 2015a, 2015b). A single administration of fentanyl (4 μg/kg) IV to Thoroughbred foals at 1, 3 and 6 weeks of age induced sedation characterized by a wide-based four-legged stance, lowered head, and lack of arousal to a stimulus in all but one foal (Knych et al., 2015a). The times to onset were varied and the duration was short, between 4.5 and 15 min. Measurement of plasma fentanyl concentrations revealed that fentanyl is cleared more rapidly in foals than in adult horses. In the second study, foals aged 5–13 days were administered doses of fentanyl of 2, 4, 8, 16, and 32 μg/kg at 10 min intervals (Knych et al., 2015b). Six of eight foals were sedated with the fentanyl dose of 4 μg/kg, but increased locomotor activity, head pressing, and muscular rigidity occurred after the 8 and 16 μg/kg doses. Although fentanyl (4 μg/kg) induced sedation and potentially could be utilized for preanesthetic medication, the duration is so short that additional fentanyl would have to be administered during anesthesia. Fentanyl and remifentanil (an ultrashort-acting mu-opioid agonist) have been administered as CRIs to adult horses anesthetized with either isoflurane or sevoflurane (Thomasy et al., 2006; Benmansour et al., 2014). In one study evaluating three dose rates for loading dose and CRI of fentanyl, a reduction in isoflurane requirement was obtained only at the highest dose rate studied, and one of the five horses administered that dose exhibited excitement during recovery (Thomasy et al., 2006). Studies are required to identify the optimal dose rate in foals that will provide prolonged analgesia without inducing the adverse postoperative effects of CNS excitement and decreased gastrointestinal motility.

Tramadol is structurally related to codeine with a weak mu-receptor agonist action and a blocking effect on

serotonin and norepinephrine uptake in pain pathways within the spinal cord. Although not considered to be a strong analgesic, it is a popular prescription drug for postoperative analgesia in dogs. However, a recently published study measuring plasma concentrations of tramadol and its metabolite in 1-, 2-, 3- and 6-week-old foals observed short-lived (about 15 min) signs of sedation only in the older foals that also exhibited pronounced muscle tremors after tramadol administration (Knych et al., 2016). Without additional information, the use of tramadol in foals cannot be recommended.

Premedication

The objectives of premedication are to minimize anxiety in the foal and to decrease dose rates of anesthetic agent(s) used for induction of anesthesia. Foals up to 10–14 days of age can be sedated by administration of diazepam or midazolam (0.05–0.20 mg/kg) IV with an opioid, such as butorphanol (0.01–0.05 mg/kg) (Table 35.1). Clearance of diazepam is slow in foals <3 weeks of age, thus repeating the premedication dose of diazepam in the induction protocol, will result in accumulation of the drug and is not advised (Norman et al., 1997). Older foals up to 2 months of age also can be administered xylazine (0.1–0.4 mg/kg) or romifidine (0.01–0.04 mg/kg) IV. The dose rates of the α_2-agonist can be progressively increased as the foal's age increases, up to dosages used in adult horses; in all cases, the dosage should be based on the health status of the foal. Assessment of the foal after premedication allows the anesthetist to judge the dose rate of the induction drugs, whether they are injectable agents or mask induction in very young foals. Foals with a mare should be sedated and anesthesia induced with the mare present.

Induction

Anesthesia may be induced in very young or depressed foals by using light sedation and an inhalation agent delivered through a facemask or nasotracheal tube. Masks with a rubber diaphragm manufactured for anesthesia of large dogs will produce an airtight seal between mask and muzzle, facilitating speed of induction and minimizing room pollution with anesthetic gas. Homemade masks can be constructed from a plastic bottle with the bottom removed and the sharp edge covered with elastic bandage material to protect the foal's skin. The foal should first be allowed to breathe only oxygen through the mask to become accustomed to the equipment. Then, the vaporizer setting is increased by 0.5% every few breaths or approximately every 5 s to a concentration appropriate for the gas, the degree of sedation, and the physical status of the foal. When the foal is lightly anesthetized, it should be placed in lateral recumbency, if this has not occurred already, for endotracheal intubation (tube sizes with an internal diameter of 10–14 mm). Pollution of the room with the anesthetic gas can be eliminated by using a nasotracheal tube instead of a facemask. A nasotracheal tube, size 8–11 mm, is introduced at one nostril and pushed ventrally with one finger to enter and remain within the ventral nasal meatus. The other hand advances the nasotracheal tube until the tip is in the pharynx. The foal handler then extends and

Table 35.1 Selected anesthetic protocols for premedication and induction of anesthesia in foals before maintenance of anesthesia with an inhalation agent. Drug combinations and dose rates should be chosen based on the foal's age and physical health.

Premedication		Induction		
Drug	**Dose rate (mg/kg IV)**	**Drug**	**Dose rate (mg/kg IV)**	**Comments**
Diazepam *or* Midazolam	0.05–0.10	Ketamine	1.0–2.2	Neonatal foals; lowest doses for foals <2 weeks old
Butorphanol	0.01–0.10			
Xylazine *or* Romifidine	0.4–0.6 0.04–0.06	Ketamine	1.0–2.2	Foals >2 weeks old
± Butorphanol	0.02	± Diazepam *or* Midazolam	0.05	
Xylazine	0.6–1.0	Ketamine *or* Ketamine Guaifenesin	 2.0–2.2 1.7 20–50	Foals >2 months old
Butorphanol Midazolam	0.05 0.1	Propofol	0.5–1.0 slowly IV to effect	Foals <2 weeks old (Lascola et al., 2013)

straightens the foal's head and neck by pushing down between the ears so that the tube can be gently advanced into the larynx. Presence of the tube within the larynx can be confirmed by loosely cupping a hand over the end of the tube and feeling air flow as the foal breathes. The nasotracheal then is advanced down the trachea, connected to the delivery system, and the foal is allowed to breathe the inhalation agent. The nasotracheal tube must be held firmly in position during induction of anesthesia to avoid movement of the tip against the tracheal mucosa or accidental extubation if the foal shakes its head. The cuff can be inflated to minimize dilution of inspired anesthetic gas by air inhaled around the tube. When this technique is used for healthy foals, the nasotracheal tube is removed when the foal is fully anesthetized and a larger tube is inserted orotracheally. Switching tubes is not advisable for foals with gastrointestinal distension, even when a nasogastric tube is in place, because of the risk of regurgitation of gastric fluid when the foal lies down or the nasotracheal tube is removed. This can result in pulmonary aspiration if the airway is unprotected. If regurgitation occurs before the change can be made, the nasotracheal tube will have to be used for anesthesia, resulting in resistance to breathing if a small tube has been inserted and necessitating IPPV.

Foals weighing <110 kg are frequently induced to general anesthesia while standing beside or lying on the surgery table. Ketamine (1.0–2.2 mg/kg) IV is the most commonly used agent administered for induction of anesthesia, with the lowest dose rate being used for foals <2 weeks of age (Table 35.1). Ketamine (2.0–2.2 mg/kg), with or without diazepam or midazolam, provides satisfactory induction of anesthesia in foals ≥2–3 months of age, with sufficient anesthesia time for endotracheal intubation and transportation to the adjacent surgical facility. Large premedicated foals can be anesthetized with ketamine combined with guaifenesin (20–50 mg/kg) IV (Table 35.1).

Propofol is frequently administered to adult horses during induction of anesthesia with ketamine to improve muscle relaxation as the horses slowly fall to the floor. Propofol has also been used instead of ketamine for induction of anesthesia in foals. In one recent study, healthy Standardbred foals, 2.5–13 days old, were sedated for computed tomography by IV administration of butorphanol (0.05 mg/kg) and midazolam (0.1 mg/kg) followed by propofol (Lascola et al., 2013). Although the investigators had a calculated dose of propofol (4 mg/kg) available, propofol was administered slowly and titrated to effect. As a result, the actual dose of propofol required for these foals was 0.5–1.0 mg/kg.

Alfaxalone has attracted some interest for its potential use as a supplement or for TIVA in adult horses. The pharmacokinetics and effects of alfaxalone were determined in five Australian Stock Horse foals aged 12 days (Goodwin et al., 2012). The foals were premedicated with butorphanol (0.05 mg/kg) and 10 min later alfaxalone (3 mg/kg) was injected slowly IV over 1 min. Endotracheal intubation was performed and oxygen (6 L/min) insufflated into the endotracheal tube. The duration of immobility was 19 ± 7 min and time to standing was 49 ± 1 min. Induction of anesthesia was smooth and endotracheal intubation was accomplished easily. The results of that study indicated that the pharmacokinetic profile in the foals differed from that of alfaxalone administered to adult horses, and that hypoxemia occurred in the 5 min after induction of anesthesia despite oxygen insufflation. These effects of alfaxalone in butorphanol-premedicated neonatal foals are promising.

Maintenance of Anesthesia

Anesthesia for laparotomy is usually maintained by administration of isoflurane or sevoflurane in oxygen. The vaporizer settings for foals on a small circle circuit will be much lower than those required for a large animal circle because the dilution effect is less. Oxygen flowmeter settings for a small circle can be reduced to 1–2 L/min once the nitrogen has been washed out of the system and sufficient anesthetic gas has accumulated to produce adequate anesthesia. This may take up to 10 min. Vaporizer settings for a small circle are approximately 1.5% for isoflurane and 2.5% for sevoflurane.

Lidocaine is commonly administered by infusion for its anti-inflammatory effects in horses with colic. Because lidocaine also provides some sedation, it is important to decrease the vaporizer setting to avoid an excessive depth of anesthesia that induces vasodilation and hypotension (Fischer & Clark-Price, 2015). One recommendation is to administer a loading dose of lidocaine (1.3–1.5 mg/kg) IV over 15 min to be followed by a continuous infusion of 0.05 mg/kg/min (3 mg/kg/h). If hypotension develops, this is an indication to decrease the vaporizer setting. However, the desired improvement in blood pressure also may be achieved by decreasing the lidocaine infusion rate.

Monitoring During Anesthesia

Monitoring the anesthetized foal is key to patient safety and one person should be dedicated to this responsibility for each foal. Anesthesia is a dynamic process and early recognition of an imminent complication is often facilitated by the knowledge of the physiologic variables recorded in the previous 10–15 min (Figure 35.1). Monitoring equipment provides detailed information that can be combined to yield a better overall interpretation of the animal's status than can be obtained from limited measurements or subjective interpretations. However, the latter skills can become useful as they develop as experience in anesthetizing horses increases.

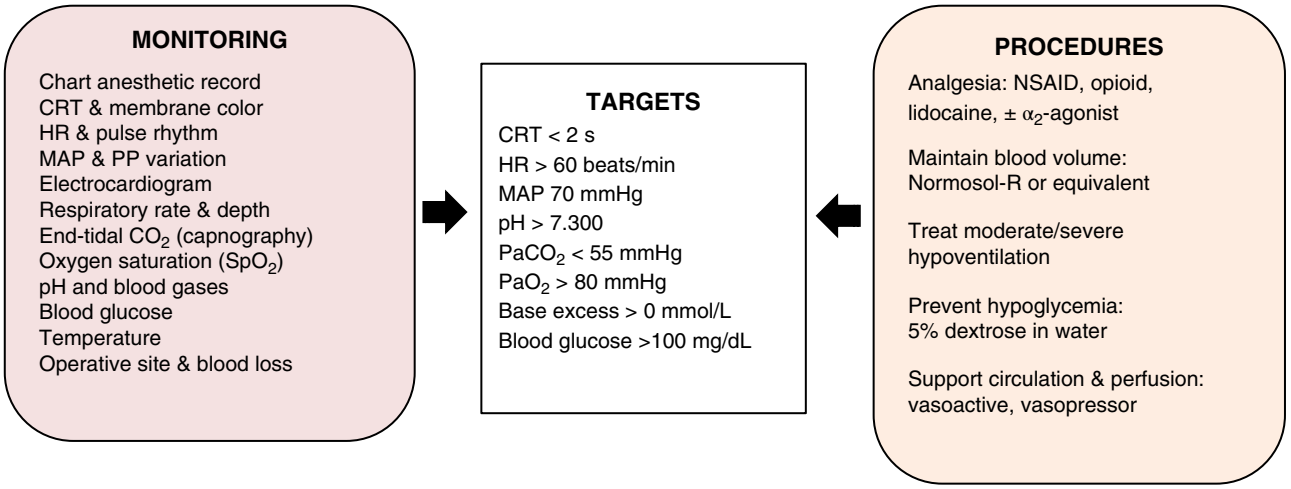

Figure 35.1 Desired target values for variables monitored in foals during general anesthesia, with monitoring and procedures required to achieve these values. CRT, capillary refill time; HR, heart rate; MAP, mean arterial pressure; PP, pulse pressure (systolic – diastolic pressure); NSAID, non-steroidal anti-inflammatory drug.

Depth of Anesthesia

The depth of anesthesia may be difficult to judge based simply on lack of limb movement, eye position, palpebral reflex, heart rate, respiratory rate, and breathing pattern. In fact, heart and respiratory rates may be unchanged at moderate and deep planes of anesthesia. Gradual reduction in anesthetic administration until obvious signs of light anesthesia (moderate strength of palpebral reflex and increases in heart rate, arterial pressure, and respiratory rate) may be an effective strategy for avoiding excessively deep anesthesia. When an anesthetic gas analyzer is available, the end-tidal isoflurane or sevoflurane concentration may be measured and maintained at a value not more than 1.5 times the minimum alveolar concentration (MAC) value for that agent. Depending on which analgesic drugs are being administered and the health status of the foal, the end-tidal isoflurane or sevoflurane value for adequate surgical anesthesia may be achieved at concentrations as low as 0.5 × MAC. Foals <2 months of age require a lower concentration of inhalation agent for anesthesia than adult horses. Typically, MAC values in adult horses are approximately 1.1% for halothane, 1.3% for isoflurane, 2.8% for sevoflurane, and 8.1% for desflurane, although ranges exist for these agents depending on the methodology and the horse population used in the determination. Lower MAC values, such as 0.72% for halothane and 0.87% for isoflurane, have been measured for neonatal foals.

Ventilation

Adequacy of ventilation is quantified by measuring arterial carbon dioxide partial pressure ($PaCO_2$) and indirectly by measuring end-tidal CO_2 ($ETCO_2$) using capnography. $ETCO_2$ may not correspond accurately to $PaCO_2$ in foals that are breathing spontaneously and this is more likely with spontaneous breathing as the duration of anesthesia progresses (Geiser & Rohrbach, 1992). Therefore, it is advisable to make at least one blood gas measurement early during anesthesia to determine if IPPV is warranted. Measurement using arterial blood is advisable to obtain information about oxygenation and also ventilation, but venous blood samples can be used to provide an approximation of ventilation as $PaCO_2$ should be lower than venous PCO_2. Furthermore, the base excess measurement, which is an indicator of metabolic acid–base status, should be identical in arterial and venous blood.

The reported $PaCO_2$ in healthy conscious foals <2 weeks of age is 40–44 ± 3 mmHg (5.3–5.9 ± 0.4 kPa) (Carter et al., 1990; Lascola et al., 2013) when standing and 49 ± 4 mmHg (6.1 ± 0.5 kPa) when recumbent (Wong et al., 2011). Mild hypoventilation is indicated by an increase of 10 mmHg in $PaCO_2$ [≤50–55 mmHg (6.7–7.3 kPa)], moderate hypoventilation by an increase in $PaCO_2$ of 20 mmHg [≤60–65 mmHg (8.0–8.6 kPa)] and severe hypoventilation by $PaCO_2$ of >60–65 mmHg (>8.0–8.6 kPa). Controlled ventilation should be started when moderate hypoventilation is identified. Generally, a respiratory rate of 10–12 breaths/min and a tidal volume of 12–15 mL/kg applied with an inspiratory time of 1.5 s will achieve $PaCO_2$ close to normal. Peak inspiratory pressure should be monitored to ensure that it does not exceed 25 cmH_2O, a pressure that will decrease cardiac output and may cause barotrauma.

Oxygenation

Oxygenation of arterial blood is determined by adequate ventilation, cardiac output, and arterial pressure. The arterial oxygen partial pressure (PaO_2) should be approximately 80–90 mmHg (10.6–12.0 kPa) at sea level, but

lower at higher elevations. Mean PaO_2 values for 15 foals in lateral recumbency at an altitude of 1500 m were 53.0 mmHg (7.1 kPa) after birth and 68 mmHg (9.0 kPa) at 48 h, with an oxygen saturation of 88% (Hackett et al., 2010). Foals born at high altitude will have a higher hemoglobin concentration with increased oxygen affinity, but anesthesia will prevent other compensatory mechanisms, such as increased frequency of ventilation and increased cardiac output. Consequently, the significance of the measured PaO_2 value must be considered with respect to the local altitude.

Hypoxemia is defined at sea level as $PaO_2 \leq 60$ mmHg (8.0 kPa). The impact of low PaO_2 on patient outcome is largely influenced by the state of systemic perfusion. Even when hemoglobin is fully saturated, as is likely to occur when the foal is breathing >90% inspired oxygen, oxygen delivery to the brain, heart, or gastrointestinal tract will be compromised when the animal is hypotensive. Hypoxemia may not be apparent by observation of gum color and the status of oxygenation is best determined by blood gas analysis of arterial blood. Pulse oximetry gives an estimate of peripheral hemoglobin oxygenation, and interpretation of the results may depend on the internal algorithm of the monitor used. The peripheral capillary oxygen saturation (SpO_2) recorded by some oximeters is consistently lower than the level of saturation (SaO_2) determined by blood gas analysis in foals (Chaffin et al., 1996; Wong et al., 2011). In one study, a reflectance pulse oximeter placed on the ventral surface of the base of the tail in foals had 100% sensitivity for detecting $SaO_2 < 90\%$ but consistently underestimated the actual value (Chaffin et al., 1996). In another study, a reflectance transducer (Oxisensor II RS10, Tyco Healthcare Group, Pleasanton, CA, USA, and Passport 2, Datascope Patient Monitoring, Mahwah, NJ, USA) taped at the same location provided a good recording of pulse rate but SpO_2 measurements were 3% lower than SaO_2, leading the authors to recommend blood gas analyses to verify hypoxemia (Wong et al., 2011).

Circulation

Cardiovascular function can be assessed using capillary refill time, pulse rate, arterial blood pressure, color of blood, and bleeding at the operative site. Some facilities may have equipment to measure the cardiac output using the noninvasive method of partial CO_2 rebreathing [noninvasive cardiac output (NICO)] (Novametrix Medical Systems, Wallingford, CT, USA) to assess trends in cardiac output or the more invasive technique of lithium dilution cardiac output (LiDCO) (LiDCO, London, UK) (Valverde et al., 2007). The capillary refill time, assessed by finger compression and release on the gum, should be less than 2 s. Measurements of hemodynamic changes from birth to 2 weeks in one group of healthy neonatal Thoroughbred/Quarter horse foals indicated some rapid changes occurring in the first 24 h of life followed by gradual changes (Thomas et al., 1987). In these foals, heart rates increased from a mean of 83 bpm in the first 10 h after birth to 95 bpm at 2 days and 114 bpm at 8 days of age, mean aortic pressures increased from 86 mmHg at 10 h after birth to 91 mmHg at 2 days and 100 mmHg at 8 days, and cardiac outputs increased from 188 mL/kg/min at 10 h to 234 mL/kg/min at 8 days; cardiac output indices were up to three times higher than recorded in adult horses. Similar values of heart rate 110 bpm, MAP 100 mmHg, and cardiac output 225 mL/kg/min in the first 2 weeks of life have been published (Dunlop, 1994).

Mean arterial pressure in healthy isoflurane-anesthetized, ventilated, laterally recumbent neonatal foals was measured noninvasively using two oscillometric methods and the values were compared with pressures measured from a catheter in the metatarsal artery (Giguère et al., 2005). Significant differences were obtained between the monitors and site of cuff placement. MAP measured by the Cardell Veterinary Monitor 9402 at the coccygeal artery and the DINAMAP Pro 100 at the metatarsal or coccygeal arteries had the best correlations to MAP measured directly. The range of cuff widths used in this study was wide (36–90%) and there was no correlation between cuff width and the mean differences between invasive and noninvasive measurements. Although noninvasive measurement of blood pressure may be adequate for healthy foals anesthetized for a short time, the invasive method should be used for foals anesthetized for laparotomy. Reasons for this strong recommendation are that measurement using oscillometric monitors may be interrupted by body movement from the surgical procedure and, importantly, owing to the intermittent nature of oscillometric monitoring and the variation in accuracy, early recognition of hypotension and response to treatment are less efficient than when guided by continuous pressure measurement from an arterial catheter.

Catheters can be inserted in the facial, transverse facial, and metatarsal arteries for measurement of arterial pressure, and details are available elsewhere (Clarke et al., 2014). In foals that are young, depressed, and easily restrained in lateral recumbency on the table, after clipping the hair and aseptic preparation of the skin, a 22-gauge catheter should be inserted into a metatarsal artery before induction of anesthesia. Arterial pressures will then be available immediately before anesthesia, after induction and tracheal intubation, and as soon as the foal is positioned in dorsal recumbency, allowing immediate observation of low MAP and the need for intervention. Insertion of the arterial catheter may be delayed until after induction of anesthesia in foals that are less ill and standing before anesthesia. In foals,

insertion of a catheter in the facial artery where it curves around the mandible may be more difficult than catheterization of the artery where it is adjacent to the rostral border of the masseter muscle on the side of the face. Catheterization at this site is facilitated by rotating the foal's head into a partially lateral position.

After insertion of the catheter, it should be capped or a three-way stopcock attached, flushed with sterile heparinized saline without preservative, and then sutured or stapled to the skin using a white tape tab around the hub of the catheter. Low-compliance (ideally) tubing filled with heparinized saline should connect the catheter to a pressure transducer placed level with the thoracic inlet or sternum when the foal is lateral or the thoracic inlet or point of the shoulder when the foal is in dorsal recumbency. Electrocardiography leads should be attached in a base–apex configuration for monitoring cardiac rate and rhythm.

Temperature

Hypothermia is a common consequence of anesthesia in foals, especially in an air-conditioned operating room. The most accurate means of measuring core temperature to identify hypothermia is through the use of a rectal probe; a nasal probe may provide a reading substantially lower than the core temperature. Several methods can be employed to minimize heat loss and prevent the development of hypothermia. A warm waterbed is available in a size that fits a small-animal operating table, allowing the foal to sink into the mattress and be cradled by the warmth. A hot-air blanket can be positioned over the foal's thorax, forelimbs, and neck. Fluid bags for IV fluid therapy can be warmed although, depending on the rate of infusion, the temperature of the fluid may have decreased by the time it reaches the indwelling catheter. A warm recovery room is also advisable.

Fluid Administration

A foal in its first week of life retains some of the fetal physiologic mechanisms that predispose it to fluid overload (Palmer, 2004; Fielding, 2014). For example, the nature of the neonatal capillary epithelium allows high filtration of fluid that is counterbalanced by a high lymphatic flow rate (Palmer, 2004). Increases in venous pressure may result in increased retention of interstitial fluid by impeding lymph return. Further, the high capillary filtration results in movement of fluid out of the capillaries, thereby diminishing intravascular retention of administered fluids. Many foals requiring abdominal surgery are also critically ill. A recent study found that critically ill dogs developed a significantly greater degree of fluid overload when compared postoperatively with systemically healthy dogs; the results confirmed that the critically ill dogs were administered more fluid in the course of intensive management, but excreted a smaller fraction of administered fluids (Cavanagh et al., 2016). Although there is an association between increased fluid overload and mortality, this has yet to be confirmed (Cavanagh et al., 2016). Given that hypovolemia and hypotension must be treated and fluid loss during laparotomy from evaporation and blood loss replaced, the choice of fluid composition and volume of fluid administered must be carefully balanced. One recommendation for fluid therapy for foals in the intensive care environment is to avoid hyperchloremia, colloids, and fluid overload (Fielding, 2014). Imposition of cardiovascular depression from anesthetic agents and altered fluid balance from surgery may necessitate some deviations from recommended daily maintenance therapy.

An increase in arterial pressure in the neonatal foal over the normal value may decrease the intravascular fluid volume and cause increased protein leak (Palmer, 2004). Because it may be important to avoid generating high arterial pressures when treating hypotensive foals, accurate information regarding blood pressure must be obtained rapidly using invasive pressure monitoring. Resuscitation from hypovolemia should be achieved with an initial IV infusion of 20 mL/kg balanced electrolyte solution, Normosol R, Plasmalyte, or lactated Ringer's solution before anesthesia is induced. While this fluid should be continued during anesthesia at 5–10 mL/kg/h, an additional administration of 10 mL/kg, or more, may be necessary to adjust for the decrease in MAP resulting from isoflurane- or sevoflurane-induced peripheral vasodilation, and mesenteric vasodilation and evaporation after the abdomen is opened. Effectiveness of fluid therapy should be assessed by MAP, adequate pulse pressure (systolic minus diastolic pressure), acceptable mucous membrane color, capillary refill time <2 s, and warm ears and legs. Postoperatively, assessment of adequate blood volume may be further monitored by noting the volume of urine output and by weighing the foal twice daily. When the urinary bladder has been catheterized to avoid operative site contamination with urine or for monitoring of urine output during anesthesia, normal urine flow should be >1 mL/kg/h. Decreased urine output during anesthesia may not only be caused by hypovolemia because inhalation anesthesia significantly decreases renal blood flow even in healthy animals.

The recommendations for colloid administration have varied considerably in the last decade because of reported renal damage after administration of hetastarch in human patients. A concern for foals in the first few days of life is that colloids may leak into the interstitial space and prolong fluid retention (Palmer, 2004). The focus now in human medicine is to balance carefully the volumes of the different fluids administered to avoid fluid overload. When hemodynamic stability has failed to be achieved by decreasing anesthetic administration, infusing crystalloid fluid, and administering vasoactive agents, infusion of plasma or 6% hetastarch (10 mL/kg) may be required.

Hypoglycemia may develop in foals during anesthesia, particularly in those foals anesthetized within 48 h of birth (Holdstock et al., 2004). Hyperglycemia develops in response to administration of xylazine in adult horses but does not occur in foals <4 weeks of age (Robertson et al., 1990) and is not a consideration when evaluating a blood glucose result in neonatal foals. Measurement of blood glucose concentration is recommended at 30–60 min intervals during anesthesia. Based on the results obtained, 5% dextrose in water (D5W) should be infused IV at 3–5 mL/kg/h, in addition to the balanced electrolyte solution, to maintain blood glucose >100 mg/dL (5.55 mmol/L) (Adams & Trim, 1990). The infusion rate should be adjusted according to each measurement result. The infusion of D5W should be continued until the end of anesthesia because the blood glucose concentration can decrease significantly in the hour after anesthesia. Continued administration of D5W is particularly important in foals in the first week of life, as postanesthetic nursing will not result in a substantial increase in blood glucose until the foal is ≥5 days old (Holdstock et al., 2004). Blood glucose concentration should be measured in older unweaned foals but dextrose infusion may not be necessary.

Measurement of blood glucose with a point-of-care glucometer is convenient but significant differences have been identified when results obtained using various models were compared with results obtained from a standard laboratory chemistry analyzer. One such study determined that glucose concentrations measured with a glucometer (Accu-Check) were consistently on average 20 mg/dL (1.1 mmol/L) lower than those from the chemistry analyzer (Russell et al., 2007).

Circulatory Support

There are many causes of hypotension, including hypercarbia, hypovolemia, anesthetic agents that cause bradycardia, myocardial depression, or excessive systemic vasodilation or vasoconstriction, myocardial depression from endotoxemia or severe metabolic acidosis, or dysrhythmias (see Table 40.3 in Chapter 40). An initial assessment of membrane color, capillary refill time, MAP, arterial pulse pressure, and heart rate and rhythm may indicate the root source of the hypotension. The target values for MAP and capillary refill time should be 70 mmHg and <2 s, respectively. The first line in treatment of hypotension should be a decrease in anesthetic administration with or without an infusion of 10 mL/kg of crystalloid solution. Hypercarbia from hypoventilation may cause sympathetic stimulation and hypertension or decreased myocardial contractility and vasodilation resulting in hypotension. When hypoventilation has been identified either from shallow breathing or by $PaCO_2$ > 55 mmHg (7.3 kPa) and arterial pressure improves after several minutes of controlled ventilation, IPPV should be continued. Significant acidemia (pH ≤7.250) should be investigated to identify a cause (respiratory, metabolic acidosis, or mixed) and treated accordingly.

The vasoactive strategies described in Chapter 40 can be used to support cardiovascular function in foals. Frequently, the first choice in foals is IV infusion of dobutamine (0.5–1.5 μg/kg/min to increase MAP or 2.0–5.0 μg/kg/min to increase cardiac output and MAP) (Table 35.2). A solution of dobutamine, 100 or 200 μg/mL depending on the size of the foal, is used with the rate of infusion being regulated by a fluid pump or a syringe

Table 35.2 Suggested intravenous dose rates for vasoactive drugs used for circulatory support in foals.

Drug	Dose rate	Comments
Dobutamine	1–5 μg/kg/min	Low dose increases MAP by mild vasoconstriction and higher dose increases cardiac output and MAP by increasing contractility. Efficacy diminished with hypovolemia. Infusion rate adjusted according to MAP
Ephedrine	0.03–0.06 mg/kg	Duration approximately 30 min. Can be administered concurrently with dobutamine
Dopamine	7–10 μg/kg/min	Increases cardiac contractility with some vasoconstriction and increase in heart rate. Recommended for treatment of atrioventricular heart block and cardiovascular collapse. Can be administered concurrently with dobutamine
Norepinephrine	0.1–1.0 μg/kg/min	Vasoconstriction at low doses increases MAP but may decrease cardiac output and higher doses increase MAP and cardiac output (Hollis et al., 2006; Valverde et al., 2006; Craig et al., 2007). Can be administered concurrently with dobutamine
Phenylephrine	0.1–2.0 μg/kg/min	Dose rate in adult horses. High dose significantly increased MAP but decreased cardiac output and oxygen delivery (Fantoni et al., 2013)
Arginine vasopressin	0.1–2.5 mU/kg/min	Not for first-line treatment; included when hypotension persists after resuscitation with fluids and treatment with dobutamine and norepinephrine; cardiac arrest
Epinephrine	0.01 mg/kg every 2–3 min until spontaneous heart beat	Cardiac arrest; combine with controlled ventilation and external cardiac massage

driver (see Table 40.5 in Chapter 40). Dobutamine may increase cardiac output but cause sufficient vasodilation to preclude an increase in MAP (Craig et al., 2007). Ephedrine (0.06 mg/kg bolus or in divided doses) IV may improve MAP when administered either alone or concurrently with dobutamine. Dopamine infused IV is the agent of choice in foals with bradycardia (7 μg/kg/min) or third-degree atrioventricular heart block (7–10 μg/kg/min) or acute cardiovascular collapse (10 μg/kg/min).

When the selected vasoactive agents have been ineffective in counteracting vasodilation, the vasopressors norepinephrine or phenylephrine may be utilized to increase MAP (Table 35.2). Varying effects on heart rate and cardiac output have been reported during infusions of norepinephrine (0.05–1.0 μg/kg/min) in foals (Hollis et al., 2006; Valverde et al., 2006; Craig et al., 2007). Norepinephrine (0.2 and 0.4 μg/kg/min) increased MAP without changing the heart rate or cardiac output in anesthetized foals (Craig et al., 2007; Hollis et al., 2008b), whereas in another study, norepinephrine (0.3 and 1.0 μg/kg/min) increased MAP and cardiac output dose dependently without changing the heart rate (Valverde et al., 2006). Concurrent administration of dobutamine with norepinephrine is likely to result in a greater improvement in MAP than that obtained with either drug alone (Hollis et al., 2006). Arginine vasopressin is frequently included in resuscitation from cardiac arrest. In one study of hypotensive anesthetized healthy foals, vasopressin infusion was not effective in increasing heart rate, cardiac output, or MAP and evidence of decreased gastric perfusion was found (Valverde et al., 2006). Infusion of vasopressin may be effective in septic foals with depleted endogenous vasopressin concentrations.

An extensive review of the interaction of physiologic changes resulting in hypotension and the mechanisms of action of vasoactive drugs that may contribute to cardiovascular support in equine anesthesia has been published (Schauvliege & Gasthuys, 2013).

Recovery from Anesthesia

The foal should not be disconnected from the oxygen supply immediately at the end of surgery. After the foal has been turned into a lateral position, the oxygen flow rate should be increased to flush anesthetic gas from the circuit and the foal allowed to breathe oxygen for up to 10 min. As the depth of anesthesia lightens during this period, the foal can be weaned from controlled to spontaneous ventilation by squeezing the reservoir bag about four times per minute. Oxygen should be supplied after the foal has been moved to a foam mat in the recovery stall. Foals can be intermittently artificially ventilated by connecting either a demand valve or a resuscitator (ambu) bag with oxygen flow to the endotracheal tube. The demand valve is used with larger foals as is done for adult horses, whereas the resuscitator bag is used with small foals. When breathing appears to be adequate, the assisted modes can be replaced by oxygen insufflation (5–7 L/min). After endotracheal extubation, rubber tubing delivering the oxygen can be inserted into the ventral nasal meatus of one nostril. In the interval between assisted ventilation and extubation, oxygen should be insufflated into the endotracheal tube, but care must be taken to avoid occluding the lumen. A variety of tubes and catheters intended for other uses can be used for this purpose, including a cut length of IV administration set tubing with one end inserted securely into the rubber tubing from the flowmeter and the other end into the endotracheal tube.

Personnel usually remain with small foals during the recovery period. The foal's head should be elevated with towels or a foam wedge to reduce nasal congestion and decrease the incidence of nasal obstruction after extubation. When evidence of nasal mucosa swelling is detected by palpation at the end of anesthesia, unless regurgitation has occurred, the orotracheal tube should be replaced with a nasotracheal tube for recovery until the foals stands. Young foals are manually restrained in lateral recumbency until judged ready to stand. If hypoxemia was present during anesthesia, supporting the foal in sternal position at this time may improve oxygenation. Foals >2 months of age can be left to recover unassisted in a padded recovery stall, although kept under continuous observation.

Small foals that are being manually assisted to stand, and foals that were administered a continuous infusion of an α_2-agonist, will not need additional sedative administration to facilitate recovery. Large foals may benefit from IV administration of romifidine (0.02 mg/kg) or xylazine (0.2 mg/kg) approximately 10 min after the inhalation agent has been discontinued. Assistance with standing may be provided by manual lifting by the tail with someone steadying the foal at its head.

Once the foal is standing with minimal ataxia, the mare can be brought to the recovery stall and mare and foal then returned to their regular stall. As the swallowing reflex and the gastroesophageal sphincter may be compromised by residual effects of anesthesia, foals that nurse immediately may aspirate some milk into the trachea. Furthermore, milk may flow down the esophagus into the pharynx if they lie down to sleep soon after nursing. Both events carry the risk of pulmonary aspiration of milk. Therefore, the muzzle used before anesthesia should be reapplied before the foal rejoins the mare until 45–60 min have elapsed after discontinuing anesthetic administration. Although this time period is arbitrary, it has been used successfully for many years. The mare's behavior should be monitored when the foal tries to nurse with the muzzle in place.

Conclusion

Anesthesia of neonatal foals involves consideration of physiologic and pharmacologic differences from older foals and adult horses. The best outcome will occur when abnormalities of cardiopulmonary function, fluid, and electrolyte balance are treated before induction of anesthesia, minimizing the risk of anesthesia exacerbating the severity of the animal's condition. Intraoperative monitoring is essential to identify deviations from healthy conscious foals and anesthetic management must be adjusted to restore the variables to within normal ranges. The choice of drug combinations will be partly dictated by the availability of specific agents but dose rates should be decreased in young and ill foals. Provision of analgesia is important and is an ongoing field of study to determine the dose rates of drugs that are effective in horses without inducing adverse behavioral responses.

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36

Specific Diseases of the Foal

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The number and variety of conditions resulting in colic or abdominal distention in the foal are extensive, as in the adult. Although many conditions that affect the foal also occur in the adult, there are a few conditions that are unique to foals, or for which the management and outcomes are slightly different. Most cases of colic in the foal are managed medically, with only 11% of foals presented for colic requiring surgery (Mackinnon et al., 2013). In that study, the most common diagnoses were enterocolitis, meconium retention, and idiopathic colic. Of foals that required surgery, the most common diagnosis in Mackinnon et al.'s study was small intestinal strangulation (Mackinnon et al., 2013), whereas in another study, uroperitoneum, meconium impaction, enteritis, and intussusception were most commonly seen (Cable et al., 1997) (see Chapter 34).

Stomach

Gastric Outflow Obstruction

Gastric outflow obstruction is most commonly a consequence of chronic gastroduodenal ulceration leading to fibrosis and stricture of the duodenum, although congenital pyloric stenosis has been reported (Munroe, 1984; Barth et al., 1980; Kol et al., 2005). This condition appears to be less commonly recognized now than in the past, perhaps owing to the widespread and common use of acid suppressive medications; however, some published information does not support the idea of reduced incidence of duodenal ulceration or increased use of anti-ulcer medication (Elfenbein & Sanchez, 2012). In one postmortem study of 691 foals, the overall incidence of duodenal ulceration (alone or combined with other sites) was only 5% (Elfenbein & Sanchez, 2012). This report also found that the incidence of anti-ulcer medication use had not increased in the study period, which spanned 20 years.

In addition to the impact of management and medication use, age is important in lesion location. For example, a recent retrospective study of colic in 137 foals less than 30 days of age found that only 15 foals were managed surgically, and of these none had pyloric outflow obstruction due to gastroduodenal ulceration (Mackinnon et al., 2013), whereas an earlier study reported that 30% of exploratory celiotomies for colic in juvenile horses (older than 30 days) had a diagnosis of gastric ulcer-associated disease (either stricture or gastric rupture) (Santschi et al., 2000). The true incidence of duodenal ulceration and associated illness is currently unknown.

Clinical signs of gastric outflow obstruction, regardless of the cause, include mild to moderate intermittent colic associated with interrupted suckle, weight loss or failure to thrive, bruxism, and salivation in the later stages. Medical treatment with anti-ulcer medications such as ranitidine or omeprazole may result in clinical improvement that is incomplete or temporary (for a more detailed discussion of the treatment of gastric ulceration, see Chapter 50). Ulceration can progress to gastric perforation, resulting in peritonitis and/or sudden death. Abdominocentesis may reveal peritonitis or the fluid may be normal, and ultrasound evaluation of the abdomen may detect increased fluid or fibrinous exudates around the stomach. Endoscopic examination typically reveals ulceration of the esophagus and also diffuse and severe ulceration of the squamous region of the stomach. Outflow obstruction can be confirmed with an upper GI series as described in Chapter 32. Treatment for gastric outflow obstruction is surgical bypass of the obstruction

The Equine Acute Abdomen, Third Edition. Edited by Anthony T. Blikslager, Nathaniel A. White II, James N. Moore, and Tim S. Mair.

Companion website: www.wiley.com/go/blikslager/abdomen

by gastrojejunostomy (see Chapter 34). Extensive and prolonged aftercare is necessary in such cases, as it appears that establishing a new gastric emptying pattern develops slowly. Long-term use of anti-ulcer medications is necessary, along with normal postoperative management of ileus. Complications include infection of the surgical site, septicemia, ileus, breakdown of the anastomosis site, and stricture of the anastomosis, leading to persistent colic. Foals should not be fed for at least a week after gastrojejunostomy, and nutritional support must be provided intravenously. Early reports had poor overall outcomes (Campbell-Thompson et al., 1986), but more recent studies have demonstrated better short- and long-term success (Coleman et al., 2009)

Small Intestine

Obstruction of the small intestine occurs in 25–45% of foals with gastrointestinal diseases requiring surgery (Cable et al., 1997), although a lower incidence was reported in more recent studies (Mackinnon et al., 2013). Of foals that required abdominal surgery, 44% had a small intestinal lesion, compared with only 15% with a large colon disorder (Figure 36.1 and Figure 36.2) (Cable et al., 1997). Reported conditions of the small intestine include volvulus, ileus, ascarid impaction, bezoars, pyloric or ileal hypertrophy, intussusceptions, and jejunal incarceration through mesenteric rents. Clinical signs and methods of treatment are not substantially different from those used in adult horses. The overall short-term recovery rate ranges from 60 to 80%, with much better overall outcomes reported more recently than in older reports. One significant difference among foals, however, is the greater tendency toward the development of intestinal adhesions compared with older horses (Lundin et al., 1989). The rate was up to 33% of foals in one report (Cable et al., 1997), compared with only 7% of adult horses (Philips & Walmsley, 1993).

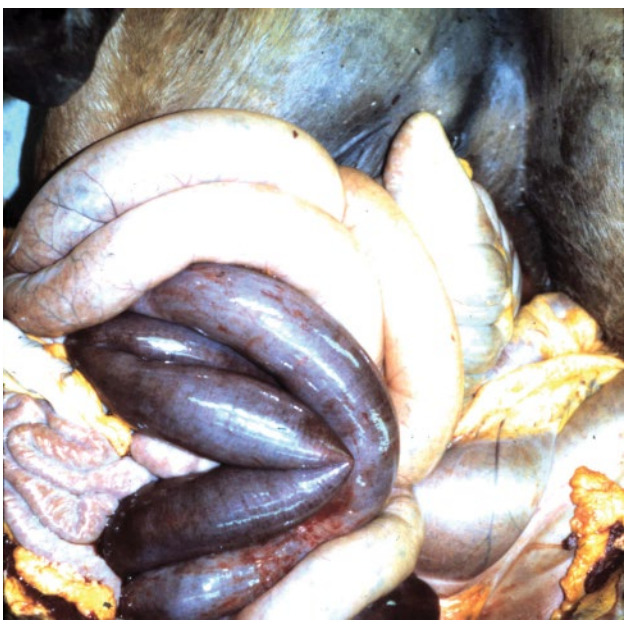

Figure 36.1 Characteristic strangulated and necrotic bowel in a foal.

Large Intestine

Meconium Impaction

Meconium impaction is one of the most common causes of colic in the neonate, exceeded only by enteritis, and may lead to complete obstruction, requiring surgical intervention (Mackinnon et al., 2013). Clinical signs of meconium impaction include a failure to pass meconium, progressive colic associated with straining to defecate, and abdominal distention. Digital palpation will often reveal the presence of an obstructing fecal mass, but in some cases the meconium may be lodged too far orad in the small colon. If meconium impaction is suspected but cannot be determined digitally, then ultrasound can be performed to visualize the impaction. Alternatively, lateral radiographs and/or barium enemas may be diagnostic. Abdominocentesis is not usually necessary, and the peritoneal fluid is normal in most cases.

The primary principles of treatment include pain control, correcting dehydration, and measures to aid passage of the meconium either by lubrication or dissolution of the mass. An enema should be administered to affected foals using either warm soapy water or a commercial phosphate enema (e.g., a Fleet enema; C. B. Fleet, Lynchburg, VA, USA). Fleet enemas work well and are convenient, and the short insertion tube is safe. To perform a soapy water enema, a lubricated soft red rubber

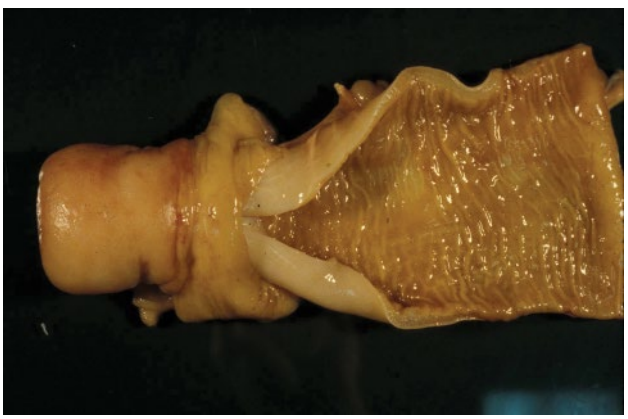

Figure 36.2 Intussusception demonstrating fixed position of the invaginated segment.

stallion catheter can be gently passed to the approximate level of the pelvic inlet and the solution (approximately 1 pint/0.7 L) gently administered by gravity flow. The operator should be careful not to tear the rectum, which is very delicate in the neonate. If the meconium is not passed, the enema can be repeated in 1–2 h. In the author's experience, additional treatments are rarely successful if two to three enemas have not led to significant improvement.

Retention enema using 4% acetylcysteine has been advocated and reported to be effective when conventional enemas have failed (Madigan & Goetzman, 1990). In this technique, 100–200 mL of 4% acetylcysteine solution are infused into the rectum via a 30 F Foley catheter, and held there for 30–45 min. The treatment can be repeated after several hours. This method was effective in 41 foals in which it was employed; some treated foals had received multiple soapy water or phosphate enemas prior to the acetylcysteine. It took an average of 1.5 enemas per foal and resolution took from 1 to 96 h (mean ± SD 29.6 ± 17.5 h) (Pusterla et al., 2004). This technique appears to be very safe and effective, causing no mucosal inflammation at the concentrations described. It is important to recognize, however, that the effects are not immediate, and complete obstruction with intestinal distention may necessitate surgery in select cases.

Additional treatments used for meconium impactions include oral laxatives such as mineral oil (200 mL) or linseed oil (15–20 mL). Dioctyl sodium succinate (15 mL of a 5% solution in water) has also been advocated and can be useful, but should not be repeated as multiple doses can lead to dioctyl sodium succinate toxicity. The use of irritant cathartic laxatives such as castor oil is not recommended in most cases as these compounds produce severe enteritis and diarrhea if not used judiciously. Manual removal of meconium using forceps should not be attempted because of the risk of rectal trauma or penetration.

If after several enemas there is continued pain and/or increasing distension, surgical removal is indicated, as more enemas are not likely to be curative. Surgical treatment should not be delayed at this point, owing to the risk of intestinal compromise or rupture and subsequent peritoneal contamination. At surgery, the impaction can usually be broken down and "milked out" of the small colon and rectum by massage. Fluid can be injected proximal to the mass to aid its breakdown, and in severe cases the impaction may be removed through a colotomy in the antimesenteric tenia in a healthy segment of bowel. These procedures seem to be rarely needed; in one recent report at a surgical referral center, three of 27 foals with meconium impactions had surgery and all survived (Mackinnon et al., 2013). This is consistent with the author's experience of treating persistent meconium impactions; surgical treatment is usually uncomplicated and has a high success rate if performed early and prior to the development of significant intestinal distention. If the fecal mass is simply broken down by manipulation and forced out, without enterotomy, then food does not need to be withheld after surgery. If the bowel is compromised, and resection is necessary, then the outcome is less favorable, and withholding feed becomes necessary.

Atresia

Atresia of the colon, terminal ileum, and cecum, in association with an all-white coat color, has been referred to as the "lethal white syndrome," owing to its association with the recessive gene for white coat color in the progeny of overo–overo breedings. As this is a simple recessive trait, it occurs in one out of four foals from such matings. The genetic abnormality leads to a failure of migration of the neural crest cells into the bowel during embryonic development. These cells are responsible for myenteric plexus development in addition to forming melanocytes. Most foals are presented at 24–48 h of age with a history of no fecal passage with progressive abdominal distention and colic. The diagnosis is supported by the clinical signs and history, in concert with the observation that the foal has no pigment in the skin (Hultgren, 1982; Young et al., 1992). Even if surgery to connect proximal and distal segments is possible, the possible lack of neurons in the myenteric plexus is the reason for a poor prognosis in these cases.

Atresia coli can also occur in foals not associated with the recessive lethal white gene. In affected foals, there is an absence of a segment of bowel sometimes including the mesentery. The atresia can consist of a total missing segment, an atretic segment consisting of a fibrous band, or a membranous tissue separating two adjacent patent segments of bowel. It is believed that these abnormalities are the result of a loss of blood supply to the affected segment during development. Clinical signs are similar to those described earlier for foals with lethal white syndrome; however, foals have normal pigmentation and are not necessarily the offspring of overo–overo breeding. Radiographs of the abdomen may reveal the absence of a colon, with a blunt gas-distended stump; barium enemas may be helpful. Surgical correction has been attempted, but results are often disappointing unless the proximal and distal segments are sufficiently formed and can be surgically connected (Cho, 1986; Young et al., 1992) (Figure 36.3).

Atresia ani has been reported in foals, and can be of variable severity, ranging from nothing more than a simple lack of skin perforation to complete absence of several inches of anus. In foals with an intact anal ring and simple lack of perforation of the skin, surgical correction can be attempted; however, results are variable. In more

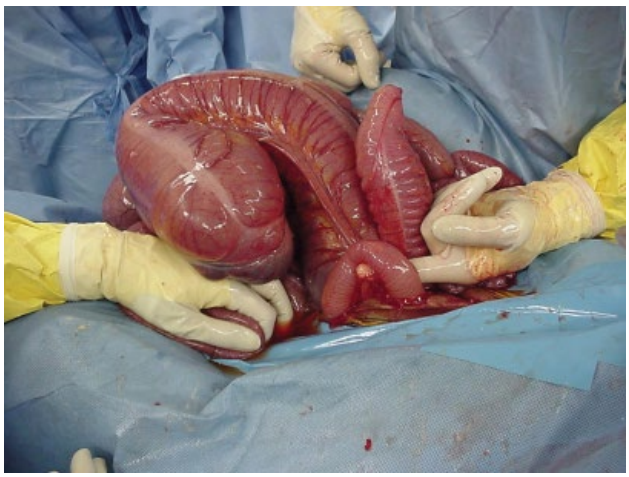

Figure 36.3 Atresia coli identified during exploratory celiotomy. Note the distention caused by the blind pouch at the site of atresia of the pelvic flexure.

advanced cases, surgical correction is complicated and rarely successful. Prior to attempting surgical correction, it is prudent to examine the foal fully to ensure that other congenital lesions are not present. It has been reported that a number of other conditions occur in association with atresia ani, including cleft palate, renal hypoplasia, coccygeal vertebral hypoplasia, persistent cloaca, and rectovaginal fistula (Baker et al., 1987; Brown et al., 1988; Furie, 1983).

Urinary Tract

One of the more common causes of abdominal distention in the foal is uroperitoneum resulting from urinary tract disruption. Foals with uroperitoneum are classically 24–48 h of age, although older foals can be affected; this may be due simply to late-onset occurrence, or may be seen in foals with only a very small leak, in which the urine accumulates slowly. Although male foals are historically considered to be at greater risk (Adams et al., 1988), female foals can also be affected with almost equal frequency and constituted 17/31 cases in one case series (Kablack et al., 2000). Foals will present with clinical signs of weakness and poor nursing, urine dribbling, and straining to urinate. Foals with incomplete bladder rupture or very small leaks can often urinate a reasonable amount, and the ability to do so should not lead one to conclude that urinary tract disruption cannot be present. In addition, mild colic, tachypnea, and progressive abdominal distention can be seen. Abdominal distention may not be evident early in the course of illness, and might initially begin as mild ventral and scrotal edema, progressing to gross distention as the abdominal fluid volume increases. Rarely, rupture of the urachus between the skin and body wall can be seen, resulting in local accumulation of subcutaneous urine. Tachypnea arises secondary to respiratory compromise from increased intra-abdominal pressure and foals may be significantly hypoxic. Tachycardia is often present, presumably due to the combined effects of dehydration, pain, and abdominal compartment syndrome. Fever is not usually seen in uncomplicated cases.

The clinical workup of foals presenting with the signs described should include a complete blood cell count, clinical chemistry analysis, ultrasound examination of the abdomen, abdominocentesis, electrocardiogram, determination of immunoglobulin G concentration, and blood culture. If dyspnea or hypoxia is present, then ultrasound or radiography of the thorax is also indicated. Classical laboratory findings include hyponatremia, hypochloremia, and hyperkalemia, often associated with a metabolic acidosis. The serum creatinine is usually increased, although increased concentration of blood urea nitrogen (BUN) is more variable (Kablack et al., 2000; Adams et al., 1988; Dunkel et al., 2005). This "classic" laboratory profile may be obscured or delayed if the foal has another coexisting illness, if the urinary tract leak is very small, if the urinary tract rent is retroperitoneal, or if the foal has been on intravenous fluids. One study found that only 50% of the foals had the classic electrolyte abnormalities (Kablack et al., 2000). It is also important to recognize that similar electrolyte abnormalities can be seen in foals with enteritis/diarrhea. If there is substantial hypoventilation from abdominal compartment syndrome, hypoxemia may be present. The author has occasionally seen accumulation of pleural fluid that resolves as the abdomen is drained, and this may also contribute to hypoventilation. The hemogram is typically normal in uncomplicated cases – alterations should alert the clinician to the possibility of complications or secondary conditions.

Diagnosis is best achieved by the combination of abdominal ultrasound demonstrating an accumulation of hypoechoic fluid within the abdominal cavity, observation of an incomplete or ruptured bladder, the presence of expected electrolyte abnormalities, and the presence of a ratio of peritoneal fluid creatinine to serum creatinine of >1.5 : 1. The peritoneal fluid-to-serum ratio of creatinine is considered to be one of the most sensitive laboratory tests for the diagnosis of uroperitoneum and a ratio of >2 : 1 is considered diagnostic for uroperitoneum. Ratios were >2 : 1 in 90% of foals in one study, and did not appear to be affected by fluid therapy or the presence of concurrent disease (Kablack et al., 2000). This ratio may be <2 : 1 in foals with retroperitoneal ruptures or umbilical tears external to the abdominal wall. The ultrasound assessment is important, and the diagnosis is straightforward when an incomplete bladder is visualized, but in foals with very small leaks the bladder can be

seen to contain some fluid. In such cases, if all other signs are present, then a urinary tract disruption must be present. The positive predictive value of abnormal findings on ultrasound is very high, with ruptured bladders found in all foals in which the ultrasound appeared abnormal (Kablack et al., 2000).

Initial management includes stabilizing the foal's condition while completing diagnostic efforts and preparing the foal for surgery. If signs of dyspnea, respiratory distress, or hypoxia are present (abnormal mucous membrane color), then the foal should be supported with intranasal insufflation of oxygen while diagnostic procedures occur to prevent precipitating a crisis. Dehydration should be corrected with low potassium-containing fluids (0.45 or 0.9% NaCl) and 5% dextrose. This will help dilute serum potassium concentrations but is often inadequate by itself to reduce serum potassium concentrations to a safe level for anesthesia. This is best accomplished by peritoneal drainage; serum potassium will very quickly go back up unless the abdomen is drained. Although a number of devices can be used, the author favors a short teat cannula attached to a short (12–24 inch) catheter extension. Peritoneal fluid can be drained by gravity or gently aspirated with a 60 mL syringe and three-way stopcock (Figure 36.4). Sometimes surprising amounts of urine can be obtained (4–6 L), and this process should continue until no more fluid can be retrieved, and the foal's abdominal distention has been substantially reduced. A volume of intravenous fluids without potassium should be given during this time and in a volume approximating what was removed from the abdomen. At the completion of this process, the serum potassium and sodium concentrations are reassayed. Ideally, the serum potassium should be normal prior to anesthesia, but this is often impossible, and anesthesia can safely proceed once the potassium level is below 5.5 mg/dL, provided that the sodium concentration is near normal. Once the potassium concentration has been reduced and the foal is rehydrated and breathing easily, surgery should proceed without undue delay, as it is very difficult to maintain the serum potassium concentration at a safe level for a long period.

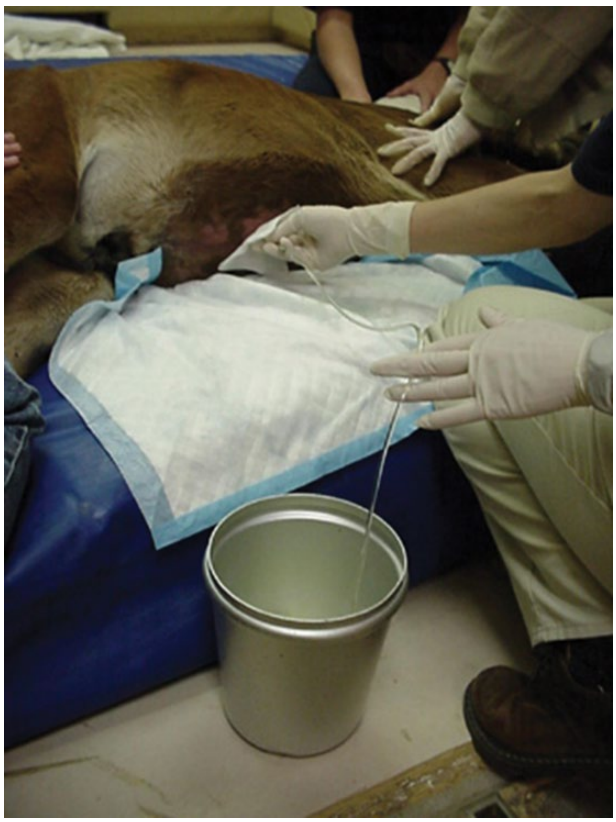

Figure 36.4 Drainage of the abdomen in a case of uroabdomen. Note the distended abdomen of the foal.

At surgery, the bladder should be inspected for tears, which typically occur on the dorsal surface, but can be on the ventral surface, or may include the apex of the bladder as it attaches to the urachus, or the tear may be in the urachus only. Small "pinholes" may be found by filling the bladder with fluid, applying some pressure and then observing the surface. It is important to remove the umbilical remnants during the procedure, and also carefully inspect for more than one rent, which occasionally occurs. Once the umbilical remnants have been removed, the bladder is closed with a two-layer inverting suture pattern and the abdomen is closed routinely (see Chapter 34). Some surgeons prefer to leave an indwelling urinary catheter in place for recovery and a short period afterwards. The need for this is questionable and does not appear necessary in cases in which a good closure with healthy margins was achieved.

Nonsurgical treatment of urinary bladder ruptures has been described, using an indwelling Foley catheter to keep the bladder decompressed (Lavoie & Harnagel, 1988). This technique is useful only in very specific circumstances (pinhole leaks) and is not likely to be of value for most cases of urinary tract disruption.

A positive outcome is expected in uncomplicated cases of urinary bladder rupture. In cases complicated by concurrent illness, the prognosis is more guarded and will be determined by the nature and severity of the concurrent illness. Potential complications include anesthetic death, sepsis, surgical site infection, peritonitis, and peritoneal adhesions. Re-rupture can occur, and rupture following urinary tract obstruction from calcified necrotic tissue in the bladder wall has been observed by the author. A final consideration is that the abdominal wall of foals is very thin, and in those that have been very distended prior to surgery the risk of herniation or dehiscence is increased. The author has observed eventration through an intact skin incision in such a case; application of a belly wrap may be indicated in select cases.

In uncomplicated cases, most foals can nurse immediately after surgery, do not require intravenous fluids, and require only routine postoperative antibiotics and pain medication for a few days. Restricted turnout is advisable for 14 days, after which routine husbandry and management are appropriate.

Hernia

A variety of different types of hernias, including diaphragmatic, inguinal, and umbilical, occur in the foal. Inguinal hernias are described as indirect, in which the bowel remains within the vaginal tunic, whereas direct hernia refers to those in which the parietal vaginal tunic is ruptured and the bowel occupies a subcutaneous position. One author refers to the latter as a "ruptured indirect hernia," whereas a direct hernia strictly refers to a condition in which the bowel has ruptured through the peritoneum and entered a subcutaneous position, never entering the parietal tunic (Van der Velden, 1988). The condition in all 14 foals of one report was described as "ruptured indirect" (Van der Velden, 1988).

Inguinal hernias appear to be more common in Standardbred and Tennessee Walking Horses, which tend to have congenitally large inguinal rings (Blikslager, 2010). Congenital indirect hernias can sometimes be managed by repeated manual reduction or application of a truss constructed of adhesive elastic tape (with appropriate padding) applied in a figure-of-eight fashion around and between the hind legs. As the foal's abdominal muscles strengthen with increasing exercise, the rings will close and prevent further herniation, although this may take several weeks. It is possible that reherniation can result, so foals need careful monitoring. In large hernias, surgical repair is often most prudent.

Ruptured indirect hernias are surgical emergencies with signs of colic and bowel obstruction, and require immediate surgical repair (Spurlock & Robertson, 1988; Van der Velden, 1988). It may be difficult to determine by examination if a hernia is merely a congenital indirect, ruptured indirect, or direct, although the ruptured indirect and direct hernias are more likely to cause obstruction, tend to have more local swelling, are more difficult to reduce, and the bowel can be palpated or visualized by ultrasound to be subcutaneous. If the signs of intestinal obstruction are present, immediate surgical repair is always indicated, regardless of the hernia type.

Umbilical hernias are not infrequently seen in foals; however; it is important to differentiate a hernia from an enlarged or abscessed external umbilical remnant. Palpation for the presence of bowel subcutaneously and ultrasound are of particular value in the examination. If the bowel can be readily reduced and no signs of colic persist, then abdominal wraps using adhesive elastic material, with or without some form of compression on the umbilical area, will often result in closure of the abdominal hernia. If the hernia cannot be reduced, and there are signs of colic or abdominal distention, then surgical correction is necessary.

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Liver Diseases in Foals

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Diagnostic tests for liver disease in foals are broadly similar to those in adults. However, in foals, many of the standard biochemical indices of liver function and damage have significantly different reference normal ranges than in adult horses. Gamma-glutamyl transferase (GGT), bile acids, and alkaline phosphatase (AP), for example, may be normally higher in healthy foals than in adult horses (Barton, 2015).

Portosystemic Shunts

Introduction

Portosystemic shunts are anomalies of the portosystemic circulation that allow direct communication between the portal circulation and a systemic vein such as the vena cava (Fortier, 2002; Gold, 2017). The shunting vessel(s) circumvent(s) portal blood from entering the hepatic circulation and being cleared of toxic metabolites by the liver. Portosystemic shunts are classified as congenital or acquired, intrahepatic or extrahepatic, and single or multiple.

In the fetus, the ductus venosus is a normal shunt that exists with the purpose of bringing oxygen and nutrients from the umbilical circulation to the heart and bypassing the liver. Intrahepatic shunts represent a failure of the ductus venosus to close normally 2–3 days after birth. Congenital extrahepatic shunts most commonly originate from the portal vein, but may also originate from the left gastric vein, splenic vein, cranial or caudal mesenteric vein, or gastroduodenal vein. These shunts typically empty into the caudal vena cava or azygous vein. The majority of portosystemic shunts noted in dogs and cats are extrahepatic, although intrahepatic shunts also occur (Ewing et al., 1974; Center et al., 1985; Birchard & Sherding, 1992; Levy et al., 1995; Lipscomb et al., 2007; Greenhalgh et al., 2010; Cabassu et al., 2011). In foals, both intra- and extrahepatic shunts have been described, with only a small number of foals surviving after surgical intervention (Buonanno et al., 1998; Hillyer et al., 1993; Fortier et al., 1996; Lindsay et al., 1998; Martens et al., 2009; Hug et al., 2012; Woodford et al., 2016).

Pathophysiology

Portosystemic shunts divert portal blood away from the liver, thereby allowing noxious substances, such as ammonia, mercaptans, short-chain fatty acids, and false neurotransmitters, which are normally cleared by the liver, to remain in the systemic circulation. This results in hepatic encephalopathy and liver atrophy.

Clinical Signs

Portosystemic shunts have been reported in foals between 2 weeks and 12 months of age. This late age of onset of clinical signs is likely related to the requirement for hind gut development to permit enough enteric ammonia to cause sufficient elevations of blood ammonia concentrations (Divers, 2015). Clinical signs associated with portosystemic shunts reflect dysfunction of the central nervous system and gastrointestinal tract, and also failure to thrive. Seizures, abnormal mentation, head pressing, obtundation, ataxia, and cortical blindness have been reported, in addition to diarrhea, constipation, and tenesmus. Alterations in growth have also been described, such as poor growth or small for age or breed. These clinical signs have commonly been reported in dogs and cats, and have been noted in foals, calves, and a camelid (Beech et al., 1977; Keane & Blackwell, 1983; Reimer et al., 1988; Hillyer et al., 1993; Johnson, 1995; Fortier et al., 1996; Ivany et al., 2002).

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Companion website: www.wiley.com/go/blikslager/abdomen

Blood ammonia levels can occasionally be high in foals with portosystemic shunts (as high as 300 µmol/L) without showing clinical signs. It would appear that the gradual development of clinical signs in some foals may somehow allow the brain to adapt to the high ammonia levels (Divers, 2015).

Diagnosis

The diagnosis of portosystemic shunts can be particularly challenging in foals owing to the vague clinical signs and the rarity of the condition (Gold, 2017). Foals with portosystemic shunts usually have normal hematocrit and total protein values, but poikilocytosis may be noted on evaluation of red blood cell morphology. Serum biochemistry values are typically within normal limits, with the possible exceptions of increased total bilirubin concentrations and either hypoglycemia or hyperglycemia. Blood ammonia and total serum bile acid concentrations are increased (Keane & Blackwell, 1983; Center et al., 1985; Reimer et al., 1988; Hillyer et al., 1993; Johnson, 1995).

Definitive diagnosis of portosystemic shunts can be achieved by computed tomography angiography, mesenteric vein portography, splenic portography, transrectal sodium pertechnetate Tc-99 m scintigraphy, and ultrasonography (Keane & Blackwell, 1983; Wrigley et al., 1987; Buonanno et al., 1998; Schulz et al., 1993; Koblik & Hornof, 1995; Fortier et al., 1996; Frank et al., 2003; Hug et al., 2012; Woodford et al., 2016). Mesenteric vein portography has been most commonly described in foals; the surgical approach for access to the portal circulation may be made through either a ventral midline celiotomy or a right flank incision. If shunt ligation is to be performed during the same anesthetic procedure as the contrast portogram, then a right flank approach is recommended as this is usually the preferred approach for shunt ligation. A catheter is advanced within the cranial mesenteric vein and an iodinated contrast agent is injected, followed immediately by radiography. If a shunt cannot be identified by positive-contrast portography, a liver biopsy should be obtained to look for hepatic dysplasia or microvascular shunting. The hepatic histological abnormalities observed in hepatic dysplasia are similar, and possibly are indistinguishable from those observed in animals with portosystemic shunts. Hepatic scintigraphy is useful for shunt confirmation, but provides no information on shunt location and is, therefore, a less rewarding technique than positive-contrast portography. Abdominal ultrasonography may identify a portosystemic shunt; however, a positive-contrast portogram should still be performed preoperatively to confirm the ultrasonographic findings. Ultrasound-guided percutaneous trans-splenic injection of 10 mL of agitated saline into the spleen with simultaneous echocardiography of the right heart ("bubblegram") is a sensitive technique (Hug et al., 2012); air bubbles appear immediately after injection if a portosystemic shunt is present. This procedure would not provide information on shunt location. Computed tomographic angiography is most commonly used in people to confirm the diagnosis, but was unable to make an accurate diagnosis of an intrahepatic shunt due to breathing artifact in one reported case in a foal (Hug et al., 2012); however, with further advances in imaging techniques, it is likely that CT angiography will become a standard diagnostic technique in the future.

Treatment

Dogs with portosystemic shunts can be managed with long-term medical treatment (Greenhalgh et al., 2010), but this has not been reported as being successful in foals. Medical treatment of affected dogs typically consists of dietary management with high-quality digestible protein in frequent small meals, orally administered antimicrobials, and lactulose to decrease ammonia concentrations. Foals are often treated with short-term medical management prior to surgery. Medical management in foals is similar to that in dogs with the use of antimicrobials, such as minocycline or neomycin and metronidazole, anti-inflammatory agents, lactulose, enemas, and intravenous fluids.

Several surgical techniques have been described in small animals, including ameroid constrictors, cellophane bands, or ligatures (Swalec & Smeak, 1990; Vogt et al., 1996; Youmans & Hunt, 1998; Havig & Tobias, 2002; Kyles et al., 2002; Hurn & Edwards, 2003; Lipscomb et al., 2007). Immediate, total ligation of the shunt vessel can cause severe portal hypertension with increased mesenteric venous pressures and intestinal congestion. Cellophane bands and ameroid constrictors are utilized to compress the shunt slowly when such portal hypertension needs to be prevented.

In foals, only one successful surgical intervention has been reported using cellophane banding for an intrahepatic shunt (Hug et al., 2012). Four successful surgical corrections of extrahepatic shunts in foals have been described in the literature, two with transvenous coil embolization (McCornico et al., 1997; Martens et al., 2009) and two with surgical ligation (Fortier et al., 1996; Woodford et al., 2016).

The preferred surgical approach for portosystemic shunt ligation is a large right paracostal incision with an 18th rib resection (Fortier et al., 1996). However, in small foals, such as the case described by Woodford et al. (2016), a technique similar to that used in dogs and cats can be utilized using a ventral midline approach. After the shunt has been located, a catheter is placed in a jejunal vessel to facilitate the measurement of portal pressures during shunt ligation. The shunt is ligated with

nonabsorbable suture while portal pressure is monitored and abdominal viscera are observed for signs of cyanosis and congestion. Cellophane banding instead of suture ligation for shunt attenuation may be considered so that progressive and partial closure of the shunt vessel is possible. Surgical mortality in foals with congenital portosystemic shunts is high, with few successful cases of portosystemic shunt ligation reported in the literature.

Tyzzer Disease and Other Infectious Causes of Liver Disease

Tyzzer disease appears to be the most common and well-reported cause of infectious hepatitis in foals. However, other infectious agents can occasionally cause hepatitis, often in association with septicemia or bacteremia, including *Listeria monocytogenes* (Warner et al., 2012), *Actinobacillus* spp., equine herpesvirus-1 (see later), *Streptococcus zooepidemicus*, and *Leptospira* spp. (Divers, 2015). Septic neonatal foals sometimes have increases in serum conjugated bilirubin concentration without evidence of hepatic dysfunction (Haggett et al., 2011).

Tyzzer disease is an acute, fulminant bacterial hepatitis and bacteremia caused by *Clostridium piliforme* (formerly known as *Bacillus piliformis*), a Gram-negative filamentous bacterium (Swerczek et al., 1973; Turk et al., 1981; Carrigan et al., 1984; Humber et al., 1988; Peek et al., 1994; Divers, 1997, 2015; Williams, 1998; Bernard, 2002; Swerczek, 2013). The disease most frequently occurs in rodents and lagomorphs, and has been reported sporadically in other domestic and wild animals. The disease has been reported in foals from 7 to 92 days of age; in a recent review of 148 cases (Swerczek, 2013), the average age at death was 20 days. Tyzzer disease in foals usually occurs sporadically (with an overall incidence of less than approximately 0.1% of foals per year), but has been reported in outbreaks, and is endemic in certain geographic locations.

The disease is not contagious. The route of infection is thought to be oral intake of feces or soil. Soil is probably contaminated by infected individuals or possibly by rodents, cats, or other mammals. The relative risk of disease appears to increase in the later months of the foaling season, suggesting that shedding of the organism by healthy mares and foals may increase environmental contamination (Swerczek, 2013). Foals normally ingest feces from their dams from 2 to 35 days, and the mare's feces may, therefore, serve as a source of infection (Swerczek, 2013). The disease has been reported in Canada, the United States, and the United Kingdom (Hall & Van Kruiningen, 1974; Pulley & Shiveley, 1974; Harrington, 1975, 1976; Whitwell, 1976; Turk et al., 1981; Brown et al., 1983; Nold et al., 1984; Scarratt et al., 1985; Peek et al., 1994; Fosgate et al., 2002; Borchers et al., 2006).

Clinical Signs

The onset of clinical signs is usually peracute, and affected foals are usually in good condition with no prior history of disease. A high carbohydrate and protein diet fed to the mare and foal has been suggested as a possible predisposing factor, by affecting the intestinal microbiome and permitting overgrowth of *C. piliforme* (Swerczek, 2013). Affected foals are often found dead on the pasture, but when observed, clinical signs include signs of liver failure and septic shock. Signs include sudden death, depression, weakness, tachypnea, tachycardia, anorexia, coma/stupor, blindness, seizures, hyper- or hypothermia, icterus, injected mucous membranes, petechiation, abdominal pain, diarrhea, and discolored urine. Tyzzer disease should be a primary differential diagnosis for a foal that is suddenly found dead. Physical examination identifies variable signs of sepsis and cardiovascular shock. Icterus of mucous membranes is variable, as the acute nature of the disease may not have resulted in a significant hyperbilirubinemia. Petechiation and high fevers may be present. Abdominal pain and/or hemorrhagic enterocolitis can be associated with this disease. The abdominal pain is likely to be secondary to colitis or acute swelling of the liver capsule. Myocarditis is an occasional postmortem finding in foals with this disease.

Diagnosis

The diagnosis is based upon the age of the foal, clinical signs, and laboratory findings indicative of septic shock and liver failure; these include severe metabolic acidosis, hypoglycemia, azotemia, and increases in serum concentrations of direct and indirect bilirubin, hepatic enzymes [aspartate aminotransferase (AST), sorbitol dehydrogenase (SDH), and GGT], and bile acids. There is also frequently a degenerative left shift on the leukogram, toxic changes in neutrophils, and thrombocytopenia.

Liver biopsy is rarely performed because the clinical signs and laboratory findings are so characteristic of Tyzzer disease that a biopsy is not required for a diagnosis. In fact, owing to the frequent occurrence of thrombocytopenia, a biopsy may be contraindicated. Blood cultures should be performed, but are rarely diagnostic. Gross necropsy identifies typical white spots in the hepatic parenchyma (Figure 37.1). Histopathology confirms a diagnosis of Tyzzer disease. Warthin–Starry stains identify filamentous bacteria in affected tissue (Figure 37.2). Routine bacterial culture techniques are usually unrewarding, although polymerase chain reaction (PCR) can be used to confirm the infection.

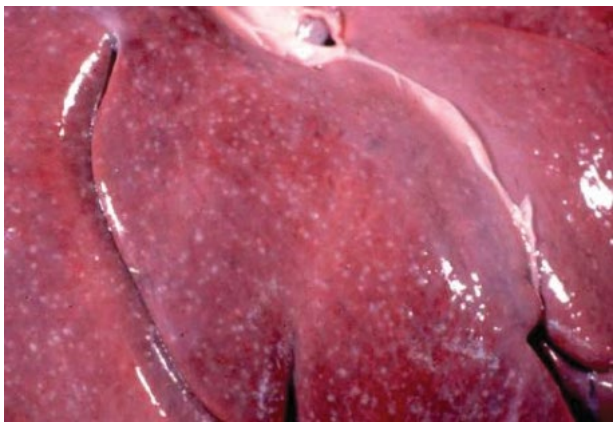

Figure 37.1 Tyzzer disease. Gross postmortem appearance. White spots are scattered over the surface and throughout the liver.

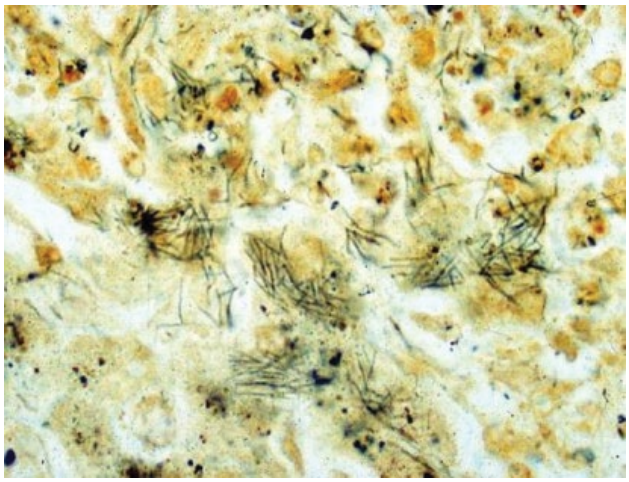

Figure 37.2 Tyzzer disease. Filamentous bacteria are present in the liver stained with Warthin–Starry.

Treatment

Successful treatment of a definitively diagnosed case of Tyzzer disease has rarely been reported in the literature (Peek et al., 1994; Borchers et al., 2006). Emergency therapy with appropriate crystalloid fluids, dextrose, and bicarbonate replacement therapy will vary depending on the foal's cardiovascular status and interference of the disease process with intermediary metabolism. Fluid therapy may be followed by vasopressor therapy, if needed, to improve blood pressure and urine production. Flunixin meglumine should be administered to decrease fever and to inhibit the production of inflammatory prostanoids. If the metabolic acidosis does not improve and the pH remains <7.25 after fluid therapy, sodium bicarbonate should be administered. If the foal is demonstrating obvious signs of hepatoencephalopathy, mannitol can be administered. Routine therapy for septic shock should be provided. The lack of antibiotic sensitivity testing necessitates a choice of broad-spectrum antimicrobial therapy. High doses of intravenous preparations of penicillin in combination with an aminoglycoside or other broad-spectrum antimicrobials are appropriate choices.

Equine Herpesvirus-1 Hepatitis

History and Clinical Signs

Mares that become infected with equine herpesvirus-1 (EHV-1) late in gestation may abort in the third trimester or deliver a stillborn foal. Sometimes infected mares will deliver a live foal that is jaundiced and weak at birth. Alternatively, the foal may appear normal at birth, but subsequently develops icterus, respiratory distress, and rarely diarrhea within the first 5 days of life (Hartley & Dixon, 1979; Perkins et al., 1999). Secondary bacterial septicemia is common.

Diagnosis and Differential Diagnosis

Icterus is a common finding in any septic foal, so any and all causes of septicemia, especially if there is concurrent evidence of pulmonary dysfunction, should be considered in EHV-1-infected foals. This should include all common bacterial agents, in addition to equine viral arteritis, which may mimic EHV-1 infection in the neonatal foal. EHV-1-infected foals commonly have concurrent bacteremia due to immunosuppression.

The diagnosis should be suspected if there is known activity of EHV-1 abortion and/or respiratory disease on the farm and a neonatal foal develops the clinical signs described. Liver enzymes may or may not be increased more than occurs in foals with bacterial sepsis, so blood chemistry profiles will not always be helpful in making the diagnosis (Perkins et al., 1999). Neonatal foals with EHV-1-associated disease are consistently neutropenic and lymphopenic, but these hematologic findings may also be present in foals with acute bacteremia. Confirmation of the disease is usually achieved at necropsy by finding severe diffuse pneumonia, icterus, and hepatic necrosis with viral inclusion bodies. *Actinobacillus*, which is also a common cause of sepsis and acute death in neonatal foals, can cause a similarly abnormal-appearing liver, but foals infected with that organism often have multifocal necrosis of the kidney and lack the diffuse pneumonia that characterizes EHV-1 infection.

Treatment

Treatments are usually unsuccessful if there is multiorgan involvement and severe neutropenia, but some foals can survive. Interferon and valacyclovir may be

helpful in the treatment of affected foals, but proper dosages and bioavailability in the foal are not known. Affected foals may also be administered granulocyte-stimulating factor, but most EHV-1-infected foals seem to have a poor response (no increase in neutrophils). Antibiotics, oxygen, fluids, and supportive care also are indicated.

Liver Failure in Foals After Neonatal Isoerythrolysis

History

Foals can develop liver failure after a prolonged or refractory course of neonatal isoerythrolysis that requires two or more transfusions (Polkes et al., 2008). The etiology of this liver failure is unknown, but may be a result of chronic hypoxia to the liver and/or iron toxicity associated with multiple transfusions or a cholangiopathy associated with the neonatal isoerythrolysis and/or its treatment. A greater number of transfusions and lower packed cell volume (PCV) on hospital admission were risk factors for liver failure.

Clinical Signs and Diagnosis

After successful treatment for neonatal isoerythrolysis, affected foals develop progressive liver disease. Signs include lethargy and the foals may be noticeably jaundiced, or may not grow as well as other foals of the same age. A blood chemistry profile confirms hepatic failure with increases in serum concentrations of bile acids, direct bilirubin, and liver enzymes. Liver failure may occur within 5 days after transfusion, or it may take up to 3 months to develop. Ultrasound findings of the liver and histological examination of biopsy specimens are both abnormal, with the ultrasound examination revealing increased echogenicity and irregularity of appearance. There is commonly evidence of hepatopathy (hepatocellular necrosis) with biliary proliferation and fibrosis on histological examination of tissue samples.

Treatment

There is no proven treatment for this poorly understood liver disease. Drugs that may decrease inflammation and/or oxidative injury in the liver and promote bile flow would be recommended. These include pentoxyfilline, 8.5 mg/kg PO one to three times daily, *S*-adenosylmethionine, 0.5 g PO once daily, and supplemental vitamin E and selenium. Subcutaneous deferoxamine may be helpful as it increases iron elimination (Elfenbein et al., 2010).

Umbilical Vein Abscess Affecting the Liver

Introduction

Foals, particularly those with inadequate colostral antibody absorption, are predisposed to infection of the umbilical structures. In many cases, the umbilical vein (which normally becomes the round ligament of the liver) may be infected and enlarged (>1 cm) with abscesses extending from the vein into the liver (Divers & Perkins, 2003; Edwards & Fubini, 1995). A variety of organisms, including Gram-negative enteric bacteria, Gram-positive cocci, and occasionally anaerobic bacteria, may be cultured from the abscessed vein. Although infection of the umbilical vein is relatively common, inflammation of the liver and increases in hepatic enzymes are rare.

Clinical Signs

Affected foals are usually between 3 and 14 days old when the diagnosis is made. Foals are febrile, depressed, and may be lame due to infectious arthritis or have signs of pneumonia. The umbilical area may or may not appear to be abnormal (Wilkins, 2004). Complete blood counts and biochemistry evaluation reveal leukopenia or leukocytosis, frequently accompanied by a left shift. Other markers of inflammation (low serum iron, high fibrinogen) are usually present as expected, but serum concentrations of liver enzymes are usually within normal limits.

Diagnosis

The diagnosis is based upon signalment and clinical signs, and ultrasound examination of the umbilical structures (Reef & Collatos, 1988; Reef et al., 1989). Occasionally, if the foal can remain relaxed in lateral recumbency, the umbilical vein can be palpated through the abdominal wall.

Treatment

If the vein is only marginally enlarged, and a positive blood culture is obtained that allows the bacterial pathogen to be identified, then appropriate antibiotic therapy may be all that is required. If the vein is more enlarged and the abnormality extends into the liver, surgery is recommended. The vein is either removed as close to the liver as possible and the stump ligated or cauterized, or the distal part of the vein is removed and the remaining vein (running into the liver) is marsupialized to allow drainage (Edwards & Fubini, 1995). Plasma is usually administered to all affected foals. Unless there is severe organ dysfunction (pneumonia),

or infectious arthritis, the prognosis with appropriate therapy is good. Marsupialization of the umbilical vein requires significant aftercare.

Portal Vein Thrombosis

Thrombosis of the portal vein is encountered rarely in foals, and develops secondary to another illness. The thrombosis may be septic, for example, with *Rhodococcus equi* infection, or may occur secondary to enteritis, generalized sepsis, and coagulopathy (Ness et al., 2013). Portal vein thrombosis has also been reported in other species secondary to sepsis, hypercoagulability, and inflammation. In older horses, hepatic neoplasia (Patton et al., 2006) and cirrhosis may occasionally predispose to thrombosis.

Clinical Signs

The signs attributed to portal vein thrombosis include depression, presumably due to hepatic shunting of gut-derived proteins, hepatic encephalopathy, and diarrhea if the thrombotic occlusion is acute and complete. The diarrhea is likely a result of increased mesenteric venous pressures and intestinal wall edema. If the thrombosis is septic, persistent fever would be expected.

Diagnosis

The diagnosis is unlikely to be made antemortem unless there is an increase in hepatic-derived enzymes and the thrombus can be identified ultrasonographically.

Treatment

In most cases, the thrombosed portal vein is identified at necropsy. Consequently, there is little experience with treatment of affected foals. One foal with abdominal lymphadenitis, septic tarsitis, and hepatitis caused by *Rhodococcus equi* infection had nearly 90% occlusion of the portal vein, and was successfully treated with long-term macrolides and rifampin (Divers, 2015). Anticoagulant therapy such as aspirin and/or pentoxifylline might be of benefit.

Hyperammonemia Syndrome in Morgan Foals

Although not well documented, this condition is presumed to occur due to an inherited abnormality in hepatic ammonia metabolism (McCornico et al., 1997).

Signalment and Clinical Signs

Affected Morgan foals are usually 4–7 months of age and have an acute onset of signs caused by cerebral dysfunction (McCornico et al., 1997; Divers et al., 1994). These signs include blindness, head pressing, circling, and seizures, and they usually arise after weaning. In some cases, there is hemoglobinuria (red discoloration of the urine). The cause of the disease is unknown, but there appears to be a disorder of ammonia metabolism and possibly other amino acids; a hereditary cause seems possible. Although cases were relatively common 10–20 years ago, they are currently rarely observed, suggesting that horses carrying the presumed defective gene responsible for the disease might no longer be in use as breeding horses.

Diagnosis

The diagnosis is based upon signalment and clinical signs in addition to measurement of blood ammonia. Blood ammonia concentrations are often very high (300–600 μmol/L), but liver enzymes are usually only mildly elevated. Liver biopsy reveals variable degrees of mild damage.

Treatment

Although the disease has been uniformly fatal, some affected foals will improve for several days only to have a second onset of severe neurologic signs. Treatments could include mannitol (0.5–1.0 mg/kg) and neomycin (4–8 mg/kg PO q 8 h), in addition to intravenous administration of crystalloids supplemented with potassium chloride.

Bile Duct Obstruction

Introduction

In the horse, there are two biliary openings into the duodenum, the major and minor biliary papillae. Both drain into the proximal duodenum in close proximity to each other. Foals with gastroduodenal ulceration may develop strictures of the duodenum associated with healing of duodenal ulcers. If the stricture is at the site of the biliary opening, bile flow may be obstructed. If the stricture is distal to the opening, there may be reflux of ingesta into the bile ducts. The clinical signs are similar with stricture at either site, but the prognosis differs.

History and Clinical Signs

There is often a history of a previous illness, such as diarrhea, from which the foal seemingly recovered. Either during the primary illness or soon thereafter, the foal begins to show clinical signs of prolonged gastric outflow, ptyalism, colic, bruxism, and decreased nursing (Sprayberry, 2003). If there is biliary obstruction, the foal may be mildly icteric.

Diagnosis

The history and clinical signs are characteristic of delayed gastric emptying due to ulceration. Ultrasound examination of the abdomen will reveal an enlarged and milk-filled stomach. Endoscopy reveals esophageal ulcers and gastric ulceration (Murray et al., 1990). The stomach may contain a large amount of milk that must be removed in order to complete the endoscopic examination. If a duodenal stricture is present and radiographs are taken prior to endoscopy, an enlarged stomach with an obvious fluid line can be seen. If the stomach is obviously enlarged, a barium study should be performed to help determine the severity of the duodenal obstruction. If the duodenal obstruction is nearly complete and distal to the biliary opening, barium may be seen in the bile ducts, but there will be little or no barium leaving the stomach 30 min after administration.

Treatment

Medical treatment of affected foals should include intravenous administration of omeprazole, H2 blockers (e.g., ranitidine), sucralfate, and misoprostil (with the dose and frequency depending upon the degree of gastric dysfunction), and bethanechol (0.025 mg/kg SQ q 4 h). If the history, clinical signs, and endoscopic and radiographic findings suggest chronic obstruction, then medical therapy is unlikely to be curative and a bypass surgery will be needed. If the duodenal stricture is at the opening of the bile duct, a hepaticojejunostomy may also be required (Orsini & Donawick, 1989).

Toxic Hepatopathy

Although several drugs administered to foals, such as nonsteroidal anti-inflammatory drugs (NSAIDs), rifampin, antifungal drugs, inhalants, herbal products, and anti-ulcer medication, have been associated with temporary increases in serum concentrations of liver enzymes, only iron has been documented to cause toxic hepatic failure (Divers et al., 1983; Acland et al., 1984). The iron-induced hepatic failure in foals occurs only when iron is administered prior to colostrum.

Clinical Signs

Typically, 3 to 5-day-old foals with iron-induced acute liver failure have an acute onset of hepatoencephalopathy (coma, blindness, seizure, etc.) that is almost uniformly fatal.

Diagnosis

The diagnosis is based upon history (iron administration prior to colostrum), clinical signs, and laboratory findings of hepatic disease and dysfunction.

Treatment

Intensive supportive care with crystalloids, dextrose, branched-chain amino acids, and "gut sterilization" with neomycin has been attempted, but has rarely been successful. Products containing iron should not be given to foals in the first days of life.

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Part VIII

Colic in the Donkey

38

Colic in the Donkey

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Introduction

Donkeys form the backbone of many agricultural societies, providing draft and traction; they help to build cities as they transport bricks from kilns to building sites, and they support those too poor to purchase a horse or motorized vehicle. In some countries, donkeys provide milk and meat, and in many urban societies they now act as companions and therapy animals, working with ease alongside children and adults.

Donkeys can be challenging patients for a number of reasons, including their behavior, physiology, and size. The authors hope that this chapter will help those dealing with donkeys to understand their requirements better and provide compassionate and informed treatment to these equids.

Anatomy of the Gastrointestinal Tract

Although there are some notable differences in the anatomy of the donkey compared with the horse, these relate mostly to external features, conformational variations, and the upper respiratory tract internally (Burden & Thiemann, 2015).

There are limited studies comparing donkey and horse gastrointestinal (GI) anatomies (Jerbi et al., 2014). The Donkey Sanctuary is working toward further anatomical measurements of the donkey's GI tract.

The structure of the donkey's GI tract, however, is remarkably similar to that of the horse, with no obvious physical features that account for its superior efficiency. One way in which donkeys adapt to high-fiber diets, such as straw, is to use the full capacity of their large intestine (cecum and colon) so forage can be retained for longer and be digested more thoroughly (Smith & Wood, 2008). Anatomic differences between the GI tract of the horse and the donkey are limited to dental differences and size/length of the viscera.

The dental anatomy of the donkey is largely similar to that described in the horse but with some subtle differences. Donkeys have a greater degree of anisognathia (27% width difference between upper and lower jaws) compared with horses (23%) and an accentuated curve of Spee. There is a greater degree of peripheral enamel infolding in mandibular cheek teeth compared with maxillary cheek teeth and a significant increase in peripheral cementum from the apical region to the clinical crown in all cheek teeth. All donkeys' cheek teeth have at least five pulp cavities, with six pulp cavities present in the 06 s and 11 s (Du Toit et al., 2008a, 2008b; Du Toit & Dixon, 2011).

The donkey's esophagus is similar to that of the horse. The average stomach weight is 3.6% of the donkey's body weight, and the capacity varies with the size of the donkey. For a standard 180 kg donkey, the usual volume that can be safely instilled via nasogastric intubation is 3 L.

The small intestine, as in horses, is divided into three parts (duodenum, jejunum, and ileum), with the jejunum being the longest part. In recent, unpublished measurements carried out at The Donkey Sanctuary's pathology laboratory, the length of the jejunum of an average 180 kg donkey was approximately 10 m (6 m per 100 kg) compared with the horse's average small intestine length of 25 m (5 m per 100 kg).

The topography and parts of the large intestine are again very similar to those of the horse. The first part of the large colon, the cecum, is an inverted comma-shaped

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sac divided into three parts (base, body, and apex) measuring 80 cm on average in a standard donkey. The large colon is divided into four parts, namely right ventral colon, left ventral colon, left dorsal colon, and right dorsal colon, and it measures approximately 3 m in total. The transverse colon is short (approximately 10 cm) and the small colon appears to be shorter than that of the horse, measuring approximately 1 m in the donkey. The rectum is the same as that of the horse. Although smaller than a horse, rectal examination is a useful part of the clinical examination, and is possible in the donkey for most clinicians, even if the internal depth of examination is reduced.

The liver is divided into three major lobes (right, left lateral, and left medial lobes) and weighs approximately 3.2% of the body weight. The liver and the pancreas do not differ from the corresponding organs in the horse.

Finally, it is important to mention that donkeys tend to accumulate more neck crest and abdominal fat than horses. Fat deposits along the linea alba have been measured up to 12 cm in depth (personal observations at The Donkey Sanctuary; Figure 38.1). As a result, abdominocentesis in donkeys is more complicated than in horses, as a catheter or a teat cannula may be required in order to obtain peritoneal fluid from a donkey.

Although the anatomies are similar, from a clinical viewpoint the donkey often appears to have a more pendulous abdomen than the horse, due to its high-fiber diet, lack of muscle tone, and intra-abdominal fat deposits. There is little space in the lumbar fossa for ultrasound examination of deeper structures and in the United Kingdom at least, fat deposits can complicate imaging and the ability to perform an abdominocentesis with ease.

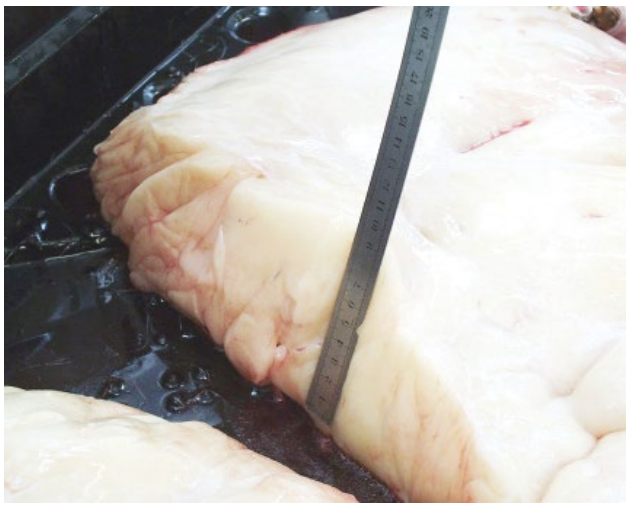

Figure 38.1 Typical fat deposits along linea alba from a donkey (postmortem specimen).

Physiology of the Donkey

Physiological Differences

The donkey's physiology is significantly different from that of the horse, which may reflect the fact that the donkey appears to be desert adapted (Figure 38.2). In relation to colic assessment, it is important to note that the reference intervals and median values for all hematological and certain biochemical parameters vary significantly from those described for non-Thoroughbred horses (Burden & Thiemann, 2015) (Table 38.1). The reported values in this study relate to clinically healthy, mature donkeys selected from the resident population of The Donkey Sanctuary in the United Kingdom. Jordana et al. (1998) compared biochemical reference ranges for different breeds of donkey and found that most values were similar, with the main exception being enzyme activities. They also found that triglyceride concentrations increased with age, although their study population was relatively small.

Donkeys may also be able to conserve blood volume more effectively than horses, as plasma volume was relatively unchanged in two donkeys that had reached a 20% level of dehydration (Yousef et al., 1970). This may result in less clinical and hematological signs of dehydration in colic patients until dehydration levels of >12–15% have been reached. Fluid balance and body water compartment partitioning also differ from those in the horse in that the donkey can survive water loss of 30% body weight and then consume sufficient water to restore the deficit within minutes. In addition, urine output is lower and correspondingly water consumption per unit dry matter of feed is less (Maloiy, 1970; Pearson et al., 2001). These are likely to be adaptations for survival in a semi-arid environment but need to be taken into consideration when monitoring colic patients.

The gut transit time in donkeys is longer than that in other equids (mean retention time for a straw diet of 53 and 35 h for donkeys and ponies, respectively) and fiber is digested more effectively. This compensates for their lower dry matter intake (Table 38.2) and results in an overall similar intake of digestible energy in ponies and donkeys (Pearson & Merritt, 1991). However, this may only apply to long-fiber forage diets, as Cuddeford & Hyslop (1996) found no difference in feed intake and digestion strategy when both species were offered a high-quality fiber-based concentrate feedstuff *ad libitum*. This has implications for how donkeys are managed from a diet point of view both during the colic recovery period and in the long term if abnormalities such as dental disease are identified. For example, donkeys with dental disease may consume excessive amounts of digestible energy when offered short chop fiber diets *ad libitum* with digestible energy of 7.5–8.0 MJ/kg (Table 38.2).

Figure 38.2 Donkeys used as pack animals in Danakil, Ethiopia.

Table 38.1 Hematologic and biochemical reference intervals in the donkey.

Parameter	Average (range)	Parameter	Average (range)
RBC (10^{12}/L)	5.5 (4.4–7.1)	Trig (mmol/L)	1.4 (0.6–2.8)
PCV (%)	33 (27–42)	CPK (IU/L)	208 (128–525)
Hb (g/dL)	11.0 (8.9–14.7)	AST (IU/L)	362 (238–536)
MCH (pg)	20.6 (17.6–23.1)	GGT (IU/L)	24 (14–69)
MCHC (g/dL)	34 (31–37)	GLDH (IU/L)	2.5 (1.2–8.2)
MCV (fL)	60 (53–67)	ALP (IU/L)	152 (98–252)
WBC (10^9/L)	10 (6.2–15)	Bile acids (μmol/L)	10 (2.6–18.6)
NEU (%)	38.3 (23–59)	Tbil (μmol/L)	1.6 (0.1–3.7)
NEU T (10^9/L)	3.7 (2.4–6.3)	TP (g/L)	65 (58–76)
EOS (%)	4.0 (0.9–9.1)	Alb (g/L)	26 (22–32)
EOS T (10^9/L)	0.4 (0.1–0.9)	Glob (g/L)	38 (32–48)
BAS (%)	0.05 (0–0.5)	Creat (μmol/L)	87 (53–118)
BAS T (10^9/L)	0 (0–0.07)	Urea (mmol/L)	3.2 (1.5–5.2)

Tbil, total bilirubin.

Table 38.2 Dry matter intake and digestible energy (DE) requirements for donkeys and ponies.

	Donkey		Pony	
	Summer	Winter	Summer	Winter
Dry matter intake (% body wt)	1.3	1.7	2.0	2.5
DE requirement (kJ DE/kg)	80	95	157	158

In a study of working donkeys in South Africa, mild dehydration resulted in increased fermentation activity in the cecum and enhanced fluid retention in the ventral colon, which were associated with an observed maintenance of appetite (Sneddon et al., 2006). Although this is a useful survival mechanism in a semiarid environment (Figure 38.2), it might conceal early signs of colic and the assessment of its severity in donkey patients where appetite is frequently found to be maintained.

Physiological parameters are also slightly different from those of the horse, which needs to be borne in mind during clinical assessment. Heart rates may range from 36 to 52 bpm and respiratory rates from 12 to 28 breaths/min, and the upper end of the range for a donkey's rectal temperature (36.5–37.8 °C) is lower than that for the horse (37.5–38.6 °C).

Donkeys are more susceptible to hyperlipemia than most horse breeds (except native ponies and Miniature Horses), with the species being a primary predisposing factor. However, this can be compounded by additional factors such as obesity, lack of exercise, and female gender. All these factors predispose to insulin resistance, which is a significant feature in affected animals. It is important to note, however, that of these risk factors only breed/species predisposition tends to be a consistent finding in clinical cases (Durham & Thiemann, 2015). In addition to preexisting risk factors, hyperlipemia is probably induced by a final trigger factor and in a recent study 72% of cases were found to have concurrent disease, which included colic, liver disease, renal disease, or colitis (Burden et al., 2011).

Epidemiology and Risk Factors

There are few studies that document the incidence of colic in donkey populations, and the information in this section is largely reliant on research derived from donkeys resident at The Donkey Sanctuary (Devon, UK). These animals are mostly inactive and range in age from foals to geriatric, with a higher proportion of mature to old animals in care. In populations of donkeys in "developing" countries with working equine populations, the incidence and risk factors for colic are expected to be focused more on inappropriate diet and parasites (Bojia et al., 2006). In a 5-year study (2000–2005) of 4596 Donkey Sanctuary donkeys (mean age 25.2 years), the incidence rate for all colic was 5.9 new cases per 100 donkeys (Cox et al., 2007), which is similar to that reported in horses. Impaction colic accounted for 54.8% of episodes (3.2 cases per 100 donkeys per year), and of these 51.4% did not survive. The sites of the impaction were identified in 62.9% of cases as pelvic flexure (39.6%), large colon (7.5%), small colon (6.8%) cecum (8.4%), and small intestine (0.6%). The highest mortality was identified in cases of cecal and pelvic flexure impactions.

The incidence and mortality of impaction colic in this population are considerably higher than those reported for horses (Proudman, 1991), although closer to results in a population of geriatric horses (Brosnahan & Paradis, 2003). Factors that affected the incidence of colic may also be related to factors that influence the clinician's overall decision to euthanize a donkey with colic, which may help to explain the high mortality rate.

Risk factors for impaction colic identified included increasing age, provision of concentrate feed (itself linked to dental disease and low body condition score), change in management, musculoskeletal disease, and dental disease. The association between musculoskeletal disease and colic may be due to a reduction in exercise and reduced water intake, particularly in geriatric donkeys. In many cases, such animals will be on pain relief medications for the musculoskeletal disease, and this can delay detection of the colic. In this aged population, surgery was usually not considered an option owing to the multiple health issues affecting aged donkeys with colic.

The association between dental disease and systemic disease was also examined in this population, where the presence of dental disease, particularly diastemata and increasing age, was the strongest risk factor for colic episodes (Cox et al., 2009; Du Toit et al., 2009). Absence of cheek teeth and the associated loss of masticatory function have been shown to relate to the number of colic episodes, especially impaction colic, and to increased mortality (Lilly, 2015). Analysis of fecal fiber length pre- and post-dentistry in donkeys showed an improvement from 4.37 to 1.94 mm, indicating that dental treatment results in improved digestibility of fiber in diets (Philips, 2014). Data from new arrivals at The Donkey Sanctuary (Lilly, 2015) and for donkeys in the United Kingdom generally (Cox et al., 2010) show that

dental disease is one of the most common conditions present and in many cases can be very severe.

To complicate the situation in the donkey, hyperlipemia can be a concurrent factor in cases of colic (Burden et al., 2011) and can reduce the prognosis for survival if not recognized and treated simultaneously.

Table 38.3 documents the prevalence of (selected) postmortem findings for 1444 donkeys resident at The Donkey Sanctuary over a 7-year period (Morrow et al., 2010). This study provides an insight into the type of conditions relating to colic; dental disease and hyperlipemia are included as these two conditions are highly relevant in the causation and treatment options for donkeys. As these findings are postmortem findings, they do not bear direct comparison with clinician-derived findings in live animals.

When the incidence of colic was studied in 1046 donkeys in the United Kingdom kept in private homes primarily as pets (92%) (Cox et al., 2010), with a mean age of 20.8 years (range 3.4–46.8 years), the rate was 1.42 new colic cases per 100 donkeys. There were 15 cases of colic in 13 donkeys (all diagnosed by a veterinarian), of which seven were impaction colic, five "spasmodic," and three unidentified. This colic incidence is lower than those recorded in previous studies on donkeys (Cox et al., 2007). The most common presenting sign was anorexia, which may be easy to overlook and nonspecific. It is notable that during the study period, 57 donkeys died or were euthanized; as there were few data available on the cause of death (one had a gastric impaction, three were found dead, and two died during treatment for an unidentified condition), it is possible that the true incidence of colic was higher than that identified.

Table 38.3 The prevalence of (selected) postmortem findings for 1444 donkeys, October 2001–2008, The Donkey Sanctuary, Devon, UK.

Description of finding	No. of donkeys	Prevalence (%)
Dental disorder	1136	78.7
Gastric ulceration	608	42.1
GI impaction	268	18.6
Cyathostomins	213	14.8
GI torsion	144	10
Peritonitis	107	7.4
GI inflammatory condition	101	7.0
Pancreatitis	69	4.8
Hyperlipemia	57	4.0
GI neoplasia	54	3.7
Abdominal organ rupture	26	1.8
GI stasis	19	1.3
Gasterophilus	6	0.4

GI, gastrointestinal.

There are isolated reports in the literature of donkeys with acute or chronic colic due to a variety of causes, such as equine grass sickness (Pirie, 2013) and pancreatic tumor (Spanton et al., 2009). However, there were insufficient data to extrapolate donkey-specific risk factors for many types of identified colic. Where information is available, it is presented in the relevant section of this chapter.

To summarize: available data suggest that impaction colic is the most commonly identified cause of colic in donkeys in the United Kingdom and that the risk factors for this condition can be largely managed by regular high-quality dentistry, careful management, and diet. Confounding factors such as age, musculoskeletal disease, and concurrent hyperlipemia may influence the decision of whether and how to treat the donkey.

Behavioral Indicators of Colic in the Donkey

It is generally accepted by those who work with donkeys and horses that there are species-specific differences in behaviors that encompass both normal and pain-related behaviors (Ashley et al., 2005). Pain behaviors tend to be subtle as befits a prey species, but the range of behaviors seen is not as limited as has been suggested (Olmos et al., 2011; Regan et al., 2015). In tests on cerebral cortical response to surgical pain, donkeys have shown equivalent or greater response to pain stimuli (Grint et al., 2015a), suggesting that donkey behavior is more correctly described as stoic or subtle.

Clinicians need to be aware that for many donkeys with colic related to impactions and mesenteric stretch, the most common pain behaviors are dullness, self-isolation, and reduced appetite. Dullness was the most common presenting sign (90.1%) seen in impaction colic in the study by Cox et al. (2009). Subtle signs such as lack of ear movement and lowered head carriage may also be seen. The more typical horse colic behaviors of flank watching, abdominal kicking, and rolling are rarely seen in donkeys, and if present indicate a severe lesion. Subtle pain-related behavior is a useful strategy to avoid attacks from predators; however, for the veterinarian it is essential to appreciate that minor changes in behavior from the normal can indicate a profoundly sick donkey (Figure 38.3). Extensive observations on normal donkeys and those experiencing pain identified several behaviors that are associated with colic and painful lesions (Table 38.4) (Burden & Thiemann, 2015).

A study on working donkeys in Pakistan found that abdominal pain presented with more severe signs, including rolling, groaning, stretching, and sweating. Although the cause of the colic was not stated in that

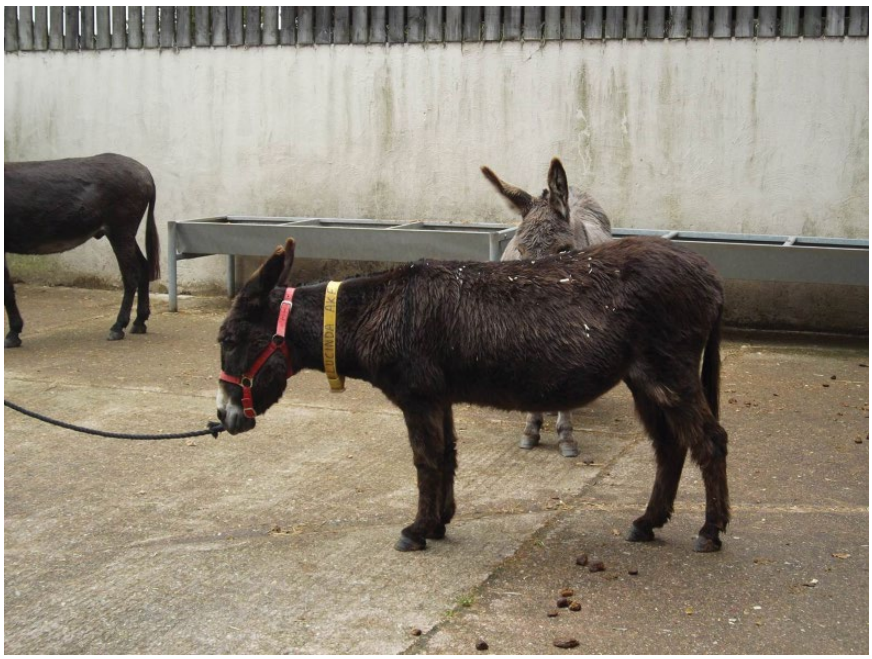

Figure 38.3 Dull donkey: typical signs include lowered head, backward-facing ears, and tightening of the muzzle.

Table 38.4 Behavioral signs of pain related to colic in the donkey, adapted with authors' experience.

Behavior	Description
Lowered head carriage	Head consistently held below withers, seen more in sick than healthy donkeys
Immobile ear position	Ears more static and unresponsive, not moving or changing direction with external stimuli. Subtle but earliest signs seen in painful donkeys
Increased time in recumbency	A common sign with impaction colic. In the absence of overt pain signs this condition should prompt a full examination every time
Reduced appetite/anorexia	An early sign of a developing clinical problem, can quickly lead to hyperlipemia
Sham eating	Careful observation shows that food is nuzzled but not swallowed, indicates a sick animal
Generalized depression/ anhedonia	Lack of response to a pleasurable stimulus – food, companion, etc. This is a common presenting sign with many underlying causes
Rolling, flank kicking	Rarely seen except in cases of severe acute abdominal disease such as torsions
Behavioral unresponsiveness	Seen in working donkeys and horses in states of severe and numerous pain-related problems
Self-isolation	The sick donkey is seen to be separate from herd companions

study (Regan et al., 2015), it may be increased severity/ duration of disease.

It is immediately obvious that dullness and depression are nonspecific signs and may be associated with a number of disease conditions in the donkey. A study by Duffield (2002) found that hyperlipemia, colic, liver disease, respiratory disease, and hoof disorders accounted for 38% of cases of dullness identified, with more than 20 other conditions also presenting primarily as a dull donkey. This means that all donkeys presenting with such symptoms should undergo a full clinical examination to differentiate the multiple factors that may be involved.

Donkeys evolved in semiarid areas of the world where food resources are scarce, and naturally live in small social groups. Hence they may experience stress (which can lead to hyperlipemia) when separated from pair-bonded companions (Murray et al., 2013). Hence, when examining and treating a donkey with colic, care should be taken to ensure that its companion is close by as much as possible during examination, treatment, and aftercare.

Working donkeys in developing countries often suffer from multiple disease states in addition to overwork and exhaustion. In these cases, animals can show an "unresponsive behavior profile" (Burns et al., 2010) and apathy. Such donkeys tend to be in very poor health and require a detailed examination to diagnose any condition.

Clinical Examination

As highlighted in the previous section, the donkey is considered a stoic species and can demonstrate subtle, nonspecific behaviors that can be easily missed or

misinterpreted as unimportant or indicative of only mild disease. Conversely, when a donkey exhibits obvious specific signs of abdominal pain, it is likely that the disease process is advanced and severe in nature. Dullness has been found to be the most common presenting sign of impaction colic, followed by reduced appetite (Cox et al., 2007).

When taking a history, particular attention should be paid to the worming history as donkeys do not appear to develop good immunity to *Parascaris equorum*. As a result, adult donkeys can have heavy burdens that might lead to small intestinal obstruction (Getachew et al., 2008). Any history of dental disease or lack of previous dental examinations should be explored further owing to the known risk of impaction colic associated particularly with diastemata (Cox et al., 2009). Dietary management and husbandry and any changes to either should be investigated as paper bedding, feeding concentrates, and limited access to pasture are all risk factors for impaction colic (Cox et al., 2009). Additionally, feeding cereal-based supplementary feed has been associated with increased risk of gastric ulceration (Burden et al., 2009).

When performing a clinical examination, it should be noted that the oral mucous membranes are normally pale pink in donkeys but with less of a yellow tinge than in the horse. Capillary refill time and pulse quality must be interpreted cautiously in view of the previously described ability of the donkey to withstand dehydration up to 20% before becoming hemoconcentrated. Furthermore, heart rates up to 70 bpm would be considered mild to moderately elevated, with anything above this level indicative of severe disease and/or pain. Severe abdominal pain may increase the respiratory rate; donkeys with respiratory diseases such as pleuropneumonia and pneumothorax also could present with signs of dullness and reduced appetite/anorexia.

Abdominal auscultation is performed in a similar manner to that in the horse and the character of normal borborygmi is also similar. Increased borborygmi may indicate spasmodic colic. However, in one study of causes of colic in the donkey, only 6% of cases were found to be spasmodic, suggesting that this is a less common finding than in the horse. More commonly, reduced or absent borborygmi are found, as was the case for 76% of donkeys with impactions (Duffield, 2002). In smaller donkeys, abdominal ballottement and external palpation may be used to assess abdominal pain and distension.

A rectal examination should always be performed and the ease and quality of this examination can be improved by the use of spasmolytics such as butylscopolamine. Fecal output and consistency should be assessed and a fecal worm egg count can be performed, if indicated. Hyperlipemic donkeys frequently have dry, mucus-covered fecal balls, which in conjunction with a reduced appetite and dullness should give a strong clinical suspicion that early treatment intervention is indicated. Although palpable structures may be limited to the most caudal part of the abdomen, abnormal structures may be palpable, as Cox et al. (2007) reported that 53% of all impactions occurred at the pelvic flexure.

In view of the associated risk of hyperlipemia in an inappetant, painful donkey, a blood sample should be taken to assess triglycerides in addition to other biochemical and hematologic parameters of interest. Duffield (2002) found that 18% of donkeys with colic were also hyperlipemic. A visual assessment of the serum can be made and any cloudiness would provide an indication for immediate treatment. It should be noted, however, that visually clear serum does not equate to triglyceride levels being within normal limits.

Gastric reflux should be assessed by passing a small-diameter (9–11 mm) nasogastric tube to reduce the risk of mucosal trauma and hemorrhage. If abdominocentesis is to be performed and is not ultrasound guided, it is important to note that the intra-abdominal fat layer can be up to 8 cm thick without the donkey appearing outwardly fat. As dental disease is known to be a risk factor for impaction colic, a thorough examination of the oral cavity should be performed, as findings may influence management changes to prevent further colic episodes or decision making on prognosis, as discussed later.

Ultrasonographic examination of the abdomen is performed in the same way as in the horse and the gut-wall thicknesses appear to be similar (<4 mm for the large colon). Gastroscopy can also be performed, although little is known regarding gastric emptying times for donkeys and care needs to be taken on how long food is withheld owing to the risk of hyperlipemia. Bedding material also needs to be considered while food is withheld as donkeys will readily eat paper-based bedding.

Little is know regarding lactate concentrations in donkeys. In a single study of healthy Brazilian donkeys, the mean serum lactate concentration was 2.2 mmol/L (Mori et al., 2003). To the authors' knowledge, no studies have examined the predictive value of blood or peritoneal fluid lactate concentration in donkeys with gastrointestinal disease.

Decision making should follow the same principles as in the horse, with the following points being taken into consideration. Donkeys may show signs at a later stage, meaning that disease processes are more advanced and the window for successful medical or surgical intervention may be reduced. Hyperlipemia may be a secondary complication that affects recovery. As a result, it must be identified early and treated aggressively, or should be factored into the prognosis. There may be other significant diseases present, particularly in geriatric donkeys, which have not presented with clinical signs. These diseases,

such as severe dental disease, liver disease, laminitis, and osteoarthritis of hips and/or shoulders, could affect prognosis.

Pharmacology

A recent survey of veterinary surgeons in clinical practice indicated that of the commonly used analgesics, phenylbutazone, flunixin, detomidine, and butorphanol, most were administered at the horse dose rate and frequency (Grint et al., 2015b). As discussed later, this suggests that many donkeys may be receiving inadequate or inappropriate therapy.

Although there are limited data regarding pharmacokinetics and pharmacodynamics in donkeys, interest in this species is increasing and several reviews and studies have been published in the past decade or so (Grosenbaugh et al., 2011; Lizarraga et al., 2004).

In general, donkeys have a greater capacity than horses to metabolize and eliminate drugs, with greater total body clearance for many drugs tested. The hepatic P450 isoenzymes appear to be more active in the donkey. As a result, altered dosing intervals may be required for drugs undergoing hepatic clearance or recirculation. It is postulated that this may be an evolutionary advantage for a species dependent on eating poor-quality vegetation and plant species avoided by horses. The previously discussed difference in water partitioning in the donkey contributes to the altered drug metabolism.

It should be noted that there are very few drugs licensed for use in the donkey and that much of the research is based on small numbers of animals. In addition, differences between miniature, standard, and mammoth donkeys have been identified.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Phenylbutazone is the most studied NSAID in donkeys; it is eliminated faster by donkeys than horses and the recommendation is to administer a loading dose of 4.4 mg/kg bid for day 1, followed by 2.2 mg/kg daily for the duration of the painful process. Prolonged use of doses at this level has not been associated with gastric ulceration or right dorsal colitis in donkeys (Burden et al., 2009). Miniature donkeys may require an even greater frequency of dosing to achieve therapeutic levels. In contrast to other NSAIDs studied in donkeys, carprofen is metabolized more slowly in the donkey. Although once-daily dosing with this drug is considered to be safe, monitoring for evidence of toxicity should be considered if long-term use is required.

The use of NSAIDs in donkeys with liver disease (hyperlipemia), or in working donkeys that may be dehydrated, should be approached with caution and reduced doses used. Current information is summarized in Table 38.5.

Sedation and Anesthesia

Doses of α_2-agonists required for sedation and premedication of donkeys are similar to those for horses, and the addition of an opioid, such as butorphanol or buprenorphine, results in synergistic sedative effects. However, mules and unhandled or feral donkeys may require up to a 50% higher dose of α_2-agonists to achieve sedation.

When using xylazine–ketamine combinations for anesthesia of donkeys or mules, there is a shorter period of relaxation and recumbency, requiring more frequent "top-up" doses, owing to the faster metabolism of ketamine in these species (Matthews et al., 1997). This is particularly marked in miniature donkeys in which

Table 38.5 Comparison of donkey and horse clearance and elimination and recommended doses of selected common NSAIDs.

Drug	Clearance donkey (horse) (mL/kg/h)	Elimination half- life donkey (horse) (h)	Recommended dose for donkeys
Equipalazone	170–215 standard, 360 miniatures (13–30)	0.6 (4–6)	2.2 mg/kg bid standard donkey, tid in miniature donkeys PO, IV
Flunixin meglumine	1.78 (1.1)	0.75–4.5 (3.4)	1.1 mg/kg bid PO, IV
Ketoprofen	414	1.3 (1.5)	1–2.2 mg/kg sid PO
Meloxicam	188 (35)	4 (8.5)	0.6 mg/kg sid PO Short $t_{½}$ means this may not be a suitable drug for donkeys
Carprofen R	2.8 (8.4) 4.9 (37)	(22)	0.7 mg/kg sid PO Slower clearance than horse, so care regarding overdosing
Firocoxib	239 (37)	0.85 (34)	0.1 mg/kg sid PO, may need more frequent dosing

Source: Adapted from Grosenbaugh et al., 2011. Reproduced with permission of John Wiley & Sons.

xylazine–ketamine–butorphanol combinations may provide only 5 min of surgical anesthesia. Xylazine (1.1 mg/kg)–butorphanol (0.04 mg/kg)–tiletamine (1.1–1.5 mg/kg) combinations are recommended (Matthews & Taylor, 2000). The addition of diazepam (0.03–0.1 mg/kg) can be useful to increase relaxation and ease intubation. Propofol (2 mg/kg) given as a bolus following administration of xylazine (0.8 mg/kg) provides good anesthesia for miniature donkeys with "top-up" doses at 0.2 mg/kg if inhalation anesthesia is not used.

Guaifenesin is cleared more rapidly in the donkey than the horse, but the dose needed to produce recumbency in the donkey is only about 60% of that of the horse dose. Owing to these various differences, the total intravenous anesthetic combination of xylazine–guaifenesin–ketamine in the donkey needs to be adjusted to avoid guaifenesin toxicity and insufficient anesthesia, by using twice the amount of ketamine compared with standard horse protocols (Taylor et al., 2008). A useful safe combination is 1 L of 5% guaifenesin, 500 mg xylazine, and 2000 mg ketamine at a dose rate of 2 mL/kg/min following premedication with xylazine at 1 mg/kg.

Opioid Analgesics

There is insufficient evidence in the donkey to recommend different dosing regimens from those used in the horse. Clinical experience indicates that good results can be obtained using morphine, butorphanol, and buprenorphine to control visceral pain. One report of the use of fentanyl patches in a miniature donkey showed that the donkey required a larger patch and more frequent change of patches to achieve plasma levels of fentanyl similar to those in a horse (Grosenbaugh et al., 2011).

Antibiotics

Although the data available are incomplete, many antibiotics have a shorter half-life in the donkey than in the horse, suggesting that an increase in dosing frequency may be appropriate. Ampicillin (10 mg/kg IV), amoxycillin (10–15 mg/kg IV), and sodium penicillin G (20,000 IU/kg IV) may require dosing at 4–6 h intervals in donkeys rather than at the 6–8 h intervals used in horses. Similarly, sulfamethoxazole/trimethoprim (12.5/2.5 mg/kg IV) may need to be administered at 8–12 h intervals rather than at 8–24 h intervals as used in horses.

The Role of Parasites

Donkeys share the same species of helminth parasites with other equids. Virtually all donkeys, especially those exposed to pasture, experience some level of parasitism. As in horses (Reinemeyer & Nielsen, 2013), strongyles, *Parascaris equorum*, *Dictyocaulus arnfieldi*, *Oxyuris equi*, *Anoplocephala perfoliata*, *Strongyloides westeri*, *Gasterophilus* spp., *Gastrodiscus* spp., *Fasciola* spp., and *Habronaema* spp. are the most commonly encountered parasites in the donkey population worldwide (Matthee et al. 2004; Getachew et al., 2010; Matthews & Burden, 2013). The life cycle of these parasites in the donkey is the same as in other equids (with the exception of *Dictyocaulus*). However, the severity of the clinical disease that they can cause might vary not only between the different species but also within the same species of equids. Most parasitic disease is a consequence of the sheer numbers of parasites present, although clinical severity can be modulated by malnutrition, coexisting diseases, or other stressors, and host genetic factors. Gastrointestinal parasites cause a wide range of clinical signs or diseases in equids; however, some manifestations are unique to specific parasites. Among gastrointestinal parasites, Cyathostomins, *Strongylus vulgaris*, *Parascaris*, and *A. perfoliata* are the parasites most often associated with equine verminous colic (Love, 1995; Reinemeyer & Nielsen, 2009).

As in horses and ponies, cyathostomin species are the most common parasitic nematodes in nonworking donkeys in the developed world (Matthews & Burden, 2013). In working donkeys in developing countries, other helminth parasites also are highly prevalent (Matthee et al. 2004; Getachew et al., 2010). Cases of colic associated with larval cyathostominosis are often reported in horses and ponies (Love, 1995; Mair & Pearson, 1995; Mair, et al., 2000). However, the common clinical signs associated with cyathostomins in horses and ponies (Love, 1995) are rarely observed in donkeys. Like other equids, donkeys vary in their susceptibility to cyathostomins, and in a well-managed population the majority of donkeys control their level of infection relatively well. However, colitis and typhilitis associated with the synchronous emergence of large numbers of encysted larvae (cyathostominosis) causing colic are sometimes observed in some donkeys at The Donkey Sanctuary (Matthews & Burden, 2013). In these cases, common presenting signs include pyrexia, inappetance, dullness, weight loss, and loose feces (but rarely diarrhea). Whether cyathostomins hibernate/encyst in working donkeys and the impact of the infection are not well documented and often unclear under tropical weather conditions.

Before cyathostomins became so prevalent, *S. vulgaris* was the major cause of verminous colic in horses and ponies worldwide (Love, 1992; Reinemeyer & Nielsen, 2009). Although this parasite is rare and no longer a major problem in the developed world, it is still highly prevalent in working donkeys in developing countries (Getachew et al., 2010; Borji et al., 2014; Getachew & Birhanu, unpublished data, 2015). As occurs in horses, pathological lesions characterized by aneurysm,

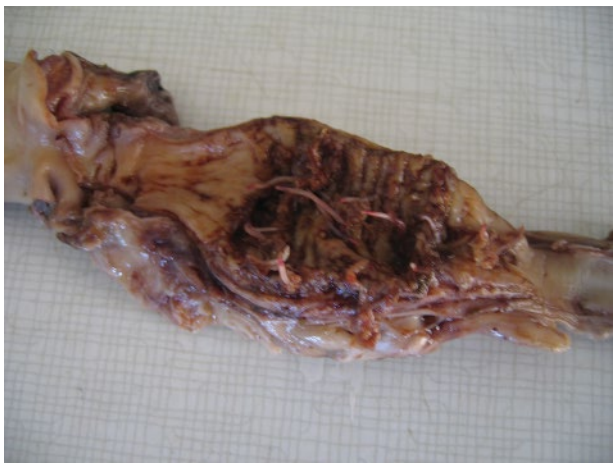

Figure 38.4 Thromboembolism associated with *Strongylus vulgaris* in the cranial mesenteric artery.

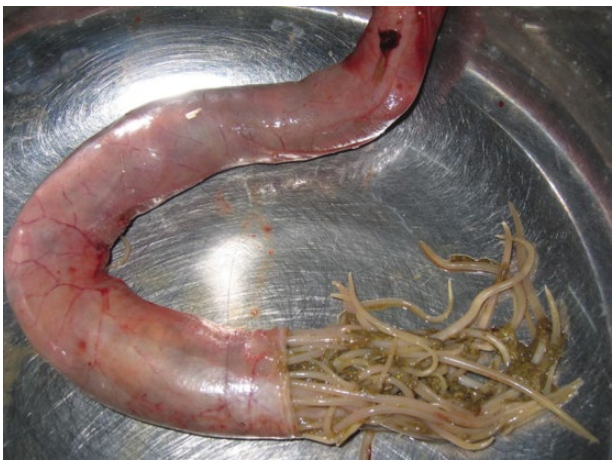

Figure 38.5 Impaction of the ileum with large numbers of *Parascaris* spp. in a 4-year-old working donkey.

thromboembolism, and arteritis/endarteritis of the cranial mesenteric artery and its branches are common findings in working donkeys (Pandey & Eysker, 1989; Borji et al., 2014). These lesions often contain numerous *S. vulgaris* larvae (Figure 38.4) and the condition is manifested by intermittent colic. The colic is mostly associated with intestinal infarction due to local ischemia caused by the parasite.

Parascaris equorum infection is a problem in foals and yearlings in horses and ponies (Clayton & Duncan, 1979), and mature working donkeys often harbor patent infections (Getachew et al., 2010). The parasite is relatively common in donkeys grazing permanent pastures and not regularly treated. Although other clinical signs, such as respiratory signs due to larval migration, exist, clinical manifestation and lesions related to the abdomen are associated with the presence of large numbers of adult worms in the small intestine. As in horses and ponies (Reinemeyer & Nielsen, 2009; Tatz et al., 2012), large numbers of *Parascaris equorum* can cause small intestinal impaction/obstruction and sometimes rupture in young donkeys (Getachew et al., 2008) (Figure 38.5). This condition is associated either with anthelmintic treatment (Cribb et al., 2006), when worms are killed resulting in tangled, dead worms mechanically obstructing the small intestine, or the accumulation of worms through repeated infections in a population of donkeys having no exposure to anthelmintics. The latter situation is particularly evident in working donkeys when their immunity is compromised through overwork, ill health, or poor nutrition (Getachew et al., 2008).

Among the three major cestode species known to affect equids, *A. perfoliata* is the most common, having a worldwide distribution. Generally, information on this parasite in donkeys is scant. In well-managed farms such as The Donkey Sanctuary in the United Kingdom, the infection prevalence of *A. perfoliata* is very low to rare

Figure 38.6 Masses of *Anoplocephala perfoliata* attached to the ileocecal valve in a donkey.

(Matthews & Burden, 2013). However, in a recent study in Ethiopia, Getachew (2006) and Getachew et al. (2012a) reported an infection prevalence of 27.9% and a seroprevalence of 34% in working donkeys. The clinical or pathological effect of *A. perfoliata* is related to its attachment to the ileocecal valve. It is common to find masses of *A. perfoliata* attached to this site and the associated lesions of local inflammation, ulceration, formation of pseudomembranes, and the development of fibrous connective tissue (Getachew, unpublished data) in working donkeys (Figure 38.6). *A. perfoliata* has been associated with increased risks of colic, particularly ileal impaction, spasmodic colic, and intussusceptions, in horses (Proudman et al., 1998; Reinemeyer & Nielsen, 2009). Although its clinical impact has not been investigated in donkeys, given its high infection prevalence in working donkeys, the same attachment site, and lesions, it is highly likely that this parasite causes colic in donkeys.

Figure 38.7 Gasterophilosis-associated rectal prolapse in a working donkey in Ethiopia.

Colic has not been reported as a prominent feature of other equine parasites. However, one recent study in Ethiopia identified that *Gasterophilus* spp. are the major cause of rectal prolapse in working donkeys leading to colic (Getachew et al., 2012b). Third-stage larvae of this arthropod parasite were found attached in the rectal mucosa (Figure 38.7), causing intense intermittent tenesmus, before they pass with feces to pupate in the soil.

Disorders of the Stomach and Small Intestine

Donkeys are susceptible to developing gastric ulcers. In a study of nonworking donkeys in the United Kingdom, 41% had evidence of gastric ulceration at necropsy. The most common site for ulcer development was the squamous area along the margo plicatus and the main risk factors appeared to be hyperlipemia, renal disease, and consuming a carbohydrate-based diet (Burden et al., 2009). The authors also reported that treatment with NSAIDs for 7 days or more prior to death did not significantly increase the risk of gastric ulceration even in the glandular region. This is in contrast to a study by Mozaffari et al. (2010), who identified glandular ulceration in 60% of healthy miniature donkeys given NSAIDs for 12 days. It should be noted, however, that in this study phenylbutazone was administered at 4.4 mg/kg IV bid whereas in the clinical study phenylbutazone would have been administered at an initial dose of 4.4 mg/kg IV followed by 2.2 mg/kg PO bid.

In a study documenting the prevalence of gastric ulcers in a group of working donkeys, 54% had evidence of hyperkeratosis, erosions, or deep ulcers in the nonglandular region, and 63% had erosions in the glandular region. All the donkeys in that study had *Gasterophilus* spp. present in their stomachs, but in only one donkey was there evidence of ulceration and inflammation at the site of larval attachment. *Draschia megastoma* was the parasite associated with the most severe lesions, which included inflammation and necrosis predominantly in the glandular region (Al-Mokaddem et al., 2015).

As in the horse, a diagnosis of gastric ulceration is made by gastroscopy. It is important to note that little information is available about gastric emptying times in donkeys. Hence, while food is being withheld, it is important to be cognizant of the type of bedding material used, as donkeys will eat large quantities of paper and cardboard. There are no data in the literature regarding the use of omeprazole in the treatment of gastric ulceration in donkeys. However, when omeprazole is used as a gastroprotectant in donkeys with hyperlipemia, it is administered at the standard equine dose.

In our experience, sick and orphan donkey foals are at high risk for developing gastric ulcers and will show similar signs to horses, including colic after feeding and bruxism. While licensed omeprazole products are contraindicated in animals weighing less than 70 kg, we have used a titrated dose (based on body weight) in donkey foals.

Donkeys also develop gastric impactions, which can be primary but often are secondary to liver disease or generalized ileus associated with gastrointestinal disturbances. Donkeys have also been reported to develop phytobezoars caused by persimmon ingestion (Banse et al., 2011). In a study of the causes of colic in working donkeys in Ethiopia, 8% of the cases were due to gastric impaction, which is higher than reported in the horse. This may reflect access to coarse feed and ingestion of foreign bodies such as polythene bags (Bojia et al., 2006). The main presenting signs for donkeys with gastric impactions are dullness and inappetance, making it difficult to differentiate gastric impaction from any primary disease. Sometimes the first indication is the presence of discomfort after the administration of enteral fluids used in the treatment of large intestinal impactions or hyperlipemia. Diagnosis is equally as challenging as in the horse, particularly in view of the risk of hyperlipemia after a prolonged fasting period prior to endoscopy. Treatment of this condition is similar to that in the horse, with careful administration of enteral fluids owing to the risk of gastric rupture.

In a large UK population of working donkeys that included a large number of geriatric animals, small intestinal lesions were identified relatively uncommonly, while small intestinal obstruction accounted for 7% of colic cases (Bojia et al., 2006). There is one report of multiple lipomas in a donkey in which the masses were

attached to the stomach, small intestine, and pancreas; these were incidental findings at postmortem (Mozaffari & Derakhshanfar, 2011). Donkeys appear to deposit fat in different areas to horses, which might explain why pedunculated lipomas appear to be less common as a cause of strangulating small intestinal lesions in geriatric donkeys.

In the literature, there are few reported cases of equine grass sickness in donkeys (Wylie et al., 2011; Mellor et al., 2013). This disease seems to be seen less commonly than in the horse, although the reasons for this are unknown.

Disorders of the Cecum, Colon, and Rectum

Impaction colic was the most common type of colic diagnosed in a large population of donkeys in the United Kingdom, with the two most common sites of impaction being the pelvic flexure and cecum (Cox et al., 2009). In that study, the mortality rate was 52%, which is considerably higher than in the horse (5%). This may be explained in part by the presence of other conditions in geriatric donkeys that will affect prognosis, such as severe dental disease that is already being managed appropriately with diet. The loss of more than eight cheek teeth, particularly if multiple adjacent teeth are lost, results in a high risk for impaction colic even when a short-chop fiber product is fed. It is also likely that donkeys exhibit more subtle signs of pain in the early stages of impaction, allowing the condition to become more advanced before being diagnosed. This delay in diagnosis and treatment is likely to affect outcome.

Diagnosis and treatment of impaction colic are similar to those in the horse, although particular attention needs to be paid to the risk of hyperlipemia both secondary to the impaction and during treatment if food is being withheld. It is advisable, therefore, to withhold long-fiber forage but allow access to grazing and moist high-fiber feeds. As mentioned previously, risk factors for impaction colic include lack of access to grass, feeding concentrates, paper or cardboard bedding, and dental disease.

Typhlocolitis can also present as colic and although the clinical signs may be nonspecific, severely affected donkeys can show marked abdominal pain and present with classic colic signs. Other presentations include ventral edema and weight loss. In contrast to the horse, diarrhea is rarely seen. For example, in a case study of 40 donkeys with typhlocolitis, none developed diarrhea (Du Toit et al., 2010). In that study, there was a seasonal pattern, with the majority of cases occurring in the fall in aged donkeys. As 50% of the cases were attributed to cyathostominosis based on histopathologic findings, it is possible that this seasonal presentation is an atypical form of cyathostominosis that might be unique to older donkeys. On histopathology, 33% of cases in that study were associated with a bacterial etiology, although no specific organisms were identified and toxin assay results were negative. Because any factor affecting the microbial flora of the cecum and ventral colon could predispose to pathogen overgrowth, careful attention should be paid to the quality of fiber products being fed. Other causes of typhlocolitis need to be considered, including NSAID-induced right dorsal colitis and antimicrobial-associated typhlocolitis; however, both of these conditions were ruled out in this study even though many of the donkeys were on long-term NSAID therapy.

Premortem diagnosis of typhlocolitis is challenging as hematologic and biochemical changes are variable and nonspecific, although severe leukopenia and hypoglobulinemia are poor prognostic indicators. Serum alkaline phosphatase (ALP) activity appears to have little diagnostic value and peritoneal ALP activity has not been investigated. Transabdominal ultrasonography is a valuable diagnostic tool for detecting increased free fluid and mural thickening. In view of the predisposition for the ventral colon to be affected, McGorum & Pirie (2010) suggested determining the ratio of right ventral to right dorsal colon thickness, as this would be expected to be significantly increased in affected animals. Peritoneal fluid analysis may be helpful to determine whether there is serosal involvement and/or peritonitis, as this will guide decision making on treatment and prognosis. A fecal sample should be visually assessed for the presence of cyathostomins, but should also be examined under the microscope to identify emerging larvae.

Treatment is similar to that in the horse, including fluid therapy, although care must be taken with the use of crystalloids as this may exacerbate mural edema in donkeys with severe ulcerative, fibrinonecrotic lesions. Although colloids are useful in helping to restore oncotic pressure, large volumes are required to increase the plasma protein concentration significantly. NSAID therapy at the recommended dose and frequency for donkeys may aid in managing clinical signs consistent with endotoxemia and provide analgesia. In very painful animals, opioids and lidocaine administered at standard equine doses may also be necessary. Other supportive treatments such as probiotics and adsorbents (e.g., di-tri-octahedral smectite) can be useful in addressing the adverse effects of intestinal pathogens. Treatment for specific conditions would be similar to that in the horse, including the use of moxidectin and corticosteroids for suspected cyathostominosis.

Similarly to horses, donkeys develop large intestinal displacements and volvulus. As mentioned previously, donkeys often present in a more advanced stage of disease and show little sign of deterioration even though

conditions are not resolving. As a result, prompt decision making is required to increase the chance of successful surgical intervention. Donkeys also develop enterolithiasis as they were overrepresented in one study (Hassel et al., 1999), and Bojia et al. (2006) reported that 24% of colic cases in a population of working donkeys in Ethiopia were attributed to enterolithiasis/foreign bodies. This may reflect different foraging behaviors and the availability of poor-quality fibrous food and indigestible material such as plastic bags. The main locations for obstruction tend to be the transverse and small colon.

Rectal prolapse occurs in donkeys. In a study by Getachew et al. (2012b), 84% of cases were associated with *Gasterophilus nasalis*. The study population was working donkeys in Ethiopia and a small percentage of cases were associated with diarrhea. Rectal prolapse has also been described in a donkey foal, although the cause was not identified. Treatment involved reduction and repositioning of the rectum using a purse-string suture to retain the tissue in position (Shanmugam et al., 2001).

Table 38.6 Prevalence of (selected) postmortem findings for 1444 donkeys, October 2001–2008, The Donkey Sanctuary, Devon, UK.

Description of finding	No. of donkeys	Prevalence (%)
Benign condition of female reproductive tract	335	23.2
Malignant neoplasia of female reproductive tract	7	0.5
Renal disease	284	19.7
Malignant renal neoplasia	6	0.4
Liver disease (excluding neoplasia)	261	18.1
Liver neoplasia (malignant)	60	4.2
Liver neoplasia (benign)	10	0.7
Gastrointestinal neoplasia	54	3.7
Urolithiasis	45	3.1
Pancreatitis	69	4.8
Peritonitis	107	7.4

Colic Due to Abdominal Neoplasia and Other Abdominal Organs

In older donkeys, abdominal neoplasia is a significant cause of colic. Affected animals exhibit the typical signs of weight loss, recurrent pyrexia, inappetance, and altered plasma proteins. In contrast to the findings in intestinal neoplasia in horses (Taylor et al., 2006), diarrhea is not a common finding in our experience of donkeys with intestinal neoplasia, although the other clinical signs are similar, including manifestations of paraneoplastic syndromes.

Data from the postmortem survey of 1444 aged donkeys by Morrow et al. (2010) (Table 38.6) document abdominal neoplasia of the gastrointestinal tract, liver, kidney, and female reproductive system. In that study, the prevalence was 9.5%, which is more than twice the 4% incidence of abdominal neoplasia in the horse (Knottenbelt & Leverhulme, 2014).

A typical case report of abdominal neoplasia in a donkey (Thiemann, 2008) highlights the challenges of diagnosis in a geriatric stoic species already on low-dose NSAID therapy for chronic foot pain. The 26-year old-donkey presented with acute colic and distension of the small intestine after a history of low-grade anemia and weight loss. At postmortem examination, a 17 kg mass (a leimyosarcoma) was found, occupying 20% of the abdominal cavity.

Pain and colic symptoms due to abnormalities affecting other abdominal organs have been reported in the donkey, typically as isolated case reports. For example, Thiemann et al. (2007) described five cases in which pyometra and enlarged ovarian tissue caused colic in jennies, Spanton et al. (2009) documented chronic colic in a donkey due to a pancreatic tumor, and Abdel-Hady (2014) described urolithiasis in a jenny as a cause of recurrent colic symptoms. There is no large-scale review of the topic in the literature.

In at-risk populations, donkeys with infections such as rabies and tetanus may present with a multitude of symptoms, some of which resemble colic (Gizachew et al., 2012).

Colic in the Overseas Working Donkey

Of the more than 44 million donkeys worldwide (FAOSTAT, 2013), over 97% are in developing countries and specifically kept for work. These animals are maintained under poor management and husbandry conditions and are known to suffer from multiple health and welfare problems. Colic is a common abdominal condition in these animals, and often has high case fatality rates seen in a day-to-day clinical intervention run by many animal charity organizations, such as The Donkey Sanctuary and the Society for the Protection of Animals Abroad (SPANA). Although there have been few detailed epidemiologic studies of the types of colic and their predisposing factors in working donkeys, obstruction of the colon and small intestine and verminous and tympanic colic are common colic cases frequently presented at veterinary clinics. As is the case in nonworking donkeys (Cox et al., 2007), impaction colic is very common in working donkeys, although the major predisposing factors seem to be different. Retrospective clinical data

analyses in Ethiopia (Bojia et al., 2006) and Mali (Doumbia, 2011) have shown that over 40% of colic cases admitted to the clinics were impaction/obstructive colic due to foreign bodies, coarse dry feeds, and lack of access to water. Foreign body ingestion also has been described as a major cause of colic in working donkeys in Syria and Morocco (Stringer, 2011), India (Singh et al., 2010), and Kenya (Solomon, Donkey Sanctuary Kenya, personal communication). A significant number of cases of tympanic colic (23%) due to access to moldy feed and lush green grasses during the rainy season were also documented in Ethiopia (Bojia et al., 2006). Tympanic colic is seasonal and clovers are one of the main leguminous plants incriminated.

Dental problems associated with old age are one of the main risk factors of impaction colic in nonworking donkeys (Cox et al., 2009). Although some studies documented dental problems (Du Toit et al., 2008b; Mengistu et al., 2015) and indicated its association with colic in working donkeys, the extent of this association is not well studied. Given the short life span of working donkeys, their dependence on grazing, and the fact that the majority of impaction/obstructive colic is due to the ingestion of foreign bodies and coarse dry feed and lack of access to water, rather than long fibers entering the large intestine due to inadequate mastication, the reported dental abnormalities may not play a significant role in causing impaction colic in working donkeys.

As helminth parasites are one of the major health problems in working donkeys (Getachew et al., 2010, 2012a, 2012b), their role as a cause of colic cannot be overlooked. Although they are no longer a significant problem in the developed world, large strongyles, particularly *S. vulgaris*, remain highly prevalent in working donkeys (Getachew et al., 2010; Borji et al., 2014). Studies in Mali and Ethiopia (Bojia et al., 2006; Doumbia, 2011) have shown that over 26 and 19% of colic cases, respectively, were related to intestinal parasites. One study in Ethiopia has also documented gasterophilosis as the major cause of rectal prolapse in working donkeys, leading to colic (Getachew et al., 2012b).

Although there are no studies to document sand colic in working donkeys, the chance that working donkeys can be exposed to sand colic is high. Working donkeys depend entirely on scavenging/grazing on land with scarce grasses. Even when supplemented with crop residues, they eat from the ground. Furthermore, they are not supplemented with minerals such as salt. Consequently, it is common to see these donkeys ingesting sand. Many cases of sand colic have been diagnosed in the mid-lowland region of Ethiopia and coastal areas of Kenya (personal observation).

The limited number of case studies in the literature indicate that the majority of colic cases in working donkeys are work- and management-related problems, particularly owing to their scavenging habit because of shortage of feed and lack of access to water. These factors predispose them to obstructive colic secondary to foreign bodies and indigestible refuse, such as plastic materials (e.g., polythene bags) and moldy feeds (Figure 38.8).

Figure 38.8 Donkey amid plastic bags in Lamu, Kenya – typical of an unsuitable foraging area.

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Part IX

Nutritional Management

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Nutritional Management of the Colic Patient

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Nutrition and Feeding Management as It Relates to Colic Development and Prevention

As a herbivore with the bulk of its fermentative activity occurring in the hindgut, the horse has evolved and adapted to spending the majority of its day consuming long-stem forages. Modern use has placed higher nutritional demands on the horse, which are often met with higher quality forages and concentrated energy sources. Similarly, managed horses are often fed large meals, several hours apart, as opposed to their innate trickle feeding behavior. Nutritionists have the challenge of determining the nutrient requirements of horses at different types of activity or life stage, identifying suitable feedstuffs to provide such nutrients, and offering them to the horse in a way that satisfies its natural grazing behavior. Nutritionists further have the challenge of providing feeds in a way that preserves the sensitive microbial ecosystem within the horse's digestive tract. Because reports of colic in feral or wild populations are lacking, it is proposed that modern horses develop colic as a result of a disparity between current feeding regimes and the horse's natural digestive biology.

The horse has a relatively small stomach (8% of the total gastrointestinal tract) that functions to mix ingesta with hydrochloric acid, pepsin, and lipase, along with a small microbial ecosystem, to begin the digestion and fermentative processes. The small intestine is the major site of enzymatic digestion of protein, fats, and hydrolyzable carbohydrates such as starches, and is the site of absorption of these end products, including monosaccharides, amino acids, and lipids, in addition to minerals including calcium and magnesium, and the fat-soluble vitamins. Within the large colon and cecum exists a vast population of microbial organisms comprised of bacteria, fungi, and protozoa, which function primarily to ferment dietary plant fibers to short-chain amino acids (SCFAs), namely acetate, propionate, and butyrate; they are also called volatile fatty acids (VFAs), and can be used by the horse for energy production. These microbes also play a major role in the biosynthesis of vitamin K and the B complex of vitamins, and also microbial protein. The large intestine (including the cecum and large and small colon) is structured with diameter changes and flexures to optimize retention of digesta with complex motility patterns to maximize fermentative function.

This complex digestive system is perfectly adapted to the evolutionary diet of the horse – long-stemmed pasture grasses that are consumed throughout the day. Such plants are rich in fibers that are fermented to produce the SCFAs, which when absorbed and metabolized can provide the idle horse with sufficient calories to sustain itself. The increased energy demands of today's performance horses, however, require calories in amounts that exceed those that can be provided for solely by the SCFAs, largely because such grasses are bulky and the horse's upper digestive tract is simply too small to consume sufficient quantities. Therefore, today's horses are fed more concentrated energy sources, namely cereal grains and mixes, often while feeding reduced amounts of long-stemmed forages.

Cereal grains generally contain large amounts of starch, which are chains of amylose and amylopectin. The horse has very little salivary amylase, so α-amylase within the small intestine initially breaks these chains to give disaccharides and oligosaccharides, and brush-border enzymes further break them into monosaccharides. Early work by Potter et al. (1992) showed that as

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the starch intake increased, there was an increasing amount of starch entering the distal ileum that could pass into the large intestine. Further, as starch increased beyond ~350 g/100 kg body weight (BW), the amount of starch passing through the small intestine increased dramatically, suggesting that there was an upper limit to small intestinal starch digestion in the horse. This could be explained by the relatively low small intestinal α-amylase activity compared with other species as reported by Kienzle et al. (1994). Kienzle et al. further reported large variations between individual horses, and higher activity when horses had a history of grain feeding, the latter suggesting some capacity for adaptation. More recent work showed activities of the brush-border enzymes (maltase and sucrase) to be similar or elevated compared with other species (Dyer et al., 2002), suggesting that any limitation to small intestinal starch digestion is a result of inadequate α-amylase, rather than inadequate brush-border enzyme activity. As indicated, there may be capacity for dietary adaptation with respect to α-amylase activity, but this has not been directly confirmed in the horse to date. Shirazi-Beechey (2008) reported a three-fold increase in the main enterocyte's glucose transporter, SLGT1, mRNA following a 2-month adaptation to a higher (40–60%) grain diet compared with a forage only diet. As the substrates, glucose and galactose, would likely be the signal to increase transporter synthesis, this adaptation suggests that α-amylase activity may have also been up-regulated.

As cellulose is indigestible by mammalian enzymes, fibrous particles from forages and other feeds bypass the small intestine intact, to reach the large intestine – the cecum and large colon. Fibrolytic microbes, including *Fibrobacter* and *Ruminococcus* species of anaerobic bacteria, break down cellulose, hemicellulose, and pectin into the SCFAs, with CO_2, H_2, and methane as waste products, and are present in high amounts in grass-fed horses (Shirazi-Beechey, 2008; Daly et al., 2012). In horses adapted to a concentrate diet, there is a shift toward a lower population of the fibrolytic species, with an increase in Lachnospiraceae, Bacteroidetes, and *Bacillus–Lactobacillus–Streptococcus* groups (Daly et al., 2012). Daley et al. further reported a significant increase in lactic acid, an end product of starch and sugar fermentation. Similar findings have been reported following an acute change in diet, whereby cecal and colonic lactobacilli and streptococci increased 29 h after the abrupt inclusion of barley, along with an increase in lactate concentration (de Fombelle et al., 2001). Such increases in lactic acid production when horses are fed high grain concentrate diets coincide with a drop in ingesta pH (Goodson et al., 1988; Williamson et al., 2007; Julliand et al., 2001; Richards et al., 2006). Also, as lactate production increases, so does CO_2 production (Shirazi-Beechy, 2008), and a trend of higher postprandial breath methane and hydrogen levels have been reported in horses fed a high-starch diet (Pratt et al., 2002). Interestingly, despite an increase in lactic acid production with the concentrate diet, Daly et al. (2012) found no significant effects of diet (hay versus hay and concentrate) in the lactate-utilizing group of Veillonellaceae.

Taken together, the limited ability of the small intestine to digest starch results in starch reaching the large intestine, particularly when fed in large amounts. Fermentation of starch results in alterations in the microbial ecosystem, increases in lactic acid and gas production, and decreases in pH, which can lead to gut distension, dysmotility, shifts in fluid content of the digesta, and reduced integrity of the epithelium (Shirazi-Beechy, 2008; Bailey et al., 2003; Clarke et al., 1990) Therefore, it is not surprising that consumption of large amounts of soluble carbohydrates, most notably by the feeding of large grain meals, is one of the most common and important risk factors for the development of several types of colic. Tinker et al. (1997) reported an odds ratio (OR) of 4.8 when horses were fed 2.5–5 kg/day of concentrate and OR = 6.3 when horses were fed more than 5 kg/day of concentrate. Although not all commercial concentrates are high in starch, cereal grains used as ingredients in these feeds vary in their starch content (oats are 44%, corn is 70%, and barley is 54% starch) and the digestibility of the starch within the small intestine (with oats > barley > corn) (de Fombelle et al., 2001). Whereas Potter suggested ~3.5 g starch/kg BW per meal as an upper limit, Cuddeford (2001) suggested a maximum of 2 g starch/kg BW per meal based on fermentation changes observed in ponies when fed at 2.1 g starch/kg BW per meal.

Many horse trainers feed their horses only two meals per day, with one study reporting that 82% of trainers fed their horses concentrates twice per day, with only 15.3% of horses being fed three times per day and 1.4% of horses being fed four times per day (Richards et al., 2006). Similarly, show-jumping horses are fed two or three meals per day (Brunner et al., 2015). Fewer meals per day equates to larger volumes of feed at each meal. Although feeding frequency did not appear to affect fecal pH in Thoroughbred racehorses (Williamson et al., 2007), feeding large concentrate meals has been shown to affect colonic contents and fluid balance (Clarke et al., 1990; Lopes et al., 2004). In contrast, feeding multiple meals per day (and thus smaller meals) minimizes these effects. Feeding smaller meals more frequently (Houpt et al., 1988) and slowing the intake rate (Kutzner-Mulligan et al., 2013) have been shown to mitigate postprandial metabolic and hemodynamic responses, and therefore indirectly suggest that feeding smaller, frequent meals and prolonging intake rate would have less impact on the microbial ecosystem.

Pasture grazing, with a constant supply of fibrous carbohydrate to the large intestine, is typically associated with a lower risk of colic compared with management situations with little to no grazing (Hudson et al., 2001; Hillyer et al., 2002). Hillyer et al. (2002) reported an OR of 1.16 for each hour a horse was stabled, such that a horse that had no daily access to turnout or pasture would have an OR for simple colonic obstruction or distention colic of 35.2. Scantlebury et al. (2015) reported that increased pasture time decreased the risk of recurrence (OR = 0.99).

Consumption of pasture in sandy areas may, however, predispose a horse to sand colic. Psyllium has been recommended as a supplement to move sand through the digestive tract for clearance. However, in one study, feeding psyllium was not an effective way to increase sand output in the feces (Hammock et al., 1998). In contrast, another study examined the combination of probiotics, prebiotics, and psyllium fed over 35 days and reported significantly more fecal sand output after 4 days of supplementation (Hammock et al., 1998). In cases where sand has accumulated, administration of a combination of psyllium with magnesium sulfate and/or mineral oil has been shown to be effective (Niinistö et al., 2014; Hotwagner & Iben, 2008). Hotwagner & Iben (2008) reported that when 1 kg of psyllium was fed (as two 500 g meals mixed with mash feed) along with 2 L of mineral oil given via nasogastric tube, sand that had been administered previously (5 kg over 5 days) had greater output than in horses that had been administered only the mineral oil. Niinistö et al. (2014) reported that nasogastric administration of 1 g/kg BW psyllium and 1 g/kg BW magnesium sulfate for 4 days resolved the natural accumulation of sand in 9/12 horses compared with psyllium alone (3/12 horses) or magnesium sulfate (2/10 horses).

It should be noted that pasture grasses and legumes also have the potential to be high in starch and sugars, while cool-season grasses may also accumulate the oligosaccharide fructan, depending on the season or time of day (Longland & Byrd, 2006). Fructans are also fermented within the large intestine and, when fed as a bolus, result in substantial decreases in pH and alterations to hindgut health (Bailey et al., 2003; Geor, 2010). It is likely that when horses have regular access to pasture, they are not consuming a bolus of fructan similar to these experimental models. However, under some conditions, the pasture intake rate may be high and, coupled with peak climactic conditions that result in elevated fructan concentrations, a horse may be at risk of fructan-associated digestive problems.

Preserved forages are generally regarded as a suitable alternative to pasture and when horses are fed larger amounts of forage (versus lower forage and higher concentrate diets), they typically have reduced risk of colic (Tinker et al., 1997). Forages derived from grasses and legumes vary in quality depending largely on the stage of maturity at harvest, with an increase in lignin, a type of fiber that is indigestible even by microbial fermentation, as the plant ages. Although the lignin content of forages specifically has not been examined in epidemiological studies, it is intuitive that large amounts of indigestible material within the intestine would increase the risk of impaction. Round-baled hay is associated with an increased risk of colic (OR = 2.5) (Hudson et al., 2001), which may be explained by a tendency for lower quality (higher fiber) forages to be used in round-bale production. Coastal Bermuda grass hay has been implicated as a risk factor for ileal impaction (Little & Blikslager, 2002). The thin, fine stems of such hay may escape adequate chewing, resulting in large boluses of digesta within the digestive tract.

Other than feeding large amounts of grain, one of the greatest nutritional risk factors for colic is a change in diet. As shown by de Fombelle et al. (2001), the microbial population within the digestive tract is highly dynamic, and has the capacity for rapid responses following changes in diet. Changes from one concentrate feed to another (and potentially even one form of feed, for example, from textured to pelleted) may result in changes in digestibility and passage rate and, coupled with potentially different amounts and types of carbohydrates within these feeds, may be sufficient to alter the microbial system. As expected, changes in concentrate feeding result in an increased risk for colic, with reported ORs of 2.2 [multiple changes within a year (Tinker et al., 1997)], 3.6 [single change within a year (Tinker et al., 1997)], and 2.6 [change within 2 weeks (Hudson et al., 2001)]. Surprising, perhaps, is the even greater risk associated with changes in hay, such as different plant types or cuttings of the same hay. Changes in hay have reported ORs of 2.1 (Tinker et al., 1997), 4.9 (Hudson et al., 2001), and 9.8 (Cohen et al., 1999). It is likely that changes within the fibrous and sugar fractions of the hay alter microbial activity, and mastication and digestibility may also differ.

The supplementation of probiotics and prebiotics is becoming commonplace in equine feeds and diets. No study has examined odds ratios for risk of colic in horses with or without their use. However, yeast-based products containing *Saccharomyces cerevisiae* reportedly ameliorated the negative effects of a high-starch diet (providing 3.4 g starch/kg BW per meal) (Medina et al., 2002). *S. cerevisiae* also was shown to stimulate cellulose digestion and improve overall digestibility when horses were fed both high- and low-starch diets (Jouany et al., 2008; Jouany et al., 2009). Care should be taken when supplements are selected, as one study showed that many commercial products did not contain the organisms on the product label, or in the labeled quantities (Weese, 2002).

Feed and Management Recommendations to Prevent Colic

- Follow AAEP anthelmintic and other preventative healthcare guidelines.
- Ensure regular dental examinations.
- Follow guidelines for the nutritional requirements of horses (National Research Council, 2007), working with an equine nutritionist as needed.
- Aim to keep horses at an ideal body condition score (approximately 5/9 on the Henneke scale) (Henneke et al., 1983).
- Allow horses to graze well-managed pasture as much as possible.
  - Rotate, mow, and rest pastures to ensure horses graze at ideal plant heights.
    - Tall cool-season grasses such as orchardgrass: graze at 8–10 inches and remove at 3–4 inches.
    - Short cool-season grasses such as bluegrass: graze at 4–6 inches and remove at 1–2 inches.
  - Select plants based on seasonal availability for the geographic region.
  - Restrict grazing at times where sugars and fructans may be high.
    - Spring and fall.
    - Late in the afternoon of a sunny day.
    - The morning after a sunny day that was followed by a cool/frosty night.
- If pasture is not available, provide horses with high-quality dry forages suited to their needs.
  - Ensure forages are free of mold and foreign elements.
  - Select hay with green leafy plants versus coarse stems.
  - Hay analysis can indicate level of fiber, listed as ADF (acid detergent fiber) and NDF (neutral detergent fiber). Select hay with <35% ADF and 50% NDF.
    - Avoid hay with >65% NDF.
  - Offer horses *at least* 1% of their body weight as dried forage (hay) if not at pasture. Ideally, horses will consume more than 1.5% of their body weight as forage.
- If nutrient requirements exceed those that can be met with pasture or dry forage, offer high-quality concentrates in minimal amounts to meet the horse's needs.
  - Look for concentrates higher in fiber and fat and lower in starch and sugar (unless higher starch diets are required for glycogen synthesis in some performance horses).
  - Limit grams of starch per meal to less than 2 g/kg BW.
    - Example, for a feed with 50% starch, feed no more than 2 kg of feed per meal for a 500 kg horse.
  - If larger meals are fed, aim to slow the consumption rate (Kutzner-Mulligan et al., 2013).
  - Oats have the lowest amount of starch and are also highly digestible compared with other cereal grains and are therefore the safest of the cereal grains.
- Supplement energy (calorie) requirements (if needed) with vegetable oil (up to two cups/480 mL per day).
- Feed horses multiple times per day (ideally more than four times).
- When changing feeds (either pasture, forage, or concentrate), aim to make these changes over a 2-week period, by introducing the new feed at a rate of ~10% per day.
- If feeding in sandy areas, feed hay in a tub or off the ground. Consider supplementing with psyllium. Periodic nasogastric administration with psyllium, magnesium sulfate, and/or mineral oil may be warranted.
- Supplementation with *S. cerevisiae* may be recommended when horses are fed large amounts of concentrate.

Feeding Management of the Colic Patient

Horses exhibiting signs of colic should have feed and water withheld. Even while exhibiting mild colic, a horse may want to continue to eat, but this should be prevented, as it can worsen an impaction should that be the cause of the discomfort. Impaction colic can often be treated medically, with laxatives including mineral oil and/or magnesium sulfate, prokinetic agents, and fluid therapy as needed (Plummer, 2009). For horses with mild colic that quickly respond to treatment, feeding may be resumed when clinical assessment indicates adequate intestinal motility and/or there is evidence of fecal transit. In these cases, the period of feed withholding may be as short as 4–6 h. Also in these cases, supportive nutritional therapy is not warranted; however, the horse should be monitored for recurrence. Horses recovering from mild colic should have their feeding and management routine examined and owners should be given recommendations for colic prevention as above.

For horses undergoing surgical treatment of colic, it is common practice to restrict feed intake for a substantially longer period of time. In 30 horses that underwent resection and anastomosis of the small intestine, the mean duration of feed withholding after surgery was 76 h with a range of 48–91 h (Durham et al., 2003), although in another study some horses were not fed for more than 10 days after colic surgery (Cohen et al., 2004). One rationale for feed withholding appears to be concern that an early resumption of feeding (and water intake) will stress the site of enterotomy or anastomosis, thereby increasing the risk of dehiscence, peritonitis, and other

complications. Certainly postoperative complications are of grave concern, but there is no conclusive evidence that feed restriction decreases the risk for postoperative complications.

Horses that have surgical cases of colic are likely to have had feed withheld for several hours prior to surgery, and added time without feed following surgery results in negative energy balance and nutrient deprivation (Cruz et al., 2006; Edner et al., 2007). Nutrient deprivation is associated with immunosuppression and alterations in gastrointestinal function, including decreased motility, villus atrophy, and a decrease in gut barrier function associated with an increase in intestinal permeability. The latter has been associated with bacterial translocation, sepsis, and systemic inflammation (Silk & Gow, 2001). Conversely, postoperative feeding, particularly via the enteral route, is associated with a significant reduction in postoperative complications including ileus, anastomotic dehiscence and sepsis, and a decrease in the length of hospital stay (Silk and & Gow, 2001). There is evidence that early supportive postoperative nutrition improves prognosis and nutrient status in dogs (Kawasaki et al., 2009), and there is increasing awareness of such in horses.

Few studies have specifically investigated the outcome of horses with or without nutritional support post-surgery. However, one study of horses treated for surgical colic reported a significant correlation between several serum biochemical indicators of negative energy balance (e.g., increased serum bilirubin and triacylglycerol concentrations) and incisional complications (Protopapas, 2000). This observation suggests that in horses, as in humans, nutrient deprivation may be one factor that contributes to post-surgical complications, and provides rationale for initiation of nutritional support early in the postoperative period. Some authors have proposed that the monitoring of changes in serum biochemical variables, particularly bilirubin and triacylglycerol, be used to guide the need for nutritional intervention (Stratton-Phelps, 2004). Even short periods (24–36 h) of feed withdrawal can result in marked increases in serum bilirubin and triacylglycerol concentrations (>1.0 mmol/L; reference range 0.25–0.50 mmol/L) (Durham et al., 2004), suggesting that total feed withdrawal should not exceed 24–48 h. Earlier intervention (e.g., as soon as 6 h following intestinal surgery) should be considered when there is evidence of compromised nutritional status, such as horses in thin body condition (body condition score <3), a history of weight loss, and/or inadequate feed intake for more than 24–48 h prior to the colic, or those with evidence of marked hyperlipidemia. Dunkel & McKenzie (2003) described the presence of severe hyperlipidemia (serum triacylglycerol concentrations of 6.17–18.29 mmol/L) in horses with colic and/or colitis that had clinical and laboratory evidence of systemic inflammatory response syndrome (SIRS). The increase in circulating lipids likely reflects both an increase in mobilization of fat reserves (lipolysis) and a decrease in lipid clearance from blood, with both processes potentially modulated by SIRS and/or endotoxemia. Studies in other species have demonstrated that the activity of endothelial lipoprotein lipase, the enzyme responsible for tissue uptake of circulating lipids, is decreased by tumor necrosis factor-alpha (Uchida et al., 1997), and the activity of hormone sensitive lipase is increased during endotoxemia (Hughes et al., 2004). In a study by Dunkel & McKenzie (2003), treatment with intravenous dextrose or partial parenteral nutrition resulted in a decrease in serum triacylglycerol concentrations to normal limits, and appetite improved coincident with the decrease in circulating lipids.

Early nutritional intervention also may be indicated for obese ponies and horses [body condition score 7–9 (Henneke et al., 1983)] because of concern that even short periods of negative energy balance coupled with the stress of illness and/or surgery may result in disturbances in lipid metabolism, including hyperlipidemia, hyperlipemia, and hepatic lipidosis. Provision of adequate calories and protein in these horses may lessen the stimulus for lipolysis and mitigate increases in serum triacylglycerol concentrations.

Estimating Nutrient Requirements

As for healthy animals, the first consideration for postoperative nutritional support is energy (calories). A negative energy balance due to starvation or underfeeding can compromise immune function, delay wound healing, and result in a marked decrease in lean mass (e.g., skeletal muscle), the latter due to breakdown of endogenous protein for use in energy-requiring processes. On the other hand, studies in humans and other species have shown that an oversupply of energy (*hyperalimentation*) can also be detrimental, with complications such as hyperglycemia, hyperinsulinemia, hypertriglyceridemia, and insulin resistance, and increased risk of septic complications (Jeejeebhoy, 2001; Preiser et al., 2015). In septic animals, a high caloric intake results in an increase in mortality (Yamazaki et al., 1986).

Using indirect calorimetry, Cruz et al. (2006) estimated the resting energy expenditure (REE) in horses before and after a standard 90 min exploratory laparotomy. They reported an REE of ~24 kcal/kg BW/day in horses prior to surgery and 26 kcal/kg BW/day following anesthesia and surgery. For a 500 kg horse, this represents an increase in energy expenditure above baseline of about 1 Mcal/day (12 Mcal/day versus 13 Mcal/day post-surgery). The resting energy requirement (RER) (or "stall maintenance") reported by Pagan & Hintz

(1986) is RER = 21 kcal × BW (kg) + 975 kcal, which for a 500 kg horse equates to 11,475 Mcal/day, similar to the pre-surgery, stall-rested value of Cruz et al.

The current edition of the National Research Council (NRC)'s *Nutrient Requirements of Horses* (National Research Council, 2007) reports an average of 30.3 kcal/kg BW/day from several studies that had measured heat production in horses at maintenance. These data, however, were derived from horses that were confined during experiments, and therefore when average voluntary activity is included, the digestible energy (DE) requirement for maintenance in horses is 33.3 kcal/kg BW, or 16.7 Mcal/day for a 500 kg horse. Therefore, it can be deduced that horses following colic surgery have energy requirements that are about 80% of their normal energy requirements. However, in one study that examined 79 cases of gastrointestinal disease, the mean energy intake at the time of peak infusion of parenteral nutrition was 29 kcal/kg BW, and ranged from 18 to 50 kcal/kg BW/day! (Lopes & White, 2002). Similarly, horses that underwent resection of the small intestine gained weight when fed closer to true maintenance (i.e., 32–33 kcal/kg/day) during the postoperative period (Spurlock & Spurlock, 1989).

Energy requirements are also affected by the level of feed intake. Thermogenesis associated with the digestion, fermentation, and metabolism of feed can account for 15–25% of daily energy expenditure (Rooney, 1988). As horses recovering from colic will most often consume less feed than normal, some reduction in the energy losses associated with digestion and nutrient processing is to be expected. One author has suggested that stall maintenance energy needs are reduced by approximately 15–20% in the face of decreased feed intake (Rooney, 1988).

On balance, it appears that energy needs are minimally altered by surgery or injury unless there are major complications such as generalized burns or sepsis, in which case energy requirements may increase by up to 40–100% (Mechanik & Brett, 2002). Given the paucity of data on the effects of illness on the energy needs of horses and in light of concerns regarding increased risk of complications during overfeeding, the authors recommend that the caloric requirements of horses recovering from colic initially be based on the resting energy requirement or stall maintenance equation (i.e., 20–24 kcal/kg BW/day). Thereafter, there should be a gradual increase in the ration, although true maintenance DE may not be required until the horse returns to normal management such as field turnout. Importantly, regular measurement of body weight or assessment of body condition score (Henneke et al., 1983) should be undertaken during convalescence to judge the adequacy of energy provision and to provide a basis for adjustments in feeding.

Protein serves an important role in tissue maintenance, immune function, wound healing, and the slowing of endogenous protein catabolism. Protein requirements must be considered in light of caloric intake and underlying disease process. When the energy supply from carbohydrate and fat is limited, endogenous protein will be used for energy, contributing to a loss of lean body mass. Therefore, in developing a nutritional plan, first ensure that minimal energy needs are met, and then calculate protein requirements. For humans, suggested protein requirements range between 1.2 and 2.0 g protein/kg/day, with the higher end of this range recommended for patients undergoing major intestinal surgery (Waitzberg et al., 1999). Feeding 1.5 g/kg BW per day to critically ill humans is recommended (Preiser et al., 2015). The current NRC recommends a crude protein (CP) requirement of 1.26g/kg BW for an average horse (National Research Council, 2007). This equation is based on endogenous losses of nitrogen and digestibility of protein in most equine feeds.

For parenteral feeding, slightly lower protein feeding is reasonable given the higher availability of amino acids administered via the intravenous route versus the gut (Durham et al., 2003, 2004). Reports of parenteral feeding of horses suggest 0.7–1.0 g protein/kg/day (1 g/40–50 kcal) (as a balanced amino acid solution) (Durham et al., 2003, 2004; Waitzberg et al., 1999). There may be justification for higher levels of dietary protein (e.g., 2 g CP/kg/day), particularly for horses in poor body condition (body condition score <3) or those with hypoproteinemia and/or hypoalbuminemia. McDermott et al. (2015) reported hypoalbuminemia (<3.5 g/dL) as an independent predictor of anastomotic leak and sepsis in humans. Lysine requirements are calculated as 4.3% of the crude protein requirement (National Research Council, 2007).

Although there are no defined requirements for other amino acids (National Research Council, 2007), work in humans suggests that the amino acids arginine and glutamine are beneficial (Wang et al., 2015; Vermeulen et al., 2007). Immune-modulating diets (IMDs) are specialized nutritional formulas that offer balanced nutrition (carbohydrates, protein, lipids, minerals, and vitamins) that are supplemented with nutrients that improve immune function and modulate inflammation. Supplemental arginine stimulates the proliferation of immune cells, while glutamine serves as a fuel for immune cells, particularly within the mucosa (Vermeulen et al., 2007). Mice supplemented with 2% glutamine in their parenteral nutrition formula had significantly lower bacterial enteroinvasion compared with mice that were not supplemented (Wang et al., 2015). In the horse, glutamine supplementation also appears to support mucosal healing (Rötting et al., 2003). In contrast, branched-chain amino acid supplementation of parenteral nutrition (Huang et al., 2014) did not offer a clinical advantage in terms of biochemical markers, mortality, or postoperative hospital stay.

Omega-3 fatty acids are also included in IMDs, as anti-inflammatory agents (Gultekin et al., 2014; Marik & Flemmer, 2012). One study showed that 10 g of fish oil-enriched total parenteral nutrition resulted in significantly decreased inflammatory mediators, and improved biochemical markers in patients with sepsis (Gultekin et al., 2014).

It should be noted that refeeding syndrome may be a consequence of postoperative nutrition (Blumenstein et al., 2014; Mehanna et al., 2008), particularly if a horse presents with malnutrition prior to surgery or is fasted for more than 5 days (Witham & Stull, 1998). Refeeding syndrome results from a shift in metabolism to a starvation state that results in an intracellular depletion of phosphate, potassium, and magnesium. Refeeding, particularly with carbohydrates and glucose, triggers an increase in insulin that helps to move glucose from the blood and stimulates protein synthesis, which results in an uptake of phosphate, magnesium, and potassium into cells. This can in turn result in hypophosphatemia, hypomagnesemia, and hypokalemia, and shifts in fluids that can cause respiratory failure and cardiac arrest. This gives further support to offering calories, and particularly carbohydrate in controlled amounts, but also warrants supplementation with minerals, especially potassium, phosphorus, and magnesium, and also thiamine (Fuentebella & Kerner, 2009; Mehanna et al., 2008). In humans, the recommended supplementation rates are potassium 2–4, phosphate 0.3–0.6, and magnesium 0.2–0.4 mmol/kg BW/day (Mehanna et al., 2008). Monitoring phosphorus and magnesium during nutritional therapy is advised (Witham & Stull, 1998). In the horse, the recommendation for refeeding starved horses involves offering alfalfa hay, initially in limited amounts and increasing daily (Witham & Stull, 1998; Stull, 2003).

Micronutrient supplementation of zinc, selenium, copper, and vitamins C, E, and B is recommended for humans following surgery and may be warranted for the horse (Preiser et al., 2015).

Modes of Nutritional Therapy

The mode of nutritional therapy for the colic patient will depend on the underlying cause of the colic, the horse's appetite, and complications that arise during convalescence. The three primary modes of nutritional therapy are (1) voluntary enteral feeding, (2) assisted enteral feeding, and (3) parenteral nutrition. The preferred option is a controlled return to normal voluntary intake. Prerequisites are absence of gastric reflux, good intestinal motility, and a willingness to eat. As a general recommendation, horses that underwent celiotomy without enterotomy and have good gastrointestinal motility can resume feeding within 12–24 h. As discussed, however, some clinicians prefer to withhold feed for a longer period (>24 h) in horses that have undergone enterotomy or anastomosis (Rooney, 1988). Voluntary intake should provide at least 50–75% of the horse's resting or stall maintenance DE and crude protein requirements by the second or third day of feeding. For example, 75% of the resting energy requirement of a 500 kg horse (~9 Mcal DE) would be met by the consumption of about 4 kg of first-cut timothy hay that contains approximately 2.3 Mcal DE/kg (as fed). Although labor intensive, weighing the offered hay and the feed remaining in the stall is the only means to determine the adequacy of caloric intake, and requires knowledge and analysis of the hay's nutrient content.

More challenging is the nutritional management of anorexic or inappetant horses, or horses with severe intestinal compromise that restricts feeding by the enteral route because of ileus or intestinal dysmotility. Inappetant horses should be offered a variety of palatable feedstuffs, including fresh grass, in an attempt to stimulate intake. However, failure to consume at least 50% of the resting DE requirement for more than 24–36 h is an indication for initiation of assisted enteral feeding. Earlier intervention is justified for horses in poor body condition (body condition score <3) or a recent history of weight loss, old horses (>20 years of age), horses with suspected or confirmed endotoxemia/SIRS, lactating mares or those in the last trimester, and animals with severe hypertriglyceridemia (Rooney, 1988; Magdesian, 2003). Parenteral nutrition should be considered for horses with ileus and other intestinal conditions that prevent voluntary or enteral feeding, particularly when the withholding of oral feeding is expected to exceed 48–72 h (Magdesian, 2003; Durham et al., 2004).

In human clinical nutrition, there has been considerable debate on the relative merits of enteral versus parenteral nutrition. In humans, enteral nutrition (EN) feeding has been reported to result in fewer septic complications than parenteral nutrition (PN). Hospital pneumonia, intra-abdominal abscesses, anastomotic leaks, and catheter complications are more frequent in patients on PN (Anastasilakis et al., 2013; Mazaki & Ebisawa, 2008; Abunnaja et al., 2013). Villus atrophy, epithelial cell apoptosis, and increased mucosal permeability are also adverse effects of PN (Anastasilakis et al., 2013), as enteral nutrients feed the gut (which uses 15–35% of the body oxygen consumption) (Stoll et al., 1998). To date there have been no studies comparing PN with EN in horses. Although PN has been used successfully in horses, high cost is a concern (Durham et al., 2003).

Although EN is advocated when the gastrointestinal tract is functional, the weight of evidence from human studies indicates that PN is an important alternative to EN when a risk of malnutrition is present and EN is not tolerated or not possible owing to poor gastrointestinal

function. The same principles can be applied when developing a plan for nutritional management of colic patients. "If the horse will eat, feed it. If the gut works, use it."

Voluntary Feeding

For horses with a good appetite, nutritional management will comprise a gradual increase in voluntary intake, with an emphasis on high-fiber feeds. One author has recommended that hay be offered as soon as 12 h after colic surgery (Naylor, 1999). In another study, feeding grass hay to horses after colic surgery was associated with a decreased incidence of severe diarrhea during the postoperative period (Cohen & Honnas, 1996). Initially, small amounts (e.g., 0.3–0.5 kg) of good-quality forage (e.g., grass hay, alfalfa) should be fed four to eight times daily, with a steady increase in the volume of feedings and a decrease in frequency over a 3–5 day period. Limiting the size of feedings during the early phase of refeeding may reduce the risk of intestinal distension and anastomotic dehiscence (Naylor, 1999). For the same reason, some clinicians prefer to feed processed fiber products (e.g., chopped grass or alfalfa "chaff," alfalfa meal, soaked beet pulp shreds, wheat bran, or combinations) rather than long-stem hay during the early postoperative period. Alternatively, the horse may be allowed to graze pasture for 5–10 min several times throughout the day, or provided a highly digestible, low-bulk pelleted feed such as those marketed for use in older horses – "senior feeds."

In general, grain-concentrate feeds (e.g., straight grains or sweet feed) should be avoided for 10–14 days post-surgery (or colic) because of concern that an excess of starch may disturb an already disrupted hindgut microbial community. Thereafter, grain or grain-concentrate feeding can be resumed, starting at a rate of about 500 g/day (for a 500 kg horse), split into several meals and increasing by no more than 0.5–0.75 kg/day. An additional concern with the feeding of grain concentrates relates to the potential for high glycemic feeds that exacerbate hyperglycemia and hyperinsulinemia during the postoperative period. In humans, surgery is associated with the development of insulin resistance and hyperglycemia, and these are associated with increased morbidity. Further, glucose management can result in reduced morbidity and mortality (Evans et al., 2015). The implications of these findings for the management of equine colic patients are unknown. Preliminary studies have demonstrated hyperglycemia and hyperinsulinemia after emergency celiotomy in horses (A. Durham, personal communication with R. Geor, 2005), suggesting that insulin resistance also may occur in horses after colic surgery. Blood glucose monitoring is advocated for human patients (Evans et al., 2015), and should be considered in horses. Avoidance of high glycemic feeds (i.e., those rich in starch) may be particularly important in overweight horses, ponies, and donkeys in which there is an association between insulin resistance and development of laminitis (Kronfeld et al., 2004). Kronfeld et al. preferred to feed alternative sources of energy when hay or other forage alone does not meet estimated DE needs, for example, fat from stabilized rice bran (0.5–1.5 kg/day) or vegetable oil (100–300 mL/day mixed with hay cubes that have been softened in water). The feeding of a small amount of a protein supplement, for example, 0.25–0.50 kg casein, 93% CP [dry matter (DM) basis], also may be indicated, particularly in horses with hypoproteinemia.

Assisted Enteral Feeding

Assisted enteral feeding is accomplished by the infusion of a liquid diet through a nasogastric tube. Even if the majority of the nutritional support is being maintained through parenteral feeding (below), the combined used of enteral feeding has benefits for gastrointestinal health and, at least in human medicine, enteral feeding is associated with fewer complications (Grecu, 2013; Abunnaja et al., 2013).

Diet options for assisted enteral feeding include human enteral products, commercial pelleted horse feeds, commercial enteral products, and homemade recipes (Naylor, 1999; Sweeney & Hansen, 1990). Human formulations that have been administered to adult horses include Vital HN and Osmolyte HN (Ross Laboratories, Columbus, OH, USA). Both formulations are devoid of fiber, an advantage with respect to ease of administration through a small-diameter nasogastric tube but also a possible reason for the high incidence of diarrhea when these products are fed to horses. There also have been anecdotal reports of laminitis. Risk of these complications may be mitigated by gradual introduction to the liquid diet over a 3–4 day period, but diarrhea remains common, perhaps indicating the importance of dietary fiber for maintenance of normal hindgut function. It should also be recognized that the mix of energy substrates in these fiber-free human enteral formulas differs from that in typical equine rations(Stratton-Phelps, 2004). Osmolyte contains approximately 29% of calories from lipid and 54% calories from hydrolyzable carbohydrate (mostly sugars), whereas Vital HN provides about 10% of calories from lipid and 74% from carbohydrate. The high lipid content of Osmolyte may contribute to digestive disturbances in horses not adapted to fat-supplemented rations, and the use of a high-carbohydrate diet such as Vital HN may be contraindicated for horses with abnormal glucose metabolism (Stratton-Phelps, 2004). Collectively, these considerations argue against the use of fiber-free human enteral products in horses recovering

from gastrointestinal disease. Diets containing a moderate amount of fiber (10–20% crude fiber, DM basis) appear to be a more suitable choice for assisted enteral feeding in horses (Stratton-Phelps, 2004).

Recently, an enteral diet has been formulated specifically for horses (WellSolve Well-Gel®, Land O'Lakes Purina Feed, St. Louis, MO, USA). The product contains 36% CP, 6% fat, 14% maximum fiber, 4% starch, and 7% sugar (Vineyard et al., 2011). When fed at 0.3% BW per day (1.5 kg for a 500 kg horse), it provides 100% of the NRC requirements for protein, vitamins, and minerals (National Research Council, 2007). It can be offered as voluntary consumption when hydrated (with 1 : 1 to 2 : 1 water to WellSolve Well-Gel) or by enteral nasogastric administration (3 : 1 water to WellSolve Well-Gel). Neither voluntary consumption nor enteral administration of the product resulted in significant glucose or insulin responses. When used in the field, 76% of clinicians reported a positive or potentially positive effect on the horse's health status, with the remaining 24% indicating no effect (i.e., there were no negative effects) (Vineyard et al., 2011). This product appears to be safe and provides a higher fiber alternative to human products (Vineyard et al., 2011; Stratton-Phelps, 2004). Critical Care® (Oxbow Animal Health, Murdock, NE, USA) is another high-fiber (21–26% minimum–maximum) feed designed for small herbivores that has been used for horses (Carr & Holcombe, 2009).

Another approach is to use a commercially available pelleted feed that contains a source of fiber, such as "senior feeds" or "complete feeds" that contain added fiber, the latter of which are designed to be fed without hay. These products contain about 14–25% crude fiber and can provide between 2.6 and 3.1 Mcal DE/kg diet (as fed). Therefore, 3.5–4.0 kg of diet would be needed to meet the stall energy requirements of a 450 kg horse. Vegetable oils (¼ to 1½ cup or 75–375 mL per day) can be added to increase the caloric density of the diet (Table 39.1). Vitamin E (100–200 IU per 100 mL of oil) should be added to the ration as an antioxidant if supplemental vegetable oil is provided. When providing supplemental fat to a sick horse (450–500 kg body weight), 75–25 mL/day (¼ to ½ cup) should be given initially and then gradually increased if no adverse response is seen (e.g., diarrhea, steatorrhea, or lipemia). As indicated earlier, fish oil may be a better alternative than vegetable oil to increase the omega-3 intake in the ration (Gultekin et al., 2014). Feeding oil may be contraindicated in horses and ponies with hypertriglyceridemia (triglyceride concentration >300 mg/dL) or hepatic lipidosis.

Variations in the alfalfa/dextrose/casein enteral formulation first described by Naylor (1999) also can be used for assisted enteral feeding (Table 39.2). The recipe designed by Naylor provides about 3 Mcal DE/kg diet and is 33% crude protein and 12% crude fiber. The higher protein content compared with typical equine diets may be beneficial for debilitated and/or hypoproteinemic horses. In healthy horses, the administration of this diet was reported to maintain body weight and serum biochemical parameters within reference limits. However, occasional diarrhea and laminitis were reported complications.

Suggested feeding protocols for a completed pelleted feed with supplemental vegetable oil and for the alfalfa/dextrose/casein formulation are presented in Table 39.1 and Table 39.2, respectively. The rate of diet administration should be gradually increased over a 3–5 day period. A suggested rate of introduction is to administer one-quarter of the final target volume of feed on day 1, half of the total volume on day 2, three-quarters of the total volume on day 3, and the total volume on day 4 or 5.

Alternatively, WellSolve Well-Gel can be offered in increasing amounts. For enteral feeding, it is recommended to offer it in 3 : 1 ratio of water to WellSolve Well-Gel, but a ratio of 4 : 1–6 : 1 may help the flow through the nasogastric tube. Similarly, increasing the volume of water will help prevent dehydration for the horse. On day 1, 0.1% BW (~500 g for a 500 kg horse) could be mixed with (at least) 2 L of water, increasing by about 250 g/day to reach the 0.3% BW recommended to

Table 39.1 Enteral formulation based on a complete pellet ration and recommended feeding schedule for a 500 kg horse[a]. Source: Adapted from Fascetti & Stratton-Phelps, 2003.

Ingredient (complete pelleted)	Day 1 (¼ ration)	Day 2 (½ ration)	Day 3 (¾ ration)	Day 4 (full ration)
Horse feed (g)[b]	885	1770	2650	3530
Vegetable oil (mL)	100	177	265	354
Water (L)	8	16	24	24
Digestible energy (Mcal)	3	6	9	12

a) Energy requirements are at *stall maintenance* for a 500 kg horse (~12 Mcal DE/day). These allowances should be divided and administered as a minimum of four feedings daily.

b) Equine Senior® (Land O'Lakes Purina Feed, St. Louis, MO, USA), 2.6 Mcal DE/kg (as fed).

Table 39.2 Alfalfa/dextrose/casein enteral formulation and recommended feeding schedule for a 500 kg horse[a]. Source: Adapted from Naylor et al., 1984.

	Day						
Parameter	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Electrolyte mixture (g)[b]	230	230	230	230	230	230	230
Water (L)	21	21	21	21	21	21	21
Dextrose (g)	300	400	500	600	800	800	900
Dehydrated cottage cheese or casein (g)	300	450	600	750	900	900	900
Dehydrated alfalfa meal (kg)	2	2	2	2	2	2	2
Digestible energy (Mcal)	7.4	8.4	9.4	10.4	11.8	11.8	2.2

a) These allowances should be divided and administered as three or four feedings daily. Stall maintenance requirements for a 500 kg horse are 12 Mcal DE/day.

b) Composition of electrolyte mixture: sodium chloride (NaCl) 10 g; sodium bicarbonate ($NaHCO_3$) 15 g; potassium chloride (KCl) 75 g; potassium phosphate (dibasic anhydrous, K_2HPO_4) 60 g; calcium chloride ($CaCl_2{\cdot}2H_2O$) 45 g; magnesium oxide (MgO) 25 g.

meet 100% of a horse's protein, mineral, and vitamin requirements. More than 0.3% of BW can be offered if warranted – up to 0.6% of BW (~3 kg for a 500 kg horse). WellSolve Well-Gel provides 2.8 Mcal/kg, and thus provides 8.4 Mcal/day if fed at the 0.6% BW amount. If additional calories are required, vegetable oil can be included at rates similar to those in Table 39.1 (although this is not recommended for hyperlipidemic horses or those with liver failure). Further calories can be provided in the form of dextrose (starting with 300 g/day and increasing up to 900 g/day) or molasses (starting with 100 mL/day and increasing up to 500 mL/day). Dextrose and/or molasses should be minimized or avoided for horses that are insulin resistant.

Clinical signs of intolerance to enteral feeding (see below) will dictate a slower rate of introduction. In hospital settings, the enteral diet should be administered in a minimum of four and preferably six feedings per day with no more than 6–8 L per feeding for a 450–500 kg horse (including the volume of water used to flush the tube), as the size of such horse's stomach is only about 9–12 L (Carr & Holcombe, 2009). This volume should be administered over a 10–15 min period. In field settings, a more practical approach is to administer two treatments per day, although it will not be possible to meet maintenance nutritional requirements with this treatment regimen.

Pelleted feeds should be soaked in warm water to soften before mixing in a blender. If using WellSolve Well-Gel, it does not need to be blended. A fresh batch of diet should be made before each feeding. The tube with the smallest possible internal diameter should be chosen for diet administration. A tube with a ½ inch (12 mm) inner diameter is suitable for most enteral diets that contain fiber. The end of the tube should be open-ended, rather than fenestrated, to prevent the tube from becoming clogged. Fiber-free diets can be administered via a smaller tube (e.g., 18 Fr, 100 inch feeding tube; NG18100, MILA International, Florence, KY, USA). Intermittent nasogastric intubation or placement of an indwelling nasogastric tube can be used to facilitate feeding. In hospitalized horses, feeding tubes can be left in place for up to 7–8 days although some degree of nasopharyngeal irritation and mucoid nasal discharge are to be expected. Softer silicone rubber tubes are less irritating than tubes made of poly(vinyl chloride), do not tend to harden when left in place, and are generally recommended for horses requiring assisted enteral feeding for a number of days (Stratton-Phelps, 2004; Naylor, 1999). Before placement of the tube, the clinician should establish that the diet solution flows adequately through it. It may be necessary to add more water or to mix the feed in a blender a second time. The tube should be positioned in the stomach rather than the distal esophagus to minimize the risk of reflux of feed around the tube. The tube should be secured to the halter; between feedings, application of a muzzle may be necessary to prevent the horse from dislodging the tube. A stomach pump is recommended for infusion of fiber-containing diets. After administration of the diet, the tube should be flushed with approximately 1 L of water followed by a small volume of air to ensure that no feed material remains in the tube. The end of the tube should be capped with a syringe case between feedings. An excellent guide for the placement of an indwelling feeding tube was described by Carr & Holcombe (2009, p. 96).

Valle et al. (2014) developed a feeding plan for nutritional management for horses following colic surgery based on the level of risk associated with the surgery: (1) low, uncomplicated; (2) moderate (colon–cecum enterotomy, small colon anastomosis, no ischemia, and low distension); (3) high (ischemia–anastomosis of

the small intestine, heavy intestinal distension, proximal jejunitis); and (4) very high (ischemia of the large colon–cecum, anastomosis of the large colon). Levels 1 and 2 were fed 12 h after surgery, whereas the feeding plan began after 36 h for level 3 (or 8 h after reflux) and after 24 h for level 4. Feeding included good-quality hay soaked in water, and a pelleted fiber mix that was ground and soaked to make a slurry. The hay-to-pellet ratio varied depending on the risk level, with the low-risk level 1 group having 80 : 20 hay to pellet and the level 4 group being offered 20 : 80 hay to pellet. Few complications were reported (Valle et al., 2014).

Close clinical monitoring, particularly of gastrointestinal function, is imperative for horses receiving assisted enteral feeding. Repeated ultrasonographic examinations can be useful for the evaluation of gastric distension and intestinal motility. The presence of residual gastric fluid should be assessed (i.e., siphoning) before each feeding. Substantial gastric reflux (>1–2 L) is an indication to withhold enteral feeding for at least 1–2 h with re-evaluation prior to recommencement of diet administration (Naylor, 1999). Persistent gastric reflux indicates intolerance to enteral feeding and the need for parenteral feeding. Similarly, signs of colic, ileus, abdominal distension, and/or increased digital pulses suggest intolerance to enteral feeding and are an indication to discontinue therapy or decrease the volume and frequency of feedings. The passage of loose feces is not uncommon in horses receiving assisted enteral feeding and of minimal concern if not accompanied by clinical signs of depression, dehydration, ileus, and/or colic (Naylor, 1999; Rooney, 1988). It is important to measure the total volume of water administered via the nasogastric tube. Daily water requirements (approximately 50 mL/kg/day) can generally be met during assisted enteral feeding if the horse is fed four or five times per day. Frequent measurements of hematocrit and plasma total protein concentration also are useful for monitoring hydration status and the adequacy of water administration. Frequent measurements of serum electrolytes and ionized calcium and magnesium are recommended during assisted enteral feeding. Supplementation with potassium, calcium, and/or magnesium may be necessary. Horses should also be monitored for the development of complications associated with repeated or indwelling nasogastric intubation, including rhinitis, pharyngitis, and esophageal ulceration (Stick et al., 1981). Body weight should also be assessed daily, to monitor energy intake and to make adjustments as needed. It should be noted, however, that hydration status will greatly affect body weight, so a combination of body weight measurement and body condition score (Henneke et al., 1983) assessment is suggested. If adequate nutrition is not being met by enteral feeding, the use of parenteral nutritional support is advised.

Parenteral Nutritional Support

There have been several reports of use of parenteral nutrition in colic patients, with ileus, gastric reflux, and gastrointestinal conditions mandating complete bowel rest (e.g., small intestinal resection, duodenitis–proximal jejunitis) being the most common indications for instigating this form of nutritional therapy (Durham et al., 2003, 2004; Lopes & White, 2002; Holcombe, 2003; Carr & Holcombe, 2009). To date, few studies have evaluated the clinical benefits of parenteral nutrition in colic patients. Durham et al. (2003, 2004) examined the effects of postoperative parenteral nutrition in 15 horses (versus 15 control horses) recovering from resection and anastomosis of strangulated small intestine. They reported no beneficial effect of parenteral nutrition on time to first oral feeding, duration of hospitalization, costs of treatment, or short-term survival (up until 5 months after discharge), although the parenteral nutrition protocol did confer improved nutritional status as reflected by lower serum concentrations of triglycerides and total bilirubin and higher concentrations of glucose. However, the duration and volume of postoperative gastric reflux were longer in the parenteral nutrition group than in the control horses, perhaps due to alterations in gastric and/or small intestinal motility, and there was a nonsignificant trend for catheter-site complications in the parenteral nutrition group. It was concluded that further study of a larger number of horses is required to determine the clinical benefits and possible harmful side effects of parenteral nutrition in horses recovering from small intestinal surgery.

Studies of the effects of parenteral nutrition in perioperative human patients also have yielded equivocal findings. Several studies have demonstrated that perioperative parenteral nutrition is associated with reduced morbidity and mortality in malnourished patients (Evans et al., 2015; Abunnaja et al., 2013; Desky et al., 1987; Silk & Green, 1998). In contrast, peri-operative parenteral nutrition in well-nourished human patients has been associated with increased morbidity, particularly septic complications of the catheter (Farinas-Alvarez et al., 2000; Cohen & Chin, 2013). Nonetheless, as discussed earlier, the current consensus in human clinical nutrition is that parenteral nutrition is an important component of overall case management, particularly in patients with evidence of malnourishment, gut failure, and/or increased nutritional requirements (e.g., pregnancy, lactation, growth). Although further studies are needed to examine the putative benefits of parenteral nutrition in equine colic patients, there is rationale for the use of parenteral nutrition in horses that are prevented from eating for more than 48 h post-colic, particularly those in poor body condition (body condition score <3) or with increased nutritional demands (e.g., pregnant or lactating mares).

As with enteral nutritional support, the goal of parenteral nutrition is to administer calories and amino acids such that the loss of body protein (and lean body mass) is minimized. Therefore, parenteral nutrition formulations will include carbohydrates (dextrose), amino acids, and fats (as long-chain fatty acids), and also minerals and vitamins. Recent work in humans supports the further addition of supplemental glutamine and arginine (Cohen & Chin, 2013; Vermeulen et al., 2007; Wang et al., 2015). Additionally, fish oil lipid emulsions are included in many formulations (Gultekin et al., 2014; Cohen & Chin, 2013). Formulations should not be hyperosmotic, as this is associated with an increased risk of thrombosis (Carr & Holcombe, 2009).

Carbohydrates in the form of a 50% dextrose solution (3.4 kcal/g or 1.7 kcal/mL; osmolarity 2525 mOsm/L) and lipid, as a 10–20% emulsion (20% emulsion: 9 kcal/g or 2 kcal/mL; osmolarity 260 mOsm/L), are the primary sources of energy used in parenteral nutrition solutions, while an amino acid solution (e.g., Travasol 8.5% or 10%; Baxter Health Care, Deerfield, IL, USA) is used to meet protein requirements (e.g., protein synthesis, immune function). Commercial lipid emulsions (e.g., Intralipid 20%; Baxter Health Care) consist of soybean oil, egg yolk phospholipid, and glycerin. These emulsions provide mainly unsaturated fatty acids (linoleic, 44–62%; oleic, 19–30%; linolenic, 4–11%; palmitic, 7–14%). Parenteral nutrition solutions with and without lipid can be used, that is, dextrose–amino acid or dextrose–lipid–amino acid mixtures. The addition of lipids to the parenteral nutrition formula results in a solution with lower osmolarity compared with a dextrose–amino acid mixture of similar caloric density. Hence the lipid-containing solution should be less irritating to peripheral veins. Ideally, 30–40% of the nonprotein calories are derived from lipids, but higher levels may be tolerated (Carr and Holcombe, 2009). Lipid solutions must be included in the formula if the target calorie provision approaches true maintenance (32–33 kcal/kg/day), because this level of calorie delivery from a dextrose–amino acid parenteral nutrition solution often results in marked hyperglycemia and glucosuria. However, when the target daily energy provision is 20–24 kcal/kg/day, dextrose–amino acid mixtures can be used. In human medicine, this approach is referred to as *partial parenteral nutrition* and is often employed in postoperative patients who require only a few days of intravenous nutritional support (Jeejeebhoy, 2001). A similar rate of calorie provision has been applied in recent reports of parenteral nutrition in postoperative colic patients (Durham et al., 2003, 2004). As discussed previously, provision of amino acids (protein) at a rate of 0.6–0.8 g/kg BW/day is one guideline for meeting protein requirements in adult horses, although some authors have recommended 1.0–1.5 g/kg/day, and provision of amino acids at 0.6–2.0 g/kg/day has been used in sick horses without apparent complications. Again, supplementation with glutamine and/or arginine may be advised. Fat-soluble vitamins may be solubilized to make them water soluble and added, depending on the anticipated reserved stores of these vitamins within the body and the amount provided (if any) via the digestive tract. Although the microbes within the horse's intestine generally produce sufficient amounts of B vitamins, the microbial population post-surgery may be compromised and B vitamin status affected. Vitamin C is not required by mature horses, but its antioxidative function may be beneficial during convalescence. Vitamin B complex and vitamin C solutions should be protected from light sources.

A suggested parenteral nutrition formula (Table 39.3) comprises 1 L of 50% dextrose (0.5 g/mL dextrose × 3.4 kcal/g × 1000 mL = 1700 kcal), 1 L of a 10% amino acid solution (0.1 g/mL of amino acids × 4 kcal/g × 1000 mL = 400 kcal), and 500 mL of 20% lipid emulsion (0.2 g/mL lipid × 9 kcal/g × 500 mL = 900 kcal). These components are diluted with 4 L of isotonic fluid, yielding a final volume of 6.5 L and a caloric density of approximately 0.45 kcal/mL. A multivitamin supplement (American Pharmaceutical Partners, Los Angeles, CA, USA) may be added to this mixture. This solution can be prepared up to 24 h in advance of administration, with storage at 4 °C until use. Administration of parenteral nutrition solutions should be through a dedicated intravenous catheter, preferably one inserted into a large vein such as the jugular to minimize the risk of complications associated with the infusion of hyperosmotic solutions. Alternatively, a double-lumen catheter can be used, allowing the parenteral nutrition solution to be given through one port and medications and other fluids through the other port. To minimize the risk of thrombophlebitis, nonthrombogenic catheters such as those made from polyurethane are recommended. Meticulous attention to sterile technique is needed during catheter placement to minimize further the risk of thrombophlebitis and other septic complications. The fluid lines used for delivery of the parenteral nutrition solution should be changed every 24 h. An infusion pump is required to ensure accurate delivery of the parenteral nutrition solution.

Table 39.3 provides a recommended rate of parenteral feeding for a 450 kg horse. The initial rate of parenteral nutrition solution administration should be approximately 35% of target calorie provision, increasing to 60–65% after 12 h and 100% (23 kcal/kg/day) at 24 h, provided that there are no complications such as the development of marked hyperglycemia, glucosuria, or hyperlipemia. Hyperglycemia and hyperlipemia were the most common complications of postoperative parenteral nutrition in horses following intestinal surgery. In one report, hyperglycemia was observed in 52 of 79 (66%)

Table 39.3 Parenteral nutrition formula and recommended administration rate for a 500 kg horse[a]. Source: Adapted from Holcombe, 2003.

Formula	First 12 h	Second 12 h	Day 2 on
Dextrose 50% (mL)	1000	1000	1000
Lipid 20% (mL)	500	500	500
Amino acids 10% (mL)	1000	1000	1000
Isotonic fluids (mL)	4000	4000	4000
Total volume (mL)	6500	6500	6500
kcal/bag	3000	3000	3000
kcal/h	210	333	480
Rate (mL/h)	470	740	1070
Bags required	0.90 per 12 h	1.4 per 12 h	4.0 per 24 h
kcal/day	–	–	~12,000

a) For parenteral nutrition, daily energy needs are estimated at 22–23 kcal/kg/day (~11.0–11.5 Mcal/day for a 500 kg horse).

horses receiving parenteral nutrition (Lopes & White, 2002), perhaps due to insulin resistance, an excessive rate of administration, or both. Hyperglycemia is also associated with a poor prognosis for survival (Hassel et al., 2009). Urine and blood glucose concentrations should be measured every 4–8 h in horses receiving parenteral nutrition, and the rate of dextrose administration should be decreased if glucose concentrations exceed the renal threshold (approximately 180 mg/dL or 10 mmol/L). A constant-rate insulin infusion (e.g., regular insulin at a starting dose of 0.05–0.1 IU/kg/h) can be instituted if the reduction in dextrose administration rate fails to correct the hyperglycemia. Blood glucose concentrations should be closely monitored, using on-site blood gas analyzers rather than hand-held monitors that may be less accurate. In humans, a goal of ~145 mg/dL (~8 mM) is currently recommended, and has been shown to decrease the incidence of complications (Mesotten & Van den Berghe, 2012). In horses, this goal value may be lower, as each 10 mg/dL increase in glucose above 100 mg/dL resulted in a 1.15 × odds ratio of failure to survive to discharge (Hassel et al., 2009). Adjustments in insulin dose may be required to achieve glycemic control. As mentioned, tight regulation of glucose concentrations has been associated with improved outcome in critically ill human patients. Serum blood urea nitrogen (BUN), triglycerides, and electrolytes should be monitored at least daily. Hypokalemia, hypocalcemia, and hypomagnesemia have been reported in horses receiving parenteral nutrition, and it may be necessary to supplement these nutrients if parenteral feeding is used for more than 48–72 h. Finally, body weight should be recorded daily or every second day; maintenance of body weight will provide the best guide to the effectiveness of nutritional support, again accounting for changes due to hydration status.

Transition to Voluntary Feeding

As appetite returns (or when voluntary oral feeding is no longer contraindicated), small amounts of palatable feed (e.g., fresh grass) should be offered. The WellSolve Well-Gel product may also be fed directly (versus via nasogastric tube) as a slurry, with a water-to-product ratio of 1 : 1 to 2 : 1 to bridge the gap of voluntary feeding by offering a concentrated nutrition source, and decreasing the dependency of parenteral or enteral nutrition. If these feedings are tolerated, the level of tube or parenteral feeding can be gradually reduced as the provision of feed for voluntary consumption is increased. Nutritional support can be withdrawn when voluntary feed intake provides at least 75% of stall maintenance calorie and protein requirements. Recommendations for the resumption of oral intake in horses with small or large intestinal problems are discussed in the next section.

Feeding Management of Specific Gastrointestinal Conditions

Small Intestinal Disorders

Disorders of intestinal motility are of primary concern following small intestinal surgery, particularly in horses requiring resection and anastomosis of the small intestine. Complications include peritonitis, impaction or leakage at the site of enterotomy or anastomosis, and adhesion formation (MacDonald et al., 1989). There has been little study of the impact of postoperative nutrition on these complications, or of the effects of nutritional therapy on short- and long-term survival rates. There have been anecdotal reports that early application of enteral or parenteral nutritional support is associated with decreased incidence and/or severity of postoperative ileus, but there are no data from controlled studies. However, as discussed previously, parenteral nutrition may be beneficial for the nutritional management of horses following small intestinal surgery, particularly for the first 24–72 h when there is rationale for restriction of enteral feeding to minimize the risk of incisional leakage and dehiscence. Parenteral nutritional support is also advocated for horses with duodenitis–proximal jejunitis because of the protracted nature of the ileus and gastric reflux in these cases. A concern with the feeding of high-bulk feeds, such as long-stem hay, in the early postoperative period is distension at the site of enterotomy and/or anastomosis. In horses with sutured esophageal wounds, a traditional hay–grain diet can result in the development

of fatal complications, presumably because this high-bulk diet promotes distension at the incision site, increasing the probability of wound dehiscence (Stick et al., 1983). On the other hand, horses with esophageal injuries that are sutured closed can make a full recovery if fed a soft diet (e.g., slurry made from pelleted feeds) for 8–10 weeks following the injury (Stick et al., 1983). These findings may be applicable to the nutritional management of horses following small intestinal surgery. Specifically, if cost is not prohibitive, it is recommended to administer parenteral nutrition for 24–48 h after surgery with a subsequent gradual introduction to enteral feeding and concomitant reduction in the level of parenteral feeding. If parenteral nutrition is not feasible, feed should be withheld for 24–36 h. In all cases, enteral feeding should not be started until gastrointestinal function is adequate, as indicated by the presence of borborygmi and the absence of gastric reflux. Initially, small amounts of water should be offered (e.g., 1 L every hour over a 5–6 h period) as a test of intestinal function. If no gastric reflux develops, intake of solid feed can be started. A soft, low-bulk ration is recommended initially. Fresh grass (hand grazing) and mashes or slurries made from alfalfa pellets or pelleted complete feeds are also suitable feedstuffs following small intestinal surgery. Molasses may be added to the mash or slurry to enhance the palatability of the ration. Small meals (0.5–0.75 kg) should be fed every 3–4 h, to avoid excessive distention. In uncomplicated cases of resection and anastomosis, there should be a gradual introduction to long-stem hay following initial feeding of soft diet feeding.

Long-term Dietary Modification

Resection of greater than 50% of the small intestine requires long-term modification of diet. Ponies fed a complete pelleted feed were able to maintain body condition following resection of less than 50% of the small intestine (Tate et al., 1983). However, ponies fed the same diet after removal of more than 60% of the small intestine developed diarrhea and substantial weight loss, likely due to significant malabsorption. Clinical experience has also indicated difficulty in maintaining body condition of horses following resection of 50% or more of the small intestine. A diet based on alfalfa has been recommended (e.g., chopped alfalfa, alfalfa pellets, high-quality hay). Beet pulp shreds and stabilized rice bran (a source of digestible fat) also are suitable feedstuffs, and vegetable oil (e.g., 100–500 mL/day divided bid or tid) can be gradually introduced to increase the energy density of the ration. If the ileum has been resected, the ability of the horse to absorb lipids and fat-soluble vitamins may be limited. Therefore, when providing vegetable oil, the feces should be monitored closely for steatorrhea. Fat-soluble vitamins may be administered by monthly injections. Supplementation of calcium, magnesium, and zinc may be warranted.

Large Intestinal Disorders

Diarrhea is a complication of all types of colic surgery, but the risk appears to be highest in horses undergoing celiotomy for large intestinal disorders (Cohen & Honnas, 1996). In one study, the risk for the development of diarrhea after surgery was two-fold higher in horses with large intestinal disorders than in horses with other lesions (Cohen & Honnas, 1996). There was a further increase in risk in horses that had an enterotomy. Conversely, horses fed grass hay were half as likely to develop severe diarrhea as horses not fed grass hay. Horses should be fed small amounts of grass or soft grass hay at frequent intervals (every 2–3 h) as early as 12 h post-surgery, provided that there is no evidence of gastric reflux or poor intestinal motility. First-cut hay is preferred because of the higher dry matter digestibility compared with more mature forages. No grain or concentrate should be introduced until 10–14 days post-surgery. However, the feeding of a low-bulk pelleted feed such as Equine Senior or WellSolve Well-Gel may be beneficial during this period.

Horses with impaction of the large colon should be fed soon after resolution of the impaction. Fresh grass, alfalfa pellets, chopped alfalfa hay, and other sources of highly digestible fiber are preferred. It has been suggested that pelleted feeds may allow for increased rates of passage owing to the smaller particle size compared with long-stem roughage (Naylor, 1999). Careful dietary management of horses recovering from cecal impaction is required. Affected horses are prone to reimpaction after resumption of feed intake, perhaps reflecting a persistent decrease in cecal motility associated with marked distension of the cecum. Low-bulk pelleted feeds rather than long-stem hay are recommended during the first 10–14 days after cecal impaction. Careful clinical monitoring (e.g., repeat ultrasonographic examinations and palpations per rectum) is paramount during the first 48–72 h when the risk of reimpaction is highest. Thorough oral examination should be undertaken to establish whether inadequate mastication of the feed is an underlying cause of the impaction.

Long-term Dietary Modification

Longer term dietary modification is required for horses with extensive resection of the large colon, but not when the cecum alone is removed. Bertone and colleagues demonstrated that gastrointestinal passage time and fiber, protein, and phosphorus digestion are decreased after resection of more than 90% of the large colon (Bertone, 1989; Bertone et al., 1989a, 1989b). In one clinical report, chronic diarrhea, weight loss, and hypophosphatemia were complications of extensive large colon resection (Arighi et al., 1987). With appropriate dietary

management, however, these horses can maintain adequate body condition. In the early postoperative period, horses that have undergone extensive resection should be fed small amounts of a low-bulk feed such as alfalfa pellets or a pelleted commercial feed (e.g., Equine Senior). Subsequently, legume forage should be the predominant component of the ration. Following experimental colon resection, a ration of alfalfa hay or an alfalfa–timothy hay mix provided better results than straight grass hay, perhaps owing to higher digestibility and protein content of the alfalfa-based rations. Hypophosphatemia was reported in half of a group of ponies that had undergone large colon resection and all had lower phosphate concentrations than control ponies (Ducharme et al., 1987). Supplemental phosphorus can be provided in supplement form or by feeding 0.5 kg wheat or stabilized rice bran daily. If additional calories are required for weight maintenance, a "fat and fiber" concentrate rather than grain or sweet feed is recommended.

Conclusion

Nutrition plays an extensive role in equine health and disease. Excellent feeding management can reduce the risk of colic development, while the provision of adequate nutrition to the horse during convalescence from a colic episode is also vital to the horse's prognosis. Further research is warranted to refine nutrient requirements and feeding recommendations for horses recovering from colic surgery.

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Part X

Anesthesia for Abdominal Surgery

40

Anesthesia for Horses with Colic

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Surveys of mortality in horses anesthetized for surgery for colic consistently identify an increased mortality compared with healthy horses undergoing elective surgery. Although improvements in patient monitoring and anesthetic protocols have contributed to better outcomes over the last several decades, strict attention to individual patient requirements is essential to maintaining this increased level of success. Most deaths associated with emergency abdominal surgery reported in recent surveys are due to cardiac arrests occurring in the first 30 min of anesthesia or to fractures or dislocations in the immediate recovery period (Dugdale & Taylor, 2016). The objectives of this chapter are to emphasize that:

- preanesthetic evaluation (including appropriate patient preparation) is a key step toward optimum anesthesia;
- being prepared for emergency surgery, which includes equipment, checklists, plans, and assigned duties, increases efficiency;
- knowledge of the pharmacology and interaction of anesthetic agents allows appropriate choice of a protocol for the individual patient;
- intensive monitoring and availability of monitoring equipment are the key to minimizing physiologic abnormalities;
- experience in anesthetizing horses is important for early recognition of complications, but attention to checklists helps both inexperienced and experienced anesthetists;
- anesthetic management in recovery must counter adverse effects of equine anatomy, physiology, and behavior to achieve a satisfactory outcome.

Preanesthetic Assessment

An efficient and thorough preanesthetic evaluation can have a major positive influence on the course of anesthesia. The aims of preanesthetic evaluation are to assess the horse's status regarding (1) preoperative abnormalities of fluid and electrolytes that should be treated before anesthesia, (2) administration of treatments to ensure adequate cardiovascular function after induction of anesthesia, (3) the optimal reduction in dose rates of anesthetic agents, and (4) treatment strategies for possible complications. Evaluation of the animal's mental state may be used to avoid behavior that may result in situations dangerous to horse and handler. The anesthetist must review the history and consider details when determining how to manage the anesthetic period. Important factors include the horse's usual work or job and extent of animal–human interaction, reproductive status, duration of colic, and recent drug administration. The physical examination provides relevant details such as breed (some breeds respond differently to a drug; some breeds are excitable or dominant whereas others are less concerned and more relaxed), age (senior animals may require a lower dosage of drugs and be more susceptible to onset of hypotension), sex (pregnancy introduces several problems; stallions may be temperamentally unpredictable), weight (hypoventilation will be greater in heavy horses), current behavior [central nervous system (CNS) depression and hyperexcitability will have opposite influences on drug dose rates], evidence of self-trauma (indication of pain and individual response to pain), and the degree of abdominal distention (excessive abdominal distention impairs ventilation and decreases cardiac output). Consideration of these factors may dictate an adjustment in the usual method of induction of anesthesia.

The current status of the cardiovascular system should be evaluated by observation of mucous membrane color and capillary refill time (CRT), palpation of pulse strength and rhythm, noninvasive measurement of blood pressure, and auscultation of cardiac sounds for dysrhythmias. Laboratory test results provide further insight into the progression of the horse's disease. Preanesthetic

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treatment is advisable for some abnormalities, such as increased packed cell volume (PCV), hypocalcemia, and metabolic acidosis. Suspicion of a specific surgical lesion may further guide the choice of anesthetic management. For example, mortality rate is higher in horses with strangulating intestinal lesions or ischemic bowel (Pascoe et al., 1983; Driscoll et al., 2008; De Bont et al., 2013; Suthers et al., 2013).

Possible complications associated with anesthesia of pregnant mares are related to the impact of the gravid uterus on adequacy of ventilation and possible aortocaval compression resulting in hypotension during dorsal recumbency. A reduction in cardiovascular function due to the stress of anesthesia and surgery may result in fetal mortality. A retrospective study identified the foaling rate after colic surgery to be lower than after surgery for noncolic-related conditions (Drumm et al., 2012). Furthermore, a live foal is more likely to be born to mares aged ≤15 years and at ≥40 days of gestation, and when the duration of anesthesia is <3 h (Proudman et al., 2002; Chenier & Whitehead, 2009).

A high PCV before anesthesia has been associated with decreased survival (Pascoe et al., 1983; McCarthy & Hutchins, 1988; Trim et al., 1989; Proudman et al., 2006; Ludders et al., 2009; Archer et al., 2011; Suthers et al., 2013). Indicators of hypovolemia observed before anesthesia include clinical signs of dehydration, weak peripheral pulses and prolonged CRT, low blood pressure [systolic arterial pressure (SAP) <100 mmHg or mean arterial pressure (MAP) <80 mmHg], and values of PCV, total protein concentration, creatinine, and anion gap that exceed normal values. Since hypotension is likely to develop in a hypovolemic horse after induction of anesthesia, restoration of blood volume with an intravenous (IV) infusion of balanced electrolyte solution, such as acetated or lactated Ringer's solution at 20 mL/kg, is advisable before induction of anesthesia in horses with evidence of hypovolemia. Hypertonic 7.5% saline solution, 2–4 mL/kg administered IV over 10–20 min, can be used to expand blood volume rapidly and promote improved hemodynamic function for about 1.5 h (Dyson & Pascoe, 1990; Schmall et al., 1990). Hypertonic saline should be followed by administration of balanced electrolyte solution to avoid tissue dehydration.

Hypocalcemia and hypomagnesemia are present in a high proportion of horses with colic and in healthy animals with experimentally induced endotoxemia (Carlstedt et al., 2000; Garcia-Lopez et al., 2001; Delesalle et al., 2005; Toribo et al., 2005). In horses with colic, the serum calcium and magnesium concentrations were not predictive of survival or length of hospital stay (Garcia-Lopez et al., 2001). Because hypocalcemia can contribute to hypotension during anesthesia, administration of 23% calcium gluconate, 0.5 mL/kg IV, over 20 min before induction of anesthesia appears to provide a temporary increase in serum calcium concentration. Anesthesia with isoflurane, sevoflurane, or halothane decreases serum calcium concentrations significantly, ionized Ca^{2+} more than total Ca^{2+}, in healthy horses (Grubb et al., 1999; Driessen et al., 2002). This effect should be taken into consideration when evaluating measurements of calcium concentration intraoperatively. Finally, moderate to severe metabolic acidosis (base excess > –8.0 mEq/L) should be at least partially corrected by administration of sodium bicarbonate solution, 1.5 mEq/kg, given IV over 30 min.

Auscultation of the heart should be done routinely as part of the preanesthetic evaluation. Identification of atrial fibrillation or a mitral murmur will forewarn of the probability that during anesthesia blood pressure will be low and difficult to treat effectively. Premature ventricular depolarizations are occasionally present in endotoxemic horses and may or may not require specific treatment. Electrolyte abnormalities such as hypokalemia, hypocalcemia, and hypomagnesemia occurring in critically ill patients may contribute to the arrhythmias and also the direct effect of endotoxin on the myocardium (Marr, 2004).

Increased intra-abdominal pressure not only impairs lung excursion, but also decreases cardiac output. In an extreme case of excessive abdominal distention, where the horse is cyanotic and death is imminent, the dose rates of anesthetic agents for induction of anesthesia may be reduced by 50% or more. Additionally, oxygen should be insufflated during induction, and endotracheal intubation and controlled ventilation with oxygen must be started immediately the horse loses consciousness. These efforts may keep the horse alive until the surgeon can explore the abdomen.

Intravenous administration of antibiotics, particularly penicillin and occasionally gentamicin and ceftiofur, may decrease cardiac output and cause hypotension, which will further reduce cardiovascular stability during anesthesia (Hubbell et al., 1987). These drugs should be administered at least 30 min before induction of anesthesia, whenever possible and, if administration has to occur during anesthesia, the drugs should be given in small increments and administration stopped if arterial pressure decreases.

One classification of health status (American Society of Anesthesiologists) assigned before anesthesia is based on a scale consisting of five classes. Healthy horses comprise class 1, and horses with colic are included in classes 3, 4, and 5 as follows: class 3, horses with a disease that is not immediately life threatening; class 4, horses with severe diseases that require life-saving surgery; class 5, horses that are severely ill and cardiovascular collapse is present or imminent. This preanesthetic health status is a composite single value that correlates with the prevalence of anesthetic complications and mortality, such

that prevalence of complications increases from being the lowest for horses in class 1 to the highest for horses in class 5. It is important to note that this may not provide an accurate prediction of risk. Risk assessment tools are advocated for preanesthetic evaluation of human patients undergoing emergency laparotomy and several models of varying discrimination are in use (Oliver et al., 2015). Surveys have identified horses to be at a greater risk for death than anesthetized human patients, cats, and dogs. The risk factors associated with anesthesia and surgery in a survey of 35,978 horses without colic included horses older than 14 years of age, horses that were anesthetized outside regular daily working hours, and horses with a long duration of anesthesia (Johnston et al., 2002). The mortality rate during anesthesia and for the first 7 days after anesthesia for these horses was 2.4%. Of the horses that died or were euthanized because of perioperative complications, more than one-third had cardiac arrest or cardiovascular collapse, or were found dead, and one-third suffered a fracture or myopathy after anesthesia. In contrast, the overall mortality rate of 5330 horses with colic in this survey was 34.6%; 23% had an operable lesion but died or were euthanized because of a problem occurring during anesthesia or postoperatively. Clearly, colic surgery carries a substantial increase in risk for horses and supportive treatment before and during anesthesia is critical for reducing mortality.

Anesthetic Agents

An anesthetic protocol that best serves the patient is one that combines several agents to produce unconsciousness, analgesia, and muscle relaxation. Preanesthetic medication (premedication) often includes xylazine, detomidine, or romifidine, because these agents produce mild to good sedation and some analgesia; some anesthetists prefer to use medetomidine or dexmedetomidine (Table 40.1). Low dosages of these drugs are recommended as they significantly decrease cardiac output and gastrointestinal motility in a dose-dependent manner (Merritt et al., 1998; Wagner et al., 1991; Doherty et al., 1999). The results of recent studies indicate that inclusion of a peripheral α_2-receptor antagonist (MK-467) decreases the adverse cardiovascular effects of detomidine. This finding suggests that future use of α_2-agonists in combination with MK-467 may produce fewer peripheral effects (Pakkanen et al., 2015). Although the addition of butorphanol contributes to sedation and analgesia, this approach will exacerbate the impairment of gastrointestinal function caused by other agents, most notably detomidine (Sutton et al., 2002). Acepromazine may be omitted from the anesthetic protocol for ill horses as the vasodilation induced by this drug may interfere with treatment of low blood pressure during anesthesia.

Induction of anesthesia after premedication is most commonly accomplished by IV injection of ketamine (1.7–2.2 mg/kg), with the addition of either diazepam or midazolam (0.05 mg/kg), propofol (0.4 mg/kg), or guaifenesin (20–50 mg/kg) to improve muscle relaxation (Table 40.1). Thiopental (2.2–4.4 mg/kg) with guaifenesin (50–110 mg/kg), or tiletamine–zolazepam (1.1 mg/kg) are alternative drugs that can be used for induction. Currently, investigators are assessing the effects of a combination of alfaxalone with guaifenesin and ketamine for induction of anesthesia in horses.

An opioid is frequently included in the anesthetic protocol to provide analgesia, increase the intensity of sedation, and decrease the dose rate of the inhalation agent. Although these beneficial effects of opioids have been documented in anesthetized dogs, there is little published evidence that the same benefits occur in horses (Bennett & Steffey, 2002). The present author's clinical experience is that butorphanol contributes to an efficient induction of anesthesia in horses and that it can lessen the tachycardia and high blood pressure during

Table 40.1 Commonly used anesthetic agents for induction of anesthesia.

Stage of anesthesia	Anesthetic agent	Dose rate (mg/kg IV)	Dose for 450 kg (1000 lb)	Comments
Premedication	Xylazine *or* Romifidine ± Butorphanol	0.4–1.1 0.04–0.1 0.02	1.8–5.0 mL (100 mg/mL) 1.8–4.5 mL (10 mg/mL) 0.9 mg (10 mg/mL)	Dose reduced according to drugs (e.g., detomidine) administered in the hour prior to anesthesia
Induction of anesthesia	Ketamine	1.7–2.2	10 mL (100 mg/mL)	Dose of ketamine can be decreased by 20–50% in sick horses
	Diazepam or midazolam *or* propofol *and/or* guaifenesin	0.05 0.04 20–50	5 mL (5 mg/mL) 18 mL (10 mg/mL) 180–450 mL (5%, 50 mg/mL)	In addition to ketamine, diazepam/midazolam or propofol with or without guaifenesin to increase relaxation during induction

anesthesia presumed to be due to an inadequate anesthetic plane. Some evidence of analgesia and decreased stress response was observed in horses that had had surgery for colic and were given butorphanol (0.013 mg/kg/h) as an IV infusion postoperatively (Sellon et al., 2004). Improved behavior scores and lower plasma cortisol concentrations were documented in the horses that were administered butorphanol. Opioids decrease intestinal motility to varying extents depending on the drug and dose rate administered, and synergistically prolong the duration of decreased intestinal motility induced by xylazine or detomidine. Healthy horses that received a continuous IV infusion of butorphanol (0.024 mg/kg/h) for 24 h (Sellon et al., 2001) and horses with colic given butorphanol (0.013 mg/kg/h) (Sellon et al., 2004) had a decrease in fecal output. The decrease in intestinal motility was not considered to have a significant clinical impact other than introducing the need to include the influence of butorphanol during assessment of the patient's postoperative clinical progress.

Administration of morphine sulfate, 0.05 and 0.1 mg/kg IM or IV, to awake healthy horses resulted in no behavior change and no evidence of colic, but neither was there evidence of analgesia during experimental thermal or electrical threshold testing (Figueiredo et al., 2012). Gastrointestinal motility assessed by auscultation was decreased for 60 or 120 min by the two dose rates, respectively, but the fecal output was unchanged. Morphine (0.1–0.17 mg/kg) administered IV after induction of anesthesia has also been used as an adjunct to anesthesia in horses without observable adverse effects during recovery from anesthesia in one study (Mircica et al., 2003). However, in a retrospective study of risk factors for colic in horses after orthopedic surgery, intraoperative systemic use of morphine, median dose 0.1 mg/kg, was associated with a four-fold increase in risk of colic compared with either butorphanol or no opioid (Senior et al., 2004). It is important to recognize that many factors may affect intestinal motility in horses that are anesthetized for surgery. Although opioids, including butorphanol, morphine, meperidine, methadone, and fentanyl, have been incorporated into anesthetic protocols for horses, there is a need for more controlled studies evaluating their use and adverse effects.

Preparation for Anesthesia

The time from the decision for surgery to induction of anesthesia for many patients must be as short as possible. This can only be accomplished when all team members perform their assigned duties efficiently. Rapid preparation is implemented when the anesthesia machine, monitoring equipment, endotracheal tubes (with cuffs already checked for leaks), and mouth speculum are ready for use at all times. The only steps remaining are to connect the oxygen supply and hang IV fluids on a stand. After completion of the preanesthetic evaluation, the anesthetist must prepare drugs for the anesthetic protocol and assemble any drugs needed to treat potential complications. A checklist for preanesthetic preparation can be useful to facilitate this process and avoid forgetting items, particularly after normal working hours.

A person other than the anesthetist should prepare the horse for anesthesia. By the time the decision to proceed with surgery has been made, the horse should have a large indwelling catheter present in a jugular vein and appropriate crystalloid or colloid fluid administered to restore blood volume and treat electrolyte imbalances. If not done already, a second 14-gauge catheter should be inserted into the opposite jugular vein. The second catheter is necessary during anesthesia because the pressure exerted by infusion of crystalloid fluid will interfere with accurate delivery of adjunct drugs if all are delivered through a single catheter. Hair should be clipped over a facial or transverse facial artery to save time between induction of anesthesia and initiation of invasive arterial pressure monitoring. Preferably, the abdomen should also be clipped to minimize the time between induction and surgical incision. An attempt should be made shortly before induction of anesthesia to remove gastric fluid through the nasogastric tube to minimize the risk of gastric fluid refluxing into the pharynx before endotracheal intubation. The mouth should be flushed with water and the feet cleaned. Leg wraps should be applied, if that is normal hospital procedure.

Induction of Anesthesia

The condition of horses with colic requiring anesthesia varies from relatively healthy to moribund. Consequently, anesthetic administration must be adjusted to accommodate the status of the individual patient.

Many horses with colic will have a decreased requirement for anesthetic drugs owing to CNS depression from exhaustion and multiple administrations of sedatives, electrolyte imbalances, or azotemia. Further, the ability of the horse's cardiovascular system to adjust to the effects of anesthetic agents may be decreased as a result of hypovolemia and endotoxemia. Ventilation, cardiac output, and arterial pressure decrease after induction of anesthesia, recumbency, and change in body position. Consequently, the dose rates of drugs used for sedation and induction will depend on which and how many drugs have recently been administered, and the horse's clinical status. Dose rates of the drugs having the most depressant effects on cardiovascular function (i.e., the α_2-agonist sedatives, ketamine, and

thiopental) can be decreased by 20–50% in some horses. Drugs having less profound effects on the cardiovascular system (i.e., opioids and benzodiazepines) are used at the dose rates used in healthy animals.

Horses at risk for cardiovascular collapse at the onset of anesthesia will benefit from infusion of dobutamine initiated before induction and continued through the induction period and body position change to dorsal recumbency. Horses with considerable abdominal distention can be given oxygen by nasal insufflation during induction of anesthesia until the trachea can be intubated and oxygen is administered using a demand valve. This is a precaution in a horse with cyanosis or labored breathing, as apnea induced in horses that are already hypoxemic may rapidly progress to cardiovascular collapse (Guedes et al., 2016).

Methods used to ease a standing horse to a recumbent position during induction of anesthesia vary among hospitals. Options are to allow a horse to free-fall with or without a parallel restraining wall (swing-door) or to use a hydraulic table induction. Transportation from the induction stall to the operating room may involve manual positioning on a moveable table or cart. Many hospitals use a hoist attached to hobbles around all four pasterns so that the horse can be elevated into dorsal recumbency and transferred to the next room on a ceiling track. Regurgitation and pulmonary aspiration of gastric fluid during induction are a concern. Regurgitation may occur despite the presence of a nasogastric tube and this risk can potentially be decreased by (1) removing gastric fluid shortly before induction of anesthesia and (2) maintaining the horse in a sternal position after induction of anesthesia while performing endotracheal intubation followed by inflation of the cuff before moving the horse into lateral recumbency.

An endotracheal tube is inserted for delivery of oxygen and the inhalation agent. The cuff is inflated to produce an airtight seal to prevent leakage of anesthetic gases into the room and entry of any refluxed gastric fluid into the lungs. A thin film of K-Y lubricant gel on the cuff is recommended as an aid to preventing leakage of fluid past the cuff. Because pharyngeal, laryngeal, and tracheal damage after endotracheal intubation in horses has been reported (Trim, 2015), insertion of the endotracheal tube must be performed gently, without force. Furthermore, the endotracheal tube should be disconnected from the anesthesia delivery system, with few exceptions, whenever the horse is moved or the body position is substantially changed. Since overinflation of the endotracheal tube cuff to 100 mmHg causes tracheal epithelial damage (Touzot-Jourde et al., 2005), the cuff pressure should be limited to <80 mmHg as measured with an aneroid manometer (e.g., Posey cufflator). Although this procedure does not guarantee absence of tracheal mucosal injury, the cuff is commonly overinflated when other estimates of cuff inflation, such as palpation of the pilot balloon or listening/feeling for air escaping around the tube during positive pressure inflation of the lungs, are used.

The horse's head must be supported at a higher level than the heart to minimize congestion of nasal mucosa that will contribute to airway obstruction in recovery (Figure 40.1). The horse must lie on sufficient padding to allow muscle perfusion and the legs should be supported to avoid complete flexion (i.e., frog-legging) that may lead to myopathy or neuropathy. Use of foam pads for support

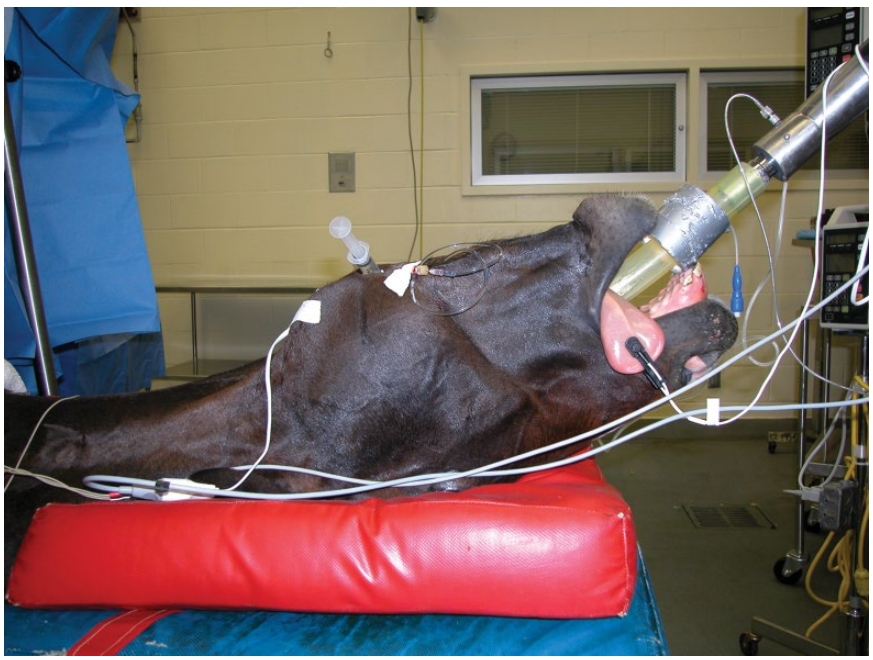

Figure 40.1 The horse's head should be elevated above the level of the heart to decrease the risk for nasal mucosa swelling and airway obstruction in recovery.

must be thoughtful because forcing a pad between the horse's shoulder or hindquarter and the table can result in myopathy, rather than the intended protective effect. The eyes should be lubricated with ophthalmic ointment, and a urinary catheter commonly is inserted in male horses to divert urine away from the operative site.

During the transition from injectable anesthetics used for premedication and induction of anesthesia to inhalation anesthesia, the depth of anesthesia may lighten to the point where the horse may move. When anesthesia has been induced with a xylazine– or romifidine–ketamine combination, appropriate supplementation within the first 15 min after induction is bolus doses of the sedative and ketamine at one-third of the initial doses. As the duration of anesthesia increases toward 30 min or more, appropriate supplemental doses are one-tenth to one-fifth of the initial doses. This approach also is applicable when thiopental has been used for induction of anesthesia.

Administration of >90% inspired oxygen has been associated with absorption atelectasis as the depletion of oxygen in the alveolae results in collapse (Hedenstierna & Edmark, 2010). This has led some anesthetists to decrease the inspired oxygen concentrations to 40–60% during anesthesia in healthy horses with the aim that the degree of lung collapse at the end of anesthesia will be less than that occurring after administration of >90% oxygen throughout anesthesia. Horses with abdominal distention will develop considerable lung collapse as they lose consciousness and probably will require >90% inspired oxygen to avoid or treat hypoxemia.

Maintenance of Anesthesia

Anesthesia is most commonly maintained with a volatile anesthetic agent with or without administration of boluses or a continuous infusion of one or more adjunct agents. The technique of combining constant-rate infusions (CRIs) with a low concentration of inhalation agent may be called partial intravenous anesthesia (PIVA).

Isoflurane and sevoflurane are the most commonly used agents, as halothane is no longer available in all countries. Moreover, isoflurane and sevoflurane have been documented to cause less depression of cardiac function, less reduction in intestinal and renal blood flows, and better muscle blood flow than halothane (Steffey & Howland, 1980; Manohar et al., 1987; Sertyn et al., 1987; Grosenbaugh & Muir, 1998; Raisis et al., 2000). Isoflurane and sevoflurane result in similar decreases in cardiac output with increasing depth of anesthesia. However, Driessen et al. (2006) confirmed that less dobutamine (dose and duration of infusion) was needed to maintain MAP >70 mmHg in racehorses anesthetized with sevoflurane compared with isoflurane at approximately equipotent doses. The mechanism suggested for this difference was that sevoflurane causes less peripheral vasodilation than isoflurane. Deep anesthesia in healthy horses decreases renal and intestinal blood flows to less than 50% of the awake value, and serum creatinine kinase and aspartate transaminase enzymes are significantly increased the day after anesthesia (Manohar et al., 1987; Steffey et al., 2005).

A more recent investigation in healthy research horses documented a significant correlation between the depth of isoflurane anesthesia and decreases in cardiac output and MAP (Hopster et al., 2015). Measurements of perfusion and oxygenation of the jejunum and colon showed rapid deterioration at a cardiac output of <50 mL/kg/min and MAP 60 mmHg, corresponding to an end-tidal isoflurane concentration of 2%. Values improved when the depth of anesthesia was lightened.

Desflurane is another inhalation agent that is used for anesthesia in horses and it has properties that facilitate rapid changes in the depth of anesthesia and rapid recovery. Unfortunately, desflurane is expensive and requires a costly specialized vaporizer, which limit its use in the general population of horses.

In a prospective observational study of human patients undergoing general anesthesia and major surgery, independent predictors of mortality in the year after surgery were the patient's disease, the duration of anesthesia (cumulative deep hypnotic time), and intraoperative hypotension (Monk et al., 2005). This information adds incentive to the need to avoid deep anesthesia, to treat hypotension, and to complete the surgical procedure as rapidly as feasible.

Adjunct Agents

Continuous IV infusion or intermittent bolus administrations of injectable agents during anesthesia can be used to provide analgesia or sedation and to decrease the concentration of inhalation agent delivered. Depending on which adjunct agents are used, the decrease in inhalation agent may or may not translate into improved arterial pressure (Wagner et al., 2011). Agents used for this purpose are lidocaine, opioids (butorphanol, morphine, remifentanil), α_2-agonist sedatives, and ketamine. In-depth reviews of the use of these agents for PIVA have been published (Gozalo-Marcilla et al., 2014, 2015).

Lidocaine

Lidocaine is commonly administered IV to horses as a loading dose of 1.3 or 1.5 mg/kg over 15 min followed by a CRI of 0.05 mg/kg/min (3 mg/kg/h). Although these dose rates are administered to both awake and anesthetized horses, published studies have documented higher plasma lidocaine concentrations in anesthetized horses than in conscious horses administered the same dose (Feary et al., 2005). This difference in drug disposition caused by anesthesia is similar to that described for

gentamicin in anesthetized horses and in critically ill septic and endotoxic human patients (Smith et al., 1988; Tang et al., 1999).

The administration of a lidocaine CRI during anesthesia was originally recommended for four reasons: to provide sedation and decrease the amount of inhalation agent required with the hope of improving cardiovascular performance and decreasing postanesthesia ataxia, to induce a central antihyperalgesic effect (preemptive analgesia), and decrease the amount of analgesic agents required postoperatively, to promote early resumption of gastrointestinal motility postoperatively, and to provide an anti-inflammatory effect.

The anesthetic potency of an inhalation agent is described by its minimum alveolar concentration (MAC) value [i.e., the lowest end-expired (end-tidal) concentration that will prevent a response to an electrical stimulation or skin pinch in 50% of a group of animals]. Lidocaine infusion has been shown to decrease the halothane, isoflurane, or sevoflurane requirement (decreased MAC), in some cases in a dose-dependent fashion and with increasing duration of infusion (Doherty & Frazier, 1998; Dzikiti et al., 2003; Feary et al., 2005; Rezende et al., 2011). Importantly for clinical use, the decrease in anesthetic requirement varies among animals. For example, in one study of lidocaine CRI, the MAC of sevoflurane was decreased from a mean of 2.42% to a mean of 1.78%. Although this was a mean reduction of 27%, values ranged from 6 to 45% in the horses studied (Rezende et al., 2011). This variation means that the vaporizer setting must be adjusted according to the assessment of depth of anesthesia in each animal. Presumably the addition of lidocaine to another anesthetic agent results in a combination that exerts an increased sedative effect. By contrast, infusion of lidocaine alone in conscious horses did not cause significant sedation, although a CRI at ≥0.04 mg/kg/min was documented to provide antinociception to an electrical stimulus (Risberg et al., 2014).

Administration of a large loading dose of lidocaine may result in decreased blood pressure; infusing the dose over 15 min may diminish this effect on the cardiovascular system. Use of a loading dose before the CRI will rapidly increase plasma lidocaine concentrations, thereby facilitating a decrease in inhalation agent requirement. In a study in which plasma lidocaine concentrations were measured in awake horses, one group of horses was not administered a loading dose. The results of that study revealed that without a loading dose a steady state was not achieved until 3 h after the start of the infusion (Dickey et al., 2008). The results also confirmed that plasma lidocaine concentrations decreased rapidly within 1 h after the infusion was discontinued. Nonetheless, another clinical study of horses with colic demonstrated that only a short duration of decrease in isoflurane requirement occurred in horses administered a loading dose of lidocaine compared with those that were not (Nannarone et al., 2015).

The contribution of lidocaine to intraoperative analgesia is not fully defined. In one study of healthy horses, a lidocaine infusion was accompanied by a 25% decrease in the isoflurane vaporizer setting during anesthesia (Dzikiti et al., 2003). However, there were no significant differences in blood concentrations of stress-related hormones or physiologic variables between the horses administered lidocaine and those not administered lidocaine. Evidence of preemptive analgesia was observed in human patients administered lidocaine when undergoing general anesthesia for major abdominal surgery (Koppert et al., 2004). Pain scores after anesthesia did not differ when the patients were at rest, but patients administered lidocaine during anesthesia had reduced pain intensity during movement. Similarly, morphine consumption was significantly lower in the patients administered lidocaine, especially on the second and third days postoperatively, with maximum effect at 36 h. There was no difference between the two groups in the time to first bowel movement.

In one investigation of lidocaine infusion in horses with colic administered lidocaine (0.65 mg/kg followed by 0.025 mg/kg/min during anesthesia and then at twice that rate after anesthesia), no differences were detected in the time to first passage of feces compared with horses not given lidocaine (Brianceau et al., 2002). One study has identified that horses at risk for ileus are those with small intestinal lesions, high PCV preoperatively, and duration of anesthesia exceeding 3 h (Cohen et al., 2004). Administration of adjunct agents during anesthesia may also have an impact on postoperative gastrointestinal function. For example, administration of hypertonic saline decreased mucosal injury and ileus in laboratory animals subjected to intestinal ischemia and reperfusion and improved the survival rate in animal models of shock and sepsis (Coimbra et al., 1997; Attuwaybi et al., 2004; Wu et al., 2015). Increased intestinal permeability to endotoxin was prevented in anesthetized endotoxemic pigs by administration of a combination of lactated Ringer's solution, hetastarch, and dobutamine (Fink et al., 1991). The mechanism for this effect was attributed to maintenance of mesenteric perfusion, with the greatest effect achieved by the combination of blood volume expansion and dobutamine administration.

Both lidocaine and hypertonic saline modulate the inflammatory response to tissue injury by altering polymorphonuclear neutrophil activity and may have a beneficial influence in horses with colic when given early and within 12 h of onset (Ciesla et al., 2000; Hollmann & Durieux, 2000). Lidocaine infusion has been documented to decrease markers of inflammation, including prostaglandin E2 (PGE_2) concentration and mucosal cyclooxygenase-2 (COX-2) expression (Cook et al., 2008,

2009), and tumor necrosis factor-alpha (TNF-α) (Peiró et al., 2010a). The deleterious effects of reperfusion injury on gastrointestinal smooth muscle may also be attenuated by administration of lidocaine (Guschlbauer et al., 2010, 2011).

Opioids

An IV injection of butorphanol (0.02–0.024 mg/kg) can be followed by an infusion of the same agent at 0.02 mg/kg/h to maintain steady plasma concentrations, or supplemental injections of butorphanol (0.02 mg/kg) can be administered at 45–60 min intervals. The addition of butorphanol to detomidine in conscious, healthy horses produces a significant increase in the nociceptive threshold over detomidine alone and prolongs the duration of antinociception (Schatzman et al., 2001). Butorphanol may not significantly decrease the inhalation agent requirement (Doherty et al., 1997), although it is the clinical impression of some anesthetists that administration of butorphanol (0.02 mg/kg) IV intraoperatively effectively deepens anesthesia (Hofmeister et al., 2008).

Remifentanil is an ultrashort-acting mu-opioid that can be used as a continuous infusion during anesthesia in horses. A research study in horses evaluated isoflurane anesthesia with a CRI of dexmedetomidine (0.25 µg/kg loading dose and 1.0 µg/kg/h), with dexmedetomidine combined with remifentanil (6.0 µg/kg/h), and with dexmedetomidine combined with morphine (0.15 mg/kg loading dose and 0.1 mg/kg/h) for 1 h (Benmansour et al., 2014). The cardiac index and MAP were similar with all treatments. The dexmedetomidine CRI was continued for 15 min after the opioid infusions had been discontinued. The recoveries were similar among the treatments and no excitement or colic was observed.

α_2-Agonists and Ketamine

CRIs of xylazine, romifidine, medetomidine, dexmedetomidine, and ketamine are infused individually during inhalation anesthesia in horses in an attempt to provide analgesia and improve the quality of recovery, even though medetomidine and dexmedetomidine are not licensed for use in horses (Gozalo-Marcilla et al., 2015). In a recent comparison of infusions of dexmedetomidine (1.5 µg/kg/h) and ketamine (1.0 mg/kg/h) during anesthesia with controlled ventilation, the isoflurane requirement was decreased in some horses and oxygenation overall was improved, but cardiac index and MAP were decreased (Duke-Novakovski et al., 2015).

Monitoring During Anesthesia

Adequate monitoring supports clinical judgment and facilitates adjustments in anesthetic delivery, ventilator modes, and administration of IV fluids and vasoactive drugs to maintain physiologic variables within accepted normal ranges. The use of monitoring equipment providing real-time values ensures a rapid response that limits the swings of over- or undercorrection. Completing a record during anesthesia allows the anesthetist to assess at a glance changes over time in the variables being monitored and to identify a trend that requires an adjustment in anesthetic management (Figure 40.2).

Depth of Anesthesia

Monitoring of the depth of anesthesia is based on absence of movement, presence or absence of a palpebral reflex, eyeball position, and presence or absence of increased MAP in response to surgical stimulation. Eye signs can be difficult to assess when the horse is on its back, and rotating the head to one side may expose one eye for evaluation (although the eyes often differ in their positions). A light plane of anesthesia maintained largely with an inhalation agent is judged when the eye is rotated rostroventrally and a weak palpebral reflex is present. The horse may be too deeply anesthetized when the eye has rotated into a central position and the palpebral reflex is absent. Concurrent administration of infusions of an α_2-agonist or ketamine may alter the eye signs so that the eye is positioned more centrally in the orbit during light anesthesia.

Anesthetic Gas Analyzer

An anesthetic gas analyzer aspirates a continuous sample of gas from within the endotracheal tube or from the junction of the endotracheal tube with the delivery system, and then measures the inspired concentration of isoflurane or sevoflurane and the exhaled end-tidal concentration (FE′Iso or FE′Sevo) (Figure 40.3). The inhaled concentration of anesthetic from large-animal delivery systems is usually substantially less than the vaporizer setting because the exhaled anesthetic concentration is low and dilutes the concentration in the ventilator bellows (the major source of inspired gas). Measurement of the inspired anesthetic concentration warns the anesthetist when the inspired concentration is becoming too low to maintain anesthesia. The anesthetic concentration at the end of exhalation (alveolar, end-tidal) is considered to be representative of the concentration in the brain. When compared with the reported MAC value for that anesthetic agent in horses, the measured end-tidal concentration may provide a warning signal that the level of anesthesia is becoming too deep. The mean MAC values reported for halothane, isoflurane, and sevoflurane in horses are 0.9, 1.3, and 2.3%, respectively, although ranges of values have been reported owing to variations among animals and methodological differences. Satisfactory maintenance of anesthesia is usually achieved in healthy horses at FE′Iso or FE′Sevo 1.0–1.5 × MAC. Horses with colic that are

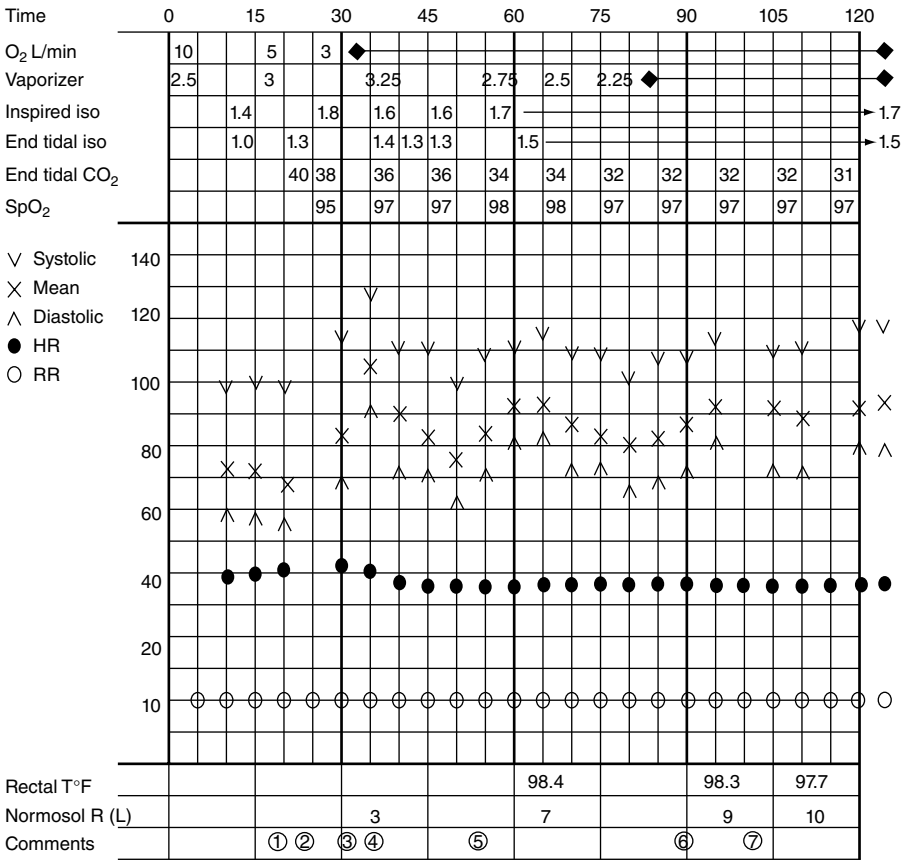

Figure 40.2 Anesthetic record of a 3.5-year-old 456 kg Appaloosa cross mare with ileal impaction. Ventilation is controlled. Comments on record: 1. Started 1 L hypertonic saline solution. 2. Started dobutamine infusion at 0.5 µg/kg/min; surgery start. 3. Started lidocaine loading dose followed by infusion. 4. Dobutamine off. 5. Restart dobutamine infusion. 6. Starting abdominal closure. 7. Dobutamine off, removed nasogastric tube, stop lidocaine. Recovery was good and quiet with horse showing no movement for 50 min and then standing at the second attempt 67 min after isoflurane discontinued.

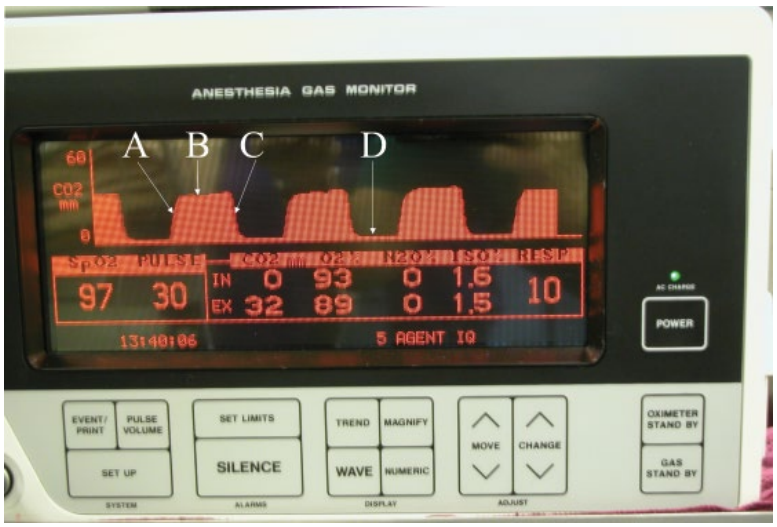

Figure 40.3 Photograph of a gas analyzer screen displaying inspiratory and expiratory values for carbon dioxide (CO_2) and the inhalation agent, and hemoglobin oxygen saturation (SpO_2). Upsweep (A) of the CO_2 waveform is exhalation, the end-tidal CO_2 partial pressure is measured at the end of the plateau (B), and downsweep (C) is inhalation. The trough (D) is inspiratory CO_2 and should be zero. This horse has an end-tidal CO_2 pressure of 32 mmHg (within normal limits) and a respiratory rate of 10 breaths/min. The end-tidal concentration of isoflurane is 1.5%.

endotoxemic and are administered CRIs of analgesic or sedative drugs can often be maintained at 0.5–1.0 × MAC. Once a satisfactory depth of anesthesia has been achieved, the FE′Iso or FE′Sevo can be used to guide changes in the vaporizer setting to maintain the plane of anesthesia within a narrow range of anesthetic concentrations, thereby avoiding depths of anesthesia that are either too light or too deep (Parviainen & Trim, 2000).

Ventilation and Oxygenation

Monitoring the ventilation of anesthetized horses determines the severity of hypoventilation and identifies horses that are hypoxemic. Unless the respiratory rate is <5 breaths/min, indicating a strong likelihood of significant hypoventilation, respiratory rate is not a useful measure of adequacy of ventilation. Hypoventilation can be monitored noninvasively using capnography or invasively by the collection of arterial blood for blood gas analysis. The capnograph continuously aspirates gases from a port next to the endotracheal tube connector and measures the exhaled carbon dioxide (CO_2). The gases exiting the monitor must be discharged back into the expiratory limb of the circle circuit or into the waste-gas scavenging system. The waveform should indicate no CO_2 during inspiration and the peak of the waveform is a measurement of end-tidal CO_2 partial pressure ($P_E'CO_2$) (Figure 40.3). These measurements are useful when the horse's lungs are artificially ventilated. However, the $P_E'CO_2$ may differ considerably from arterial CO_2 pressure ($PaCO_2$) when the horse is breathing spontaneously. The difference is usually the result of lung collapse exacerbating ventilation–perfusion mismatch. In healthy horses during artificial ventilation, $PaCO_2$ is 4–6 mmHg (0.5–0.8 kPa) higher than $P_E'CO_2$. The difference is greater in horses with colic and is on average 10–13 mmHg (range: 5–30 mmHg) [1.3–1.7 kPa (range: 0.7–4.0 kPa)] (Trim, 1998; Koenig et al., 2003). Normal $PaCO_2$ in horses is around 40 mmHg (5.3 kPa) and values up to 50 mmHg (6.7 kPa) are considered mild hypoventilation (Table 40.2). A blood gas analysis performed early in anesthesia will determine the difference between $P_E'CO_2$ and $PaCO_2$, and with knowledge of the difference capnography can be used during anesthesia to assess adequacy of ventilation. Further information on pulmonary function can be acquired by monitoring respiratory mechanics: airway pressures and pulmonary compliance (Moens, 2013).

Intermittent Positive Pressure Ventilation

Controlled ventilation (intermittent positive-pressure ventilation; IPPV) is advisable for most horses with colic as abdominal distention caused by either ingesta or gas causes cranial movement of the diaphragm and lung collapse. IPPV is most effective when instituted immediately after induction of anesthesia rather than after a delay. High $PaCO_2$ resulting from moderate to severe hypoventilation has unpredictable effects on cardiovascular function. In some animals, hypercarbia is associated with sympathetic nervous system stimulation and increased heart rate, even tachycardia, and increased MAP. Hypercarbia causes decreased myocardial contractility and systemic vasodilation, thereby resulting in hypotension in some animals. The acidemia that accompanies hypercarbia will contribute to a significantly low arterial pH in horses with metabolic acidosis that has developed as a result of the intestinal disease.

Use of a mechanical ventilator should ensure consistent adequate ventilation and allow the anesthetist to attend to other functions. IPPV will achieve satisfactory $PaCO_2$ in most horses when $P_E'CO_2$ is 35–40 mmHg (4.7–5.3 kPa). This is achieved in healthy horses with a respiratory rate of 10 breaths/min and a tidal volume of 10–12 mL/kg or peak inspiratory pressure (PIP) of 20–30 cmH_2O (15–23 mmHg).

Artificial ventilation with a normal PIP of 20–30 cmH_2O (15–23 mmHg) may not adequately ventilate a horse with abdominal distention, at least until the abdomen has been opened. Increasing PIP may achieve a $PaCO_2$ close to normal, but at the expense of a decrease in cardiac output resulting from the high intrathoracic pressure. Recommendations for maximum PIP vary from 40 to 50 cmH_2O (30–38 mmHg); pressures ≥50 cmH_2O may result in alveolar rupture. In spite of the risk for damage, transiently higher pressures may be utilized in a ventilation strategy for horses that are hypoxemic. A compromise may be "permissive hypercarbia," where mild hypoventilation [$PaCO_2$ < 50–55 mmHg (6.7–7.3 kPa)] is permitted in order to use a lower PIP.

Oxygenation

Hypoxemia can be difficult to identify using only clinical signs. Mucous membranes of horses that are hypoxemic, defined as arterial oxygenation (PaO_2) <60 mmHg (8.0 kPa), are frequently dusky pink rather than cyanotic, and the expected responses to hypoxemia of increased respiratory rates or attempts to breathe against the ventilator may not be observed in horses. Pulse oximetry using a probe clipped on the tongue, lip, or nostril (Figure 40.1) generally accurately identifies hypoxemia when the monitor displays a hemoglobin O_2 saturation (SpO_2) ≤90%. However, not all pulse oximeters provide similar readings in horses and for some, SpO_2 < 93% corresponds to hypoxemia. Furthermore, almost all pulse oximeters fail to produce a reading some of the time. Ambient light may cause erroneous SpO_2 readings, so the probes should be covered. Moistening the tongue with water and moving the clip periodically may be necessary to restore a reading in these instances.

Blood gas analysis with an automatic analyzer provides an accurate measurement of PaO_2 (Table 40.2). Handheld or portable analyzers, such as the i-STAT and IRMA TRUpoint, are available to provide point-of-care analysis of pH and blood gases that are sufficiently accurate for the management of clinical patients. Early studies with equine blood identified discrepancies for potassium and ionized calcium (iCa^{2+}) concentrations, blood glucose, and PCV measurements when compared with a laboratory analyzer (Grosenbaugh et al., 1998; Looney et al., 1998; Klein et al., 1999). For example, in one study the i-STAT underestimated

Table 40.2 Arterial pH and blood gas analysis, capnography (end-tidal carbon dioxide; $P_E'CO_2$) and pulse oximeter (SaO_2) measurements in two anesthetized horses with colic. Horse A: 430 kg American Saddlebred with small intestinal volvulus has a low normal pH, mild respiratory acidosis, and mild metabolic alkalosis. Horse B: 500 kg Quarter Horse with sand colic having values within the normal ranges.

Variable	Horse A	Horse B	Normal values
pHa	7.38	7.43	7.38–7.44
$PaCO_2$ (mmHg)	48.2	39.2	38–44
PaO_2 (mmHg) breathing oxygen	320	523	Up to 600 (sea level) (<60 = hypoxemia)
HCO_3^- (mmol/L)	29.0	26.0	24–29
Base excess (mmol/L)	+3.1	+2.0	0 to +5
$P_E'CO_2$ (mmHg) Capnography	39	27	34–40
SaO_2 (%) Pulse oximeter	98	99	>90

$PaCO_2$, arterial carbon dioxide partial pressure; PaO_2, arterial oxygen partial pressure.

the iCa^{2+} at normal to high values, although the low-value measurements were closer to the real measurements, and glucose values were substantially overestimated (Grosenbaugh et al., 1998). Hematocrit values were measured as substantially lower than actual values by several monitors, including the i-STAT (Peiró et al., 2010b). PCV values from several monitors were substantially lower than actual values. Hence it is recommended that results obtained before and after treatment should be interpreted using analyzer-specific reference ranges and the same analyzer. Care is essential when preparing self-filled heparinized syringes that only a minimal volume of heparin is drawn into the syringe to avoid acidification of the sample and significantly different pH and iCa^{2+} values.

Cardiovascular

Administration of anesthetic drugs and turning the horse onto its back frequently result in a dramatic decrease in MAP. As soon as the horse is on the table, electrodes for the electrocardiogram (ECG) should be quickly attached in case of cardiac arrest. The ECG will also provide essential information for the diagnosis of abnormal cardiac rhythms. A clear pink mucous membrane color and a CRT <1 s should be an indication of satisfactory peripheral perfusion. Prolonged CRT will occur when the cardiac output is decreased; as a result, peripheral perfusion will be decreased. White, bluish, deep-red, or fuchsia colored membranes are present when peripheral perfusion is decreased.

Palpation of the facial artery may provide an initial assessment of arterial pressure (soft and compressible = low pressure, hard like a pencil = adequate pressure). It is important for arterial pressure to be measured as soon as possible after the horse is connected to the anesthesia machine. The vaporizer should be turned to a lower concentration than usually used in healthy horses at the start of anesthesia, particularly for horses in which preanesthetic evaluation identified hypovolemia or decreased cardiovascular function. Since the vasodilation induced by inhalation agents is dose dependent and vasodilation promotes decreased arterial pressure, the use of a low vaporizer setting for the first 20 min of anesthesia will offset a decreased anesthetic requirement and may avoid hypotension during the period when monitoring equipment is being attached. Noninvasive measurement of arterial pressure provides useful information before anesthesia and arguably is adequate for a healthy horse under inhalation anesthesia for a short time. However, an invasive technique with a catheter in an artery and arterial pressure display on a monitor is more appropriate for a horse with colic (Figure 40.4) (Clarke et al., 2014). Accurate values for SAP, MAP, and diastolic arterial pressure (DAP) can be then observed without delay.

Acceptable values for heart rates are 24–46 bpm and for MAP >70 mmHg. Hypotension in horses is defined as MAP ≤70 mmHg; lower values may be life threatening. Intestinal perfusion and oxygenation decrease in horses at MAP <70 mmHg (Hopster et al., 2015). Observation of the arterial pulse waveform reveals the rate and rhythm of the cardiac beats, and the steepness of the upsweep of the wave is related to contractility.

Systolic Pressure Variation and Pulse Pressure Variation

The presence of "cycling" [marked fluctuations in SAP in sequence with the ventilator; systolic pressure variation (SPV)] can be observed on the monitor in some patients. The increase in intrathoracic pressure produced by the

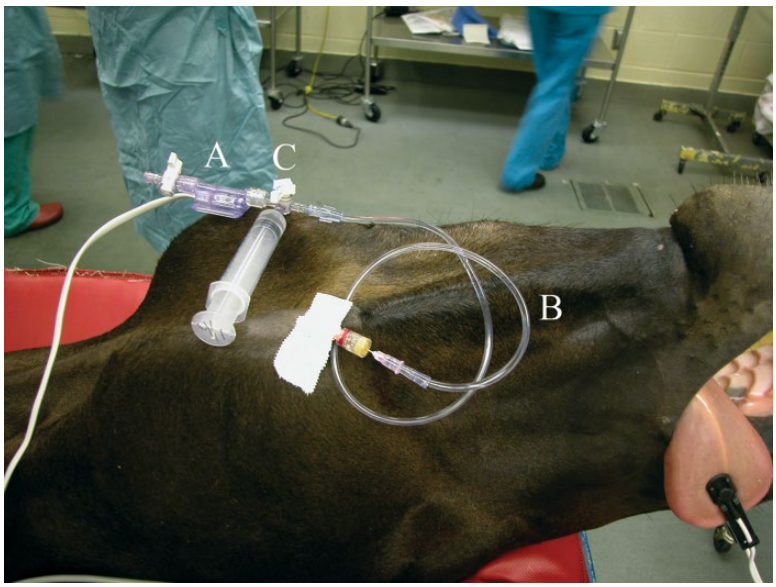

Figure 40.4 Measurement of arterial blood pressure with a 20-gauge catheter in the facial artery. The pressure transducer (A) is connected by a heparinized saline-filled low-compliance extension tube (B) to the catheter in the artery. The transducer must be filled with heparinized saline before calibrating by gently back-flushing the transducer from stopcock (C) and then permanently closing a second stopcock at the opposite end of the transducer. The transducer must be calibrated to zero pressure on room ambient pressure before measuring the patient's pressure for the first time. The transducer must be placed at the level of the thoracic inlet or point of the shoulder or lateral tuberosity of the humerus when the horse is in dorsal recumbency to correspond with heart level.

ventilator during inspiration decreases venous return, which in turn decreases stroke volume, an effect that is greatest in the presence of hypovolemia. A mild degree of cycling is a normal effect of IPPV, but observation of pronounced cycling has been used by the present author as an indicator of the need for volume loading. Pulse pressure is calculated by SAP–MAP. Increases in cardiac output in response to fluid loading have been correlated with measurements of a pulse pressure variation (PPV) of >13% in the respiratory cycle during mechanical ventilation in humans (Marik et al., 2009; Freitas et al., 2013) and in dogs (Fantoni et al., 2017; Sasaki et al., 2016). These studies have also determined that changes in cardiac function after a fluid challenge were poorly correlated with central venous pressure measurements.

Body Temperature

Hypothermia is a complication of colic surgery performed in an air-conditioned room. This decrease in body temperature is a result of the air conditioning, exposure of the abdominal organs, decreased metabolism cause by the anesthetic agents, and lack of muscle movement. Obvious consequences of hypothermia are ataxia during recovery from anesthesia when the rectal temperature is <35.5 °C and a prolonged recovery time. Attempts to slow the rate of fall of body temperature during anesthesia include use of a warm-water mattress under the horse, IV administration of warmed replacement fluids, and application of a hot air-blanket, for example a Bair Hugger, over the head, neck, and shoulders of the horse. Heat loss may be increased if the horse's back becomes wet after lying in water accumulated during preparation of the surgical site and recovery in a cold recovery room.

Management of Abnormalities

Plans and flow charts for different abnormalities should be developed before anesthesia to optimize patient management during the stress of a difficult anesthetic management by reminding the anesthetist of the options. For example, hypotension may have any of several causes and different treatments may be appropriate in different patients. Furthermore, a measured physiologic variable should not be considered in isolation when assessing the significance of the value and treatment options. For example, MAP should be evaluated with the heart rate and observation of mucous membrane color and CRT. Thus, even when the MAP is within an acceptable measurement range, if the oral membrane color is white or gray, indicating vasoconstriction, or the CRT is >2 s, indicating low cardiac output, that MAP may not, in fact, be an acceptable value. Oxygen delivery to tissues depends on cardiac output, arterial oxygen content (hemoglobin concentration and saturation) and tissue perfusion, all of which may be adversely affected in a variety of situations. The causal effect of many abnormalities on morbidity and mortality in horses after anesthesia is not known. Therefore, it is advisable to maintain physiological variables within the normal ranges that are associated with healthy conscious horses.

Hypercapnia and Hypoxemia

A variety of respiratory rates and tidal volume values can be used to achieve a $PaCO_2$ of 40–44 mmHg (5.3–5.9 kPa). A combination commonly used in our hospital is a frequency of 10 breaths/min, with each breath being approximately 10 mL/kg with an inspiratory time ≤2 s for juvenile and adult horses. If a slower respiratory rate is used, the volume must be increased, resulting in a higher

PIP. Measurement of $PaCO_2$ will accurately determine the efficiency of ventilation.

Several anesthesia machines with ventilators are available for horses (Figure 40.5 and Figure 40.6). In most cases, a separate source of oxygen or compressed air is used to drive the ventilator. The Tafonius is an example of an electrically driven piston ventilator. Waste gases must be scavenged from the anesthesia delivery system, the ventilator, and the capnograph or gas analyzer. The ventilator control panel (Figure 40.5 and Figure 40.6) provides control of the respiratory rate (frequency), the tidal volume (flow rate), the duration of inspiration, and the inspiratory pressure. The duration of inspiration should be 1.5–2 s, as a longer inspiration than this impedes venous return to the heart and decreases cardiac output. The control for inspiratory time may differ depending on the manufacturer and model of the ventilator. On one ventilator, inspiratory time may be changed by altering the inspiration-to-expiration ratio (I : E). While setting an I : E of 1:2 or 1:2.5 is satisfactory for

(A)

(B)

Figure 40.5 **(A)** Large-animal anesthesia machine from Mallard Medical (Redding, CA, USA) and **(B)** the ventilator control panel. The volume per breath is adjusted by increasing or decreasing the flow rate of anesthetic gases into the animal, and the tidal volume is assessed by observation of the displacement of the bellows or indirectly from the inspiratory pressure read from the pressure gauge in the delivery circuit (above the CO_2 absorber).

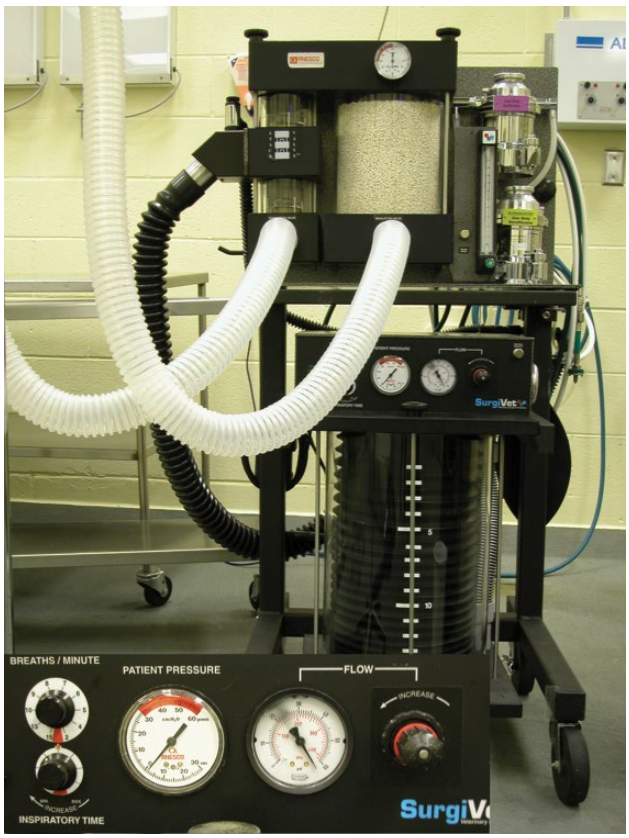

Figure 40.6 Large-animal anesthesia machine from Surgivet (Waukesha, WI, USA) and the ventilator control panel (inset). The circle circuit is stacked above the ventilator and the capacity of the ventilator bellows can be limited by using a hand crank on the side of the ventilator to raise or lower the base of the bellows. The tidal volume is adjusted by increasing or decreasing the inspiratory flow rate.

10 breaths/min, on another ventilator the inspiratory time is controlled by using the inspiratory time knob. The PIP can be read from the pressure gauge on the circle delivery circuit; target values are 20–24 cmH_2O (15–18 mmHg) in healthy horses, and up to a maximum pressure of 40 cmH_2O (30 mmHg) in a horse with a distended abdomen. A more detailed description of ventilation and use of ventilators in horses is available elsewhere (Moens, 2013).

Hypoxemia may develop during anesthesia as a consequence of lung collapse. Although cyanosis is uncommon, the mucous membranes appear muddy red or pale in color. Hypoxemia may be suspected when dark-colored blood is observed during placement of the catheter for arterial pressure measurement. Measurement of $PaO_2 < 60$ mmHg (8 kPa) will confirm hypoxemia. PaO_2 may increase after the abdomen has been opened and an improvement in ventilation is achieved. In the event of hypoxemia, controlled ventilation should be started if the horse is breathing spontaneously and the $PaCO_2$ is high. Although IPPV may open collapsed regions of lung, rather than increasing PaO_2, occasionally oxygenation will decrease at the onset of ventilation because the pressure on the diaphragm is so great that only already ventilated parts of lung are further distended. If circulation is poor, infusion of dobutamine may improve cardiovascular function but may not increase PaO_2.

The reported prevalence of hypoxemia during anesthesia is 6.0–37.8% (Trim et al., 1989a; Wilson & McFeely, 1991; McCoy et al., 2011), but hypoxemia has not yet been associated with a poor outcome in retrospective studies. Nonetheless, further investigation is needed to determine if hypoxemia influences intestinal oxygen delivery and subsequent tissue viability. Consequently, efforts should be made to treat hypoxemia that develops during anesthesia. There are several treatments and ventilation strategies that can be implemented to decrease the ventilation–perfusion mismatch and intrapulmonary shunt fraction, including administration of albuterol (salbutamol), application of continuous positive airway pressure (CPAP), positive end-expiratory pressure (PEEP), and an airway recruitment maneuver (ARM).

Albuterol

Administration of a bronchodilator into the inspired air may increase the airflow into underventilated parts of the lung, improving the ratio of ventilation to perfusion in those areas. Albuterol (salbutamol) has a direct effect on bronchial smooth muscle and is a treatment for horses with recurrent airway obstruction (Derksen et al., 1999; Bertin et al., 2011). Albuterol (Ventolin) is available in a metered-dose inhaler delivering 90 µg per actuation. In conscious horses, an average of six actuations (540 µg) resulted in bronchodilation lasting 30–60 min, but with considerable variation among individuals (Derksen et al., 1999). In one study of administration of albuterol (2 µg/kg) to horses with colic during anesthesia, a significant increase in PaO_2 was measured within 20 min (Robertson & Bailey, 2002). Albuterol should be administered through a port at the junction of the circle circuit with the endotracheal tube during inspiration, with the dose divided between two or three successive respiratory cycles.

Continuous Positive Airway Pressure (CPAP)

The Tafonius ventilator (Hallowell EMC and Vetronic Services) can be modified at the factory to be able to sustain a positive airway pressure on inspiration and exhalation (Mosing et al., 2016). In a recent study, the effects of CPAP of 8 cmH_2O (6 mmHg) were evaluated in spontaneously breathing healthy horses anesthetized with isoflurane. Although higher PaO_2 decreased shunt and no decreases in cardiac output were measured during CPAP compared with no CPAP, there was no clinically relevant effect on calculations of oxygen delivery to tissues (Mosing et al., 2016).

Positive End-expiratory Pressure (PEEP)

Imposition of a PEEP of 10 cmH_2O may increase oxygenation in some horses, but the results are variable (Wilson & McFeely, 1991; Moens, 2013). PEEP may be accompanied by hypotension that must be treated with vasoactive support. In healthy anesthetized horses ventilated at 9 breaths/min, PIP of 30–33 cmH_2O (23–25 mmHg) and I : E of 1 : 2, PEEP of 10 and 15 cmH_2O (8 and 11 mmHg) significantly increased PaO_2 without adversely affecting cardiac output (Ambrósio et al., 2013). In another study, horses ventilated with 10 cmH_2O (8 mmHg) PEEP from the start of anesthesia maintained higher PaO_2 than horses without PEEP (Hopster et al., 2011).

Alveolar Recruitment Maneuver (ARM)

For some horses with severe lung collapse, the lungs must be forcibly expanded before PEEP can be most effective, a strategy known as ARM. The use of ARM in humans is controversial because of the potential for the high pressure to cause alveolar membrane damage (Santos et al., 2016). Current issues under discussion include the speed of recruitment, the magnitude and duration of PIP, use of a fixed value for PEEP for all patients, and methods for identifying the optimum PEEP for an individual patient (using oxygenation and respiratory system mechanics). In a recent study in rats with severe acute lung inflammation arising from cecal puncture-induced sepsis, a step-wise increase in PEEP with ARM followed by decremental PEEP resulted in a lower lung damage score than in application of CPAP with ARM, and significantly less atelectasis when compared with no ARM (Santos et al., 2016). Techniques described for horses involve applying PEEP in increments of 5 cmH_2O each for a duration of 3–10 min up to 25 cmH_2O, while maintaining the difference in pressure between PIP and PEEP the same (20 cmH_2O), and then decreasing PEEP to a lower value of 10 cmH_2O (Hopster et al., 2011, 2017). Of concern is the impact of these high airway pressures on cardiac output and MAP, and thus on organ blood flow. In a recent study of ARM in healthy horses, blood flow to the stomach, jejunum, and colon remained constant until PIP was increased to 45 cmH_2O and PEEP to 25 cmH_2O, at which point blood flow abruptly decreased (Hopster et al., 2017). The cardiac output and MAP progressively decreased after PEEP reached 15 cmH_2O and, despite a significant increase in PaO_2, oxygen delivery to tissues was also decreased. The authors commented that no vasoactive support was provided, and the results might have been different if it had been provided, but also that the results may be different in horses that are hypoxemic or hypovolemic. Further studies are needed to identify the sequence and the PEEP that will increase PaO_2 without adversely affecting cardiac output and intestinal blood flow.

Cardiovascular Support

Adequate blood volume and venous return are essential for cardiac output to be satisfactory. Ideally, blood volume should be restored with balanced electrolyte solutions or expanded by administration of hypertonic saline solution before anesthesia. Infusion of acetated or lactated Ringer's solution should be continued during anesthesia, at a rate of 5–10 mL/kg/h depending on an estimated blood volume status. Inadequate circulation may be recognized by a MAP <70 mmHg, CRT ≥2 s, and white, bluish, or deep-red mucous membrane color and significant PPV. All available cardiovascular measurements should be assessed in conjunction with knowledge of the concentration of the anesthetic agent administered, time elapsed since induction of anesthesia, and the status of surgical manipulations to determine the cause(s) of suboptimal circulation and choice of appropriate therapy. The causes of decreased circulation fall primarily into two physiologic abnormalities: decreased venous return to the heart and decreased cardiac function (Table 40.3). Both mechanisms are in effect at the start of anesthesia. The low MAP present immediately after induction of anesthesia may respond to infusion of dobutamine, 0.5–5 μg/kg/min, and hypertonic saline, 2–4 mL/kg, if not already administered preoperatively. Other treatments are available depending on the underlying cause (Table 40.4).

Dobutamine

Dobutamine is a synthetic catecholamine that stimulates β_1-receptors to increase cardiac contractility and cardiac output, thereby increasing MAP (Swanson et al., 1985). Heart rate may be unchanged, increased, or decreased during infusion of dobutamine. Limited β_2- and α_1-receptor activity causes vasodilation or vasoconstriction, respectively. A convenient dobutamine solution concentration (200 μg/mL) is made by adding 8 mL of 12.5 mg/mL dobutamine to 500 mL of N saline. The infusion rate can be regulated by counting drops per minute or drops per second through a 10, 15, or 20 drops/mL administration set or by administration using a volume pump that is programmed in milliliters per hour. Some calculated infusion rates are listed in Table 40.5. Inappropriate bradycardia or tachycardia that occurs during administration of dobutamine is managed by decreasing the rate of dobutamine administration and by adding alternative cardiovascular support such as ephedrine.

Ephedrine

Injection or infusion of ephedrine may be an effective treatment of hypotension in anesthetized horses (Grandy et al., 1989). Ephedrine is a plant alkaloid that increases cardiac contractility through release of norepinephrine

Table 40.3 Flow chart to aid diagnosis and management of hypotension (mean arterial pressure <70 mmHg).

Evaluation	Rule outs	Management
Obvious initiating event	Recent administration of antimicrobial drug	If before anesthesia, consider delaying induction; during anesthesia, treat for decreased cardiac contractility
	Injection of anesthetic supplement	Depending on severity of hypotension, consider waiting for drug to redistribute; dobutamine or ephedrine
	Change from lateral to dorsal position	If severe, consider temporarily returning horse to lateral; decrease administration of inhalant, dobutamine
	Excessive depth of anesthesia	Decrease anesthetic administration
	Hemorrhage	Decrease anesthetic administration, balanced electrolyte solution 2.5× volume loss, dobutamine, HSS, colloid, (eventually) blood transfusion
	Release or manipulation of ischemic intestine	Decrease administration of inhalation agent, dobutamine, HSS, assess pH, blood gas and base excess
Heart rate and rhythm normal	Check for mechanical causes: Check delivery system pressure gauge for increased pressure	Resistance to expiratory relief (pop-off) valve
	High intra-abdominal pressure	Observe surgical site; consult with surgeon
	Aortocaval syndrome	Compression of the aorta or caudal vena cava by heavy intestine or enterolith, pregnant uterus, surgical manipulation, left lateral tilt
Heart rate abnormal	Bradycardia <24 beats/min; evaluate ECG for sinoatrial block or atrioventricular heart block	Hyoscine or atropine or glycopyrrolate, and/or ephedrine or dopamine
	Tachycardia >55 beats/min; check monitors for hypercarbia (hypoventilation, stuck circle one-way valve), hypoxemia (SpO_2, mucous membrane color, surgical site blood color, collapsed bellows), endoxemia (observe ischemic bowel, surgical manipulation of ischemic bowel, bright-red oral membranes), inadequate anesthesia or analgesia, administration of vasoactive agents especially with aortocaval compression	Identify and treat cause; tachycardia may be the cause or the result of hypotension: Includes start IPPV or increase tidal volume, check anesthesia machine, see text for managing hypoxemia, treat release of endotoxin as for decreased cardiac contractility; if suspected, decrease infusion rate of dobutamine, consider gastric or urinary bladder distention
Irregular cardiac rhythm, irregular peripheral pulses	Evaluate ECG for: Premature atrial depolarization	Treatment not usually necessary
	Atrial fibrillation	Fluid volume and dobutamine
	Atrioventricular heart block	Hyoscine or atropine, treat advanced atrioventricular block with dopamine
	Premature ventricular depolarizations (endotoxemia, hypercarbia)	Lidocaine
	Significant pulse pressure variation PPV (on palpation of peripheral artery)	Indicative of hypovolemia, balanced electrolyte, HES
Diagnosis not made, check for other causes	Hypocalcemia Hypoglycemia	Measure and treat accordingly with calcium borogluconate or 5% dextrose in water, respectively

HSS, hypertonic saline solution; ECG, electrocardiogram; IPPV, intermittent positive-pressure ventilation; HES, hydroxyethylstarch; PPV, pulse pressure variation.

from neurons and a mild direct agonist effect on α-, β_1-, and β_2-receptors. Cardiac output and arterial pressure are increased by ephedrine; heart rate may be slightly increased, some vasoconstriction is induced, and blood volume is mobilized from viscera, especially the spleen. When ephedrine is administered IV as a bolus, 0.03–0.06 mg/kg, the onset of action is slow, generally taking several minutes to be evident, and the duration is 30–40 min. Limiting the initial dose of ephedrine to 0.03 mg/kg should avoid tachycardia. An IV infusion of ephedrine at 0.02 mg/kg/min for 10 min in healthy anesthetized horses increased MAP, cardiac output, and oxygen delivery for

Table 40.4 Drugs and dosages for treatment of complications.

Drug	Indication	Dosage
Atipamezole (5 mg/mL)	Detomidine antagonist	0.006–0.2 mg/kg IV. Inject slowly in increments
Atropine (0.5 or 15 mg/mL)	Bradycardia with hypotension, atrioventricular heart block	0.005–0.02 mg/kg IV. Time of onset may be several minutes
Calcium gluconate 23%	Serum Ca ≤9.5 Not for cardiac arrest	0.5 mL/kg IV over 20–30 min
Dobutamine	Hypotension	2–5 µg/kg/min using 100, 200, or 500 µg/mL solution, decrease rate as pressure rises
Dopamine	Hypotension Advanced atrioventricular heart block or cardiac arrest	5 µg/kg/min using 100, 200, or 400 µg/mL solution, decrease rate as pressure increases 7–10 µg/kg/min
Ephedrine (50 mg/mL)	Hypotension; to induce splenic contraction	0.06 mg/kg IV bolus, divided dose; 0.02 mg/kg/min to effect
Epinephrine (1 mg/mL)	Cardiac arrest	0.015 mg/kg IV = 6–7 mL for 450 kg (1000 lb) horse
Glycopyrrolate (0.2 mg/mL)	Bradycardia	0.0025–0.005 mg/kg IV
Hetastarch	Hypovolemia Cardiac arrest	5 mL/kg over 30 min IV 2 mL/kg with hypertonic saline
Hyoscine (20 mg/mL)	Bradycardia	0.2 mg/kg IV
Hypertonic saline 7.5%	Rapid treatment of hypovolemia or hemorrhage Cardiac arrest	2–4 mL/kg over 10–15 min. Must be followed by lactated Ringer's solution if patient is dehydrated 2 mL/kg
Lidocaine	Premature ventricular depolarizations, ventricular tachycardia, ventricular fibrillation	1–2 mg/kg IV bolus, 0.05 mg/kg/min IV infusion
Naloxone (0.4 mg/mL)	Opioid antagonist	0.01–0.02 mg/kg IV; usually 2 mL per large horse
Phenylephrine	Hypotension unresponsive to other treatments	0.2–2.0 µg/kg/min
Sodium bicarbonate	Metabolic acidosis	1.5 mEq/kg (mmol/kg) over at least 20 min (treats a deficit of 5); or base excess × 0.3 × kg body weight = mEq given over at least 1 h. Do not treat a deficit of more than 10 mEq/L in less than 1 h; repeat pH/blood gas analysis first
Tolazoline (100 mg/mL)	Xylazine antagonist	0.5–2 mg/kg IV in divided dose to effect; must be given over several minutes to avoid hypotension

Table 40.5 Infusion rates of dobutamine calculated using a solution concentration of 200 µg/mL and an administration set delivering 15 drops/mL.

Body weight		Infusion 2 µg/kg/min		Infusion 5 µg/kg/min	
kg	lb	mL/h	drops/s	mL/h	drops/s
100	220	60	1 drop/5 s	150	~1 drop/2 s
227	500	136	~1 drop/2 s	340	3 drops/2 s
350	770	210	~1 drop/s	525	2.2 drops/s
454	1000	273	~1 drop/s	681	~3 drops/s
550	1210	330	4 drops/3 s	825	3.4 drops/s

90 min without changing the heart rate (Fantoni et al., 2013). Ephedrine also can be used when splenic contraction is needed to facilitate surgical manipulation.

Phenylephrine

Phenylephrine is a synthetic drug that may counter hypotension associated with vasodilation by stimulating α_1-receptors and causing vasoconstriction. Phenylephrine infusions (0.25–2.00 μg/kg/min) increased MAP but decreased cardiac output in anesthetized healthy horses (Fantoni et al., 2013; Ohta et al., 2013). Since oxygen delivery to tissues is dependent on cardiac output, phenylephrine infusion also significantly decreased oxygen delivery (Fantoni et al., 2013). Consequently, phenylephrine should be used only when other methods for treating hypotension (decreasing depth of anesthesia and dobutamine, ephedrine, and volume administration) have failed.

Dopamine

Dopamine is a catecholamine that can be administered to improve cardiovascular performance. Because dopamine causes initial vasodilation and a decrease in MAP, it is less often used as the first vasoactive drug for treating hypotension in horses. Dopamine is a natural precursor of norepinephrine and part of dopamine's cardiovascular effects are mediated through norepinephrine and part by stimulation of dopamine DA_1, α_1-, β_1- and β_2-receptors. The effects of dopamine are dose and time dependent. In horses, low dosages of dopamine, 1–3 μg/kg/min, increase renal and mesenteric blood flow, may increase MAP, and produce a mild increase in cardiac output. Moderate dosages of dopamine, 3–10 μg/kg/min, increase cardiac contractility and cardiac output, and heart rate at the higher dose. Vasodilation produced at these dose rates may result in a decrease in MAP in the first 5–7 min followed by an increase in blood pressure and cardiac output over 15–30 min, as plasma concentrations of norepinephrine increase (Trim et al., 1985). The high dose of dopamine, ≥10 μg/kg/min, causes vasoconstriction and is preferentially used over dobutamine and ephedrine in cases of acute severe hypotension, in the treatment of advanced third-degree atrioventricular heart block, and during management of cardiac arrest. Dopamine infusion has been documented to increase cardiac output and blood pressure in healthy and endotoxemic anesthetized horses and to increase intestinal and renal blood flow (Clark & Moore, 1989; Trim et al., 1989b, 1991). Despite evidence that administration of dopamine increases oxygen delivery to the gastrointestinal tract and attenuates the endotoxin-induced decrease in intestinal villus blood flow, there is evidence that the distribution of blood flow is modified, resulting in a disproportionate decrease in mucosal blood flow (Neviere et al., 1996; Schmidt et al., 1996). In some horses in which an unsatisfactory response to dobutamine is obtained, the combination of low-dose dopamine with dobutamine may improve cardiovascular function.

Vasopressin

Vasopressin can be used in the treatment of cardiac arrest. Although it is not recommended as the first line of treatment for hypotension, it has been used in human patients in advanced septic shock who have become refractory to the administration of catecholamines (Dellinger et al., 2013).

Calcium

Infusion of calcium gluconate during anesthesia significantly increases cardiac output and MAP and decreases heart rate in healthy horses (Grubb et al., 1999). Administration of calcium gluconate should be avoided during the performance of an intestinal anastomosis as gastrointestinal activity increases, intestinal diameter decreases, and intestinal sutures may become loose.

Specific Clinical Scenarios

Aortocaval Compression

Occasionally, hypotension occurs as soon as the horse is positioned on its back and treatment to improve cardiovascular performance is unsuccessful. In these patients, increasing the infusion rate of a catecholamine results in tachycardia, but does not increase arterial pressure. The hypotension may be due to high intra-abdominal pressure or to compression of the aorta or caudal vena cava (aortocaval syndrome) from the weight of the gastrointestinal tract. This latter problem is most likely to occur in horses with impaction of the transverse colon, or from a gravid uterus, or from gastric distention. The arterial pressure increases only after the pressure in the abdomen has been decreased by incision and intestinal decompression or when the intestines are lifted by the surgeon. Although the surgeon can identify a severely distended stomach, attempts at decompression using the nasogastric tube may or may not be successful. The impact of such severely impaired circulation on cerebral function will depend on the duration. Although severe hypotension after induction of anesthesia may have other causes, start of surgery is urgent when aortocaval syndrome is suspected. Sometimes tilting the horse 10–15° to one side results in sufficient repositioning of the intestines or uterus and less pressure on the caudal vena cava to allow the arterial pressure to be restored. Once the abdomen is open, aortocaval compression has been relieved, and the arterial pressure remains adequate, the horse should be repositioned into dorsal recumbency to avoid gluteal or thoracic limb myopathy.

Endotoxin Release

Surgical manipulation of poorly perfused or ischemic intestines can result in the release of vasoactive substances that cause an abrupt decrease in cardiovascular function, a severe decrease in arterial pressure, tachycardia, and metabolic acidosis. Endotoxins have been detected in the circulation after manipulation or enterotomy of the large colon in horses with colic anesthetized for abdominal surgery (Trim et al., 1997a). At the start of untwisting a strangulated intestine, even before significant changes occur in cardiovascular measurements, counter measures can be instituted that include a decrease in the vaporizer setting and preparation for administration of dobutamine or ephedrine, if those solutions are not already available. When decreased cardiovascular function is observed, arterial blood should be collected for measurement of pH, PaO_2, base excess, and lactate concentration to assess the magnitude of the responses to toxin release.

Hemorrhage

Rupture of a large blood vessel may occur during intestinal manipulation, resulting in blood loss, decreased venous return and cardiac output, and hypotension. Clinical assessment of the severity of the situation must recognize that cardiac output decreases faster and earlier than MAP as the volume of blood loss increases. Without cardiovascular support other than lactated Ringer's solution at 10 mL/kg/h, loss of 10 L has a significant adverse impact on a 500 kg horse (Wilson et al., 2003). Treatment involves decreasing the concentration of the inhalant anesthetic, possibly decreasing the CRI infusion rate(s) of adjunct drugs, and administering fluid for volume expansion. The objective is to achieve an adequate circulation (MAP >70 mmHg, CRT <2 s, and no tachycardia). Hypertonic saline (2–4 mL/kg) IV will maintain cardiac output and MAP for 1 h in the face of severe hemorrhage (Schmall et al., 1990). Blood loss will be augmented if overtreatment results in a high arterial pressure and the source of the bleeding cannot be stopped. Hydroxyethylstarch, plasma, and dextran 70 are useful colloids for blood volume expansion and to retain fluid within the vascular space. Blood transfusion, if feasible, should be considered if blood loss exceeds 20% of the total blood volume. The blood volume of most horses is 100 mL/kg and that of draft horses and ponies is 72 mL/kg.

Cardiac Dysrhythmias

Abnormal cardiac rhythm may be responsible for decreased cardiac output. Second-degree atrioventricular (AV) heart block is characterized by the presence of a P wave without a QRST complex on the ECG and loss of a corresponding peripheral pulse (Figure 40.7). Xylazine and detomidine may initiate this rhythm and no treatment is indicated. Blood pressure may decrease when this rhythm is initiated by dobutamine and this effect is usually reversed by decreasing the rate of dobutamine infusion. The presence of AV block on other occasions is a cause for concern because it may progress to advanced heart block or cardiac arrest. Second-degree AV block may be treated with infusion of dopamine, 6 µg/kg/min, or an IV bolus of atropine, 0.005–0.02 mg/kg.

Bradycardia can be effectively treated by IV administration of atropine, 0.01 mg/kg, or glycopyrrolate, 0.005 mg/kg. Onset of action may be slow for several minutes followed by tachycardia and hypertension (Teixeira Neto et al., 2004; Pimenta et al., 2011). Both atropine and glycopyrrolate are associated with ileus lasting for several hours, occasionally days, after administration during anesthesia. Hyoscine (Buscopan) may be preferable to atropine or glycopyrrolate because, although the heart rate is increased for a shorter time, hyoscine should have a shorter duration of impact on gastrointestinal motility (Pimenta et al., 2011).

Differentiating the cause of tachycardia is by process of elimination of the many potential causes: sinus tachycardia from distention of a viscus such as the stomach or the urinary bladder, excessively low arterial pressure (cardiac output) from decreased venous return, hypoxemia, hypercarbia, endotoxemia, dobutamine or ephedrine, and ventricular tachycardia.

Atrial fibrillation is an occasional complication that may be responsible for hypotension during anesthesia (Figure 40.8). This dysrhythmia may be present before induction of anesthesia or may develop at any time during anesthesia. Knowledge of this complication before

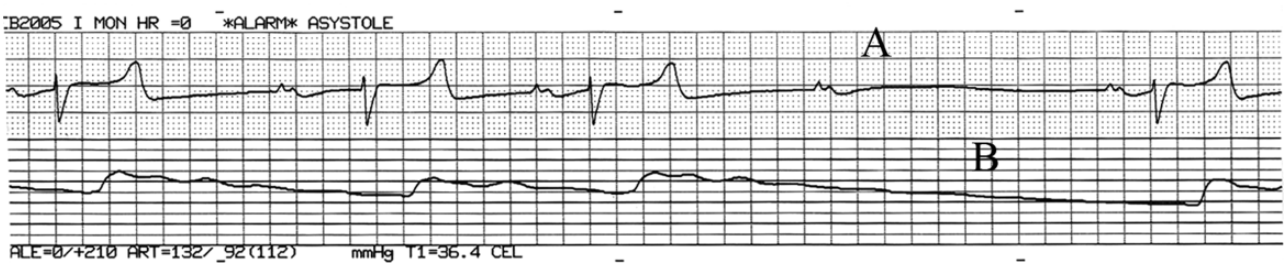

Figure 40.7 Second-degree atrioventricular heart block at A on the electrocardiogram seen as a P wave without a corresponding QRS complex and subsequent loss of pulse at B observed on the arterial waveform below.

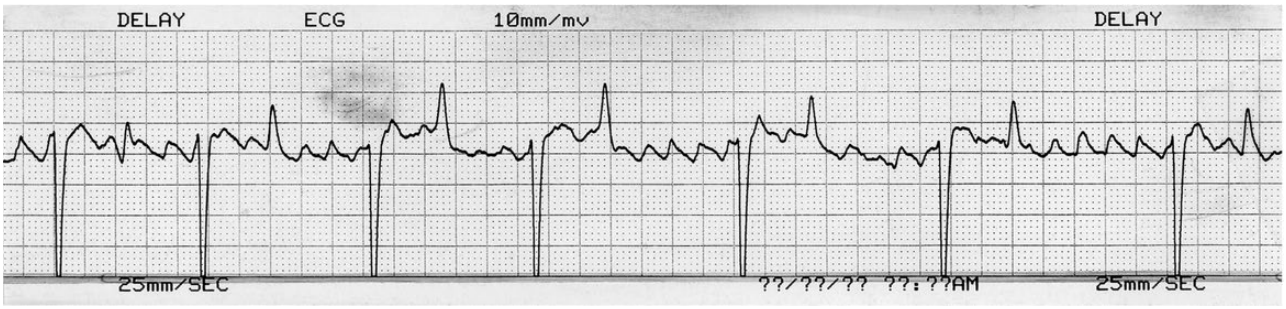

Figure 40.8 Atrial fibrillation identified on a base apex lead electrocardiogram. Ventricular rate for atrial fibrillation may vary from normal to fast.

anesthesia affects preanesthetic evaluation and choice of anesthetic agents because of the potential for severe hypotension during anesthesia that is unresponsive to usual treatments. The premedication dose rate for an α_2-sedative should be kept as low as possible and sevoflurane or isoflurane used in preference to halothane anesthesia. When hypotension is present, infusion of dobutamine may maintain adequate MAP. Spontaneously occurring atrial fibrillation usually persists for the duration of anesthesia and for several hours afterward before reverting to normal rhythm.

Hyperkalemic Periodic Paralysis

When the horse with colic carries the gene for hyperkalemic periodic paralysis, serial measurement of serum potassium concentration during anesthesia will identify development of the syndrome. Mild muscle fasciculations on the face or body may be observed during anesthesia at the onset of the syndrome, which can be at any time during anesthesia. Tachycardia, hypertension, and dysrhythmias are not always features of this syndrome in anesthetized horses. Treatments that should be available include normal saline to replace balanced electrolyte potassium-containing solutions for IV fluid therapy, calcium gluconate and 5% dextrose solutions to induce movement of potassium into cells, and sodium bicarbonate to address acidosis.

Diaphragmatic Rupture

Some horses exhibiting signs of colic may be identified at the time of surgery as having a diaphragmatic rupture with intestine in the thorax. The inability to ventilate the horse adequately and hypoxemia may be problems for the anesthetist, especially after extraction of the intestine and introduction of pneumothorax. Adjusting the table to a head-up tilt may be requested by the surgeon, and the change in position may improve ventilation. Other alterations in anesthetic management include repositioning the pressure transducer level with the heart to maintain an accurate arterial pressure measurement and realizing that this position may induce bilateral gluteal myopathy. Insertion of a chest tube may be necessary in horses with this condition.

Recovery from Anesthesia

Management of horses with colic during recovery from anesthesia should be similar to that applied to healthy patients: recovery in a quiet, warm, darkened, and padded recovery area with a foam- or air-filled pad for the horse to lie on, and administration of oxygen. Loud noises outside the recovery room can startle a horse awake and induce a premature attempt to rise, which, based on personal observations of these scenarios, should be avoided. A slower recovery time to standing has been associated with better quality recoveries (Young & Taylor, 1993). In contrast, longer recovery times have been associated with factors that contribute to poor-quality recoveries, such as a longer duration of anesthesia, a longer duration of intraoperative hypotension, hypothermia, and horses with surgery for colic (Voulgaris & Hofmeister, 2009; Mayerhofer et al., 2005). Recovery of horses in a stall with dimmed lights or placing a towel over the horse's head and eyes is more an intuitive decision rather than based on data. In one study comparing recoveries in darkened or illuminated recovery rooms, there was no difference in the quality of unassisted recoveries or the times to first movement or standing (Clark-Price et al., 2008). Designs of equine recovery rooms are described in detail elsewhere (Clark-Price, 2013).

The quality of recovery from anesthesia is influenced by many factors, such as breed, health status, anesthetic agents administered, intraoperative hypotension, surgical procedure, duration of anesthesia, and hypothermia. Different scoring systems have been used to assess factors and interventions that potentially may worsen or improve recovery. One study comparing four scoring systems concluded that all four systems were equally reliable methods for scoring "good" and "bad" recoveries, with similar scores recorded from scorers who were experienced or inexperienced in equine anesthesia

(Vettorato et al., 2010). However, some of these systems are not objective, requiring some subjective interpretation by the scorer.

Airway Management

Although airway obstruction is a complication that must be dealt with during recovery, the problem often originates during anesthesia. Congestion and edema of the nasal mucous membranes will develop when the horse's head is positioned level with the thorax. Consequently, elevation of the head plays an important part in preventing the occurrence of nasal mucosal swelling. Reflux of gastric fluid into the nostrils around the nasogastric tube appears to irritate the mucosa and cause nasal mucosal swelling. An attempt at lavaging the nasal cavity with water, performed with the horse's head lower than its neck, may reduce mucosal irritation. When gastric reflux has been observed to occur during anesthesia or when nasal hemorrhage occurs after removal of the nasogastric tube, the horse should be allowed to recover from anesthesia with the orotracheal tube in place and the cuff should remain inflated to prevent pulmonary aspiration of fluid. Packing of the nasal cavities with gauze may be necessary to control hemorrhage, which can be life threatening (Trim et al., 1997b). The mouth speculum is removed and the endotracheal tube positioned so that it exits the mouth through the interdental space and secured to the nose or head with tape or a length of gauze. The nasal packing must be removed before extubation. The endotracheal tube is not removed until the horse is standing and can lower its head and expel fluid or blood clots from the nasopharynx and upper trachea.

Alternative techniques for managing nasal obstruction by mucosal swelling include replacing the orotracheal tube with a nasotracheal tube and/or topical application of phenylephrine to the nasal mucosa: 5 mL of 0.15% phenylephrine solution for a 500 kg horse (Lukasik et al., 1997). In recovery, the head should be supported with a foam pad or towels above the level of the heart. In the absence of nasal swelling or gastric reflux, the presence or absence of the endotracheal tube during recovery is the clinician's preference.

One reason why a horse in recovery should be constantly watched is that occasionally airway obstruction occurs whether or not the endotracheal tube is present. The endotracheal tube can be kinked or the horse's nostrils occluded when the horse's neck is twisted or its nose is pushed up against the wall when recumbent or standing. Laryngospasm, which is a rare occurrence in the horse, may develop as the horse tries to stand. This complication is life threatening. Airway obstruction or excessive inspiratory effort in recovery can result in severe pulmonary edema, recognized by fluid flowing from the horse's nostrils when the head is lowered and abnormal lung sounds heard on auscultation (Ball & Trim, 1996). Treatment with furosemide and oxygen therapy will be necessary for a period from a few hours up to 48 h.

Oxygenation

Oxygenation of hemoglobin will decrease rapidly once the horse starts to breath air during recovery. The author's preference is simultaneously to turn off the vaporizer and oxygen flow and to disconnect the endotracheal tube from the anesthesia machine. The horse is hoisted in dorsal recumbency into the recovery room (<2 min), placed in lateral recumbency, and controlled ventilation applied at 8–10 breaths/min with oxygen using a demand valve for about 10 min. Weaning to spontaneous breathing is accomplished by decreasing the respiratory rate to 4 breaths/min for several minutes. When spontaneous breaths begin, each breath is augmented by the demand valve. At approximately 20 min, the demand valve is disconnected and oxygen insufflated at 15 L/min into the endotracheal tube or into the dorsal nasal meatus when the endotracheal tube has been removed. This flow rate of oxygen is low, perhaps enriching the inspired oxygen to 29%, but has been shown to maintain oxygenation in recumbent horses with adequate ventilation (McMurphy & Cribb, 1989). A flow rate of 10 L/min will not provide sufficient oxygen to improve oxygenation (Mason et al., 1987). Weaning from IPPV using positive-pressure ventilatory support should prevent hypoxemia and will speed elimination of the inhalation agent (Ida et al., 2013a). For horses with high PaO_2 at the end of anesthesia, IPPV should be continued until the horse is disconnected from the anesthesia machine immediately prior to being moved to the recovery room. Apnea at this time may prevent a decrease in SaO_2 (Blaze & Robinson, 1987). The endotracheal tube should be connected to a demand valve as soon as possible. In contrast, horses that are hypoxemic at the end of anesthesia may experience a rapid and potentially life-threatening decrease in oxygen saturation during apnea (Guedes et al., 2016) and should breathe oxygen throughout the transfer process. Once the horse has been weaned from the demand valve to spontaneous breathing, oxygen should be insufflated through the endotracheal tube or the dorsal nasal meatus at 15 L/min for an adult horse.

Sedation in Recovery

Poor recoveries from anesthesia in horses are often associated with successive uncoordinated movements and repeated attempts to rise, not necessarily occurring within a short time of extubation. Reasons for this include panic reactions as the horse regains consciousness while still retaining residual effects of anesthesia,

sedation and muscle weakness from anesthetic agents, hypothermia, and sometimes hypokalemia or myopathy. Lidocaine infusions should be discontinued 15–30 min before the end of anesthesia as continuance of lidocaine infusion until transfer to recovery has been associated with increased ataxia when standing (Valverde et al., 2005). Administration of small doses of α_2-agonist sedatives, specifically xylazine or romifidine, is recommended for many horses in an attempt to slow their return to consciousness while allowing more time for elimination of anesthetic agents before the horse attempts to stand. The timing of the supplemental sedative dose in recovery will depend on the depth of anesthesia assessed at the time of transfer from the operating room; an assessed light plane of anesthesia with observation of nystagmus would indicate the immediate need for administration, whereas transferring a horse at a deeper plane of anesthesia may warrant delaying administration of the sedative for 5–10 min. Waiting a long time between discontinuing inhalation anesthesia and sedative administration when the horse is already becoming aware of its surroundings often results in an undesirable or less efficacious effect because circulating catecholamines have begun to increase. Xylazine, 0.1–0.2 mg/kg, or romifidine, 0.01–0.02 mg/kg, is frequently administered IV approximately 5 min after the inhalation anesthesia has been discontinued to improve the quality of recovery. In a recent evaluation of horses recovering from isoflurane anesthesia, romifidine at 0.02 mg/kg resulted in significantly better recovery than xylazine or a lower dose of romifidine (Woodhouse et al., 2013). In another study of horses after isoflurane anesthesia for arthroscopy, recovery scores were better after administration of 0.5 mg/kg xylazine compared with 0.25 mg/kg (Ida et al., 2013b). The fewer attempts to stand at the higher dose were attributed to a 66% longer recumbency period before standing. Some horses in the high xylazine dose group were hypoxemic, a further indication that oxygen insufflation during prolonged recoveries is important. In the author's opinion, caution must be exercised in the administration of a high dose of xylazine in recovery after colic surgery as hypotension or apnea may develop after a bolus administration. When a horse is unacceptably ataxic after standing and the cause is attributed to the xylazine supplementation, administration of a very low dose of tolazoline IV, such as 2 mL for an adult horse, will result in more stable footing. Additional sedative may be unnecessary in horses that have received injectable agent supplements during anesthesia, especially medetomidine infusion.

Studies of recoveries after using different inhalation agents have yielded inconsistent results. In one study of healthy research horses, recovery from sevoflurane anesthesia, with or without postanesthetic administration of xylazine, was better and associated with less time taken to achieve coordination than recoveries observed after isoflurane anesthesia (Matthews et al., 1998).

Unassisted Versus Assisted Recovery

The need for assistance to standing using ropes attached to the head halter and tail will be determined primarily by hospital routine and the design of the recovery room. However, these approaches should be considered for those horses that are likely to have weakened muscle function. Factors that influence muscle strength include endotoxemia, hypocalcemia, hypokalemia, body temperature below 96 °F (35.5 °C), anesthesia time longer than 3 h, old age, major blood loss, and when the horse's hind limbs were in the full flexed position during anesthesia. Recovery room designs are varied, but the arrangement of ropes to assist a horse to stand is facilitated by metal rings high on the walls. The head halter must be secure and unable to slide over the ears. Likewise, the rope tied to the tail must be with a knot that will not slip when subjected to the horse's full weight. One arrangement is to tie the head rope to the noseband, passing the free end through a metal ring on the wall and then through a hole in the wall to the outside where it can be held by one person. The rope attached to the horse's tail is passed through a separate ring on the inside wall before passing through a second hole in the wall and being held by a second person. Although the horse must make the effort to stand, the ropes restrain the horse, preventing forward movement that could lead to stumbling. The head rope must not be too tight as the horse attempts to stand, allowing some head and neck movement, and upward traction on the tail rope can provide some lifting action.

Postoperative Analgesia

Attempts to provide analgesia after surgery have included use of a nonsteroidal anti-inflammatory agent (NSAID) with continuous administration of butorphanol, morphine, or lidocaine. Evidence of a decreased stress response associated with butorphanol administration was present in an investigation of 27 horses with colic (Sellon et al., 2004). Half of the horses received butorphanol infusions, 0.013 mg/kg/h for 24 h after celiotomy, and had decreased plasma cortisol concentrations. Heart rates and respiratory rates were not affected by the administration of butorphanol, but the time to first passage of feces was significantly delayed and the total fecal output in 24 h was decreased. This effect on gastrointestinal transit was confirmed in another study, and the authors suggested that postoperative infusions of lidocaine and ketamine may be administered to better effect (Elfenbein et al., 2014).

Pain scoring scales based on observation of the horse's behavior and demeanor and physiologic measurements

have been developed specifically for horses (Pritchett et al., 2003; Graubner et al., 2011; Gleerup et al., 2015; Taffarel et al., 2015; De Grauw & Van Loon, 2016).

Conclusion

As more information is published about the pathophysiology of endotoxemia and sepsis, ischemia, and multiple organ failure, it is increasingly obvious that changes occurring in horses with colic are exceptionally complex. At present, goals in the management of anesthesia should be to maintain MAP, peripheral perfusion, $PaCO_2$, and depth of anesthesia within a tight range of values, with treatment to prevent hypoxemia. Since morbidity and mortality from colic surgery frequently are attributable to complications during recovery from anesthesia, further studies are needed to identify methods to ensure a safe transition from the operating table to return to the hospital stall. Currently, there is insufficient evidence for the use of individual anesthetic agents. Additional controlled studies are needed with emphasis on oxygen delivery and tissue oxygen content in the gastrointestinal tract, effects occurring during anesthesia that may impact organ function after anesthesia. Provision of analgesia during and after anesthesia in horses is largely influenced by the clinician's preference and further well-designed studies incorporating the new pain scoring systems for horses are essential to provide a scientifically based recommendation for this problem.

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Part XI

Surgery for Acute Abdominal Disease

41

Preparation of the Patient for Abdominal Surgery

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The primary goals of patient preparation for surgery are simplification of the surgical procedure and reduction of intra- and postoperative complications. Equine colic surgery most often is performed in an emergency setting and in a compromised patient. A longer duration of anesthesia will have negative effects on the clinical outcome; therefore, preparation of the patient should be organized to take as little time as possible under general anesthesia. This chapter focuses on the most commonly performed ventral median approach. The procedures and principles can be applied to other surgical approaches as needed.

Patient Preparation and Positioning

Colic surgery most often is an emergency procedure and keeping horses off feed before surgery is not an option. In those patients with elective procedures, feeding restrictions should be applied as needed for the procedure (e.g., laparoscopy) or the anesthetic regime. If possible, horses should be cleaned and their feet picked before entering the surgical rooms. In horses with gastric reflux or a full stomach, a nasogastric tube should be inserted and left in place before induction of anesthesia. This will minimize any risk of gastric rupture during induction of anesthesia and of spontaneous gastric reflux occurring when placing the horse in dorsal recumbency with the subsequent risk of aspiration of gastric fluid.

After induction of general anesthesia, horses are placed in dorsal recumbency. In this position, the sternal region of the horse and all four feet are higher than the abdomen, and falling loose hair and debris can contaminate the surgical site before and during surgery (Figure 41.1). Therefore, the feet should be covered during surgery and all debris and loose hair removed from the limbs and the sternal region before beginning preparation of the surgical field. Use of a heavy-duty vacuum cleaner helps with this process. Most shoes do not have to be removed, but all feet should be covered with tape during surgery and recovery to minimize contamination of and damage to the padded recovery stall. During surgery, the distal limbs should be covered, and rectal sleeves can be used for this purpose (Figure 41.1). In male horses, the penis is packed into the prepuce with gauze sponges and the external ring of the prepuce is closed with a monofilament suture in a simple continuous suture pattern (Figure 41.2). Alternatively, towel clamps can be used to close the prepuce, but they do not provide as good a seal as a sutured closure. As an alternative, the penis can be exteriorized, the penis and prepuce cleaned, a urinary catheter placed, and the penis secured toward the side or caudally. This will minimize the risk of urinary leakage and subsequent contamination of the surgical field but will occupy additional time under general anesthesia.

Preparation of the Surgical Field

The initial preparation of the surgical field, including the removal of hair and the initial cleaning of the surgical site, should be performed outside the surgery room if possible. This will minimize contamination of the surgery room, and a higher number of colony-forming units (CFU) of bacteria in the air of the surgery room has been associated with a higher rate of postsurgical wound infections in ventral median incisions in horses (Galuppo et al., 1999).

Removal of Hair

For a ventral median incision, the hair from the ventral abdomen should be removed in a region from cranial of the prepuce or mammary glands to slightly cranial of the

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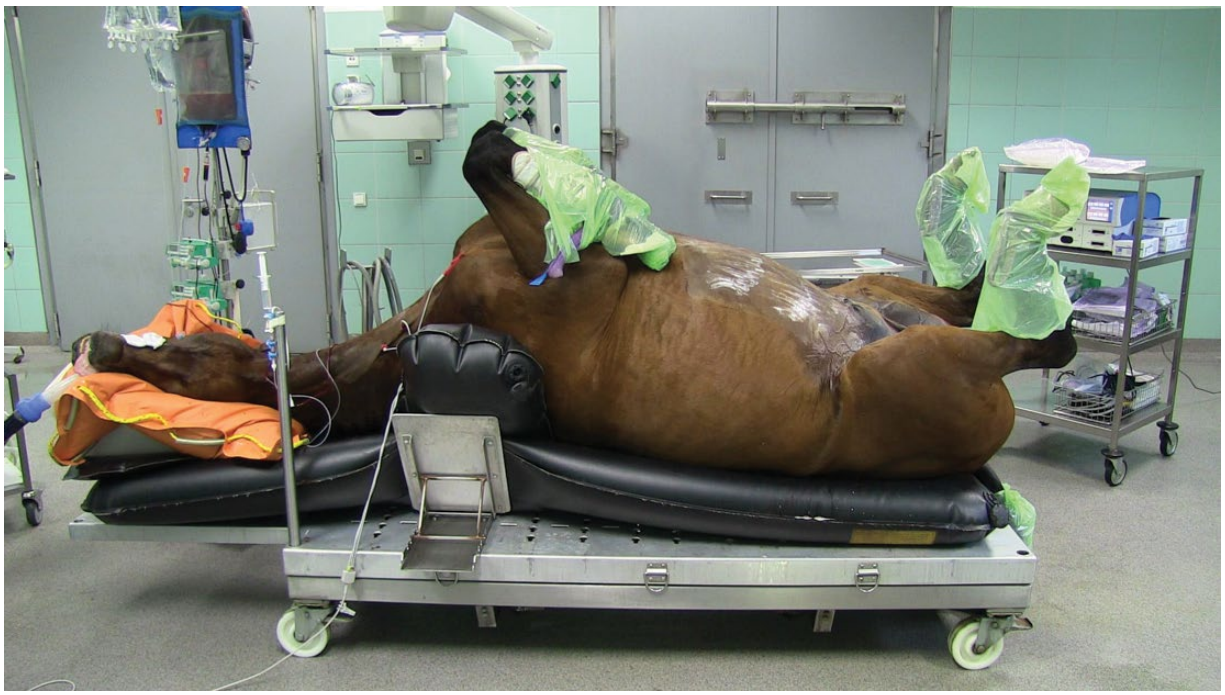


Figure 41.1 Positioning of a horse on a surgery table in dorsal recumbency. Note that the sternal region and all 4 feet are located at a level above the proposed site for a ventral median laparotomy, and falling loose hair and debris can contaminate the surgical site before and during surgery. All 4 feet are covered with rectal sleeves to protect the surgical site.

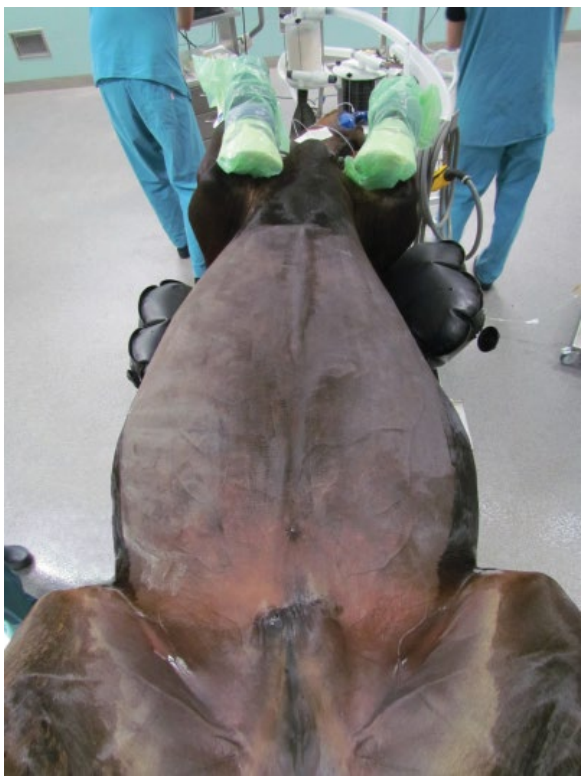


Figure 41.2 Surgical site prepared for a ventral median laparotomy. The hair from the ventral abdomen has been removed in a region from cranial of the prepuce to slightly cranial of the xiphoid and lateral to the midline to the level of the flank folds. The preputial orifice has been sutured close. The feet have been taped and the distal limbs covered with rectal sleeves.

xiphoid and lateral to the midline to the level of the flank folds (Figure 41.2). As soon as the decision for surgery has been made, hair should be clipped using a #40 blade on the standing horse if possible, because this will minimize time under general anesthesia. If needed, clipping can be completed when the horse has been placed under general anesthesia. The clipper blades should be cleaned and disinfected before each use to avoid contamination of the surgical field. Clipping of the hair is to be preferred over shaving, because shaving will cause more skin damage (Figure 41.3). Bacteria can colonize damaged skin and the risk for wound infections will increase in parallel with an increasing period between shaving and surgery. Therefore, even in cases of elective surgery, hair should be removed as close to the time of surgery as possible (Brown et al., 1997). In human medicine, shaving significantly increased the risk of postoperative wound infections compared with clipping (Tanner et al., 2011). In cattle, clipping alone resulted in significantly less skin irritation than clipping followed by shaving (8.7 versus 47.8%), but there was no difference in the rate of postoperative wound infections (Bédard et al., 2001).

Skin Cleaning and Disinfection

Optimally, initial skin preparation is performed before the horse is moved into the surgery room and is followed by a final sterile preparation. The initial preparation focuses on cleaning the surgical site from fat and all

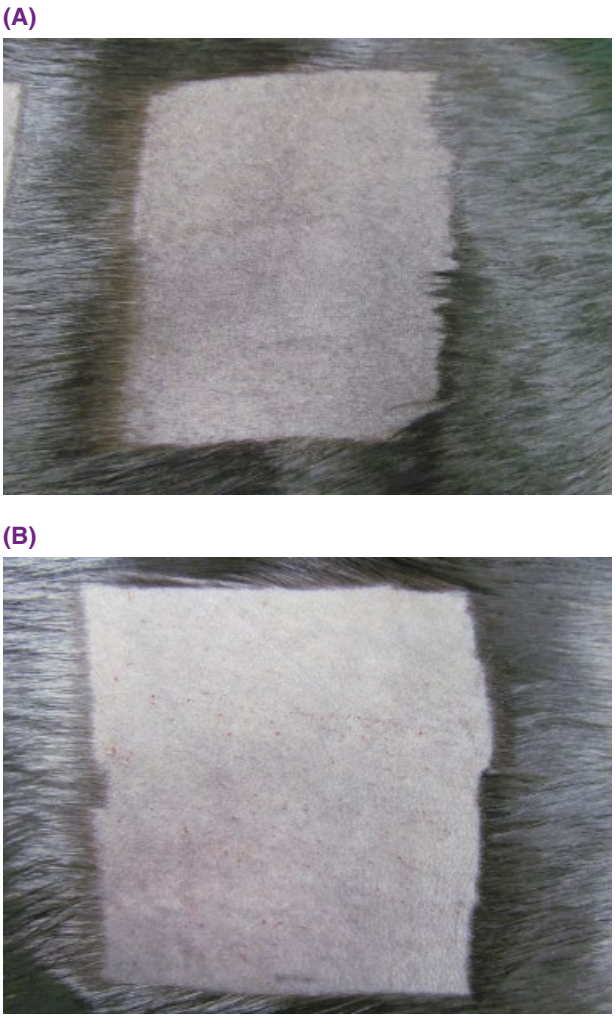


Figure 41.3 Area of skin on the ventral abdomen of a horse after hair removal with clippers **(A)** or a razor **(B)**. Clipping and shaving were performed carefully by the same person. For clipping a new #40 blade and for shaving a new razor blade were used. Note that shaving caused more skin damage, and bacteria can colonize damaged skin, increasing the risk for postoperative wound infections.

visible dirt, and the final preparation must disinfect the surgical site. After successful skin disinfection, approximately 20% of the original bacterial flora will remain in the deeper layers of the skin and can recolonize the skin surface after approximately 30–60 min.

In veterinary medicine, the antiseptic agents most commonly used and most extensively evaluated are alcohol, iodine formulations, and chlorhexidine. Successful disinfection relies on mechanical scrubbing, needed to clean the skin, and a sufficient contact time of the disinfectant with the surgical site. Use of polyvinylpyrrolidone (PVP)–iodine will liberate free iodine from the PVP–iodine complex (see later). The disinfection time should therefore be controlled and this is not a step that can be abbreviated to reduce anesthesia time.

Alcohol

For disinfection, one of the alcohols 1-propanol, 2-propanol (isopropyl alcohol), and ethanol is most often used, and their effectiveness for disinfection decreases in the order listed. Alcohols are effective against vegetative bacteria and some fungi and viruses. They do not provoke allergies but can irritate and dehydrate the skin. Because of their cytotoxicity, alcohols should not come in contact with open wounds.

Alcohols denature proteins, which will damage the cell membrane. Dilution with water quickly makes alcohols ineffective. Very high alcohol concentrations can also limit the disinfection properties because at high concentrations carbohydrates from the cell membrane precipitate and will retard diffusion of the alcohol to and into the cell (Larson & Morton, 1991).

Alcohols are among the fastest acting disinfectants, but the skin must be kept wet with alcohol during the entire disinfection time. The presence of organic debris can reduce the effectiveness of alcohols and therefore thorough cleaning of the skin before disinfection is paramount. After evaporation, there is no residual activity of alcohol.

Alcohols reduce the residual activity of chlorhexidine diacetate (but not of chlorhexidine gluconate) and inactivate hexachlorophene-based products. Because they increase the availability of free iodine, alcohols increase the antimicrobial activity of PVP–iodine.

Iodine

Iodine is microbiocidal because it causes metabolic interferences and is effective against a broad spectrum of bacteria, viruses, and fungi. There is no known resistance that can develop against iodine. Iodine can irritate tissue, has strong staining properties, and is radiopaque and corrosive. Some of these disadvantages can be reduced through the formation of complexes with carrier substrates, which reduce tissue irritation and staining while not interfering with the bactericidal properties of alcohols. The complex most often used for skin disinfection is PVP–iodine (povidone–iodine), the carrier substance being PVP. PVP–iodine is available as a 10% aqueous solution with 1% available iodine.

Iodine is tightly bound to PVP but must be released in order to be bactericidal. Iodine is liberated from PVP in an equilibrium reaction with water, and therefore iodine that has been removed, such as through a reaction with bacteria, will be replaced from the PVP–iodine complex. The necessary presence of water can explain why higher concentrations of an aqueous PVP–iodine solution are less bactericidal, and the standard 10% solution contains insufficient free iodine to kill bacteria (LeVeen et al., 1993). Dilution of the 10% aqueous solution up to 1 : 100 will increase the amount of available free iodine up to 2.5-fold. Higher dilutions than 1 : 100 will rapidly decrease the

amount of available free iodine. Alcoholic iodine solution must be used undiluted.

Iodine is inactivated by organic debris, so the skin must be cleaned before disinfection with iodine. Addition of detergents also reduces the release of iodine (LeVeen et al., 1993). Iodine can cause allergic reactions and is cytotoxic, particularly at high concentrations. Therefore, iodine should be diluted before contact with mucous membranes (to at least 1 : 40) and should not come in contact with open wounds. In contrast to chlorhexidine, octenidine–iodine complexes do not irritate the cornea and can be used as skin disinfectant in the area of the eyes (Brühl et al., 1964).

Alcohols will increase the liberation of free iodine from PVP–iodine complexes. When disinfecting a surgical field, PVP–iodine should be used alternating with alcohols.

Chlorhexidine

Chlorhexidine is effective against a wide range of bacteria, fungi, and viruses and there are no known resistances. Chlorhexidine is cytotoxic and should not come in contact with open wounds. It can damage the cornea and therefore is not suitable for use in the skin around the eyes.

Chlorhexidine is bactericidal through precipitation of proteins and destruction of cell membranes. It will bind to proteins in the stratum corneum of the skin and through this mechanism can have a residual action for up to 6 h. The bactericidal properties of chlorhexidine are little or not impaired by the presence of organic debris.

Whereas chlorhexidine gluconate is almost unaffected by the presence of alcohols, the bactericidal properties of chlorhexidine diacetate are markedly reduced by alcohols.

Octenidine

Octenidine is available as octenidine dihydrochloride and is effective against bacteria, fungi, and viruses, but not against endospores. There are no known resistances. In contrast to PVP–iodine, alcohols, and chlorhexidine, octenidine is not licensed for general use for the aseptic preparation of a surgical field in human medicine, where it is licensed for surgical preparations in the area of the anus and the urogenital tract.

Octenidine will be effective after approximately 1 min and has a residual effect for up to 24 h. The cation of octenidine interferes with negative charges in cell membranes of microorganisms.

Octenidine is not as irritant to tissues as are alcohols, PVP–iodine, and chlorhexidine, and can therefore be used to lavage wounds. However, it is chondrotoxic and should not come in contact with articular cartilage and should not be used in the area of the ears. Also, it can damage the cornea and should not be used in the area of the eyes. Lavage of very deep wounds or wounds with insufficient egress is not recommended in human medicine, because it has caused cases of severe and therapy-resistant tissue swelling and necrosis with subsequent fibrotic changes of affected muscles and permanent movement impairment. Octenidine therefore should not be applied with pressure into body and wound cavities and after wound lavage, free egress of lavage and wound fluid must be ensured (Hülsemann & Habenicht, 2009, 2011).

Octenidine should not be used in conjunction with PVP–iodine because this can lead to the liberation of iodine radicals that can irritate tissue and stain it brown to violet.

Comparison of Different Antiseptic Agents for Use as Skin Disinfectants in a Surgical Setting

Several studies have compared the use of PVP–iodine and chlorhexidine in the aseptic preparation of a surgical field. In human medicine, most often chlorhexidine has been recommended. In a study of 849 patients, aseptic preparation of the surgical field with chlorhexidine gluconate and alcohol resulted in significantly less postoperative wound infections than aseptic preparation with PVP–iodine (Darouiche et al., 2010). In 18 ponies, three protocols for aseptic preparation of ventral midline incisions were compared: PVP–iodine and alcohol, chlorhexidine gluconate and alcohol, and chlorhexidine gluconate and saline (twice, 5 min each). The authors concluded that both PVP–iodine and alcohol and chlorhexidine gluconate and saline were suitable protocols and resulted in low numbers of CFU after aseptic preparation, but chlorhexidine and saline reduced CFU after the initial scrub more effectively than PVP–iodine and alcohol. Skin preparation with chlorhexidine and alcohol was not recommended, because in this group higher numbers of CFU of bacteria were found after the surgery (Wilson et al., 2011). In a study of 117 cattle skin preparations with PVP–iodine, soap and alcohol was as effective in the prevention of postoperative wound infections as a skin preparation with chlorhexidine gluconate and alcohol, but the number of CFU of bacteria was lower after the use of chlorhexidine (Desrochers et al., 1996). A combination product for preoperative skin preparation containing 2% chlorhexidine gluconate and 70% isopropyl alcohol provided significantly more persistent antimicrobial activity at 24 h than either of the components used separately (Hibbard et al., 2002).

In summary, both chlorhexidine and PVP–iodine seem suitable for aseptic surgical skin preparation in horses, although PVP–iodine has no residual activity and chlorhexidine has a wider range of antimicrobial activity

and is only minimally inhibited by organic material. Chlorhexidine preferably should be used in conjunction with saline.

Other Skin Preparation Products

Film-forming Iodophor Complex

This complex consists of isopropyl alcohol and iodine povacrylex (a proprietary iodine–acrylate copolymer) and after a one-step application to the skin will form a water-insoluble and air-permeable film with a residual effect for up to 12 h. It was as effective as a two-step surgical preparation with PVP–iodine in the reduction of CFU in horses (Zubrod et al., 2004). Similarly, in ponies with ventral midline incisions, skin preparation with PVP–iodine and alcohol and with a film-forming iodophor complex applied after a hexachlorophene scrub were equally effective in reducing bacterial CFU and resulted in a similar incidence of incisional drainage (Galuppo et al., 1999).

Glutaraldehyde

Skin preparation with stabilized glutaraldehyde was as effective at reducing and maintaining low bacterial CFU in dogs as was skin preparation with chlorhexidine (Lambrechts et al., 2004).

Skin Sealing

Products based on cyanoacrylate glue have been developed for use in the preparation of surgical fields. These products aim to prevent mechanically the migration of bacteria from hair follicles into the surgical wound, and cyanoacrylate can actively prohibit bacterial growth. Use of cyanoacrylate glue can reduce bacterial CFU and may reduce surgical site infections in human medicine (Daeschlein et al., 2014; Dohmen, 2014). In horses, no difference was found in intravenous catheter contamination rates after catheter site preparation with PVP–iodine with and without a cyanoacrylate microbial sealant. The sealant was well tolerated by the horses (Pasolini et al., 2015).

Draping

The ideal surgical field draping is sterile and impermeable to water and bacteria. Reusable surgical drapes are made from cotton, which is not waterproof and, if wet, not sufficiently impermeable to bacteria. In particular in surgeries with higher amounts of liquids in the surgical field (e.g., arthroscopies, colic surgery), the use of cotton as the sole draping material is less suitable.

Disposable drapes are available from several manufacturers. For use in ventral midline laparotomies, the surface of the drape should be smooth and remain smooth when wet to avoid irritation of bowel placed on the drape. Horses can be covered with several smaller drapes, and the principles for draping in general surgical procedures apply. Several manufacturers produce drapes specifically designed for use in ventral midline celiotomies, and these single drapes will greatly simplify the draping process (Figure 41.4). Some drapes incorporate barriers around the proposed incision site to prevent bowel from moving too far away from the incision site. Alternatively, nonpenetrating towel clamps can be used to create similar barriers (Figure 41.4B).

Adhesive incisional drapes are available and can help to secure the drapes to the skin around the proposed surgical site (Figure 41.4B). Adhesive incisional drapes impregnated with antimicrobials are supposed to minimize migration of bacteria from hair follicles into the surgical wound. However, no difference was found in humans in the incidence of surgical site infections when comparing adhesive incisional drapes with or without iodine impregnation (Kramer et al., 2010).

Common Pitfalls When Preparing the Surgical Field

Clothing

The person preparing the surgical field should not wear long-arm sleeves or very loose clothing. Loose closing can inadvertently and repeatedly contact the surgical field and make effective disinfection impossible.

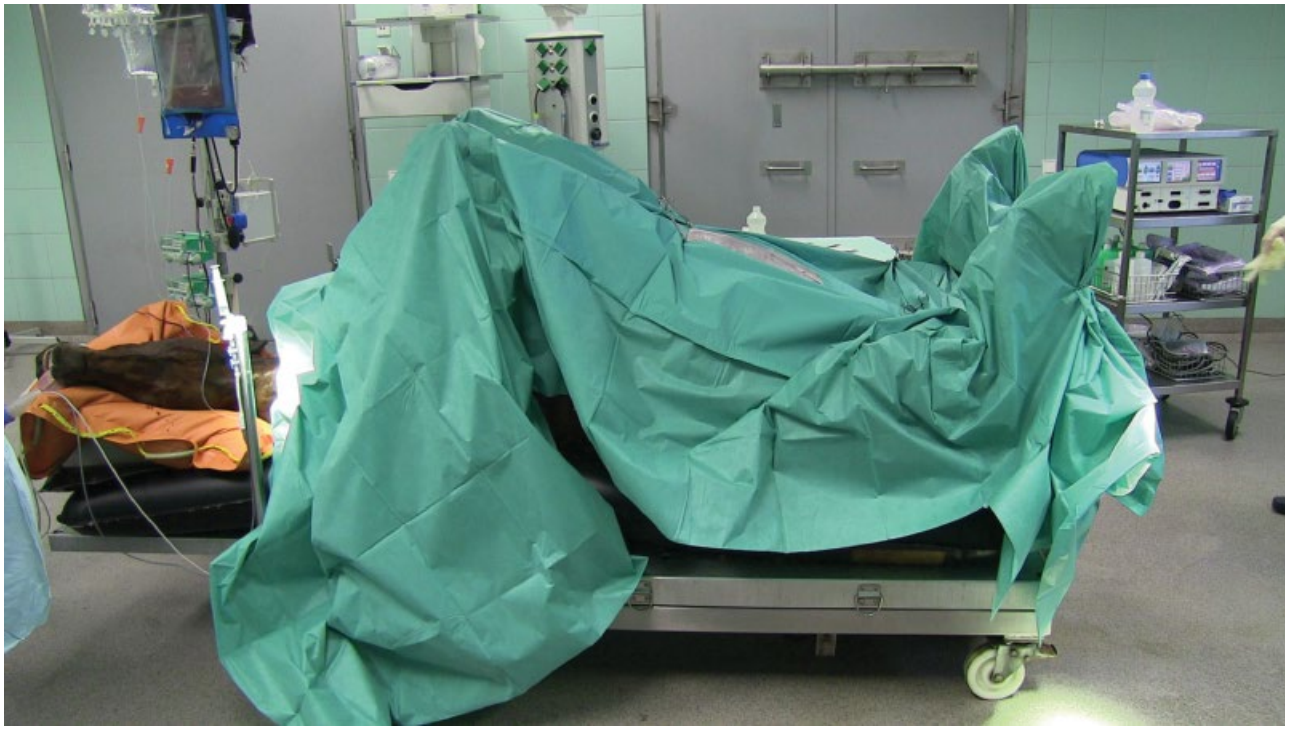
Location of the Surgical Site

When performing a ventral midline laparotomy, the surgical site is not the highest point of the animal: all four limbs and the sternal region are located higher that the ventral abdominal midline. Loose debris and hair can fall and move toward the surgical site after draping when surgical manipulation of bowel inside and outside the abdomen causes movement of the horse. Also, the preparation of the surgical site should be performed with as little free liquid as possible. If too much fluid is used when preparing for a ventral midline laparotomy, liquid can run from the cranial edges of the surgical field caudally and recontaminate the surgical site (Figure 41.5).

Sponges

The part of the sponge touching the surgical field should not have previously been touched by the person performing the aseptic preparation (Figure 41.5 and Figure 41.6). Even though the hand of the person preparing the surgical field should not directly contact the skin, in most cases some of the liquid used for cleansing and disinfection will contact the hand. Since the bacterial

(A)



(B)

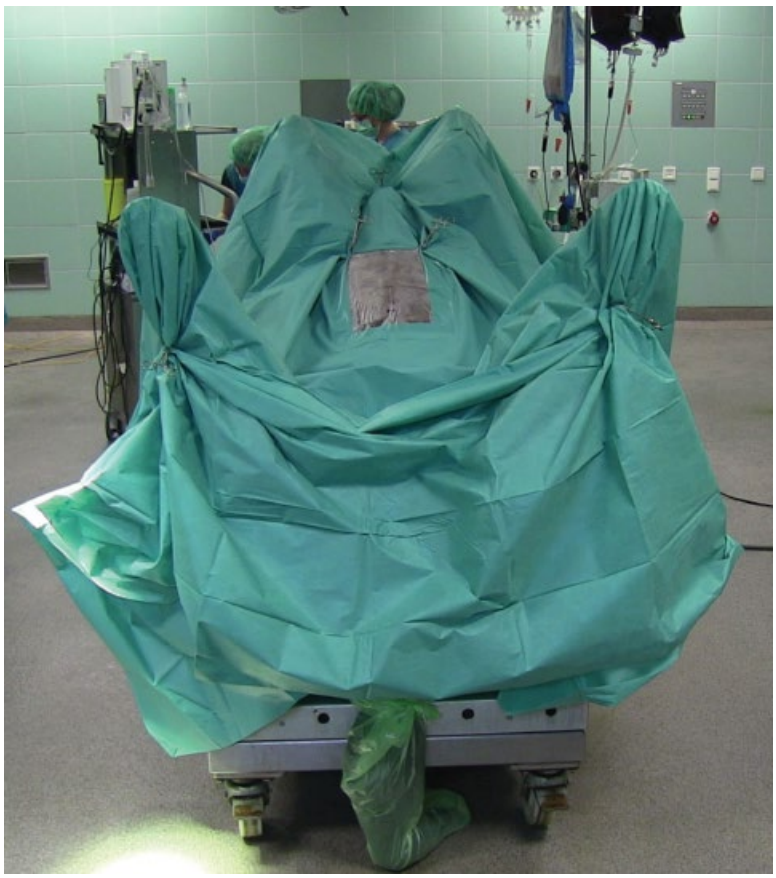


Figure 41.4 **(A)** Use of a single drape to cover the horse before performing a ventral median laparotomy. The drape is water impermeable and retains its smooth surface even when wet. It is fenestrated in the area of the proposed surgery site and incorporates an adhesive incisional film to secure the drape to the skin near the surgery site. **(B)** Note how towel clamps are used to create barriers lateral and caudal to the proposed incision site to prevent bowl falling away from the sterile field.

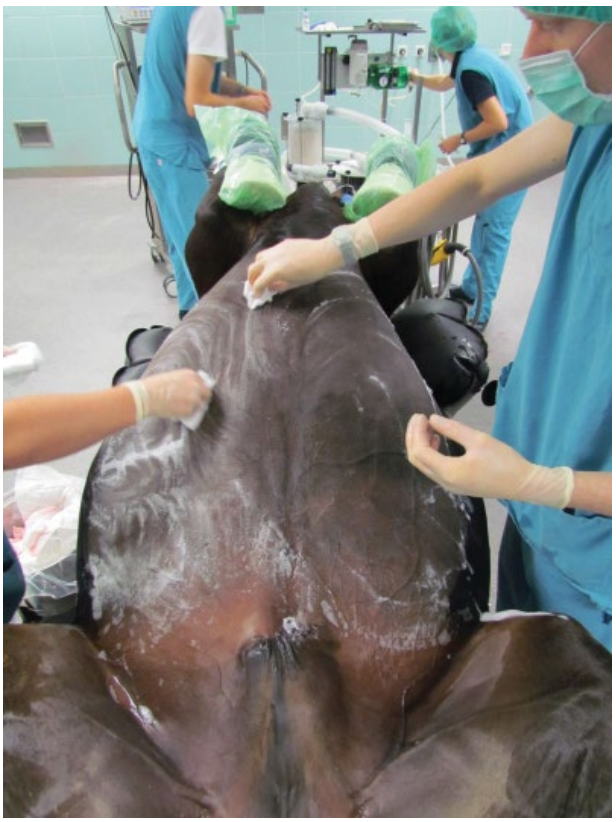


Figure 41.5 Aseptic surgical preparation for a ventral median laparotomy. The surgical site should be cleaned from the inside to the outside, and a sponge that has come into contact with a region further away from the proposed site of the incision should not be moved toward the center of the surgical site. If too much fluid is used when preparing for a ventral midline laparotomy, liquid can run from the cranial edges of the surgical field caudally and recontaminate the surgical site. Note that the hand of the person performing the scrub does not come in direct contact with the skin.

count on the skin of the surgical site is expected to decrease during aseptic preparation, the hand of the person performing the preparation will be more likely to contain higher counts of bacteria than the skin at the surgical site toward the end of aseptic preparation.

Figure 41.6 Handling of sponges for aseptic surgical field preparation. The part of the sponge touching the surgical field should not have previously been touched by the person performing the aseptic preparation. The sponge is removed from the stack from the top with the left hand, and the untouched side of the sponge is then placed on the skin.

Touching the side of the sponge later applied to the skin therefore might recontaminate the surgical site. Using latex examination gloves for skin preparation helps to avoid human contact with the surgical site.

Cleaning and Disinfection

Principles from general surgery apply. The surgical site should be cleaned from the inside to the outside, and a sponge that has come into contact with a region further away from the proposed site of the incision should not be moved toward the center of the surgical site to avoid any recontamination (Figure 41.5). This principle is often inadvertently disregarded when preparing for a ventral midline laparotomy, probably because of the potentially long longitudinal incision that can be very close to the preputial orifice in male horses. The latter region cannot be disinfected easily and must be regarded as an "outside" region of the surgical field.

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42

Surgical Exploration and Manipulation

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In horses with colic, abdominal exploration can be performed through a variety of approaches, and some approaches may be preferable to others depending on the tentative diagnosis made before surgery or the procedure planned. For most colic cases, a ventral median or paramedian approach will be used because these approaches result in direct access to most of the abdomen. Surgical exploration should include the entire abdomen, including nonintestinal organs and structures such as the liver, spleen, diaphragm, bladder, and reproductive organs. Following the same system during every abdominal exploration can be helpful to identify the anatomic structures quickly and make a definitive diagnosis, and also to ensure that all abnormalities are identified.

Ventral Midline Celiotomy

As indicated by its name, the ventral midline incision is located on the midline of the ventral aspect of the abdomen and includes skin and subcutaneous tissue, the linea alba, retroperitoneal fat, and peritoneum (Figure 42.1). For most abdominal surgeries, the incision will extend from approximately 2 cm cranial to the umbilicus cranially to the length desired. A length of 20–25 cm is sufficient for many colic surgeries, in particular for small intestinal lesions. The main advantage of a shorter incision is that it takes less time to close and it may increase owner's acceptance. However, if the incision is short enough to hamper bowel manipulation, this can prolong the surgery time and increase the amount of mechanical irritation to the incisional margins, which in turn can have negative effects on wound healing. Also, some lesions, especially large colon lesions, may necessitate a longer incision to manipulate the bowel safely and correct the lesion. Therefore, a ventral midline incision should be as short as possible without interfering with necessary surgical manipulations, but as long as necessary to expedite the surgery. Depending on the intended procedure and the anticipated lesion, the ventral midline incision may be located more cranially or caudally than described. A more cranial incision may be needed for lesions such as a diaphragmatic hernia, gastroduodenal lesions, or liver lobe torsion. Diseases involving the uterus and the bladder or the small colon and rectum may necessitate a more caudally located incision caudal to the umbilicus or near the pelvis.

For a ventral midline incision, sharp dissection of all tissues layers with a scalpel has been recommended and is guided by the ridge of the linea alba that can often be palpated on the ventral midline or, alternatively, on the dorsal aspect of the linea alba after an initial incision has been performed. The initial incision includes skin and subcutaneous tissue and exposes the ventral aspect of the linea alba (Figure 42.2 and Figure 42.3). Separating the skin or subcutaneous tissue from the abdominal tunic is unnecessary and should be avoided. It is traumatic and increases the inflammatory response, creates dead space, and could reduce vascular perfusion of wound margins, and all of these factors can interfere with wound healing. Bleeding from subcutaneous and skin vessels will be encountered. Hemorrhage into the incision can increase postoperative wound edema and provides a good environment for bacterial growth. Electrocautery can be used to reduce hemorrhage, but it is unclear if this effectively reduces incisional wound healing complications. Often the bleeding will stop after the abdomen is opened, releasing pressure on the skin.

After the linea alba has been exposed, it is carefully transected using the belly of a scalpel blade. Especially in horses with severe intestinal distention, this tissue layer will be under a high degree of tension, and after incision the distended intestine will push against the incisional opening. Care must therefore be taken to avoid injury to the bowel during incision. Thumb forceps can be introduced dorsal to the linea alba and used to guide and

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Figure 42.1 Transverse cut through the ventral abdominal wall. The rectus muscles are held with forceps on either side of the central linea alba lying beneath the subcutaneous fat. Note the retroperitioneal fat in the lower portion of the figure.

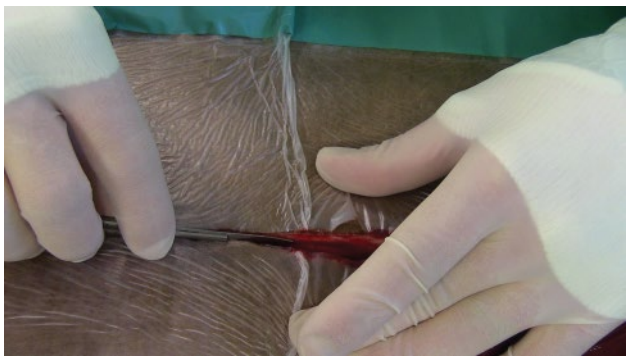


Figure 42.2 Midline skin incision. The skin and subcutaneous tissues are incised using the belly of the scalpel blade in one smooth motion.

Figure 42.3 Exposure of the linea alba. Once the incision through the skin and subcutaneous tissues has been made, the linea alba can be seen as a thin, linear, white structure on midline.

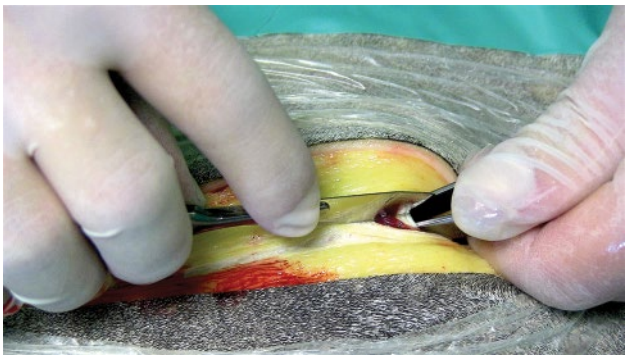


Figure 42.4 Incision through the linea alba. After initial penetration of the linea alba, thumb forceps are inserted through the incision within the retroperitoneal fat to elevate the linea alba during incision, thereby protecting the abdominal contents.

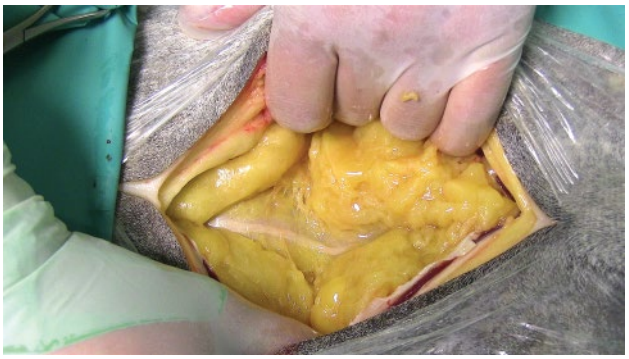


Figure 42.5 Appearance of tissues following incision through the linea alba. Note the appearance of the retroperitoneal fat, with the falciform ligament clearly visible within the peritoneum.

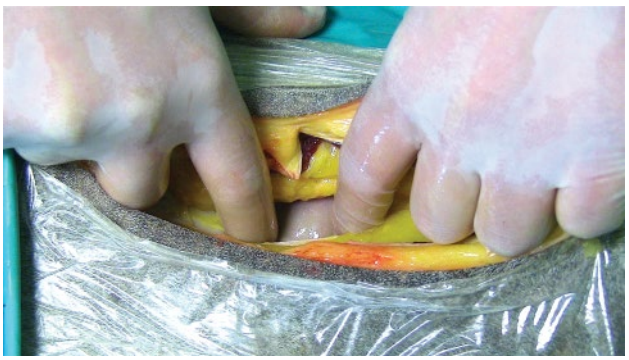


Figure 42.6 Opening of the peritoneum. The peritoneum can be opened along the length of the incision using the fingers to make a longitudinal blunt dissection.

isolate the scalpel during incision (Figure 42.4). After transection of the linea alba, variable degrees of retroperitoneal fat will be visible (Figure 42.5). Excess fat can be removed if needed. Dissection is continued bluntly and this will expose the peritoneum and the falciform ligament (Figure 42.5). To open the abdomen, the peritoneum can be punctured with a finger and two fingers are then used to tear the peritoneum longitudinally (Figure 42.6). Alternatively, the falciform ligament can be elevated with forceps and incised in a longitudinal direction using scissors or a scalpel (Figure 42.7).

The linea alba is wider near the umbilicus and is thinner as it courses cranial. Exact positioning of the incision in the linea alba is therefore more difficult in a

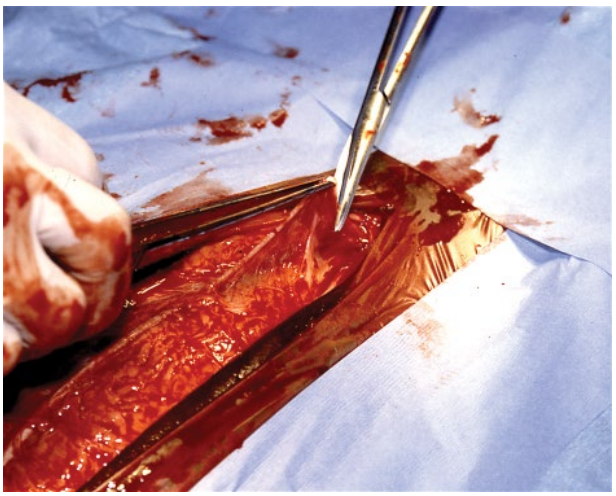


Figure 42.7 Elevation of the falciform ligament. An alternative approach to entering the peritoneal cavity is to elevate the falciform ligament with forceps, and sharply incising the ligament to open the peritoneum.

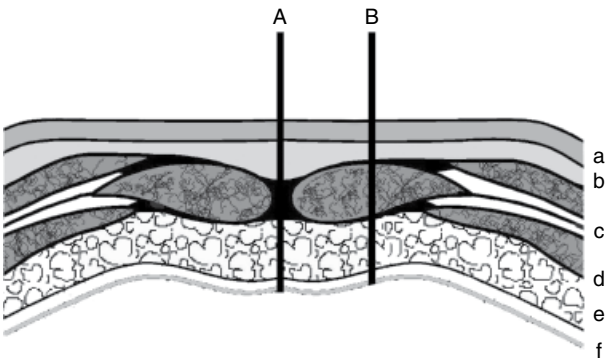


Figure 42.8 Difference between layers incised through a ventral midline approach (A, through linea alba) and paramedian approach (B, through muscle sheaths and rectus abdominis muscle). a, skin; b, external abdominal oblique; c, internal abdominal oblique; d, transverse abdominis muscle; e, retroperitoneal fat; f, peritoneum. The external abdominal oblique and internal abdominal oblique muscles form the external rectus sheath and the transverse abdominis muscle forms the internal rectus sheath.

more cranial location. Caudal to the umbilicus, there is an increased amount of subcutaneous fat, resulting in a larger dead space after surgery, increasing the risk for postoperative wound healing complications. A ventral midline incision in mares can be extended as far as the pubic bone, splitting the udder into two halves. In male horses, for a caudal ventral midline incision the skin incision must be directed paramedian around the prepuce, and these structures must subsequently be reflected laterally to expose the linea alba.

Ventral Paramedian Celiotomy

The ventral paramedian approach, most often a right ventral paramedian approach, is an alternative to the ventral median approach and is the approach routinely used for colic surgery by some surgeons (Anderson et al., 2013). It may also be indicated in a horse with a repeat laparotomy after an initial ventral midline incision. Reasons to avoid reusing the ventral midline incision include an incisional infection or suspected intra-abdominal adhesions to the ventral midline. In addition, reopening an incompletely healed ventral midline incision may be associated with an increased risk for postoperative wound healing complications (Mair & Smith, 2005).

This approach differs from the ventral median approach in its location lateral to the linea alba, most commonly at a distance of 5–10 cm from the linea alba. Tissues layers transected with this approach include skin and subcutaneous tissue, the external rectus sheath, the rectus muscle, the internal rectus sheath, retroperitoneal fat, and the peritoneum (Figure 42.8). During transection of the rectus muscle, larger vessels may be encountered, and bleeding can be more pronounced than in a ventral midline incision.

Comparisons of the Ventral Median and the Ventral Paramedian Approaches

Although the ventral median incision is the approach most commonly used for a first ventral laparotomy in horses, some surgeons prefer the ventral paramedian incision for the initial approach to the abdomen. It has been suggested that the higher vascularity of the incisional margins of the ventral paramedian approach, because it is made through muscle, may aid in wound healing. In addition, the rectus abdominis muscle may help to support the viscera and thereby decrease tension on the external rectus sheath (Anderson et al., 2011).

The ventral median incision was biomechanically superior to a right ventral paramedian incision in a single cycle to failure bursting strength model. However, both incisions were thought to have adequate strength for *in vivo* use (Anderson et al., 2013). Wound healing complications after ventral paramedian incisions have compared favorably with ventral midline incisions (Anderson et al., 2011). In a study comparing the clinical and histological features of wound healing in a repeat ventral median or paramedian incision in horses 72 h after an original ventral median incision, both approaches for repeat laparotomy had similar tensile strength and similar incisional healing (Boone et al., 2014). In summary, both ventral median and ventral paramedian approaches can be used for initial and repeat laparotomies and should result in similar success rates for wound healing in clinical patients.

Ventral Median Celiotomy in Foals

In young foals, the umbilical vein is located dorsal to the linea alba and care must be taken to avoid incising this structure, especially if an umbilical infection cannot be ruled out. For this reason, some surgeons prefer a paramedian incision, at least for the initial opening of the abdominal wall. However, with careful technique, incision through the linea alba can also be used, and a small layer of retroperitoneal fat usually separates the umbilical vein and the linea alba. This approach is helpful if removal of the umbilical vein is necessary due to infection.

After incision of the skin, only small amounts of fat and subcutaneous tissue are visible, and the linea alba and its separation near the umbilicus can usually be seen (Figure 42.9). Incision of the linea alba should begin cranial to its separation near the umbilicus to avoid internal umbilical structures. After the initial incision, a finger is inserted dorsal to the linea alba and used to palpate the umbilical vein and bluntly separate it from the linea alba. Incision of the linea alba is continued with forceps guiding the scalpel as used in the adult (Figure 42.4). The peritoneum can then be bluntly penetrated on either side of the umbilical vein and torn longitudinally to open the abdomen (Figure 42.10). Umbilical resection can be performed at the end of colic surgery in foals if the foal is stable and anesthesia time is not overly long. This will eliminate the risk of the development of an umbilical infection.

Inguinal and Parainguinal Celiotomy

The external inguinal ring is a slit in the aponeurosis of the external abdominal oblique muscle and can be located by palpation. The abdomen can be approached through the inguinal ring and inguinal canal, and if needed the inguinal ring can be enlarged. When approaching the external inguinal ring, care must be taken to avoid damage to large vessels located in this region, particularly the external pudendal vein and its branches that pass through the abdominal wall through a foramen caudal to the inguinal canal. After sharp incision of the skin and fascia over the external inguinal ring, blunt dissection with two fingers can be used to dissect the loose connective tissue and approach the external inguinal canal. The inguinal approach most often is used to correct a nonreducible inguinal hernia or to locate a cryptorchid testicle.

As an alternative, the abdomen can be approached through a parainguinal incision. This approach is located craniomedial and parallel to the external inguinal ring. Using this approach, the large vessels encountered near the external inguinal ring can be avoided more easily and the incision can be longer than in an inguinal approach. A parainguinal approach can allow for easier exteriorization of some organs, for example the ovaries, than could be achieved using a ventral midline approach. Use of a parainguinal incision has been described for ovariectomies, cryptorchidectomies, and cystotomies and for the treatment of lesions involving the small colon.

Flank Laparotomy

A flank incision is not frequently used for colic surgery, but can be useful for certain lesions. In cases with a known diagnosis accessible by standing flank laparotomy, such as nephrosplenic ligament entrapment of the large colon, this approach can be useful and will eliminate costs and risks of general anesthesia. For some diagnoses, such as uterine torsion, a standing flank laparotomy may be the preferable approach. Not all regions of the abdomen are accessible through a flank incision, making a complete abdominal exploration impossible so that not all lesions can be detected or treated using this approach.

Figure 42.9 Appearance of the linea alba in the foal. Note the relative lack of subcutaneous fat in the neonate, with the faint white appearance of the linea alba separating toward the umbilicus (left of the figure).

Figure 42.10 Opening the peritoneal cavity in the foal. Note the umbilical vein coursing through the central part of the incision adjacent to the opened peritoneal cavity.

However, surgery for acute colic through a flank incision has been described as an alternative to a ventral midline celiotomy in cases with limited treatment options because of financial constraints (Hardy, 2003).

For most standing flank laparotomies, horses should be restrained in stocks. During some surgeries, such as correction of a uterine torsion, stocks can interfere with necessary manipulations and the flank incision can be performed without stocks. The tail should be wrapped to avoid contamination of the surgical field. For most procedures, light sedation with an α_2-agonist with or without butorphanol is sufficient. Local analgesia at the incision site can be achieved by a paravertebral block, an inverted L-block, or a line block, or by infiltration of the surgery site. Flank laparotomy can be performed on the left, right, or both sides depending on the suspected lesion and the procedure planned. The standard approach is midway between the tuber coxae and the last rib, beginning 2–3 cm above the prominent ridge of the internal oblique muscle and extending ventrally to the desired length. Skin and subcutaneous tissues are incised, exposing the external oblique muscle. For abdominal exploration, an incision using a grid approach may be sufficient. The grid consists of splitting all three muscle layers in the direction of their fiber alignment. This approach will result in less bleeding and less trauma and should reduce the rate of wound healing complications. For larger incisions, a modified grid approach is preferred over sharp transection of all muscle layers. In the modified grid approach, only the fibers of the external oblique muscle are transected with a scalpel, while the internal oblique and the transverse abdominal muscles are bluntly separated in the direction of their fiber alignment. In this approach, the intact internal oblique muscle edges can help keep the intestine inside the abdomen (Freeman, 2008; Hardy, 2003). For intestinal manipulation, all layers, including the external oblique muscle, the internal oblique muscle, and the transverse abdominal muscle, must be transected. After transection or separation of the muscle fibers, the exposed retroperitoneal fat and the peritoneum can be bluntly penetrated to open the abdomen.

A flank laparotomy incision carries a higher risk of wound healing complications than a ventral midline incision, if more muscle needs to be transected and if there is more manipulation with irritation of the incisional edges. Careful closure that minimizes dead space will limit incision complications.

Abdominal Exploration

Before exploring the abdomen, the surgeon applies waterproof sleeves to both arms if the gown does not include them, and then sterile saline is poured onto the sleeves to lubricate them and remove glove powder before the arm is inserted in the abdomen. Exploration of the abdomen is largely dictated by the preoperative findings, which are usually fairly accurate in determining if the small or large intestine is involved, but not at identifying the specific lesion (Blikslager & Roberts, 1995). Once the ventral abdomen has been opened, the affected bowel is usually immediately evident and, in some horses with advanced intestinal strangulation, the odor of necrotic tissue will be present. Intra-abdominal gas and odor will escape in horses with a ruptured viscus. Any abnormalities in peritoneal fluid should also be noted at this time, such as evidence of peritonitis (fibrin and excess serosanguinous or purulent fluid), rupture (luminal contents), and hemorrhage.

If the lesion cannot be seen or palpated immediately through a ventral midline incision, it is located by the following methods, combined with a sound knowledge of the abdominal anatomy of a horse in dorsal recumbency (Figure 42.11). Manual palpation of intra-abdominal contents is used locate a tight band, bowel distended with gas, fluid, impacted digesta or foreign material, bowel drawn tightly across the abdomen, an intra-abdominal mass or enterolith, mesenteric mass or abscess, thickened bowel wall, or distended bowel that can be traced into an internal site of strangulation. This part of the examination should be brief and, if it fails, the next step is to examine all of the intestine starting from a fixed or easily located segment.

To start a thorough examination, the apex of the cecum is exteriorized, which is usually the first structure found where it lies on the midline or to right of the midline with the apex directed cranially. The portion exteriorized is followed to the body and base of the cecum, and the correct alignment with the colon can be checked by tracing the lateral cecal band to the cecocolic ligament (Figure 42.12). In horses with small intestinal lesions, the cecum is empty and usually more to the right side, where it can be difficult to find. If the cecum cannot be found, it might be involved in a displacement. After the cecum has been partly exteriorized, the apex is drawn upwards to display the ileocecal fold as it traces from the dorsal cecal band to the ileum (Figure 42.13). Traction on the cecum should tense the band so that it becomes more obvious. From that point, the ileum (about 50 cm) is followed to the jejunum (20 m) to the duodenocolic ligament, which attaches the duodenum to the proximal small colon. The proximal 25–30 cm of jejunum, the distal 25–30 cm of ileum, and ileocecal junction cannot be exteriorized.

The ileum is distinguished from the jejunum by its thicker wall, less obvious vascular pattern on its wall, the ileocecal fold, and the single ileal artery along the mesenteric attachment, and, in some horses, hemomelasma ilei appears as hemorrhagic nodules on the ileal serosa

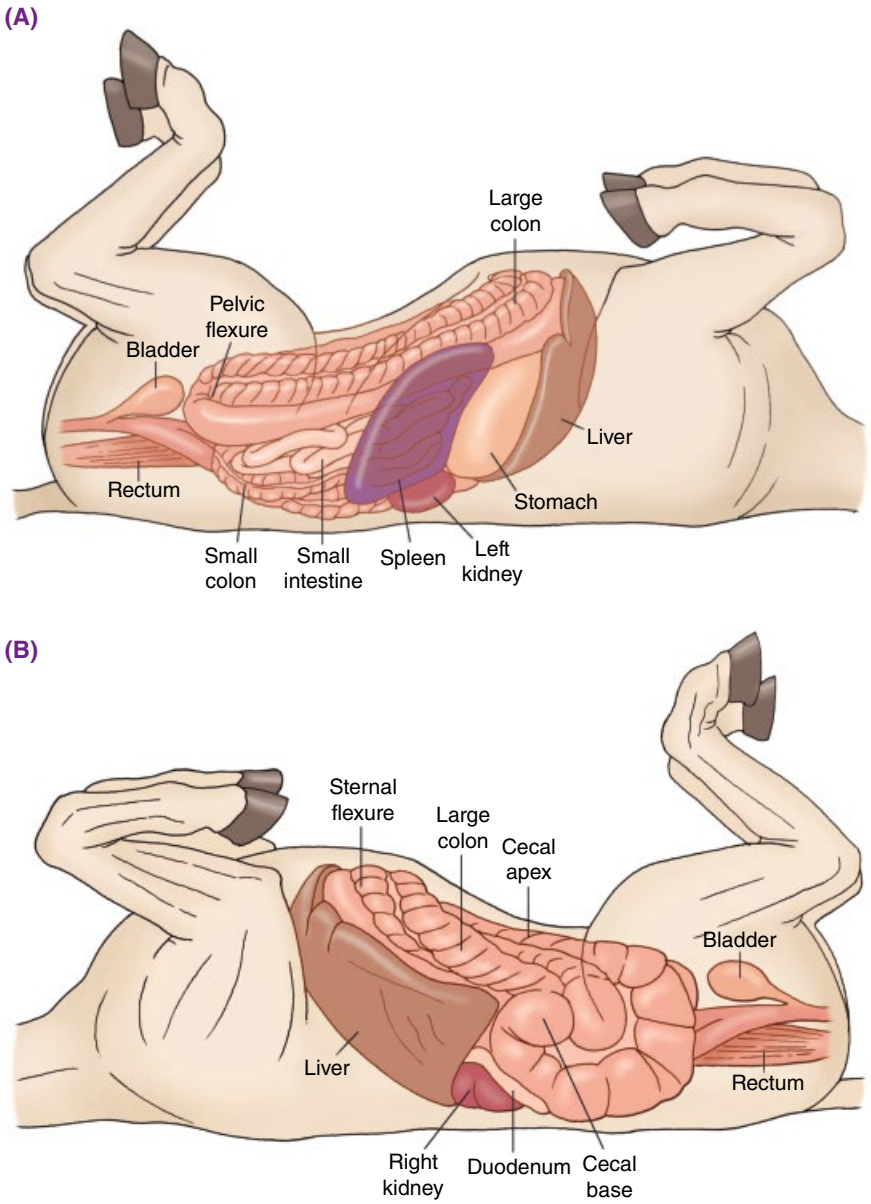


Figure 42.11 Diagram of the abdominal structures. The structures in the abdomen stay relatively fixed even when the horse is turned on its back. Structures in **(A)** include the stomach, left kidney, spleen, left colon, and small colon. Structures in **(B)** include the liver, duodenum, right colon, and cecum. Source: White, 1986.

(Figure 42.14). The cause of hemomelasma ilei is unknown, although this change is considered an incidental finding that does not create problems. In the horse in dorsal recumbency, the small intestine is located in the middle of the abdomen, dorsal to the large colon. If the distal small intestine is empty and collapsed, a more proximal strangulation should be suspected and sought by tracing orally. A segment of jejunum and a fold of associated mesentery are elevated from the abdomen and the mesenteric edge thus formed is traced to the cranial mesenteric artery and right kidney (Figure 42.15). Any abnormality in the cranial mesenteric artery, a mesenteric volvulus, or abscesses and enlargements in the lymph nodes in the mesenteric root can be found by this technique.

The lateral band of the cecum can be traced to the cecocolic fold and its attachment on the ventral aspect of the right ventral colon (Figure 42.13). From this point, the large colon (3–4 m) can be followed and exteriorized. Failure to find the cecocolic fold could indicate a colonic displacement. Parts of the large intestine can be recognized readily by location and characteristic bands or tenia. The cecum and right and left ventral colons have four bands, the left dorsal colon has one band that is buried in the mesenteric attachments and close to the mesenteric lymph nodes

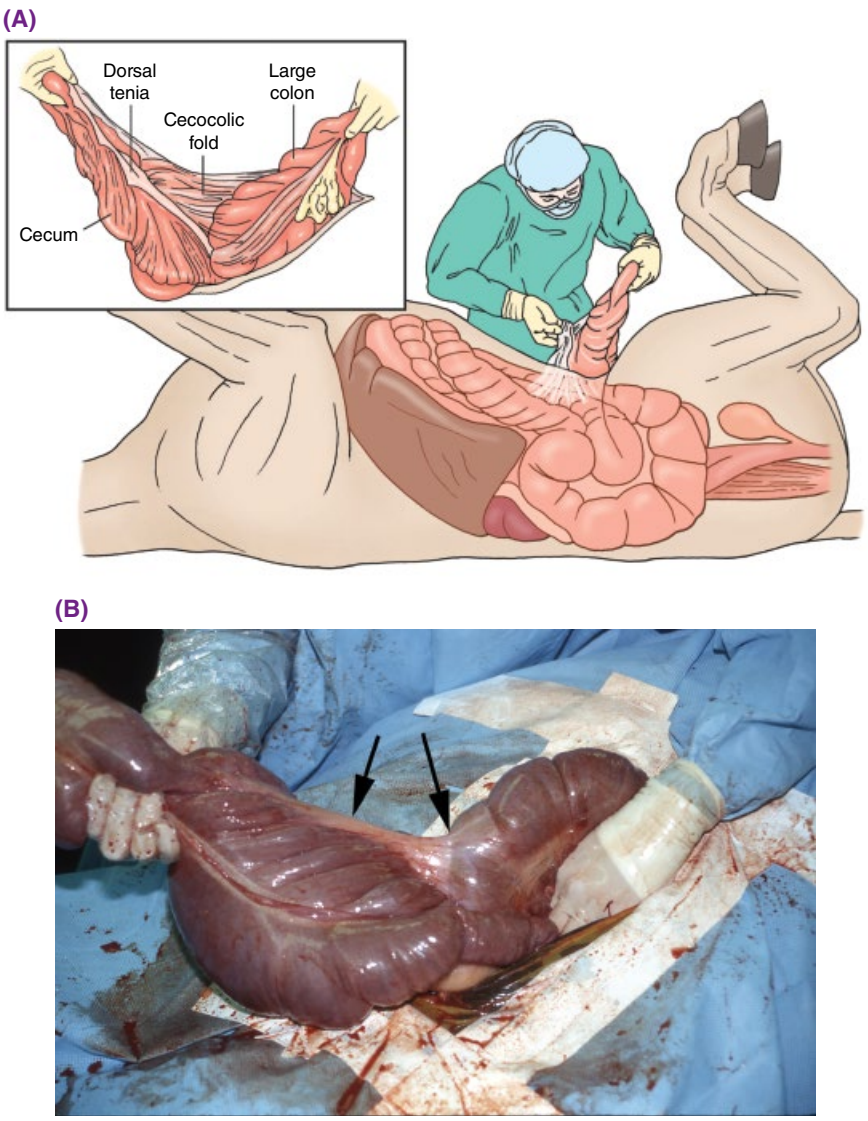


Figure 42.12 **(A)** Exteriorization of the cecum. The apex of the cecum is grasped and brought out of the abdomen and pulled caudally. The lateral band of the cecum is followed to the cecocolic fold, which attaches to the right ventral colon. **(B)** By elevating the cecum (left arrow) and right ventral colon (right arrow), the cecocolic fold can be seen connecting these segments of the intestine. Cranial is to the right. Correct visualization of the cecocolic fold confirms correction of a colon displacement. Source: White, 1986.

and colonic vasculature, and the right dorsal colon has three bands.

The small colon has two bands, one in the mesenteric attachment and the other that is antimesenteric (Figure 42.16). The mesentery of the small colon contains abundant yellow fat, except in severely underweight horses, and the small colon can be readily identified by fecal balls in the lumen. The pronounced sacculations disappear when the small colon becomes distended. The major mesenteric vessels of the small colon are obscured in the mesenteric fat, but the terminal branches are obvious for a short distance from the mesentery on the bowel wall and are closely spaced. Sacculations or haustra are obvious on the cecum and ventral parts of the large colon, disappear at the pelvic flexure and along the left dorsal colon, and are sparse and shallow in the right dorsal colon. The medial and lateral cecal bands contain cecal vessels and lymph nodes, but the dorsal and ventral bands are free of any vasculature. The ventral band does not extend as far as the others and ends close to the medial band.

The easiest method for examining the colon is to trace along the left parts toward the pelvic inlet where the pelvic flexure can be located. This part should be carefully cupped in the hand and then drawn back to the incision. The remainder of the colon is then worked out of the abdomen in segments and cradled over the surgeon's arm to elevate it away from the incision (Figure 42.17). It is critical that tension is not applied to the dorsal colon as it is elevated, especially if it is impacted, because it is

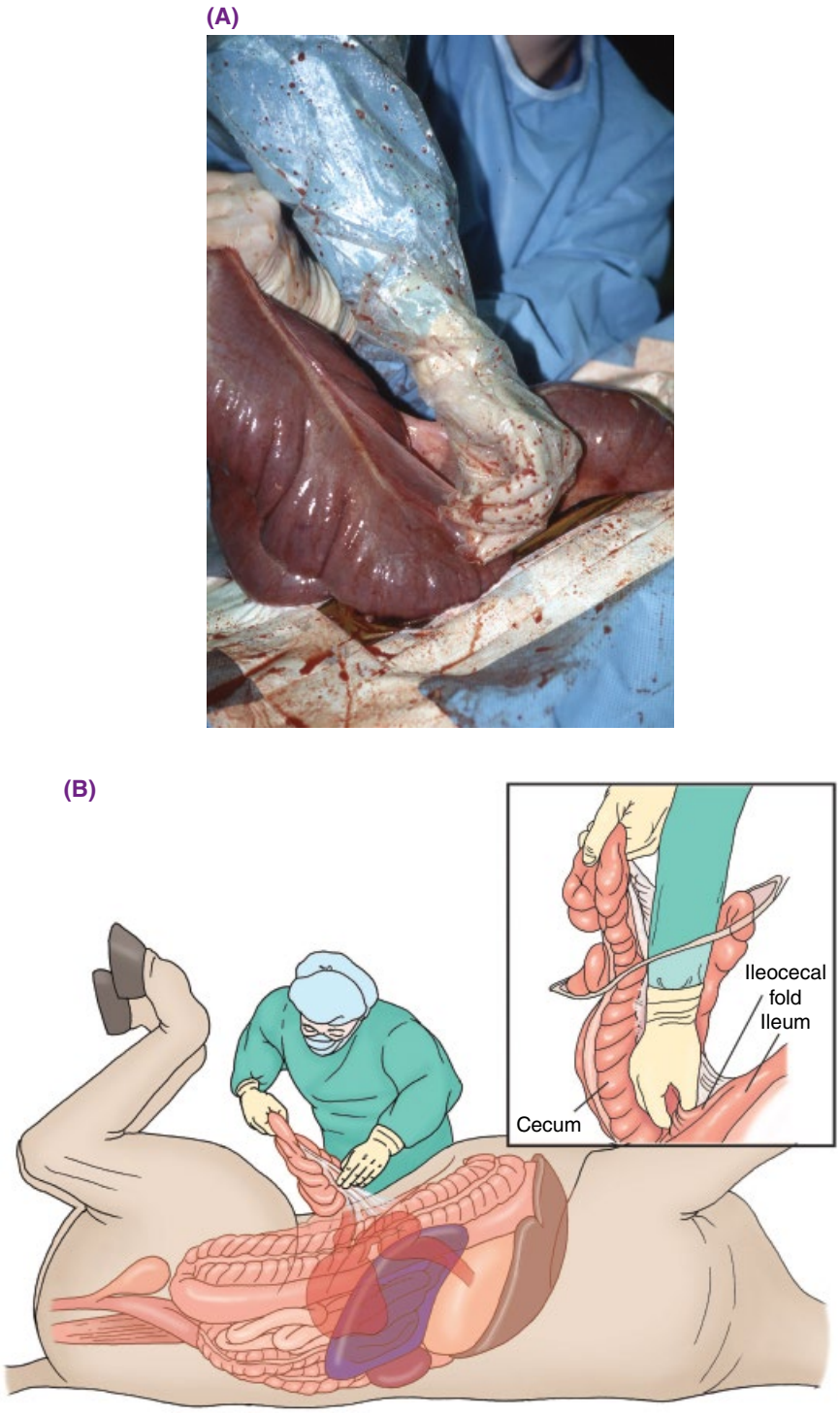


Figure 42.13 Identification of the ileum. To find the ileum, the dorsal cecal band is grasped **(A)** and followed into the abdomen **(B)**, where it forms the ileocecal fold on the antimesenteric surface of the ileum (inset). Palpating the ileocecal fold helps to locate the ileocecal junction and leads to the ileum, which is brought out of the abdomen to initiate examination of the small intestine by tracing it orally **(C)**. Source: White, 1986.

(C)

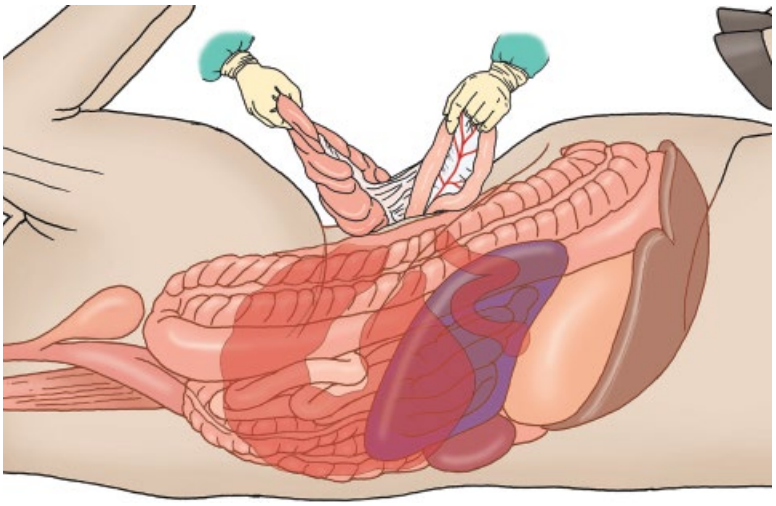


Figure 42.13 (Continued)

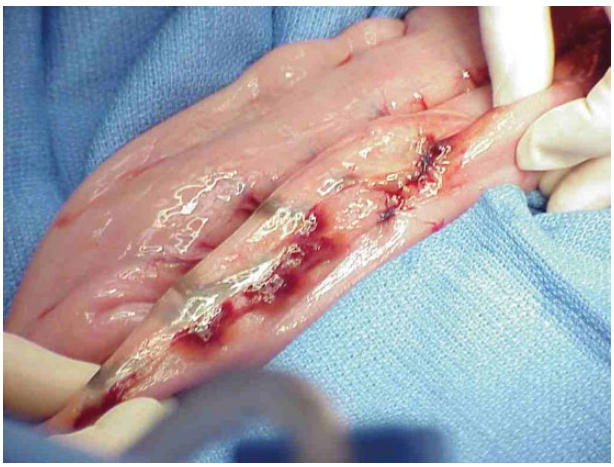


Figure 42.14 Typical appearance of a hemomelasma ilei. Note the focal hemorrhagic tissue on the ileum, grossly identified as hemomelasma ilei. This is considered a benign area of focal inflammation which is not related to diseases causing colic. Source: Courtesy of Anthony Blikslager, DVM.

prone to rupture close to its attachments to the dorsal body wall. The rectum (Figure 42.18) is traced to the aboral part of the small colon that cannot be exteriorized and then to a portion of the small colon that can be exteriorized (3–4 m), the transverse colon, and right dorsal colon. In the horse in dorsal recumbency, the small colon is located in the middle of the abdomen, further caudally than the small intestine. The transverse colon is too deep in the abdomen to see, but can be located running transversely across the middle of the abdomen by tracing the small colon orally or the right dorsal colon aborally (Figure 42.19). It should be palpated by a surgeon on the left side of the horse, for example, with the right hand coming from the right dorsal colon and the left hand from the small colon simultaneously to ensure that it is not impacted with an enterolith along the intervening portion.

Against the left body wall, the caudal edge of the spleen is traced manually to the dorsal edge, and then medially to the nephrosplenic (renosplenic) ligament, and left kidney (Figure 42.20). The dorsal edge of the spleen forms a sizable notch, dorsal to its line of attachment to the renosplenic ligament, which can trap large colon when displaced into this area. Both kidneys should be palpated for enlargement or renal calculi. When the small intestine becomes strangulated through a rent in the gastrosplenic ligament, the entrapped bowel can be palpated in the left cranial part of the abdomen, cranial to the spleen.

The vaginal ring is the point at which the peritoneum is evaginated into the inguinal canal to form the parietal layer of the vaginal tunic, and is different to the internal inguinal ring (Figure 42.21). The deep or internal inguinal ring is an approximately 15 cm line of separation between the muscular edge of the internal abdominal oblique and the inguinal ligament. The vaginal rings are on both sides of the abdomen, slightly ventral and cranial to the brim of the pelvis, and caudal to the muscular edge of the internal abdominal oblique muscle. Each ring is evident as a small, ventrally directed slit that will accommodate one or two fingertips, and is bound medially by a 2–4 cm long flap with the free edge dorsal to the opening. The rings are more obvious and larger and penetrated by well-formed testicular vessels in a stallion compared with a gelding, and small intestine can be palpated entering the vaginal ring in a horse with an inguinal hernia. In this part of the abdomen in a mare, the uterus should be checked for torsion and the broad ligaments for a hematoma from ruptured uterine artery or for a tear that has strangulated small intestine. The bladder can also be examined in this area (Figure 42.22).

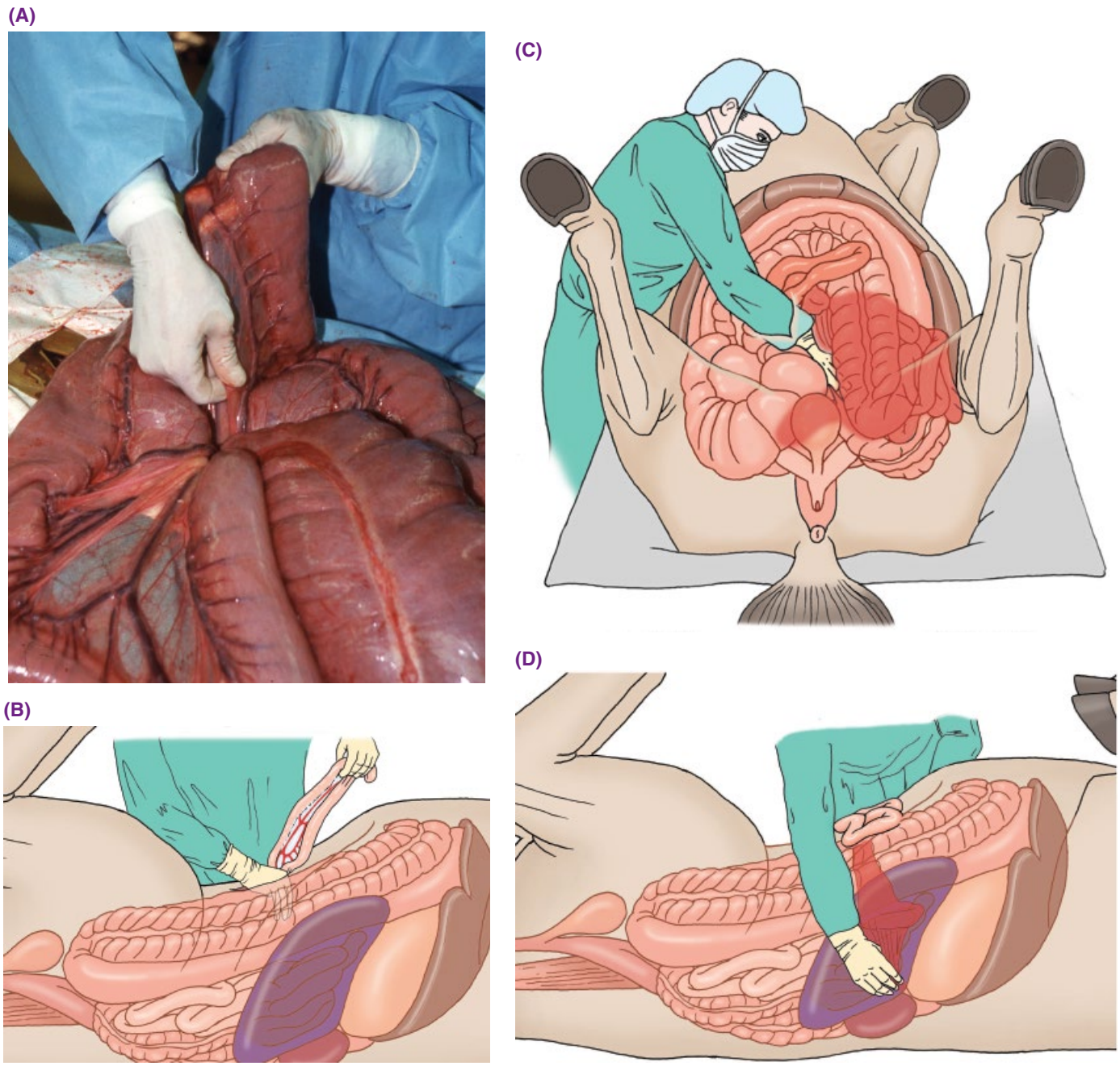


Figure 42.15 Examination of the mesenteric root. To examine the small intestine and the mesenteric root, one hand stretches the small intestine from the abdomen while the other hand is slid down the mesentery (**A** and **B**) to the dorsum of the abdomen. The mesentery is felt for any thickening and twisting that would indicate a volvulus. The attachment of the mesentery (highlighted) is on midline at the level of the first lumbar vertebra (**C** and **D**). Source: White, 1986.

In the cranial abdomen (Figure 42.23), the surgeon can palpate the stomach to left of midline, pylorus to right of midline, the duodenum (1 m long) along the right dorsal abdomen, the liver (right and left sides), and the diaphragm (Figure 42.24). The stomach is readily apparent when distended and can be recognized by the omental attachment and the prominent gastric veins and superimposed arteries that branch extensively toward the greater curvature. When empty, the stomach is flaccid, thick walled, and difficult to locate because it is not visible through most incisions and can be difficult to distinguish from the large colon by palpation. The pylorus is readily palpated as an approximately 8 cm long thickening in the transition zone between antrum and duodenum to right of midline (Figure 42.25). The duodenum, pylorus, and antrum can be exposed to view in foals but are rarely

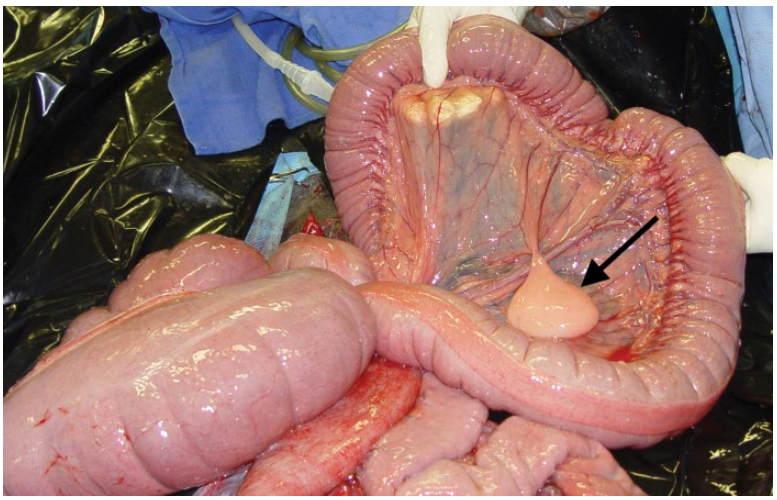
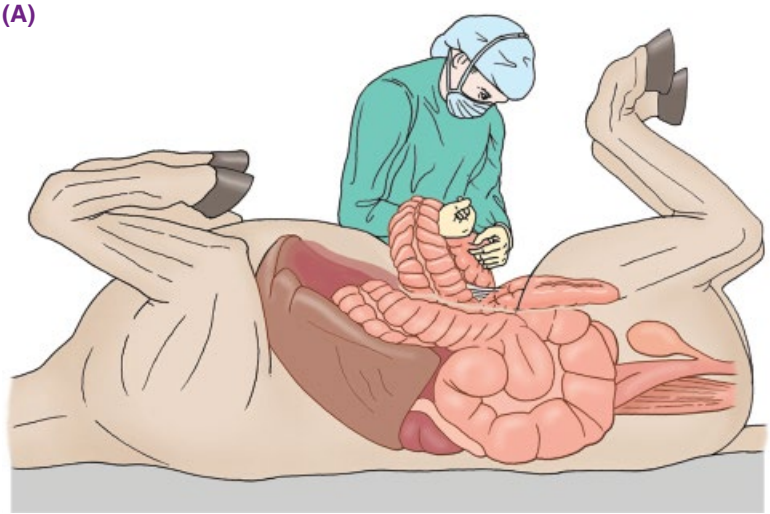


Figure 42.16 Examination of the small colon. The small colon has one tenia on the antimesenteric border. There is a lipoma on the small colon mesentery (arrow).

(A)



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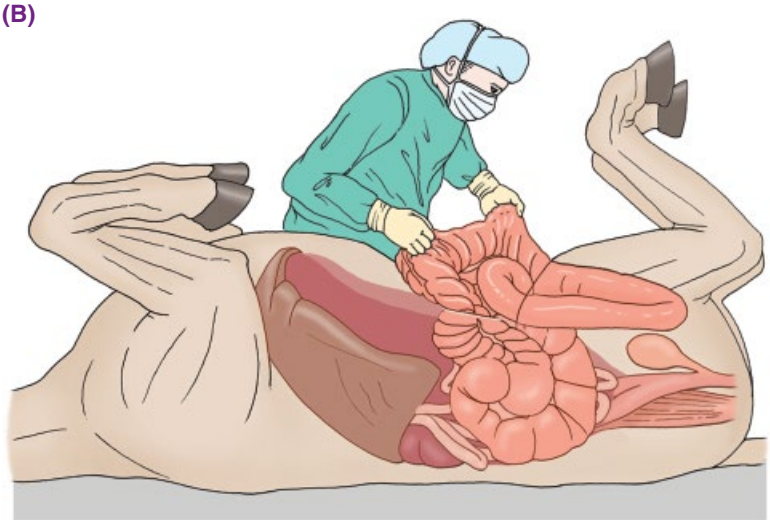
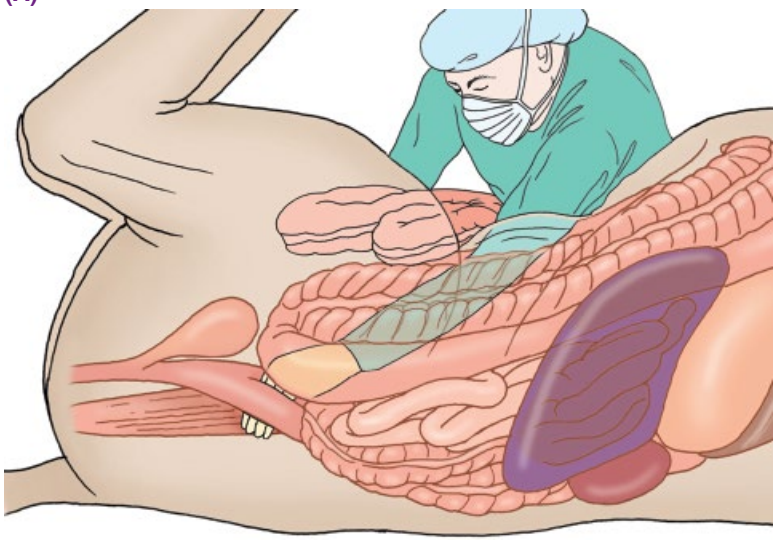


Figure 42.17 Exteriorization of the large colon. The large colon should be lifted carefully. Laying the colon over the forearm helps to elevate it out of the abdomen, decreasing the risk of seromuscular tears or rupture **(A)**. The entire colon is brought out of the abdomen for inspection **(B)**. Source: White, 1986.

(A)



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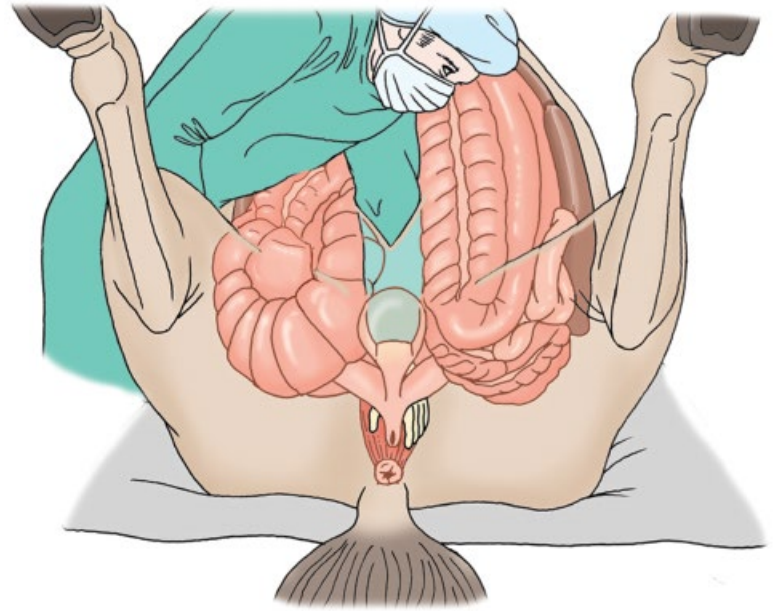


Figure 42.18 Palpation of the rectum. The rectum can be located in the pelvic inlet or by following the small colon aborally **(A)** and **(B)**. The right-handed operator will find it easiest to palpate the rectum from the left side of the horse. Source: White, 1986.

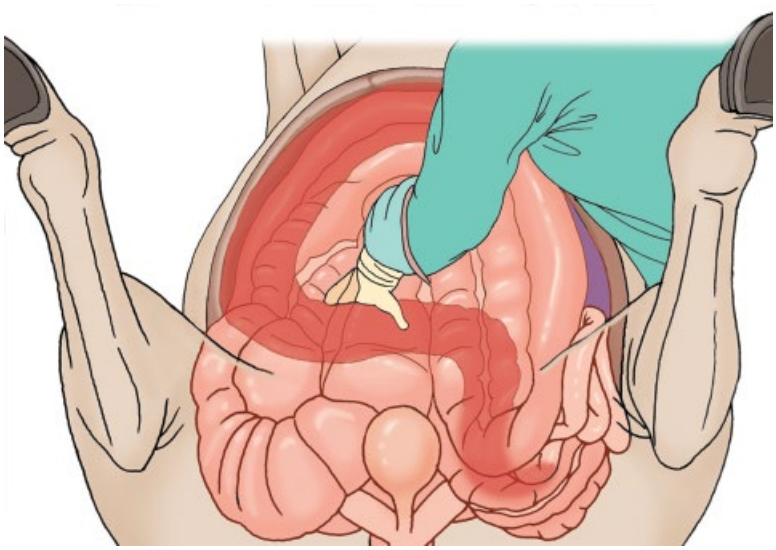


Figure 42.19 Palpation of the transverse colon. The transverse colon (highlighted) is palpated by following the right dorsal colon aborally or the small colon orally. It is found in the center of the abdomen just cranial to the mesenteric stalk and cannot be exteriorized. Source: White, 1986.

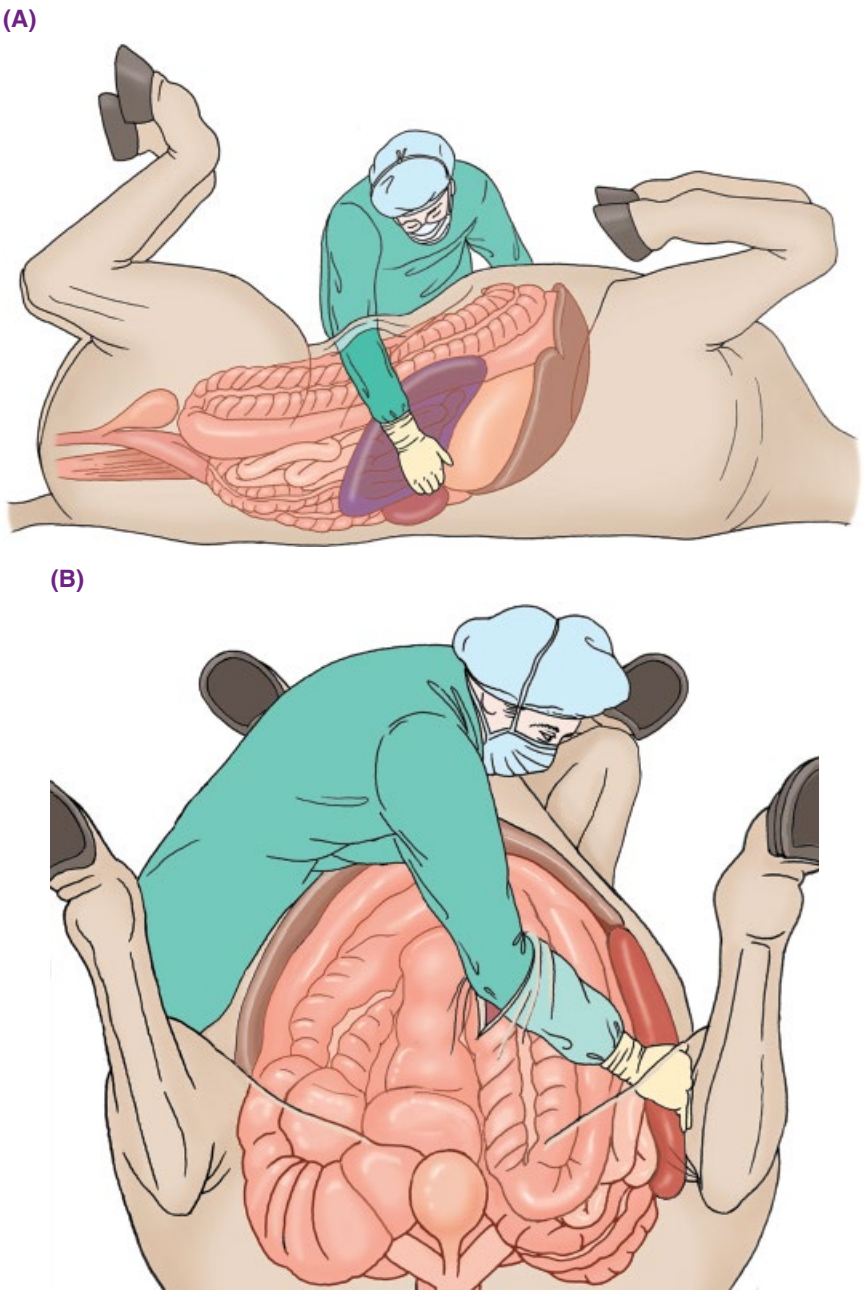


Figure 42.20 Palpation of the renosplenic space. The spleen and renosplenic space are palpated on the left side lateral to the incision by passing the hand dorsally along the caudal edge of the spleen **(A)** and **(B)**. The renosplenic space and the gastrosplenic ligament should always be checked for intestinal entrapment or incarceration. Source: White, 1986.

visible in adults through a ventral median incision. The diaphragm should be carefully palpated to detect any defects in it. The surface of the tendinous portion of the diaphragm is normally rough on palpation. On the left dorsal and cranial part of the abdomen, the left liver lobe can be found and part of it can be seen so that hepatic disease and enlargement can be determined by this means. The liver should be palpated for any evidence of rounding of the normally smooth and sharp edges, and a biopsy can be taken from the left lobe if needed.

To find the epiploic foramen, the surgeon stands on the left side of the horse and inserts the right hand through the most rostral commissure of the incision, to direct it with the arm at right-angles to the incision along the right body wall. When the fingertips encounter the edge of the liver, the fingers are traced medially along the visceral surface of the right lobe of the liver, until the caudate process and lobe are encountered. The fissure separating the right lobe from the caudate lobe is ignored and the back of the fingertips are traced medially along the caudate lobe until a slit-like passageway (1–3 fingers or 4 cm wide in a 450 kg horse) is encountered between the caudate lobe and the portal vein (Figure 42.26). This is the epiploic foramen. Incarceration of the small

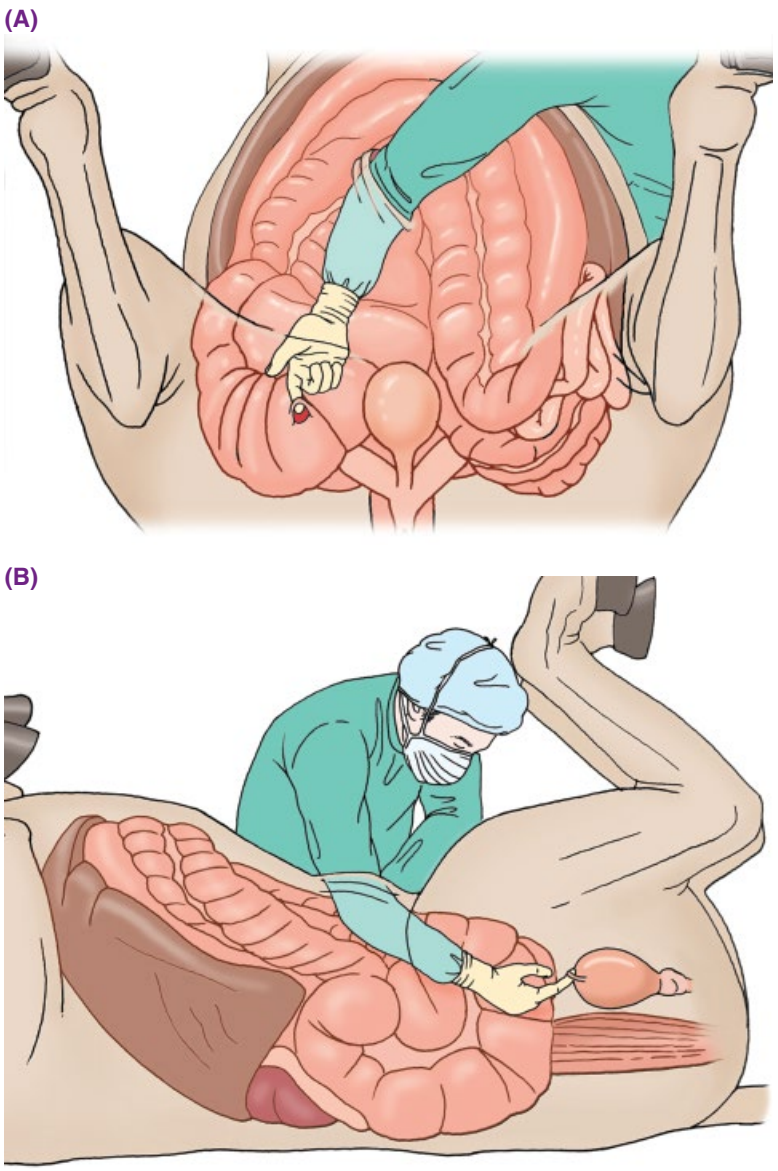


Figure 42.21 Palpation of the vaginal rings. The vaginal rings are found on both sides of the pelvis at the level of the pubis. The surgeon uses a forefinger to check the thin vaginal ring for entrapped intestines or adhesions **(A)**. The ductus deferens can be followed from the bladder to its entry into the rings **(B)** . The vaginal ring will vary in size in the stallion and will be closed in the gelding. Source: White, 1986.

intestine can pass from the right side of the abdomen into the omental bursa or from the left, rupturing the omental bursa, and palpated on the right side of the abdomen (Figure 42.27).

Examination and Handling of the Small Intestine

In a horse with extensive small intestinal strangulation and distention, loops of distended small intestine can emerge from the abdomen as soon as it is opened (Figure 42.28). If possible, the surgeon should resist exteriorization of several discontinuous loops, because these will only create taut mesenteric bands that will trap other fluid-filled loops as they are drawn from the abdomen, and slow the process considerably. Instead, the surgeon should exteriorize the affected loops in an orderly fashion, arranging them on the left side of the horse and maintaining their oral to aboral alignment. In this way, the bowel is positioned appropriately for jejunocecostomy (if required), it facilitates the flow of contents from oral to aboral during decompression, and decreases the risk of disorientation and incorrect positioning. For example, small intestinal volvulus usually involves several feet of small intestine that need to be exteriorized to allow rotation of the bowel in the direction required to correct the mesenteric twist, usually followed by drainage and jejunocecostomy. By exteriorizing all of the small intestine the mesentery can be followed to its attachment

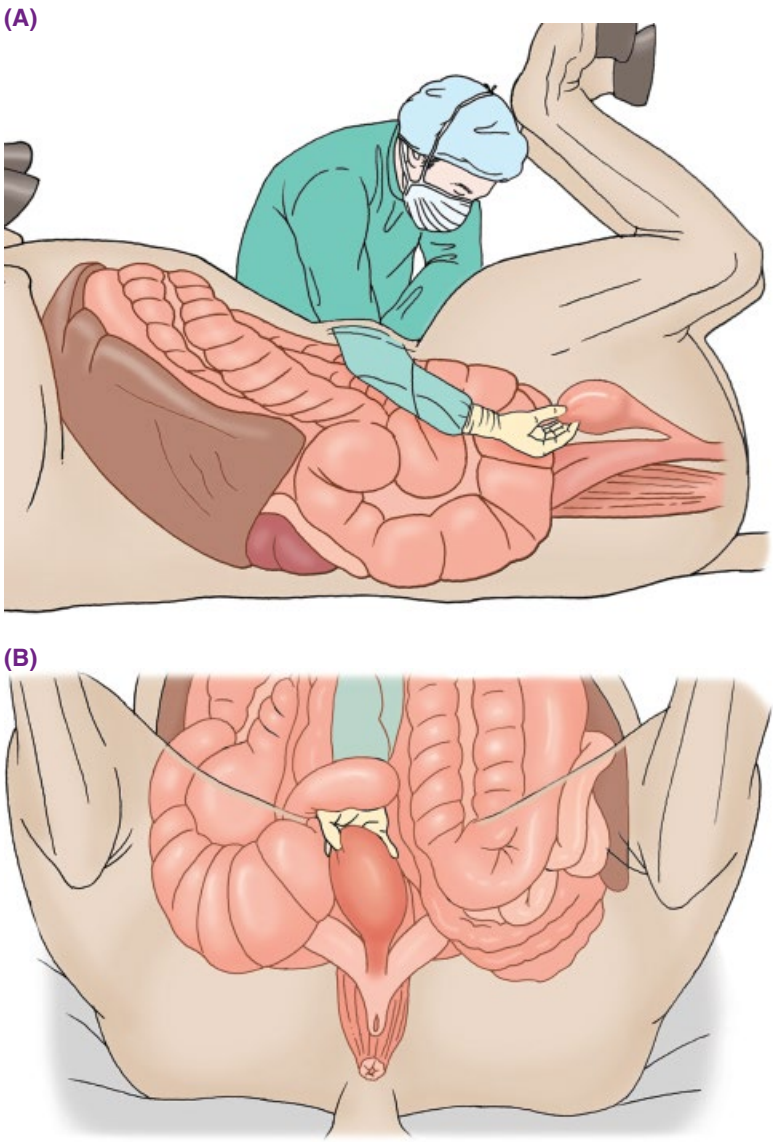


Figure 42.22 Palpation of the bladder. The bladder is easily palpated if distended and if empty feels like a thick elastic sac. The bladder is in the pelvic canal and can be identified on midline and ventral to the rectum (the uterus in the mare) **(A)** and **(B)**. The bladder can be exposed for inspection, but the incision must be made caudal to the umbilicus up to the pubis or parainguinal. Source: White, 1986.

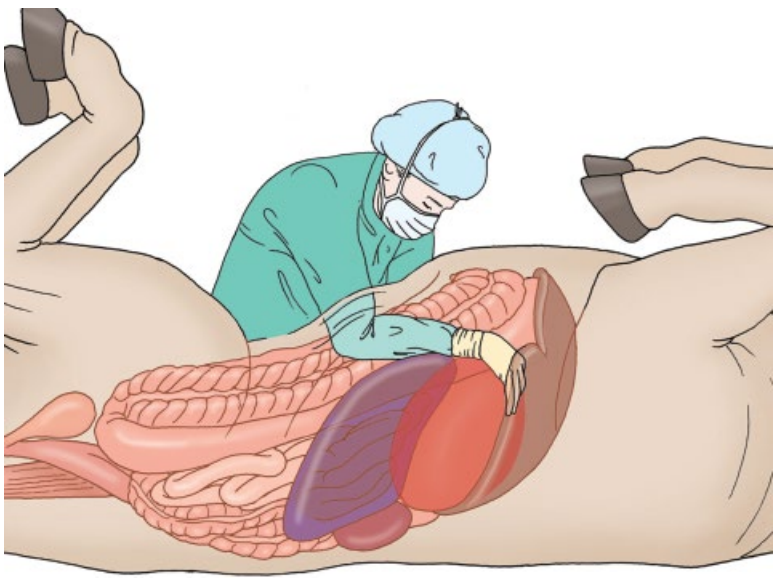


Figure 42.23 Palpation of the stomach and liver. The stomach and liver are palpated on the left side in the cranial part of the abdomen. The greater curvature of the stomach can be seen in the abdomen if the incision is made on ventral midline just behind the xiphoid or if the stomach is severely distended. Source: White, 1986.

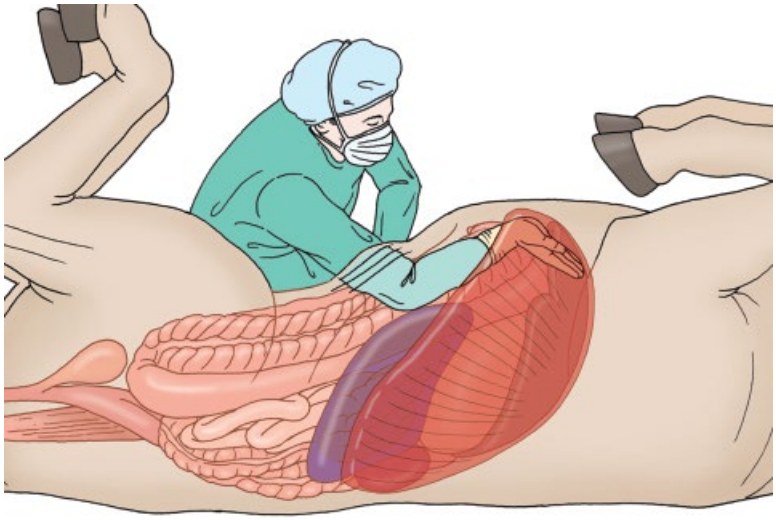
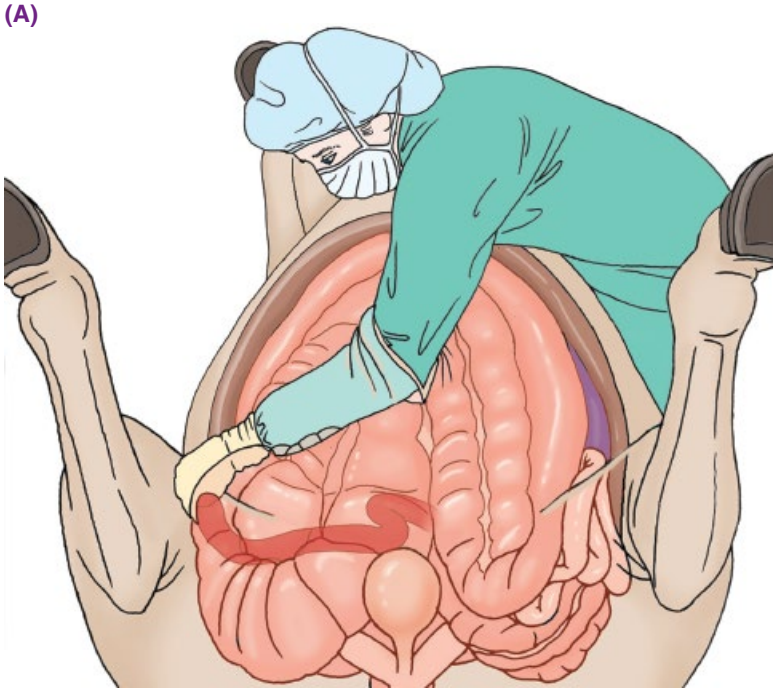


Figure 42.24 Palpation of the diaphragm. The diaphragm is palpated cranial to the stomach and liver. Most lesions occur in the ventral central portions of the diaphragm and in the central region at the musculotendinous junction. Source: White, 1986.

(A)



(B)

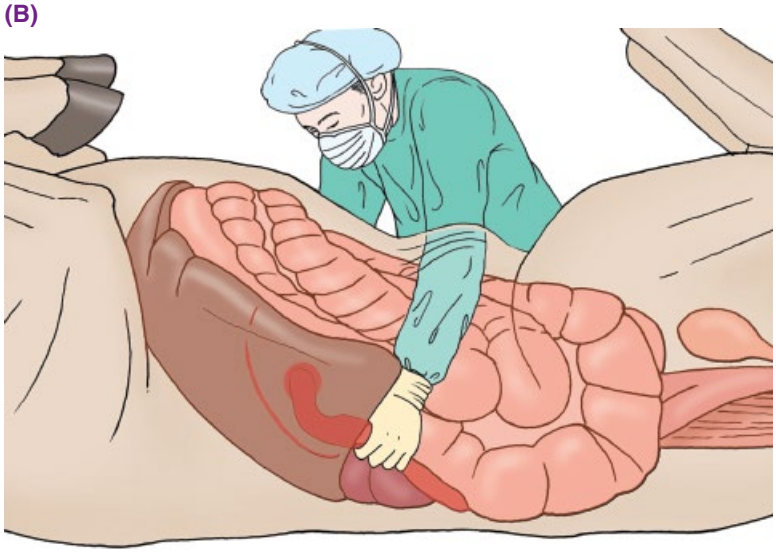


Figure 42.25 Palpation of the pylorus and duodenum. The duodenum and pylorus are palpated from the left side, reaching to the right with the left hand **(A)** and **(B)**. The duodenum is attached to the body wall by the mesoduodenum and is normally thin and pliable. The pylorus is normally muscular and thick and can only be seen through a ventral midline incision just behind the xiphoid by retraction of the intestine and the stomach. Source: White, 1986.

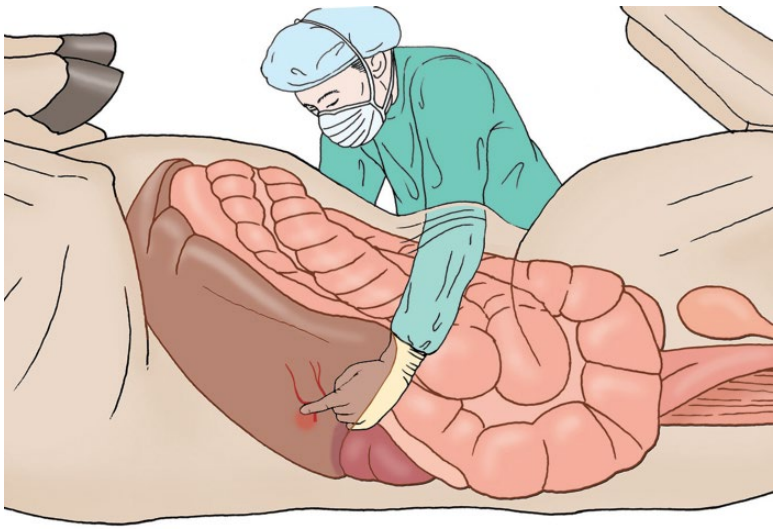


Figure 42.26 Palpation of the epiploic foramen. The epiploic foramen is palpated on the right side of the abdomen on the visceral surface of the liver between the vena cava and caudate lobe of the liver dorsally and the portal vein and gastropancreatic fold ventrally. This space should always be checked for incarcerations of the small intestine.
Source: White, 1986.

(Figure 42.15). The rotation of the surgeon's hand following a twisted mesentery is the direction the entire small intestine must be rotated to correct the volvulus. Once the volvulus has been corrected, the ileocecal ligament with its alignment of the cecum is exposed so the intestine can be followed to the duodenum (Figure 42.29).

Most lesions can be corrected by manipulating the distended bowel without an enterotomy. Small intestine must be handled carefully to prevent the fingertips from tearing intestinal wall and mesentery, especially in foals. Before the intestine is manipulated, the serosal surface is lubricated with sterile saline delivered from a spray bottle, a bulb syringe, or a rotary fluid pump. Some surgeons like to coat the bowel wall with sterile 1% sodium carboxymethylcellulose to facilitate handling.

Examination and Handling of the Large Intestine

Correction of large colon displacement requires recognition of the abnormal bowel orientation and returning the bowel to its normal anatomic position. The colon usually needs to be exteriorized and decompressed to accomplish this. Excess gas is removed by needle aspiration from an accessible portion of the cecum or colon before the abdomen can be adequately examined and before the colon can be exteriorized (Figure 42.30). After incomplete correction of a displacement, the cecocolic fold might be difficult to exteriorize or, if it can be exteriorized, but is directed caudally, further correction is required.

To correct large colon volvulus, the direction of the twist must be determined, and this is usually clockwise as viewed from the back of the horse (the ventral colon rotates in a medial and dorsal direction). As much colon as possible is exteriorized, both arms are placed deep in the abdomen, and the bowel is manipulated as close to the twist as possible with open flat hands. From the surgeon's perspective through the abdominal incision, the direction for derotation of large colon volvulus is clockwise (the ventral colon is rotated lateral and dorsal) in most cases. As the twist is corrected in the abdomen, the correction should then be applied to the exteriorized portion to eliminate resistance from this against further rotation of the intra abdominal segment. The most difficult part of correction is to turn the fluid-filled right dorsal colon around the right ventral colon.

To prevent rupture of bowel during manipulation and exteriorization, the surgeon must not grab the wall with fingertips and should relieve distention if necessary by needle decompression or by enterotomy. Some surgeons partly fill the abdomen with sterile saline or lactated Ringer's solution before they exteriorize the colon to help it float to the incision with minimal handling. The abdominal incision should be enlarged as needed to allow more room for manipulation of heavy bowel, to release entrapment of a heavy intra-abdominal portion as it is drawn out of the abdominal incision, and to remove some of the abdominal compression that holds the colon in place. The healthy colon is more likely to tear from tension than the strangulated colon, because the wall is thinner and more likely to stretch to its limit than the wall that is splinted by congestion and edema; however, the congested colon wall is more susceptible to tearing by finger penetration. Partial thickness tears, usually through the seromuscular layer (submucosa and mucosa intact) are not uncommon, but should be sutured, preferably after tension in the wall is reduced by removal of gas or fluid, or an impaction.

Special Circumstances

A mare in advanced pregnancy can pose a considerable challenge to complete exploration of the abdomen, because the gravid uterus can occupy a majority of the

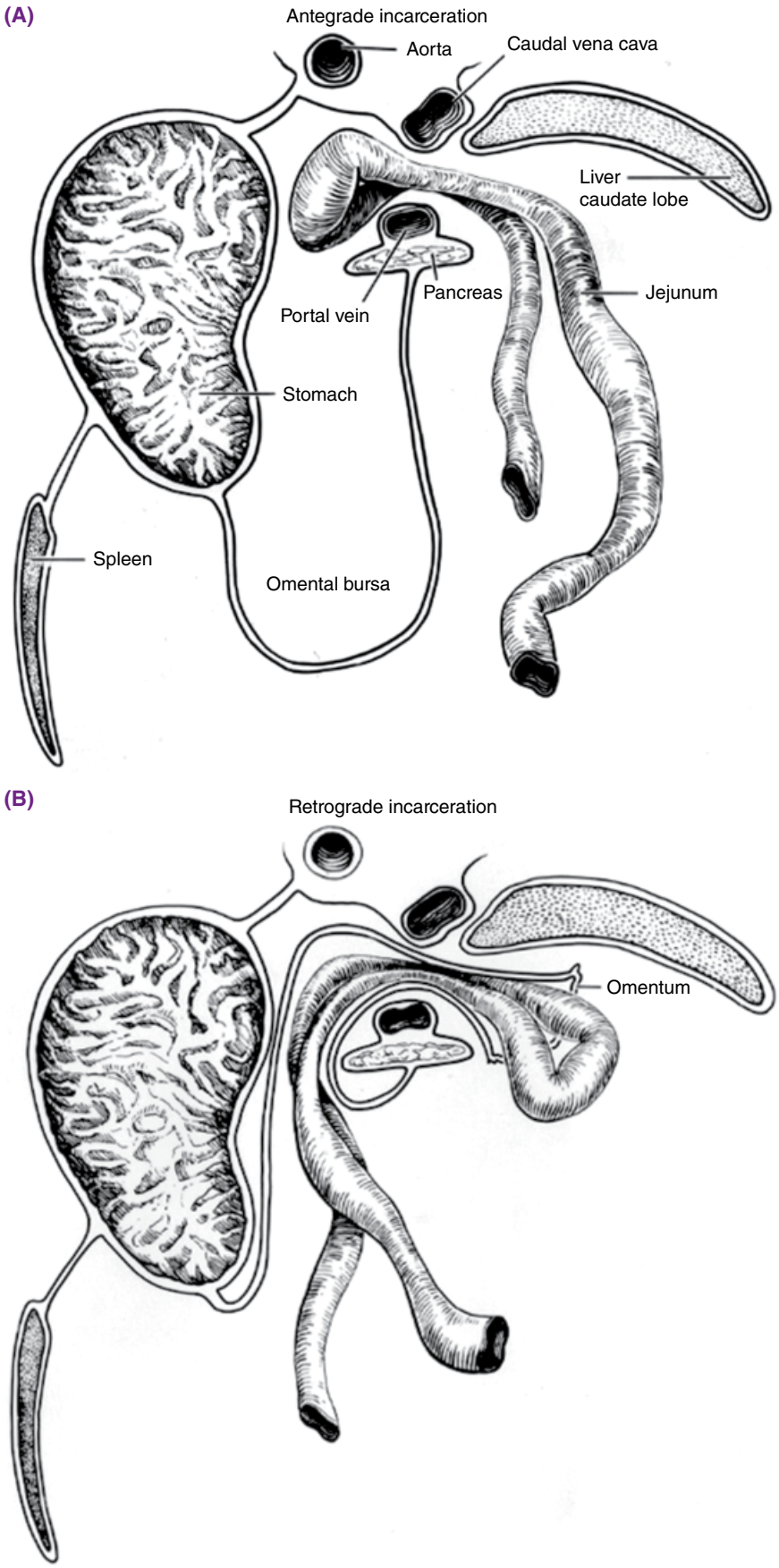


Figure 42.27 The small intestine can be incarcerated in the epiploic foramen passing right to left into the omental bursa **(A)** or left to right rupturing the omental bursa **(B)**.

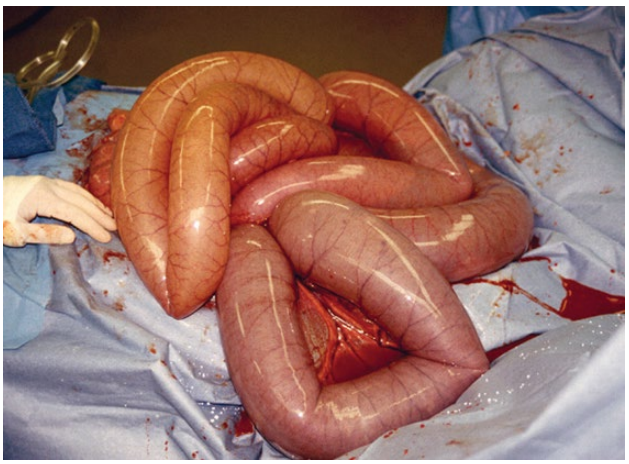


Figure 42.28 Typical appearance of strangulated small intestine emerging though the incision in a horse with a small intestinal obstruction.

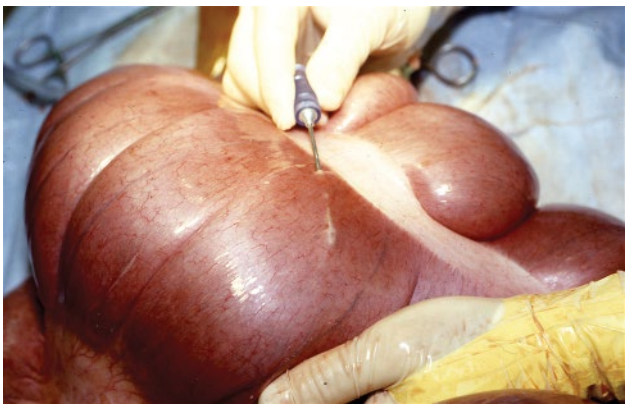
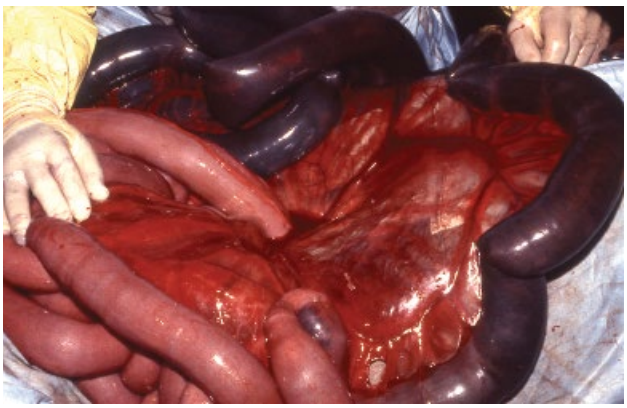


Figure 42.30 Decompression of gas may be necessary to allow a complete exploration of the abdomen. Puncture of the cecum or colon by threading a 16-gauge needle within the submucosa for 2–3 cm prior to puncturing the mucosa decreases contamination during needle removal. Connecting the needle to suction expedites gas removal.

(A)



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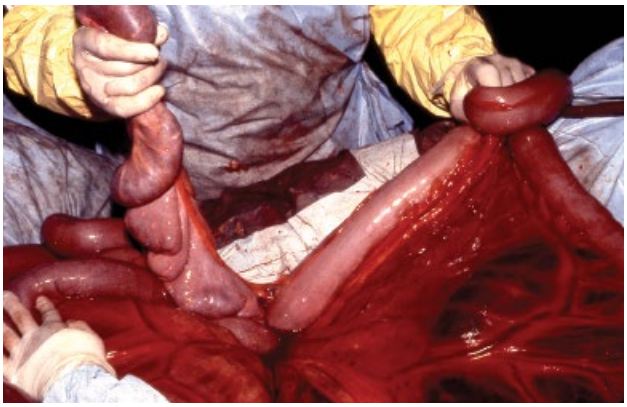

Figure 42.29 Presentation of a small intestinal volvulus with twisted mesentery preventing the normal anatomic alignment of the ileum and cecum **(A)**. The corrected volvulus allows the normal presentation of the cecum and ileum and enables the surgeon to lay out of the mesentery and small intestine in a normal position on the left side of the abdomen **(B)**.

abdomen and hinder access to many areas. However, thorough and complete examination and correction of the lesion should still be possible. Cesarean section should not be used as a means of facilitating the exploration and surgery, because this imposes another major procedure on the mare and jeopardizes the life of the foal if it is premature. In addition, it should be possible to complete the procedure under these conditions and the abdominal incision can be bolstered with retention sutures to protect it during a rough recovery from anesthesia.

Enteroliths are usually found in the right dorsal colon, transverse colon, and small colon, where they become tightly impacted and easy to identify as solid objects covered by stretched intestinal wall. Less solid foreign materials, such as plastic bags and rubber or bailing twine, can be less obvious when incorporated into a mass of intestinal contents. Also, an enterolith that has a flattened surface is a strong indication that others have formed in the colon, but these can be difficult to locate, especially smaller ones that are hidden in contents. Therefore, a thorough search through the large colon is indicated while its contents are drained through an enterotomy.

It is not unusual to find a segment of strangulated small intestine lying free in the abdomen, apparently displaced spontaneously from a strangulation. The cause of the strangulation is rarely found and there is little to be gained by searching for it in many cases. Exceptions are diaphragmatic defects, inguinal hernias, and some tears in the small intestinal mesentery; these should be sought because strangulation in them can recur. Diaphragmatic defects and obvious mesenteric tears should be repaired

immediately, although this can be difficult in many cases. The owner should be allowed the option of surgical prevention of an inguinal hernia as an elective procedure. In all horses that have evidence of a released small intestinal strangulation, the diaphragm must be examined carefully because a tear in this structure would be easy to implicate as the cause and repair would be strongly indicated (Dabareiner & White, 1999). If the horse fits the age category for a lipoma, the small intestinal mesentery should be examined as several may be found. A strangulating pedunculated lipoma that detached, spontaneously releasing the intestine, might be located by a manual sweep of the abdomen or might float to the surface during abdominal lavage. Failure to find a detached lipoma does not appear to cause future problems.

Although lipomas are less common in the small colon than the small intestine (Garcia-Seco et al., 2005), the small colon mesentery should be examined for lipomas if a strangulating lipoma is found in the small intestinal mesentery (Figure 42.16). More importantly, the remainder of the small intestinal mesentery should also be searched for other lipomas, and those that have an obvious stalk and are close to the intestinal attachment should be removed, regardless of size. The long-term prognosis is good enough after colic surgery that remaining lipomas will have time to enlarge, acquire a stalk, and strangulate bowel.

In horses with clinical signs of large colon volvulus or some strangulating lesion of the large colon, the colon can be found in its normal position, but with obvious edema and congestion, as if it had experienced recent compromise of blood flow. It is not unusual to find no abnormality in a horse that had evidence of a surgical lesion beforehand, suggesting spontaneous correction of a displacement. Relaxation of the abdominal muscles under general anesthesia, rotating the horse into dorsal recumbency, and elevating the horse onto the surgery table are all procedures that could lead to spontaneous correction before the abdomen is opened.

Rarely, a horse may suffer from two, apparently unrelated, strangulating lesions of the small intestine (Van der Velden, 1989) or from a strangulating lesion (inguinal hernia) and a secondary small intestinal volvulus (Moll et al., 1991). More commonly, a small intestinal lesion and a large intestinal lesion can develop concurrently in the same horse (Stephen et al., 2004). History and known risk factors (e.g., sand ingestion, previous surgery) should also prompt examination of the structure most likely affected when the primary surgical lesion is not related. Regardless, a thorough exploration should be completed in all cases, and can be performed rapidly with or without extra-abdominal examination of intestine.

Not all causes of colic are related to the gastrointestinal tract, and this should be considered when the abdomen is explored. For example, splenic infarction has been reported to cause mild colic and intra-abdominal hemorrhage (Roy et al., 2000); subcapsular splenic hematoma can cause mild colic. Anemia, anorexia (McGorum et al., 1996), and splenomegaly have been documented as rare causes of recurrent colic (Varra & Nelson, 1976). Torsion of the liver involves the left liver lobe and should be suspected based on preoperative ultrasonographic findings, changes in liver enzymes, and finding hemoperitoneum and a necrotic odor during surgery (Turner et al., 1993). In normal horses, the common hepatic duct is 1.0–1.5 cm wide and 5 cm long and not readily located, but, in horses with cholelithiasis, this duct is an enlarged can be palpated on the right side of the abdomen, close to the duodenum, about 12–15 cm from the pylorus (Traub et al., 1982). Usually, preoperative elevations in liver enzymes, preoperative ultrasonographic findings, and marked liver enlargement at surgery will direct the surgeon to examine this area. In the same location, swelling and hemorrhage might be evident in cases of pancreatitis, which is rare (Baker, 1978). The adrenal glands are rarely the site of disease in horses, although ruptured pheochromocytoma can cause nonspecific signs that can be confused with colic and lead to exploratory celiotomy (Yovich & Ducharme, 1983). These glands are embedded in retroperitoneal fat on the medial and cranial poles of the kidneys and measure approximately 8 cm long, 3–3.5 cm wide, and up to 1.5 cm in thickness.

Intestinal Placement

After exploration is completed, the bowel is returned to the abdomen and replaced according to its normal anatomic position in the dorsally recumbent horse (Figure 42.11). The large colon is replaced first, usually by elevating the left segments and using gravity and manipulation to place the sternal and diaphragmatic flexures in the cranial part of the abdomen. The left ventral and dorsal colons are then positioned to the left of the incision, while the pelvic flexure is grasped gently in one hand and worked back into the caudal abdomen. The small colon is positioned in the caudal part of the abdomen and the small intestine is placed in the middle of the abdomen, between the right and left parts of the large colon. The cecal base and body are positioned as far caudally as possible, and the apex is then replaced so that it can be laid under the abdominal incision and thereby act as a means of retaining loops of small intestine in the abdomen. If lesions have been corrected and all bowel arranged and replaced according to the recommended system, no special attempts need be made to prevent any error in placement.

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43

Intestinal Viability

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Determining intestinal viability is a critical part of intraoperative decision making by the surgeon. It has been proposed that enhanced methods of assessing tissue viability could improve long-term survival after colic surgery by better informing the need for resection (Gonzalez et al., 2015c; Proudman et al., 2002). Currently, the determining factors for and against resection remain controversial among surgeons (Fiege et al., 2015). The proponents for resection argue that debulking compromised tissue removes the source of possible postoperative complications. However, resection is not an option when the affected bowel is inaccessible or too much bowel is involved. Additionally, intestinal resection is not a benign procedure and is associated with multiple complications that include anastomotic site stricture or leakage, peritonitis, and incisional infection. Finally, resection increases the financial impact on the owner that may limit postoperative treatment options. Accurate determination of tissue viability is therefore key to prognosis and intraoperative decision making.

Small Intestine

In horses with colic necessitating exploratory celiotomy, the best outcomes are usually associated with resolution of disease during the first surgery. Furthermore, in many cases, a second surgery may not be an option. Therefore, in cases with diseased bowel, the intraoperative decision by the surgeon to resect or not is critical to outcome. Decreased short- and long-term survival rates and also a high rate of repeat celiotomy, adhesion formation, and progressive bowel necrosis are all associated with small intestinal segments incorrectly judged as viable and left *in situ* (Mair & Smith, 2005; Parker et al., 1989). However, intestinal resection is not a benign procedure and is associated with a multitude of disadvantages. These include extra expense, complications (adhesions, anastomotic complications, and short bowel syndrome) and increased duration of surgery. The expense of resection, due to longer anesthesia time, more complicated surgery, and intensive aftercare, could lead an owner to elect for intraoperative euthanasia. Increased duration of surgery needed for resection could also extend the anesthesia time beyond safe limits for horses of large body size or mares in advanced pregnancy. In addition, some portions of the bowel are inaccessible for surgical resection. Finally, extensive bowel resection may lead to the development of malabsorption, resulting in chronic weight loss and unthriftiness (Freeman et al., 2000). In such cases, leaving damaged bowel in place and recovering the horse may be a reasonable decision. This option is further strengthened by the fact that the intestine is amazingly resilient and injured intestine has an incredible capacity to repair (see Chapter 2) (Gonzalez, 2015). Furthermore, the short duration of surgery and the decreased expense without resection together with the relative lack of complications all make leaving injured, but viable, bowel a more acceptable choice than performing a high-risk anastomosis (Freeman et al., 1988a, 2001). Therefore, it is critical that the surgeon weigh the risks and benefits of leaving compromised bowel *in situ* against those of small intestinal resection.

Clinical Judgment

Clinical criteria of viability are serosal color, bowel wall thickness, presence or absence of mesenteric arterial pulses, spontaneous motility or motility evoked by snapping a finger against the intestinal wall, and improvement in color after correction of the strangulation. In the normal bowel, snapping a finger against or pinching the bowel wall will induce motility, and will also create a transient focal contraction that appears as a blanched raised plaque of muscle activity. Spontaneous or evoked

The Equine Acute Abdomen, Third Edition. Edited by Anthony T. Blikslager, Nathaniel A. White II, James N. Moore, and Tim S. Mair.

Companion website: www.wiley.com/go/blikslager/abdomen

motility can appear sluggish in viable strangulated bowel, however, because edema and hemorrhage thicken the wall, creating a physical barrier to the muscular contractions. Gross signs of edema and hemorrhage are common because most strangulations are classified as hemorrhagic owing to occlusion of venous return prior to arterial delivery of blood to the affected segment. Veins are thin walled compared with arteries and are therefore less resistant to occlusion. This results in the palpable wall thickening and the purple to black discolored appearance of the bowel that is associated with strangulation. These gross alterations, however, do not signify an irreversible change. In fact, short intestinal segments with these changes may survive and, depending on the degree of damage, the intestine may not be predisposed to intraabdominal adhesions (Freeman et al., 2014). For this reason, additional methods to help determine tissue viability have been and continue to be studied. Unfortunately, enterotomies performed to evaluate mucosal appearance as a means to determine tissue viability are currently considered of little use. The mucosa is the first and most severely affected of all the intestinal layers following intestinal ischemia and therefore may erroneously lead a surgeon to perform resections (Figure 43.1) (Freeman et al., 1988b). Furthermore, performing an enterotomy to obtain a biopsy could introduce a site for adhesion formation. For this reason, the risk of enterotomy to assess viability outweighs the benefit and contributes little to the clinical picture. This recommendation, however, may change with the development of new tests to determine tissue viability (Kinnin et al., 2014). Improved methods of assessing small intestinal viability could reduce unnecessary resection and anastomosis and improve long-term survival (Proudman et al., 2002; Freeman et al., 2014). This is important because horses with strangulating obstruction of the small intestine that requires resection have a poorer short-term survival than horses with simple obstruction of the small intestine not needing resection (Mair & Smith, 2005).

Methods of assessing viability in equine (pony) jejunum have been compared with clinical judgment in only one study (Freeman et al., 1988b). In that study, all intestinal segments recovered from different types of ischemia without developing complications, including adhesions, although clinical judgment and fluorescein fluorescence predicted otherwise (Freeman et al., 1988a, 1988b). Interestingly, another study using identical types and durations of ischemia to injure the jejunum resulted in adhesions (Sullins et al., 1985). However, similarly to the previously described study, the fluorescein pattern remained inaccurate for determining tissue viability (Sullins et al., 1985). Differences between the studies that could have favored the formation of adhesions in the one study were strangulation of four segments versus one segment per animal, more traumatic methods for inducing ischemia, and omission of antibiotics and flunixin meglumine in the postoperative management (Sullins et al., 1985; Freeman et al., 1988a).

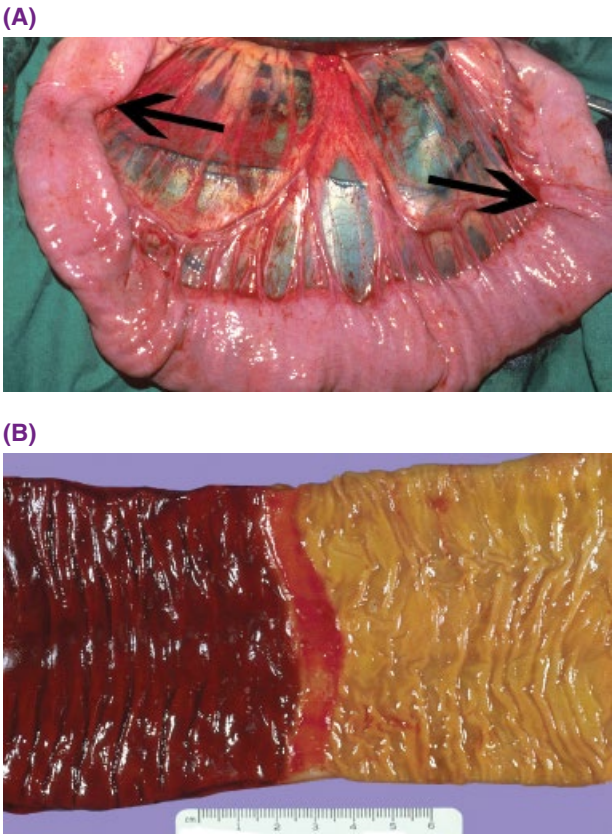

Figure 43.1 Segment of jejunum 15 min after it was subjected to 3 h of arterial and venous occlusion (**A**, between arrows). Although the bowel appears viable based on the appearance of its serosal surface, the mucosal surface of a segment treated in a similar manner has undergone more severe changes **(B)**.

A retrospective evaluation of short- and long-term outcomes in horses after surgery for small intestinal strangulating lesions led to the development of a clinical grading system for small intestinal viability (Table 43.1) (Freeman et al., 2000, 2001). In that study, horses with segments scored as grade I, II, and III (Figure 43.2, Figure 43.3, and Figure 43.4) did not have a resection and had a more favorable outcome than horses that had resection (Freeman et al., 2000, 2001). Although the former horses had milder intestinal lesions than the horses that required resection (Figure 43.5 and Figure 43.6), they were also allowed to recover from surgery with those lesions *in situ*, which could have placed them at risk for development of adhesions (Sullins et al., 1985). However, they did not appear to be at any greater risk for adhesions than those that had a resection. Factors that tended subjectively to worsen the prognosis for these horses were prolonged surgeries, failure to decompress distended bowel at surgery, and failure to distinguish accurately between grade III and grade IV lesions (Figure 43.7). In a more recent study, these classifications were modified by dividing the original grade III score

Table 43.1 Grades of mucosal injury used to decide on the need to resect strangulated small intestine (Freeman et al., 2014).

Grade	Features
I	Improves within 15 min after correction of the lesion and is similar to healthy adjacent bowel, but slightly darker pink, with mild edema and ecchymoses (Figure 43.2). Motility spontaneous or induced by snapping a finger against the intestinal wall
II	Improves within 15 min after correction of the lesion and has marked edema, with extensive ecchymoses, coalescing into diffuse patches of red against a background of dark pink, and no circumferential constrictions at points of strangulation (Figure 43.3). Motility is weak or induced by snapping a finger against the intestinal wall
III	Similar to Grade II, with one or more of the following: black strips or patches against a red background (Figure 43.4), and/or constrictions at points of strangulation that are equal to or less than half the intestinal circumference
IV	Improves slightly or not at all within 15 min after correction of the lesion, and is predominantly dark red, blue, or purple (Figure 43.5), has little or no motility even after snapping a finger, has bowel wall thickness ranging from thin to thick, has presence or absence of black striations, has a necrotic odor, or has constrictions at points of strangulation
V	Diffusely gray, black, or green discoloration, amotile, with or without necrotic odor (Figure 43.6).

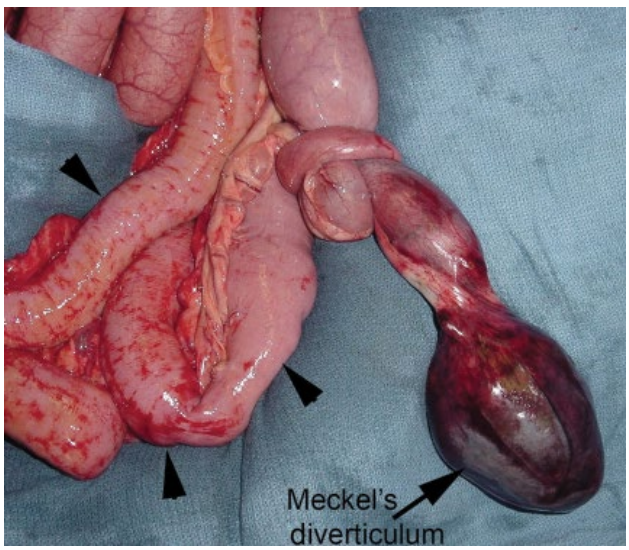

Figure 43.2 Grade I changes in a segment of foal jejunum and ileum (to the left, arrowheads) involved in strangulation by a Meckel's diverticulum (arrow).

into a modified classification of grade III and grade IV and by changing grade IV to grade V (Freeman et al., 2014). This study found that this subjective method of assessing small intestinal viability could reduce the need for resection and anastomosis. However, it is important

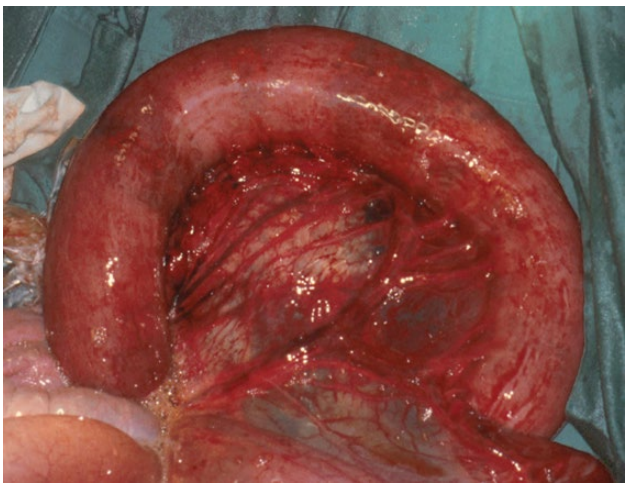

Figure 43.3 Grade II changes in small intestine that was strangulated in the epiploic foramen and was not resected. The horse recovered and did not develop a known problem over a 2 year follow-up.

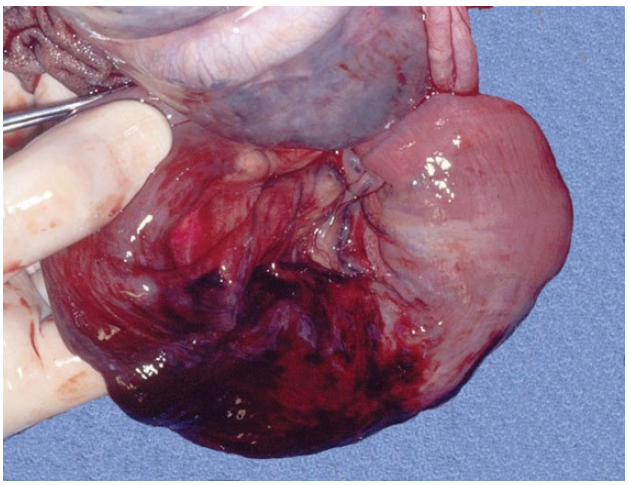

Figure 43.4 Grade III changes in jejunum strangulated in an inguinal hernia. Note that the changes are grade II in the segment in the surgeon's hand but the black discoloration was attributed to hemorrhage in that portion.

to note that the number of cases with the most severe grades of injury were too small to allow conclusions that such segments should be left *in situ*.

A grading system such as that already described is potentially valuable. The basic premise of such grading systems is that changes consistent with early venous strangulation obstruction are consistent with a correct viability score. Such changes include red discoloration and even some black patches or stripes in the bowel with a thick and edematous wall (Figure 43.2, Figure 43.3, and Figure 43.4). Bluish discoloration of the bowel (grade IV and V) suggests arterial occlusion and potentially a poorer prognosis for survival, especially if the affected area of bowel wall is thin. Even a small area of bluish discoloration or an area that ultimately becomes nonviable

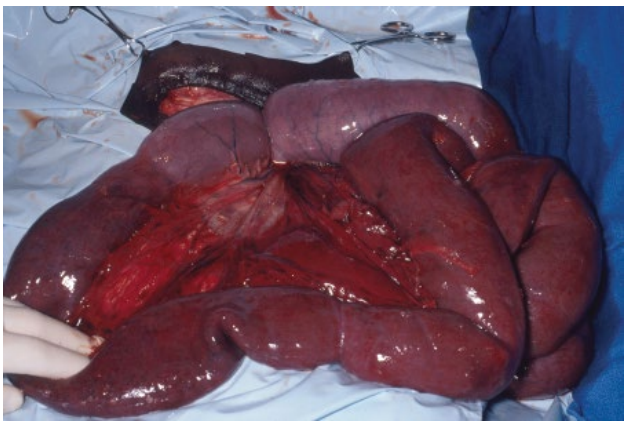

Figure 43.5 Grade IV in bowel that has undergone diffuse dark-red and purple discoloration, with marked edema.

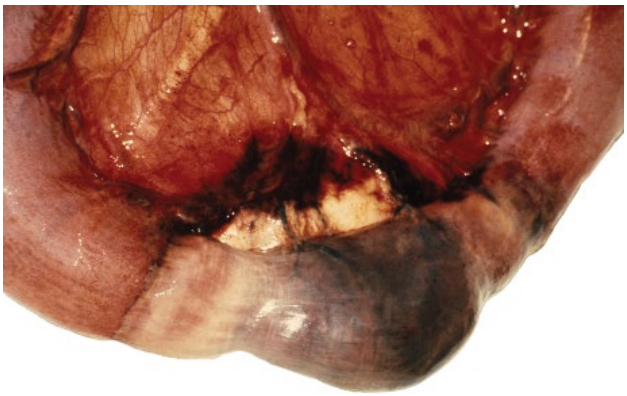

Figure 43.6 Grade V in bowel strangulated in an inguinal hernia, with black discoloration, complete circumferential constrictions, and blanching. Compare with Figure 43.4.

may cause postoperative obstruction and abdominal pain (Figure 43.7). It is important to note that this system is based on observation of subtle color changes in the bowel wall, and is very dependent on the lighting conditions and quality of the surgery lights.

Bowel that becomes ischemic after evisceration tends to progress through these grade changes very rapidly, but the viability does not necessarily decline to the same extent in these segments. This clinical observation is consistent with the experimental finding that a closed-loop model (Figure 43.8) produces similar mucosal lesion grades as an open-loop model of strangulation in ponies, but with milder serosal evidence of ischemia (Figure 43.9A and B) (Ruggles et al., 1993). This difference can be explained by a more rapid filling of veins and tissue in the open-loop model similar to that which may occur in eviscerated bowel because of the lack of opposing pressure on the bowel wall.

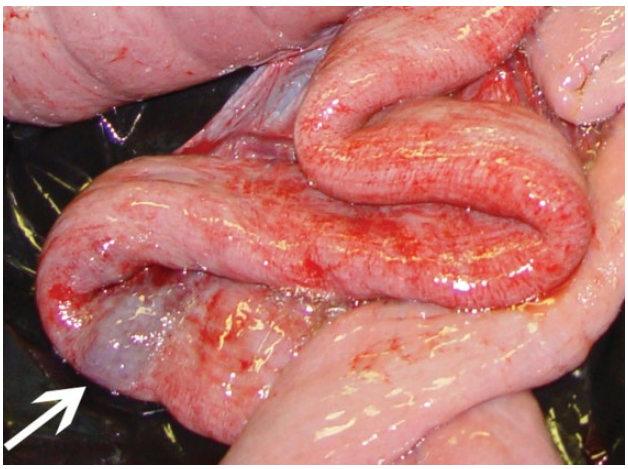

Figure 43.7 Patch of bluish discoloration (grade IV, arrow) in a jejunal segment that had undergone grade I changes following strangulation and was therefore not resected. This was missed at the first surgery but caused severe postoperative obstruction and pain and was resected at this (second) surgery.

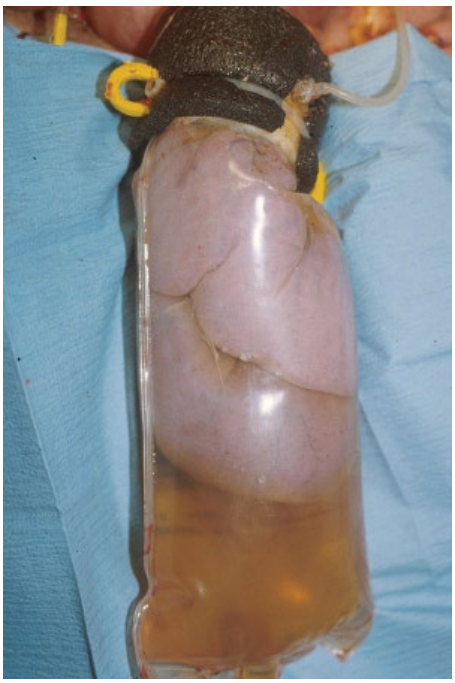

Figure 43.8 A closed-loop strangulation model created by placing strangulated jejunum in a 1 L IV fluid bag with sufficient physiologic solution to create a peritoneal fluid medium. See Ruggles et al. (1993) for more details.

Fluorescein Fluorescence

The advantages of fluorescein fluorescence (visual or qualitative fluorescence) in the equine small intestine include rapid assessment of large areas of bowel and the fact that it is simple to use, safe, and inexpensive (Figure 43.10) (Bulkley et al., 1981; Freeman et al., 1988b). Fluorescein is administered through the jugular catheter

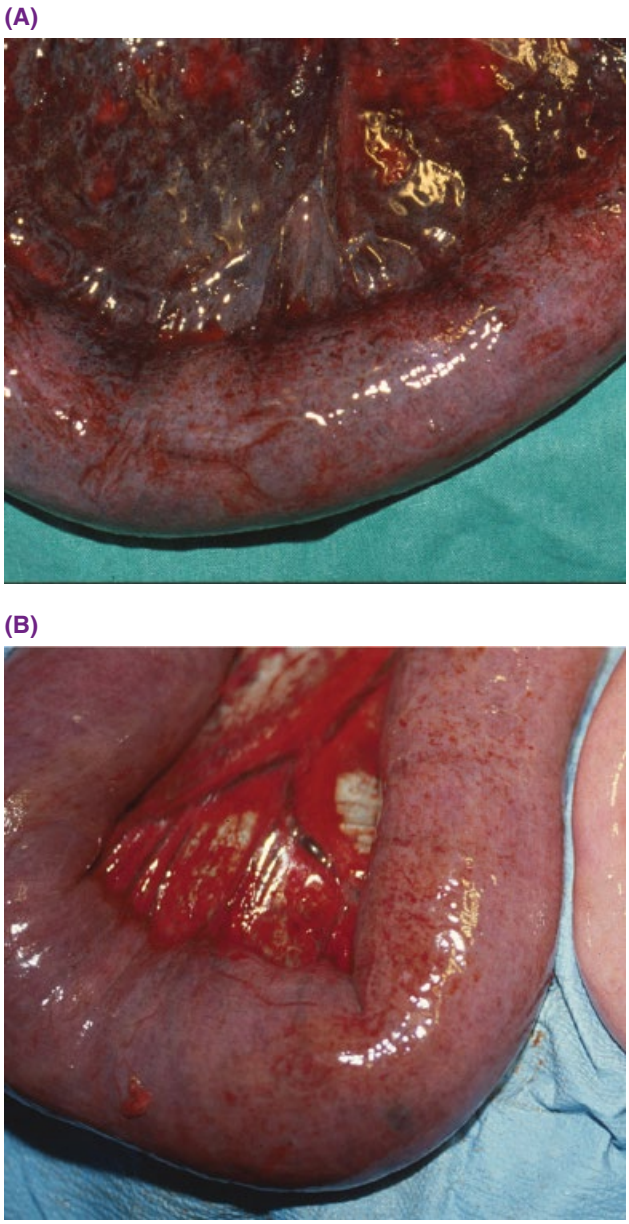

Figure 43.9 Segments of small intestine 15 min after release from 3 h of venous strangulation obstruction created in an open abdomen (Freeman et al., 1988a) **(A)** and 15 min after release from 6 h of venous strangulation obstruction in a closed-loop model shown in Figure 43.8 (Ruggles et al., 1993) **(B)**. Although both segments had similar mucosal grades of injury, the external appearance in **(A)** is worse (representative of bowel strangulated by evisceration) than in **(B)** (representative of an enclosed intra-abdominal strangulation).

as a 10% solution at a dosage of 15 mg/kg of body weight and a portable UV lamp is used to demonstrate fluorescence in the darkened room, approximately 5 min after injection (Freeman et al., 1988b). Unfortunately, interpretation of equivocal fluorescein patterns is subjective and prone to error, and patterns that characterize nonviable intestine in other species are viable in the horse

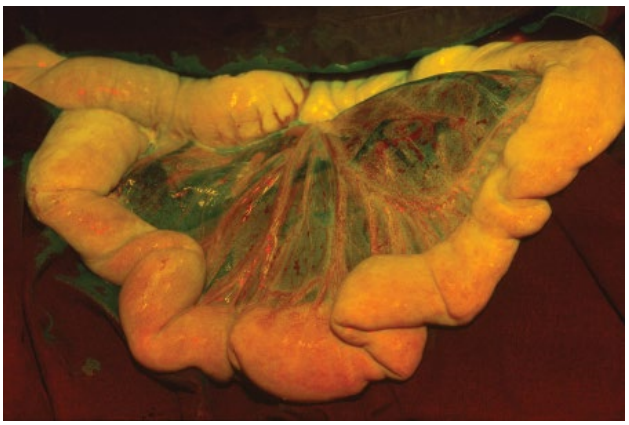

Figure 43.10 Normal pony jejunum illuminated with a Wood's lamp in a darkened room shortly after injection of fluorescein through the jugular vein. This is a normal fluorescent pattern.

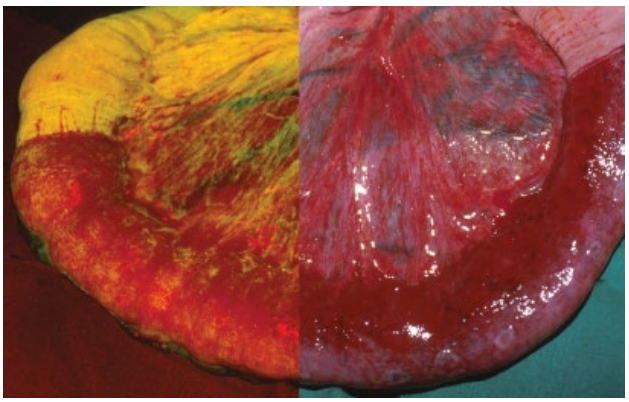

Figure 43.11 Segment of small intestine 15 min after release from 3 h of venous strangulation obstruction, before (right) and after fluorescein administration (left). Long-term follow-up confirmed that this segment was viable and did not form adhesions, although it was judged as nonviable based on clinical and fluorescent criteria. Note that the seromuscular hemorrhage interfered with fluorescence on the mesenteric border, so that this is an indeterminate pattern in equine jejunum.

(Bulkley et al., 1981; Freeman et al., 1988b). In viable intestine rendered hemorrhagic and edematous by venous occlusion, intramural hemorrhage shields fluorescein in the tissues from the UV light, and a hypofluorescent or nonfluorescent pattern is produced even when the intestine has perfusion (Figure 43.11). This accounted for the high false-positive results, low overall accuracy, and low overall specificity for fluorescein in one study of jejunum in ponies (Freeman et al., 1988b). Fortunately, the hyperfluorescent pattern caused by perivascular leakage in nonviable bowel (Brusie et al., 1989; Bulkley et al., 1981) seems rare in horses. This could lead to the assignment of viable to nonviable bowel. Furthermore, the concern that nonviable bowel will stain from surface contact with dye in peritoneal fluid does not appear valid. Although a viable fluorescent pattern

usually means that a segment can be left in place, overall, fluorescein fluorescence offers little improvement over clinical judgment because a nonviable fluorescent pattern is an inconclusive finding (Freeman et al., 1988b).

Doppler Flowmeter

The Doppler pencil probe (9 mHz) is calibrated to a Doppler flowmeter, and can be used to detect blood flow at several points in the mesenteric vessels and in the intestinal wall (Freeman et al., 1988b). After the tip of the gas-sterilized probe has been coated with sterile, water-soluble gel to enhance contact, it is held at a 45° angle to the tissue surface while it is directed upstream to the direction of blood flow (Figure 43.12). Doppler arterial signals are judged as being present (viable) or absent (nonviable). The Doppler technique is most suitable for identifying small areas of ischemia and for selecting well-perfused margins for intestinal anastomosis (Bulkley et al., 1981). Because of this limited range of application, the Doppler probe cannot scan large segments of ischemic bowel adequately and can miss foci of infarction.

In a study of pony jejunum, Doppler ultrasound was superior to fluorescein fluorescence and clinical judgment in predicting the viability of intestinal segments after they were subjected to venous occlusion (Freeman et al., 1988b). However, the Doppler technique has been shown to be inferior to fluorescein fluorescence and to clinical judgment in detecting nonviable segments, regardless of the method of inducing ischemia (Bulkley et al., 1981). The superiority of fluorescein fluorescence has been attributed to its ability to assess microvascular perfusion, which correlates closely with tissue viability, whereas the Doppler device detects blood flow in large vessels (Bulkley et al., 1981; Freeman et al., 1988b).

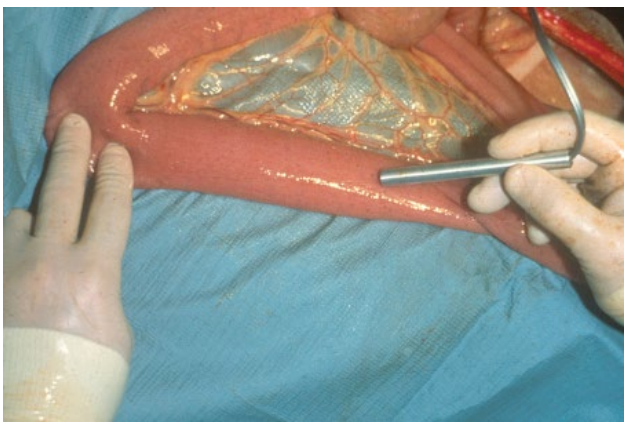

Figure 43.12 Method of applying the Doppler flow probe to the jejunal wall to detect pulsatile blood flow. The tip is held at a 45° angle and a coating of water-soluble lubricant enhances contact. Unlike fluorescein (Figure 43.10 and Figure 43.11), this method can only assess small segments at a time.

Miscellaneous

The perfusion fluorometer (quantitative fluorescence), laser Doppler flowmeter, and tetrazolium analysis of the mucosa have some potential but are cumbersome and require special equipment (Brusie et al., 1989; Bulkley et al., 1981). Thermography has been evaluated in a preliminary study in pony jejunum, and some criteria were established that could have clinical application (Purohit et al., 1982). For example, a temperature gradient of <0.5 °C between mesenteric and antimesenteric margins and a difference of >1.5 °C between mesenteric border temperatures of ischemic and nonischemic bowel could indicate inadequate revascularization (Purohit et al., 1982). In clinical cases, a mean intraluminal hydrostatic pressure of 15 cmH_2O in the small intestine proximal to an obstruction was significantly associated with low survival (Allen et al., 1986); however, this would seem to be more useful as an indicator of prognosis than intestinal viability.

Pulse oximetry has been evaluated in normal equine small and large intestine and could be attractive for clinical use (Figure 43.13), because there is no equipment

Figure 43.13 Portable hand-held monitor suitable for use as a pulse oximeter in detecting bowel viability (Nonin Medical, Plymouth, MN, USA). The reflectance sensor demonstrated or the clip-on sensors can be applied to the serosal surface of the bowel to obtain a rapid recording for blood oxygen saturation.

calibration involved and an objective display of information is presented rapidly (Schmotzer et al., 1991). The high-intensity ear probe or the flat reflectance sensor (Figure 43.13) can be applied easily and rapidly to intestinal segments. Pulse oximeter oxygen values, pulsatile flow, or the detection of a pulse, alone or in combination, could be used to assess tissue perfusion and intestinal viability. In a study of canine jejunum, ileum, and colon, pulse oximetry and surface oximetry were capable of estimating tissue blood flow, but pulse oximetry was faster and easier to use (MacDonald et al., 1993). Despite these findings, pulse oximetry is not widely used to determine intestinal viability.

Large Colon and Cecum

In the equine large colon, the term viable refers to the ability of the affected segment to recover fully without risk of further mucosal necrosis and death of the horse secondary to endotoxemia and peritonitis. Unlike the small intestine, adhesions are less likely to form in the large colon after a mild to moderate ischemic injury (Sullins et al., 1986). It is also important to consider the risk of recurrence of large colon displacement, particularly the very dangerous risk of large colon volvulus (Hughes & Slone, 1997). This risk will weigh heavily on the side of resection in horses prone to this condition, even if the horse might survive with the colon left in place after correction (Hughes & Slone, 1997). Another important consideration is the benefit of debulking the colon of ischemic tissue that could allow transmural passage of endotoxin and other bacterial products into the circulation (Hughes & Slone, 1997). The large intestinal disease most likely to present the most difficulty with viability assessment is large colon volvulus, and the decision to resect is further complicated by poor access to viable intestinal margins.

Clinical Judgment

Clinical assessment of viability is considerably more difficult in the large colon than in the small intestine. A segment that appears viable based on serosal appearance can have irreversible mucosal changes and microvascular thromboses. Conversely, a segment with similar or more severe serosal evidence of ischemia can recover if left in place. A pelvic flexure colotomy can be useful in such cases, as it allows the assessment of bleeding from the cut edges. Also, a thin slice of one edge of the enterotomy can be harvested for histological examination (Van Hoogmoed et al., 2000a; Gonzalez et al., 2015c; Levi et al., 2012). Most surgeons agree that if the mucosa is dark red and bleeding is brisk, the prognosis is better than if the mucosa is black. However, dark discoloration of the mucosa and failure to bleed do not rule out viability. Additionally, visual assessment of motility in the large intestine is not as reliable as in the small intestine because large intestinal motility normally appears sluggish.

Pelvic Flexure Biopsy

The degree of epithelial injury to the equine large colon can be determined using histological assessment of pelvic flexure biopsies (Van Hoogmoed et al., 2000a; Van Hoogmoed & Snyder, 1998; Gonzalez et al., 2015c; Levi et al., 2012). Intestinal biopsies can be evaluated freshly frozen or fixed, followed by embedding, sectioning, and staining. Morphologic changes that include interstitial tissue-to-crypt ratio (I : C ratio), percentage loss of superficial and glandular epithelium, and the degree of hemorrhage and edema have been used to predict viability in cases of large colon volvulus (Figure 43.14) (Van Hoogmoed et al., 2000a). Intestinal viability was decreased when >50% loss of the crypt epithelium and an I : C ratio >3 were measured (Van Hoogmoed et al., 2000a). An increased I : C ratio is attributed to hemorrhage that causes architectural damage as the interstitium expands and glandular epithelium is compressed (Van Hoogmoed & Snyder, 1998; van Hoogmoed et al., 2000b). Loss of glandular epithelium is associated with decreased tissue viability due to the integral role of stem and progenitor cells, which reside within this region, in the renewal of the mucosal lining (see Chapter 2) (Van Hoogmoed et al., 2000a; Gonzalez et al., 2014, 2015b; Gonzalez, 2015).

Importantly, one study has shown that histological changes identified at the pelvic flexure are uniformly distributed throughout all colonic tissue involved in the volvulus, including those at less accessible regions and at the site of resection and anastomosis (Van Hoogmoed et al., 2000b). Furthermore, in another study comparing the accuracy of dorsal colon versus pelvic flexure biopsy in predicting survival in cases of large colon volvulus, no difference was found (Gonzalez et al., 2015a). These findings contribute to the value of histological assessment in grading tissue damage. It should be noted that, in one study, the accuracy of pelvic flexure biopsies to predict short-term survival were called into question (Levi et al., 2012). In this study, however, histopathologic measures were not assessed individually, but were grouped and then assigned a numerical score. The benefit of pelvic flexure biopsy to determine short-term outcome has been further confirmed in a more recent study that found that horses with an I : C ratio >1 were 12-fold more likely not to survive to discharge (Gonzalez et al., 2015c). This work identified evidence of the importance of hemorrhage score as a means to determine tissue viability, a parameter not found significant

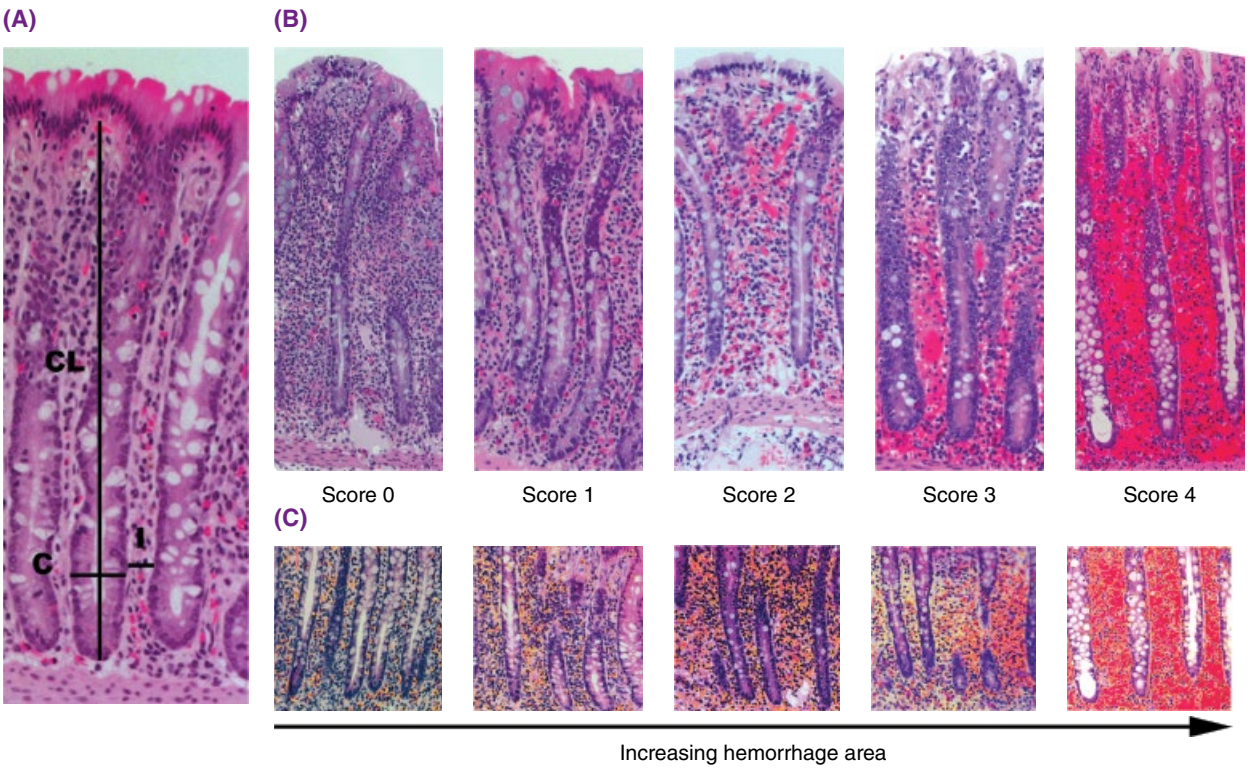

Figure 43.14 Histomorphometric evaluation of pelvic flexure mucosal biopsies of horses. **(A)** The interstitium-to-crypt ratio (I : C) is defined as the ratio of the width of the intercrypt lamina propria (I) to the width of the crypts (C). The crypt length (CL) can also be measured. **(B)** Hemorrhage score within the lamina propria of the mucosal biopsy is assigned a score from 0 to 4 (score 0, no hemorrhage; score 1, a few individual red blood cells within the lamina propria; score 2, increased number of individual red blood cells; core 3, appearance of clumps of red blood cells; and score 4, no clear demarcation between red blood cells, obscuring the lamina propria. **(C)** Hemorrhage area was digitally quantified using ImageJ. Source: Gonzalez et al., 2014b. Reproduced with permission of John Wiley & Sons.

in the original work by Van Hoogmoed and colleagues (Van Hoogmoed et al., 2000a; Gonzalez et al., 2015a). In fact, the accuracy of hemorrhage measurements in predicting survival or nonsurvival was 79%. Mortality was found to be 8.8- and 26-fold more likely in cases with a mucosal hemorrhage score of ≥3 and a hemorrhage area of ≥0.84 ppi, respectively (Figure 43.14) (Gonzalez et al., 2015c). The strong association of poor short-term outcome with increasing area of hemorrhage is likely due to the architectural damage that results from extravasation of red blood cells into the lamina propria.

The limitation of histological evaluation of fixed biopsy samples is the delay in obtaining results. However, many cases can recover with nonviable colon after correction of large colon volvulus and remain stable for 3–4 days after surgery before they start to deteriorate from failure of mucosal repair. In these cases, histological results provide an assessment of viability in the postoperative period that may help determine the need for further treatment, surgery, or euthanasia, if the horse's clinical condition deteriorates after surgery.

Surface Oximetry

Surface oximetry has been applied for viability assessments in both equine small and large intestine (Van Hoogmoed & Snyder, 1998). The results of a study combining evaluation of tissue blood flow (surface oximetry or laser Doppler) and histological injury (frozen tissue sections) support the use of these modalities to assess large colon ischemia (Van Hoogmoed & Snyder, 1998). Surface oximetry provides a measure of the partial pressure of oxygen on the tissue surface (PsO_2) and is determined by the oxygen content in blood beneath the probe, the diffusion distance from the vessels to the surface, local tissue oxygen consumption, and blood flow (Van Hoogmoed & Snyder, 1998). A good outcome is associated with a $PsO_2 > 20$ mmHg (Van Hoogmoed & Snyder, 1998). The disadvantages are that the equipment is expensive, only small areas of tissue can be evaluated, and contact between the probe and tissue should be constant. Pulse oximetry can also be used to assess oxygen saturation but may not be as sensitive as surface oximetry to decreases in local tissue blood flow (Van Hoogmoed & Snyder, 1998). Ultimately, this technique has not been found to be clinically useful and is not widely used.

Fluorescein Fluorescence

A viable vascular pattern in the large intestine may indicate the potential for complete recovery, compared with the small intestine where observation of the same pattern was associated with possible adhesion formation (Sullins et al., 1986). The fiber-optic perfusion fluorometer has the advantage over qualitative fluorescence that it provides quantitative information and therefore gives an objective measure of perfusion (Brusie et al., 1989). Results with the fiber-optic perfusion fluorometer were inconclusive in one study of experimental ischemia in equine small and large intestine, although it did identify the ventral colon as more susceptible than the dorsal colon to ischemia (Brusie et al., 1989).

Colonic Luminal Pressure

Colonic luminal pressure has been evaluated in horses with large colon disease (Moore et al., 1996). In horses with a large colon obstruction, intraluminal hydrostatic pressures exceeding 38 cmH_2O had a high sensitivity, specificity, and positive and negative predictive values for predicting low survival in one study (Moore et al., 1996). The predictive value of colonic luminal pressure to determine survival was reassessed in a more recent study that focused on this tool to predict survival in horses undergoing large colon resection anastomosis (Mathis et al., 2006). This study concluded that colonic luminal pressures for nonsurvivors were not significantly different from those of survivors with and without resection and anastomosis. Furthermore, a colonic luminal pressure of 38 cmH_2O had poor sensitivity, specificity, and positive predictive values. Finally, no optimal colonic luminal pressure value was found, in this study, to group horses accurately into survivors and nonsurvivors in either manually corrected or resected groups. Both studies noted that the validity of using 38 cmH_2O as a cutoff value to predict outcome among different hospital populations could be influenced by a hospital's overall mortality rate. Unfortunately, the value of colonic luminal pressure measurement was further undermined since no cutoff was found to predict death or survival. This study concluded that colonic luminal pressure measurements have variable accuracy in predicting outcome in horses with large colon volvulus after manual correction and poor accuracy in horses after large colon resection anastomosis.

Miscellaneous

The evaluation of colonic serosal microvascular perfusion as a means to determine the degree of tissue injury has been performed using dark-field microscopy (Hurcombe et al., 2014). A video microscope is placed lightly on the colonic serosa while an accompanying computer allows for real-time viewing and recording of vessels. Microvascular perfusion indices were found to correlate with histological mucosal injury scores from pelvic flexure biopsies. Unfortunately, no conclusions could be drawn as to the utility of this technique to predict outcome in cases of severe colonic tissue injury (Hurcombe et al., 2014). Furthermore, the authors described major challenges in the use of this technology in the clinical setting, including the need for specialized equipment and software and the time and expertise required for detailed analysis and post-processing of images.

Small Colon

Assessment of small colon viability has not been studied to the same extent as for the large colon and small intestine in horses. This is likely because small colon lesions account for only 2.8–4% of surgical colic cases (Prange et al., 2010; Mair & Smith, 2005). Fecaliths, enteroliths, and feed impactions can all cause intraluminal obstructions that result in focal or multifocal areas of pressure necrosis in the small colon wall (Figure 43.15). Strangulating lipomas, mesenteric tears, and incarcerations of the small colon can all cause vascular compromise and ischemic injury (Prange et al., 2010). Determining tissue viability is critical for making the intraoperative decision to perform a resection, and further research to evaluate the impact of different forms of injury on small colon viability is needed.

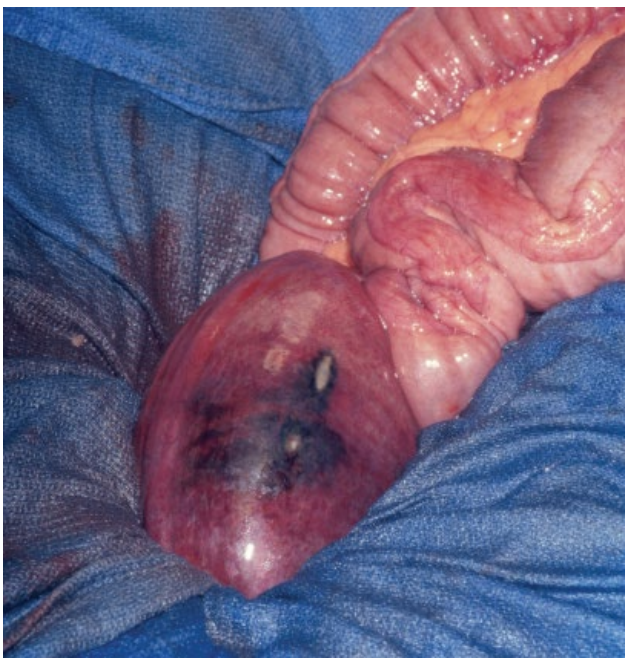

Figure 43.15 Small colon containing a firm fecalith impaction, with black and green discoloration and mural thinning suggesting pressure necrosis.

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44

Small Intestinal Resection and Anastomosis

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Small intestinal resection and anastomosis become a necessity when segments of small intestine are deemed nonviable or nonfunctional during colic surgery. The survival rates after small intestinal resection have improved over the years and short-term survival rates after small intestinal resection in more recent papers are mostly reported to be around or above 80% of horses recovered from surgery (Freeman et al., 2000; Morton & Blikslager, 2002; Müller et al., 2009; Stewart et al., 2014). Resection of the small intestine in adult horses seems to have little or no negative effects on short- or long-term survival compared with horses with small intestinal lesions not requiring resection (Freeman et al., 2000; Müller et al., 2009; Wormstrand et al., 2014), but in foals long-term survival was lower after small intestinal resection (Cable et al., 1997) and long-term prognosis for adult horses has been reported to decrease with increasing length of resected small intestine (Proudman et al., 2002). However, small intestinal resection has been associated with an increased risk for postoperative complications such as postoperative ileus or colic symptoms (Mair & Smith, 2005; Torfs et al., 2009). The type of small intestinal anastomosis performed can also influence postoperative survival and complication rates, and a jejunocecostomy has been associated with a higher complication and a lower postoperative survival rate than a jejunojejunostomy or a jejunoileostomy (Freeman et al., 2000; Morton & Blikslager, 2002; Proudman et al., 2002). This chapter deals with the techniques for and potential complications of small intestinal resection and anastomosis.

Extent of Resection

The small intestine is responsible for the absorption of many nutrients, and resection of more than 50% of the small intestine will result in the development of malnutrition and malabsorption problems in human patients (Debas, 2003). In ponies without gastrointestinal disease, resection of more than 60% of the small intestine was associated with postoperative weight loss, changes in the hepatic parenchyma, and an increase in serum alkaline phosphatase activity (Tate et al., 1983). In a subsequent study, resection of 70% of the distal small intestine in ponies without gastrointestinal disease was well tolerated and ponies regained their normal weight by week 10 after resection. In addition, serum alkaline phosphatase levels returned to normal by 6 months after resection (Haven et al., 1992). These studies were performed in ponies without intestinal disease, but venous strangulating obstruction for 3 h and venous strangulating obstruction for 1.5 h followed by 1.5 h of reperfusion increased the length of the affected small intestine by approximately 30% in horses (Freeman & Kilgallon, 2001). This could lead to an overestimation of the length of small intestine resected in clinical patients, and evaluation of the length of remaining small intestine might prove more useful in these cases. A guideline of at least 4.5 m (15 ft) of remaining small intestine in an adult horse has been suggested (Freeman, 2008).

Decompression

Severe distention will increase intramural pressure in the affected small intestine with subsequent compression of venous blood vessels, intramural edema formation, and serosal damage. This may predispose to the development of postoperative ileus and adhesion formation, and intestinal distention can be painful. Intraoperative decompression of distended small intestine is recommended, and its benefits will likely outweigh the negative effects of the mechanical handling of the small intestine needed to achieve decompression (Hopster-Iversen et al., 2014).

The Equine Acute Abdomen, Third Edition. Edited by Anthony T. Blikslager, Nathaniel A. White II, James N. Moore, and Tim S. Mair.

Companion website: www.wiley.com/go/blikslager/abdomen

Manipulation of the intestine should be reduced to the minimum amount needed and performed as carefully as possible, and lubrication with saline lavage or carboxymethylcellulose can be used to reduce mechanical damage to the serosa. Decompression is achieved by manually stripping the bowel in a proximal to distal direction. Small intestinal contents can be emptied into the cecum, but this may require handling of nondistended distal small intestinal sections and, if too much fluid is emptied into the cecum, this fluid may need to be removed through a typhlotomy to avoid postoperative colic symptoms. If the section of small intestine to be resected is long enough to allow sufficient exteriorization after transection of the mesentery, a better method for decompression can be emptying of the distended proximal segment through the opened strangulated segment into a bucket.

Ligation of Mesenteric Vessels

When transecting the mesentery of strangulated small intestine, all major and some smaller mesenteric vessels must be ligated to prevent postoperative bleeding. Ligation can be performed with single or double absorbable suture ligatures, surgical staples (e.g., with the Ligate Divide Stapler, LDS) or using an electrosurgical vessel-sealing device. For suture ligation, both monofilament and polyfilament sutures can be used, but monofilament sutures were more resistant to pressure in an *in vitro* setting (Gandini et al., 2014a). Size 2-0 USP (3 metric) has been recommended most often for suture ligation, but the size of the artery and degree of mesenteric edema may make a size 1 USP (4 metric) or a size 3-0 USP (2 metric) suture more appropriate in some clinical patients. A sliding knot was comparable in resistance to pressure to a surgeon's knot but was faster to perform (Gandini et al., 2014a). In a study comparing vascular occlusion with double-suture ligation, LDS staples, and an electrosurgical vessel sealing device (LigaSure Atlas; Valleylab, Boulder, CO, USA), the bursting pressure was greater than the expected systolic pressure in conscious or anesthetized horses for all three methods and therefore all methods were deemed appropriate, but suture ligation was strongest, followed by electrosurgical vessel sealing and LDS staples (Rumbaugh et al., 2003). For resection of longer sections of small intestine, vessel ligation using LDS staples or a vessel-sealing device will be much faster than suture ligation. The benefit of the surgical time gained can outweigh the additional costs associated with both LDS staples and the use of a vessel-sealing device. Regardless of the ligation method used, all transected arteries should be re-evaluated at the end of the surgical procedure to ensure adequate hemostasis (Figure 44.1).

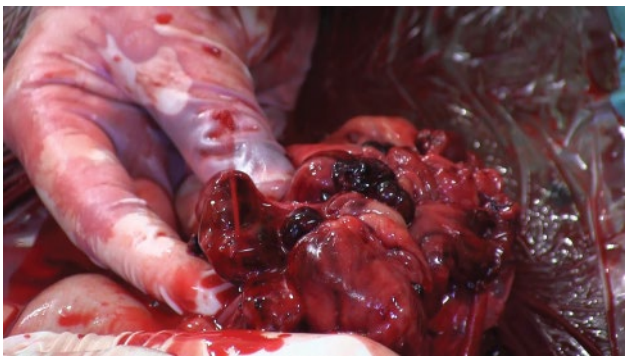


Figure 44.1 Hemorrhage of a mesenteric artery 24 h after small intestinal resection causing life-threatening hemoperitoneum. The mesenteric arteries had been ligated with 4 metric polyglactin 910. Hemorrhage was evident only after release of tension on the exteriorized mesenteric stump.

Suture Material for Anastomosis

Materials evaluated for small intestinal anastomosis in horses include different types of surgical sutures and surgical staples. A hand-sewn anastomosis has the advantage of not requiring expensive specialized equipment and can be individually designed in shape and size. A stapled anastomosis often is quicker and may be cleaner to perform. Closure of an anastomosis must provide a good seal while leaving enough lumen. Any type of suture material exposed on the serosal surface may predispose to adhesion formation, as may exposure of mucosal tissue. Although nonabsorbable suture materials have been used for intestinal sutures and monofilament nonabsorbable suture material can be used safely in a contaminated environment with minimal tissue response, absorbable suture materials are preferred by most equine surgeons. Polypropylene suture material used to close small intestinal incisions in dogs has been reported to be extruded into the lumen and serve as a site for attachment of foreign bodies, supporting the preference for absorbable suture material in intestinal surgery (Milovancev et al., 2004).

For hand-sewn anastomoses, both monofilament and polyfilament suture material can be used. Intestine heals very rapidly and suture tensile strength is needed for only 2–3 weeks. Polyfilament suture materials used in equine intestine include polyglactin 910 and lactomer 9-1 and have good handling characteristics and good knot security. The greatest disadvantage of a polyfilament suture in intestine is the significant tissue drag associated with these materials, and care must be taken not to cut through the intestinal wall while tightening the sutures. Monofilament absorbable sutures used in equine intestine include polydioxanone and polyglyconate, and both will retain their tensile strength longer than is needed in equine intestine. Shorter acting monofilaments such as

glycomer 631 can be an alternative and have been used in equine intestine. Absorbable sutures are available as barbed sutures that eliminate the need for a knot and thereby decrease the amount of exposed suture material and potentially decrease adhesion formation. Barbed sutures have been evaluated *in vitro* and the anastomosis was faster to perform. They provided a lower bursting pressure than a comparable standard suture with knots, but the bursting pressure was considered to be well above pressures encountered clinically (Nelson & Hassel, 2014). The choice of suture material used for hand-sewn anastomoses should also depend on the surgeon's preference and his or her experience and comfort in handling and tying knots with the material chosen. Surgical staples including skin staples have been used for anastomosis and are well tolerated, and the choice between hand-sewn and stapled anastomosis should be based on factors including cost and training, experience, and comfort level of the surgeon. If staples other than skin staples are chosen, 4.8 mm staples (green cartridge) are preferable to 3.8 mm staples (blue cartridge) for intestinal surgery in adult horses, because the 3.8 mm staples close to a height of 1.5 mm (compared with 2 mm for 4.8 mm staples), and this could crush tissues and weaken the closure. However, in foals the 4.8 mm staples might not produce an effective seal (Freeman, 2008).

Jejunojejunostomy

End-to-End Jejunojejunostomy

Before beginning a jejunal resection, the small intestine should be exteriorized and oriented on the abdomen with the proximal small intestine positioned toward the head and the distal small intestine directed toward the tail. If decompression of the jejunum into the cecum has been selected, this step should be completed before starting the resection. The cecum and all other segments of intestine not needed should then be replaced into the abdomen. The proposed site of resection is chosen and whenever possible should be located in a segment of intestine that is as healthy as possible. The resection site should be as close as possible to a major mesenteric artery. If resection is performed too far away from a major mesenteric artery toward the middle of an arcuate mesenteric artery, the jejunum involved in the anastomosis may not receive adequate blood supply. The segment of jejunum near the middle of an arcuate mesenteric artery receives blood supply from the two mesenteric arteries on either side of the arcuate artery, and after resection the blood supply from one of these two sides will be interrupted.

Resection is then started with transection of the mesentery. Mesenteric transection should be performed from one end to the other, beginning at either the proximal or the distal end. An absorbable suture (e.g., size 1 USP, 4 metric, polyglactin 910) is used to ligate the first mesenteric artery. This suture is not cut, and instead the needle is left attached to a needle holder and the short end is kept slightly longer and secured with a hemostat (Figure 44.2A). The mesenteric arteries are then ligated and transected with the method chosen (LDS, electrosurgical vessel sealing device, suture) in a step-by-step fashion. During resection, the long end of the initial ligature is used to gather the mesentery. This ensures that all mesentery is secured and no holes will be left after completion of the resection. When gathering the mesentery, it should be penetrated close to each mesenteric artery (Figure 44.2B). This will make a final inspection of each ligated artery at the end of the anastomosis easier and will avoid individual arteries withdrawing into the abdomen and hemorrhaging unnoticed.

If decompression of the bowel through the strangulated intestine has been selected, the jejunum that has been freed from its mesenteric attachment can now be exteriorized further, between the hind legs of the horse or toward either side of the abdomen. Additional drapes are used to pack off the surgical site before this step and will be left until the anastomosis has been completed. An assistant must have a secure grip on the proximal and distal ends of the jejunum to be resected before it is exteriorized further to avoid excessive pull on and damage to the intact mesentery. The exteriorized jejunum to be resected is placed in a bucket and transected or incised by a nonsterile assistant (Figure 44.2C). The surgeon can then empty the proximal and if needed the distal parts of the remaining intestine into the bucket. After decompression, any segments of intestine not needed for the anastomosis should be replaced in the abdomen and additional drapes should be used to pack off the abdominal incision site. This should result in an organized and clear surgical field.

The jejunum at the proximal and if needed at the distal side of the proposed anastomosis should be occluded to avoid contamination with intestinal contents during the procedure. Intestinal clamps such as Doyen clamps are not ideal for this purpose, since they are not atraumatic and will damage the bowel (Figure 44.3A and B) (Hopster-Iversen et al., 2014). Penrose drains seem to be less traumatic. Small hemostats can be used to perforate the mesentery in an area without blood vessels and very close to the jejunum. The Penrose drain is then pulled through and tightened only as much as needed to occlude the intestinal lumen (Figure 44.2D). This occlusion should be performed at a distance well away (15–30 cm) from the proposed site of anastomosis to avoid constricting the bowel at the anastomosis site and thereby reducing the lumen of the anastomosis.

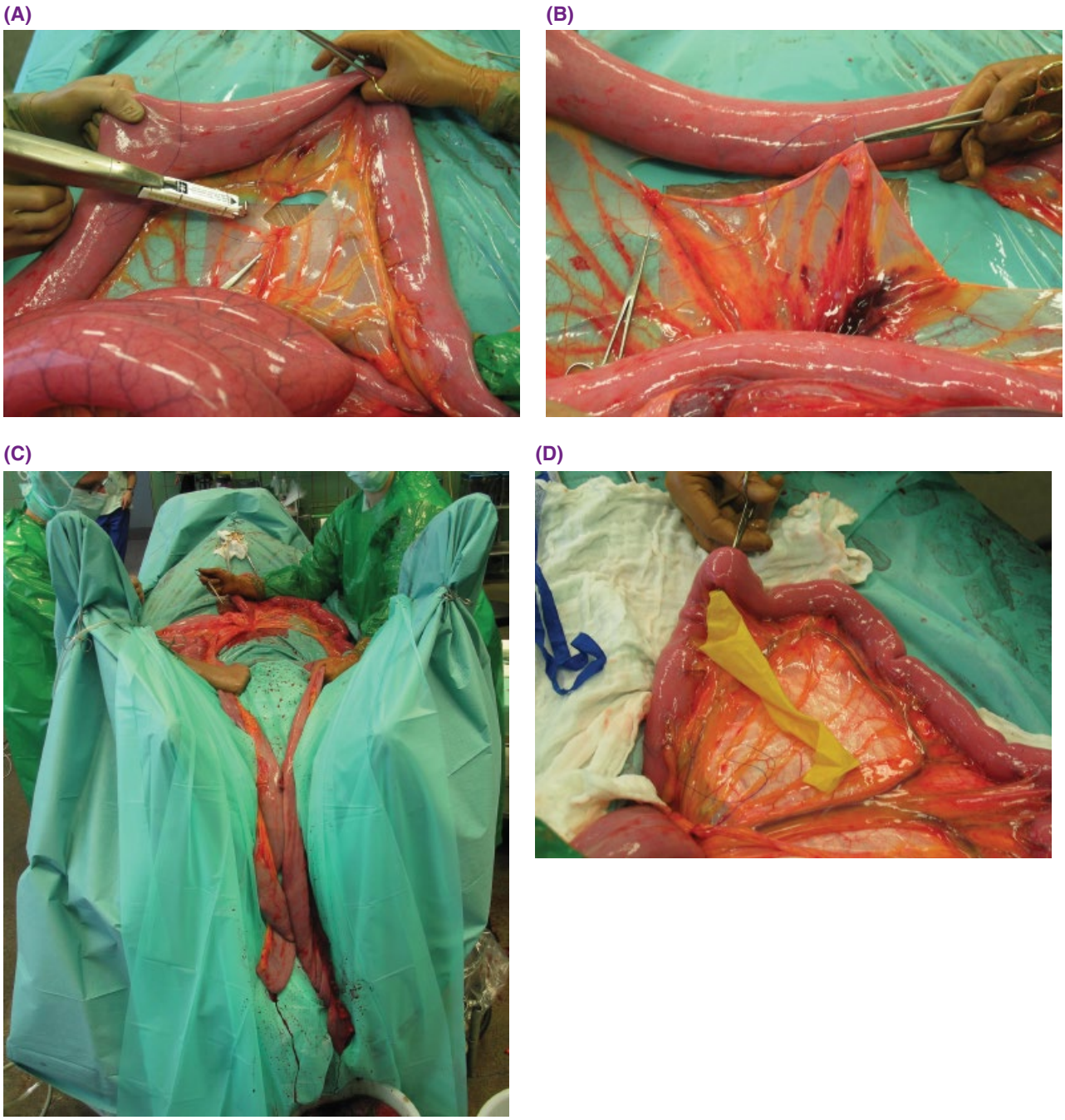
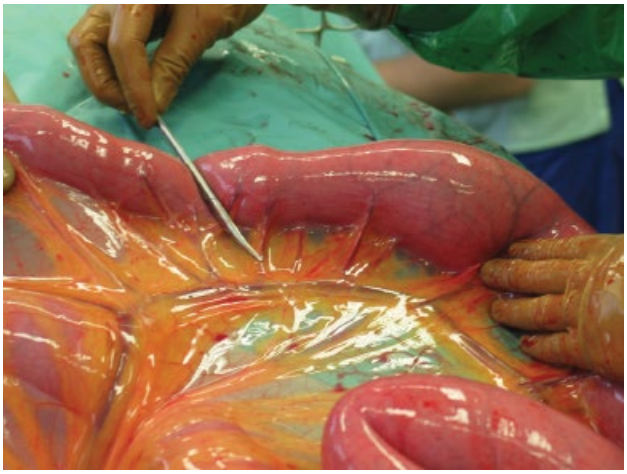


Figure 44.2 **(A)** Beginning of mesenteric transection. The first mesenteric artery is ligated but the suture is not cut. The short end is secured with a hemostat and the long end is left attached to the needle holder. An LDS stapler is being used for ligation and transection of the mesenteric artery and vein. **(B)** Gathering the mesentery during transection, taking care to penetrate the mesentery near each major mesenteric artery. **(C)** Decompression of the jejunum through the strangulated intestine. An assistant must have a secure grip on the proximal and distal jejunal ends to avoid excessive pull on and damage to the intact mesentery. **(D)** A hemostat is pushed through the mesentery near the jejunal attachment and used to pull a Penrose drain through, which is then tied to occlude the lumen. **(E)** Line of transection of the jejunum at a 60° angle from the mesentery toward the intact bowel near a major mesenteric artery. **(F)** Placement of interrupted Lembert sutures on the mesenteric and antimesenteric sides to provide traction and adapt the proximal and distal jejunal lumen. Note the strong contraction of the proximal jejunal segment on the right side that significantly reduces the lumen. **(G)** Traction has been applied to the stay sutures to adapt the lumen and a continuous Lembert suture pattern has been started at the mesenteric edge. **(H)** After completion of a 180° continuous Lembert pattern, the intestine is turned, which allows access to start the second 180° suture line to complete the anastomosis. **(I)** After completion of the anastomosis, the short and long ends of the suture used to gather the mesentery are tied to each other. An assistant can hold the mesenteric stump away from the intestine while suturing the mesenteric defect to avoid shortening of the mesentery at the level of the anastomosis. **(J)** Completed anastomosis using a single-layer continuous Lembert pattern. The lumen in an adult horse should be large enough for a surgeon with a size 7 glove to pass three or four fingers through the stoma.

(E)



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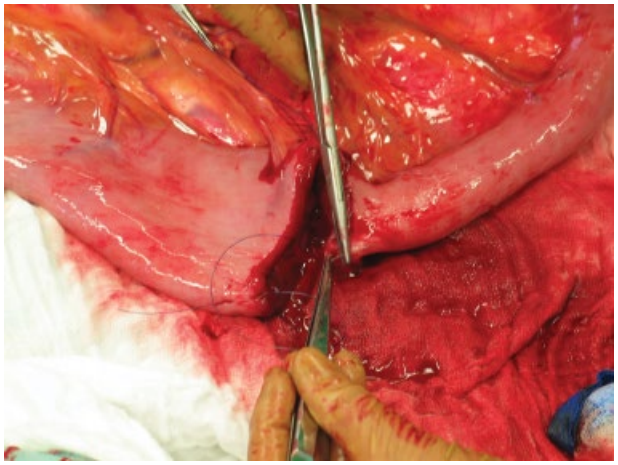

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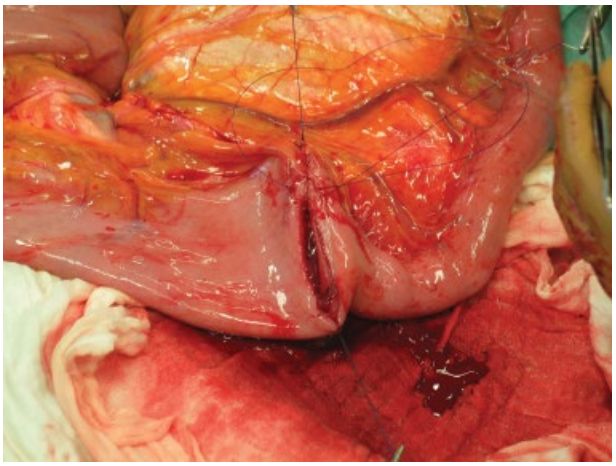

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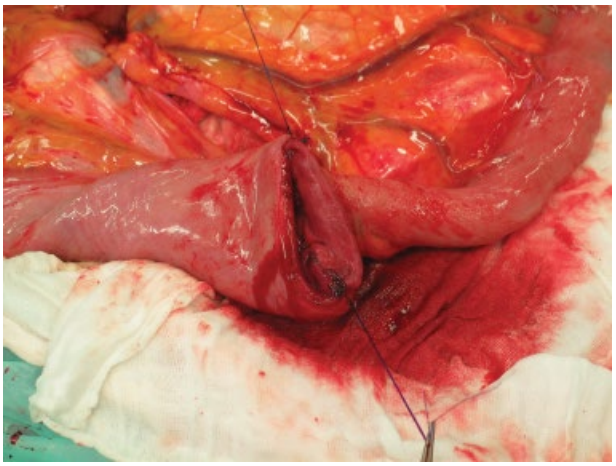

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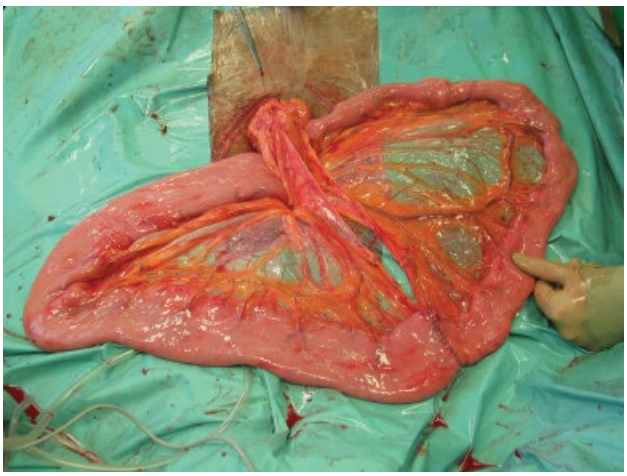

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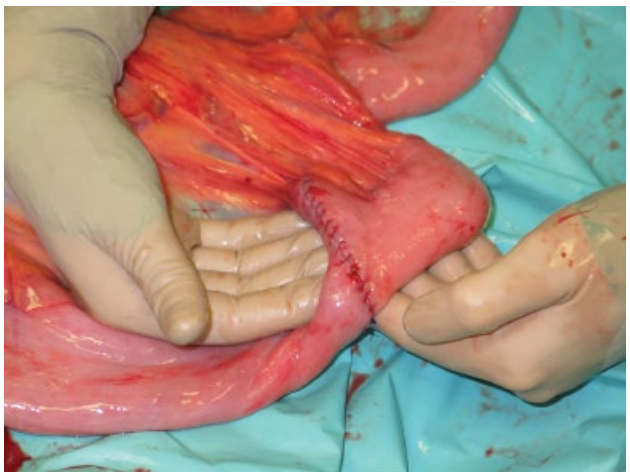

Figure 44.2 (Continued)

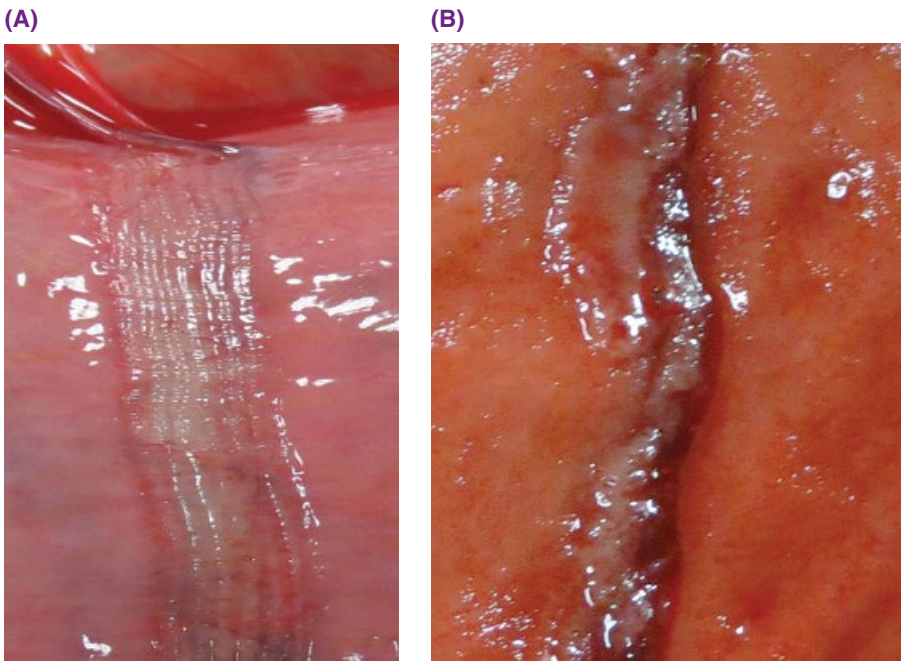

Figure 44.3 Macroscopic damage to equine jejunum ((A) serosal side; (B) mucosal side) after placement of Doyen clamps for 30 min.

Before transecting the jejunum, both proposed sites of the anastomosis should be placed without tension close to each other on a moist absorbable surface (e.g., moistened lap sponges) that can absorb any intestinal contents during the procedure. This surface should be tilted away from the abdominal incision and can be the body wall or a sterile tray if needed. During the entire procedure, care must be taken to avoid any contamination of the abdomen. The jejunum is transected at a point nearest a major mesenteric artery at an angle of 45–60° from the mesenteric attachment toward the intact bowel (Figure 44.2E). This angulation will increase the lumen of the anastomosis and to a certain extent will allow for adaptation of different lumen diameters between the proximal and distal jejunal segments for anastomosis, with the proximal segment usually having a smaller diameter than the distal segment. If the transection is performed in a straight line, sharp angles are created at the mesenteric border that may make a leakproof seal in this location more difficult. To avoid this problem, the line of transection can be shaped in an S-curve, beginning in a 90° angle at the mesenteric border, then redirecting to the desired 45–60° angle, and finishing in a 90° angle to the antimesenteric border (Freeman, 2008). After transection, the two parts of jejunum to be anastomosed must be adjusted to the same maximum diameter. This can be complicated by an often higher contractility of the proximal jejunal segment that will further reduce the lumen (Figure 44.2 F). Intestinal clamps placed near the anastomosis site often do not allow for an adequate lumen in addition to damaging the bowel (Hopster-Iversen et al., 2014). Instead, two single Lembert sutures can be placed on the mesenteric and antimesenteric border and the ends secured with hemostats (Figure 44.2F). An assistant can then provide gentle traction to adjust both sides of the anastomosis and to maximize its lumen (Figure 44.2G). The anastomosis is then sutured with the pattern chosen (Figure 44.2G and H), with special attention to the mesenteric and antimesenteric sides, because these locations are most prone to leakage. For this reason, traction on the hemostats should be minimized while suturing the mesenteric and antimesenteric borders. When hand suturing an anastomosis, it has been recommended that the submucosa should be incorporated into the suture bites in addition to the seromuscular layer (Freeman, 2008). The submucosa is the strongest layer in human intestine, contributing 70–75% of the strength of the intestinal wall and providing the stability, strength, and resistance to intensive deformations of long duration in human small intestine (Raikevitch, 1963; Egorov et al., 2002).

Different suture patterns have been suggested for end-to-end jejunojejunostomy, and interrupted and continuous patterns can be used. Interrupted patterns avoid the purse-string effect that can be associated with continuous suture patterns, but usually take longer to perform and leave more suture material exposed on the serosal surface that may predispose to adhesion formation (Freeman et al., 2000). Continuous patterns should be interrupted at least twice to span a maximum of 180° of the anastomosis. In comparison with continuous patterns, interrupted sutures may allow for a certain degree of expansion between sutures and a subsequent enlargement of the anastomotic lumen that is not possible

with continuous sutures. However, this may also make interrupted sutures more prone to leakage. Double- or single-layer suture patterns can be used, and intuitively double-layer suture patterns should provide a better seal. However, a double-layer pattern takes longer to perform, increases inversion of intestine, and thereby reduces the lumen and leaves more suture material at the anastomosis site. On comparing a one-layer continuous Lembert and a two-layer simple continuous and Cushing pattern, the single-layer Lembert was quicker to perform and resulted in less lumen reduction, and there was no difference in bursting pressure and bursting wall tension between the two patterns (Nieto et al., 2006). In an *in vitro* comparison of continuous suture patterns for jejunojejunostomy, the single-layer Lembert pattern was fastest to perform and had the highest bursting pressure when compared with a double-layer Lembert pattern and a Gambee pattern (Auletta et al., 2011). Another *in vitro* study compared a double-layer simple continuous and Cushing pattern, a single-layer Lembert pattern. and a single-layer Cushing pattern and found all three patterns to be comparable in lumen reduction and bursting pressure, but the single-layer patterns were faster to perform (Sherlock et al., 2011). Although the single-layer Cushing pattern in that study was faster to perform than the single-layer Lembert pattern, the Cushing pattern will be more prone to reduction of the lumen though a purse-string effect. Gandini (2006) reported a single-layer inverting closed-bowel technique for end-to-end jejunojejunostomy using a modified Doyen clamp to occlude the apposed proximal and distal jejunal ends in one clamp. A 180° Cushing pattern from the mesenteric to the antimesenteric edge was sutured on one side of the Doyen clamp. The clamp was rotated and the proximal and distal ends of the jejunum were transected on the other side of the Doyen clamp. A Parker–Kerr oversew of the Doyen clamp was performed to complete the anastomosis. Gandini found this technique to be faster to perform than a double-layer simple continuous and Cushing pattern. Bursting pressures for the closed Doyen clamp technique were lower but were considered adequate for the intended purpose (Gandini, 2006). A continuous single-layer Lembert pattern has performed well in clinical cases, supporting the assumption that a double-layer pattern is not necessary to provide an adequate seal (Mendez-Angulo et al., 2010). In a clinical study, both an interrupted Lembert and a continuous pattern Lembert with a carboxymethylcellulose and hyaluronate membrane performed well and similarly in the short term, but the latter pattern was associated with less colic and mortality from colic in the long term (Freeman & Schaeffer, 2011). In a retrospective clinical study, no differences in surgical time, complications, or survival rate were found between a single-layer Lembert and a double-layer simple continuous and Cushing pattern (Close et al., 2014).

Skin staples have been evaluated for use in end-to-end jejunojejunal anastomosis (Gandini & Bertuglia, 2006). The anastomosis with skin staples was faster to perform than a two-layer hand-sewn anastomosis and resulted in less lumen reduction. The bursting pressure was less for the stapled technique but was considered sufficient for a clinical application. It is unknown if the presence of the skin staples will have negative effects in the horse such as promotion of adhesions, but they have been used for intestinal anastomosis without direct complications in dogs, pigs, and humans (Fraser, 1994; Edwards & Galbraith, 1998; Coolman et al., 2000). Another type of staple that can be used for end-to-end anastomosis is a circular stapling device. However, the lumen that can be achieved with this stapling device is limited and its use is restricted to resection in ponies (Robertson-Smith & Adams, 1987; Zoettl et al., 1999).

After the anastomosis is completed, the surgery site should be thoroughly cleaned and lavaged and the additional drapes that were added to pack off the abdomen before the beginning of the anastomosis should be removed. The surgeon should change gloves, gown, and instruments before proceeding. The mesenteric stump is gathered and all transected arteries are inspected to ensure adequate hemostasis. The short end of the suture used to gather the mesentery is tied to the long end, firm enough to close any hole remaining in the mesenteric stump (Figure 44.2I). After tying, the long end of the suture can be used to close the remaining gap in the mesentery without tension in a simple, continuous pattern. An assistant can hold the mesenteric stump away from the intestine to ensure that no purse-string effect will shorten the mesentery and result in a kink in the intestine at the level of the anastomosis (Figure 44.4 and Figure 44.5).

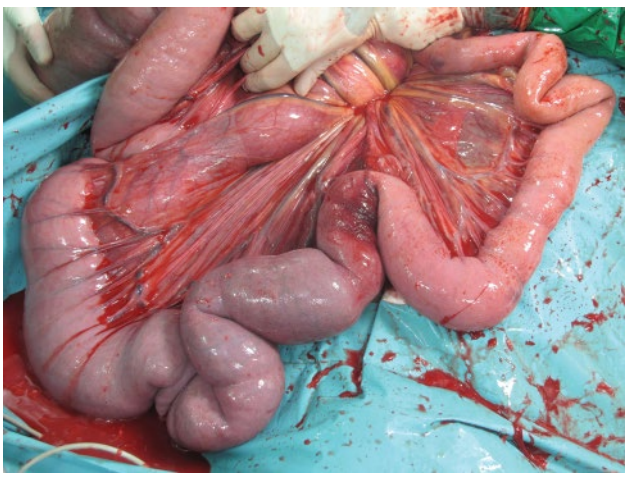

Figure 44.4 The mesenteric defect in this horse was closed in a way that left it too short. This resulted in a kink of the jejunum at the level of the anastomosis and made this jejunojejunostomy nonfunctional.

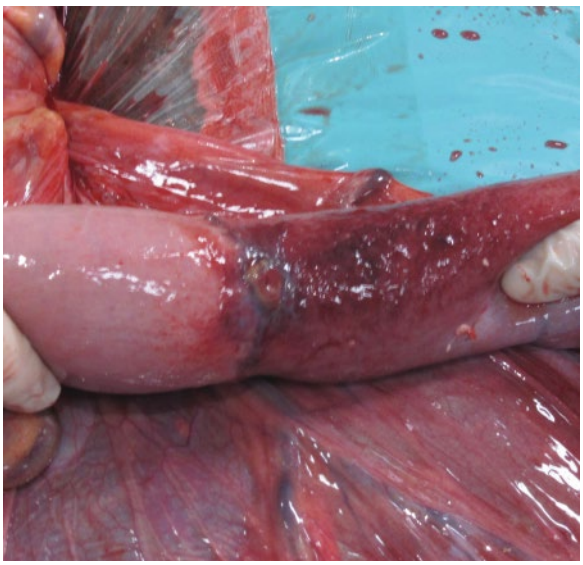

Figure 44.5 Same intestine as in Figure 44.4. The kink caused severe serosal irritation and possibly a mild leak at the antimesenteric side of the anastomosis.

The Penrose drains used to close the jejunal lumen are cut and removed. The remaining gap in the mesenteric attachment is very small and does not need to be closed. At this point, the anastomosis is inspected to ensure adequate suture placement. The anastomosis must have a sufficient lumen to be functional. A surgeon with a size 7 glove should be able to pass three or four fingers through the anastomosis (Figure 44.2J). Inadequate traction on or alignment of jejunal ends, excessive inversion during suturing, and pulling sutures so tight as to create a purse-string effect can all result in a stoma lumen that is too small to function (Figure 44.6A–C). Manual distention of the anastomosis site to control for leakage puts unnecessary stress on the anastomosis and may predispose to failure. It should therefore be avoided and the anastomosis replaced in the abdomen without additional mechanical handling.

Functional End-to-End Jejunojejunostomy

All procedures and principles described in the section on end-to-end jejunojejunostomy apply. After transection of the mesentery and decompression of the bowel, the jejunal ends to be anastomosed are lined up in antiperistaltic fashion, with the antimesenteric sides of each bowel segment opposing the other. In the open technique, both bowel ends are transected and a stoma is created along the antimesenteric side through the open lumen. As an alternative, both bowel ends can be closed before positioning them for the anastomosis. The forks of a linear stapling instrument are then inserted through stab incisions close to the overseen ends to create the stoma. The mesentery is sewn so that part of the mesenteric suture line covers the blind end of the apposed segments (Freeman, 2008).

Latimer et al. (1998) described a closed one-stage functional end-to-end jejunojejunostomy in horses with the use of linear stapling equipment. After transection of the mesentery, Doyen clamps were clamped across the oral and aboral jejunal segments near the proposed transection of the bowel. Two stay sutures, 12–14 cm apart, were applied close to the Doyen clamps to the antimesenteric side of each segment and brought the bowel segments into alignment. Stab incisions into the antimesenteric side near the Doyen clamps were created and used to introduce the arms of a 100 mm linear anastomosis stapling instrument (ILA-100). The stoma was then created along the antimesenteric sides of the jejunum and the stapling instrument removed. A linear stapler (PI-90) was placed diagonally across both jejunal ends on the side of the stab incision near the created stoma and fired, then the jejunum was transected near the linear stapler and interrupted sutures were placed in the seromuscular layer at the antimesenteric side of the anastomotic staple line and along the linear staple line at the junction of the anastomotic staple lines with the linear staple line and at the mesenteric border of the anastomosed bowel segments (Latimer et al., 1998).

After a functional end-to-end anastomosis, the bowel remodels in an end-to-end fashion with a circular lumen of the anastomosis after 16 weeks, and the mesentery will eventually cover exposed mucosa at the linear staple line (Latimer et al., 1998). Intussusception has been described as a complication after functional end-to-end jejunojejunostomy in two ponies 2 and 26 days after surgery and in a horse 8 months after surgery (Frankeny et al., 1995; Semevolos et al., 2002). The lead point for the intussusception in all horses was the stapled anastomosis site, and the authors suggested that the acute angle created in the jejunum by the functional end-to-end anastomosis could predispose to the formation of an intussusception (Frankeny et al., 1995). Other complications described for this type of anastomosis include impaction at the anastomosis site, dehiscence of the staple line, peritonitis, and postoperative ileus (Latimer et al., 1998).

Side-to-Side Jejunojejunostomy

All procedures and principles described in the section on end-to-end jejunojejunostomy apply. After transection of the mesentery and decompression of the bowel, the jejunal ends to be anastomosed are transected and the ends closed with a Parker–Kerr technique or a stapling instrument. The jejunal segments with the blind ends are then lined up in isoperistaltic fashion. The stoma can be created at the antimesenteric side or between the antimesenteric and the mesenteric sides of the jejunal segments. Placing the stoma at the

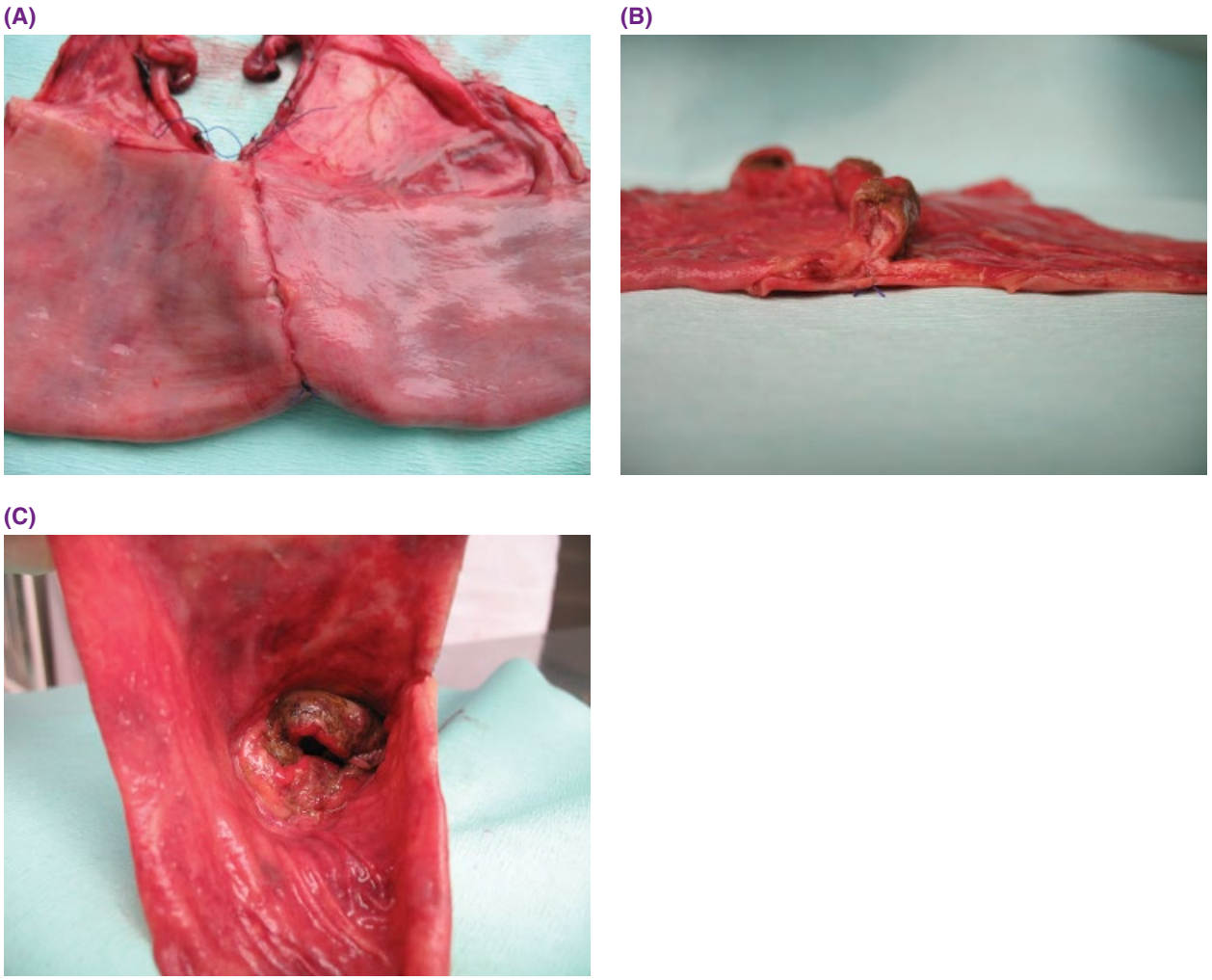

Figure 44.6 Failed anastomosis 24 h after completion of surgery. Doyen clamps were used near the anastomosis to adapt both jejunal ends and a double-layer suture pattern was used to complete the anastomosis. The Doyen clamps probably did not allow for enough lumen. In addition, too much inversion was created, leaving a large ridge of tissue further occluding the anastomotic lumen. **(A)** Anastomosis viewed from the serosal side. Note the imprints of the Doyen clamps in the serosa that can still be seen 24 h after removal. **(B)** Anastomotic suture line in a transverse view demonstrating the amount of inversion. **(C)** View into to the inside, demonstrating the very small lumen remaining.

antimesenteric side may not be regarded as anatomically correct but was less likely to leak when compared with a stoma created half way between the antimesenteric and the mesenteric sides. This could be due to difficulties in accessing the latter location for staple application and for inspection of the completed anastomosis (Mackey et al., 1987). The stoma is created with the help of linear stapling instruments inserted through stab incisions. If a shorter stapling instrument (GIA 50) is used, the stab incision is placed in the center of the planned stoma and the stapling instrument is placed and fired in both directions (proximal and distal) from the stab incisions. When longer stapling instruments are used (GIA 80, GIA 90, ILA 100), a single application of the stapling instrument through a stab incision at one end of the proposed stoma is sufficient (Freeman, 2008). If two staple lines are used, the most likely location for a leak will be at the junction of the two lines (Mackey et al., 1987). If one stapling line is used, the most likely point of failure is at the stapled end of the anastomosis, not at the end with the hand-sewn stab incisions (Bickers et al., 2002). The placement of stay sutures at either end of the anastomosis has been recommended to prevent leakage and staple separation (Freeman, 2008). The stoma should begin and end as close to the two blind ends as possible. If the blind ends are too long without connection to the stoma, this can predispose to the accumulation and impaction of intestinal contents, dilation, and ulceration (Freeman, 2008). After completion of the stoma, the two mesenteric edges are sutured to the adjacent mesenteric surface at the points of overlap (Freeman, 2008).

Jejunoileostomy

Jejunoileostomy can be performed when sufficient healthy ileum is available as an alternative to jejunocecostomy. The procedures and techniques for jejunoileostomy are comparable to those for jejunojejunostomy. Since this anastomosis must be performed in close proximity to the abdominal incision, special attention must be given to careful draping and packing off the surgical site and to removing any leaking intestinal contents before they can gain access to the abdominal cavity. Most reports describe an end-to-end jejunoileostomy, using a single-layer continuous Lembert pattern (Lee et al., 2012), a two-layer simple continuous and Cushing pattern (Lee et al., 2012), or a two-layer simple continuous and simple continuous pattern (Loesch et al., 2002). A one-layer Lembert pattern was faster to create, and resulted in a larger anastomotic lumen and no difference in bursting pressure compared with a two-layer jejunoileostomy (Lee et al., 2012). Anderson & Blackford (2012) described a stapled closed one-stage functional end-to-end jejunoileostomy in five horses.

A jejunoileal anastomosis will leave the intestinal anatomy more intact than its alternative, the jejunocecostomy, and can function well. In the past, several concerns have been raised regarding this anastomosis. This anastomosis has been thought to be susceptible to failure owing to vascular compromise because of the absence of a collateral arcuate blood supply to the ileum (Edwards, 1986), but later this complication was considered to be rare (Freeman, 2008). Freeman (2008) suggested that a jejunoileal anastomosis could have a tendency to impact. This could be due to the difference in intestinal wall thickness between the jejunum and ileum, and horses with a large gastric impaction at surgery may be most prone to anastomotic impaction (Freeman, 2008). Also, intense handling of the ileum can result in significant edema formation, and an edematous ileum could predispose a jejunoileal anastomosis to impaction.

Ileoileostomy

This anastomosis can be performed if only a short segment of ileum must be resected, both ileal ends can be exteriorized, and the ileal vasculature is intact. It involves ligation and transection of the vasa recti that leave the ileal artery and trimming the mesentery in a semicircle with the curve facing the ileal artery. A hand-sewn end-to-end anastomosis is performed as described in the section on end-to-end jejunojejunostomy. The mesentery is closed, making sure that the ileal artery is not kinked (Rayner, 2003).

Jejunocecostomy

Jejunocecostomy can be performed when the ileum is compromised to such an extent that a jejunoileostomy cannot be completed. This anastomosis will change the intestinal anatomy significantly, removing a valve between the small intestine and the cecum and creating a stoma far more distal on the cecal body than the position of the ileocecal junction. In addition, the jejunum has a thinner and less muscular wall than the ileum, which can make propulsion of intestinal contents into the cecum more difficult. The thin wall of the jejunum in conjunction with the new location of the stoma also make correct positioning of the jejunum and the stoma critical to avoid kinks in the bowel after the horse stands up that can lead to anastomotic failure.

A jejunocecostomy can be performed in a side-to-side or an end-to-side fashion. A side-to-side jejunocecostomy may allow for the creation of a wider stoma that is less likely to be associated with problems resulting from stomal swelling and obstruction (Röcken & Ross, 1994). If a side-to-side jejunocecostomy is made too large (>10 cm), it can distend with time, which can lead to a delayed failure of the anastomosis. This may be explained by effects of delayed transit through this type of anastomosis and by reflux of cecal contents (Freeman, 2008). The size of the final stoma can be critical for success of the side-to-side jejunocecostomy. If the stoma is too large, it will be more difficult for the jejunum to build up enough pressure to overcome the intraluminal pressure exerted by the cecum (Giusto et al., 2014). If the stoma is too small, the jejunum can create more pressure, but passage of solid intestinal contents may be inhibited. As a guide, the final stoma of a side-to-side jejunojejunostomy should be close to the diameter of the jejunum at the level of the anastomosis (Freeman, 2012). Giusto et al. (2014) compared different sizes of hand-sewn and stapled jejunocecostomies *in vitro*. He found that with both techniques the final stoma was approximately 6–12% larger than initially intended. In a 400 kg horse, an initial stoma length of 80 mm was sufficient to produce a stoma as wide as the jejunum proximal to it.

For jejunocecostomy, the principles described for jejunojejunostomy apply. After transection of the mesentery, the intestinal contents should be drained though the strangulated segment into a bucket if possible and not into the cecum. Excessive filling of the cecum will predispose to reflux of cecal contents into the surgery site during the anastomosis. In a first step, the ileum is resected, followed by the anastomosis of the jejunum to the cecum. The final step will be closure of the mesenteric defect if possible, and this is less straightforward than it is after a jejunojejunostomy or jejunoileostomy is performed.

Resection of Ileum

The ileum should be resected at a point that is still accessible to seal the ileal lumen securely, but leaving the ileal stump as short as possible because a long stump could intussuscept into the cecum, be passed on, and then obstruct the cecocolic orifice (Schumacher & Hanrahan, 1987). To obtain access to the ileum as close to the ileocecal junction as possible, the cecum should be exteriorized as far as possible, any gas distention of cecum and large colon removed, and, if necessary, the large colon can be exteriorized to improve access further. The surgery site should be packed off with plastic drapes and laboratory sponges to minimize the risk of abdominal contamination. Closure of the ileum can be achieved with stapling instruments or a Parker–Kerr technique. If the ileum is compromised at the level of transection, the thickness of the ileal wall often does not allow for secure closure with staples. Both staples and a Parker-Kerr suture should be oversewn with an inverting suture pattern until the stump is securely sealed. If needed, ileum of questionable viability and even some necrotic ileum can be left *in situ*, but closure of compromised ileum can be difficult (Freeman, 2008). Remaining compromised ileum can be tolerated, probably because this segment of intestine remains nonfunctional. Also, the ileum can atrophy with time or intussuscept into the cecum, which is well tolerated if the ileal stump is not so long as to obstruct the cecocolic orifice (Toth et al., 1998; Freeman, 2008). For ileum that is deemed too compromised to leave in the abdomen with a secure closure, the ileum can be inverted into the cecum during surgery with the help of a nasogastric tube (Vasey & Julian, 1987). As an alternative, linear stapling equipment with 4.8 mm staples can be used to transect the ileum close to the ileocecal orifice in healthy bowel. This has to be done blindly and care must be taken to include the entire diameter of the ileum in the stapling line and to avoid including any other abdominal contents (Bladon & Hillyer, 2000; Freeman, 2008). Use of a TA90 stapler across a fold of everted cecum at the level of the ileocecal orifice has also been described, and this required a considerable amount of traction (Bladon & Hillyer, 2000). When extensive ileal resection is performed, the ileal vessels must be ligated at the same level. To do this, Bladon & Hillyer (2000) suggested making a defect in the ileal mesentery on the side of the ileal artery opposite from the ileum and a second defect in the ileocecal fold after completion of the ileal transection. Both defects were extended dorsally into the abdomen to the level of the transection. A strand of polyglactin 910 (5 metric) was passed through the mesenteric defect and the first throw of a knot tied to form a loose loop around the ileum. The loop was guided down into the abdomen to the level of the transected ileum and there tied around the ileal mesenteric artery and vein. The ileum was transected free from the mesentery up to level of the abdominal incision, and its vasculature and the mesenteric vessels were ligated again under direct visualization (Bladon & Hillyer, 2000). An alternative for blind ligation of the ileal vessels at a level near the cecocolic ligament could be the use of a laparoscopic electrosurgical vessel sealing device, but care must be taken to include only the vasculature and to protect the surrounding abdominal contents from the heat generated with this instrument. Also, the use of stapling equipment has been suggested for hemostasis, either as a separate stapling line across the ileal artery (Robertson, 1990) or by placing the vasculature on the ileum and including it in the staple line used when transecting the ileum (Freeman, 1997).

Side-to-Side Jejunocecal Anastomosis

After decompression of the bowel, the jejunum is transected at a 90° angle at a level near a major mesenteric artery. The distal end is closed using a Parker–Kerr technique oversewn with a Cushing suture line or another inverting suture pattern. Alternatively, a dividing stapling instrument can be used. The everting mucosa can then be covered using an inverting suture line to avoid adhesion formation (Bladon & Hillyer, 2000).

The stoma for this anastomosis should be half way between the dorsal and the medial bands of the cecum and as far toward the base of the cecum as possible. The cecum must be exteriorized as far as possible and as a guideline the stoma should be placed so far proximally on the cecum that it is approximately at the same level as the cecocolic fold (Figure 44.7). The segment of cecum chosen for the anastomosis can be lifted with Babcock forceps or stay sutures or be clamped off (Freeman, 2008).

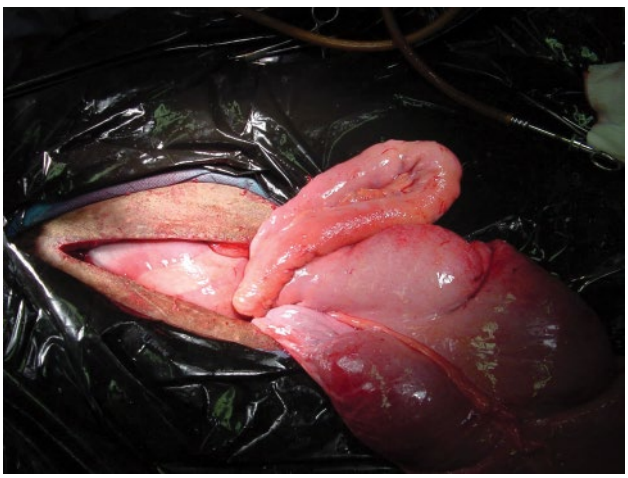

Figure 44.7 Completed hand-sewn side-to-side jejunocecostomy. The stoma of the anastomosis is at a level with the cecocolic fold and the blind end of the jejunum is pointing towards the base of the cecum.

The stoma will be created between the antimesenteric side of the jejunum and the cecum. The antimesenteric side of the jejunum as close to the blind end as possible is attached to the selected wall segment of the cecum as close to the cecal base as possible. A second suture is used to secure the antimesenteric side of the jejunum approximately 10–12 cm further proximal from its blind end to the cecum half way between the dorsal and medial bands. This should result in the jejunum being positioned on the cecum half way between the dorsal and medial bands, running parallel to these bands with the blind end pointing toward the base of the cecum. Both the jejunum and the cecal wall should be in apposition without folds and without tension. The stoma can then be created using a hand-sewn technique, stapling instruments, or a "cutting or sawing thread" technique. A stapled suture line is more rigid than a hand-sutured line, and resulted in a spindle shaped stoma that was curved dorsoventrally in an *in vitro* study (Giusto et al., 2014).

Hand-sewn Technique

The goal is to create a stoma exactly between the antimesenteric side of the jejunum and the cecum, with two layers of sutures surrounding the stoma. The suture line are created in the following order: outer suture line on one side, inside suture line on the same side, inside suture line on the other side, and outer suture line on the other side. Since the first suture line is an outer suture line it must be created slightly (5–8 mm) closer to the mesentery of the jejunum than its antimesenteric side. Failure to do this will place the stoma more toward the mesentery of the jejunum, causing rotation of the jejunum and a kink at the anastomosis (Freeman, 2008). The first outer suture line is completed using a Cushing pattern to join the jejunum and the cecum between the two interrupted sutures previously applied. It is tied at both ends but the ends are left long and can be secured with hemostats. The jejunum is then incised at its antimesenteric side for approximately 8–10 cm and about 5 mm shorter than the first suture line on either end. The cecum is incised about 5 mm away and parallel to the first suture line and 5 mm shorter than this suture line on either end. The second suture line can be a simple continuous pattern that joins the cecum and the jejunum inside the first suture line. This line should incorporate the corners of the stoma on either side. It is tied but the suture ends are left long. The third suture line must be an inverting pattern, such as a Lembert pattern, to join the cecum and the jejunum of the opposing side of the created stoma and including the corners. It is tied on both sides, and the long ends of the two inside suture lines (second and third suture lines) can then be tied together to secure complete closure of the anastomosis on both ends of the stoma. The last suture line is then completed in a Cushing pattern and tied on both sides (Figure 44.7). The long ends of the first and the last suture lines are then tied together on both ends of the stoma to ensure a secure seal at these critical points.

As an alternative, Gandini (2010) described a technique for a hand-sewn, semiclosed, single-layer jejunocecal side-to-side anastomosis. In this technique, the blind-ended jejunum is positioned on the cecum with its antimesenteric side as described earlier, but two proximal and two distal stay sutures are used to attach the jejunum to the cecum in a rectangular shape. A continuous Lembert pattern is then used to join the jejunum and cecum on both long sides and on the short side of the rectangle near the cecal base. Two 25–30 mm full-thickness incisions were made into the cecum and jejunum on the short side of the rectangle near the apex of the cecum. Two crushing Hartmann bowel clamps were introduced to connect the jejunal and cecal walls on either side along the long axis of the proposed stoma. The stoma was then created with scissors introduced between these two clamps. After removal of the clamps, the jejunal and cecal walls along the short side of the rectangle near the apex of the cecum were joined with a continuous Lembert suture pattern, closing the incisions and completing the anastomosis.

Anastomosis with Stapling Instruments

After securing the blind-ended jejunum to the cecum with interrupted sutures on the proximal and distal aspects of the proposed stoma as described in the section on the hand-sewn technique, stab incisions are made into the antimesentric side of the jejunum and into the cecum, both near either end of the proposed stoma between one interrupted suture and the stoma to be created. The arms of a linear intestinal anastomosis stapling device with a length between 80 and 100 mm are introduced into the jejunum and cecum and the stapling instrument is secured and fired to create the stoma. The stab incisions are then closed with an inverting hand-sewn pattern. Oversewing the entire staple line is optional, but interrupted sutures can be used to stabilize the anastomosis at its most critical points, either end of the anastomotic lumen and at the midpoint of each side of the anastomosis (Freeman, 2008). With this technique, the formation of a blind-end pouch in the distal jejunum is unavoidable, in contrast to the hand-sewn technique (Giusto et al., 2014).

To avoid blind-pouch formation, Freeman & Schaeffer (2010) described an alternative method for stapled anastomosis using stapling instruments. In this technique, the jejunum is not blind-ended before attaching it to the cecum with stay sutures. A stab incision is created into the cecum at the level of the open end of the jejunum. A linear intestinal anastomosis stapling device is introduced into the jejunum and cecum and used to create the

stoma. The jejunum and the cecum are then closed in a Y-shaped suture line. Another technique to avoid the formation of a blind pouch was described by Gandini et al. (2014b, 2014c) and involves a modified GIA80 stapler and transection of the jejunum after the stoma has been created. Both modified techniques could almost completely reduce the formation of a blind pouch compared with a standard stapled side-to-side jejunocecostomy (Gandini et al., 2014b, 2014c).

"Cutting or Sawing Thread" Technique

The jejunum is secured to the cecum with interrupted stay sutures on the proximal and distal aspect of the proposed stoma and jejunum and cecum are joined with a Cushing suture line as described in the section on the hand-sewn technique (first suture line). The site of the stoma is prepared by cutting through the seromuscular layers of both cecum and jejunum about 5 mm away from and parallel to the Cushing suture line. This will be the site of the proposed stoma. Care must be taken not to penetrate the mucosa during this step of the surgery. A simple continuous suture line incorporating all intestinal wall layers is placed joining the jejunum and cecum on the inside of the first suture line (similarly to the second suture line in the hand-sewn technique). A 12-gauge catheter is then introduced through the mucosa into the lumen of either the cecum or jejunum at the proposed end of the stoma near the cecal base, and passed distally and through the mucosa toward the serosal side at the proposed end of the stoma near the cecal apex. A 6 or 8 metric polyfilament steel suture or other strong polyfilament suture is then passed through the catheter until it exits near the cecal base and the catheter is removed. The same procedure is repeated in the other intestinal segment (jejunum or cecum), and the same suture strand passed through the catheter. This should result in the suture entering the cecal lumen near the cecal base, leaving it near the cecal apex, entering the jejunal lumen near the cecal apex, and leaving it near the cecal base. A third inverting suture line corresponding to the third suture line described in the hand-sewn technique is completed, leaving a short segment near the cecal base open. A sawing motion on the passed suture is used to create the stoma. After the mucosa has been transected and the suture removed, the third suture line is completed, followed by a fourth suture line in a Cushing pattern as described in the hand-sewn technique (Toth et al., 1998). This method has been adapted using a diathermy wire instead of a suture wire (Sandh, 1991).

End-to-Side Jejunocecal Anastomosis

This anastomosis is created in a hand-sewn fashion and the types and sequence of suture lines are performed as described in the section on hand-sewn side-to-side jejunocecal anastomosis. The location of the stoma on the cecum is the same as for the side-to-side anastomosis. The jejunum can be transected at an angle to increase the lumen of this stoma, and a longitudinal incision on the antimesenteric side ("fishmouth") can be used to increase the stoma size further (Freeman, 2008).

For this anastomosis, the jejunum is not closed to form a blind end. Instead, the open jejunal end is attached at its mesenteric and antimesenteric sides to the selected region of the cecum with simple interrupted sutures. A Lembert or Cushing pattern attaches the back side of the jejunum to the cecum (first suture line). The cecum is incised 5 mm from this suture line in a length corresponding to the jejunal opening and a simple continuous suture line is placed to connect the cecum and the jejunum near the first suture line (second suture line). Two inverting suture lines are then placed at the near side of the jejunum similarly to those described for the side-to-side jejunocecostomy to complete the anastomosis (third and fourth suture lines).

Mesenteric Closure

Closure of the mesentery is only possible if the ileum was transected near the abdominal incision. It is impossible if the ileum was transected near or at the level of the ileocecal orifice or if it was inverted into the cecum (Bladon & Hillyer, 2000). If closure of the mesentery is not possible, it has been suggested to leave the defect as large as possible to avoid incarceration of intestine passing through the defect (Robertson, 1990).

If the ileum was transected near the abdominal incision, the mesentery is closed beginning at the gathered mesenteric stump with a simple continuous suture pattern. The suture line is continued to suture the mesentery to the cecum near the blind end of the jejunum, then to the ileocecal fold and along the antimesenteric side of the ileum to the ileal stump, and then back to the gathered mesenteric stump. This should result in complete closure of the mesentery without any remaining gaps. During mesenteric closure, the ileal stump and the anastomosis should be separated as much as possible to prevent distortion of the anastomosis when the horse stands (Freeman, 2012).

Comparisons of Anastomosis Types

For jejunojejunal and jejunoileal anastomosis, the end-to-end anastomosis will cause the least disturbance from the normal anatomy of the intestine. Potential problems inherent to other methods of small intestinal anastomosis (intussusception of a functional end-to-end anastomosis, blind-end formation in a side-to-side anastomosis) are avoided with this technique, and the end-to-end

anastomosis is the technique of choice in most publications concerning small intestinal resection. In a direct comparison between jejunojejunostomies using a hand sewn end-to-end, a stapled functional end-to-end, and a stapled side-to-side technique, there was no difference in postoperative survival or complication rates between these techniques (Semevolos et al., 2002). A stapled functional end-to-end anastomosis was faster to perform and needed less tissue manipulation than a stapled side-to-side jejunojejunostomy, and there was no difference in bursting pressure and bursting wall tension between these two techniques (Bickers et al., 2002). Close et al. (2014) found no difference in postoperative complications and survival between small intestinal end-to-end anastomoses created with a single-layer or a double-layer suture pattern. For jejunojejunal and jejunoileal anastomosis, the technique chosen should depend on the experience and level of comfort of the surgeon, with a preference for an end-to-end anastomosis. The choice between a single-layer and a double-layer suture pattern also depends on the experience of the surgeon, but single-layer Lembert patterns are faster to perform and at least as strong as double-layer patterns.

Whenever possible, a jejunoileal anastomosis should be preferred over a jejunocecal anastomosis. A jejunoileostomy results in similar survival rates to a jejunojejunostomy (Rendle et al., 2005; Close et al., 2014), but may result in a higher rate of colic during the immediate postoperative period (Close et al., 2014). In most reported clinical studies, the mortality rate for horses with a jejunocecal anastomosis was higher than that with a jejunojejunal anastomosis (Freeman et al., 2000; Morton & Blikslager, 2002; Proudman et al., 2002). Stewart et al. (2014) reported similar survival rates between jejunojejunal, jejunoileal, and jejunocecal anastomoses, but horses with a jejunocecostomy had more colic episodes after the surgery. A higher rate of postoperative complications after jejunocecostomy than after jejunojejunostomy has also been reported by other authors (Freeman et al., 2000; Proudman et al., 2002), and the highest risk for complications occurs in the first week after surgery (Freeman et al., 2000).

When a jejunocecal anastomosis becomes necessary, a side-to-side technique should be preferred because it has a lower mortality rate than an end-to-side jejunocecostomy (Röcken & Ross, 1994). Both stapled and hand-sewn techniques can be used in accordance with the comfort level of the surgeon, and both suture methods had similar survival rates (Freeman & Schaeffer, 2010; Proudman et al., 2002). However, stapling resulted in a higher rate of postoperative complications in one report (Freeman & Schaeffer, 2010).

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45

Large Colon Enterotomy, Resection, and Anastomosis

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Large Colon Enterotomy

Pelvic flexure enterotomy is a commonly performed procedure in horses with abnormalities affecting the large colon. Typically, this procedure is performed to evacuate the colonic contents. However, enterotomy procedures are also performed for removal of foreign bodies (usually from the right dorsal colon), and right ventral colon enterotomy is used to access the viability of the cecum in horses with a cecocolic intussusception.

Pelvic Flexure Enterotomy and Large Colon Evacuation

For this procedure, the large colon is exteriorized and placed on a colon tray (Kimzey Enterotomy Surgery Table; Kimzey Welding Works, Woodland, CA, USA) on the left side of the horse or caudally between the horse's hind legs. If a colon tray is not available, the colon is best exteriorized between the horse's hind legs. Some surgeons place the end of the laparotomy drape on the tray to create a shelf to help support the weight of the colon. The enterotomy drape is then placed on top of the laparotomy drape and secured with towel clamps. The colon tray is angled at about 20° (Figure 45.1). A modified trash can with an ingesta strainer and a liquid outflow hose can be used to collect and evacuate the contents of the colon (Figure 45.2) (Markel et al., 1988). Alternatively, the end of the tray can be positioned over a disposal system built into the surgery room (Figure 45.3). In anticipation of colonic evacuation, a lavage system should be established. This can be accomplished with two garden hoses, or one hose with a Y connection. One hose is used for intraluminal lavage and evacuation of the contents, and the other for extraluminal lavage of the colon, using warm water (37 °C, 98.6 °F) or a warm balanced electrolyte solution (Markel et al., 1988). If these are not available, stomach tubes, buckets, and pumps can be used.

A full-thickness 8–12 cm incision is made on the antimesenteric border of the pelvic flexure (Hardy & Bertone, 1992). One hose is inserted and gently advanced into the colon, while the other is used to lavage continuously the serosal surface of the colon to reduce fecal contamination (Figure 45.1). During the evacuation procedure, it is useful to lift the colon to ensure that the underside is also lavaged. A sterile assistant helps to feed the hose into the colon and massage its contents. A modified colon tray has been developed that stabilizes the colon in a funnel, and the enterotomy is fixed using hooks (Marien et al., 2000). This modification has not been deemed necessary by most surgeons, and the author prefers to be able to manipulate the colon during evacuation. Furthermore, if the colon has an impaction associated with a displacement, the author prefers to evacuate the colon before correcting the displacement, in order to avoid rupture of a heavy colon during surgical manipulations.

If colonic evacuation is performed as part of correction of a large colon volvulus, an intestinal biopsy can be collected to evaluate the severity of damage at the time of surgery. Prior to closure, di-tri-octahedral smectite (Bio-Sponge®, Platinum Performance, Buellton, CA, USA) (0.5 kg per 500 kg body weight in 4 L of water) can be pumped into the right ventral colon to help reduce the likelihood of postoperative diarrhea (Hassel et al., 2009). Closure of a pelvic flexure enterotomy is performed using 2-0 absorbable suture material in two layers: a simple continuous seromuscular layer followed by a Lembert or a Cushing pattern (Young et al., 1991). Alternatively, a thoracoabdominal stapling device (TA™ 90, Covidien Products, Medtronic, Minneapolis, MN, USA) can be

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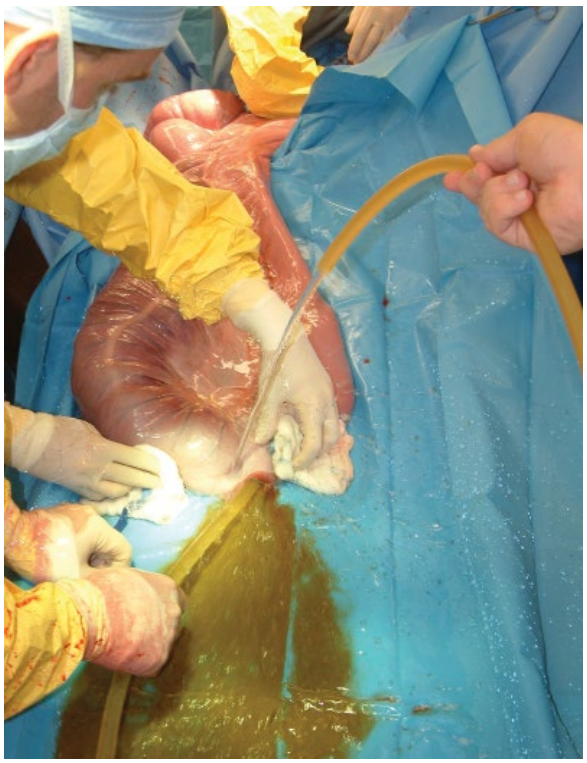

Figure 45.1 Exteriorization of the large colon onto a colon tray for evacuation through a pelvic flexure enterotomy.

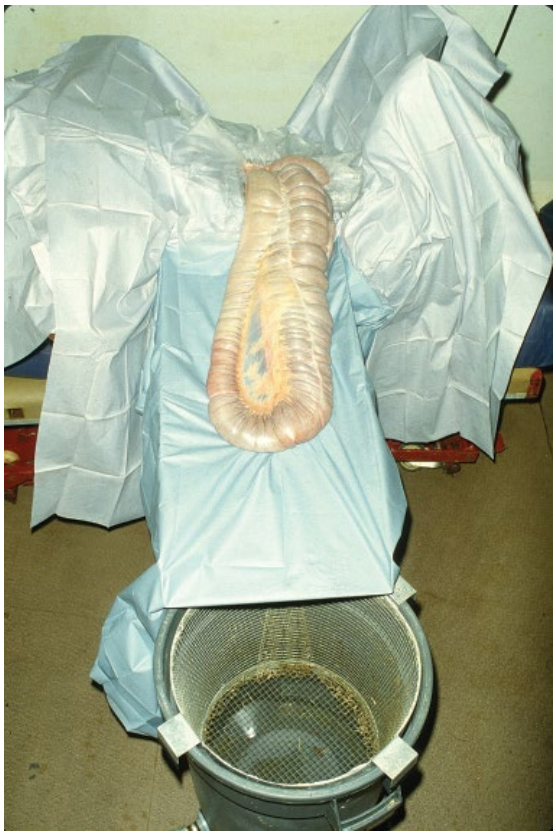

Figure 45.2 Illustration of a modified trash can used to collect colonic contents during evacuation.

Figure 45.3 Disposal system used to evacuate biological fluids and intestinal contents during large animal surgery.

used to apply a double row of staples to close the enterotomy site in an everting pattern, making sure that only the seromuscular layer is apposed and that no mucosa protrudes through the edges of the incision. In one experimental study, the stapled closure was significantly faster to perform, resulted in less reduction of the luminal diameter, and resulted in no difference in bursting strength compared with a double-layer hand-sewn closure (Rosser et al., 2012). The colon is rinsed with sterile saline or lactated Ringer's solution and replaced in the abdomen.

Enterotomies in the right dorsal or ventral colons are performed after the colon has been draped off from the main surgical field. Enterotomies made in the ventral colon are performed between tenial bands as the fibrous nature of the teniae precludes successful inversion during suturing. The location of the enterotomy in the dorsal colon is not as critical. Because enterotomies performed at these sites are more likely to bleed postoperatively, a full-thickness closure (simple continuous or Connell patterns) is performed on the first layer to achieve better hemostasis (Doyle et al., 2003). A Lembert or Cushing suture pattern is used as the second layer.

A modified Heineke–Mikulicz technique for pelvic flexure enterotomy closure has been described in two

horses having extensive stricture of the large colon (Rose et al., 1991). A longitudinal incision was made centered over the stricture and the incision was closed using a transverse closure, effectively increasing the diameter of the colon at that site.

Large Colon Resection

Indications

Resection of the large colon is performed for removal of full-thickness mural defects in the large colon. Causes include strangulation, infarction, thromboembolic disease, neoplasia, or scar tissue formation (Rose et al., 1991; Watt et al., 2001; Dabareiner et al., 1996; Embertson et al., 1982; Rottman et al., 1991; Steenhaut et al., 1993; Trostle & Markel, 1993; Wilson, 1983; Robertson & Tate, 1982). In addition, large colon resection may be recommended to prevent recurrence of large colon displacement or volvulus.

Techniques

Surgical techniques for removal of 50–95% of the large colon have been described (Arighi et al., 1987; Bertone et al., 1986, 1987; Boening & Von Saldern, 1986; Ducharme et al., 1987a, 1987b). Techniques for resection of the large colon include resection and end-to-end anastomosis, and resection and side-to-side anastomosis. Because large colon volvulus of a partially resected colon has been reported (Hughes & Slone, 1997), amputation of the entire colon within the limits of the abdominal incision is recommended.

End-to-end procedures are performed for removal of the colon up to 10–12 cm from the cecocolic ligament (Hughes & Slone, 1998). When resection of the colon closer to or proximal to the cecocolic ligament is required, a side-to-side technique is preferred as the end-to-end technique places too much tension on the anastomosis site. This increased tension places the anastomotic site at increased risk for dehiscence.

For an end-to-end resection, the colon is exteriorized on a colon tray and draped off; the cecum is replaced into the abdomen. All ingesta are massaged into the segment to be removed. If the colon is full, a pelvic flexure enterotomy is performed to evacuate the contents of the colon; care must be taken to remove all ingesta and water from the right dorsal and ventral colons to minimize contamination during the resection. The site for resection is identified by choosing a site that is easily held by the assistant surgeon without tension on the mesentery (Hughes & Slone, 1998). The colon is positioned to expose the right colic artery and the colic branch of the ileocolic artery within the mesocolon; the colonic vessels are isolated by blunt finger dissection and double ligated using #1 polyglactin 910. Alternatively, two double rows of staggered staples (TA 90) are applied across the mesocolon followed by a third double-staggered row 4 cm distally. The mesocolon is transected between the proximal and distal staple lines. Hemostasis is verified and any bleeding vessels are ligated. The right ventral colon is transected in a line transverse to its long axis. The dorsal colon is transected at a 30° angle to its long axis, with the antimesenteric border shorter so that the diameters of the dorsal and ventral colons are similar. In the original description of the procedure, a V-shaped stoma was created between the mesenteric border of the dorsal and ventral colons using an inverting linear anastomotic instrument reinforced with a double-layer, simple continuous pattern. This step was omitted in later descriptions of the procedure (Hughes & Slone, 1997). Starting at the mesenteric border, and suturing from the lumen, the colons are apposed with a double-row, simple continuous pattern using #0 polydioxanone or polyglactin 910 (Figure 45.4). Once the mesenteric portion of the anastomosis is completed, the remainder of the end-to-end anastomosis is performed using a double layer starting with a Connell followed by a Lembert pattern (Figure 45.5). The colon is lavaged and replaced in the abdomen. In a clinical study regarding the use of end-to-end resection anastomosis in 73 horses with strangulating large colon volvulus, 74% of horses survived to discharge, and the 1, 2, and 3 year survival rates were 67.8, 66.0, and 63.5, respectively (Ellis et al., 2008).

For a side-to-side anastomosis, the site of resection is usually at the level of the cecocolic ligament or orad to it. The colon is exteriorized to the left of the horse on a colon tray and the colonic vasculature is transected as described above. The stoma is created first, taking advantage of the weight of the colons to facilitate exposure of the anastomotic site. The site for creation of the stoma is identified, taking care to end it just proximal to the level at which the colonic vessels have been ligated, so a blind sac is not formed. A three-tier side-to-side stoma is created; the first layer apposes the colons using #1 polyglactin 910 in a Lembert or Cushing layer for a length of 20 cm (Figure 45.6). A full-thickness incision is made in each colon and a full-thickness, simple continuous circumferential closure, interrupted at the 180° mark, is made to create the stoma. The upper layer is then apposed using a Cushing or Lembert pattern. Alternatively, the stoma can be created using stapling instruments. This may minimize contamination, but may not be possible if the colons are too thick and edematous as a result of the underlying disease process. For an adequately sized stoma, the stapling instrument is fired twice if the ILA-100 or the GIA 90 is used, and three times if the GIA 55 is used, keeping in mind that the staples in the latter stapling instrument have a shorter staple length. Staple lines should be oversewn. Once the staples have been applied, the down layer cannot be approached for oversewing. Therefore, this layer should be performed first,

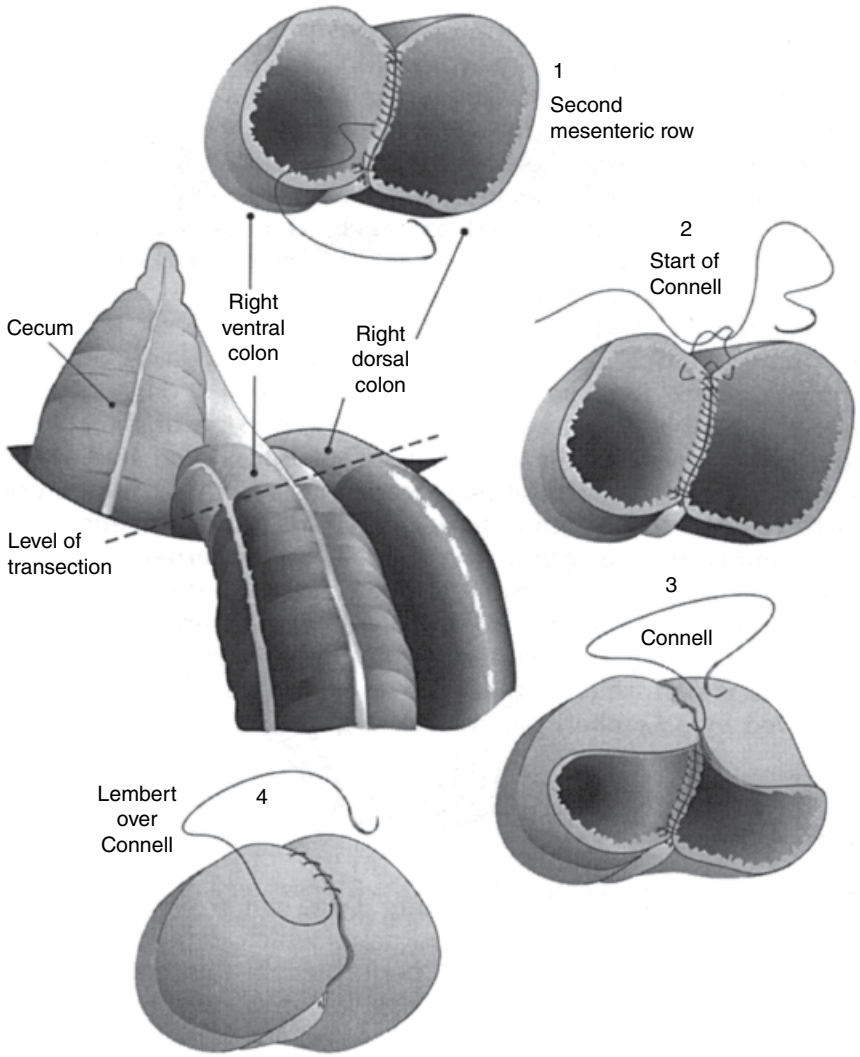

Figure 45.4 Illustration of an end-to-end resection and anastomosis of the equine large colon. Source: Hughes & Slone, 1997. Reproduced with permission of Elsevier.

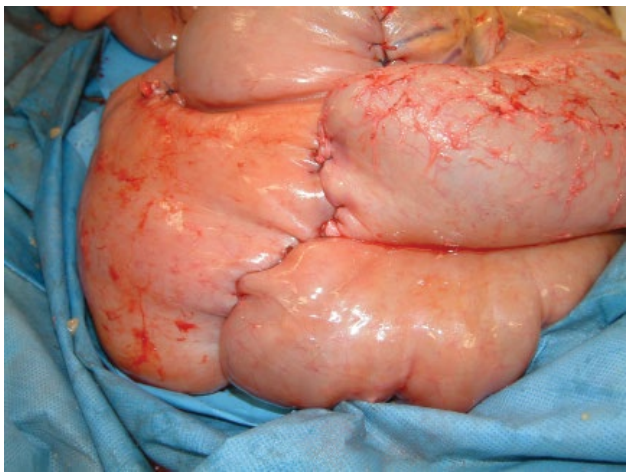

Figure 45.5 Intraoperative photograph of the large colon of a horse after end-to-end resection and anastomosis.

before application of the stapling instrument. Once the stoma has been created, the colons are resected, starting with the ventral colon, taking care to resect them at the site of colonic vessel ligation. The lumens are closed using a full-thickness, simple continuous or Connell pattern, and are oversewn with a Lembert or Cushing pattern (Figure 45.7). The resected colons are lavaged and replaced in the abdomen. Although resection of the large colon has been performed using stapling instruments, this is usually not possible after correction of large colon volvulus, as the intestinal edema and congestion do not allow proper closure of the instruments and adequate formation of the staples. In one study on the use of side-to-side resection of the large colon in 52 horses with large colon volvulus, 68.2% of horses survived to discharge; however, 77.8% of horses with nonstrangulating large colon lesions survived to discharge compared

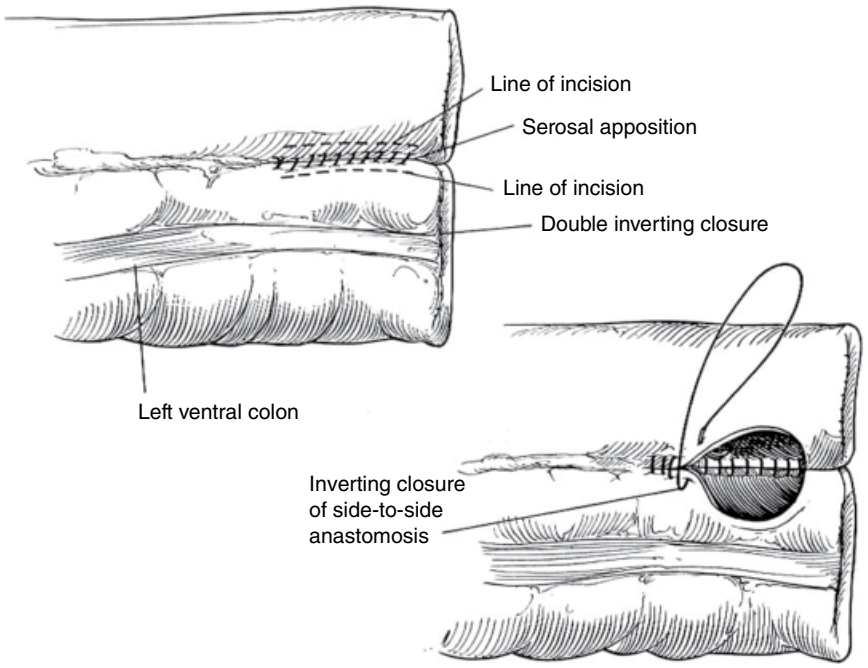

Figure 45.6 Illustration of a stapled side-to-side resection and anastomosis of the equine large colon. Source: McIlwraith & Robertson, 1998. Reproduced with permission of John Wiley & Sons.

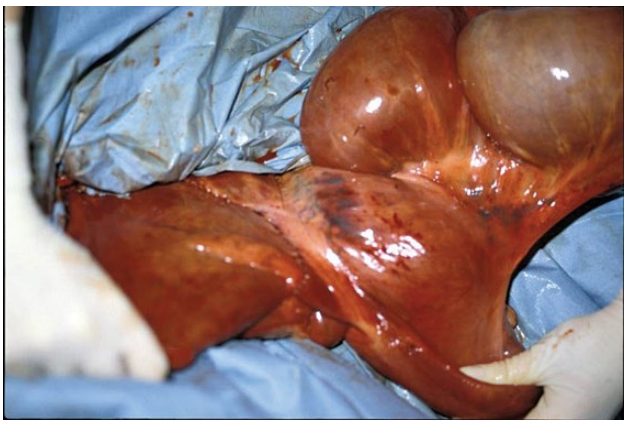

Figure 45.7 Intraoperative photograph of the large colon of a horse after side-to-side resection and anastomosis at the level of the cecocolic ligament.

with 47% of horses with strangulating large colon lesions (Driscoll et al., 2008).

An early method for large colon resection has been described that uses a luminal approach to create the side-to-side anastomosis, followed by closing the ends of the colons, essentially creating a functional end-to-end anastomosis (Boening & Von Saldern, 1986). The technique described above for end-to-end resection represents a modification of this technique.

Successful bypass of the right dorsal colon for the treatment of large colon volvulus has been described in one horse (Freeman & Richter, 1998). In that report, the large colon was judged to be nonviable after reduction of a large colon volvulus. The right dorsal colon was transected as far distally as possible within the abdomen, using a TA 90 stapling instrument, and the suture line was partially oversewn. The right ventral colon was transected 10 cm from the cecocolic ligament and an end-to-side anastomosis was made between the right ventral colon and the descending colon using a double-layer inverting pattern. Two mild episodes of colic and diarrhea for 1 week were the reported complications. In a similar fashion, anastomosis of the right ventral colon to the descending colon to bypass a nonfunctional descending colon anastomosis in a miniature pony was reported (Dowling et al., 2000). A two-layer, hand-sewn, end-to side anastomosis was performed between the right ventral colon and the descending colon. One episode of colic successfully treated with medical therapy was the only postoperative complication encountered in this case.

Complications

Complications arising from large colon resection are usually a result of the primary disease and include persistent endotoxemia and peritonitis as a result of continued bowel devitalization. This is because the site of volvulus is usually at or proximal to the site of resection, such that some portion of compromised large colon cannot be removed. Therefore, it is essential for the surgeon to remove as much of the devitalized colon as possible. In the author's experience, this requires a side-to side resection at or proximal to the cecocolic ligament. Even then, a segment of devitalized colon may remain in the abdomen, leading to subsequent complications. Most horses that succumb to endotoxemia and peritonitis do so within 3–7 days after the procedure, and require

considerable intensive care. In contrast, horses that survive have an improvement in clinical signs within 24 h after the procedure.

Postoperative pain is common in horses after large colon resection. This procedure induces clinical signs of pain even in healthy horses. Administration of non-steroidal anti-inflammatory drugs (NSAIDs), lidocaine, and opiates can help alleviate the pain.

Signs of endotoxemia are common after large colon resection for large colon volvulus. Signs include fever, tachycardia, injected mucous membranes, dehydration, and hypoproteinemia. Signs of large colon ileus, manifested by moderate to severe distention, can also occur. Supportive care with fluids, plasma, and treatments designed to counteract the effects of endotoxins are important. Horses should be monitored for signs of postoperative hemorrhage, which is more prevalent with large colon procedures and occasionally require a blood transfusion.

Postoperative diarrhea is commonly observed after large colon resection, because of mucosal damage or reduced surface area available for fluid absorption. The diarrhea is usually self-limiting and resolves within a few days if it is not infectious in origin. However, isolation procedures should be followed as dictated by hospital protocol, and infectious diseases should be ruled out.

Horses with successful resection of the large colon will usually regain normal fecal consistency in 5–7 days. Because of the decreased surface area available for digestion and water absorption, these horses will have increased water and phosphorus requirements, and will require a highly digestible diet.

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46

Abdominal Closure

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Closure of the abdomen is the final step of surgery for the acute equine abdomen. Once the intestinal lesion has been corrected and the end of surgery approaches, the importance of abdominal closure is often overlooked. However, meticulous closure of the abdomen is critical for a successful outcome, as complications such as acute failure or infection can be catastrophic. Many factors have been identified that contribute to incisional complications, ranging from suture choice and pattern to patient factors that affect wound healing. Research is continually being performed to evaluate new suture patterns and suture type and therefore the dedicated surgeon must continually evaluate the literature to keep current on advances in abdominal closure.

Although closure of the linea alba is obviously the most critical layer in providing strength to the body wall, handling of each tissue layer is important in a successful outcome and therefore these will be considered in turn.

Peritoneum

There is much debate, even in human surgery, as to whether or not the peritoneum should be sutured prior to closing the linea alba. This contention exists because closing the peritoneum could potentially increase or conversely decrease the incidence of adhesions forming between the intestine and the body wall. The original theory was that suturing the peritoneum avoided the presence of denuded areas where adhesions could occur, and therefore suturing the peritoneum was recommended (Robbins et al., 1949).

A study was performed to evaluate the effect of nonsuturing of the parietal peritoneum on the incidence of adhesions in horses assessed 5–11 days after surgery (Swanwick & Milne, 1973). In horses in which the peritoneum was not sutured, the adhesion rate was approximately 27%, but this increased to 50% if the peritoneum was sutured. Interestingly, in the presence of fecal contamination, this difference was amplified with the adhesion rate in horses in which the peritoneum was sutured rising to 75%, but remaining constant at 25% in horses in which the peritoneum was not sutured (Swanwick et al., 1973). However, in this study, nonabsorbable suture was used, which may have exacerbated the difference by creating a permanent nidus for inflammation. Overall, no adverse effects of not suturing the peritoneum were noted. Therefore, the conclusion can be drawn that suturing the peritoneum in horses appears to increase the incidence of adhesions, especially in the presence of fecal contamination, and therefore it is not recommended.

Closure of the Body Wall

Most colic surgery uses an approach through the linea alba. The anatomy of the body wall through a ventral median celiotomy is shown in Figure 46.1. However, some surgeons prefer a right ventral paramedian approach, either as a first incision or in a repeat laparotomy. Closure of each of these approaches is considered separately. Other approaches, such as a diagonal paramedian or parainguinal approach, are used infrequently and will not be discussed here.

Closure of the Linea Alba

The surgeon must make critical decisions in selecting the type of suture, suture size, and suture pattern. In addition, meticulous attention must be paid to tissue bite size and knot security. Many studies have evaluated these

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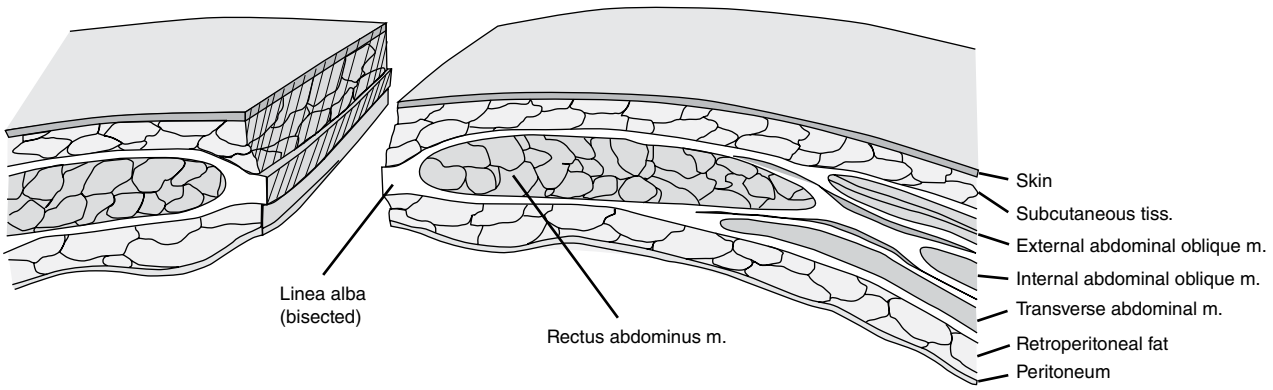

Figure 46.1 Anatomy of equine body wall through ventral median incision. Source: Freeman et al., 2002. Reproduced with permission of Elsevier.

criteria, and the evidence should factor into the surgeon's decision. In addition, the strength of the healing incision over time must be considered.

Suture Type and Size

Appropriate selection of suture type and size is critical to achieve a secure closure of the linea alba while minimizing the risk of complications such as infection. A comprehensive study that tested seven different suture materials in their largest available size at the time that the study was performed in the early 1990s in the equine linea alba (Trostle et al., 1994). Sutures tested included #3 polyglactin 910, #5 polyester, and #2 polydioxanone (see Table 46.1 for metric equivalents). Interestingly, all sutures failed before the tissue did. Therefore, none of these sutures maximized the strength of the linea alba. Size 5 polyester had the highest breaking strength and stiffness of all suture material tested. However, it cannot be recommended for closure of a ventral median celiotomy because it is nonabsorbable and multifilament and therefore there is a high risk of suture sinus formation. Both #3 polyglactin 910 and #2 poly(glycolic acid) were significantly weaker than #5 polyester, but were the strongest sutures excluding polyester. Polyglactin 910 in size 3 is a popular choice for closure of abdominal incisions. Although it is multifilament, which could increase the risk of infection, it is absorbable and therefore the infection should resolve once the suture degrades. Also of note from this study is that #2 nylon was significantly weaker than other sutures and therefore cannot be recommended for closure of a ventral median celiotomy (Trostle et al., 1994).

A more recent study repeated this evaluation of suture for closure of the equine linea alba using the larger sizes of polydioxanone and polyglactin 910 that are now commercially available in Europe and Canada (Fierheller & Wilson, 2005). It was found that #7 polydioxanone had the highest breaking strength, which was significantly higher than that of #6 polyglactin 910, followed by #3 polyglactin 910 and #2 polydioxanone. Despite this high breaking strength, again in 98% of specimens it was the suture that failed, usually adjacent to the knot. Therefore, even with the larger sized polydioxanone and polyglactin, the suture is still not as strong as the linea alba.

Table 46.1 Metric measures and USP suture diameter equivalents for synthetic absorbable and non-absorbable materials. Source: Freeman et al., 2002. Reproduced with permission of Elsevier.

USP size	4–0	3–0	2–0	0	1	2	3
Metric measures	1.5	2.0	3.0	3.5	4.0	5.0	6.0

An important consideration when using absorbable suture is the length of time that the suture maintains its strength compared with the gain in tissue strength as the linea alba heals. Tensile strength of the linea alba was tested at 2, 4, 8, 16 and 24 weeks after a 30 cm ventral median celiotomy was performed (Chism et al., 2000). It was determined that specimens were weakest after 2 weeks of healing, being less that one-fifth as strong as normal linea alba. However, the tensile strength rapidly increased after 2 weeks such that by 4 weeks after surgery, the tensile strength was not significantly different from normal linea alba.

The poor incisional strength at 2 weeks is concerning given that braided absorbable sutures undergo rapid hydrolysis (Bourne et al., 1988; Campbell & Bailey, 1992). In particular, the tensile strength of poly(glycolic acid) and polyglactin 910 was found to decrease by approximately 50% after 2 weeks of subcutaneous implantation, and had negligible strength after 4 weeks (Bourne et al., 1988; Campbell & Bailey, 1992). In contrast, polydioxanone, which is a monofilament absorbable suture, was found to retain 50% of its strength after 6 weeks of subcutaneous implantation. This difference is probably due to the fact that braided absorbable sutures have a larger surface area over which hydrolysis can occur, and therefore degrade more quickly than monofilament

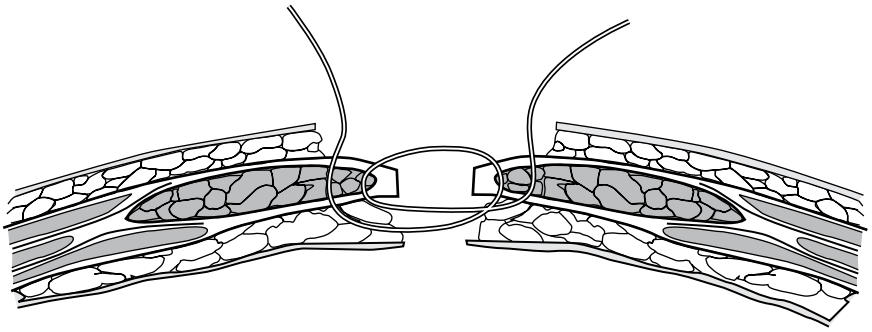

Figure 46.2 Far–near–near–far suture pattern for the linea alba. Source: Freeman et al., 2002. Reproduced with permission of Elsevier.

absorbable suture. Overall, polyglactin 910 is still preferred by most surgeons for closure of the linea alba and the rapid loss of tensile strength does not appear to be a problem in most cases. However, care should be taken not to stress the incision unduly at the 2 week time point, for example, by extended transportation of the horse.

Suture Pattern and Knot

Many suture patterns have been used to close the equine linea alba. A near–far–far–near pattern (Figure 46.2) was popular with surgeons 20 years ago, but was identified as a risk factor for purulent incisional drainage compared with a simple interrupted pattern, with incidence of infection rates of 40% and 0%, respectively (Kobluk et al., 1989). The authors hypothesized that this was due to the extensive undermining of tissues that is required to place near–far–far–near sutures, which results in an increase in dead space. The larger amount of foreign material in the incision as a result of this suture pattern would also likely contribute to an increase in infection rate.

Currently, a simple continuous pattern is the most popular method for closure of the equine linea alba. A study by Magee & Galuppo (1999) evaluated the incisional bursting strength of the equine linea alba closure when using #3 polyglactin 910 in a simple continuous or inverted cruciate suture pattern (Figure 46.3). The simple continuous pattern resulted in a significantly higher incisional bursting strength. This is most likely because any increase in tension in the incision can be better distributed along the length of the incision when a simple continuous pattern is used, instead of the force being isolated over one suture (Jenkins, 1976). Additionally, the simple continuous pattern used an average of 40 cm less suture than the inverted cruciate pattern, which may result in a decreased incidence of incisional infection.

Whichever pattern or suture type is selected, tissue bite size is also critical. An important study showed that the breaking strength of the linea alba increased with tissue bite size up to 15 mm (Trostle et al., 1994). With bite sizes greater than 15 mm, the breaking strength did not significantly increase further. The authors hypothesized

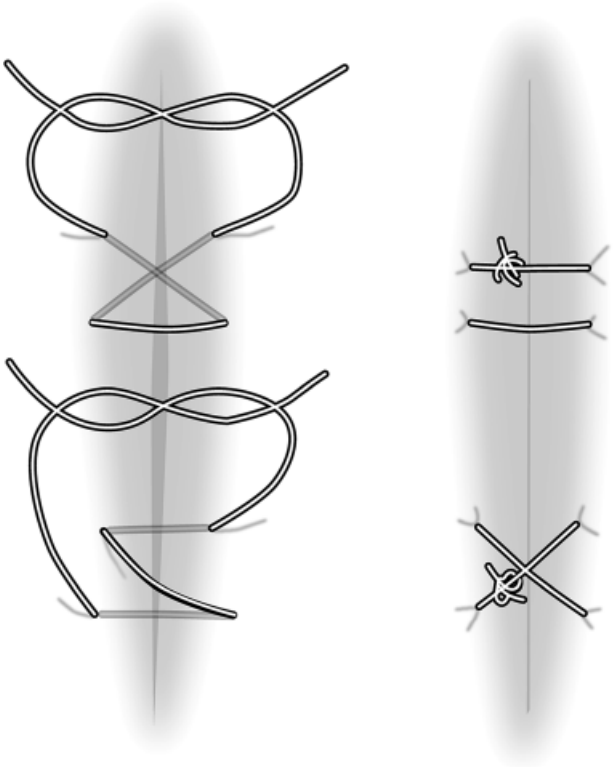

Figure 46.3 Inverted cruciate, or figure-of-eight (top), and cruciate patterns, placement (left) and on completion (right). The difference is that the crossover point of the sutures is close to the knot in the cruciate pattern, which could stress this vulnerable part of the suture. Source: Freeman et al., 2002. Reproduced with permission of Elsevier.

that this is because tissue bites of 15 mm or greater are placed lateral to the transition zone between the linea alba and the rectus abdominis sheath (Figure 46.1), which is stronger than the linea alba itself. Therefore, care should be taken to ensure that tissue bites are taken at least 15 mm back from the edge of the incision.

Additionally, the breaking strength of the abdominal wall was greatest near the umbilicus and decreased cranially, as would be expected based on the thickness of the linea alba (Trostle et al., 1994). This finding was also verified in a separate study (Chism et al., 2000). Hence a

surgeon could presume that the cranial portion of the incision would be more at risk for dehiscence than the caudal part.

It is well established that the knot is the weakest point of the suture line. This is likely because the knot changes the direction of the suture material, resulting in the forces placed on it being redirected at an angle to the suture. Indeed, in *all* the studies that evaluated the effect of suture pattern and size on incisional strength, the suture line failed at the knot (Figure 46.3) (Trostle et al., 1994; Magee & Galuppo, 1999; Fierheller & Wilson, 2005). Therefore, it is not surprising that a simple continuous pattern, which inherently contains fewer knots, has been shown to be stronger than an interrupted pattern (Magee & Galuppo, 1999). In fact, the addition of a knot to a suture line profoundly decreases the tensile strength of a suture by 30–35% (Bourne et al., 1988). Therefore, when closing the linea alba with a simple continuous pattern, it would be prudent to use greater length suture with two surgeons suturing from each end of the incision and tying to each other in the middle in order to minimize the number of knots required.

An additional consideration is knot security. The type of suture, number of throws, suture pattern, and surgeon experience have all been shown to influence knot security (Marturello et al., 2014). Polyglactin 910 was found to have poor knot security when it was dry, but it was substantially higher when the suture was wetted with saline (Bourne et al., 1988). A braided absorbable glycolide–lactide copolymer suture (Polysorb™; Covidien, Norwalk, CT, USA) has been shown to have superior knot security to polyglactin 910 in several studies (Kearney et al., 2014; Sanders et al., 2015). USP size 2 glycolide–lactide polymer was also found to have a higher initial yield strength than the same sized polyglactin 910 and polydioxanone. Therefore, it would seem to be an ideal choice for closure of the equine linea alba. However, it lost strength very rapidly when incubated in phosphate-buffered saline, serum, urine, or inflamed peritoneal fluid (Kearney et al., 2014; Sanders et al., 2015). Clamping the first throw of a knot to hold it when it is under tension did not weaken the knot, at least when tested with #2 nylon and #2 polypropylene (Huber et al., 1999), hence it seems to be an acceptable method to prevent slippage when tying a knot under tension to close the linea alba. The number of throws is also important in preventing slippage, especially when a continuous suture pattern is used. When #2-0 polyglactin 910 was tied with a secure square knot, three throws provided sufficient security to the start of the suture line, but six throws were necessary on the ending knot to prevent slippage (Rosin & Robinson, 1989). Another study using size 3-0 suture also confirmed that the knot at the end of a simple continuous line is at increased risk for failure compared with the knot at the beginning of a simple continuous pattern (Marturello et al., 2014). This is likely because the ending knot is created with a suture loop, which adds bulk to the knot and may result in it being less secure. Larger sized suture is also less secure. Therefore, when using larger suture many surgeons will chose to place six throws on each knot and leave 1 cm ears to reduce the risk of untying due to slippage (Magee & Galuppo, 1999). Additionally, the tying technique is important, as a loosely tied square knot is not as secure as a snug square knot (Rosin & Robinson, 1989).

Closure of a Paramedian Approach

Occasionally, a ventral paramedian incision, usually placed 5 cm to the right of midline, is used to approach the abdomen. Surgeons may select this approach because of personal preference, in order to avoid a previous ventral median celiotomy, and because it has a low incidence of incisional complications (Anderson et al., 2011). However, surgeons also need to be aware that right ventral paramedian incisions have a significantly lower bursting strength than ventral median celiotomies, with the body wall usually failing along the right side of the suture line (Anderson et al., 2013). Additionally, when performing a second celiotomy subsequent to an initial ventral median celiotomy, no difference in tensile strength was found between the right ventral paramedian approach and a repeated ventral median approach (Boone et al., 2014). Therefore, a right ventral median celiotomy approach may not confer much of an advantage at a repeat celiotomy, compared with reopening the original incision.

Comparisons of suture type, pattern, and tissue bite size have not been performed as extensively for paramedian incisions as for ventral median celiotomies. However, it is likely that much of the same findings apply to paramedian incisions. Closure of a right ventral paramedian incision differs slightly in that only external rectus sheath is closed. (Anderson et al., 2011) This may contribute to the documented lower bursting strength.

Subcutaneous Closure

There is much debate as to whether the skin and subcutaneous tissues should be closed in a single layer to create a two-layer closure including the linea alba, or two separate layers giving a more traditional three-layer total closure. Advocates for a separate subcutaneous closure argue that the additional layer over the suture in the linea alba will help protect it against ascending infection, closes dead space, and reduces tension on the skin. Others would argue that this inserts an additional layer of foreign material that could potentiate infection.

A recent study compared the incidence of incisional drainage after exploratory celiotomy in cases sutured

with a two- or three-layer closure (Colbath et al., 2014). The incidence of incisional drainage was found to be up to five times higher in horses that had a three-layer closure, compared with those that had a two-layer closure. The two-layer closure applied in this study used polydioxanone in a modified subcuticular pattern in which tissue bites take a small amount of subcutaneous tissue and advance at 45° to exit at the dermal/epidermal interface. The subsequent bite is taken directly across the incision from the exit point, entering through the opposite dermal/epidermal junction and advancing 45° through the subcutaneous tissue (Colbath et al., 2014). A previous study also compared a two- and three-layer closures of laparotomy incisions and found no difference between the techniques in the incidence of suppuration, which was defined as drainage of pus from the incision (Coomer et al., 2007). However, the two-layer closure used in this study simply eliminated the subcutaneous closure with the second layer consisting solely of skin suture. Therefore, dead space was not specifically eliminated. This may explain the difference in findings between the two studies, as in the Colbath et al study the modified subcuticular pattern specifically closes the dead space and suture material is buried, which may reduce the risk of ascending infection.

Absorbable size 2-0 suture in a simple continuous pattern is usually used for subcutaneous closure. An antibacterial (triclosan)-coated version of #2-0 polyglactin 910 was evaluated to determine if it might decrease the likelihood of incisional complications after ventral median celiotomy (Bischofberger et al., 2010). There was no beneficial effect of the antibiotic-impregnated suture on incisional complication rates and, in fact, incisions sutured with the triclosan-coated suture had a trend toward an increase in incisional edema, although this was not significant. Therefore, there appears to be no evidence to suggest a benefit to using triclosan-coated suture to close the subcutaneous layer of ventral median celiotomies.

Skin Closure

If a three-layer closure is used, the technique utilized for skin closure is also important. For many years, stainless-steel skin staples have been the surgeon's choice for skin closure in ventral median celiotomies because they are quick and easy to use. However, when the use of skin staples was compared with simple continuous suture with #0 polypropylene, the incidence of infection was 27% compared with 10% with the suture (Torfs et al., 2010). These findings have resulted in the majority of surgeons no longer using staples for skin closure in colic cases and switching to suture instead.

An alternative would be to use absorbable subcuticular staples for closure of the skin (Biedrzycki et al., 2015). The potential advantages of these staples is that they may reduce the risk of ascending infection and also do not need to be removed. However, the subcuticular absorbable staples had a low tensile strength and failed by staple fracture. Furthermore, their reactivity in equine tissue is unknown. Therefore, further investigation is necessary before recommending their use in clinical cases.

Additionally, although the risk of incisional drainage was higher when the skin was closed separately than with a two-layer closure, a simple continuous pattern only increased the odds ratio to 2.6, whereas other skin sutures patterns, such as a horizontal mattress and intradermal, increased the odds ratio to 4.9. Therefore, if the surgeon chooses to use a three-layer closure, a simple continuous pattern in the skin appears to be the one that results in the lowest risk of incisional complications.

Conclusion

Closure of the abdomen is a critical step in clinical cases. Meticulous attention must be paid by the surgeon to ensure that a secure closure is created that also minimizes the risk of postoperative complications.

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Part XII

Intensive Care and Postoperative Care

47

Monitoring Treatment for Abdominal Disease

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Monitoring the effectiveness of treatment is an essential part of the overall management of horses affected by a wide variety of abdominal conditions. Careful monitoring of gastrointestinal function is important so that the response to therapy can be assessed, and any derangements or deteriorations of gastrointestinal function can be identified and supportive therapy instituted rapidly. However, the critically ill patient may develop abnormalities and dysfunction of many organ systems in addition to the system affected by the primary disease. The result can be multi-organ dysfunction, and ultimately multi-organ failure, which is invariably fatal. It is important, therefore, that monitoring allows assessment of the function of all of the major organ systems, and not just gastrointestinal function. This monitoring includes repeated physical examinations and pain assessment, monitoring of temperature and pulse and respiratory rates, and collection of clinical pathological data. Accurate medical records are essential to monitor trends in an animal's response to treatment.

Frequency of Examinations

The frequency of examinations is dependent on the condition of the horse and the underlying abnormalities. Thus, seriously ill horses will need continuous supervision and frequent (at least hourly) re-examinations, whereas less critically ill horses require less frequent re-examinations. Suggested protocols for the monitoring of horses with different types of gastrointestinal disease are summarized in Table 47.1. It should be recognized that these are guidelines only, and the precise monitoring protocol must be tailored to the needs of individual clinical cases.

Physical Examinations

Horses receiving intravenous fluid therapy (which includes most horses with significant bowel damage such as strangulating and ischemic lesions and colitis/enteritis) should be examined hourly, and the hydration status evaluated by packed cell volume (PCV) and total protein (TP) estimations at least every 6 h. Horses with less serious gastrointestinal diseases are generally examined every 3–4 h until the condition has stabilized or is improving. These examinations should include assessments of the following:

- degree of pain;
- cardiovascular status (heart rate, mucous membrane color, capillary refill time, etc.);
- rectal temperature;
- respiratory rate;
- gastrointestinal function (fecal production, intestinal sounds);
- appetite;
- urine production;
- assessment of the feet for evidence of laminitis (pain, increased digital pulses);
- assessment of intravenous catheter sites for evidence of thrombophlebitis (heat, swelling, pain, distention of the vein);

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Table 47.1 Guidelines for monitoring intensive treatment of horses with gastrointestinal diseases.

Condition	Common complications	Frequency of physical examinations	Nasogastric intubation	PCV/TP	Full hematology	Electrolytes and urea/creatinine
Postoperative simple obstruction of small intestine	Ileus	q 1 h while on IV fluids	q 4 h or if painful or if increase in heart rate	q 6 h until no gastric reflux	q 24 h	q 12 h until no reflux
Postoperative simple obstruction of large intestine	Diarrhea	q 3–4 h	Not routinely necessary	q 24 h	q 24 h or if febrile or diarrheic	q 24 h
Postoperative strangulating obstruction of small intestine	Ileus Endotoxemia Adhesions Thrombophlebitis Laminitis	q 1 h while on IV fluids	q 4 h or if painful or if increase in heart rate	q 6 h until no gastric reflux	q 24 h	q 12 h until no reflux
Postoperative strangulating obstruction of large intestine	Endotoxemia Hypoproteinemia Diarrhea Laminitis	q 1 h while on IV fluids	Not routinely necessary	q 6 h	q 24 h or if febrile or diarrheic	q 12 h
Postoperative simple obstruction of small colon	Small colon impaction Diarrhea	q 3–4 h	Not routinely necessary	q 24 h	q 24 h or if febrile or diarrheic	q 24 h
Postoperative strangulating obstruction of small colon	Endotoxemia Adhesions	q 1 h while on IV fluids	q 4 h or if painful or if increase in heart rate	q 6 h	q 24 h	q 12 h
Small colon impaction	Small colon impaction Diarrhea Salmonellosis	q 3–4 h	Not routinely necessary	q 24 h	q 24 h or if febrile or diarrheic	q 24 h
Large intestinal impaction	Diarrhea	q 3–4 h	Not routinely necessary	q 24 h	q 24 h	q 24 h
Proximal enteritis	Ileus Laminitis	q 1 h while on IV fluids	q 4 h or if painful or if increase in heart rate	q 6 h until no gastric reflux	q 24 h	q 12 h until no reflux
Acute colitis	Endotoxemia Laminitis Thrombophlebitis Acute renal failure	q 1 h while on IV fluids	Not routinely necessary	q 6 h	q 24 h	q 12 h

- assessment of the surgical incision in postoperative cases;
- abdominal shape and "pings";
- volume of IV fluid administered.

Pain

Analgesic therapy is necessary in all horses in the immediate postoperative period. Provision of adequate analgesia and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) are important in minimizing the negative effects of pain and inflammation on healing. Postoperative pain may originate from peritoneal inflammation, the abdominal incision, and/or intestinal distention. Pain relief should be provided without impeding gastrointestinal motility or masking any deterioration of the horse's condition that might require another type of treatment (e.g., re-laparotomy). Flunixin meglumine is the most commonly administered analgesic drug for the first 24 h after surgery, being effective in controlling pain in addition to combating some of the effects of endotoxemia/systemic inflammatory response syndrome (SIRS) (see Chapters 17 and 28). Thereafter, analgesic drugs are used as necessary. "Low-dose" flunixin meglumine (0.25 mg/kg) is commonly used for several days after colic surgery. This dose has been shown to counteract the cardiovascular effects of endotoxemia (Semrad et al., 1987), but is unlikely to mask a clinical deterioration in the horse's condition. Most horses show an immediate cessation of abdominal pain after colic surgery. However, a small number may demonstrate bouts of pain within the first few days after surgery. If there is no improvement in these horses after gastric decompression, they may require further analgesic therapy. Several pain scales for colic have been developed (see Chapter 12), but they have not been universally accepted (Pritchett et al., 2003; Sutton et al., 2013). This lack of acceptance may be due to the fact that individual horses respond differently to abdominal pain, and older horses and draft breeds often appear to be more stoic. Head position, ear position, location, locomotion, response to other horses, response to opening of the stall door, response to approach, and lifting feet are factors that are often included in pain scores (Pritchett et al., 2003; Gleerup & Lindegaard, 2016). As an alternative to categorical simple descriptive pain scales, some clinicians and hospitals devise their own visual analog scales. Although it is common for horses to appear quiet and depressed in the immediate postoperative period, usually within 6 h they become bright and responsive; however, horses that were sicker prior to surgery are more likely to remain quiet after surgery.

Recurrence of significant signs of colic within 24–48 h after surgery is not usual, and may be an indication to consider early re-celiotomy (Dunkel et al., 2014). Horses with postoperative ileus may also demonstrate pain due to gastrointestinal distention. This pain usually abates after nasogastric intubation and gastric decompression. A full description of the different analgesic drugs is provided elsewhere in this book (see Chapter 27).

Lidocaine (lignocaine) is administered IV by some clinicians as a treatment for postoperative ileus (Malone et al., 1994, 2006; Lefebvre et al., 2016). Lidocaine is also effective in treating visceral pain, has synergistic effects with other analgesic drugs, and allows the dose of other analgesics to be reduced. Other strategies for controlling postoperative pain are described in Chapters 12 and 27.

Cardiovascular Status

Monitoring the horse's cardiovascular status (based on physical examinations coupled with clinical pathological monitoring) is important to assess the adequacy of intravenous fluid therapy and to identify ongoing fluid and electrolyte losses, and acid–base disturbances. These examinations are used to determine and monitor the type and rate of intravenous fluid therapy. Deteriorating cardiovascular status despite adequate fluid therapy may suggest ongoing intestinal damage, ileus, or "third space" fluid loss. In some circumstances, particularly in combination with other signs, this may be an indication to consider an early re-celiotomy.

Horses are usually mildly to moderately tachycardic (heart rate 50–70 bpm) for the first 12–24 h after colic surgery (Southwood, 2004). However, heart rate usually rapidly decreases to normal thereafter. Tachycardia is most commonly caused by either pain or shock, however primary cardiac diseases should also be considered if the heart rate is not consistent with other clinical signs. Persistent tachycardia (>50–60 bpm) should warrant investigation, and a nasogastric tube should be passed to relieve any gastric distention. Prolonged tachycardia (>80–90 bpm for longer than 24 h) generally indicates a poor prognosis. The mucous membranes may be initially bright red after surgery, but should improve during the first 24 h. The mucous membranes should be moist and the capillary refill time should be less than 2 s in an adequately hydrated horse. Assessment of peripheral temperature (of the ears and distal limbs) can be a helpful qualitative measure of tissue perfusion. Pulse quality is a crude marker of cardiac output and peripheral tissue perfusion. Additional monitoring of the cardiovascular system could include central venous pressure, arterial blood pressure, and blood lactate concentration.

Central venous pressure is used as a marker of blood volume, vascular tone, and cardiac function; it can be measured using a catheter placed in the intrathoracic portion of the cranial vena cava. The catheter is attached

to a water manometer positioned with zero at the point of the shoulder. Normal central venous pressure in an adult horse is approximately 8–12 cmH_2O. In postoperative colic patients, the goal should be to maintain a pressure exceeding 5 cmH_2O.

Arterial blood pressure can be used to assess adequate blood volume and cardiac performance. Indirect (noninvasive) monitoring is most commonly performed in conscious horses using an occlusion cuff placed around the base of the tail (Marsh, 2010). Normal indirect mean arterial pressure in adult horses is 85–95 mmHg (Parry et al., 1984). Arterial blood pressure is typically maintained at a normal level until shock becomes decompensated, so it is important to monitor other indicators of poor tissue perfusion and not rely totally on blood pressure measurements.

Fever

Postoperative fever is common within the first 24 h after surgery, but usually resolves thereafter. A persistent fever is abnormal, and could indicate the development of peritonitis, ischemic intestine, impending colitis, septic thrombophlebitis, wound infection, or pneumonia. Fever may also occur as a result of endotoxemia/SIRS. Consequently, horses with persistent fevers should be thoroughly investigated to determine the cause of the fever. In a review of 113 horses monitored postoperatively after colic surgery, 43% were diagnosed with a postoperative infection (Freeman et al., 2012). In this study, peak rectal temperature >39.2 °C (102.5 °F), time after surgery to peak temperature >48 h, and duration of pyrexia >48 h were significantly associated with infection. The authors concluded that slight to mild pyrexia (38–39.4 °C or 100.4–102.9 °F) in the early postoperative period is not necessarily associated with impending bacterial infection in colic patients, and the use of antimicrobials in these patients may be costly and unnecessary.

Septic peritonitis is an uncommon complication of colic surgery. Clinical signs include depression, fever, low-grade abdominal pain, anorexia, and ileus (see Chapter 29). These signs are not unique for peritonitis, and can be seen with many other gastrointestinal problems, including enterocolitis, endotoxemia, and ileus. Recognition of these signs in horses after surgery should therefore initiate a full clinical and laboratory evaluation so that their cause can be identified. Septic peritonitis in the postoperative period may develop as a result of devitalized intestine or leakage from a previous anastomosis; surgical exploration may be necessary in such cases. Abdominal ultrasonography may be helpful in establishing a diagnosis of septic peritonitis. Peritoneal effusion and thickening of the intestinal walls (>0.2 cm) are characteristic findings in horses with septic peritonitis. Peritoneal fluid changes are expected in all horses after abdominal surgery, and persist for at least 7 days (Santschi et al., 1988). Such changes include increased total nucleated cell counts and increased total protein concentrations; these features cannot, therefore, be used to diagnose septic peritonitis in the postoperative case. The diagnosis should be based on the cytologic appearance of peritoneal fluid, including the identification of toxic and degenerate neutrophils, and intra- or extracellular bacteria. Serum to peritoneal fluid glucose concentration differences exceeding 50 mg/dL (>2.8 mmol/L), peritoneal fluid pH <7.3, glucose concentration <30 mg/dL (<1.7 mmol/L), and fibrinogen concentration >200 mg/dL (>2 g/L) are indicative of septic peritonitis (Van Hoogmoed et al., 1999).

Inflammatory Markers

Plasma fibrinogen and serum amyloid A concentrations can be used to monitor the inflammatory response, and both of these markers increase after surgery. An uncomplicated colic patient is expected to have a fibrinogen concentration of 500–800 mg/dL (5–8 g/L), but infection (e.g., wound infection, peritonitis, septic thrombophlebitis) should be suspected if values exceed this level (Jacobsen & Andersen, 2007). In a recent study of 18 horses after colic surgery, significant increases in serum amyloid A concentrations occurred in all horses whereas fibrinogen concentration only increased mildly after surgery. Serum amyloid A concentrations were also significantly increased in horses identified with SIRS prior to surgery and at 48 and 72 h postoperatively in horses that developed complications (Daniel et al., 2016).

Respiratory Rate

The respiratory rate is variable in horses after colic surgery. Increased respiratory rate may indicate pain (including abdominal pain and laminitis), acidosis, or secondary respiratory tract complications (such as pleuropneumonia). Thoracic auscultation should be routinely performed to monitor for any changes in lung sounds, and thoracic ultrasonography performed if pleuropneumonia is suspected.

Gastrointestinal Function

Gastrointestinal function is assessed by monitoring bowel sounds and fecal production. Decreased gastrointestinal borborygmi are associated with reduced motility

and withholding feed (Naylor et al., 2006). In many horses after colic surgery, gastrointestinal sounds are reduced initially, but improve during the first 24 h. In most cases, the return of normal gastrointestinal function is accompanied by resolution of abdominal pain, normalization of the horse's cardiovascular status, cessation of gastric reflux, and return of normal defecation patterns. Walking in hand and grazing can be helpful to stimulate intestinal motility. Prolonged absence of gastrointestinal sounds, in combination with signs of abdominal pain, and possibly evidence of abdominal distention, are poor prognostic signs. A healthy 500 kg horse passes approximately 5–7 piles of feces per day (depending on the type and amount of food, and the time since surgery). If the large colon or cecum was evacuated during surgery, or if the horse is placed on a low-bulk diet, fecal production will be reduced. Any sudden change in the amount of feces being produced, or the nature of the feces (e.g., development of soft feces or diarrhea), may indicate a deterioration in gastrointestinal function. Horses affected by small intestinal diseases are at particular risk for developing postoperative ileus, whereas diarrhea is more commonly seen in horses with large intestinal lesions.

Adynamic ileus is defined as a functional obstruction of the aboral transit of gastrointestinal contents, and is an important problem in horses after colic surgery (see Chapter 13). However, adynamic ileus can also occur in horses with other nonsurgical diseases of the gastrointestinal tract, including enteritis, colitis, and peritonitis. Although adynamic ileus occurs most commonly in horses after surgery involving the small intestine, it can also occur after surgery for other lesions, such as large colon volvulus (Hardy & Rakestraw, 2002). Postoperative ileus is serious, and is responsible for 40% of postoperative deaths in horses with abdominal crisis. The disruption of the normal propulsive motility results in sequestration of fluid and ingesta in the segment of the intestinal tract that is dysfunctional and in the intestine orad to this area. This process occurs most commonly in the small intestine and stomach, but can also occur in the large intestine, especially with severe damage to the large intestinal wall associated with colonic volvulus or colitis, resulting in severe endotoxemia.

The signs of ileus relate to the accumulation of gas and fluid within the gastrointestinal tract (see Chapter 13). Affected horses become depressed and anorexic and show signs of increasing abdominal pain. Borborygmi are reduced or absent, and there may be abdominal distention. The sequestration of fluid within the intestinal tract results in increasing heart rate, discolored mucous membranes, and prolonged capillary refill time. PCV and total protein increase as a result of hemoconcentration. All of these signs should alert the clinician to the possibility of the development of postoperative ileus. Nasogastric intubation and gastric decompression should be performed every 2–4 h if the horse produces more than 2 L of nasogastric reflux. As the amount of reflux decreases, the frequency of nasogastric intubation can be reduced. If a stomach tube is left in place for subsequent decompressions, it should be removed after reflux volume decreases to allow for normal gastric emptying. In most horses, the volume of gastric reflux gradually decreases as normal gastrointestinal motility returns. However, in some horses, an initial reduction in the volume of reflux is followed by a sudden increase in reflux that is then followed by a decrease again (Holcombe, 2003).

Information about gastrointestinal function can also be gained by repeated diagnostic ultrasound examinations (see Chapter 23). Transabdominal ultrasound can be used to monitor distention, wall thickness, and contractility of the intestines, and also the volume of peritoneal fluid (Reef, 1998). Small intestine is normally identified in the caudoventral and cranioventral abdomen. In healthy horses, small intestinal loops measure 1.8 ± 0.8 cm in diameter, with a wall thickness of 0.16 ± 0.05 cm, and contract 6–15 times per minute (Holcombe, 2003). The position, degree of distention, and content of the stomach can also be assessed by abdominal ultrasonography. This examination should be performed before nasogastric intubation because the latter may introduce air into the stomach that alters the position and causes distention. In healthy horses, the stomach can be viewed in the left cranial abdomen, between the 9th and 12th ribs (Epstein et al., 2008). The gastric wall is thick (0.75 cm) and a bright gas echo is usually seen within the lumen of the stomach. If the stomach is identified beyond the 12th intercostal space or if it is distended by fluid contents, then gastric decompression should be performed (Holcombe, 2003). Recently, the ultrasonographic examination of the duodenum in postoperative colic patients was studied (Belz et al., 2014) and shown to be valuable in the diagnosis and monitoring of postoperative ileus. Whenever the duodenum appears to be at least partially fluid filled, the authors recommend nasogastric intubation to definitely rule out gastric dilatation.

Motility problems affecting the cecum or large colon can arise after strangulating obstructions (such as colonic volvulus) or secondary to colonic impaction. Gas distention of the cecum and large colon is identified by auscultation, percussion of the abdomen, and rectal palpation. Abdominal ultrasound examinations are less helpful than with small intestinal distention. If the horse is painful as a result of large bowel tympany, then percutaneous decompression may be attempted if a gas cap can be identified in the paralumbar fossa (usually on the right side). After clipping and aseptic preparation of the skin in the paralumbar fossa, a bleb of local anesthetic

solution is injected subcutaneously. A 14-gauge intravenous catheter is then advanced through the skin and body wall and into the gas-distended viscus. Once the gas has been removed, the catheter is withdrawn (3–5 mL of antibiotic solution, such as gentamicin, can be injected as the catheter is withdrawn if deemed necessary). This procedure carries a risk of inducing septic peritonitis or abdominal wall abscess, and should only be performed if deemed essential. In a review of cecal decompression in 145 horses (Witte et al., 2014), complications were observed in 23 (15.9%) horses with the following incidence: fever (9.7%), diarrhea (9.0%), peritonitis (5.5%), local inflammation (4.1%), and hematoma (2.1%).

Monitoring gastrointestinal function is important in helping to determine when feeding can be safely resumed after surgery. In horses affected by ileus, feeding can usually be safely resumed when the horse has become pain free with normal cardiovascular parameters and has not refluxed for 12 h. In the absence of ileus, early (by 6 h) postoperative feeding after all forms of colic surgery, including small intestinal resection and anastomosis, has been recommended by several surgeons (Snyder & Van Hoogmoed, 2000; Freeman et al., 2000). However, there is little published information about the effects of early enteral nutrition after small intestinal surgery, and the optimum type of feed, quantity, and precise timing of feeding are largely unknown. Although feeding can be a stimulus for intestinal motility, early feeding can also result in pain and accumulation of fluid and ingesta in the stomach and small intestine in some cases (White, 2009). Prior to offering food, many surgeons recommend offering small amounts of water (e.g., 1 L) every hour until the horse is no longer thirsty, then offering hay or a pellet feed (up to 0.5 kg) every 3 h, increasing over 24–48 h until *ad libitum* hay or a full ration of pellets (based on the basal energy requirements of the horse) can be fed (White, 2009). If early feeding is introduced after small intestinal surgery, the cessation of oral intake may be required if the horse subsequently shows signs of pain or ileus. At present, there appear to be no objective measures of bowel function that can be used to predict when it is safe to allow enteral feeding after small intestinal surgery, and the decision as to when, how much, and how often to feed an individual horse after surgery needs to be made on a case-by-case basis. Water intake should be monitored. Average water intake for an adult stalled horse being fed hay is approximately 50–65 mL/kg body weight/day; however, horses that are not eating (or are receiving intravenous fluids) will not drink this volume. This fact should also be taken into consideration when determining intravenous fluid administration rates for horses that are not eating normally.

Gastrointestinal function needs to be very carefully monitored in horses after treatment for intestinal impactions (including ileal, cecal, large colon, and small colon impactions) as these horses are at risk of reimpaction after the reintroduction of food. Colonic impaction may also occur when feeding is reintroduced or when intravenous fluids are discontinued in horses recovering from other gastrointestinal problems. These impactions are usually easily resolved by administering water, electrolytes, and mineral oil by nasogastric tube. The horse can also be stimulated to drink more by giving oral sodium chloride or potassium chloride (30–60 g).

Cecal impactions are less common, but potentially more serious. The development of such impactions may occur in any horse after general anesthesia and surgery. Use of α_2-adrenergic drugs may also disrupt normal cecal motility patterns and predispose to impaction (Ross, 1989). Clinical signs of cecal impaction include reduced fecal production, decreased appetite, depression, and mild abdominal pain. These signs may be particularly mild if the horse is being treated with NSAIDs. The diagnosis is confirmed by rectal palpation, when a large, firm viscus is palpated from the middle to the right side of the abdomen, with a taut ventral cecal band. The most dorsal part of the impacted cecal base cannot be felt because it is attached to the dorsal body wall and out of reach. Monitoring the size and consistency of the cecal impaction is important because cecal rupture can occur if the condition does not resolve. Treatment with oral and intravenous fluid therapy, laxatives, and prokinetic drugs is often successful. However, if the impaction fails to resolve with this treatment, or if the clinical signs worsen, then surgical treatment should be considered (Ross, 1989; Smith et al., 2010; Plummer et al., 2007) (see Chapter 53).

All horses undergoing intensive therapy for gastrointestinal disease are at risk of developing diarrhea (see Chapters 15 and 30). Specific risk factors include antimicrobial drug administration, gastrointestinal surgery, anorexia, ileus, oral fluid and laxative therapy, and being housed in the intensive care unit (Cohen & Honnas, 1996). Important infectious agents associated with diarrhea in horses with abdominal disease include *Salmonella* spp., *Clostridium difficile*, and *Clostridium perfringens*. Identification of these agents or their toxins is important in view of the possibility of spread to other susceptible horses in the hospital. All horses that develop diarrhea should be considered as potential sources of these infectious agents, and those with associated pyrexia and neutropenia should be isolated pending microbiological testing. Noninfectious causes of diarrhea, including resolution of pelvic flexure impaction, can be very difficult to differentiate from the early stages of infectious causes. Because more than 40% of horses with gastrointestinal disease are positive for *Salmonella* spp. based on polymerase chain reaction testing (Cohen et al., 1996), routine daily fecal cultures (for a minimum of 5 days) are recommended for all horses in intensive care units (Holcombe, 2003). Routine infection control measures

(e.g., use of disposable shoe covers and gloves for each stall, regular disinfection of equipment and facilities, individual equipment for each horse) should be used to limit the spread of infectious agents before they become clinically apparent (see Chapter 26).

Horses undergoing intensive therapy will also be at risk for developing gastric ulceration (see Chapter 10). Risk factors include starvation, NSAID therapy, hypovolemia, and stress. Clinical signs of gastric ulceration may include inappetence, depression, mild abdominal pain, bruxism, and ptyalism. These signs are not pathognomic for gastric ulceration, and can be seen with many other gastrointestinal diseases. The diagnosis is achieved by gastroscopy. This technique and the treatment of gastric ulcers are described elsewhere (see Chapter 50).

Urine Production

A healthy 500 kg horse will produce between 5 and 15 L of urine per day. If the horse is receiving intravenous fluids, the urine output is expected to be greater. Decreased or absent urine production should be immediately investigated. Potential causes include hypovolemia, "third space" fluid loss, and acute renal failure (Divers et al., 1987).

Laminitis

Laminitis is a potential complication for all horses with intestinal disease, especially those with concomitant endotoxemia (see Chapter 49). Horses that have had significant bowel wall damage should be carefully monitored for signs of laminitis. In view of the fact that many of the treatments for laminitis are most effective when used as prophylactic therapies, some clinicians advocate their use on horses at particular risk for laminitis rather than waiting for the development of clinical signs of the condition (Hardy & Rakestraw, 2002). Such therapies include sole and frog supports, cryotherapy (Van Eps, 2010), acepromazine, and topical nitroglycerine vasodilator creams. Treatments for endotoxemia should also be employed to try to prevent laminitis.

Thrombophlebitis

Horses with endotoxemia, diarrhea, fever, and generalized debility are predisposed to thrombophlebitis, particularly if catheterization is prolonged (Traub-Dargatz & Dargatz, 1994; Lankveld et al., 2001) (see Chapter 48). The catheter site should be regularly checked for evidence of heat, swelling, pain, or drainage. Ultrasonography can be used to detect early (subclinical) evidence of thrombophlebitis (Geraghty et al., 2009)

Monitoring Clinical Pathology Parameters

Regular monitoring of certain clinical pathology parameters is necessary to assess both cardiovascular and renal function, and to identify electrolyte and acid–base derangements. Monitoring should include the following:

- PCV and total plasma protein concentration – if synthetic colloid therapy is used, measurement of plasma osmolality can be helpful in directing fluid therapy;
- plasma lactate concentration;
- urea and creatinine concentrations;
- sodium, potassium, chloride, calcium, and magnesium concentrations;
- acid–base status and blood gas analyses;
- blood glucose concentration;
- serum triglyceride concentrations.

Blood lactate concentrations can be used as a marker of peripheral tissue perfusion. Hyperlactatemia (plasma lactate >1 mmol/L) may indicate hypovolemia, hypoxia, hypotension, or endotoxemia/SIRS. Plasma creatinine concentrations can also be used to assess tissue perfusion. Azotemia (plasma creatinine >1.5 mg/dL; 115 µmol/L) may be due to prerenal (e.g., hypovolemia and poor tissue perfusion), renal (e.g., acute kidney injury), or postrenal (e.g., obstruction of the lower urinary tract) causes. Differentiating between these causes depends on other diagnostic tests and monitoring the response to fluid therapy.

Hyperglycemia can occur as a result of stress or endotoxemia. Severe hyperglycemia (blood glucose >195 mg/dL; 10.7 mmol/L) is associated with a worse prognosis for survival (Hassel et al., 2009) (see Chapter 25). Daily monitoring of blood glucose concentration can be helpful, but if horses are receiving intravenous dextrose supplementation, blood glucose concentration should be monitored every 4–6 h. Hyperglycemia can worsen endotoxemia-related gastrointestinal dysfunction and increase bacterial translocation in humans, and insulin therapy might be considered in horses with severe hyperglycemia. Blood glucose and serum triglyceride concentrations should also be monitored in horses at risk for developing hyperlipemia (e.g., ponies, donkeys, Miniature horses, pregnant and lactating mares, or animals with pituitary pars intermedia dysfunction). Hypertriglyceridemia (serum triglycerides >50 mg/dL; 0.56 mmol/L) is common after colic surgery, but the triglyceride concentration usually returns to normal values within 72 h of surgery. Severe or prolonged hypertriglyceridemia (triglycerides >400 mg/dL; 4.5 mmol/L) should be managed using intravenous dextrose supplementation and insulin therapy if necessary.

Fluid Balance

Most horses affected by serious gastrointestinal disease develop varying degrees of hypovolemia and dehydration, and require fluid therapy. Careful monitoring of PCV and total protein is essential (along with other measurements of hydration and circulatory status) during intensive therapy. The rate of fluid administration may require modification depending on the results of this monitoring. Fluid therapy is discussed in detail elsewhere (see Chapters 27 and 28). In most cases, reasonable indicators of successful cardiovascular support include maintaining the heart rate at <80 bpm, PCV < 50%, and total protein >4.5 g/dL (45 g/L) (Hardy & Rakestraw 2002).

Continued fluid losses occur in horses with ileus (due to loss in gastric reflux and sequestration into the intestine) and horses with diarrhea. In addition, "third space" loss of fluid can occur as a result of endotoxemia. In these horses, increased capillary permeability results in loss of fluid and protein into the interstitium. As a result, it can be difficult to maintain the plasma volume despite fluid therapy because of decreased plasma oncotic pressure (due to plasma protein loss) and fluid sequestration into the tissues. The PCV may continue to increase and the total protein continue to fall despite fluid therapy. In most cases, maintenance of the PCV at <50% and the total protein at >4.5 g/dL (45 g/L) is adequate to sustain effective cardiac output. These parameters should be measured every 6 h in critically ill horses, and the rate of fluid administration altered accordingly. If the total protein falls to <4.1 g/dL (41 g/L) (corresponding to a decrease in plasma oncotic pressure to less than 12 mmHg) (Allen et al., 1986), colloid administration is likely to be beneficial in order to increase the plasma oncotic pressure and allow continued fluid administration without causing severe edema. Commonly available colloids for use in horses include equine plasma, 25% human albumin, dextrans, and hydroxyethylstarch (see Chapter 28). Plasma has several advantages over synthetic colloids in that it not only provides oncotic support (through albumin), but also provides coagulation factors and antithrombin III. Frozen plasma should be thawed slowly at 37 °C, and then administered immediately. It should be administered slowly using an in-line filter. The volume of plasma to be administered can be estimated from the following equation:

$$\text{volume} = (\text{PPg} - \text{PPr}) \times (0.05 \times \text{BW})/\text{PPd}$$

where PPg is the goal plasma protein concentration, PPr is the plasma protein concentration of the recipient, PPd is the plasma protein concentration of the donor, and BW is body weight. Although this may underestimate the actual end measurement, in most cases a volume of 4 mL/kg is a standard initial treatment.

Although measuring total protein is typically used to assess colloid oncotic pressure, when synthetic colloids are used, a colloid osmometer should be used, if available. This is necessary because values of total protein measured on a refractometer will no longer be reliable. The objective is to maintain the plasma oncotic pressure above 12 mmHg. If unavailable, clinical parameters such as decreases in edema and PCV can be used to assess the efficacy of therapy. Dextran-40 (molecular weight 40,000) and dextran-70 (molecular weight 70,000) are available as 6% solutions, and are generally administered at a rate of 4 mL/kg over 15–20 min. Hydroxyethylstarches are available as either hetastarch or pentastarch. Pentastarch is more rapidly degraded than hetastarch (half-life 2.5 h compared with 25 h) (Rudloff & Kirby, 1997). Hetastarch infusion (10 mL/kg) to healthy ponies has been shown to increase significantly the plasma colloid oncotic pressure for 120 h (Jones et al., 1997). Hetastarch exerts a dose-dependent effect on hemostasis, which may be significant at doses >20 mL/kg. Recently, 25% human albumin has been safely given to horses and this product has the highest oncotic value.

Hemorrhage is uncommon in the postoperative colic case; however, a decrease in both PCV and total protein, along with evidence of depression, tachycardia, tachypnea, pale mucous membranes, cold extremities, and abdominal pain, are indications of possible hemorrhage.

Urine specific gravity can be useful for assessing the horse's hydration status. The normal urine specific gravity (SG) of adult horses is 1.025–1.050, but horses receiving intravenous fluids are often isosthenuric (SG 1.008–1.012) or hyposthenuric. If a horse receiving intravenous fluids is hypersthenuric (SG >1.020), this may indicate hypovolemia. Urine can also be assessed for the presence of glucose, which would indicate hyperglycemia.

Renal Function

Horses with abdominal disease may develop acute renal failure as a result of vasomotor nephropathy, which arises secondary to sepsis, systemic inflammatory response syndrome, and/or hypotension (Divers et al., 1987). The renal disease occurs as a result of intravascular depletion, coagulopathies, poor vasomotor tone, and capillary leak syndrome, all of which affect renal perfusion and intrarenal vasoconstrictor–vasodilator forces (Divers, 2003). Monitoring renal function by way of recording urine production and serum urea, creatinine, and electrolyte concentrations is important to identify early stages of acute renal failure. Increasing the intravenous fluid administration rate will frequently be successful in restoring normal renal function if such changes are identified early. Persistently high creatinine concentrations should be followed up with urinalysis. If the horse

has elevated creatinine concentrations with oliguria or anuria, diuretic therapy (furosemide 1–2 mg/kg every 2 h, or dopamine 3–7 μg/kg/min) can be instituted in the hope of improving urine production. If aminoglycosides are being administered, the measurement of peak and trough levels can help insure that adequate yet nontoxic amounts are being given.

Electrolyte Balance

Electrolyte abnormalities, especially hypocalcemia, hypokalemia, and hypomagnesemia, can develop in horses after colic surgery (Hardy & Rakestraw, 2002). If possible, it is more informative to monitor the ionized calcium concentration rather than total calcium. The total calcium concentration can be affected by a variety of other factors and therefore can be misleading. For example, the total calcium concentration is usually low if the total plasma protein concentration is low, but the ionized calcium may be normal. Alternatively, the total calcium concentration may be normal yet ionized calcium abnormally low if the horse is alkalotic. Hypocalcemia may develop as a result of lack of dietary calcium intake, diuresis, endotoxemia, and acid–base disorders. Calcium is essential for intestinal motility, and hypocalcemia may therefore contribute to ileus. Low serum ionized calcium concentrations are common in horses after colic surgery, and such horses will benefit from having calcium added to the intravenous fluids (50–100 mL of 23% calcium gluconate added to every 5 L of fluid) (Dart et al., 1992; Toribio et al., 2005). However, excessive calcium administration should be avoided as this may exacerbate cellular death associated with reperfusion injury.

Hypokalemia is common in horses after colic surgery and horses suffering from diarrhea. Hypokalemia can develop as a result of lack of dietary intake, diuresis, and gastrointestinal loss. Horses with metabolic acidosis can become hyperkalemic as a result of the exchange of intracellular hydrogen and potassium ions. Excessive potassium excretion may follow correction of acidosis. Most of the total body potassium is intracellular, and therefore measurements of serum potassium concentration may be misleading. Provided that renal function is adequate, routine potassium supplementation is recommended in horses with reduced or lack of intake and continued fluid therapy for more than 24 h. Potassium can be safely supplemented at a rate of 20–40 mEq of KCl per liter of fluids. Supplementation should not exceed 0.5 mEq/kg/h to avoid hyperkalemia.

Hypomagnesemia has been documented in horses with a variety of gastrointestinal diseases, and appears to be particularly prevalent in horses affected by ileus. Magnesium supplementation can be achieved by administering magnesium sulfate at a rate of 5 mg/kg/h.

Acid–Base Balance

Acid–base disturbances are most commonly the result of hypovolemic shock resulting in lactic acidosis. In these cases, correction of acid–base balance is generally achieved by correction of the hypovolemia and circulatory support. However, bicarbonate therapy may be beneficial in severely acidotic horses (pH <7.2, when blood bicarbonate concentration is <15 mEq/L, or when base excess is >10 mEq/L). The bicarbonate deficit can be calculated from the following equation:

$$\text{bicarbonate deficit}(\text{mEq}) = \text{base deficit} \times 0.3 \times \text{body weight}(\text{kg})$$

Half of the calculated bicarbonate requirement should be administered intravenously over 1 h and the remainder administered over 12–24 h. Acidosis is also common in horses affected by colitis due to bicarbonate loss in the intestine, and these horses can also benefit from bicarbonate supplementation once the anion gap and/or high blood lactate have been corrected. Horses continually receiving ≥0.9% saline solutions as the predominant crystalloid therapy may become acidotic from the disproportionately high chloride concentration in these fluids.

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Postoperative Complications

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Postoperative complications commonly occur following ventral midline celiotomy for treatment of colic despite many recent advances in both surgical and postoperative management. This chapter addresses the pathophysiology and treatment of the most commonly observed complications following ventral midline celiotomy. Conditions to be described include postoperative pain, postoperative ileus, incisional complications including dehiscence, incisional infection, and hernia formation, fever, septic peritonitis, and coagulopathy with associated conditions including thrombophlebitis and infarction. Other commonly observed postoperative complications in horses with surgical gastrointestinal disease include systemic inflammatory response syndrome (SIRS), colitis, adhesion formation, and laminitis. Pathophysiology and treatment of the latter conditions are described in depth in Chapters 15, 16 (SIRS), 13, 14 (adhesions), and 49 (laminitis).

Postoperative Pain

At various times in the postoperative period, horses that have undergone colic surgery may show recurrence of abdominal pain. Recognition of postoperative pain is straightforward when overt signs of colic are observed (see Chapters 12 and 20); however, recent advances have been made in monitoring equine visceral pain using a composite pain score that may improve our ability to detect problems early on and provide greater consistency among different observers (Van Loon et al., 2014) (see Chapter 12). It is atypical for horses undergoing ventral midline celiotomy to lie down in the early postoperative period, which may be of significant concern as it may lead to contamination of the surgical incision and subsequent incisional infection. Development of colic is the most prevalent complication reported, described as occurring in 28–32% of postoperative colics in the short term (Proudman et al., 2002; Mair & Smith, 2005a, 2005b, 2005c), 35.1% with long-term follow-up (Mair & Smith, 2005a, 2005b, 2005c), and as high as 69–75% following relaparotomy (Mair & Smith, 2005a, 2005b, 2005c; Dunkel et al., 2015). The prevalence of postanesthetic colic in horses undergoing nonabdominal surgeries, in comparison, is only 5.2% (Senior et al., 2006). Other reported factors that influence the prevalence of postoperative colic include whether a resection/anastomosis was performed (Mair & Smith, 2005a, 2005b, 2005c), the type and location of anastomosis (Proudman et al., 2007; Freeman & Schaeffer, 2010; Close et al., 2014; Stewart et al., 2014; Brown et al., 2015), and the intraoperative diagnosis, with large colon volvulus (French et al., 2002) and right dorsal displacement of the large colon compared with other forms of displacement implicated as higher risk at 42% (Smith & Mair, 2010). Although end-to-side versus side-to-side jejunocecostomy (Brown et al., 2015), and single- versus double-layer small intestinal anastomosis (Close et al., 2014) did not differ with respect to the prevalence of development of postoperative colic, jejunocecostomy poses a higher risk for postoperative colic than jejunjojejunostomy or jejunoileostomy (Proudman et al., 2007; Stewart et al., 2014). Among horses undergoing jejunocecostomy, those with a stapled anastomosis had a significantly greater prevalence of postoperative colic than those with hand-sewn anastomoses (Freeman & Schaeffer, 2010), but survival did not differ between hand-sewn and stapled jejunocecostomy techniques (Proudman et al., 2007; Freeman & Schaeffer, 2010). If pain is observed in the postoperative period, it is essential to make an effort to determine the underlying cause in order to implement effective management strategies.

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The timing and nature of postoperative colic relative to surgery may provide clues to the possible etiology (Proudman, 2009):

Colic within 48 h of surgery:
- incisional/surgical pain;
- persistent ischemic bowel, for example, ileal stump;
- continued ischemia/reperfusion injury of bowel;
- leakage at an enterotomy or anastomosis site;
- postoperative ileus;
- recurrent displacement.

Colic within 2 – 7 days of surgery:
- obstruction at an anastomosis (e.g., hematoma, impacted ingesta);
- "delayed adaptation" at an anastomosis;
- peritonitis/anastomotic leakage;
- postoperative ileus;
- large colon impaction;
- gastric ulcers.

Colic at least 7 days after surgery:
- adhesions;
- recurrence of previous problem, for example, colon displacement.

Response to therapy plays a key role in the effort to determine an underlying cause. Although the majority of horses with postoperative colic will respond to medical therapy, an attempt to determine the underlying cause is essential to avoid delays in performing a repeat laparotomy. Two primary indications for repeat laparotomy in postoperative colics are poor or short-lived responses to analgesics and evidence of development of septic peritonitis. The most challenging decisions come with the management of postoperative ileus, as differentiating between physiologic ileus secondary to postoperative inflammation versus obstruction from surgical error or physical obstruction. In these cases, and in situations with ischemic bowel or anastomotic leakage, serial monitoring to ascertain trends in clinical parameters may provide important clues to optimizing treatment.

"Delayed adaptation" to an anastomosis occurs most often 48–72 h postoperatively as horses are being reintroduced to feed. Transient colic episodes may be observed after feeding, and these may be of sufficient duration to cause small intestinal distention. The precise cause of these episodes, which respond well to administration of analgesic or spasmolytic agents, is unknown but may be associated with delayed adaptation of electrical conduction across the new anastomosis site or inflammation of the previously distended small intestine (Atanassova et al., 1976; King & Gerring, 1989).

Treatment

A multimodal approach to treatment of postoperative pain is often appropriate to minimize the adverse effects of high doses of any given drug. The most commonly utilized analgesic agents in the postoperative colic patient include nonsteroidal anti-inflammatory drugs (NSAIDs), α_2-agonists, lidocaine administered as a continuous-rate infusion (CRI), and opioid analgesics. Table 48.1 provides a list of these drugs and their most commonly used dosages. Other commonly used analgesic therapies in horses that are generally not indicated in the postoperative colic unless painful complications such as laminitis occur include ketamine CRI (0.4–1.2 mg/kg/h IV), fentanyl patches (one or two 10 mg transdermal patches applied q 48–72 h), and epidural analgesia (see Chapter 27).

It is important to note that both α_2-agonists and opioids negatively impact propulsive motility in the equine gastrointestinal tract (Merritt et al., 1998). These agents should be administered cautiously when concern for postoperative ileus exists. One study of postoperative colic patients identified benefits in recovery characteristics and plasma cortisol levels when butorphanol was

Table 48.1 Mechanism of action and dosages of the most commonly used analgesics for treatment of postoperative visceral pain. Doses provided for α_2-agonists and butorphanol are administered as needed for pain.

Drug	Dosage	Mechanism of action
Xylazine	0.25–1.0 mg/kg IV PRN	α_2-Agonist
Butorphanol	0.01–0.02 mg/kg IV or IM PRN or 13 µg/kg/h IV	Opioid agonist–antagonist
Detomidine	0.01–0.02 mg/kg IV or IM	α_2-Agonist
Flunixin meglumine	0.25–1.0 mg/kg IV q, 8–12 h	NSAID – nonspecific COX inhibitor
Firocoxib	0.27 mg/kg (loading), then 0.09 mg/kg IV q 24 h	NSAID – COX-1 sparing
Meloxicam	0.6 mg/kg IV q 24 h	NSAID – COX-1 sparing
Lidocaine	50 µg/kg/min IV	Anti-inflammatory, analgesic, sympathoadrenal inhibition
Romifidine	0.04 mg/kg IV	α_2-Agonist

administered as a CRI (0.013 mg/kg/min IV for 24 h), but significant delays in time to passage of first feces was also observed (Sellon et al., 2004).

Lidocaine is commonly administered as a CRI in postoperative colic patients primarily for its prokinetic qualities, believed to be due in part to an anti-inflammatory effect and sympathoadrenal inhibition. Although somatic analgesia has been shown to occur with lidocaine IV infusions, the visceral analgesic effects of lidocaine have yet to be proven, and there is some evidence to indicate it has limited to no effect (Robertson et al., 2005), despite anecdotal evidence suggesting some benefit. Interestingly, lidocaine administered as a CRI will delay fecal transit in normal horses (Rusiecki et al., 2008), so administration in all postoperative colic patients may not be appropriate.

The most commonly used NSAID in postoperative colic patients is flunixin meglumine, as it appears to be unmatched in its visceral analgesic effects and has been proven to be beneficial both in the treatment of endotoxemia (Moore et al., 1986) and the prevention of adhesion formation (Sullins et al., 2004). Its disadvantages are potentiation of both gastric and colonic ulceration, delayed mucosal healing in models of jejunal ischemia (Cook et al., 2009), and nephrotoxicity. The use of COX-1-sparing NSAIDs, including firocoxib and meloxicam, has shown promise for providing visceral analgesia with fewer known adverse side effects (Cook et al., 2009) (see Chapter 27). The degree of analgesia achieved with meloxicam compared with flunixin meglumine was shown to be less in one study, but its use did not negatively impact clinical outcome and was associated with higher neutrophil counts 48 and 96 h postoperatively (Naylor et al., 2014).

Figure 48.1 Nasogastric decompression of large volumes of reflux obtained from the stomach of a horse with small intestinal ileus.

Postoperative Ileus (POI)

Postoperative ileus typically refers to stasis of the small intestine from failure of coordinated small intestinal motility resulting in progressive fluid distention of both the small intestine and stomach (Figure 48.1). Although large colon ileus may also occur, the focus of this discussion will pertain to the small intestine. For a more thorough discussion of intestinal physiology and transit, see Chapter 9.

Prevalence

The prevalence of POI lies between 10 and 21% of surgical colic cases, but has been reported to occur in 30–50% of cases when only horses with small intestinal resection are considered, with 30% of affected horses dying or requiring euthanasia as a result of the condition (MacDonald et al., 1989; Freeman et al., 2000; Roussel et al., 2001; French et al., 2002; Proudman et al., 2002; Cohen et al., 2004; Mair & Smith, 2005a, 2005b, 2005c; Holcombe et al., 2009). In these retrospective reports, the clinical definition of POI varies, but a useful diagnostic criterion is more than 2 L of gastric fluid on at least two consecutive occasions within 24 h (French et al., 2002; Proudman, 2009). Median time to onset of reflux was 24 h postoperatively (Proudman et al., 2002).

Risk Factors

Consistently reported risk factors for development of POI include increased packed cell volume (PCV) prior to surgery, presence of strangulating lesions of the small intestine, and prolonged surgical and anesthetic time (Blikslager et al., 1994; French et al., 2002; Cohen et al., 2004). Other proposed risk factors include intestinal ischemia, distention, peritonitis, electrolyte imbalances, endotoxemia, traumatic handling of bowel, resection and anastomosis, anesthesia, Arabian breed, high serum protein at admission, hyperglycemia, presence of >8 L reflux at admission, high heart rate at admission, and length of resection (Roussel et al., 2001; Cohen et al., 2004; Holcombe et al., 2009; Torfs et al., 2009; Hardy & Rakestraw, 2012).

Prevention

Prevention of POI begins intraoperatively, as surgical errors including traumatic handling of distended bowel, luminal stenosis at the site of anastomosis, and shortening of the small intestinal mesentery at the anastomotic site may result in development of POI that may be physiologic or mechanical in nature. All horses that have undergone small intestinal surgery should be monitored for POI until successfully returned to a normal diet. Early postoperative feeding is advocated by some surgeons as a means to prevent POI; however, most advocate a more judicious approach. Monitoring should take the form of clinical examinations every 2–4 h for the first 48 h postoperatively, with particular attention to intestinal sounds, cardiovascular parameters [membrane color, heart rate, and PCV/TP (total protein)] and passage of feces. Twice-daily ultrasonographic monitoring for small intestinal and gastric fluid distention for the first 72 h postoperatively may provide early recognition of the onset of POI before it is recognizable by other means. Ultrasonographic examination of the ventral abdomen and inguinal regions may reveal early evidence of fluid distention and reduced contractile activity of the small intestine (Figure 48.2) (see Chapter 23). Transcutaneous ultrasound of the left lateral abdomen in the 12–15th intercostal spaces near the thoracoabdominal junction may show evidence of fluid accumulation in the stomach ventrally or a generalized enlargement of the stomach (i.e., extension caudal to the 13th intercostal space) (Figure 48.3). The development of POI is often accompanied by increases in PCV without concurrent increases in plasma TP due to protein losses accompanying fluid losses in the gastrointestinal tract.

Treatment

If mechanical obstruction is suspected as a cause of POI, relaparotomy is indicated. Persistent and insidious postoperative pain is a feature of these cases, although differentiating mechanical from physiologic ileus can be very difficult. Treatment of physiologic POI has two major components: nursing care and the use of prokinetic agents. To date, there is little scientific evidence to aid clinicians in the management of these cases, and no studies that unequivocally document the efficacy of prokinetic agents in clinical cases.

Supportive Care

The primary considerations for supportive care of horses with POI include fluid replacement, gastric decompression, and anti-inflammatory therapy, with parenteral nutrition playing an important role when POI persists. Horses with compromised small intestinal motility should not be fed or offered water to drink, and therefore require intravenous fluid therapy. Isotonic fluids should be administered to restore deficits from dehydration, meet maintenance requirements that are reduced in anorexic animals, and replace ongoing losses associated with gastric reflux. Monitoring PCV/TP every 4–6 h is a helpful indicator of the success of fluid therapy and can provide clues toward resolution of POI as indicated by decreases or no change in PCV in the face of increasing TP. Serum electrolyte concentrations should be monitored and potassium, magnesium, and calcium should be supplemented as needed. As anorectic horses will undergo total body depletion of potassium over time, potassium supplementation at a minimum of 20 mEq/L

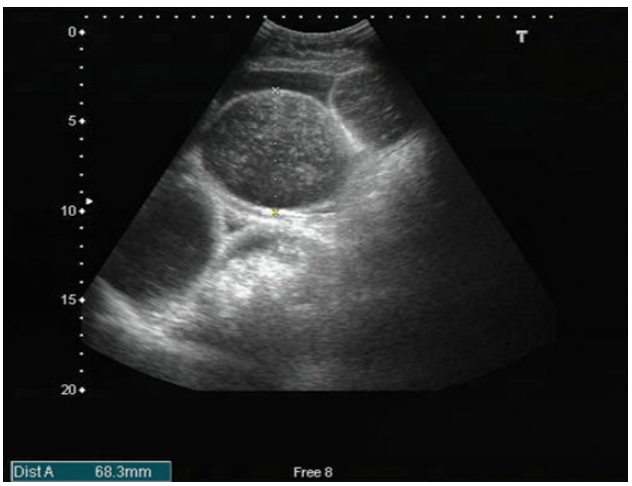

Figure 48.2 Ultrasonographic image of the ventral abdomen in a horse with postoperative ileus showing marked fluid distension of multiple loops of amotile small intestine.

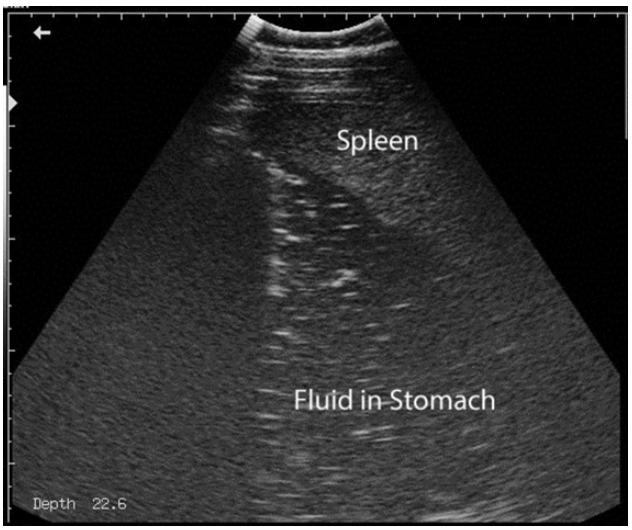

Figure 48.3 Transcutaneous ultrasound of the left lateral abdomen in the 13th intercostal space near the thoracoabdominal junction showing evidence of fluid accumulation in the ventral aspect of the stomach.

of intravenous fluids should be considered. Monitoring of urine specific gravity may provide evidence of systemic dehydration in the face of a relatively normal PCV and plasma protein concentration. As fluid secretions of the proximal intestine cause small intestinal distention and subsequent distention of the stomach, nasogastric decompression of the stomach is an essential component of treatment to avoid gastric rupture. Frequency of decompression is dictated by volume produced, but most often occurs every 2–4 h. As complications associated with prolonged nasogastric intubation may occur (Hardy et al., 1992), and the presence of the nasogastric tube within the stomach induces some degree of delayed gastric emptying (Cruz et al., 2006), periodic relief by pulling the tube for short periods of time can improve the attitude of the patient while reducing the risk of development of complications. The volume of reflux obtained over a defined time period can be a useful indicator of the success, or otherwise, of therapy. As an inflammatory component to POI is likely, treatment with NSAIDs (flunixin meglumine or firocoxib) is an additional key component of treatment. Horses with ileus appear to benefit from frequent short walks as physical activity may stimulate motility. Judicious timing of initial access to water and feeding is indicated in horses with POI and those with persistent POI (>48 h) may benefit from initial dextrose supplementation in fluids (1.25–5%) followed by implementation of partial parenteral nutrition.

Prokinetic Therapy

A wide variety of promising new prokinetic drugs have been reported in horses and other species, such as tegaserod (Delco et al., 2007), mosapride (Okamura et al., 2008, 2009a, 2009b), levosulpride, prucalopride (Pandolfino et al., 2000), and methylnaltrexone (Van Hoogmoed & Boscan, 2005; Boscan et al., 2006), but they are not currently in clinical use.

Comprehensive discussions of prokinetics, including mechanisms of action, dosages, and usage in the horse, are presented in Chapters 9 and 13. A survey of the use of prokinetic agents by equine surgeons in both 2004 (Van Hoogmoed et al., 2004) and 2016 (Lefebvre et al., 2016) indicated that the predominant prokinetic used in the management of POI is lidocaine. Table 48.2 illustrates the dosages of the most commonly used prokinetic agents in horses.

Table 48.2 The most commonly used prokinetic agents in horses and recommended dosages.

Drug	Dosage
Lidocaine	1.3 mg/kg IV bolus, then 0.05 mg/kg/min IV as a CRI
Metoclopramide	0.25 mg/kg IV in 500 mL saline over 30–60 min q, 6–8 h or CRI at 0.01–0.05 mg/kg/h
Erythromycin	1.0 mg/kg in 1 L saline over 1 h q 6 h
Cisapride	0.1 mg/kg IM or IV q 8 h (compounding required owing to poor oral bioavailability)
Neostigmine	0.0044–0.022 mg/kg IM or SQ q 20–60 min
Bethanechol	0.025 mg/kg IV or SQ q, 4–6 h
Domperidone	5 mg/kg PO

Incisional Complications

The most commonly encountered incisional complications that may occur following ventral midline celiotomy for treatment of colic include acute incisional dehiscence (Figure 48.4), incisional infection, and incisional hernia formation. The prevalence, risk factors, and treatment for each are discussed.

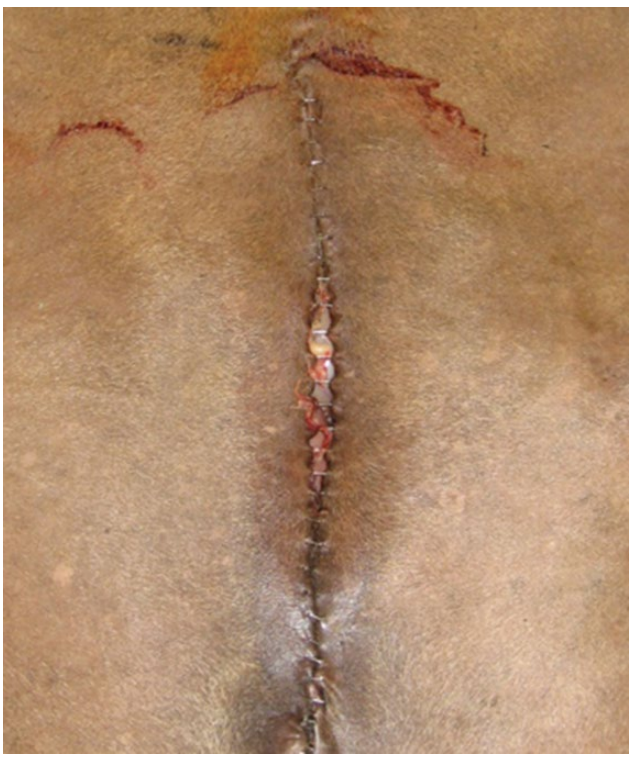

Figure 48.4 Dehiscence of the abdominal wall with retention of skin staples in a horse that had ventral midline celiotomy 4 days prior.

Dehiscence

Acute incisional dehiscence occurs in only 1–3% of postoperative colic patients (Kobluk et al., 1989; Stone et al., 1991; Wilson et al., 1995), but the consequences are potentially fatal if not immediately addressed. Dehiscence most commonly occurs within the first

8 days postoperatively and should be managed by application of an abdominal bandage (Figure 48.5), followed by immediate surgical repair including debridement of incisional edges and thorough incisional and abdominal lavage under general anesthesia. A reinforcing suture pattern such as preplaced horizontal mattress sutures in combination with a continuous pattern in the linea alba, or application of 18–22-gauge stainless-steel wire stents through the body wall when infection is suspected or body wall strength is compromised (Figure 48.6), is often appropriate to maintain the integrity of the body wall. As seen in Figure 48.6, pressure necrosis of the skin and surrounding tissues is a consequence of wire stent application. These wounds heal once the wires are removed.

Serosanguinous discharge often precedes dehiscence (Stone et al., 1991), so its presence should initiate investigation of incisional integrity via palpation and ultrasound. Factors believed to increase risk of dehiscence include violent anesthetic recoveries, postoperative pain, and conditions or activities associated with increased intra-abdominal pressure. These may include abdominal distention, straining, excessive exercise, or whinnying.

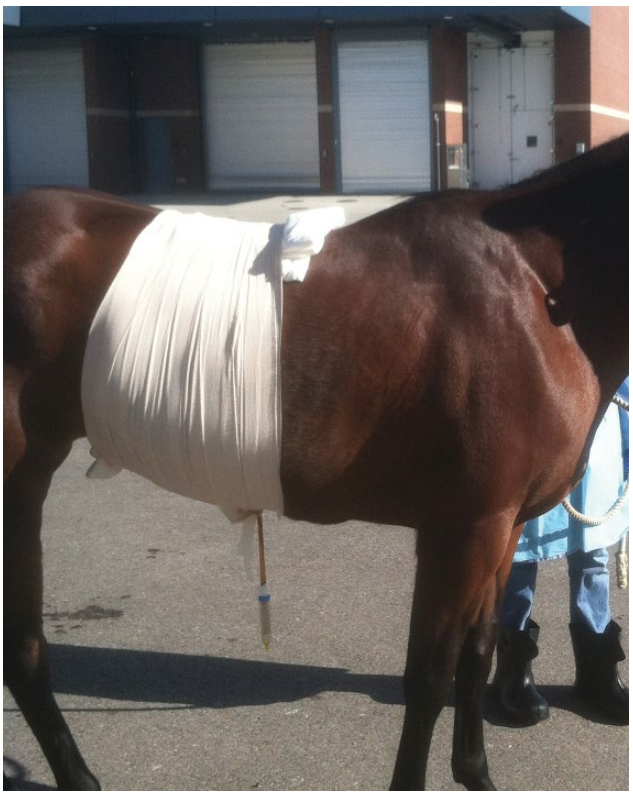

Figure 48.5 Example of a snugly applied Elastikon abdominal bandage with sterile bandages over the surgical incision that may be used for temporary retention of bowel during acute incisional dehiscence. The presence of the bandage may help limit further evisceration and bowel contamination during induction for repair.

Incisional Infection

Infection of the laparotomy wound is a common complication of colic surgery. Recent reports describe a prevalence of postoperative incisional infection of 12–42% (Mair & Smith, 2005a, 2005b, 2005c; Durward-Akhurst et al., 2013; Tnibar et al., 2013; Colbath et al., 2014; Costa-Farre et al., 2014; Anderson et al., 2015). The prevalence increases to 68–87% following repeat celiotomy (Kobluk et al., 1989; Dunkel et al., 2015). This complication causes patient discomfort, prolonged hospitalization, and increased cost to the client. Wound suppuration also increases the risk for incisional hernia development (Ingle-Fehr et al., 1997).

Clinical Signs and Treatment

An early indication of the development of incisional infection is postoperative fever. This is often followed by increased edema and tenderness to palpation directly over the incision line. Infection most commonly develops three or more days after surgery and drainage may be delayed as long as 14 days (Hardy & Rakestraw, 2006).

Incisional infections can be managed effectively by promoting drainage of purulent material from the subcutaneous space. This is achieved by removal of skin staples or sutures at the site of infection and daily cleaning of the wound with removal of crusted exudates and massage of the surrounding area toward the wound opening to promote drainage (Figure 48.7). Aerobic and anaerobic culture and sensitivity of exudate are used to determine antimicrobial therapy. Systemic antibiotics are appropriate when fever, significant tissue reaction, or

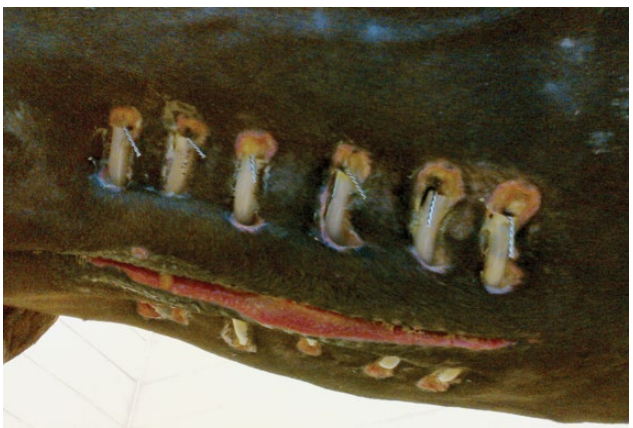

Figure 48.6 22-Gauge stainless-steel wire with Argyle tubing placed in a vertical mattress pattern full thickness through the body wall in a horse with a severe incisional infection and subsequent incisional dehiscence. The image was taken 10 days postoperatively and demonstrates pressure necrosis of the skin and surrounding tissues as a consequence of wire stent application.

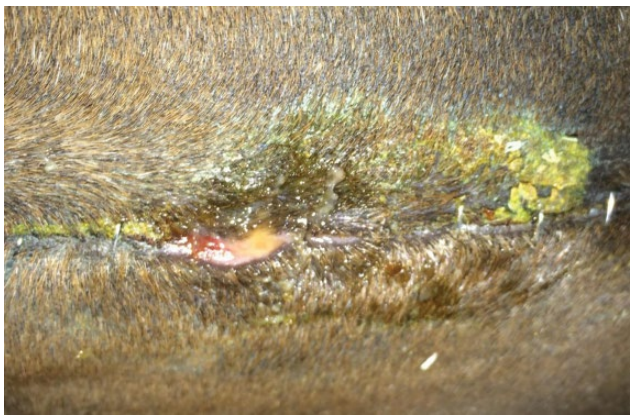

Figure 48.7 Ventral abdominal incisional infection 12 days following celiotomy for treatment of colic. Note the removal of two skin staples to facilitate drainage from the infected subcutaneous tissues.

systemic signs of illness are present. However, prolonged postoperative antibiotic therapy is ineffective in the prevention of surgical site infection (Durward-Akhurst et al., 2013). As drainage decreases, granulation tissue will fill the subcutaneous defect and the draining sinus tract will contract and close. It is unusual for subcutaneous infection to migrate dorsally into the peritoneal cavity, but risk for incisional hernia formation increases 17–62-fold with the presence of an incisional infection (Gibson et al., 1989; Ingle-Fehr et al., 1997). Because of the substantial increase in risk of hernia formation, application of a properly fitted abdominal bandage or hernia belt designed for prevention and treatment of abdominal hernias (CM Heal hernia belt; CM Equine Products, Norco, CA, USA) reduces the risk for hernia formation (Klohnen, 2009). The cost of the hernia belt must be considered and also the increase in cost and labor associated with frequent bandage changes that become necessary when the belt is applied.

Risk Factors and Protective Practices

Multiple studies have identified risk factors associated with postoperative incisional infection with occasional conflicting results. One study identified an increased risk associated with performing an enterotomy or resection (Honnas & Cohen, 1997), whereas others found no such association (Kobluk et al., 1989; Phillips & Walmsley, 1993; French et al., 2002). Use of a stent bandage over the incision was found to increase risk in one study (Mair & Smith, 2005a, 2005b, 2005c), but decreased risk in another (Tnibar et al., 2013). There is evidence to suggest that bacterial contamination that contributes to incisional infection occurs primarily in the postoperative period during anesthesia recovery and in the 24 h after surgery (Ingle-Fehret al., 1997; Galuppo et al., 1999; Klohnen, 2009). This is further supported by several studies showing protective effects of various methods of surgical wound coverage including iodophor-impregnated incise drapes (Kobluk et al., 1989; Ingle-Fehr et al., 1997; Galuppoet al., 1999), stent bandages (Tnibar et al., 2013), and application of abdominal bandages (Smith et al., 2007). Maintenance of an aseptic environment during both anesthesia recovery and in the early postoperative period is essential to lessen the risk for incisional infection. Other protective factors include lavage of the subcutaneous tissues with sterile saline during closure (Smith et al., 2007), increased experience of the surgeon (Torfs et al., 2010), and use of a two-layer modified subcuticular pattern for closure rather than a three-layer sutured closure (Colbath et al., 2014). Influence of type of suture used and method of closure of the abdominal wall, subcutaneous tissue, or skin has also been investigated. The near–far–far–near suture pattern in the linea alba was significantly associated with an increased prevalence of infection in one study (Kobluk et al., 1989), and also the use of skin staples compared with monofilament suture for closure of the skin (Torfs et al., 2010), poly(glycolic acid) suture for closure of the subcutaneous tissues, and prolonged anesthetic time (Costa-Farre et al., 2014). Patient factors reported to increase the risk of wound suppuration include low intraoperative PaO_2, increased time under anesthesia (Costa-Farre et al., 2014), increased peritoneal fluid fibrinogen (Honnas & Cohen, 1997), leukopenia, postoperative pain, older age (>1 year), and undergoing repeat celiotomy (Wilson et al., 1995; Mair & Smith, 2005a, 2005b, 2005c).

Incisional Hernia Formation

Published reports suggest that between 2.6 and 3.6% of horses undergoing colic surgery that do not develop incisional infection will develop incisional herniation (Honnas & Cohen, 1997; Mair & Smith, 2005a, 2005b, 2005c; Anderson et al., 2015), whereas risk of hernia formation with the presence of incisional infection increases by a factor of 17.8–62.5 (Gibson et al., 1989; Ingle-Fehr et al., 1997). Hernia formation at the incision site can be detected by visual observation of a defect in the abdominal wall and by palpation of the edges of a hernial ring (Figure 48.8). Some hernias are single, others constitute two or more discrete hernial rings in a stretched, thinned area of abdominal wall. The significance of the hernia is dependent on its size and the intended use of the horse. Small hernias, with minimal distortion of the profile of the abdominal wall, are well tolerated and need not be repaired, especially in horses undertaking only light exercise. Large hernias are cosmetically unacceptable and are at risk for ulceration and dehiscence These should be surgically repaired in most instances. The CM Heal hernia belt has been advocated both for treatment and prevention of incisional hernias (Figure 48.9).

Figure 48.8 Large ventral abdominal incisional hernia 3 months following ventral midline celiotomy for treatment of colic. Source: Courtesy of Nat White.

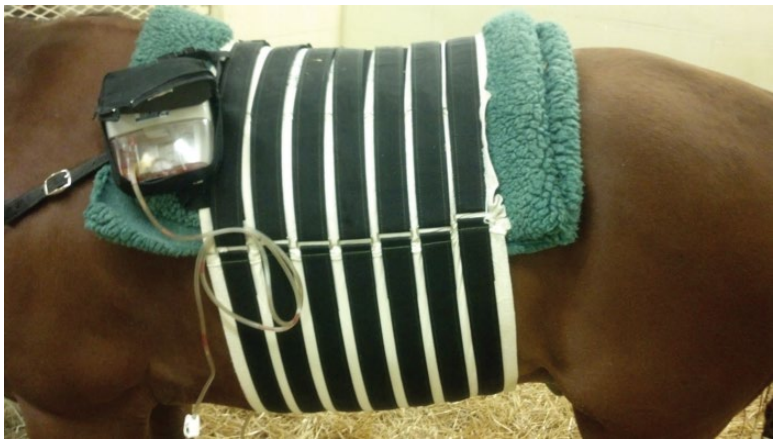

Figure 48.9 CM Heal hernia belt in place in a postoperative colic patient. These have utility for incisional support, reducing incisional edema, hernia repair, and hernia prevention. Source: Courtesy of Clarisa Krueger.

Prophylactic use of this belt in 993 postoperative colics resulted in an 8% incidence of incisional complications, with only 0.5% of all horses developing an incisional hernia, and 6% with incisional infection developing a hernia (Klohnen & Lores, 2008). The hernia belt has been shown to provide superior and persistent sub-bandage pressure over elastic bandages and nylon binders (Canada et al., 2015), and anecdotal reports suggest favorable responses for healing of incisional hernias without surgical intervention.

The appropriate management of horses with incisional hernias is important to the success of subsequent surgical repair. Once the hernia is recognized, the horse should be confined to a stall to minimize further increases in size and a CM Heal hernia belt should be applied and reset daily. It is recommended that hernia repair is delayed for 3–6 months after colic surgery to allow the abdominal wall to heal and for maturation of collagen along the edge of the hernia. This is important to maximize the suture-holding capacity of the tissue and it provides an opportunity to recognize the degree of improvement achieved with the hernia belt alone. Preoperative preparation for larger hernias should include feeding a pelleted diet for 1–2 weeks followed by perioperative fasting to reduce the volume within the gastrointestinal tract (Hardy & Rakestraw, 2012) and prophylactic antimicrobial therapy.

Surgical options for herniorrhaphy include primary closure, subperitoneal mesh implantation with a fascial overlay, subperitoneal mesh placement with hernia ring apposition, subcutaneous mesh placement with hernia ring apposition, and laparoscopic intraperitoneal mesh overlay (Caron & Mehler, 2009; Kummer & Stick, 2012). Available mesh materials include knit polypropylene (Marlex), coated polyester (Mersilene), and polyglactin 910 (Vicryl). An advantage of Vicryl mesh is that it is absorbable and may not require removal in the event of infection developing postoperatively (Kummer & Stick, 2012). Facilitation of apposition of the hernial ring may be achieved with intraoperative paralysis using atracurium besylate to allow for enhanced relaxation of the muscles of the lateral abdominal body wall. Postoperative complications following mesh herniorrhaphy include tearing of the internal abdominal oblique muscle, seroma

formation, and incisional drainage and infection. Use of mesh should be avoided when possible (i.e., primary closure performed if feasible) to decrease complications associated with mesh implantation.

Postoperative Fever

Development of postoperative fever [>38.3 °C (101 °F)] is very common, occurring in up to 85% of colic patients, but the presence of mild fever may not necessarily be associated with impending bacterial infection (Freeman et al., 2012). However, peak postoperative temperature >39.2 °C (102.6 °F), time from surgery to peak temperature >48 h, and duration of pyrexia >48 h are significantly associated with infection (Freeman et al., 2012). If postoperative fever is recognized, a thorough investigation of the etiology of the fever should be pursued, as delays in diagnosis of conditions such as septic peritonitis or septic thrombophlebitis may have devastating consequences. More common causes of fever in the postoperative colic patient include endotoxemia or SIRS secondary to the primary disease process, incisional infection, colitis or enteritis, septic peritonitis, thrombophlebitis, pneumonia, and viral respiratory disease. A list of these common causes of fever and initial recommended diagnostic tests is provided in Table 48.3. The author has commonly observed postoperative fever with specific surgical conditions, including extensive colonic feed impactions, sand impactions requiring surgery, and obstructions of the descending colon, presumably a result of mucosal injury and disruption of the gastrointestinal mucosal barrier. In the author's experience, prophylactic use of di-tri-octahedral (DTO) smectite [1 lb (450 g) via nasogastric tube q 12–24 h] with these cases has been helpful in ameliorating fever and preventing and treating postoperative diarrhea.

If postoperative fever is identified, a complete blood count (CBC) should be submitted. Leukopenia and neutropenia are common in the postoperative colic patient, but persistent neutropenia may be a consequence of an underlying disease process such as colitis from salmonellosis or other pathogens, ischemic or infarctive conditions, peritonitis, or other Gram-negative infections. Hyperfibrinogenemia also commonly occurs postoperatively, but rarely exceeds 700 mg/dL (7 g/L) in the uncomplicated colic patient. Serum amyloid A (SAA) has been shown to be a more sensitive indicator of inflammation than fibrinogen in postoperative colic (Daniel et al., 2016), and increased levels have been correlated with development of complications and nonsurvival (Westerman et al., 2016).

Pneumonia is an infrequent, but potentially serious, cause of postoperative fever, reportedly occurring in less than 1% of postoperative colics (Mair & Smith, 2005a, 2005b, 2005c). Viral upper or lower respiratory disease should also be considered when fever of unknown origin is present. Thoracic auscultation including a rebreathing examination and auscultation of the trachea should be performed. If a viral respiratory disease is suspected, nasal swabs should be obtained for herpes and influenza polymerase chain reaction (PCR) testing. If pneumonia is suspected, transtracheal wash with aerobic and anaerobic culture and sensitivity followed by broad-spectrum antimicrobial therapy is indicated, along with clinical monitoring, thoracic radiography, and thoracic ultrasound.

For detailed discussions of the diagnosis and treatment of the following common causes of postoperative fever, see the following chapters: SIRS, Chapters 16 and 28; peritonitis, Chapter 29; and enteritis/colitis, Chapter 30.

Septic Peritonitis

Septic peritonitis in postoperative colic is a life-threatening complication with a reported fatality rate of 56% (Hawkins et al., 1993). Prompt diagnosis of this condition is essential as early relaparotomy is indicated in the majority of cases to optimize outcome. Although some degree of

Table 48.3 Common causes of fever in the postoperative colic patient and recommended initial diagnostic tests.

Cause of postoperative fever	Recommended initial diagnostic tests
Endotoxemia/SIRS	PE; CBC
Incisional infection	PE; CBC; ultrasound evaluation of incision
Colitis/enteritis	PE; abdominal ultrasound; CBC
Septic peritonitis	Abdominal ultrasound; abdominocentesis; peritoneal fluid analysis; CBC
Thrombophlebitis	PE; ultrasound jugular vein; remove and culture IV catheter
Pneumonia	Thoracic auscultation with rebreathing examination; thoracic ultrasound; CBC
Respiratory viral disease	PE; auscultation of thorax with rebreathing examination; nasal swabs for virus isolation

CBC, complete blood count; PE, physical examination.

peritonitis occurs in every postoperative colic patient, making the interpretation of nucleated cell counts in peritoneal fluid difficult (Santschi et al., 1988; Hanson et al., 1992), septic peritonitis is a relatively rare complication, reported to occur in only 3.1% of postoperative colics (Mair & Smith, 2005a, 2005b, 2005c). Clinical signs of septic peritonitis may include fever, tachycardia, colic, diarrhea, and decreased borborygmi (Dyson, 1983).

Diagnostic methods to differentiate septic peritonitis from nonseptic postoperative peritonitis may include the presence of large quantities of free peritoneal fluid with or without fibrin tags visualized on ultrasound, increased echogenicity of peritoneal fluid, peritoneal fluid analysis indicating presence of degenerate neutrophils and/or bacteria, low pH of peritoneal fluid (<7.3), and a low glucose concentration in peritoneal fluid compared with the systemic blood glucose concentration [>50 mg/dL (2.77 mmol/L) difference] (Rodgers, 1994). A peritoneal fluid sample should be submitted for aerobic and anaerobic culture and sensitivity if septic peritonitis is suspected. Conditions that may lead to septic peritonitis in the postoperative period include surgical contamination, necrotic bowel present prior to surgery or secondary to ischemic injury postoperatively, or leakage from the site of an anastomosis or enterotomy (Hardy & Rakestraw, 2006).

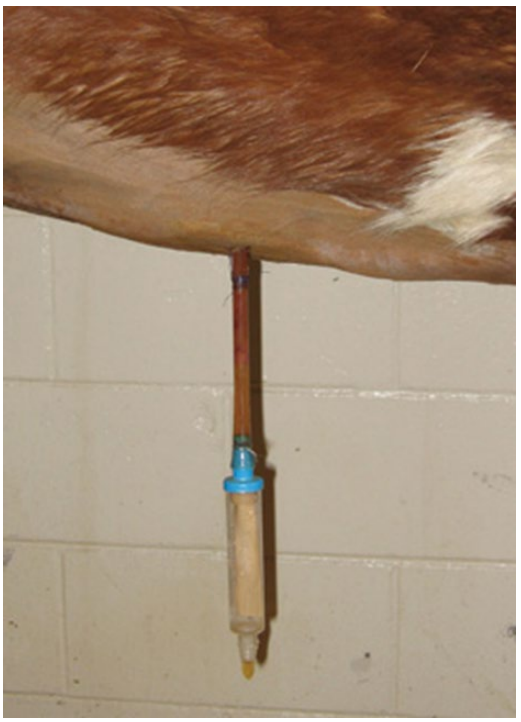

Figure 48.10 Indwelling 30-French Argyle trocar catheter with Heimlich valve attached with 18-gauge stainless-steel wire to allow for continuous drainage and lavage of the peritoneal cavity for treatment of septic peritonitis.

Treatment

Considering the conditions that lead to septic peritonitis in the postoperative colic, relaparotomy immediately following the recognition of septic peritonitis is almost always indicated. Even if a continued source of gastrointestinal leakage or necrosis is not identified, relaparotomy provides an opportunity for a thorough abdominal lavage, omentectomy, and placement of an indwelling abdominal drain for continued peritoneal lavage postoperatively. Abdominal lavage provides a mechanism to remove bacteria, cellular debris, inflammatory mediators, fibrin, and free fluid (Maetani & Tobe, 1981), and is effective at reducing the potential for adhesion formation (Hague et al., 1998). Omentectomy at the time of abdominal drain placement will facilitate proper functioning of an indwelling abdominal drain by limiting omental occlusion of drain fenestrations. Although there are several options for peritoneal drains, the method of choice in the author's hospital is use of a 30-French Argyle trocar catheter (Covidien, Mansfield, MA, USA) with 4–6 added fenestrations toward the tip created with a #10 scalpel blade. This drain may be placed in the standing sedated horse as well as under general anesthesia. The drain is secured to the skin with a Chinese finger trap suture pattern. A Heimlich one-way chest valve (BD, Franklin Lakes NJ, USA) is secured to the tube with 18-gauge wire to limit the potential for ascending infection (Figure 48.10). Strict attention to aseptic technique is utilized while handling the drain during all lavages. Warmed sterile isotonic fluids (e.g., Plasmalyte) are administered through the drain (Figure 48.11) using a modified high-flow IV set (High Flow IV administration set; Mila International, Florence, KY, USA) with a connector to attach to the Argyle trochar catheter (Figure 48.12) (double-ended barb connector 4–12 mm; JorVet, Loveland, CO, USA). The volume administered may be dictated by patient tolerance, but a minimum of 5 L and a maximum of 15 L is infused intra-abdominally. If possible, the patient is walked for 5 min prior to drainage of the peritoneal cavity via gravity into the same sterile fluid bag used to administer fluids. This procedure may be repeated 2–4 times daily depending on the severity of the peritonitis. Discontinuing abdominal lavage should be dictated by daily peritoneal fluid analysis indicating progressive resolution of septic peritonitis. The duration of peritoneal lavage rarely exceeds 72 h.

Important therapies in addition to abdominal lavage include broad-spectrum antimicrobial therapy, including extended anaerobic spectrum treatment with metronidazole (15 mg/kg PO q 8 h) until culture and sensitivity results dictate otherwise, along with therapy for fluid volume and electrolyte replacement. Anti-inflammatory therapy with NSAIDs, treatment with polymyxin B sulfate if endotoxemia is present, and cryotherapy (e.g., ice boots) for laminitis prevention are often indicated.

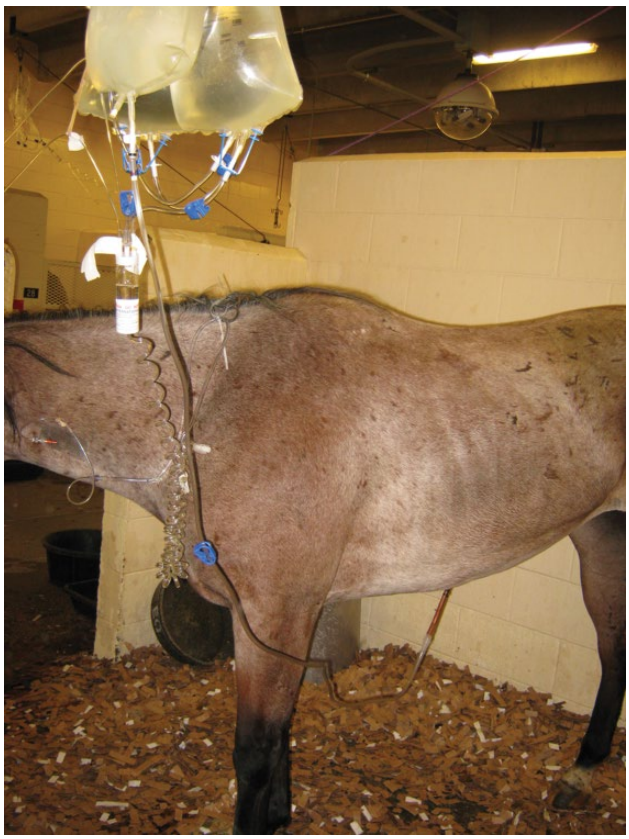

Figure 48.11 Gravity-flow lavage with sterile warmed isotonic fluids into the peritoneal cavity in a horse with septic peritonitis. Once the fluids have infused, the tube may be occluded, the empty fluid bag held, and the horse may be walked. Fluid collection may take place by lowering the fluid bag to the ground and releasing the roller clamp on the fluid infusion set. A Heimlich valve should be applied using 18-gauge stainless-steel wire following collection of most of the infused fluid to allow for continued drainage of residual fluid.

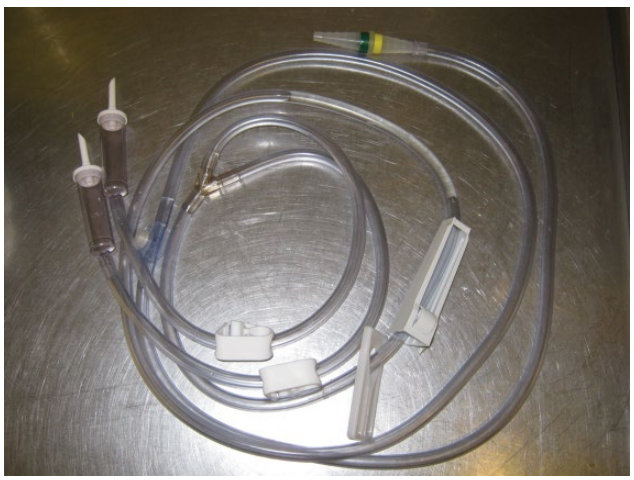

Figure 48.12 High-flow IV set modified with a double-ended barb connector to allow connection to the 30-French Argyle trocar catheter for peritoneal lavage.

Coagulopathy and Associated Complications

Dysfunction of coagulation and fibrinolysis is a frequent event in horses with gastrointestinal disease exhibiting SIRS, and has been reported to occur in 70% of horses with large colon volvulus (Dallap et al., 2003). Those with strangulating, inflammatory, and ischemic gastrointestinal disease are at greatest risk for development of coagulopathy of varying severity from subclinical to overt disseminated intravascular coagulation (DIC). Manifestations of coagulopathy in its most severe form include a persistent hypercoagulable state, resulting in fibrin deposition, and microthrombi deposition in multiple tissues, resulting in multiorgan failure. A consumptive coagulopathy over time may be characterized by a hemorrhagic syndrome with gross evidence of bleeding (Monreal & Cesarini, 2009). Diagnosis can be determined with a hemostatic profile that includes platelet count, clotting times, fibrinogen concentration and D-dimer concentration. Two common manifestations of colic-associated coagulopathies include jugular vein thrombosis and postoperative infarction of the gastrointestinal tract and other organs resulting in multiorgan dysfunction or failure.

Jugular Thrombosis and Thrombophlebitis

The prevalence of jugular thrombosis has been reported as being between 7.5 and 10% of horses recovering from colic surgery (Proudman et al., 2002; Mair & Smith, 2005a, 2005b, 2005c), so frequent monitoring of the catheter site and jugular vein should occur in horses with colic. The risk of thrombophlebitis is increased by catheter type, dwell time of the catheter, presence of fever, inappropriate site preparation, poor catheter care, endotoxemia, salmonellosis, hypoproteinemia, and large intestinal disease (Lankveld et al., 2001; Dolente et al., 2005).

The clinical signs of septic jugular thrombophlebitis are firm swelling with edema, heat, and pain in the area overlying the catheter insertion site, typically accompanied by fever. Nonseptic thrombosis is primarily characterized by "cording" of the jugular vein with vascular congestion proximal to the vein. If thrombosis is bilateral, swelling of the muzzle and face may occur. Ultrasonographic imaging of jugular veins is helpful to confirm the diagnosis of thrombophlebitis, monitor response to treatment, and identify the best site for aspiration for bacterial culture and sensitivity (Gardner et al., 1991).

Thrombosis commonly develops following removal of an indwelling catheter, but if signs of thrombosis are identified while the catheter is in place, it is important to remove the catheter immediately. At this time, the

catheter tip may be cultured for bacterial contamination. Some clinicians consider that it is helpful to apply hot packs to the affected area several times daily in order to stimulate blood flow. The topical use of dimethyl sulfoxide (DMSO) or topical diclofenac cream has also been advocated, although there is no evidence to support the efficacy of these treatments. If infection is suspected or confirmed by bacterial culture, appropriate antibiotic therapy should be used. The majority of thrombi that are unilateral resolve and the affected veins will recannulate, although this may take weeks to months. If venous access is necessary, alternative veins to the jugular (lateral thoracic, cephalic) should be used if a venous catheter is still necessary.

Infarction of the Gastrointestinal Tract and Other Organs

Postoperative infarction of the gastrointestinal tract most often will result in euthanasia or death of the postoperative colic patient as multiple organ dysfunction and failure ensue. The author has most commonly observed this syndrome in the postoperative colonic volvulus patient. The infarction may be a result of the primary disease process (i.e., nonviable colon remaining postoperatively), or may occur several days postoperatively as a consequence of the development of a hypercoagulable state and thrombi formation within the vasculature of the colon and other organs. Based on work in other species on the efficacy of low-dose aspirin for impairing thrombin generation and reactions catalyzed by this enzyme (Undas et al., 2001), and actions of aspirin in ponies on prolongation of bleeding time and inhibition of platelet cyclooxygenase (Cambridge et al., 1991), every other day therapy with aspirin (10 mg/kg PO q 48 h) in postoperative colonic volvulus patients considered at increased risk for thrombotic disease can be considered. Clopidogrel (2 mg/kg PO q 24 h) has been shown to be superior to a low dose of aspirin (5 mg/kg) on adenosine diphosphate (ADP)-induced platelet aggregation and may have therapeutic potential (Brainard et al., 2011). Heparin therapy is considered to be the most effective and safe treatment for the hypercoagulable state in horses (Monreal & Cesarini, 2009), but unfractioned heparin (40 IU/kg q 12 h SQ) has detrimental side effects, including anemia and prolongation of clotting times (Monreal et al., 1995; Feige et al., 2003). Low molecular weight heparin (LMWH) may be somewhat cost prohibitive, but has fewer reported side effects and is more effective than unfractioned heparin (Feige et al., 2003). The recommended dosages for dalteparin (Kabi Pharmacia, Stockholm, Sweden) and enoxaparin (Sanofi-Aventis US, Bridgewater, NJ, USA) are 50 IU/kg subcutaneously every 24 h and 0.5 mg/kg subcutaneously every 24 h, respectively (Monreal & Cesarini, 2009). An added potential benefit of LMWH is prophylaxis for laminitis (De la Rebière de Pouyade et al., 2009). Some clinicians hesitate to use heparin therapy in postoperative colic patients undergoing resection and anastomosis owing to concern for postoperative hemorrhage, although LMWH has limited impact on clotting times (Feige et al., 2003). Fresh plasma or fresh frozen plasma may have benefits in those patients with spontaneous hemorrhages and may be used in combination with LMWH.

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Laminitis Associated with Acute Abdominal Disease

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Pathogenesis: Physiologic Considerations

In the past two decades, laminitis research, using both experimental models of laminitis and investigations of clinical cases of laminitis, has greatly expanded our understanding of the disease and has resulted in the separation of the disease into three basic types: sepsis-related laminitis, supporting limb laminitis, and endocrinopathic laminitis. In sepsis-related laminitis, any disease that results in systemic sepsis (commonly termed endotoxemia) may put an animal at risk of laminitis; however, there appears to be a higher prevalence in disease states associated with Gram-negative bacterial organisms (Belknap et al., 2009; Garner et al., 1978). Although numerous diseases ranging from acute metritis to pleuropneumonia can predispose horses to the development of acute laminitis, the most common instigator of sepsis-related laminitis is acute abdominal disease (Slater et al., 1995). Acute laminitis is commonly associated with horses exhibiting signs consistent with sepsis/endotoxemia due to compromised bowel in diseases that require surgical intervention (e.g., intestinal strangulation obstruction, particularly of the large colon) and horses with severe inflammatory bowel diseases (e.g., enterocolitis, proximal enteritis) (Moore & Allen, 1996). Overall, large intestinal disease is more commonly associated with laminitis than small intestinal disease, most likely owing to the large concentration of Gram-negative organisms in the large intestine.

We have made more progress in both (1) determining the pathophysiology and (2) establishing effective therapies for sepsis-related laminitis compared with endocrinopathic and supporting limb laminitis, primarily because the most commonly used experimental models for laminitis are models of sepsis-related laminitis. These models involve intragastric administration of either an excessive amount of carbohydrate [either a starch/wood flour gruel (Garner et al., 1975; Sprouse et al., 1987; Leise et al., 2011) or oligofructose (van Eps & Pollitt, 2006, 2009b; Van Eps et al., 2014) dissolved in water] or the aqueous extract of the heartwood of black walnut trees (Minnick et al., 1987; Galey et al., 1991; Faleiros et al., 2011c). In both carbohydrate overload models, the delivery of excessive carbohydrate to the hindgut results in enterocolitis, injury to the large intestinal mucosal surface, and subsequent systemic absorption/translocation of bacteria and/or bacterial toxins from the compromised intestine. This results in clinical signs consistent with the systemic inflammatory response syndrome (SIRS) component of sepsis (e.g., hyperemic to cyanotic mucous membranes, elevated heart rate, hypo- or hyperthermia) (Bailey et al., 2009; Sprouse et al., 1987). In both carbohydrate overload models, horses develop diarrhea in the developmental stages of the model, and develop clinically apparent lameness (Obel Grade 2–3 laminitis) within 40–48 h (slightly sooner in the oligofructose model) (van Eps & Pollitt, 2006; Garner et al., 1975, 1978).

The black walnut extract (BWE) model of sepsis-related laminitis was developed after the discovery that horses bedded on shavings made from heartwood of black walnut trees developed laminitis (True et al., 1978; Minnick et al., 1987). In this model, black walnut heartwood shavings are soaked in water overnight, the shavings filtered out, and the extract is administered via nasogastric tube. This is a much more rapid model of laminitis, in which the animals exhibit clinical signs

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of laminitis within 10–12 h post-administration (Minnick et al., 1987; Galey et al., 1991). However, the animals usually demonstrate only a mild, transient form of laminitis (commonly Obel Grade 1), and do not usually undergo lamellar failure. Therefore, although valuable data have been obtained from both the carbohydrate and BWE models, the carbohydrate overload models are more commonly used because they more closely mimic the clinical course of laminitis (in both timing and severity of lamellar injury/failure).

The pathophysiology of lamellar failure in laminitis has been a controversial topic in veterinary medicine over several decades, primarily regarding the role that lamellar blood supply plays in the lamellar injury. As therapies for laminitis were based on the purported pathophysiology of the disease, the controversy regarding pathophysiology followed into the clinical arena regarding appropriate therapy for the disease. A primary reason for this controversy is that the location of the lamellar tissue between two relatively impenetrable surfaces, namely the hoof wall and the distal phalanx, prevented laminitis researchers from using many of the advanced physiologic techniques that are/were readily applicable to study the microvasculature in other tissues (intestines, etc.). As a result, investigators used less precise techniques as proxies for lamellar blood flow (e.g., hoof warmth) to report either an increase or decrease in lamellar blood flow in the early stages of laminitis (Pollitt & Davies, 1998; Hood et al., 2001b). With the recent establishment of a technique in which a microdialysis catheter is placed in the lamellar tissue in the standing horse and from which real-time data can be obtained, investigators have been able for the first time to assess physiologic events occurring in the lamellar tissue in real time (Nourian et al., 2010). Using this method in the oligofructose model of sepsis-related laminitis, lamellar perfusion was noted actually to increase during the development of laminitis (Medina-Torres et al., 2016b), thus questioning the role that ischemia may play in the pathophysiology of sepsis-related laminitis.

Establishment of the role of inflammatory events in the pathophysiology of lamellar injury in sepsis-related laminitis has followed many of the same findings reported in organ injury in human sepsis. In both carbohydrate overload models of sepsis-related laminitis, low levels of circulating endotoxin have been detected (Sprouse et al., 1987; Bailey et al., 2009). Similarly to human sepsis, one of the early events found to occur in sepsis-related laminitis is systemic activation of circulating leukocytes (Hurley et al., 2006; Loftus et al., 2010; Lunn & Hurley, 2009), followed by adhesion of these leukocytes to the endothelial surface in the lamellar microvasculature and emigration of these leukocytes into the lamellar tissue (Faleiros et al., 2009b, 2011a; Fontaine et al., 2001; Black et al., 2006). The activated leukocytes are likely stimulated to enter the lamellar tissue owing to both (1) platelet activation resulting in leukocyte activation (Bailey et al., 2009; Weiss et al., 1997; Weiss & Evanson, 1997) and (2) activation of the endothelial surface of the lamellar microvasculature from circulating bacterial products and inflammatory mediators, combined with the demonstrated expression of chemokines (molecules chemotactic for leukocytes) by host lamellar cells including the lamellar epithelial cells (Leise et al., 2015; Faleiros et al., 2009a). A marked increase in lamellar inflammatory mediator expression including cytokines, chemokines, and COX-2 has been detected in models of sepsis-related laminitis (Faleiros et al., 2009a, 2011b; Leise et al., 2011; Fontaine et al., 2001; Waguespack et al., 2004a, 2004b; Blikslager et al., 2006; Belknap et al., 2007); the increases in lamellar inflammatory mediator expression is dramatically higher than that observed in visceral organs (e.g., liver and lung) at risk of injury in human sepsis (Stewart et al., 2009).

Although lamellar inflammatory events have been well documented in the early stages of sepsis-related laminitis, the link between inflammatory signaling and lamellar failure has been more difficult to establish. Interestingly, similarly to a consistent failure of over 100 clinical trials using drugs to block signaling mechanisms related to systemic inflammation in human sepsis, administration of anti-inflammatory pharmaceutical therapies to septic horses has anecdotally and experimentally provided minimal protection against lamellar injury in laminitis. The two primary histological findings in sepsis-related laminitis are stretching of the epidermal lamellae and separation of the epidermal lamellae from the underlying basement membrane and dermis. The stretching of the lamellar epithelial cells is likely due to dysregulation of cellular maintenance of the cytoskeleton, which normally allows cells to maintain a morphologic "rigidity" (De Laat et al., 2013). The separation of the lamellar basal epithelial cells from the underlying basement membrane attached to the dermal lamellae most likely occurs as a result of dysregulation of the primary protein adhesion complexes that keratinocytes use to adhere to the underlying matrix: type I hemidesmosomes (Pollitt, 2010; Nourian et al., 2007). These protein complexes, which include integrins that span the cell membrane to attach to matrix components of the basement membrane, have been demonstrated to be disrupted in the oligofructose model of sepsis-related laminitis (Nourian et al., 2007).

How does the marked lamellar inflammatory response lead to these two lamellar epithelial events (stretching and dysadhesion), which then lead to lamellar failure? A likely answer may come from epithelial cell tumor formation secondary to inflammatory diseases. When a normal epithelial cell makes the transition to a

tumor cell, two of the primary events are the same two events thought to lead to stretching and dysadhesion of the lamellar epithelial cells in laminitis: (1) dysregulation of the cytoskeleton (Medina-Torres et al., 2016a) and (2) dysregulation of the hemidesmosome adhesion complexes (Underwood et al., 2015). In inflammatory bowel disease, epithelial tumor formation has recently been reported to be driven by the cytokine IL-6 (Italiani and Boraschi, 2014), the same cytokine as present in extremely high levels in the lamellae in sepsis-related laminitis (Leise et al., 2011; Van Eps et al., 2012; Loftus et al., 2007). As we have also recently documented increased lamellar concentrations of the same two signaling proteins/pathways (JAK/STAT3 and MTORC1/RPS6) that are activated when IL-6 drives normal epithelial cells to become cancer cells (Italiani & Boraschi, 2014; Obel, 1948), it is likely that IL-6 is driving the same changes in lamellar epithelial cells, starting with disrupted cytoskeletal and adhesion dynamics, and leading to lamellar failure. Finally, local hypothermia (cryotherapy), the only therapy found to be protective against lamellar failure in sepsis-related laminitis (see the discussion under Treatment), decreased lamellar concentrations of both IL-6 and phospho-RPS6. It is hoped that this signaling pathway will provide pharmaceutical targets in the future for sepsis-related laminitis.

Pathogenesis: Structural Considerations of the Equine Digit

The stresses on the lamellae are related to weight bearing and locomotion. The forces coming to bear on the lamellae include the downward force of the horse's weight through the osseous structures of the digit, the ground reaction force, and the moments around the distal interphalangeal joint, namely the extensor moment generated by the ground reaction force and flexor moment generated by the tension of the deep digital flexor tendon exerted on the caudal aspect of the distal phalanx (Figure 49.1). Intuitively, it would appear that the more weight bearing is concentrated on the distal wall (versus the solar ground surface), the greater the stresses would be in the lamellae; however, the relationship between weight bearing and the distribution of load across the ground surface of the foot is potentially significantly more complex than this simple supposition. At rest, the center of weight bearing is approximately at the center of the ground surface of the foot, but the distribution of weight bearing on the ground surface of the foot is related to the nature of the ground surface. In a shod horse standing on a flat, hard surface, including the artificial surfaces upon which horses commonly stand, weight bearing is through the ground surface of the wall and sole immediately adjacent to the wall. In a bare-footed horse standing on a yielding surface, such as sand, weight bearing is more broadly distributed across the ground surface of the foot, resulting in more weight being borne by the sole and less weight concentrated on the ground surface of the wall (Hood et al., 2001a). Intuitively, this would suggest that housing a horse on a soft surface would decrease the tension on the lamellae compared with a hard surface. However, in the latter instance, it has not been determined how weight is transferred from the sole to the distal phalanx. It has been hypothesized that, in a healthy horse, the load on the ground surface of the sole is directed to the wall and thence to the lamellae (Thomason, 2007). If this is correct, then it may not actually make much difference whether the horse is standing on a soft or firm surface. Additionally, if weight were directly transferred through the sole to the distal phalanx, it would suggest that the subsolar dermis is in a state of compression, which would likely be deleterious to the dermal blood supply of the sole, particularly if the horse remained stationary rather than moving about the stall (Thomason, 2007). To contradict this, clinical experience suggests that thin-soled horses, whether they are laminitic or not, are more comfortable on a soft substrate than on a firm surface, which would support the intuitive position. There are at least three aspects about being housed on a soft surface that might explain this. First, moving around on a surface that yields with pressure means that the foot decelerates more slowly on impact, which should make movement more comfortable. Second, the weight is distributed across the ground surface of the foot, reducing the strain on the lamellae when a horse is motionless. Third, a soft surface may permit a horse to position its foot differently on the ground. The mechanism by which weight is transferred from the sole to the distal phalanx is perhaps the most pressing question in need of answering that could have the most impact on supportive care of the foot in horses with laminitis.

During locomotion, the stresses associated with weight bearing are also centered on the ground surface of the foot for most of the stride. However, during the breakover phase of the stride, they are concentrated at the toe. Consequently, at breakover, the ground reaction force is located at the toe of the hoof so the length of the moment arm is considerably longer than when the horse is standing at rest or at mid-stance in the stride (Figure 49.1). How much this affects the stresses in the dorsal wall (and hence the lamellae) is most likely a function of what the bending (extensor) moment is at breakover, and the extensor moment dependent on the other magnitude of the ground reaction force as well as the length of the moment arm. Therefore, although the moment arm peaks at breakover, the magnitude of the ground reaction

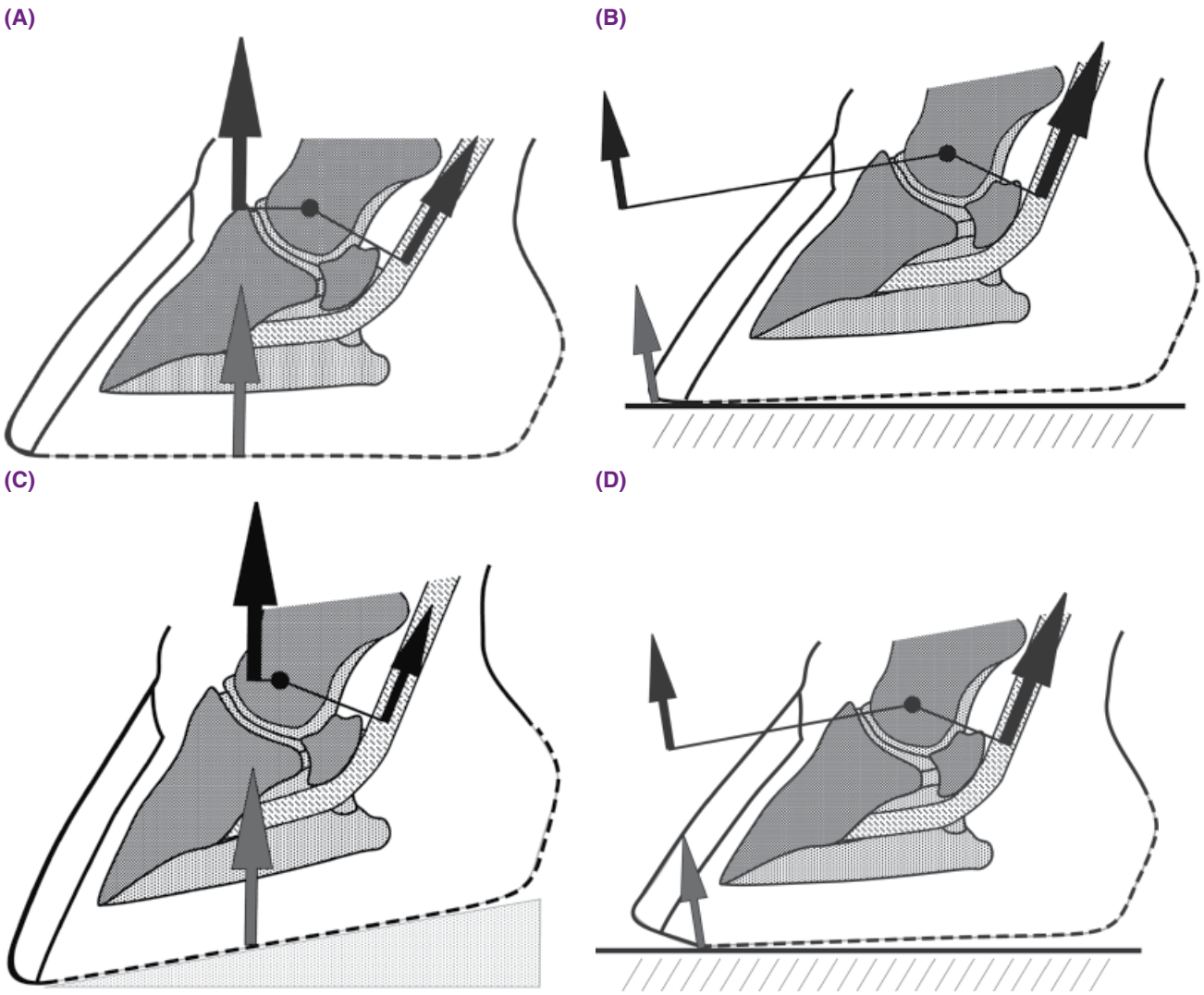

Figure 49.1 Schematic diagrams representing the effects of heel elevation and moving the breakover palmarly on the moments about the distal interphalangeal joint. The thin black lines extending from the center of rotation of the distal interphalangeal joint represent the moment arms for the ground reaction force and the tension in the deep digital flexor tendon (black arrows; size approximates the force). Note the gray arrows indicative of the ground force that is transferred to the moment arm. **(A)** Normal foot at rest; **(B)** normal foot at breakover – note that the ground reaction force is no longer vertical; **(C)** 10° heel elevation (assuming the point of action of the ground reaction force remains constant) – note that the component of the ground reaction force perpendicular to the moment arm is reduced compared with (A) and hence the torque about the distal interphalangeal joint is reduced; **(D)** breakover moved palmarly – note that the length of the moment arm of the ground reaction force and the force perpendicular to it are both decreased, hence the torque about the distal interphalangeal joint is reduced. All the vectors illustrated by the arrows are for illustrative purposes only and are not meant to indicate actual values. Images are copyrighted to Andrew Parks. Used with permission.

force has decreased substantially such that by the time the horse breaks over, it is already past peak extensor moment, which is maximal at around 65% of the stride (Clayton et al., 1998). However, there is also a spike in dorsal wall strain at breakover in trotting ponies that is 45–90% of peak strain (Thomason et al., 1992), which supports the hypothesis that breakover is associated with an increase in dorsal lamellar stress.

In a healthy horse, the strength of the lamellae greatly exceeds the stresses applied, thereby allowing the distal phalanx to be retained in its normal position. However, in horses with laminitis, the strength of the lamellar attachment to the distal phalanx is reduced, most likely due to the aforementioned lamellar epithelial stretching and dysadhesion of the epidermal lamellae from the underlying dermal lamellae. Once lamellar integrity is diminished during the developmental and acute stages of acute laminitis, partial loss of the lamellar integrity causes the remaining intact lamellae/portions of lamellae to endure the entire load of weight bearing

and locomotion. As a result, the remaining lamellae are potentially exposed to a cycle of exacerbated mechanical injury. The transition from acute/subacute laminitis to chronic laminitis is partially defined by displacement of the distal phalanx within the hoof capsule. Displacement of the distal phalanx occurs when stresses on the lamellae exceed the mechanical properties of the dermal and epidermal lamellae to resist them. The pattern of displacement of the distal phalanx within the hoof capsule varies among horses, and sometimes even between the feet in an individual horse. The distal phalanx may displace evenly around the circumference of the hoof wall, which is usually termed symmetrical distal displacement or sinking (Figure 49.2A). Alternatively, the distal phalanx may displace unevenly in relation to the hoof wall, the most common pattern of which is seen when the dorsal distal margin of the distal phalanx descends and the dorsal surface of distal phalanx diverges from the dorsal surface of the hoof wall distally (Figure 49.2B). This pattern is termed rotation of the distal phalanx. Rotation is frequently divided into capsular rotation and phalangeal rotation. Capsular rotation refers to divergence of the dorsal wall away from the dorsal parietal surface of the distal phalanx, whereas phalangeal rotation refers to divergence of the dorsal surface of the distal phalanx from that of the pastern in a palmar direction, that is, flexion. Immediately following rotation, capsular and phalangeal rotation occur equally and concurrently. However, it is possible later in the disease to have a situation in which one is more marked than the other; it is not uncommon for the phalangeal axis to become more closely realigned to its original position while marked capsular rotation persists (see later). In addition to symmetrical distal displacement and rotation of the distal phalanx, a less frequent pattern of displacement occurs in which the distal phalanx displaces asymmetrically in a dorsal (frontal) plane, either medially or laterally. Asymmetric displacement most commonly occurs on the medial/axial side of the foot (commonly termed a "medial sinker"; Figure 49.2C). In most horses, the pattern of displacement is a combination of distal displacement and rotation of the distal phalanx, although one pattern usually dominates.

After displacement has occurred, the space created by separation of the damaged lamellae between the hoof wall and the parietal surface of the distal phalanx is filled with blood and necrotic tissue. As the injured tissues heal, the coronary dermal papillae may not realign with the parietal surface of the distal phalanx and the space between the wall and distal phalanx fills with hyperplastic tissue (commonly termed the lamellar wedge). Both of these changes may prevent the realignment of the dorsal hoof wall with the distal phalanx with new wall growth.

Laminitis in the Acute Abdomen Patient: Clinical Presentation and Treatment

History

The history of horses with laminitis may vary considerably; however, there are distinct patterns that are recognizable in horses with either acute or chronic laminitis. In most diseases, the terms acute and chronic are used solely to designate temporal characteristics of the disease. However, in horses with laminitis, the term acute is typically applied to the first 3 days after onset, whereas chronic is frequently used to designate that displacement has occurred regardless of the duration of the disease. This is unfortunate because it suggests that the events associated with the acute phase of the disease have yielded to a separate set of events associated with the chronic phase, whereas in reality, the pathogenesis is a continuum. Therefore, we would prefer to separate the duration from the development of rotation in the classification, because medical therapy is typically related in part to duration, whereas hoof care is largely directed at mechanically maintaining or improving the relationship between the hoof capsule and the distal phalanx; these two objectives do not necessarily coincide temporally. However, in the laminitis literature, the term acute not only denotes laminitis of short duration (specifically less than 3 days), but also indicates that displacement of the distal phalanx has not occurred. In contrast, the term chronic with reference to laminitis is used to indicate that the distal phalanx has displaced regardless of the duration the disease process. Furthermore, disease of longer than 3 days in which displacement has not occurred is referred to as subacute. Thus, whereas the acute phase is truly acute, the subacute phase may refer to a horse that has survived the acute phase for several weeks without rotation of the distal phalanx, but whose symptoms have not resolved. The chronic phase may extend indefinitely from as little as 1 or 2 days after the onset of the disease.

Horses with acute laminitis frequently have a history of a prior or concurrent disease for which laminitis is a recognized sequela; the onset of signs is usually rapid. Horses with chronic laminitis may have a history of chronic disease as a direct sequela to acute laminitis, a recurrence or continuation of chronic laminitis of a long-standing nature, or have an insidious onset in which the acute phase was never pronounced. Horses with either acute or chronic laminitis may present with no history of a prior predisposing disease process.

The majority of animals with acute abdominal disease that suffer from laminitis do not have a previous history

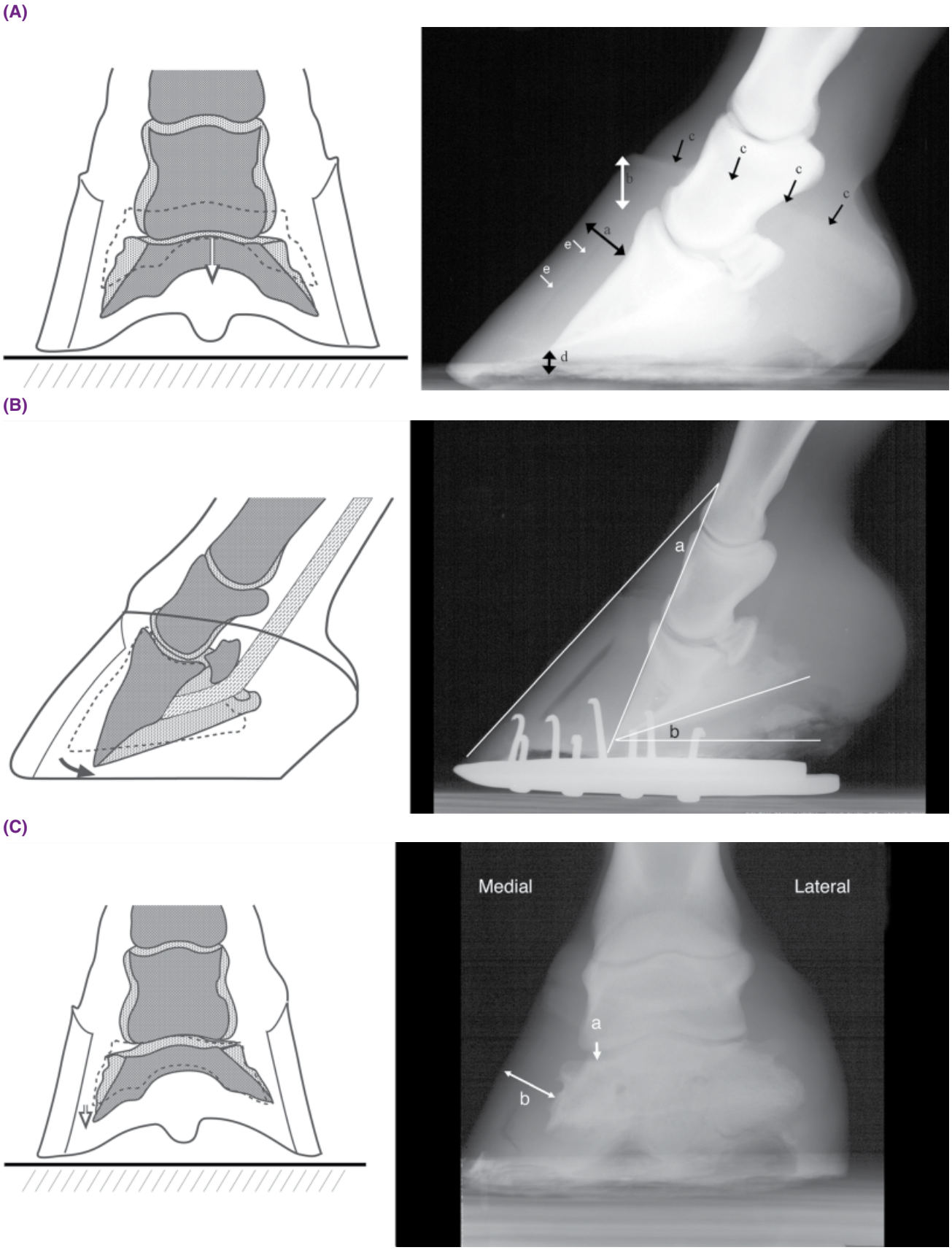

Figure 49.2 Schematic diagrams and radiographs that show three different patterns of displacement. **(A)** Distal displacement – the schematic illustration shows descent of the distal phalanx from the dorsal perspective, and the radiograph shows features of distal displacement from the lateral perspective including increased width of the dorsal hoof (a), increased distance between the coronary band and the extensor process of the distal phalanx (b), a prominent "sinker" line (c), reduced thickness of the sole (d), and a prominent radiolucent line between the dorsal hoof capsule and underlying tissues (e); **(B)** rotation – the parietal surface of the distal phalanx is diverging from the dorsal hoof wall (a, capsular rotation), and from the axis of the phalanges evidenced by an increased angle of the solar surface of the distal phalanx to the ground (b, phalangeal rotation); **(C)** asymmetric mediolateral distal displacement – in this radiograph the distal phalanx has distally displaced medially (a), and the medial wall is increased in thickness (b). Images are copyrighted to Andrew Parks. Used with permission.

of laminitis, and suffer an acute onset of sepsis-related laminitis secondary to the systemic effects of the abdominal disease. However, it is also not uncommon for the acute abdomen patient to have a history of endocrinopathic laminitis, or at least to have a history suggestive of metabolic syndrome. Therefore, it is important in these instances for the clinician to attempt to ascertain if displacement of the distal phalanx may have been present from the predisposing endocrinopathy, as the prognosis given may not be quite as poor if the radiographically detected amount of displacement did not occur rapidly over a short period of time (i.e., was a more insidious displacement from endocrinopathic laminitis that is commonly associated with more lamellar stability and a better prognosis than an acute displacement in sepsis-related laminitis). Without a previous history of laminitis, the most common history obtained in the acute abdomen patient suffering from acute laminitis is an acute onset of lameness following the onset of clinical signs of systemic sepsis (described later). In most instances of sepsis-related laminitis, signs of laminitis will occur 24–72 h after the onset of clinical signs of sepsis. However, the timing may be variable in animals owing both to the severity of disease and/or a genetic susceptibility of the septic animal to laminitis (in experimental models of sepsis-related laminitis, only approximately 70–80% of the animals develop laminitis with some animals being "nonresponders"; the same thing appears to occur in clinical sepsis cases, as some horses develop laminitis and some do not). In some horses with acute abdominal disease, the clinical signs of systemic sepsis may actually be subsiding when signs of laminitis occur, whereas there may be ongoing signs of sepsis in other animals.

Clinical Symptoms

Clinical signs in horses with acute laminitis include those signs of systemic sepsis (i.e., those of the systemic inflammatory response), which animals commonly exhibit prior to onset of clinical signs of laminitis, and the clinical signs associated with the digits. The clinical signs of systemic sepsis most commonly observed in these cases include mucous membrane changes, tachycardia, depression, and hypo- or hyperthermia. It may be difficult to ascertain from the physical examination whether the tachycardia is due to systemic sepsis, the pain from laminitis, ongoing pain from abdominal disease, or all three [tachycardia from digital pain can be assessed if temporary digital anesthesia (e.g., abaxial sesamoid nerve block) is performed; the heart rate should decrease precipitously with local anesthesia of the affected digits]. The clinical signs of acute laminitis are characterized by lameness, an increase in the temperature of one or more hooves, increased digital pulses, and elicitation of a painful withdrawal response to hoof testers. Any combination of feet may be affected, although both front feet are most frequently affected. The magnitude of lameness may vary from mild to severe; horses with mild lameness demonstrate repeated shifting from one foot to another, whereas horses with severe lameness may stand planted, refusing to move or to even permit a foot to be picked up off the ground. The characteristic stance of a laminitic horse with both forefeet affected is placement of the forefeet well in front of the normal position in order to put more weight onto the palmar half of the feet, and anterior placement of the hind feet in order to shift more weight to the hindlimbs (Figure 49.3) (Hood et al., 2001c). The characteristic gait of a laminitic horse is stiff limb movement, including an arched back, appearing to shift weight to the hind limbs, short strides, and landing on the toes of the forelimbs, all of which are exacerbated when the horse is turned. However, horses with milder forms of laminitis may not have this characteristic gait. Horses with distal displacement of the distal phalanx more frequently have a more normal stance but are usually intensely resistant to movement as all four feet are frequently affected. It is at times difficult to determine whether the forefeet or all four feet are affected; anesthesia of the forefeet with abaxial sesamoid nerve blocks (usually with lidocaine owing to its short-term effect) will help determine whether any lameness exists in the hind feet, or if any abnormality noted in hindlimb gait is merely compensation for the painful forelimbs. Horses in which hind foot pain predominates may occasionally have a hypermetric gait with quick withdrawal of the rear limb upon weight bearing that is similar to the gait of a horse with stringhalt.

Increased hoof temperature and the strength of digital pulses must be interpreted in the context of the lameness and other systemic symptoms, because it is not unusual for an increase in hoof temperature to be transient, and the interpretation of digital pulses is highly subjective. Application of hoof testers is useful to confirm the presence of pain around the dorsal margins of the sole in a horse that is suspected of having laminitis.

Horses with long-standing chronic laminitis usually present with a combination of lameness and characteristic deformation of the hoof capsules. However, they may present with lameness without deformation of the hooves, or deformation of the hooves with minimal signs of lameness. The lameness varies from being barely detectable to the characteristic gait previously described. Changes to the hoof capsule vary with the duration of the disease and may be visible in both the wall and the sole. Immediately after a horse has suffered rotation of its distal phalanx, the wall is unchanged. However, depending on the degree of rotation, the sole dorsal to the apex of the frog may be flattened or even convex. A palpable groove at the junction of the skin of the pastern

Figure 49.3 Classic stance of a horse with laminitis. The front feet are placed forward while the rear limbs are brought under the body and accept more weight.

and the coronary band may develop at any point around the circumference of the foot, indicating that the distal phalanx has displaced. This palpable groove is typically located dorsally for horses with rotation, around the entire circumference in horses with distal displacement, and on one side of the foot (medial or lateral) for horses with asymmetric distal displacement. In horses with prolonged rotation, the dorsal wall may assume a characteristic concave appearance, and the heels may become elongated (Figure 49.4). The disparate growth of the hoof wall between the toe and heels is visible in the growth rings, which are more widely spaced at the heels than at the toe. The texture of the hoof wall may also be rougher and the appearance duller than normal. The sole may be flatter than normal, show evidence of bruising where it is flattened, and be softer than normal. The white line may be wider than normal, frequently with elongated keratinized lamellae, and contain old hemorrhages.

Figure 49.4 Chronic laminitis has caused foot deformity with dishing of the front of the foot and wider growth rings in the horn at the heels.

Radiography

Radiography is important in laminitis as a diagnostic tool, to monitor progress of the disease, and to guide treatment. Radiographs demonstrate the position of the distal phalanx in relation to the hoof capsule, and changes in the shape and density of the distal phalanx. Three main radiographic projections are used: lateral, dorsopalmar, and 45° oblique. For the lateral and dorsopalmar projections, it is important that the foot is placed on a block. It is best if the ipsilateral foot is also placed on a block at the same height above the ground and the metacarpi are vertical to ensure even weight bearing, although the latter can be very difficult. The X-ray beam is centered as close as possible to the solar margin of the distal phalanx (approximately 1.5 cm proximal to the weight-bearing surface of the hoof capsule). It is important to ensure that the radiograph is a true lateral projection; alterations of the axis of the foot by more than 10° will cause the degree of rotation to be underestimated (Koblik et al., 1988). Most veterinarians now use digital radiography, which allows manipulation of contrast to

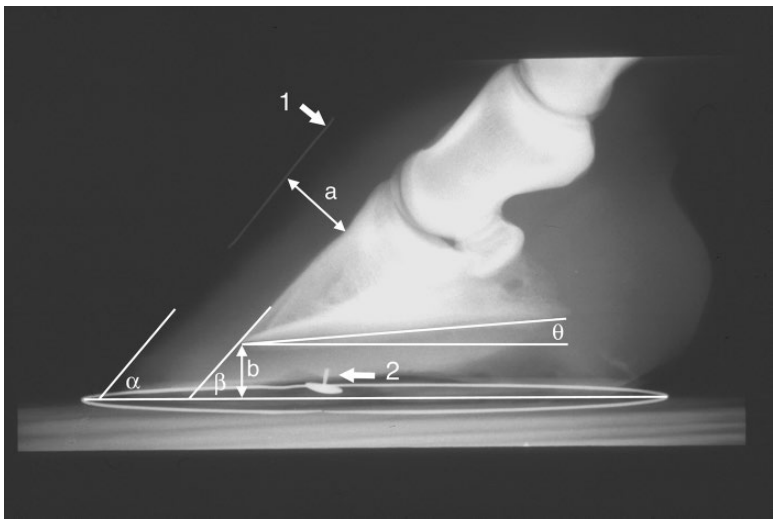

Figure 49.5 Lateral radiograph of the foot. (1) Linear radiopaque marker on the dorsal hoof wall; (2) marker to identify the dorsal extent of the frog. a, Thickness of the dorsal hoof; b, thickness of the solar hoof; α, angle of the dorsal hoof wall to the ground; β, angle of the dorsal parietal surface of the distal phalanx to the ground (β – α = degree of capsular rotation); θ, angle of the solar margin of the distal phalanx in relation to the ground surface of the hoof. Image is copyrighted to Andrew Parks. Used with permission.

depict accurately the outer margin of the hoof capsule, the dorsal border of the distal phalanx, and the junction between hoof capsule and the underlying dermis. Film-based radiography may require the use of two different exposures for the lateral and dorsopalmar views to discern the position of the distal phalanx in relation to the hoof capsule and the radiographic morphology of the distal phalanx because of the extreme difference in density of the hoof capsule and the distal phalanx. Additionally, it is helpful to define the position of the hoof capsule in relation to the distal phalanx by placing a linear marker on the dorsal hoof wall with the proximal aspect of the marker touching the coronary band, and contrast material on dorsal solar surface of the foot with or without a marker on the apex of the frog (Figure 49.5) (Grundmann et al., 2015).

Assessing the position of the distal phalanx in relation to the hoof capsule is dependent on the chronicity of the disease. Immediately after the distal phalanx has rotated or displaced distally, the external contour of the hoof capsule is not changed, whereas as the condition becomes chronic, the deformation of the hoof capsule changes the interpretation of the radiographs. Immediately after distal phalanx rotation, the most useful radiographic signs are the degree of rotation between the dorsal hoof wall and the parietal surface of the distal phalanx (capsular rotation, β – α in Figure 49.5), the angle of the abaxial solar margins of the distal phalanx to the ground (θ in Figure 49.5), and the distance between the dorsal–distal margin of the distal phalanx and the ground (b in Figure 49.5). In horses in which the distal phalanx has displaced distally, the distance between the dorsal surface of the hoof capsule and the adjacent parietal surface of the distal phalanx is a relatively repeatable measure of the displacement (13–20 mm in normal horses depending on size; a in Figure 49.5) (Cripps & Eustace, 1999b). In horses in which the distal phalanx has rotated and displaced distally, this measurement should be made at the base of the extensor process. The distance between the proximal limit of the extensor process and the coronary band is another commonly used measure of distal displacement [commonly termed the coronary–extensor (C–E) distance or the founder distance; b in Figure 49.2A] (Cripps and Eustace, 1999a). Owing to the broad range of this measurement in normal horses (–2 to 10 mm), this measurement is commonly not as useful in the initial workup of horses with laminitis unless there are previous lateral radiographs available to which the current C–E distance can be compared. This measurement is useful when serial radiographs are taken throughout the course of disease.

After prolonged chronic rotation of the distal phalanx, there is frequently remodeling or resorption of the distal aspect of the dorsal solar margin that is visible on the lateral and dorosopalmar oblique views, and a lip of new bone on the dorsal aspect of the dorsal solar margin visible on the lateral view (Figure 49.6). Additionally, rotation of the distal phalanx may be associated with

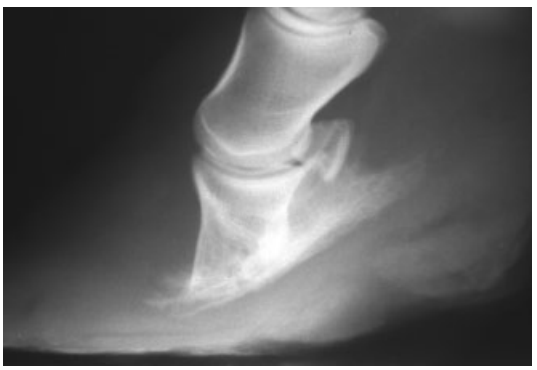

Figure 49.6 Lateral radiograph of chronic laminitis. There is remodeling of the dorsal tip of the distal phalanx due to pressure and bone lysis.

displacement and reorientation of the dorsal solar papillae, which then cause lysis of the parietal surface of the distal phalanx immediately proximal to the solar margin (Collins et al., 2010). Furthermore, small tangential fractures may be present at the dorsal solar margin of the distal phalanx on the lateral and dorsopalmar oblique views. Ideally, the same measurements used after recent rotation would be used to indicate the position of the distal phalanx in relation to the hoof capsule following prolonged rotation. However, distortion of the contour of the dorsal hoof capsule may make it impossible to obtain a precise measurement of capsular rotation. Therefore, measurement of the angle that the top one-third of the hoof capsule makes with the parietal surface of the distal phalanx most likely provides the closest indication of what the rotation would be without the dorsal concavity. Unfortunately, resorption of the dorsal solar surface of the distal phalanx makes it harder to measure the angle of the solar margin of the distal phalanx to the ground, but, by extrapolating from the palmar processes, an approximate angle can be obtained. Digital venography in the standing horse has been developed as a prognostic aid to assess the vasculature of the digit. Venograms in which there is no filling of contrast of the lamellar vessels, the circumflex area, and the terminal arch are reported to indicate an extremely poor prognosis for recovery (Redden, 2001).

Treatment

The treatment of horses with laminitis varies according to the phase (i.e., acute versus chronic) of the disease process; this discussion will focus on the horse in the acute phase of sepsis-related laminitis. In horses with acute laminitis, the goals of treatment are (1) to halt or limit any systemic disease process that predisposed the horse to laminitis, (2) to prevent or limit the digital changes leading to separation of the injured lamellae, and (3) to control pain. Therefore, in the acute phase, therapy is primarily medical and supportive. In horses with chronic laminitis the treatment varies with the pattern of displacement that has developed. For horses with rotation of the distal phalanx, the treatment goals are (1) to realign the solar margin of the distal phalanx with the normal weight-bearing surface of the hoof, (2) to encourage realignment of the dorsal surface of the hoof capsule with the parietal surface of the distal phalanx, (3) to control pain, and (4) to manage secondary complications such as distal phalanx sepsis. For horses with asymmetric distal displacement of the distal phalanx (e.g., "medial sinker"), realignment of the distal phalanx is also a goal, but must be implemented differently. For horses with symmetrical distal displacement of the distal phalanx, the overall goals are similar, except that because the phalangeal axis has not changed, realignment of the position of the distal phalanx to the ground is unnecessary. As such, treatment of the chronic phase consists primarily of foot care, pain medication and, if necessary, surgery. However, the boundaries between the treatment of acute and chronic laminitis are more blurred than their definitions might suggest. Medical therapy initiated in the acute stage of the disease continues into the subacute and early chronic stages, and, occasionally surgical treatment, which is usually reserved for chronic laminitis, but may be used in the acute stages.

Medical Therapy

Medical therapy for horses with acute laminitis is ambiguous at best and contentious at worst, because there are no controlled clinical studies indicating which therapies are effective. Medical therapy for laminitis associated with acute abdominal disease is directed at the pathophysiologic processes presumed to be involved in the disease, namely vascular dysfunction, inflammation, and endotoxemia.

Therapies to Address Vascular Dysfunction

Therapies used to address possible vascular dysfunction include both vasodilators and anticoagulants. Overall, medical therapies to improve lamellar blood flow have not been found to be effective in the treatment of laminitis. Two types of pharmacologic agents have been used to improve digital blood flow, vasodilators and rheological agents (agents that increase the malleability of red and white blood cells). The drugs most commonly used in the past decade for their vascular effects are acepromazine, isoxsuprine, pentoxifylline, and nitro-vasodilators. Acepromazine, an α-adrenergic antagonist, has been used most frequently because (1) there is some experimental evidence that administration of such agents improves digital blood flow in normal horses (Ingle-Fehr and Baxter, 1999), (2) these agents are considered to be safe, and (3) subjective clinical impressions support their use. However, more recent studies using microdialysis catheters in the lamellar tissue do not support the premise that acepromazine increases lamellar blood flow (Muller-Anstett et al., 2010). Isoxsuprine, purported as both a vasodilator and rheological agent, is poorly absorbed and does not increase lamellar blood flow at the suggested oral dosage (1.2 mg/kg bid; Ingle-Fehr and Baxter, 1999). Pentoxifylline, a rheological agent originally used to treat obstructive arteriosclerosis in humans, has been used clinically to treat laminitis. However, no data from either experimental or clinical studies support the contention that it increases blood flow in either humans or horses (Ingle-Fehr and Baxter, 1999; Dawson et al., 2002). It does appear to have a protective role at a higher dosage thought to occur as possibly a matrix metalloproteinase (MMP) inhibitor (see later). Similarly to the use of other vasodilators, early evidence supporting the use of nitro-vasodilators resulted

in a transient interest in their use in laminitis (Hinckley et al., 1996a, 1996b), whereas later studies refuted the early results and the therapy was therefore quickly abandoned (Adair et al., 2000).

Several drugs have been used to address the possible involvement of thrombus formation in laminitis; these drugs include anticoagulants, such as heparin and aspirin, and a platelet aggregation inhibitor. As already described, prophylactic administration of unfractionated heparin before induction of laminitis reduced the severity of laminitis in one study (Hood et al., 1982). However, two retrospective clinical studies provide conflicting evidence regarding its efficacy. Whereas one study reported a trend for decreased incidence of laminitis in horses with proximal enteritis treated with heparin (Cohen et al., 1994), another study reported no significant impact of heparin therapy on the incidence of laminitis in equine small intestinal surgery cases (Belknap & Moore, 1989). As unfractionated heparin has also been reported to cause agglutination of erythrocytes in horses (Moore et al., 1987), it is possible that heparin-induced red blood cell (RBC) aggregates may lodge in the lamellar capillaries and impair blood flow within the lamellae. A more recent retrospective study suggested a lower incidence of laminitis in acute abdomen cases treated with low molecular weight heparin (De la Rebière de Pouyade et al., 2009). Low molecular weight heparin may be a better choice owing to a lack of RBC aggregation with this type of heparin. Aspirin has been proposed as a treatment for laminitis owing to its ability to prevent platelet aggregation induced by arachidonic acid metabolism. In addition, aspirin has been reported to decrease thromboxane generation effectively in equine blood *ex vivo* (Baxter & Moore, 1987). However, no clinical or experimental studies have been performed to determine the efficacy of aspirin in the treatment of laminitis. Although a novel platelet aggregation antagonist was reported to reduce the incidence and severity of experimentally induced laminitis (Weiss et al., 1998), this drug was never available commercially.

Inflammation

The large amount of evidence of lamellar inflammatory signaling early in the course of experimentally induced laminitis provides a clear rationale for the use of anti-inflammatory drugs for the treatment of acute laminitis. However, both clinically and experimentally, nonsteroidal anti-inflammatory drugs (NSAIDs) have not appeared to decrease the incidence of lamellar injury in laminitis effectively. Therefore, although there is compelling evidence of lamellar injury and that NSAIDs may block some of the inflammatory signaling documented to occur in the early stages of laminitis, the main effect of NSAIDs appears to be analgesic. Although the advantages of flunixin meglumine are not as apparent to the clinical observer as the analgesic effects of phenylbutazone in horses with acute laminitis, flunixin meglumine is more effective than phenylbutazone in inhibiting endotoxin-induced synthesis of prostanoids (Moore et al., 1986), and may therefore be a superior drug to use in the horse at risk for laminitis (i.e., the horse exhibiting signs of endotoxemia). Although a reduced dose of flunixin meglumine (0.25 mg/kg tid) significantly reduces endotoxin-induced prostanoid synthesis (Semrad et al., 1987), one of the present authors (J.K.B.) uses the maximal dose of 1.1 mg/kg tid (for a short term) in most horses at risk for laminitis, for two reasons: (1) COX-2 is markedly up-regulated in the developmental stage of laminitis and (2) the reduced dose of flunixin does not always prevent the development of the clinical signs of endotoxemia as effectively as the recommended dose (1.1 mg/kg). However, close attention needs to be paid to hydration status, renal function, and signs of gastrointestinal side effects such as gastric ulceration. Although flunixin meglumine is still indicated (at least for its systemic effects) in horses exhibiting signs of systemic sepsis, a study found what most clinicians have experienced clinically: a minimal effect of flunixin, ketoprophen, or phenylbutazone in preventing or limiting lamellar failure in an experimental model of sepsis-related laminitis (Bamford et al., 2016).

Pentoxifylline has been studied in human and veterinary endotoxemia/sepsis cases owing to its ability to inhibit inflammatory gene expression. Although the drug was found to decrease inflammatory mediator expression effectively in an *ex vivo* equine endotoxemia model (Barton & Moore, 1994), little efficacy was noted in experimental endotoxemia in horses or food animals (Barton et al., 1997; Baskett et al., 1997; Ohtsuka et al., 1997; Van Miert et al., 1997). Pentoxifylline has recently been found to decrease the clinical signs of laminitis in a carbohydrate model of sepsis-related laminitis; the authors suggest that this may be through its anti-inflammatory effects (S. Eades, unpublished data).

Dimethyl sulfoxide (DMSO) was widely used for several decades as a clinical treatment for horses with acute laminitis, primarily owing to its purported value (mainly due to anecdotal observations) as an oxygen free-radical scavenger. However, its use is waning, likely because of the lack of strong experimental evidence of its efficacy. Owing to a large number of publications reporting increased expression of MMPs in the lamellae in the early stages of laminitis, drugs established to inhibit MMPs in other species, primarily tetracyclines (oxytetracycline and doxycycline), have been used to treat laminitis. However, their use is waning both as a result of recent studies demonstrating that the active forms of many of these MMPs are not present in the early stages of laminitis (i.e., the MMPs are only present in an inactive form) (Loftus et al., 2009), and a lack of efficacy of

MMP inhibitors in recent studies. Two recent studies, one using oxytetracycline and doxycycline and another using a broad-spectrum MMP inhibitor, marimastat (in which the investigators documented adequate lamellar tissue levels using microdialysis catheters), found no protective effect of these treatments against lamellar injury/failure in carbohydrate models of laminitis (S. Eades, unpublished data; C. Underwood and C. C. Pollitt, unpublished data).

Analgesia

The most common drugs used to provide analgesia in laminitis patients are the NSAIDs. Phenylbutazone is the most widely used NSAID because of its anti-inflammatory and analgesic properties; in the latter case, the clinical evidence for its benefit as an analgesic is overwhelming. Other NSAIDs used in the treatment of laminitis include flunixin meglumine, ketoprofen, and the COX-2 inhibitor firocoxib. Flunixin meglumine has been reported to be effective for the treatment of musculoskeletal pain, but less so than phenylbutazone. Ketoprofen was found to be as effective as phenylbutazone in amelioration of chronic foot pain at a dose of 3.6 mg/kg (Owens et al., 1995), but in the experience of one of the authors, ketoprofen's analgesic effects appear to be short lived. Phenylbutazone has a much higher clinical incidence of gastrointestinal and renal toxicity compared with the other commonly used NSAIDs, including flunixin meglumine and ketoprofen (MacAllister et al., 1993; Hough et al., 1999; Lees & Higgins, 1985). As phenylbutazone is a less potent inhibitor of COX-1 (purported to be the protective isoform of cyclooxygenase) than either flunixin or ketoprofen (Brideau et al., 2001), phenylbutazone's increased incidence of toxicity is most likely due to the accumulation of the active metabolite oxyphenbutazone in tissues with chronic administration (Soma et al., 1983). Many clinicians have used a combination of phenylbutazone and flunixin meglumine to maximize the anti-inflammatory effect of these compounds while attempting to avoid the toxic effects. Concurrent administration of flunixin meglumine and phenylbutazone experimentally at the suggested dosages (1.1 and 2.2 mg/kg, respectively) resulted in no effect on drug clearance, but resulted in prolongation of the effect of the two individual drugs in blocking thromboxane synthesis (Semrad et al., 1993). Hence it is possible that decreasing the phenylbutazone dosage in combination with flunixin meglumine treatment may result in adequate analgesia with decreased NSAID toxicity. Similarly, as ketoprofen has a high therapeutic index (no toxicity noted at five times the suggested dose for 15 days) (Gregoricka et al., 1991), it has been suggested that this drug may be given at more frequent intervals to improve its long-term efficacy. One of the authors has used ketoprofen at a 2.2 mg/kg dose qid in horses with renal compromise and not observed signs of toxicity. The main disadvantage of this drug is the cost and lack of an oral form, although there is anecdotal evidence that the intravenous preparation will be absorbed if administered orally. As phenylbutazone is still the most valuable NSAID for prolonged treatment of laminitis owing to its efficacy and reasonable cost, clinicians (including the authors) have attempted to decrease the toxicity by not administering the drug for a 24 h period on one out of every 5–7 days to allow a "wash out" of the oxyphenbutazone that has accumulated in the tissues. If the animal is too painful to tolerate a 24 h period without an NSAID, flunixin can be administered for that 24 h period without affecting phenylbutazone clearance (Semrad et al., 1993). Finally, the COX-2 selective inhibitor firocoxib is likely to be a much safer NSAID with less systemic side effects. However, anecdotally, it does not appear to provide the same degree of analgesia in the acute laminitis case as that provided by phenylbutazone.

In hospital settings, constant-rate infusions can be used to provide analgesia, often with one or a combination of different drugs including most commonly lidocaine (Stephenson et al., 2011; Medina-Torres et al., 2016b; Wyse et al., 2008; Williams et al., 2010; Karikoski et al., 2015), detomidine (Owens et al., 1996; Medina-Torres et al., 2016b), opioids (Wyse et al., 2008; Durham, 2016), and ketamine (Wyse et al., 2008; Karikoski et al., 2015). Especially when opioids or detomidine are used as constant-rate infusions, the clinician needs to monitor closely for side effects, the most common one being gastrointestinal ileus as evidenced by development of a large colon impaction (Durham, 2016; Medina-Torres et al., 2016b). The most commonly encountered side effects associated with lidocaine administration are due to central and peripheral nervous system/neuromuscular effects (e.g., muscle fasciculations, ataxia, depression). These side effects are transient and occur as a result of excessive blood levels of the drug.

Therapy for Endotoxemia

The frequent occurrence of laminitis as a sequela to conditions associated with endotoxemia suggests that administration of plasma or serum with high antibody titers against endotoxin may be appropriate in the treatment of horses at risk for developing acute laminitis. Although conflicting data exist regarding the efficacy of these antibodies in the treatment of horses with endotoxemia (Durando et al., 1994; Morris et al., 1986), their effect on the development of laminitis is unknown. In addition to the controversy regarding their efficacy, the expense of these endotoxin antibodies can limit their use. Polymixin B, which binds endotoxin, is used more frequently than anti-endotoxin antibodies largely because it is much less expensive and has been demonstrated experimentally to inhibit the effects of equine endotoxemia

(Barton et al., 2004). However, although polymixin B does improve clinical parameters in experimental endotoxemia (Durando et al., 1994), it had little beneficial effect in the prevention of laminitis (or limiting the severity of the lamellar changes) in an experimental model of sepsis-related laminitis (Raisbeck et al., 1989). There are several likely reasons for the failure of polymixin B to limit lamellar injury effectively in a model of sepsis-related laminitis. First, there are likely to be many more pathogen-associated molecular pattern molecules (PAMPs) in addition to endotoxin being absorbed from compromised bowel and playing a role in equine sepsis (Leise et al., 2010; Belknap & Black, 2012; Belknap et al., 2009). Second, endotoxin administration by itself has never been reported to result in laminitis (Belknap et al., 2009; Ingle-Fehr & Baxter, 1998). Additionally, it is likely that polymixin B only effectively binds endotoxin from *Escherichia coli*, and not lipopolysaccharides from other pathogens (e.g., *Salmonella* spp.) (Cavaillon, 2011). Therefore, it may have a minimal effect in horses exhibiting clinical signs of endotoxemia/sepsis if the primary source of PAMPs is not *E. coli* endotoxin.

Digital Hypothermia/Cryotherapy in the Treatment of Sepsis-related Laminitis

The only treatment that has withstood rigorous testing both within the laboratory and in the clinic as an effective therapy for sepsis-related laminitis is digital hypothermia. Although the concept of hypothermia for laminitis has been discussed for centuries, the use of profound hypothermia (3–8 °C) as a prophylactic treatment for laminitis in the septic horse was introduced only about a decade ago (Pollitt & Van Eps, 2004; Van Eps & Pollitt, 2004). Since that time, the treatment has been demonstrated to be protective not only against lamellar failure when initiated at the same time that a carbohydrate overload is administered (Van Eps & Pollitt, 2009a), but also when initiated at the time of onset of clinical signs of lameness (van Eps et al., 2014). The protection that digital hypothermia provides against structural failure of the lamellae has been dramatically demonstrated in different studies (van Eps et al., 2014; Van Eps & Pollitt, 2004, 2009a). A marked inhibition of inflammatory gene expression, including cytokines, chemokines, COX-2, and endothelial adhesion molecules (important in leukocyte extravasation into tissues), was reported in a study in which hypothermia was instituted at the same time the carbohydrate overload was administered (van Eps et al., 2012). In a recent study using the oligofructose model of sepsis-related laminitis in which hypothermia was initiated at the time point at which the horses exhibited signs of sepsis (12 h after oligofructose administration), hypothermia still conferred profound protection against lamellar injury. However, inhibition of inflammatory signaling was not present (J. K. Belknap & A. W. van Eps, unpublished data; Dern et al., 2017). In fact, hypothermia only significantly inhibited signaling more consistent with growth factor signaling (RPS6 activation was inhibited; see earlier discussion). Hence, although the efficacy of hypothermia has been well established, the mode by which it confers lamellar protection needs further assessment.

Currently, the most commonly used mode of digital hypothermia is immersion of the distal limb and digit in an ice slurry (ice and water) (Reesink et al., 2012; Van Eps & Orsini, 2016). This method is commonly performed using 5 L fluid bags in veterinary hospitals, but a commercial boot for digital hypothermia is currently available (Soft-Ride Ice Spa Therapy boot; Soft-Ride, Bacliff, TX, USA). Wrapping the distal limb in ice is not effective in maintaining the temperature below 10 °C (the target temperature used by most clinicians and researchers) (van Eps & Orsini, 2016). The foot must be immersed in the ice slurry. It is important not to use ice without water, as frostbite to the skin may occur. In the authors' opinion, digital hypothermia should be instituted as early as possible in acute abdominal patients deemed to be at risk for laminitis, which will be those suffering from medical and surgical conditions such as enterocolitis, proximal enteritis, and large intestinal volvulus. However, any acute abdomen patient exhibiting clinical signs of systemic sepsis/SIRS should probably be treated with ice slurry. Although many clinicians commonly treat only the forelimbs with hypothermia, the hindlimbs should be also treated in those horses with severe sepsis (e.g., colon volvulus, enterocolitis) in which laminitis in all four limbs commonly occurs. Again, an important point is that, even at the onset of clinical signs of lameness, a time point at which many horse owners may contact the veterinarian for the first time, rapid institution of digital hypothermia is likely to be effective because most animals with sepsis-related laminitis become lame prior to extensive lamellar failure and displacement of the distal phalanx. Because digital hypothermia is very work intensive (as the ice has to be replaced every 1–2 h) and should be performed constantly, it may be advisable to transport an animal exhibiting signs of systemic sepsis to a referral hospital where 24 h care is available. No work has been performed regarding the time period that an animal with hypothermia should be treated for; most veterinarians continue to treat the animals for at least 24 h past the cessation of clinical signs of sepsis. This will commonly result in an animal being constantly treated for 4–7 days, if not longer.

Supportive Hoof Care

In the acute stage of laminitis, supportive therapy is primarily directed at preventing or minimizing displacement of the distal phalanx and making the horse more comfortable. In the chronic phase, supportive therapy is

also directed at preventing further displacement of the distal phalanx and controlling pain. In horses with chronic laminitis, it appears that the pain experienced reflects the stresses to the injured lamellae and/or pressure on the solar surface of the hoof. Therefore, appropriate foot support can provide relief from pain in conjunction with stabilizing the distal phalanx within the hoof capsule. Additionally, an important component of the treatment of horses with chronic rotation of the distal phalanx is the realignment of the distal phalanx at the same time as (1) decreasing solar pressure (and related pathology) by the displaced distal phalanx and (2) encouraging new hoof growth to realign the wall with the parietal surface of the distal phalanx. The goals of supportive therapy in acute and chronic laminitis are sufficiently similar to allow the same biomechanical principles of stabilizing the digit to be applied to horses with either acute or chronic laminitis. These basic principles are (1) reduce weight bearing by the wall and lamellae and (2) if rotation is present, decrease the flexor moment about the distal interphalangeal joint during locomotion by decreasing the tension in the deep digital flexor tendon. The stresses in the wall due to weight bearing may be decreased by moving stresses from more severely affected wall to less affected wall, and by recruiting the sole and frog to bear weight. The flexor moment about the distal interphalangeal joint at rest may be decreased by elevating the heels and at breakover by moving the point of breakover in a palmar direction (Figure 49.1C and D). There are primary differences between the supportive foot care for horses with acute/subacute laminitis versus horses with chronic laminitis. First, the pattern of displacement is difficult to predict in the horse with acute laminitis prior to displacement, whereas the displacement has already occurred in horses with chronic laminitis. Second, the clinician is more likely to apply temporary types of foot support in the acute stage (e.g., Redden Ultimate® or Styrofoam pads/"support blocks") that can be rapidly applied with minimal trauma and can be easily interchanged if there is a lack of response. Third, application of corrective shoes with nails is usually better tolerated by horses with chronic laminitis of several weeks' duration.

Horses with acute laminitis should have stall rest to diminish the trauma caused by locomotion. In the acute stage, the shoes should generally be removed to decrease the concentration of stress around the periphery (i.e., wall) of the foot; this is not without controversy because there is some trauma associated with removing the shoes. The simplest way to redistribute weight from the wall to the sole and frog is to stand the horse on a surface that conforms to the ground surface of the foot. In this regard, sand is significantly superior to shavings because the granular nature of sand will (1) conform better to the ground surface of the foot, and therefore to provide better support to the frog and sole in addition to the wall, and (2) more readily allow the horse to adjust the position of its feet while it is standing to find the stance that is most comfortable. However, it is critical to use a bedding material in which the horse is willing to lie down to take the stress off the affected feet for extended periods of time. If a horse will not lie down in sand but will in shavings, it may be best to use deep shavings and support the feet via application of the preferred type of digital support. Peat has been used as an alternative to sand and shavings, but the authors have no experience with its use.

The simplest of the digital support devices are frog pads, either commercially available pads or those made from rolled-up gauze. Because the response to such devices tends to be highly variable, the authors use them infrequently. Weight redistribution to a greater area can be achieved by filling the concavity of the ground surface of the foot with a 5 cm thick high-density Styrofoam support block (the Styrofoam used for insulating house foundations, also called blue board). The Styrofoam crushes readily (usually over 24 h) and conforms to the ground surface of the foot. It is advantageous to continue to apply additional Styrofoam blocks as the previous ones are compressed until there are commonly 3–4 layers of Styrofoam on the bottom of the affected feet. It is possible to achieve elevation of the heels if the toe section is removed from the first one or two blocks after they are compressed. In addition to application of the Styrofoam blocks, the distal border of the wall at the toe may be beveled with a hoof rasp to move the point of breakover palmarly; it is important to avoid being too aggressive to avoid weakening the white line. It is advisable to avoid filling the concavity of the sole with hard, rigid filling materials, but commercial silicone putties, which are more pliable, are very useful for applying sole support. Closed-cell foams, frequently placed inside commercially available hoof boots, can also markedly improve a horse's comfort. As an alternative to closed-cell foams, ethylene–vinyl acetate foam either applied directly or applied to a plywood form that is attached to the foot is also a good shock absorber. A commercial cuff/wedge pad combination (Redden Modified Ultimate) used in conjunction with silicone putty (also termed digital cushion support or impression material) will redistribute weight bearing to the sole and frog, elevate the heels, and move the point of breakover palmarly. Obtaining the best results from these techniques may require some trial and error because the areas of greatest stress within the lamellae cannot usually be identified unless the distal phalanx has displaced. One author's initial approach is to try closed-cell or ethylene–vinyl acetate foam (with the plywood form), the other's preference is to apply an even layer of silicone putty (approximately 1 inch thick) to the entire ground surface of the foot. If these are not providing sufficient relief,

heel elevation, typically with a Redden Modified Ultimate, is used. The response to all of these manipulations is observed, and if it does not improve the comfort level of the horse, a change should be made. Because of the broad range of severity of the lamellar damage between affected animals (and the fact that more severely affected horses take longer to heal), the duration of use of this initial foot support can vary from weeks to months. In horses that progress from acute or subacute laminitis to chronic laminitis, the initial form of supportive therapy is usually continued for 3–5 weeks. During this period, the distal phalanx usually appears be become more stable within the hoof capsule, as evidenced by a decrease in lameness and the absence of continued displacement.

Trimming the Laminitic Foot

Once a degree of stability has been returned to the lamellar junction, it is usually appropriate to initiate corrective trimming and shoeing. The most important aspect about trimming and shoeing is that they should be guided by the position of the distal phalanx within the hoof capsule, particularly in horses with rotation of the distal phalanx. The relative position of the distal phalanx must be determined by radiography rather than based on the external surface of the hoof capsule (Figure 49.5). The objectives of trimming are to realign the solar margin of the distal phalanx with the ground surface of the hoof capsule (Figure 49.7), preserve the thickness of the sole dorsal to the frog, and position the point of breakover in relation to the dorsal margin of the distal phalanx. This can either be done by taking measurements from a radiograph or by repeating radiographs after trimming and shoe placement. The normal thickness of the sole is approximately 10–15 mm (Grundmann et al., 2015) and the ground surface of the foot is trimmed accordingly. For horses in which the distal phalanx has rotated, it may not be possible to trim the sole or walls dorsal to the mid-quarters while maintaining optimal thickness of the sole; in this case, the foot is only trimmed from the mid-quarters palmarly (Figure 49.8A). This results in an uneven ground surface of the foot, that is, after the foot has been trimmed and the palmar aspect of the foot is on the ground, the dorsal aspect may no longer be touching the ground because it was not trimmed. This may necessitate building up the wall dorsal to the mid-quarters with a composite before a shoe can be fitted (Figure 49.8B). If trimming the foot in this manner results in increased discomfort, then the height of the heels should be increased during shoeing and subsequent realignment of the distal phalanx completed over an extended period of time.

Radiographic Guidance for Trimming and Shoe Placement

The shoe is positioned such that its dorsal margin is no further dorsally than the point at which a shoe would normally be placed in relation to the distal phalanx. This point can be determined by drawing a line on the radiograph that is parallel and 15–18 mm dorsal to the dorsal parietal surface of the distal phalanx and that intersects the plane of the newly trimmed hoof (Figure 49.5). The point of breakover is usually positioned approximately 5–7 mm dorsal to the dorsodistal margin of the displaced distal phalanx (Figure 49.8C). However, some clinicians are more aggressive in moving the point of breakover further

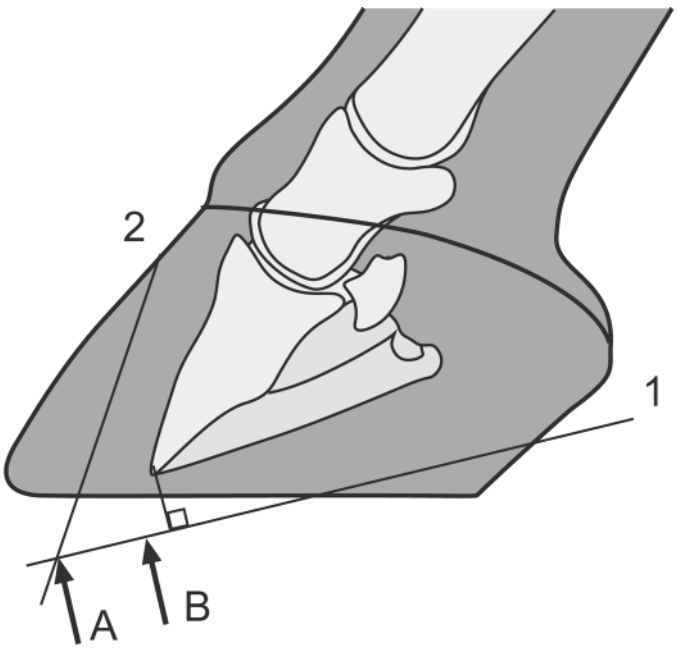

Figure 49.7 Schematic diagram of a radiograph to illustrate how the shoe should be positioned in relation to the distal phalanx. 1, A line drawn approximately 15–20 mm distal to the solar margin of the distal phalanx to guide trimming the hoof capsule; 2, a line parallel to and 15–18 mm dorsal to the parietal surface of the distal phalanx; A, intersection of lines 1 and 2, which marks the dorsal most position for shoe placement; B, a point approximately 6 mm dorsal to the dorsal margin of the distal phalanx (after trimming) that marks the approximate location for optimal breakover. Image is copyrighted to Andrew Parks. Used with permission.

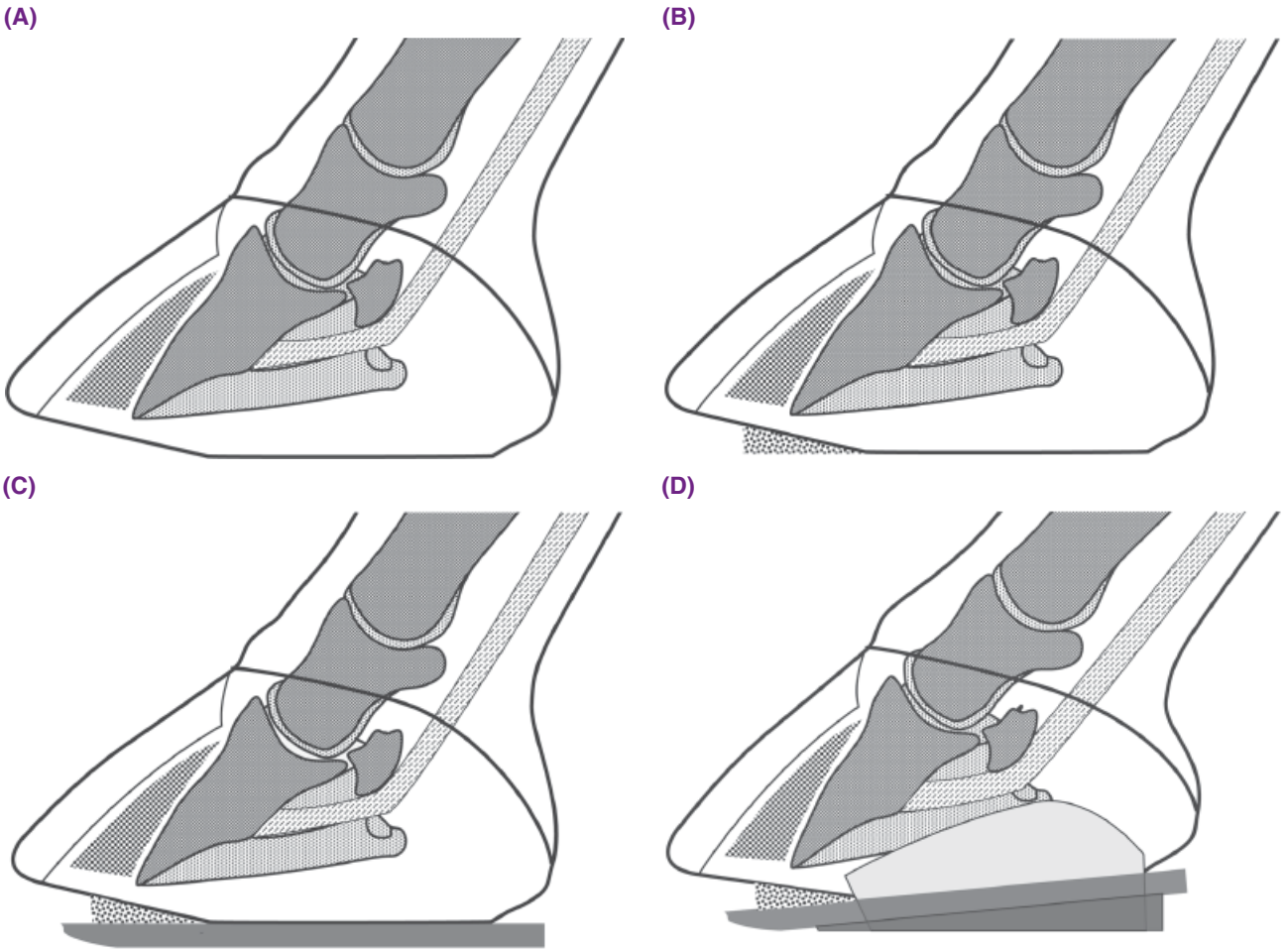

Figure 49.8 Schematic diagrams to depict trimming and shoeing of a horse's foot with rotation caused by chronic laminitis. **(A)** Immediately post-trimming; **(B)** following application of synthetic composite to build up the wall dorsal to the mid-quarters; **(C)** position of the shoe in relation to the distal phalanx; **(D)** following application of rails and silicone putty. Images are copyrighted to Andrew Parks. Used with permission.

palmarly. The mediolateral placement of the shoe on horses with asymmetric displacement is follows a different rationale discussed later.

Shoeing the Horse with Rotation of the Distal Phalanx

In horses with long-standing chronic laminitis, one author determines if the pain is due to solar pain, lamellar pain (indicating a continued instability of the lamellae), or both. That author uses a combination of hoof testers and nerve blocks to make these determinations. In his experience, the palmar digital nerve block will alleviate solar pain (i.e., from solar pressure from the displaced distal aspect of the distal phalanx) (Schumacher et al., 2000), but will not alleviate pain emanating from the dorsal lamellae. If the majority of the lameness is alleviated with palmar digital nerve anesthesia, that author feels that the lamellae are most likely stable and, therefore, the entire hoof wall is potentially available to support the foot (along with the caudal sole and frog), and the focus of the shoeing will be on taking the pressure off of the cranial sole. If lamellar pain is present, that author will also attempt to ensure that there is minimal pressure applied to the dorsal hoof wall.

The type of shoe used to treat chronic laminitis varies markedly depending on the nature of the disease. However, it is the authors' opinion that the type of shoe applied is a secondary consideration to the biomechanical goals that are desired. Once the biomechanical goals have been determined, there are usually multiple shoe–shoe combinations that can be used to achieve the given objectives.

The range of shoes that have been used is considerable and includes plain shoes, reverse shoes, egg-bar shoes, heart-bar shoes, rail shoes, full rocker shoes, and wooden shoes. One of the authors prefers to use wooden shoes or rail shoes for most horses, whereas the other prefers wooden shoes or egg-bar shoes. Both authors will adapt to what is available and the comfort of the farrier with a

technique provided that the overarching principles are followed. Regardless of shoe type, it is important that breakover can be modified and that there is no contact between the shoe and the sole at the toe. Redistribution of weight from the wall to the sole and frog may be obtained by inserting silicone putty under the frog and sole between the branches of the shoe or by applying a heart-bar to the shoe. Both authors prefer general support of the frog and caudal sole with a resilient substance (e.g., silicone putty) instead of the heart-bar shoe. There are two important goals associated with the use of cushion support material: (1) to cover the entire heel and frog approximately to the tip of the frog (the toe is not covered in horses with rotation of the distal phalanx in order to avoid putting excessive pressure on the sole in that region) and (2) to ensure that the cushion support is even with the ground surface of the shoe so that the solar surface is always supported when the limb is bearing weight. Heel elevation is commonly needed to decrease the tension on the deep digital flexor tendon and decrease the stress on the dorsal hoof wall; this is particularly important when the heels have been selectively trimmed to realign the distal phalanx with the ground surface of the foot. Heel elevation may be achieved by interposing wedge pads (either as rim or full pads) between the shoe and the ground surface of the foot, using a shoe forged with an elevated heel (e.g., a 3° egg-bar shoe), or by attaching rails to the ground surface of the shoe (Figure 49.8D). In the last instance, if commercially available detachable rails are used, heel elevation can be adjusted after the shoe has been applied. The advantage of the wooden shoes (Steward Clog) is that they are easy to make, easy to apply, and nearly infinitely adjustable (Figure 49.9) (Steward, 2003). They are attached with screws with or without casting tape. The wooden shoe functions as an extreme roller motion shoe, and is designed to allow the horse to vary the angle of the foot in relation to the ground for improved comfort. It can be used in conjunction with wedge pads to provide heel elevation if needed. In addition to being used to treat horses with rotation, the wooden shoe is also useful to treat horses with distal displacement, both symmetrical and asymmetric.

Because the severity of rotation varies in horses with chronic laminitis, shoeing must be tailored accordingly. Although all horses require accurate positioning of the shoe, the most severely affected horses require redistribution of weight bearing to the frog and sole, plus heel elevation. One of the ways to determine if heel elevation is necessary is to observe the way in which a horse with laminitis lands. If it lands toe first when walking at a straight walk (because most horses land toe first when turning), it is likely to benefit from heel elevation. Alternatively, pull the leg to be observed behind the contralateral limb and put it on the ground – if it can stand with the heels flat on the ground, it is unlikely to need heel elevation. Horses that are intermediately affected require redistribution of weight away from the walls, but do not require heel elevation. If response to treatment proceeds according to plan and the soft tissues between the hoof capsule and distal phalanx heal, the severity of symptoms decreases and the shoeing may gradually be returned toward a more routine type of shoe. However, the veterinarian and farrier must keep these animals on an aggressive trimming and shoeing schedule for the rest of their life to ensure that the foot does not "re-contract."

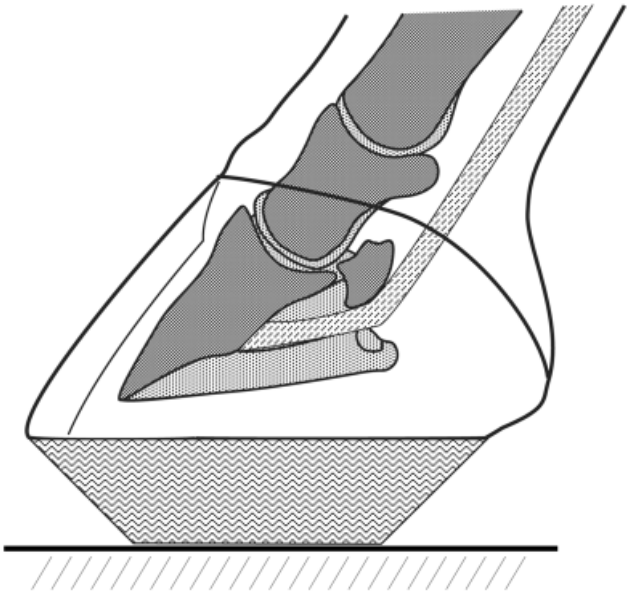

Figure 49.9 Schematic diagram to illustrate the position of the Steward Clog in relation to the ground surface of the foot and the distal phalanx. Image is copyrighted to Andrew Parks. Used with permission.

Chronic capsular rotation may persist after phalangeal rotation has been corrected, characterized by convexity of the dorsal hoof wall. This convexity is usually associated with deviation of the middle and distal thirds of the hoof wall away from the parietal surface of the distal phalanx. This condition appears to be compounded by disparate growth rates of the hoof wall, with the toe growing slower than the heels. Attempts to improve hoof wall growth have included either (1) removing weight bearing from the toe or (2) grooving the coronary band. Additionally, rasping the dorsal hoof wall parallel to the parietal surface of the distal phalanx may be successful in exposing abnormal lamellar tissue and encouraging the new hoof wall to grow parallel to the distal phalanx. However, all of these measures are unlikely to be successful at redirecting hoof wall growth if (1) the coronary papillae (which direct horn tubule growth) are no longer

parallel to the dorsal surface of the distal phalanx or (2) the dermal lamellae have been displaced away from the surface of the distal phalanx.

Shoeing the Horse with Distal Displacement of the Distal Phalanx

Horses with distal displacement of the distal phalanx or displacement involving only the medial or lateral side of the digit have different shoeing needs than horses with rotation of the distal phalanx. For example, supportive therapy must usually be continued for longer in horses with distal displacement of the distal phalanx. When these horses are ready to be shod, the shoe should be positioned and additional ground surface recruited to bear weight in a manner similar to that used for horses with rotation. However, horses with distal displacement of the distal phalanx do not appear to benefit from heel elevation, which may worsen the lameness. One author uses an egg-bar shoe and applies digital cushion support to the entire ground surface of the foot if there is no concomitant rotation of the distal phalanx. The other author's first line of treatment is a wooden shoe. Horses with distomedial or distolateral displacement of the distal phalanx require appropriate positioning of the shoe, heel elevation, and recruitment of ground surface for weight bearing. Additionally, in order to reduce the stress in the wall of the affected side, an abaxial extension should be applied contralaterally (Figure 49.10). This is most easily achieved by spreading the branches of the shoe and setting the contralateral branch wide or by using a wooden shoe and setting it flush on the affected side and wide on the unaffected side.

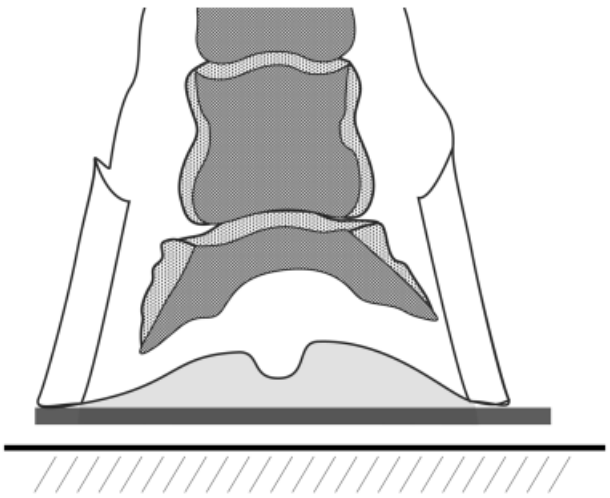

Figure 49.10 Schematic diagram to illustrate unilateral distal displacement of the distal phalanx that show the approximate position of an extension on the side contralateral to the displacement. The concavity of the sole is packed with silicone putty. Image is copyrighted to Andrew Parks. Used with permission.

Surgery

Surgery is seldom warranted in the treatment of horses with acute laminitis, but deep digital flexor tenotomy and surgical drainage and debridement of septic tissue may both be needed in the treatment of horses with chronic laminitis. Deep digital flexor tenotomy is performed to achieve a greater reduction in the flexor moment about the distal interphalangeal joint than is possible with corrective trimming and shoeing alone in horses with rotation of the distal phalanx. This procedure is indicated when (1) the distal phalanx continues to rotate within the hoof capsule despite attempts to stabilize it, (2) when a horse with rotation of the distal phalanx has unrelenting pain that cannot be managed with trimming and shoeing alone, and (3) treating secondary flexural deformity of the coffin joint. The tenotomy is usually performed in the mid-metacarpal region with a guarded bistoury in the standing horse. Tenotomy in the mid-pastern region is usually reserved for a repeat tenotomy, and is usually performed with the horse under anesthesia because the presence of the tendon sheath requires a more stringent aseptic technique than the procedure in the mid-metacarpal region.

Realignment of the solar margin of the distal phalanx with the ground surface of the hoof capsule (sometimes referred to as "derotation") is performed immediately after the tenotomy. It is critical to realize that the veterinarian and farrier only have a 4–6 week window to achieve optimal realignment of the distal phalanx. Slight, but significant, subluxation of the coffin joint occurs in most horses following deep digital flexor tenotomy, which necessitates corrective shoeing to prevent the development of degenerative joint disease. In order to minimize subluxation of the distal interphalangeal joint after tenotomy, one author uses a combination of a slightly extended heel (i.e., with egg-bar shoe) and heel elevation, whereas the other author only uses heel elevation. It is best if radiographs are taken with the shoe and pads temporarily attached in order to determine the appropriate amount of heel elevation to avoid subluxation of this joint (the amount of heel elevation needed may vary from 3° to over 10°). An additional benefit of deep digital flexor tenotomy is accelerated growth of the sole. Although desmotomy of the inferior check ligament as a more conservative surgical approach to decreasing tension on the deep digital flexor tendon has been advocated, it does not appear to provide sufficient relaxation of the tendon and neither author uses this approach.

Surgical drainage is indicated when abscessation occurs. However, both authors feel that it is important to preserve as much integrity of the sole as possible because large solar defects permit prolapse of the solar dermis; this prolapsed tissue is extremely sensitive.

Additionally, defects in the solar integument heal far more slowly in laminitic horses than they do in healthy horses. One author preserves solar integrity by making one to four small holes in the sole, whereas the other author prefers to preserve the full thickness of the sole and drain the abscess dorsally or abaxially through the distal hoof wall at its junction with the sole. Debridement of the distal phalanx is indicated whenever septic pedal osteitis is present. However, establishing the presence of septic osteitis can be problematic because many horses with drainage that have radiographic evidence of pedal osteitis do not have septic osteitis. It is the experience of one of the authors that many solar lesions dorsal to the frog caused by pressure on the sole from the distal phalanx will heal without debridement of the soft tissues or distal phalanx by altering the biomechanics of the foot. To accomplish this, appropriate biomechanical principles are used to decrease the downward pressure by the dorsal margin of the distal phalanx to relieve the solar pressure, usually by elevating the heels and/or performing a deep digital flexor tenotomy combined with corrective trimming to realign the distal phalanx with the solar surface. If conservative drainage, systemic and local antibiotics, and corrective shoeing do not resolve the problem, then surgical debridement is warranted.

Dorsal hoof wall resection used to be frequently performed when more conservative treatments failed to encourage new hoof wall growth from the coronary band to progress parallel to the parietal surface of the distal phalanx. The rationale for performing hoof wall resections was to encourage hoof wall growth by removing hyperplastic keratinized lamellar tissue, relieving pressure on the underlying tissues, and removing distracting forces within the hoof wall. However, the authors believe that this technique further destabilizes the distal phalanx because it (1) removes any remaining dorsal lamellar attachments and (2) concentrates stress at the abaxial margins of the resection. Partial hoof wall resection involving only the distal half of the wall is more acceptable because it reduces pressure on the coronary band from the weight-bearing surface of the wall while maintaining sufficient hoof to support the foot. Alternatively, the coronary band may be grooved by creating a horizontal groove through the full thickness of the stratum medium of the hoof wall parallel to and approximately 1 cm distal to the coronary band from one toe-quarter junction to the other. As a modification of this technique, one author removes the entire stratum medium proximal to the groove. Appropriate depth of the groove is indicated by the presence of pinpoint hemorrhage at the bottom of the groove. This technique mechanically dissociates the new wall from the old wall, thereby reducing any distracting forces in the dorsal wall from weight bearing and locomotion. Unfortunately, neither technique restores normal orientation of the dorsal hoof wall in relation to the distal phalanx if the coronary band horn tubules are not aligned with the distal phalanx or if a wedge of dermal tissue has developed dorsally between the bone and the lamellar epithelium. The dorsal hoof wall can be dressed back so that the exterior surface of the hoof wall is nearer to being parallel with the dorsal surface of the distal phalanx, but the wall will subsequently be thinner and not as strong.

Other Supportive Care and Miscellaneous Therapies

There are several other aspects of care for laminitic horses that need to be considered, including nutritional needs, limb edema, and pressure sores. Although the nutritional needs of laminitic horses have not been determined, the practice of starving laminitic horses for fear of exacerbating the laminitis is unwarranted. The only exception might be the first 1–3 days after the gastrointestinal disease that may have precipitated the laminitis. It is more appropriate to provide good-quality hay supplemented with a complete ration if necessary; feeding grain is inadvisable in most active cases of laminitis. If supplemental feeding is necessary (owing to inability to masticate hay, or severe loss of body condition), it is best to feed small amounts of a pelleted complete ration several times during the day to avoid the disruption of the flora in the gastrointestinal tract that can occur with one or two large feedings. It is imperative that animals be deeply bedded if there is a firm surface (concrete or rubber) in the stall.

Limb edema should be controlled in acutely laminitic horses with bandages, and pressure sores in chronically laminitic horses should be kept clean, debrided if necessary, and dressed with a topical medication such as zinc oxide. Horses that develop flexural deformities at the metacarpophalangeal joint may respond with increased comfort and mobility if the lower limb is splinted soon after the symptom is observed. Digital hypothermia, as described earlier, should always be considered as the only effective therapy available at this time to limit lamellar injury in the developmental and early clinical stages of sepsis-related laminitis.

Summary of Proposed Treatment Regimens for the Different Stages of Laminitis

Treatment of laminitic horses must take into account the variety of ways in which horses with the disease present and the ambiguities surrounding the benefits of many of the pharmacologic agents that have been advocated for use in treatment of the disease. Obviously, prevention of laminitis through appropriate prophylactic therapy is

ideal. Unfortunately, it is difficult to predict accurately when acute laminitis will occur even when a horse has a disease known to increase the animal's risk of developing acute laminitis. Therefore, treatment is frequently not started until a horse shows clinical symptoms of acute laminitis, and when treatment is started it is not on an aggressive scale because such therapy is time consuming and expensive.

Overall Prophylactic Therapy for the Horse at Risk of Laminitis

Most horses undergoing gastrointestinal crises are at risk of developing laminitis (i.e., they may be in the developmental stage of laminitis); the horses exhibiting more severe signs of systemic compromise (i.e., high heart rate, abnormally colored mucous membranes) appear to be at greater risk. The recommended treatment is aggressive supportive therapy (i.e., IV fluids, etc.) to maintain adequate circulatory function, and aggressive use of flunixin meglumine and possibly polymixin B to combat bacterial toxemia and inflammation. For horses with severe symptoms of endotoxemia, treatment with endotoxin antiserum may possibly be warranted. Broad-spectrum antibiotics should be used if systemic sepsis is suspected or should the primary condition warrant it. Shoes should be removed if present and the front feet (or all four feet) should be supported, most commonly with either Styrofoam support blocks, silicone putty, or silicone putty in conjunction with Redden Modified Ultimates. Most importantly, digital hypothermia should be performed constantly in horses with gastrointestinal crises deemed to be at risk for laminitis (especially those exhibiting clinical signs of sepsis). As clinical laminitis normally ensues 2–3 days following the initial systemic insult, it is advisable to provide aggressive prophylactic medical and foot care for at least 3 days following a gastrointestinal crisis.

Overall Therapy of the Horse in the Acute Stage of Laminitis

Horses in the acute stages of laminitis may be treated with flunixin meglumine (if there is still moderate systemic compromise), phenylbutazone (if the horse is systemically stable but lame), or a combination of these drugs. Ketoprofen or firocoxib are alternatives in horses with compromised kidneys or a history of gastrointestinal ulceration. Acepromazine can be administered to address vascular concerns, but more likely benefits the animal owing to its tranquilizing effects (i.e., decreased stress levels for the horse) as it is unlikely to increase lamellar blood flow effectively. Foot support is critical when using closed-cell foam, level rubber pads made from cushion support, or Redden Modified Ultimates (primarily for animals suspected of undergoing rotational displacement).

Overall Therapy of the Horse in the Chronic Stage of Laminitis

Horses with chronic laminitis should be treated with a combination of NSAIDs (most commonly phenylbutazone), corrective shoeing, and possibly surgery. The choice of shoeing will depend, as described earlier, on the stability of the lamellae, the pattern of displacement, and how the animal moves. Deep digital flexor tenotomy will most likely be used in the horse with severe rotation, and surgical debridement of the distal phalanx will most commonly be performed on those horses in which there is persistent drainage with radiographic evidence of lysis of the distal phalanx that has not responded to corrective shoeing.

Prognosis

The prognosis for survival and return to work has been correlated with radiographic findings. In one report, the degree of dorsal rotation of the distal phalanx on radiographs was indicative of both survival and return to work (Stick et al., 1982). In another study, the prognosis was correlated with the severity of clinical symptoms, but not severity of rotation; in that study, distal displacement negatively impacted the outcome (Hunt, 1993). Yet another study suggested that the vertical distance between the coronary band and the proximal aspect of the extensor process is the most useful prognostic indicator (Cripps & Eustace, 1999a).

In horses with acute laminitis, that is, horses without displacement, the best prognostic indicator for survival is the severity of the initial lameness, which appears to correlate with the severity of the lamellar injury. However, the prognosis varies considerably among horses, and many horses with severe acute laminitis will improve dramatically over 2–3 weeks if rotation of the distal phalanx is prevented. If displacement of the distal phalanx occurs, stabilization of the degree of lameness (and displacement) over a 2–4 week period may be a suitable goal as we continually improve our ability to address the case of chronic laminitis.

In the authors' experience with horses with chronic laminitis, numerous factors need to be considered when assessing the prognosis, including capsular rotation, phalangeal rotation, the thickness of the sole distal to the dorsal margin of the distal phalanx, and the presence of complications, including infection and secondary flexural deformities. The severity of capsular rotation is a better indicator of how much corrective shoeing will be required. The severity of phalangeal rotation is a better indicator of whether tenotomy will be necessary to facilitate the realignment of the distal phalanx. The response to corrective shoeing over 3–6 months is the best indicator of how close to normal the final appearance of the foot will be and the likelihood that the horse will return to some form of exercise.

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Part XIII

Specific Diseases of Horses

50

Diseases of the Stomach

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Gastric Ulcer Syndromes

Horses with gastric ulcers present with an array of clinical and subclinical signs that reflect varying degrees of discomfort. These signs can be as vague and nonspecific as behavioral changes, reduction of feed intake, or signs of colic. When colic is the presenting sign or in the history, it is important to perform a complete physical examination and rule out other causes of colic, even if gastric ulcers are diagnosed by endoscopy.

In foals, colic signs can be mild to severe. Several disorders can cause pronounced signs of abdominal pain in foals, and often these cannot be differentiated without a thorough evaluation, including passing a nasogastric tube, radiography, ultrasonography, complete blood count, chemistry profile, and abdominal fluid analysis. In many foals, gastric ulcers occur secondary to active enteritis or its sequelae (duodenal or pyloric stricture), and these foals often present with fever and an increased peripheral white blood cell count. Gastric ulcers in these foals can be severe; whereas enteritis may be the cause of clinical signs such as fever and lethargy, the ulcers are often the cause of the presenting abdominal discomfort. Nasogastric intubation may recover dark-brown fluid, which is indicative of bleeding ulcers. Unfortunately, signs of colic that are due to ulcers are often only apparent when ulcers are severe (Figure 50.1) or severe complications such as pyloric/duodenal stenosis (Figure 50.2, Figure 50.3), esophagitis (Figure 50.4), megaesophagus, or gastric perforation have occurred.

In adult horses gastric ulcers both cause colic and result from other disorders that cause colic (Murray, 1992). In horses in which ulcers are a primary cause of colic, discomfort is usually mild to moderate, and there are often frequent, recurrent episodes of colic. In rare cases, ulcers may cause such severe pain that exploratory surgery is performed. In some cases, the author has associated ulcers with recurrent gaseous distention of the large intestine. This may be a visceral sympathetic response to gastric pain.

Often, gastric ulcers develop secondary to another intestinal problem, and these ulcers become evident when the horse has persistent mild to moderate abdominal discomfort or impaired appetite after the primary intestinal problem has been resolved. In other cases, ulcers may contribute to abdominal discomfort but are not the primary problem. Signs of colic may even abate when the horse is treated for ulcers, but acute colic recurs as a result of the primary problem.

Diagnosis

Gastroscopic examination is the most reliable method for accurately diagnosing gastric ulcers. Abnormalities in a complete blood count or in clinical chemistry analytes do not indicate gastric ulceration as a primary problem. The presence of any such abnormalities should alert the clinician to another disorder, which may be the primary problem. A thorough gastroscopic examination should include assessment of the antrum and pyloric regions of the stomach, which usually requires a 3 m long endoscope in adult horses. In one report (Murray et al., 2001), ulcers were present in the antrum/pylorus of horses with colic that had normal-appearing squamous mucosa. Failure to identify these ulcers would have resulted in a misdiagnosis. Endoscopic examination of the proximal duodenum to the level of the major duodenal ampulla is possible in many horses, although in horses with colic the examination of this portion of the intestine usually has not been of diagnostic value.

In foals, severe gastric ulceration can accompany duodenitis and enteritis (Figure 50.5). Endoscopic examination of the duodenum should be attempted in foals. In foals 4–7 months old, the author has occasionally been able to pass the endoscope the length of the

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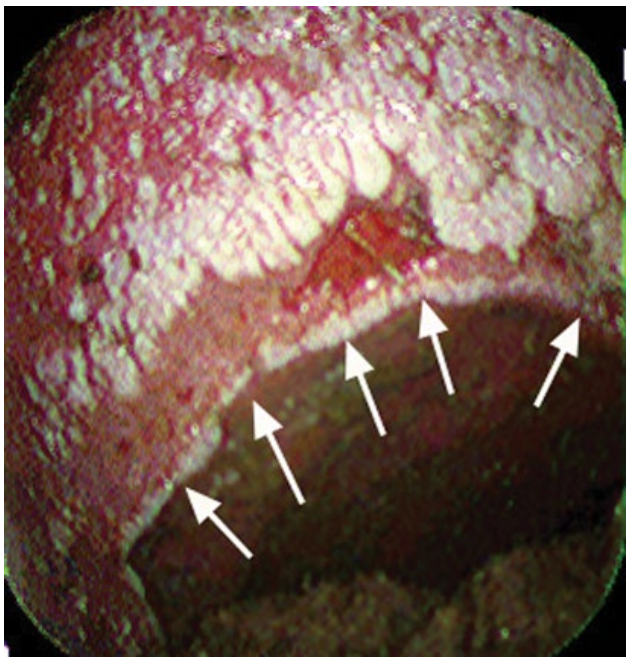

Figure 50.1 Severe ulceration of the squamous mucosa adjacent to the margo plicatus in a foal with pyloric stricture. The severe ulceration resulted from impeded gastric outflow and elevation of the normal level of acidic gastric fluid, continuously exposing the squamous mucosa to acid injury.

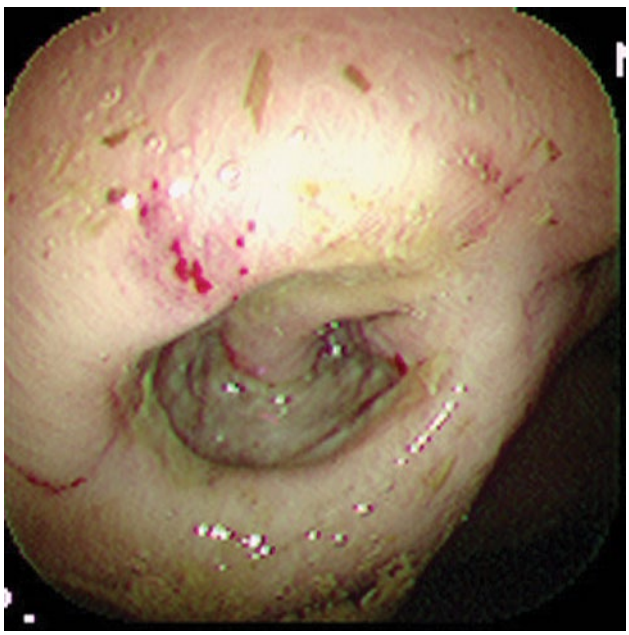

Figure 50.2 Pyloric stricture in a 2-month-old foal that had had intermittent diarrhea and colic for several weeks. The foal had responded with improved clinical signs when treated intermittently with acid-suppressive medication for 5–7 days, and relapsed when treatment was stopped.

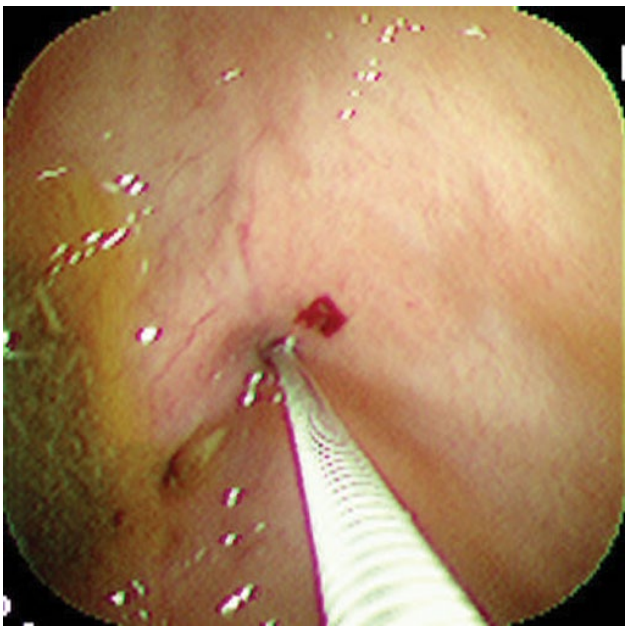

Figure 50.3 Endoscopic biopsy forceps is passed through a stricture in the duodenum, orad to the major duodenal papilla, in a 10-month-old weanling. The diameter of the lumen was approximately 2 mm at the stricture.

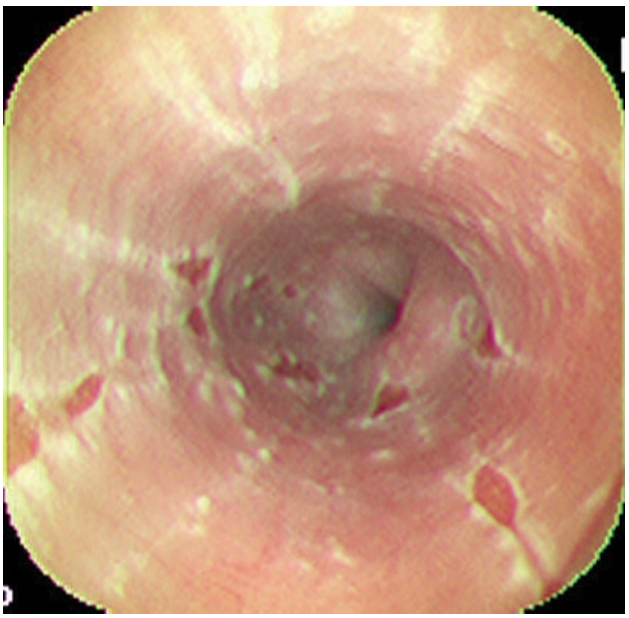

Figure 50.4 Erosions in the esophagus of the foal with pyloric stricture in Figure 50.2. Reflux of gastric contents can occur secondary to pyloric or duodenal stricture, and in chronic cases esophageal dilation (megaesophagus) can result.

descending duodenum (Figure 50.6), and in some cases this confirmed a diagnosis of enteritis. The reason for successful passage of the endoscope into the descending duodenum in foals of this age range is not known, and may reflect optimal anatomic size and configuration for the procedure. If duodenoscopy is not possible,

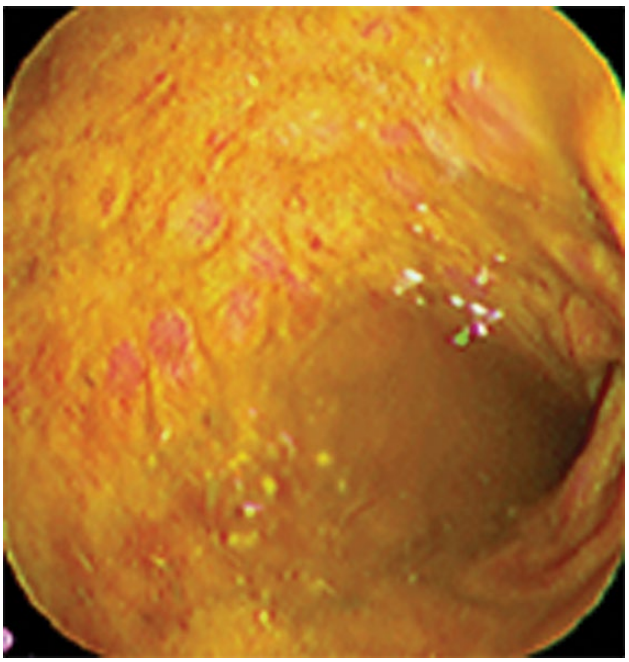

Figure 50.5 Fibrinous duodenitis in a 3-month-old foal that presented with acute fever, abdominal discomfort, and diarrhea. The foal also had severe gastric ulcers, presumably as a result of delayed gastric emptying. Several foals on the farm became similarly ill within a few days, implying an infectious cause of the duodenitis.

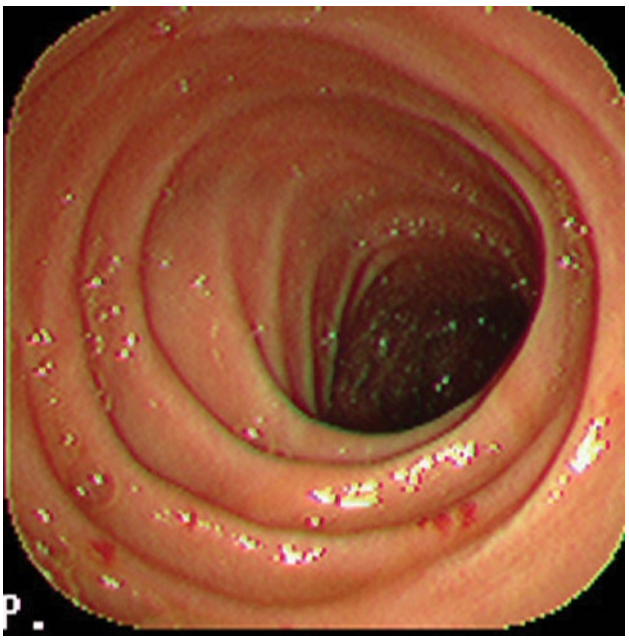

Figure 50.6 Endoscopic view of the descending duodenum in a 6-month-old foal. The endoscope could be advanced several centimeters aborad from the major duodenal papilla.

ultrasonography and contrast radiography should be performed if enteritis, duodenal ulceration, or duodenal stricture is suspected. The initial portion of the duodenum is best radiographed within 2 min of administering a barium suspension, because rapid filling of the proximal duodenum with barium highlights this portion of the duodenum where ulcers and strictures often occur.

Treatment

In all animals with gastric ulcers, reduction of gastric acidity is a primary objective. In some cases, medications that may enhance mucosal integrity or stimulate gastric emptying may be effective. Few treatments for gastric ulcers have been critically evaluated for treating gastric ulcers in horses, and currently only products containing the histamine type-2 receptor antagonist ranitidine and the H^+,K^+-ATPase inhibitor omeprazole have been approved by governmental regulatory bodies for the treatment of gastric ulcers in horses.

Suppression of gastric acidity does not stimulate ulcer healing but is permissive to ulcer healing. Mechanisms of healing are initiated with the onset of mucosal injury and removal of the acid allows healing to proceed unimpeded. When considering the use of acid-suppressive therapy in foals or adult horses, one must recognize that the horse is a continuous secretor of hydrochloric acid (Campbell-Thompson & Merritt, 1990) and thus, unlike humans, does not have a diurnal pattern to gastric acidity (Murray & Schusser, 1993). Therefore, effective treatment will require prolonged reduction of gastric acidity. The mechanism of action of an acid-suppressive agent and the dose administered will affect the potency and duration of acid suppression. Additionally, the bioavailability of orally administered drugs is generally poor, varies considerably from horse to horse, and will be affected by product formulation. Consequently, deviating from recommended dosages often results in treatment failure. In such cases, low doses of an acid-suppressive agent that appear to result in improved clinical signs may not result in ulcer healing, which has led to permanent damage to the stomach or fatal consequences in some cases.

Antacids

In humans, antacids are used primarily to control symptoms of dyspepsia (heartburn, upset stomach), and these agents are not considered primary therapy for the treatment of ulcer disease. Antacids reduce gastric acidity by neutralizing existing acid. Most antacids are based on a combination of aluminum and magnesium hydroxides or calcium carbonate. Antacids can effectively reduce gastric acidity in horses, but only briefly (Murray & Grodinsky, 1992; Murray, 1997). Liquid antacid products must be given both in large volumes (240 mL) and very frequently (6–12 times daily) to be effective in promoting ulcer healing. Feed additives that contain antacids are popularly considered to be helpful in controlling gastric ulcers in horses, but there are no supportive data.

Also, an acid-neutralizing effect is most desirable when the stomach is empty, not when it is full, because gastric pH is naturally higher when horses ingest roughage (Murray & Schusser, 1993).

Histamine Type-2 Receptor Antagonists

The histamine type-2 receptor antagonists (H2 antagonists) inhibit hydrochloric acid secretion by competing with histamine for receptor sites on the parietal cell (Nieto et al., 2001). Histamine is the most potent stimulus for hydrochloric acid secretion and, because occupation of the receptor site is by competitive inhibition, the greater the concentration of H2 antagonist at the receptor site, the greater and more prolonged is the degree of suppression of hydrochloric acid secretion. The H2 antagonists registered for use in humans are cimetidine, ranitidine, famotidine, and nizatidine, and all are available in generic formulations. Injectable formulations of cimetidine and ranitidine are also available.

In horses, ranitidine inhibits gastric acid secretion (Campbell-Thompson & Merritt, 1987), increases gastric pH (Murray & Schusser, 1993; Murray & Grodinsky, 1992; Sanchez et al., 1998), and has been associated with ulcer healing in a retrospective report (Furr & Murray, 1989). The most effective dose for increasing gastric pH was 6.6 mg/kg (Murray & Grodinsky, 1992), and increased gastric pH was best sustained when ranitidine was given at 8 h intervals (Murray & Grodinsky, 1992). Intravenous (2.0 mg/kg) and oral (6.6 mg/kg) administration of ranitidine increased the mean gastric pH for 5–8 h in young foals (Sanchez et al., 1998). Individual horses have different dose–response profiles (based on bioavailability of the drug), and as the dosage of ranitidine is decreased, the percentage of non-responders increases (Murray & Grodinsky, 1992). In some horses, reducing the dose to less than 6.6 mg/kg results in no increase in gastric pH.

Orally administered cimetidine has been shown to increase equine gastric pH (Sangiah et al., 1988), but in other studies cimetidine was not effective in promoting ulcer healing in horses given up to 20 mg/kg three times daily (MacAllister et al., 1994; Nieto et al., 2001). The effect of intravenously administered cimetidine on gastric pH in horses has not been reported, although pharmacokinetic data would support its use (Smyth et al., 1990). The author's clinical experience using cimetidine intravenously at a dose rate of 6.6 mg/kg every 6–8 h has been consistently positive, with ulcer healing progressing at a rate consistent with excellent suppression of gastric acidity.

The H^+,K^+-ATPase inhibitors, also referred to as proton pump inhibitors (PPIs), interact specifically with parietal cell H^+,K^+-ATPase because of their chemical structures and the uniquely highly acidic environments of the secretory domain of the parietal cell H^+,K^+-ATPase. Omeprazole is the only H^+,K^+-ATPase inhibitor approved for use in horses. The magnitude of inhibition of acid secretion is dose dependent, so that at higher doses more catalytic sites are blocked, and omeprazole can inhibit acid secretion by up to 99% for 24 h or longer (Daurio et al., 1999). PPIs are chemically fragile and are unstable in the presence of oxygen or acid. In fact, the PPI parent drugs do not themselves bind to parietal cell H^+,K^+-ATPase. Rather, these drugs undergo a complex chemical transformation within the acidic parietal cells' secretory canaliculi into another chemical form that binds to cysteine residues in the proton pumps (Bays & Finch, 1990). Exposure to low pH in the gastric lumen prior to absorption into the blood also chemically alters the PPI drugs, thereby rendering them inactive. Product formulations must take this into consideration, and also protect the drug from oxidation during storage. Pharmacokinetic/pharmacodynamic properties of products also can differ substantially based on formulation, even with the same dose of omeprazole. Other factors may affect the bioavailability of omeprazole, including the prandial state of the horse. In one study, bioavailability was enhanced when a paste product (GastroGard®; Merial, Duluth, GA) was given to horses from which feed was withheld (Daurio et al., 1999).

The dosage of omeprazole for treatment of ulcers in the pioneer product for horses (GastroGard) is 4.0 mg/kg once daily, which has been shown to be highly effective in treating gastric ulcers in foals and horses (Bays & Finch, 1990; Andrews et al., 1999; MacAllister et al., 1999). Omeprazole also prevented gastric ulcers in 80% of racing horses that received a reduced daily dose of 1 mg/kg for 28 days (White et al., 2005).

Drugs Acting on Gastric Motility

In some cases, ulcers are the result of accumulation of acid because of delayed gastric emptying. This may result from generalized intestinal ileus, enteritis, or pyloric/duodenal obstruction. Obstruction of the pylorus or duodenum can occur in foals as a result of chronic ulceration, and the author has observed this condition in several adult horses. Often, the pyloric stenosis is irreversible because of severe scar tissue formation, but in some cases a prolonged treatment with acid-suppression and prokinetic drugs may result in substantial recovery.

The cholinergic agonist bethanechol has been used by the author to stimulate gastric emptying in foals and horses with duodenitis, pyloric stenosis, and pyloric ulceration. Bethanechol also has been used to facilitate gastroduodenoscopy in foals and horses. Clinically, bethanechol is given subcutaneously, at a dose rate of 0.02 mg/kg, or orally, at 0.35 mg/kg, every 8 h. Cholinergic side effects are not noted at these doses unless the drug is given intravenously. Bethanechol has been given to some horses chronically (weeks to months) without apparent adverse effects.

Metoclopramide has been used effectively in humans to improve gastric emptying and in foals with suspected gastric emptying disorders. Metoclopramide has the potential to cause severe excitation in foals and horses because of its ability to cross the blood–brain barrier and its inhibitory effects on dopamine receptors. Therefore, the challenge is to administer a dose that effectively stimulates propulsive motility while avoiding adverse effects. Foals have been given doses ranging from 0.1 to 0.25 mg/kg at 6–8 h intervals. In one report, metoclopramide given to horses as a slow infusion at a dose rate of 0.125 mg/kg was shown to increase gastric emptying in a low-dose endotoxin model (Doherty et al., 1999). Bethanechol appears to be preferable to metoclopramide because it produces limited side effects.

Treatment Recommendations for Horses with Colic as the Presenting Clinical Sign

Because gastric ulcers can be both the cause of colic and the result of conditions that cause colic, effective treatment of gastric ulcers is often an important part of the treatment or aftercare of horses with colic. In horses with colic, treatment should consist of medications given at dosages that are recognized to be effective in reducing gastric acidity and promoting ulcer healing. In horses in which gastric emptying and small intestinal function are thought to be normal, an oral product can be administered. In cases of acute colic and in horses with gastric or small intestine motility concerns, intravenous treatment with an H2 antagonist or PPI drug should be given. Once the horse can utilize oral medication, oral medications can be given. Depending on the condition of the foal or horse, a prokinetic drug (bethanecol or metoclopramide) may be indicated to facilitate gastric emptying and the delivery of orally administered medication.

Gastric Impaction

Gastric impaction can occur as a primary condition, but often it is diagnosed at surgery as a finding secondary to other disorders in the intestinal tract. It can be a serious condition, because untreated cases can proceed to rupture. In some cases, there may be predisposing causes, such as ulceration or fibrosis at the pylorus, whereas in other cases, gastric impaction may occur spontaneously. Management practices that may contribute to gastric impaction include feedstuffs that can become desiccated in the stomach (beet pulp, bran, straw, wheat, and barley), dental disorders affecting masticated of feeds, and feeding a horse that has signs of colic. The last scenario occurs when the primary signs of colic have subsided but the initiating problem persists and gastric emptying is impaired along with generalized intestinal motility impairment.

Gastric impaction may be suspected during an examination for colic if it is difficult to pass a nasogastric tube into the stomach, which can occur with an impacted or dilated stomach. If the horse has not eaten for several hours, yet poorly macerated or digested feed material is recovered from the nasogastric tube, a gastric impaction may be suspected. On rectal examination, the spleen may be displaced caudally and medially because of gastric distention, but this finding is not specific for gastric impaction or dilation.

Endoscopy is often unhelpful in the diagnosis, because simply identifying a stomach full of ingesta is not diagnostic for an impaction, and it is difficult to assess distention by endoscopy. Radiography may be useful in some cases, in which the impacted stomach will be noted to displace the diaphragm cranially (Figure 50.7).

Medical treatment can include gastric lavage to remove as much ingested material as possible. This may need to be done repeatedly. Instillation of 100–200 mL of 8% dioctyl sodium sulfosuccinate (DSS) may facilitate hydration of desiccated ingesta. Treatment with analgesics and intravenous fluids should also be applied, as needed, although intravenous fluid administration is unlikely to increase the hydration of desiccated gastric contents. The author has treated horses with gastric impactions that were diagnosed at surgery with bethanecol, 0.02 mg/kg sc, every 8 h with no adverse effects. Gastric motility stimulants should be avoided if the extent of the impaction is not known, however, because of a possibility of inducing gastric rupture.

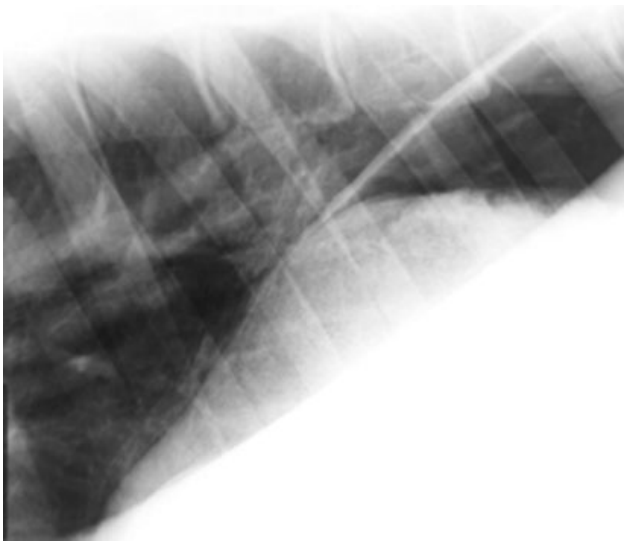

Figure 50.7 Radiograph of the caudal thorax of an adult horse with a gastric impaction. The impaction is apparent because of the contrast with the radiopaque gas cap in the stomach.

Surgical treatment can include direct infusion of balanced polyionic fluids into the impaction through the stomach wall. The stomach is massaged to break down the impaction and facilitate movement of fluid into the ingesta. Alternatively, fluid may be infused via a nasogastric tube, followed by massage of the stomach. Postoperatively, the horse should be held off feed for 48–72 h. A gastroscopic examination is indicated, both to document resolution of the impaction and to determine whether there is an underlying disorder in the stomach.

Gastric Dilation

Dilation of the stomach with fluid or gas usually results from obstruction of the small intestine, but primary gastric dilation can occur if a horse eats highly fermentable material, generating a large volume of gas. This is dissimilar to frothy bloat in ruminants, in which a stable gas/fluid froth develops in the rumen as a result of plant/rumen microbial interactions. It is possible for fluid to reflux spontaneously from the stomach into the esophagus, but with distention the gastroesophageal junction is distorted such that it is tightly closed. This promotes progressive gastric distention as fluid continues to move into the stomach from the duodenum or as gas is generated within the stomach.

The clinical signs are the same as for gastric impaction, although the onset may be more acute and the signs more severe. Affected horses are often tachypneic because of compression of the thorax by the distended stomach. Diagnosis of primary gastric dilation can be presumed if passage of a nasogastric tube releases a large volume of gas, which relieves the colic episode. If a large volume of fluid is retrieved, gastric dilation may have been temporarily resolved, but the underlying cause of enterogastric reflux will need to be determined.

Treatment is removal of excessive fluid or gas via a nasogastric tube, or at surgery via needle aspiration. An underlying reason for the gastric dilation should be determined and appropriately treated. Because the cause of gastric dilation in horses is dissimilar to that of frothy bloat in ruminants, treatments designed for the latter condition are not indicated for gastric dilation in horses. Also, products designed to treat "stomach gas" in humans, such as simethecone, are not indicated for horses with gastric distention.

Polypous Adenoma

Polypous adenomas are proliferations of mucinous glandular tissue in the antrum. These can vary in size from small enlargements to large, tortuous thickening of antral rugal folds (Figure 50.8). Lesions often have accompanying mucosal erosion or ulceration. The cause of this condition is not known. Polypous adenomas appear to be rare, and it seems that there may be a predilection for Warmblood breeds of horses. They have been associated with signs of poor appetite, failure to thrive, or recurring colic, but a definite cause-and-effect relationship is often unclear. In some cases, however, these proliferations do appear to obstruct stomach emptying during antral contractions. The primary lesions do not respond to acid-suppressive drug therapy. In one instance, polypous adenomas were successfully debulked using an electrocautery loop (Y. Nout-Lomas, personal communication, 2015).

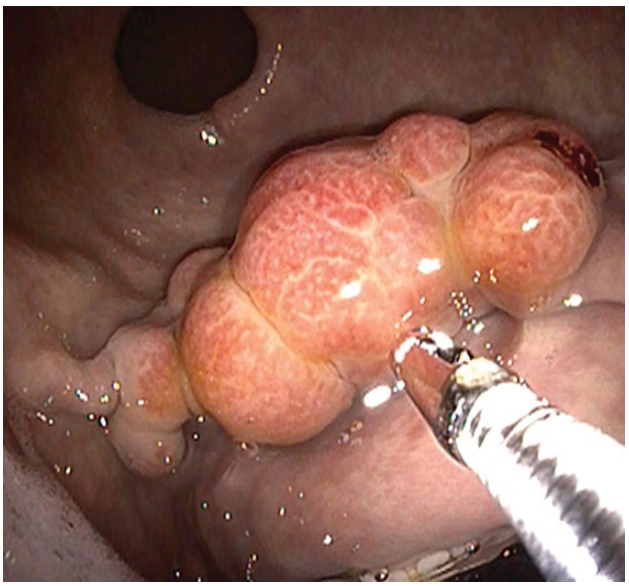

Figure 50.8 Polypous adenoma lesion in a 9-year-old Warmblood horse that presented with vague clinical signs of reluctance to work and occasional diarrhea. Note the proliferation of tissue along the rugal fold. The pylorus is in the background.
Source: Courtesy of Dr Yvette Nout-Lomas.

Neoplasia

Squamous cell carcinoma is the most frequent gastric neoplasia in horses (Taylor et al., 2009). Squamous cell carcinoma affects the esophageal and gastric squamous mucosa, and by the time the disease is recognized, treatment is rarely possible. In some horses, tumors remain localized within the stomach, whereas in other horses, tumors may extend through the stomach wall and spread to other abdominal viscera or metastasize to other locations in the body.

Typical signs associated with, but not diagnostic for, squamous cell carcinoma include chronic weight loss, poor appetite, abdominal discomfort, and lethargy.

Ascites or edema may occur in some cases. If the esophagus is involved, dysphagia or ptyalism will be the predominant sign. Involvement of the stomach with squamous cell carcinoma at the cardia may also result in dysphagia, while involvement at other sites in the stomach may result in signs of obstruction to outflow (colic) and/or weight loss. In some cases, tachypnea will be a prominent sign, because of either metastasis to the thorax or pressure on the diaphragm from an enlarged tumor.

Endoscopy is the best means for diagnosis (Figure 50.9), but other potential useful diagnostics include radiography of the caudal thorax (displacement of the diaphragm cranially or soft tissue density overlying gastric gas cap), cytologic evaluation of gastric lavage fluid, peritoneal fluid cytology, and ultrasonography.

Other gastric neoplasms cited in one report (Taylor et al., 2009) included leiomyoma, mesothelioma, adenocarcinoma, and lymphoma.

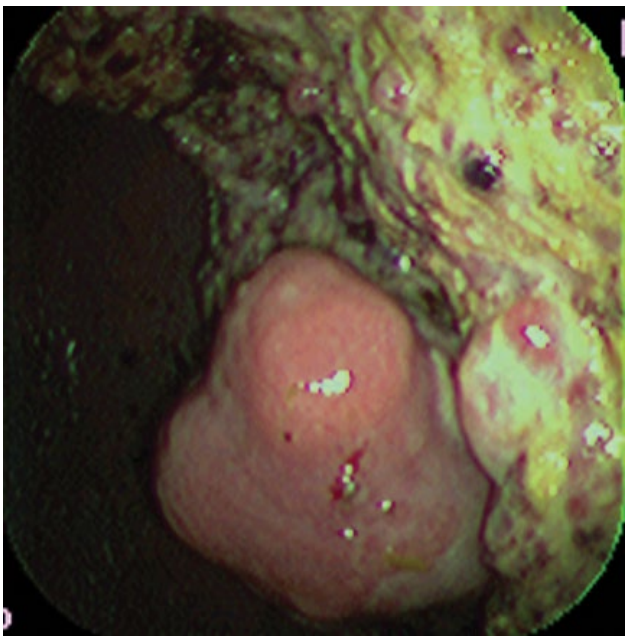

Figure 50.9 Endoscopic view of a gastric squamous cell carcinoma in an aged horse.

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51

Diseases of the Liver and Liver Failure

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One of the major functions of the liver is the filtration of enteric-derived toxins (both bacterial and chemical). As a result, the liver is exposed to many insults and liver disease is relatively common. Many disorders can cause hepatic disease (i.e., pathologic change or damage to the liver) in both adult horses and foals. Fortunately, few of these diseases result in hepatic failure. The liver carries an immense reserve capacity (approximately 80%), and liver damage, therefore, must be advanced before physiologic failure and clinical signs occur (Pearson, 1999; Divers, 2015). For example, horses with strangulating or inflammatory intestinal diseases frequently have evidence of liver disease (elevated hepatic enzymes in the serum) caused by portal hypoxia and/or increased concentrations of endotoxins in the portal circulation, but these conditions rarely progress to liver failure. In addition to the large reserve capacity, the liver also has an immense capacity to regenerate, and mature hepatocytes are capable of active proliferation by self-duplication in response to acute external stimulation and up-regulation of humoral factors (Divers, 2015). However, in some chronic insults to the liver, fibrosis develops, hepatocytes fail to proliferate sufficiently, and biliary tract cells proliferate to form ductules around the portal veins. These proliferating biliary cells associated with chronic injury may contain progenitor cells, which can give rise to both hepatocyte and biliary cells in an attempt to repair the liver (Tennant, 2008; Divers, 2015). Severe and chronic liver damage can result in irreversible fibrosis (cirrhosis).

The distinction between hepatic disease and hepatic failure is clinically important. In view of the large reserve capacity, many horses with mild hepatic disease will make a full recovery given time and removal of the inciting cause, provided that the diagnosis is made relatively early. If, however, the damage progresses to cause liver failure, then the prognosis for survival is markedly decreased, especially if progressive fibrosis occurs (Barton & Morris, 1998; Peek, 2003; Barton, 2004) (Figure 51.1). Rarely can the diagnosis of liver disease be made purely on the results of a clinical examination, unless there is fulminant hepatic failure (as evidenced by encephalopathy and jaundice).

From a clinical perspective, liver lesions can be divided into acute or chronic, and predominantly hepatocellular or biliary injury (Divers, 2015). Biochemical testing can be used in an attempt to distinguish between predominantly hepatocellular or biliary damage, although some degree of overlap between diseases is common. Distinguishing between acute and chronic diseases can be more difficult on the basis of serum biochemistry; assessment of the history, clinical signs and results of liver ultrasonography and/or histology of liver biopsies may allow this distinction to be made. The degree of fibrosis is an important prognostic indicator. Liver fibrosis is stimulated by the hepatic stellate cells (also known as perisinusoidal or Ito cells) (Hall, 2011; Divers, 2015). These hepatic stellate cells are located close to the perisinusoidal space (space of Disse), in close proximity to the hepatocytes and Kupffer cells (liver macrophages, part of the reticuloendothelial system). When the liver is damaged, the Kupffer cells produce tumor necrosis factor alpha, causing the stellate cells to become activated and to secrete collagen, resulting in fibrosis. Kupffer cells are also important in destroying enteric-derived bacteria, endotoxins, and other foreign substances. They also help recycle iron from senescent red blood cells, and as a result they accumulate hemosiderin, which can be pronounced even in disease-free horses (Divers, 2015).

Many disorders that cause chronic liver disease, such as pyrrolizidine alkaloid toxicosis, can manifest acute signs of hepatic failure. In these cases, the underlying pathologic disease of the liver may have been present for a considerable time in a subclinical state; it is only when the degree of damage throughout the liver reaches a certain level that failure of liver function occurs and clinical signs become apparent.

The Equine Acute Abdomen, Third Edition. Edited by Anthony T. Blikslager, Nathaniel A. White II, James N. Moore, and Tim S. Mair.

Companion website: www.wiley.com/go/blikslager/abdomen

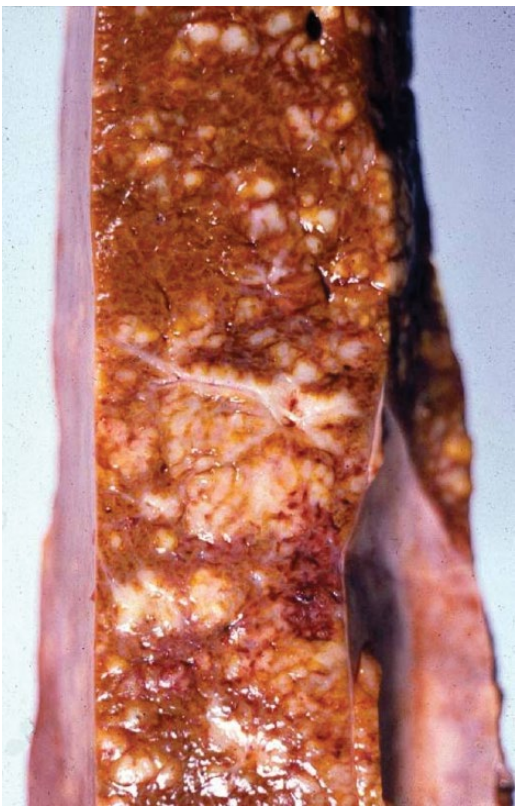


Figure 51.1 Severe fibrosis/cirrhosis of the liver.

Causes of Liver Disease

Liver disease can arise secondary to many toxic, septic, hypoxic, neoplastic, or metabolic conditions (Box 51.1).

In ponies and Miniature horses, the most common cause of acute hepatic disease and failure is hepatic lipidosis, whereas in adult horses, the most common syndromes causing both hepatic disease and failure are Theiler disease and pyrrolizidine alkaloid toxicosis. In foals, important causes of liver disease include Tyzzer disease, toxic hepatopathies (such as iron fumarate toxicity), hepatitis secondary to septicemia, and equine herpesvirus-1. Moderate increases in serum gamma-glutamyl transferase (GGT) can be present in foals with significant gastroduodenal ulceration, especially pyloric outflow obstruction and stricture formation (Peek, 2003). This may be due to restricted bile outflow through the sphincter of Oddi, or bile stasis and incomplete intrahepatic biliary clearance resulting from abnormal intestinal motility. A similar increase in serum GGT (unaccompanied by other biochemical evidence of liver disease) occurs in mature horses with protracted enteritis, or postoperative ileus (Barton, 2004). Increased liver enzymes can also occur in foals with *Rhodococcus equi* abdominal abscesses or umbilical vein remnant infection. In addition to the primary hepatic conditions listed Box 51.1, adult horses with right-sided congestive heart failure can present with increased liver enzymes, especially GGT and alkaline phosphatase (Peek, 2003).

The clinical signs of liver failure can vary, depending mostly on (1) duration – acute or chronic; (2) predominant biliary versus hepatocellular injury; and (3) specific cause.

Horses with acute liver failure are more likely to have central nervous system (CNS) signs as their initial and predominant finding. Horses with chronic liver disease leading to failure commonly (but not always) have weight loss (Figure 51.2) and/or photosensitivity (Figure 51.3) as a clinical finding (Barton & Morris, 1998; Pearson, 1999; Divers, 2002, 2015; Peek, 2003; Barton, 2004). Gastric impaction (Figure 51.4) and bilateral laryngeal paralysis

Box 51.1 Important causes of liver disease in horses

Toxic causes:
- Pyrrolizidine alkaloid toxicosis
- Alsike clover
- *Panicum* grasses
- Iron
- Mycotoxins

Infectious causes:
- Theiler disease
- Cholangiohepatitis
- Tyzzer disease
- Hepatic abscess
- Equine herpesvirus-1 (EHV-1)

Inflammatory, noninfectious causes:
- Chronic active hepatitis
- Neoplasia
- Granulomatous disease

Metabolic causes:
- Hepatic lipidosis
- Primary hyperammoninemia in horses with gastrointestinal disease (no liver disease present)
- Hyperammoninemia in Morgan foals

Obstructive causes:
- Biliary stones
- Right dorsal colon displacement
- Papillary stricture – foals with duodenal ulcers
- Neoplasia
- Hepatic torsion
- Portal vein thrombosis

Unknown causes:
- Neonatal isoerythrolysis

Congenital:
- Portosystemic shunt

Figure 51.2 Weight loss is a common presenting sign of chronic liver disease.

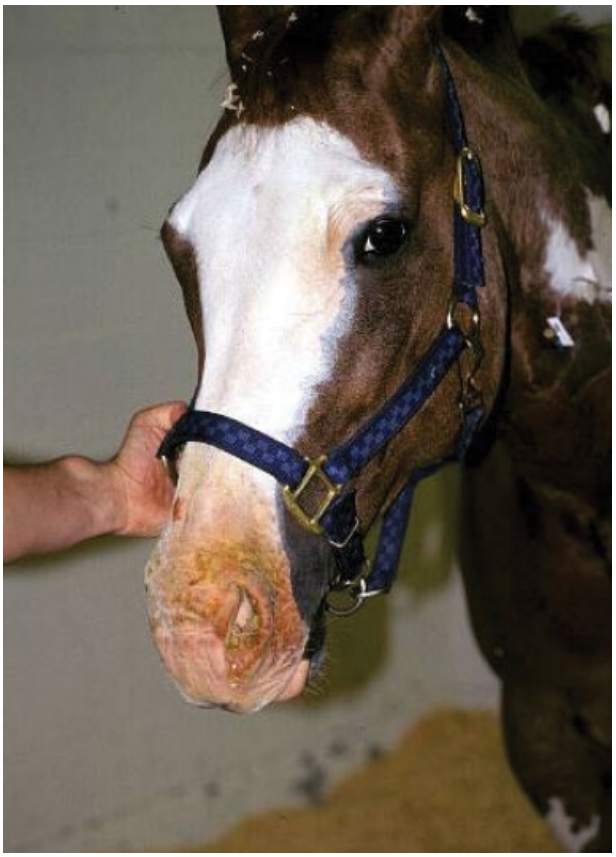
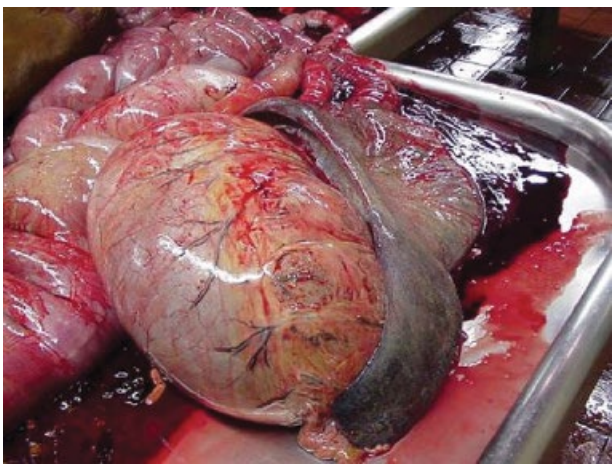


Figure 51.3 Photosensitization affecting the muzzle and nonpigmented areas on the face.

(A)



(B)

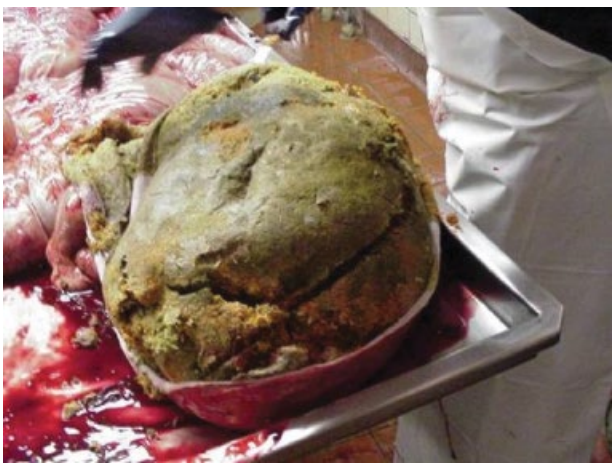


Figure 51.4 Gastric impaction secondary to liver disease – appearance at postmortem examination with the stomach wall intact **(A)** and removed **(B)**.

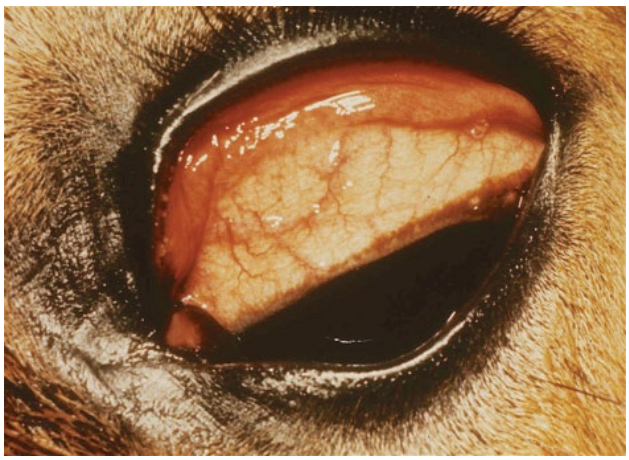


Figure 51.5 Icterus (jaundice). Yellow discoloration of the conjunctiva.

are two of many complications that may occur with equine hepatic failure (Milne et al., 1990; Pearson, 1999; Hughes et al., 2009). Horses with liver disease that initiated in the biliary system are often more jaundiced (Figure 51.5), more likely to be colicky (because of biliary obstruction and possibly an enlarged liver), have photosensitivity, and are less likely to have CNS signs. Icterus, however, is not specific for liver disease, and other causes (including hemolysis and anorexia) should be ruled out (Pearson, 1999). Specific causes of liver failure can also result in more specific findings. These include fever with cholangiohepatitis, ventral edema with hepatic lipidosis, mild abdominal distention, and abnormally tight colonic bands with right displacement of the colon that causes biliary outflow obstruction.

Diagnosis of Liver Disease

The liver has a limited number of ways to respond to various insults and, therefore, the clinical and laboratory changes tend to be similar regardless of the underlying cause. In most cases, it is appropriate first to determine if the horse has liver disease, and then to attempt to identify the cause. In horses with liver disease, some functions of the liver tend to fail before others, and this dictates the progression of clinical signs and laboratory changes (Parraga et al., 1995). In the mature horse, leakage of hepatic and biliary enzymes into the circulation, failure to convert ammonia to urea, and failure to conjugate bilirubin are generally recognized before failure to produce clotting factors or albumin (Pearson, 1999; Divers, 2015).

Biochemical Testing for Liver Damage

Biochemical testing is imperative in the diagnosis of both liver disease and liver failure (Pearson, 1999; Divers, 2015). Biochemical results can be helpful in narrowing the differential diagnosis for the liver failure and, when evaluated over time, can help predict prognosis. Biochemical testing can also be used to identify subclinical hepatotoxin exposure, for example pyrrolizidine alkaloid toxicity or drug-induced liver disease (Curran et al., 1996). Liver-specific enzymes include sorbital dehydrogenase (SDH), glutamate dehydrogenase (GLDH) and GGT, which reflect hepatocellular (SDH and GLDH) and biliary injury (GGT). Aspartate aminotransferase (AST) and alkaline phosphatase also reflect hepatocellular and biliary injury, respectively, but are not liver specific. Isoenzyme 5 of lactate dehydrogenase (LDH-5) and ornithine carbamoyltransferase are alternative indicators of hepatocellular disease, but are rarely used clinically. SDH, GLDH, and AST would be expected to increase in the serum with any mild hepatocyte injury (e.g., endotoxemia). SDH has a short half-life, which can be very helpful in determining and monitoring resolution or progression of the hepatic insult (Bernard & Divers, 1989). Not all diagnostic laboratories measure SDH, and care is required with sample handling [the enzyme is stable at room temperature only for a maximum of 12 h, or for 24 h when refrigerated (Horney et al., 1993)]. GLDH is localized in hepatocyte mitochondria and is released into the serum with acute liver disease; sensitivity of increases in GLDH for the detection of hepatic necrosis and hepatic lipidosis has been determined to be 78 and 86%, respectively (West, 1989). AST is the other most commonly used hepatocellular enzyme (also released in myopathic conditions), but it has a much longer half-life than SDH, and increased blood levels may persist for well beyond a week after resolution of the inciting event. Although GGT is released mostly from biliary epithelium, there is also some release after hepatocellular injury (Noonan, 1981), and, in the horse, GGT often continues to increase for a few days (presumably because of biliary hyperplasia) after the hepatic insult is no longer present. The half-life of GGT is probably similar to that of AST, and it is a very useful screening test for liver damage. Very rarely, serum concentrations of both GGT and SDH may return to normal with severe chronic fibrosis (Divers, 2015). Occasionally, GGT may be mildly to moderately increased (50–140 IU/L) in performance horses (usually racehorses) without any other biochemical or clinical evidence of liver disease (Divers, 2015); this persistent increase in GGT has been linked to poor performance (Snow & Harris, 1988). The cause is uncertain but could include drug administration, toxin exposure, viral infections or oxidative stress and depletion of hepatic glycogen due to over-training (McGowan, 2008). Serum GGT activity appears to be correlated with cumulative training load and racing frequency (Mack et al., 2014) and maladaptation to training (Leleu & Haentjens, 2010).

GGT levels usually return to normal in affected horses after a period of rest. Alkaline phosphatase can be released from several sites, including bone, intestine, and placenta, which limits its clinical value in assessing hepatobiliary disease. The hematocrit, serum iron concentration, and percentage iron saturation are frequently high in horses with severe liver disease.

Identification of increased hepatic-derived enzymes is used to diagnose liver damage, but the magnitude of the increases is not sufficiently reliable to predict prognosis (Divers, 2015). Prognosis is best assessed by function test abnormalities, in conjunction with identification of the etiology and the presence or absence of hepatic encephalopathy (Durham et al., 2003).

As mentioned previously, serum levels of hepatocellular liver enzymes may be increased in many systemic inflammatory diseases, probably as a result of secondary inflammatory, vascular, hypoxic, and toxic insults to the liver (Divers, 2015). Bile acids can also be increased in horses with intestinal disorders, including enteritis and equine dysautonomia (grass sickness); this is likely to be a result of both liver damage and ileus. The severity of the increase in serum bile acid concentration has been associated with prognosis in horses undergoing abdominal surgery for colic (Underwood et al., 2010).

Liver Function Tests

Liver function tests only become abnormal when approximately 80% of liver function is lost. These tests include direct (conjugated) and indirect (unconjugated) bilirubin, blood ammonia, bile acids, prothrombin and partial thromboplastin time, serum iron, and gammaglobulins (with chronic disease) (Pearson, 1999). An increase in direct bilirubin is a highly sensitive and moderately specific marker of liver failure due to either hepatocellular or hepatobiliary disease. Levels of both unconjugated (indirect reacting) and conjugated (direct reacting) bilirubin are helpful diagnostically. An increase in direct bilirubin of 25% or more of the total bilirubin is suggestive of a predominant biliary or obstructive disease (Peek & Divers, 2000). Clinically evident jaundice is associated with marked unconjugated hyperbilirubinemia, but in the absence of other biochemical evidence of liver disease is suggestive of anorexia or hemolytic anemia. Occasionally, persistent increases in unconjugated bilirubin may occur in healthy horses presumably due to decreased levels of the conjugating enzyme glucuronyltransferase (Divers et al., 1993). Septic foals and some adult horses with intestinal ileus sometimes have increases in direct bilirubin with minimal or no evidence of hepatocellular dysfunction; treatment should focus on the sepsis and intestinal ileus. Levels of both blood urea nitrogen (BUN) and albumin may be decreased with chronic liver diseases.

Serum or plasma bile acids are increased in horses with both hepatocellular and hepatobiliary disorders, and can be an early predictor of liver failure when values exceed 30 µmol/L (West, 1989; McGorum et al., 1999). Unlike in other species, fasting samples are not required to interpret bile acid results in horses, although mild increases in bile acids (up to 20 µmol/L) may occur as a result of anorexia (Hoffmann et al., 1987). Bile acids >30 µmol/L are a prognostic indicator in horses with chronic disease and fibrosis, but are not a good prognostic test in horses with acute diseases or cholangiohepatitis.

Blood ammonia concentration can also be used as an assessment of liver function; however, rapid and careful sample handling is required. Ideally, a control sample should be obtained from a healthy horse, handled identically and measured simultaneously for comparative purposes. Dye excretion tests (such as bromosulfophthalein and indocyanine green) are rarely used to assess liver function.

Other Biochemical Tests

Serum triglycerides are increased in equines with hepatic lipidosis. In states of negative energy balance, serum triglyceride concentrations increase, but in the absence of lipemia, liver failure rarely occurs (Dunkel & McKenzie, 2003). In foals with hepatic failure, hypoglycemia is often present, whereas in adult horses, blood glucose is more often normal or increased, although it may be decreased in a small number of cases (McGorum et al., 1999; Divers, 2015).

Plasma lactate concentration is often high and bicarbonate concentration low in horses with fulminant hepatic failure (Divers, 2015). Serum albumin concentration is inconsistently and only mildly decreased in both acute and chronic liver diseases. Serum globulin concentration, on the other hand, is often increased in horses with liver failure (Parraga et al., 1995; Durham et al., 2003).

There may be a decrease in BUN concentration in horses with liver failure, as a result of failure of the hepatic urea cycle. An increase in the prothrombin time (PT) and partial thromboplastin time (PTT) may also occur as a result of decreased hepatic synthesis of factors II, V, VII, IX, X, XI, and XII. Despite these abnormalities, clinical bleeding is rare after liver biopsy, and the technique can be performed safely in most horses with liver disease (Johns & Sweeney, 2008).

Liver Ultrasonography and Biopsy

Ultrasound examination and liver biopsy are the two most commonly used ancillary tests for detecting liver disease. Transabdominal ultrasonography is best performed with either a 2.5 or 5 MHz transducer (see Chapter 23). In neonatal foals, 7.5 or 10 MHz transducers are effective. The liver is best imaged from the right,

immediately caudal and ventral to the lung. Typical landmarks for imaging the liver are moving ventral to dorsal, the 6–15th intercostal spaces on the right, and the 6–9th intercostal spaces on the left. In neonatal foals, the liver can also be imaged from the ventral abdomen. In adults, the image quality and usefulness of the procedure are variable, depending on factors such as the underlying disease, normal age changes (atrophy of the right lobe occurs in old horses), extent of the lung fields, degree of gas distention of the colon, and amount of subcutaneous fat. Healthy liver tissue is less echogenic than the spleen and has a more prominent vascular pattern. The portal veins can be distinguished from the hepatic veins by the greater amount of fibrous tissue in the walls of the portal vessels. Bile ducts are not visible in the normal liver. Abnormalities that may be detected by ultrasound examination include dilated bile ducts (Figure 51.6), biliary sludge, biliary stones, hepatic fibrosis (Figure 51.7), hepatomegaly, smaller than normal liver (highly subjective), hepatic lipidosis, and hepatic masses.

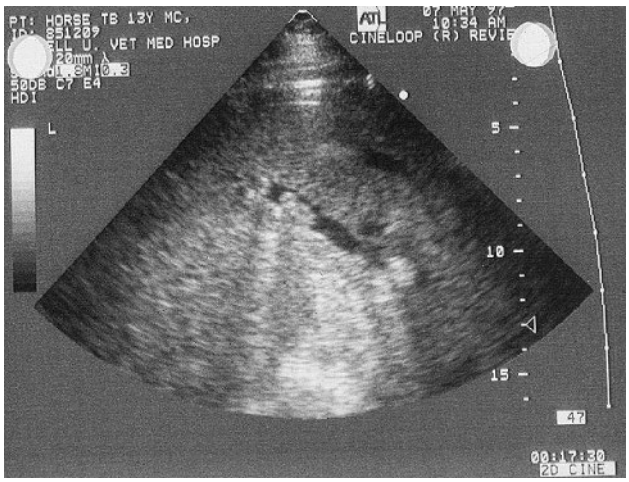


Figure 51.6 Transcutaneous ultrasonogram of the right side of the liver in a horse with cholangitis, showing a distended bile duct and cholelith.

Liver biopsy is best performed after the liver has been identified on ultrasound examination on either the right or left side. Tru-Cut biopsy needles provide excellent tissue samples in most cases; alternatively, spring-loaded biopsy needles or other ultrasound-guided techniques can be used. In the absence of ultrasound guidance, a biopsy can usually be obtained "blindly" using anatomic landmarks on the horse's right side; however, a recent study reported that using these traditional landmarks, failure to obtain liver and puncture of the lungs or intestine are likely in a significant number of cases, thereby increasing the risks of complications (Sammons et al., 2014). Biopsies are not required in many cases of liver disease; if, for example, the clinical and laboratory data suggest a specific disease (e.g., hepatic lipidosis or Theiler disease), then biopsy information is unlikely to be of added benefit. Liver biopsies are best used in cases of chronic disease or when bacterial culture is required. The results of biopsy can be used to determine the amount of fibrosis, inflammation, and predominant location of disease, and for culture purposes (Pearson & Craig, 1980). Pre-biopsy evaluation of extrinsic, intrinsic, and common clotting function, by measurement of PT and activated partial thromboplastin time (APTT), is often recommended, but hemorrhage after biopsy is rare (Johns & Sweeney, 2008). The risk of hemorrhage may be higher in adults with Theiler disease and foals with Tyzzer disease.

Occasionally, the liver will not be visible ultrasonographically on the right-hand side. In such cases, a biopsy may be obtained from the left side, but this may be associated with an increased risk of post-biopsy colic (Divers, 2015).

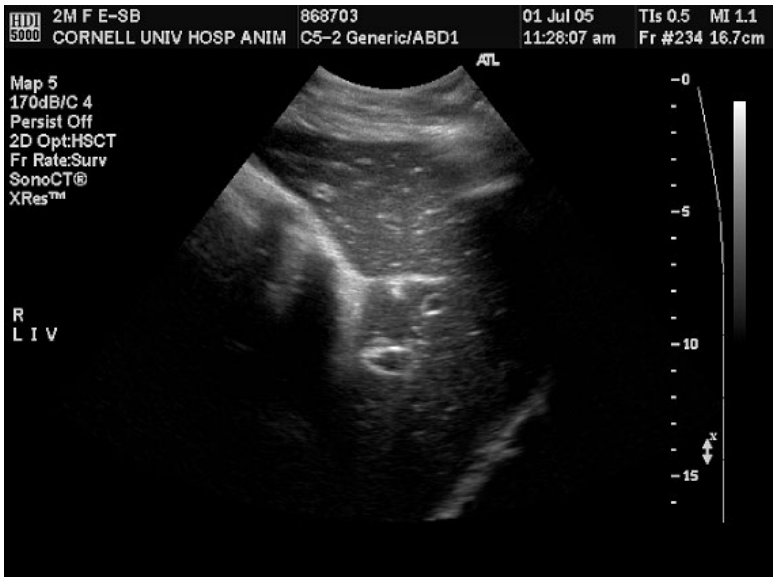


Figure 51.7 Ultrasonogram of the liver of a foal showing echogenic foci suggestive of hepatic fibrosis.

Hepatic Encephalopathy

Neurologic signs are frequently observed in patients with acute hepatic failure and are referred to as hepatic encephalopathy (hepatoencephalopathy). Hepatic encephalopathy is a metabolically induced, potentially reversible, functional disorder of the brain. Neurologic signs are the most pronounced and clinically troublesome signs in most cases of equine hepatic failure. Signs of hepatic encephalopathy may vary from depression and anorexia to bizarre maniacal behaviors. Common signs include blindness, ataxia, head pressing (Figure 51.8), propulsive circling, frequent yawning, and coma. Ataxia may be present in some cases, but not in others (Nout, 2011). Clinical examination may reveal decreased muscle tone of the lower lips, delayed or absent response to touching the inner nares, and cortical blindness, often accompanied by mydriasis (Divers, 2015). Laryngeal paralysis (Hughes et al., 2009), dysphagia, and gastric impaction (Milne et al., 1990) may also occur.

The pathophysiologic mechanism of hepatoencephalopathy is undoubtedly complex (and beyond the scope of this chapter), but involves several gut-derived neurotoxins, cerebral and systemic inflammation, cerebral vascular dysfunction, and neuroendocrine abnormalities (Sturgeon & Shawcross, 2014; Divers, 2015). The failing liver may be unable to convert colonic-derived ammonia to urea sufficiently via urea cycle enzymes located in the hepatocyte. Ammonia is toxic at high concentrations and is able to cross the blood–brain barrier. The effect of excessive ammonia on the CNS may include increases in neurotoxins (glutamine at high concentrations) in astrocytes, imbalances of neurotransmitters (glutamate and gamma-aminobutyric acid) at the neuronal synapse, systemic inflammation, structural changes in the blood–brain barrier, and changes in cerebral blood flow.

Cerebral edema with development of Alzheimer type 2 cells is characteristic of high CNS concentrations of ammonia. Alzheimer type 2 cells may result from hepatic failure, primary hyperammonemia, or severe uremia. In rare cases, the cerebral edema may be so severe that herniation occurs. Additionally, possible decreased hepatic extraction of gut-synthesized gamma-aminobutyric acid (GABA) may serve as a potent inhibitory neurotransmitter if the blood–brain barrier is abnormal. With hepatoencephalopathy, the majority of GABA (inhibitory) is produced from glutamate (excitatory) during the metabolism/detoxification of glutamine to glutamate in the neurons. The GABAergic neurotransmission is also closely linked to an increase in natural benzodiazepines. Furthermore, abnormal accumulation of glutamate may serve as excitatory neurotoxins. Complex interactions among these neurotoxins may determine if the horse with hepatic encephalopathy is depressed or maniacal. If the blood–brain barrier is abnormal, the movement of GABA into the CNS may be aided by an increased ratio of aromatic to branched-chain amino acids in the plasma, and by increased concentrations of plasma bile acids. Increased amounts of aromatic amino acids, which are normally metabolized by the liver, may also serve as false neurotransmitters. In adult horses with hepatic failure, the CNS signs of severe depression are rarely caused by inadequate hepatic gluconeogenesis and hypoglycemia. Systemic inflammation and sepsis from endotoxemia or bacterial

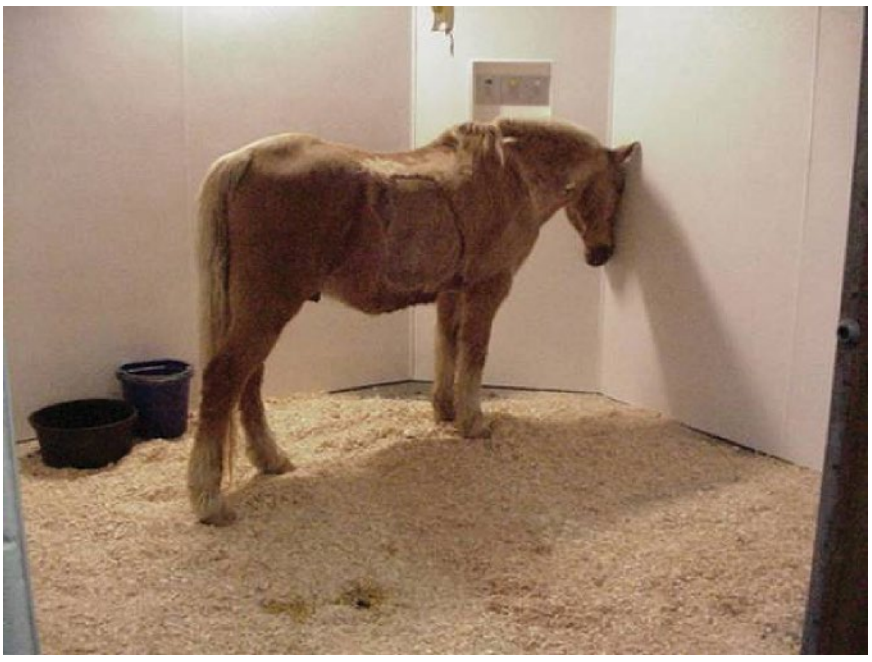


Figure 51.8 Head pressing – a common sign of hepatic encephalopathy.

translocation are often part of the syndrome of hepatic encephalopathy.

Laboratory findings that are observed in hepatic encephalopathy include hyperammonemia, occasionally hypoglycemia, and metabolic acidosis (lactic acidosis). Occasionally, horses with hepatic encephalopathy have normal blood ammonia concentrations (<90 µmol/L) (Divers, 2015). Many horses with hepatic encephalopathy will have blood ammonia concentrations in the range 100–200 µmol/L or higher.

Treatments for hepatic encephalopathy include reducing the levels of enteric-derived neurotoxins (principally ammonia), decreasing cerebral edema, correcting glucose, electrolyte, and acid–base abnormalities, and maintaining perfusion and oxygenation of the brain and other vital organs (Divers, 2015). Treatment for the underlying liver disease should also be instituted where possible. Additional supportive treatments should aim to reduce systemic and neural inflammation, reduce oxidative stress, and prevent multiple organ dysfunction. Fluid therapy should be utilized to correct intravascular fluid deficits and maintain organ perfusion; this could involve administration of hypertonic saline followed by a balanced crystalloid fluid supplemented with 50 g/L of dextrose and 20 mEq/L of KCl. If sedation is required, a low dose of detomidine (5–10 µg/kg IV) can be useful. Oversedation should be avoided to prevent excessive lowering of the head, which might exacerbate cerebral edema. Propofol (2 mg/kg IV) can also be used. If longer term sedation is required, pregabalin (3 mg/kg PO every 12 h) or gabapentin (5–12 mg/kg PO every 12 h) could be used. For profound coma, sarmazenil (0.04 mg/kg IV) or flumazenil (0.1 mg/kg IV) may be considered.

Attempts should be made to reduce the blood and cerebrospinal fluid (CSF) ammonia concentrations. Neomycin (10–20 mg/kg PO every 8 h) or another poorly absorbed antibiotic may be administered for up to 3 days to reduce the levels of ammonia-producing enteric bacteria. Metronidazole could also be administered per os to decrease enteric ammonia, but it is metabolized by the liver and high systemic concentrations are neurotoxic. Lactulose (0.3–0.5 mL/kg PO every 8 h) may help to reduce available ammonia in the large bowel. Probiotics and prebiotics have been used in people with hepatic encephalopathy and could be helpful in horses, although evidence for their efficacy is lacking. Treatments to support energy metabolism and antioxidant activity to the brain include B vitamins, vitamin C, and dimethyl sulfoxide (DMSO). Treatment of cerebral edema with mannitol or hypertonic saline may be of temporary benefit (Divers, 2015). Oral supplementation of branch-chain amino acids (valine, leucine, and isoleucine) is often recommended, but the true benefits, if any, are currently uncertain.

Primary Hyperammonemia

Primary or enteric hyperammonemia was first recognized in the 1990s (Mair & Jones, 1995; Peek et al., 1997), with more cases being described subsequently (Dunkel et al., 2011). Affected horses frequently present with anorexia and mild colic initially, followed by acute onset of neurologic signs of encephalopathy (head pressing, circling, maniacal behavior, blindness, mydriasis, etc.) 24–48 h later. Some cases follow on from primary enteritis or colitis, including horses infected by equine coronavirus (Fielding et al., 2015), salmonellosis and Potomac horse fever (Divers, 2015). This condition has also been recognized after surgical correction of a number of diseases that cause acute colic. However, in the majority of recorded cases, there is no predisposing disease. All ages, breeds, and sexes can be affected.

Affected horses have no evidence of liver disease, either on laboratory investigations or postmortem examinations. Alzheimer type 2 cells can usually be identified in the brains of horses that die. Characteristic laboratory abnormalities include hyperammonemia (often >200 µmol/L), hyperglycemia, erythrocytosis, and hyperlactatemia.

Although the cause of primary hyperammonemia is unknown, it is likely associated with increased enteric production of ammonia and increased intestinal permeability, that results in systemic absorption of ammonia that overwhelms the liver's capacity to metabolize it.

Treatment for primary hyperammonenia is the same as that for hepatic encephalopathy, with additional treatment of any underlying primary disease (if known). Approximately half of affected horses improve after appropriate treatment and half die. Those horses that survive usually show signs of improvement in 24–48 h with complete recovery by about 72 h (Divers, 2015).

Hyperlipemia and Hepatic Lipidosis

Hyperlipemia is a disorder of lipid metabolism characterized by hypertriglyceridemia and fatty infiltration of body organs (Jeffcott & Field, 1985; Watson et al., 1992; Watson & Love, 1994; Watson, 1998; McKenzie, 2011). The condition is usually precipitated by periods of anorexia, malnutrition, stress, and other diseases, and occurs most commonly in the winter months. The clinical signs are often vague initially, but the condition progresses rapidly and is frequently fatal unless early and aggressive therapy is instituted. Hepatic lipidosis with concurrent hyperlipemia is the most common metabolic disorder causing equine liver failure (Divers, 2015). Hyperlipidemia, an increase in serum triglycerides and generally without gross lipemia or hepatic lipidosis, occurs in most horses that are anorexic or withheld from feed.

Epidemiology

Hyperlipemia is most common in ponies (such as Shetland ponies and Welsh Mountain ponies), Miniature horses, and donkeys, although it occasionally affects larger horses, including horses with Cushing disease (pituitary pars intermedia dysfunction), lymphoma, and renal disease, and in foals (Moore et al., 1994; Mogg & Palmer, 1995; Hughes et al., 2002; Burden et al., 2011; Dunkel et al., 2014). Two retrospective studies from equine referral hospitals in the United States reported an incidence of hyperlipemia of 11% in Miniature ponies/horses and 18% in donkeys presented to these hospitals (Moore et al., 1994; Mogg & Palmer, 1995).

The incidence of hyperlipemia is higher in mares than in stallions and geldings. This predisposition is partly explained by the fact that hyperlipemia is common in pregnant and lactating mares; however, females also appear to be at higher risk independently of reproductive status (Reid & Mohammed, 1996). Hyperlipemia can occur in horses and donkeys of all ages, although it is uncommon in animals less than 18 months of age, with older animals being at greater risk (possibly because of an age-related decrease in insulin sensitivity). It is occasionally diagnosed in ill foals and has occurred as a congenital condition in foals born to hyperlipemic dams.

Hyperlipemia often develops as a complication of other diseases, especially gastrointestinal diseases. Some of the more common diseases identified in association with hyperlipemia are summarized in Box 51.2. Many of these diseases are thought to predispose to hyperlipemia by causing inappetence or anorexia (Naylor et al., 1980). In addition to disease, hyperlipemia may be induced by periods of enforced malnutrition, such as inadequate availability of pasture or competition for food. Pregnant mares, especially in the last trimester, and lactating mares have increased nutritional requirements and are, therefore, at greater risk of developing hyperlipemia. Obesity and stress are other important risk factors for the development of the disease. Stress factors that have been implicated include transportation, change of environment or diet, inclement weather, and the stress of pregnancy, lactation, and disease. Donkeys subjected to social reordering and donkeys that pine for missing mates can also be affected. Sometimes, hyperlipemia and hepatic lipidosis have been observed in obese adult ponies that do not have any obvious additional risk factors, suggesting that insulin resistance is the basic mechanism for the lipemia in such cases (Freestone et al., 1991).

Box 51.2 Diseases and conditions commonly associated with hyperlipemia

- Intestinal parasitism
- Colitis
- Colonic impaction
- Gastric impaction
- Dysphagia and dental disorders
- Esophageal obstruction
- Esophageal ulceration
- Lymphoma and other forms of neoplasia
- Pituitary pars intermedia dysfunction (Cushing disease)
- Peritonitis
- Metritis
- Laminitis
- Renal failure
- Liver disease
- Septicemia
- Hypocalcemic tetany
- Postinjection abscess
- Subsolar abscess

Pathogenesis

Hyperlipemia represents an excessively rapid mobilization of the body's fat reserves in response to stress or failure to maintain energy homeostasis. Decreases in feed intake, increased energy demands, such as occur with pregnancy and lactation, and increased stress hormone release are known to increase lipolysis of fat stores (Durham, 2013). In response to negative energy balance and after depletion of glycogen reserves, nonesterified fatty acids (NEFAs) are mobilized from fat stores and released into the circulation. Lipolysis associated with negative energy balance is stimulated by insulin. Increases in stress hormones enhance lipolysis by either decreasing insulin sensitivity or by up-regulating hormone-sensitive lipase and adipose triglyceride lipase (Durham, 2013). The majority of NEFAs are taken up by the liver, where they may overwhelm the oxidative, gluconeogenic, and ketogenic pathways and are esterified to form triglycerides. Triglycerides then both accumulate in the liver and are exported in the circulation as very low-density lipoproteins (VLDLs). This process occurs at such a fast rate that the VLDLs cannot be utilized by peripheral tissues, and plasma levels become excessive. VLDLs are also taken up by cells of the reticuloendothelial system, resulting in fatty infiltration of many organs.

Adipose tissues represent energy stores that form as a result of esterification of free fatty acids to produce triglycerides. This esterification is promoted by the action of insulin and glucose. In the presence of negative energy balance, lipolysis takes place in adipose tissues, mediated by glucagon, which activates the enzyme hormone-sensitive lipase. This hormone is normally inhibited by insulin and glucose, but with reduced glucose and insulin levels (which occur in negative energy

balance) and enhanced glucagon activity, lipase is activated. It can also be activated by hormones released in response to stress [such as adrenocorticotrophic hormone (ACTH), glucocorticoids, and catecholamines] and by hormones released in pregnancy and lactation (progesterone and growth hormone).

The lipolysis induced by hormone-sensitive lipase results in the release of NEFAs into the circulation, which may be used by tissues for oxidation as a source of energy. However, most NEFAs are taken up by the liver, where they can be used for ketogenesis or gluconeogenesis, or they are esterified to form triglycerides. The horse has a poor capacity for ketogenesis, and most NEFAs are used to produce triglycerides. These triglycerides are exported from the liver as VLDLs, which can be used as a source of energy in peripheral tissues or restored in adipose tissue. In the presence of food deprivation, plasma VLDLs increase excessively and triglycerides accumulate in the liver.

The clearance of VLDL triglycerides from the circulation is promoted by lipoprotein lipase. It has been suggested that increased plasma triglyceride levels in hyperlipemia may be caused by reduced clearance of VLDLs resulting from inhibition of the action of lipoprotein lipase. Lipoprotein lipase activity may be inhibited by azotemia and endotoxemia; however, studies of ponies with hyperlipemia suggest that the activity of lipoprotein lipase is increased rather than reduced.

Insulin resistance probably plays an important role in the pathogenesis of hyperlipemia. Tissue resistance to insulin results in a diminished ability to regulate hormone-sensitive lipase. Thus, when this enzyme is activated in response to a negative energy balance, or as a result of stress or concurrent disease, lipolysis progresses in an excessive and uncontrolled way. Nonesterified fatty acids are released in excessive amounts that overwhelm the liver's oxidative, gluconeogenic, and ketogenic capacity, so that triglycerides are produced, resulting in hypertriglyceridemia and hyperlipemia. Insulin resistance is common in ponies and donkeys, and is exacerbated by obesity and pregnancy and lactation.

Clinical Signs

Clinical signs of hyperlipemia are compounded by the signs relating to the underlying disease or cause, such as diarrhea or dysphagia. In addition, fatty infiltration of the liver and kidneys may produce signs of hepatic and renal failure. The initial signs of hyperlipemia are often vague and include anorexia, lethargy, and weakness (Box 51.3). Rapid progression of the disease is common, with the development of ataxia, muscle fasciculations, head pressing, profound depression, recumbency, convulsions, coma, and death. Sudden death occasionally occurs as a result of hepatic rupture (Figure 51.9). Dysphagia is observed in some cases, and may result from encephalopathy or myopathy involving the muscles of mastication. Alternatively, dysphagia may be caused by an underlying primary esophageal disease such as choke. Pregnant mares may abort spontaneously or undergo premature labor.

Box 51.3 Clinical signs of hyperlipemia

- Anorexia
- Lethargy and depression
- Weakness
- Ataxia
- Muscle fasciculations
- Dysphagia
- Sham drinking
- Profound depression
- Head pressing (Figure 51.8)
- Circling
- Recumbency
- Seizures
- Nystagmus
- Weight loss
- Ventral edema
- Ascites
- Abdominal pain
- Reduced intestinal motility and fecal output
- Pyrexia
- Tachycardia
- Tachypnea
- Congested mucous membranes
- Icterus
- Halitosis
- Abortion
- Sudden death

Some affected animals demonstrate a period of rapid weight loss and development of ventral edema at the onset of the disease. This may reflect the primary underlying disease or may occur as a consequence of subcutaneous thrombosis caused by the hyperlipemia. Edema might also develop as a result of rapid fatty infiltration of the liver, partial obstruction of the portal circulation, and increased hydrostatic pressure in subcutaneous abdominal veins. Likewise, mild intermittent abdominal pain (restlessness, flank watching, and rolling) may be caused by a primary gastrointestinal disease, or may occur as a result of hepatomegaly and stretching of the liver capsule. Intestinal motility and fecal output are often reduced, and this may predispose to colonic impaction.

The clinical course of hyperlipemia is rapid in most cases. The average interval between the onset of clinical signs and death or euthanasia is 6–10 days. In a few cases, a more protracted clinical course may occur.

Figure 51.9 Hyperlipemia. Fatty infiltration of the liver with rupture of the liver capsule.

Figure 51.10 Hyperlipemia. Gross lipemia of the serum.

Diagnosis

Gross lipemia in blood samples centrifuged or left to stand is the simplest way to diagnose hyperlipemia in practice (Figure 51.10). This is a relatively insensitive method of diagnosis, especially in animals with mild degrees of hyperlipemia and those with hyperlipidemia. Accurate measurements of plasma triglyceride levels are recommended to assess the degree of hyperlipemia and to monitor the course of the disease during treatment.

Plasma triglyceride levels exceeding 5 mmol/L (500 mg/mL) in ponies with clinical signs of hyperlipemia are diagnostic. Triglyceride concentrations of 1–5 mmol/L (100–500 mg/mL) can be present in ponies without clinical or pathologic evidence of hyperlipemia. This has been classified as hyperlipidemia or hypertriglyceridemia, and may sometimes progress to hyperlipemia if adequate nutritional support is not provided. Triglyceride levels in this range can sometimes be present in clinically normal pony mares during pregnancy. Normal plasma triglyceride levels in donkeys are higher than in ponies. Healthy, nonpregnant donkeys may have plasma triglyceride levels as high as 3.5 mmol/L (350 mg/mL). Triglyceride levels in suckling foals are also higher than in adults because of their relatively high daily intake of fat.

Plasma concentrations of other lipids, such as cholesterol, phospholipids, and free fatty acids, are also increased in hyperlipemia; however, increases in concentrations of these lipids are not as great as those of triglycerides, and they are not routinely assessed for diagnosis. Identification of fatty infiltration of liver biopsies is diagnostic but has no advantage over simple measurements of plasma triglycerides.

Clinical Chemistry

Monitoring of serum or plasma biochemistry panels can help to (1) detect the presence and severity of organ failure in hyperlipemia, (2) determine appropriate supportive therapies, (3) monitor the course of treatment, and (4) detect underlying primary conditions. Box 51.4 lists an appropriate biochemistry panel for this purpose.

Biochemical measurements of some substances may be complicated because of interference by high triglyceride levels. This can be overcome by clearing the plasma or serum of lipids prior to analysis by ultracentrifugation or chemical precipitation.

Blood glucose concentrations may be normal, low, or increased, depending on the duration of anorexia, previous glucose therapy, and the presence or absence of Cushing disease. Metabolic acidosis is often present, as shown by decreased arterial pH, decreased PCO_2, decreased bicarbonate levels, and a base deficit of up to 24 mEq/L.

Fatty infiltration of the liver results in increases of liver-derived enzymes, including GGT, LDH, SDH, and alkaline phosphatase. However, the pattern of changes in hepatic enzyme levels can be inconsistent, with nearly

Box 51.4 Biochemistry panel for investigating and monitoring hyperlipemia in equids (Watson, 1998)

Metabolic status
- triglycerides
- glucose
- hydration status –albumin
- PCV
- electrolytes – Na^+
  K^+
  Cl^-
  Ca^{2+}
- acid–base status – pH
  HCO_3^-
  PCO_2

Liver damage and function
- gamma-glutamyl transferase (GGT)
- alkaline phosphatase
- bile acids
- ammonia

Renal function
- ammonia
- urea nitrogen
- creatinine

normal GGT activities in some cases (Divers, 2015). The variability of serum activities of hepatic enzymes may reflect variations in the amount of inflammation of hepatocytes and variable biliary obstruction between cases (Divers, 2015). Liver function may be impaired, as assessed by increases in bilirubin, bile acids, and ammonia. Fatty infiltration of the kidneys can result in impaired renal function and increased plasma concentrations of urea and creatinine. These metabolites may also be increased as a result of dehydration, and reassessment after hydration is required to assess the degree of renal failure.

Plasma albumin concentrations may be normal, increased (associated with dehydration), or reduced (associated with chronic hepatopathy, a primary gastrointestinal lesion, or parasitism). Serum protein electrophoresis can be helpful in assessing underlying conditions such as intestinal parasitism.

Pathologic Findings

Typical pathologic findings in ponies and donkeys affected by hyperlipemia include fatty infiltration of the tissues, especially the liver and kidneys. The liver and kidneys are enlarged, yellow, friable, and greasy. In severe cases, the surface of the liver may be fissured, or there may be capsular rupture (Figure 51.9) and associated hemorrhage. Fatty infiltration of other organs, including the adrenals, skeletal muscle, and myocardium, may be evident. Necrotizing pancreatitis is present in some cases. Vascular thrombosis can occur secondary to hyperlipemia and fat embolism, and can result in focal hemorrhages, myocardial infarction, and renal infarction.

Figure 51.11 Small, shrunken liver from a horse suffering from Theiler disease (right) compared with a normal liver (left)

Treatment

The treatment of hyperlipemia has five different objectives (Watson, 1998):

1) treatment of underlying or concurrent disease
2) correction of dehydration, electrolyte, and acid–base imbalances
3) symptomatic therapies
4) nutritional support
5) normalization of lipid metabolism.

Treatment of Underlying or Concurrent Disease

Intestinal parasitism is a common cause of hyperlipemia in ponies and donkeys; therefore, appropriate anthelmintic therapy is required in all cases with confirmed parasitic burdens and should be administered in all other cases where no obvious cause of the hyperlipemia is identified. Other treatments for underlying diseases should be administered as appropriate, such as pergolide

therapy for pituitary pars intermedia dysfunction (Dunkel et al., 2014). Horses with Cushing disease and hyperlipemia rarely develop the metabolic crisis associated with hyperlipemia in ponies, donkeys, and Miniature horses.

Correction of Dehydration, Electrolyte, and Acid–Base Disturbances

Correction of dehydration, electrolyte, and acid–base abnormalities is essential. Intravenous fluid and electrolyte therapy are generally required. Correction of severe acidosis in the presence of liver failure may require the intravenous administration of bicarbonate. Blood gas analysis should be used when available to monitor the response to bicarbonate therapy, as too rapid an increase in blood pH may exacerbate signs of hepatic encephalopathy, and overdosing with bicarbonate can lead to persistent metabolic alkalosis and respiratory depression.

Dextrose should be added to the intravenous polyionic fluids or administered as 5% dextrose solutions in animals with hypoglycemia. When 5% dextrose solutions are being administered, serum electrolytes should be monitored, and potassium chloride or calcium gluconate administered as necessary. Care must be taken to avoid overdosing with dextrose, as this can result in transient or prolonged periods of hyperglycemia with associated diuresis, dehydration, and hyponatremia.

Symptomatic Therapies

Symptomatic therapies include the use of analgesic drugs, nonsteroidal anti-inflammatory drugs (NSAIDs), and anti-ulcer treatments. These are used as necessary on an individual basis. Therapies for hepatic encephalopathy may also be beneficial. Plasma transfusions have been used in hyperlipemic patients with hypoproteinemia and endotoxemia, and in foals with failure of passive transfer of immunity.

Nutritional Support

Nutritional support is an essential component of therapy of hyperlipemia in all cases. Affected animals should be maintained in positive energy balance in order to limit the mobilization of NEFAs from adipose tissues.

In animals that are still eating, fresh and highly palatable foods, such as grass, leafy hay, rolled grains, and high-energy feeds with added molasses, should be fed. Syringe feeding 30 mL of corn syrup two to six times per day has been recommended as a simple method for increasing caloric intake (Mogg & Palmer, 1995). In animals that are inappetent or anorexic, enteral feeding via a nasogastric tube should be undertaken. Even in animals that are still eating voluntarily, supplementation by enteral feeding should be considered if plasma triglyceride levels exceed 5 mmol/L (500 mg/mL).

Glucose and electrolyte solutions, commercial enteral formulations, and slurries made from hay or pelleted feeds can all be administered by nasogastric tube. Nutritionally complete formulations are preferred over simple glucose solutions for enteral administration (Burkholder & Thatcher, 1992; Golenz et al., 1992). Commercial enteral formulations for use in humans have been used successfully in ponies and donkeys with hyperlipemia (Golenz et al., 1992), but there is a risk of diarrhea and laminitis. Although there are numerous commercially available human enteral nutrition products, a low-fat or medium-chain triglyceride fat supplement is preferred for forced enteral feeding (Moore et al., 1994).

A common formula for enteral feeding of ponies and Miniature horses with hepatic lipidosis and hyperlipemia consists of 100–200 g of glucose, 400 g of whey, and 50–100 g of alfalfa meal mixed in 2 L of water and administered every 8 h via nasogastric feeding tube (Divers, 2015); 5–10 g of potassium chloride and multiple B vitamins are also added to the slurry. The gruel must be kept sufficiently thin to flow down the nasogastric tube. Plasma glucose levels should be monitored on a daily basis during the period of treatment, as excessive glucose administration might exacerbate lactic acidosis.

In affected animals with compromised esophageal or gastrointestinal function, such as ileus and diarrhea, intravenous (parenteral) nutrition is required (Moore et al., 1994; Durham, 2006). In most cases, constant intravenous administration of 5% dextrose at 1–2 mL/kg/h is used. Although this will not meet the animal's total nutritional requirements, it has proven effective in clinical cases. Overdosing with glucose must be avoided as it can result in diuresis, dehydration, hyponatremia, and enhancement of hepatic lipidosis. Amino acid solutions (1 g/kg body weight) can also be administered intravenously, but this significantly increases the cost of treatment. Plasma glucose levels should be monitored regularly, and electrolytes added as necessary. Human parenteral nutrition formulations can also be used, but these preparations are expensive and careful monitoring is required.

Exogenous insulin therapy may be necessary if the affected animal is hyperglycemic. Despite the inherent decrease in insulin sensitivity in hyperlipemic ponies, exogenous insulin can decrease hyperlipemia, inhibit lipolysis, and improve cellular energy balance. However, although there are several reports of the use of exogenous insulin (Dunkel et al., 2014; Durham, 2013), there have been no controlled studies that have assessed its efficacy (Divers, 2015). An intermediate or long-acting insulin suspension can be administered subcutaneously (0.10–0.15 IU/kg) every 12 or 24 h, respectively. For severe hyperglycemia, a short-acting regular insulin can be administered at 0.05–0.1 IU/kg/h as a constant-rate

infusion (Divers, 2015). Blood glucose and potassium concentrations should be monitored when insulin is being used.

Anabolic steroids and multivitamin preparations are commonly administered to hyperlipemic patients to assist hepatic function. Intravenous or orally administered B vitamins in particular are helpful. Corticosteroids should be avoided because they stimulate hormone-sensitive lipase and may induce laminitis.

The induction of abortion or premature foaling in pregnant mares has been recommended, as this significantly reduces the demands for energy. However, prematurely delivered foals have a high mortality rate because of their immaturity of body systems and susceptibility to infectious disease. A risk also exists of retained placenta and laminitis in the mare. Lactating mares that develop hyperlipemia should have their foals weaned, if possible.

Normalization of Lipid Metabolism

Two approaches to modifying lipid metabolism in hyperlipemic patients are possible: (1) reducing the net release of NEFAs from adipose tissues and (2) accelerating the removal of triglycerides from plasma VLDLs to adipose tissues and skeletal muscle.

The release of NEFAs from adipose tissue is promoted by the action of hormone-sensitive lipase. Reducing the stimulus for lipolysis may be achieved by providing a positive energy balance, removing stress factors, and removing the hormonal influences of pregnancy and lactation.

The activity of hormone-sensitive lipase is inhibited by the action of insulin, and exogenous insulin therapy has therefore been recommended in the treatment of hyperlipemia, in addition to its role in regulating blood glucose concentration.

Stimulation of lipoprotein lipase in order to increase the clearance of triglycerides from the plasma has been attempted with heparin therapy. Although not recommended, 100–200 IU/kg of heparin has been administered intravenously twice per day as treatment for hyperlipemia. The rationale for this therapy is questionable because the activity of lipoprotein lipase in affected ponies has been shown to be at its physiologic maximum. Heparin therapy also poses an increased risk of hemorrhage.

Prognosis

The prognosis for animals with hyperlipemia has been reported to be poor (Watson, 1998). The reported mortality rate for the disease (including animals that are euthanized) ranges from 57 to 85%. In individual patients, the nature and severity of the underlying disease and the promptness of treatment and nutritional support have important impacts on the prognosis and the outcome might be much better than previously reported. The degree of lipemia or increase in hepatic enzyme activities does not appear to influence the prognosis, although animals with hyperlipidemia (triglycerides <5 mmol/L) have a much better prognosis than those with hyperlipemia (triglycerides >5 mmol/L). Hyperlipemic horses with pituitary pars intermedia dysfunction that are treated with pergolide in addition to general and supportive treatment generally have a good prognosis.

Plasma triglycerides and blood biochemistry should be monitored during treatment, and the results can be helpful in assessing the prognosis. In animals that recover, plasma triglycerides usually return to normal values within 3–10 days. Early diagnosis and prompt initiation of therapy result in the best chances for survival.

Prevention

Risk factors for hyperlipemia in susceptible classes of equids include obesity, malnutrition, pregnancy, lactation, stressors such as transportation, inclement weather, social reordering, and parasitism. Avoiding these factors, therefore, will help in preventing this disease. Particular emphasis should be placed on providing adequate nutrition to susceptible animals without allowing them to become obese, and providing good routine parasite control measures. Food intake and general demeanor should be carefully monitored after periods of enforced stress, such as disease, transportation, inclement weather, and change of environment. Exercise regimes may be helpful in reducing insulin insensitivity. Plasma triglyceride levels may also be measured at times of stress and during pregnancy and lactation. The early identification and treatment of hyperlipemia are far more likely to result in recovery than identification later in the course of the disease.

Theiler Disease (Serum Hepatitis)

Theiler disease (acute hepatic necrosis, serum hepatitis, serum sickness) is a subacute hepatic necrosis often resulting in hepatic failure and acute encephalopathy in adult horses (Divers, 2015). Sir Arnold Theiler first described the disease in South Africa in 1918 after the vaccination of horses against African horse sickness with live virus and equine-origin antiserum (Theiler, 1918). It has been termed "serum hepatitis" because often the affected horses have a history of receiving an equine-origin biological product (now most commonly tetanus antitoxin) 4–10 weeks prior to the onset of clinical signs (Hjerpe, 1964; Guglick et al., 1995). Cases have been reported after administration of vaccines or antisera to African horse sickness, Eastern and Western encephalomyelitis, anthrax, tetanus antitoxin,

Clostridium perfringens, *Clostridium botulinum*, strangles, influenza, equine herpesvirus-1, pregnant mare's serum, allogenic stem-cell treatments, and commercial plasma transfusion (Hjerpe, 1964; Tennant, 1978; Reed & Andrews, 1986; Messer & Johnson, 1994a, 1994b; Guglick et al., 1995; Aleman et al., 2005). In many other cases, the affected horses may not have received an antitoxin, but may have been in contact with another horse that had received tetanus antitoxin. In other cases, no history exists of equine-origin biological products being administered. The nonbiological-associated disease (which has clinical findings, serum biochemistry findings, and liver histopathology identical with the biological administration-associated disease) appears to be more common in late summer or early fall. This apparent seasonal pattern suggests possible spread by a vector or could simply reflect the fact that many foaling mares may receive tetanus antitoxin in the spring of the year along with their newborn foal. Most commonly, only one horse on a farm is affected, although outbreaks over 4–6 week period are sometimes reported and other horses on these farm may have evidence of liver disease, such as increased enzymes, without clinical signs of hepatic failure. This would support a point-source infection and transmission or a toxicity, but no toxin has ever been found. A specific tetanus antitoxin product and/or the same batch and lot number may be responsible for a high number of cases. A nearly identical clinical and pathologic syndrome has been described in pastured horses in France (Zientara et al., 1994).

The history, onset, clinical signs, and histopathologic findings of Theiler disease are similar to those of hepatitis B virus in humans, and a viral etiology seems likely. In the last few years, three distinct equine hepatitis viruses have been discovered: nonprimate hepacivirus (NPHV, also called hepacivirus), Theiler disease-associated virus (TDAV), and equine pegivirus (EPgV), which are all close Flaviviridae family relatives of human hepatitis C viruses (Burbelo et al., 2012; Chandriani et al., 2013; Kapoor et al., 2013). Although the precise role of these viruses in Theiler disease is not yet established, it is likely that one or more of these (or other) viruses will ultimately be shown to be the cause. In fact, a previously unreported equine DNA virus has now been found in the great majority of Theiler disease cases (of both biological and nonbiological origin) (unpublished information).

Pathologic changes in Theiler disease are limited mostly to the liver (apart from widespread jaundice and intestinal hyperemia). The liver appears smaller than normal (Figure 51.11), but may be enlarged in peracute cases. Histopathologic changes include complete loss of hepatic cord architecture, widespread centrilobular to midzonal hepatocellular necrosis with hemorrhage, and mild to moderate number of lymphocytes and plasma cells in the liver (Robinson et al., 1975).

Clinical Signs

The clinical signs of Theiler disease, or any severe hepatic necrosis, are attributable to the rapid loss of hepatocyte function and collapse of the liver parenchyma (Hjerpe, 1964; Tennant, 1978; Messer & Johnson, 1994a, 1994b; Guglick et al., 1995). The most common clinical signs of Theiler disease are (1) signs of CNS disorder, (2) jaundice, and (3) discolored urine. The CNS signs (hepatic encephalopathy) are variable and may range from acute depression or coma to maniacal behavior and seizures. Affected horses may be blind and/or ataxic. Icteric membranes can be noted in most cases, although in peracute cases this may not be pronounced. The urine may be abnormally dark and have green-colored bubbles when shaken, indicating bilirubinuria, and, in a few cases, red if a microangiopathic hemolytic process is present.

Neurologic signs are frequently observed with acute hepatic failure and are referred to as hepatoencephalopathy, a metabolically induced, potentially reversible, functional disorder of the brain. Signs of hepatoencephalopathy may vary from depression to bizarre maniacal behavior. Common signs include apparent blindness, ataxia, head pressing (Figure 51.8), propulsive circling, and frequent yawning

The pathophysiologic mechanism of hepatoencephalopathy is mostly a result of abnormal hepatic protein metabolism (see the section Hepatic Encephalopathy).

Horses with Theiler disease generally have increases in both conjugated and unconjugated bilirubin, with the increase in unconjugated being the most pronounced. The unconjugated portion becomes increased because of lost hepatocellular function, with reduced uptake and conjugation of the bilirubin. Rarely, other causes of acute hepatic disease and failure may have marked increases in the conjugated bilirubin, also present if there is sufficient biliary obstruction.

Intravascular hemolysis and red discoloration of the urine may be seen occasionally with equine hepatic failure. This occurs most frequently with acute hepatic necrosis, such as in Theiler disease, and is often, but not always, a terminal event. The cause of the hemolysis may be a microangiopathic hemolytic anemia caused by the physical damage to the red blood cells as they pass through the necrotic liver.

Severe bleeding problems are not commonly observed in horses with acute liver failure. When bleeding occurs, it is generally prolonged bleeding associated with hepatoencephalopathy and self-inflicted physical trauma. Hemorrhage in horses with liver failure is generally a result of failure in both the extrinsic and intrinsic pathways of coagulation, causing prolongation of both the PT and PTT. These occur because of decreased hepatic production of clotting factors. Factor VII has the shortest half-life, so the PT should be prolonged prior to prolongation of

the PTT with liver failure. In some horses with liver failure, the PTT may sometimes be prolonged first. The reason for this is unknown. Disseminated intravascular coagulation (DIC) may be present in some horses with acute severe liver failure. The underlying cause of DIC is often multifactorial and may include decreased hepatic production of antithrombin III, plasminogen, and high molecular weight proteins that inhibit excessive coagulation. Additionally, overwhelming hepatic tissue damage and/or increased circulating endotoxin may stimulate the release of soluble proteins that affect coagulation. Fibrin degradation products (FDPs) are often abnormally high in horses with liver failure as the liver is the organ responsible for clearance of circulating FDPs. An increase in FDPs, PT, and PTT would be expected in horses with liver failure, and these findings should not be overinterpreted as being diagnostic for DIC. If a liver biopsy is required, this can generally be performed safely in spite of the prolongation in PT and PTT, because platelet counts generally remain normal in horses with liver failure.

Diagnosis

The history, clinical findings, and laboratory confirmation are used to make the diagnosis of Theiler disease. Acute severe hepatic disease can be detected most easily by measuring serum or plasma activity of liver-derived enzymes, including the following:

- GGT
- AST
- GLDH
- SDH
- LDH (isoenzyme 5).

GGT will be increased in all cases of Theiler disease and is most often in the range 100–300 IU/L. AST should be measured because it may provide an indication of prognosis: those horses having values >4000 IU/L have a poor prognosis. The repeated measurement of AST may also be used to monitor recovery, as the AST would be expected to decrease within 3–5 days if the horse is going to recover. GGT on the other hand, will frequently increase further during the first 3 days of the illness in spite of clinical improvement and eventual recovery. A decrease in SDH in the serum would be expected to occur more rapidly in improving horses than a decrease in AST, because of its shorter half-life; measuring SDH can provide prognostic information more quickly than measuring AST.

In horses with Theiler disease, measurement of serum or plasma bile acids rarely adds further information than that provided by the measurement of hepatic enzymes and bilirubins. Virtually all horses clinically affected with Theiler disease have total serum bilirubin values greater than those commonly observed with anorexia. Total bilirubin values in horses showing clinical signs caused by Theiler disease are generally in the range 12–20 mg/dL (12–20 μmol/L). The percentage of bilirubin in the unconjugated form is almost always >75%, although some increase in conjugated bilirubin occurs in all clinically affected horses. The conjugated bilirubin values are generally 1.5–5.0 mg/dL (25.5–85.5 μmol/L). The PT and PTT times are generally abnormally high in comparison with a control sample, but rarely offer information not already gathered from the measurement of direct and indirect bilirubin, bile acids, and hepatic enzyme activity in the serum or plasma. Other laboratory findings that are frequently abnormal in Theiler disease include moderate to severe acidosis, hypokalemia, polycythemia, increased plasma aromatic amino acids, and hyperammonemia.

A more definitive diagnosis of Theiler disease can only be made by liver biopsy. If the history, clinical findings, and laboratory findings are characteristic of Theiler disease, a biopsy is not necessary, and in many cases may not be easy to perform because the liver is often shrunken and may be difficult to identify with ultrasound examination. Microscopic examination generally reveals marked hepatocellular necrosis involving the entire lobule, most severe in the central and midzonal hepatocytes. There is very mild-to-moderate accumulation of lymphocytes and a few plasma cells and neutrophils. The degree of bile duct proliferation is often positively correlated with the duration of the disease. On necropsy examination, the liver is usually smaller than normal, tan, and may have markedly congestive centrilobular patterns. The borders of the liver are sharp.

Treatment

No specific therapy for Theiler disease exists; treatment focuses on treating the associated hepatic encephalopathy (Divers, 2015). The affected horse should not be stressed if at all possible. Stressful situations such as moving the animal to another facility or weaning the mare's foal often exacerbate the clinical signs of the hepatoencephalopathy. Sedation should be used only when necessary to control fulminate hepatic encephalopathy causing propulsive behavior (Figure 51.12). Xylazine, romifidine, or detomidine can be used to control bizarre behavior, prevent injury to the animal, and allow catheter placement. Doses of these sedatives that cause lowering of the head should be avoided if possible as low head position and hypoventilation may worsen cerebral edema. Phenobarbital can be used if continued and uncontrolled excitement is associated with hepatoencephalopathy. Although phenobarbital is metabolized by the liver and its use in treating hepatoencephalopathy in humans is not common, it may provide the needed effect of long-term sedation and decrease energy requirements in the brain. Phenobarbital works by increasing the

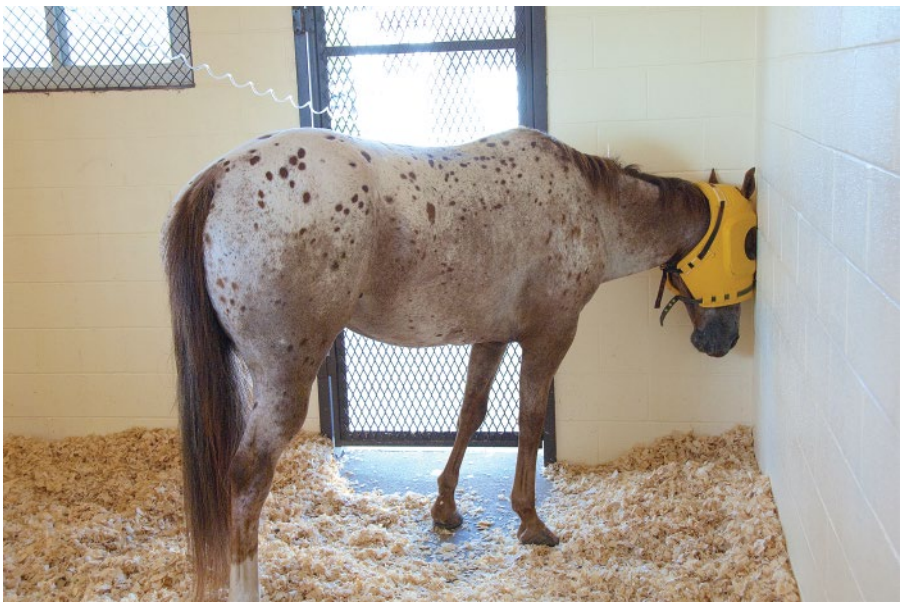


Figure 51.12 Treatment of a horse affected by Theiler disease. Intravenous fluid therapy, sedation, and the use of a head protector.

activity of the inhibitory neurotransmitter GABA. Diazepam should be avoided as it may worsen hepatoencephalopathy. The benzodiazepine receptor antagonist flumazinil (0.2 mg/kg given slowly intravenously) may be administered for uncontrolled hepatic encephalopathy, but its efficacy in both horses and humans is unproven.

Intravenous fluids are probably the most important component of treatment for hepatic encephalopathy in horses. The intravenous fluids should consist of a balanced electrolyte solution, preferably without lactate, and should be supplemented with potassium 20–40 mEq/L and 5–10 g of dextrose per 100 mL. Sodium bicarbonate should be given only if blood pH is <7.1 and/or bicarbonate is <14 mEq/L. Additional potassium may be given as potassium chloride mixed in molasses and administered per os via a dose syringe. Fresh frozen plasma may be used, but hetastarch or stored whole blood should be avoided owing to inhibition of coagulation factors (hetastarch) and high levels of ammonia in stored blood. Supplemental vitamins can be administered but are not necessary in the treatment.

An effort should be made to decrease ammonia production in the bowel. This can be done by administering neomycin (5–10 mg/kg every 8 h) orally by dose syringe for 2 days. With fulminant hepatic encephalopathy in the horse, nasogastric intubation should be avoided if possible because nasal bleeding could occur. Nasal bleeding could exacerbate the hepatoencephalopathy if the blood is swallowed; and, because of insufficient clotting proteins, the bleeding may be prolonged. Lactulose (0.2–0.5 mL/kg every 8–12 h) may also decrease ammonia production in the bowel and can be used concurrently with neomycin. Both lactulose and neomycin may cause diarrhea if given in excessive dosages or for prolonged periods. Affected animals should be fed high-carbohydrate, high-branched-chain amino acid feeds, with moderate to low total protein content. Sorghum and/or cracked corn mixed with molasses or commercially prepared branched-chain amino acid paste are ideal. Carbohydrates should be fed in frequent small amounts. A moderate protein grass hay should be fed rather than alfalfa hay or spring-cut grass hay. Affected animals should be protected from sunlight in order to prevent photosensitization.

Antioxidant, anti-inflammatory, and antiedema therapies are indicated in acute hepatic failure. The antioxidant, antiedema treatments include DMSO, acetylcysteine, and mannitol given intravenously and vitamin E given intramuscularly. Anti-inflammatory therapy should include flunixin meglumine and pentoxifylline. (7.5 mg/kg PO or IV two or three times per day). Bactericidal antibiotics should be administered to prevent bacterial translocation. Cases of fulminate hepatic necrosis that do not respond quickly to medical therapy usually succumb to the disease.

Prognosis

Horses with Theiler disease that can be maintained for 3–5 days without deterioration can make a full recovery (Divers, 2015). A decline in the SDH and PT, along with improvement in appetite, are the best positive predictive laboratory and clinical indicators of recovery. Horses that have fulminate encephalopathy that cannot be easily controlled with sedatives have a very poor prognosis, although some will recover. The degree of hyperbilirubinemia is a

less powerful prognosticator than presence of encephalopathy. Those animals that continue to eat during the first 3 days of the illness generally have a good prognosis. If the affected horse recovers, which many do within 5–10 days, the long-term prognosis is excellent. No evidence exists that severe hepatic fibrosis and/or neoplasia occur after Theiler disease in the horse.

Other Causes of Acute Hepatic Disease and Failure in Adult Horses

Only scattered reports exist of other causes of acute hepatic disease and failure in adult horses. Mycotoxicosis or other hepatotoxins make up the bulk of these reports. *Fusarium moniliforme* toxins, especially fumonisin B, may cause hepatic disease and, rarely, hepatic failure in horses eating fungi-contaminated corn. Leukoencephalomalacia is the most common disease and clinical syndrome caused by this toxin. Contamination of grain by *Aspergillus flavus* and aflatoxins B_1, B_2, and M_1 may cause hepatic necrosis and fulminate hepatic failure in horses (Vesonder et al., 1991; Caloni & Cortinovis, 2011). Fortunately, aflatoxicosis is rare in horses in most parts of the world. Pyrrolizidine alkaloid-containing plants may also cause acute hepatic disease and failure, although chronic disease with acute failure is most common. Septic portal vein thrombosis is rare in horses but should be considered in adult horses with acute hepatoencephalopathy; the condition may occur in association with hepatic neoplasia (Patton et al., 2006).

Pyrrolizidine Alkaloid Intoxication

Pyrrolizidine alkaloid intoxication is the most common cause of chronic liver failure in horses in many parts of the world (McLean, 1970; Giles, 1983; Lessard et al., 1986; Mendel et al., 1988; Carlson, 1989, 2002; Robinson & Gummow, 2015). Pyrrolizidine alkaloid-containing toxic plants (Table 51.1) tend to be unpalatable and are generally avoided by horses. Poor pasture conditions, overgrazing, or herbicide treatment may contribute to consumption of these plants; however, intoxication is more likely to occur after the feeding of contaminated hay. Pelleted or cubed hay may pose a particular risk because the presence of poisonous plants cannot be detected. Not all the parts of the plants contain pyrrolizidine alkaloids, and the concentration may vary with the season. For several of the pyrrolizidine alkaloid-containing-plants, such as *Senecio jacobaea* (Figure 51.13), toxic alkaloid concentrations are highest during budding and flowering, with the onset of flowering being the greatest period of risk of toxicity (Johnson et al., 1985). For *Crotalaria*, the seeds are most toxic.

Table 51.1 Common pyrrolizidine alkaloid-containing plants (Carlson, 2002; Burrows & Tyril, 2013).

Botanical name	Common name(s)
Amsinckia intermedia	Fiddleneck, fireweed, or tarweed
Senecio vulgaris	Common groundsel
Senecio riddelli	Woolly groundsel, Ridell's groundsel, or sand groundsel
Senecio jacobaea	Tansy or common ragwort, ragwort, or stinking Willie (Figure 51.13)
Senecio flaccidus	Threadleaf groundsel
Crotalaria spp.	Rattle box
Heliotropium europaeum	Common heliotrope or potato weed
Echium plantagineum	Patterson's curse
Cynoglossum officinale	Houndstongue

Figure 51.13 *Senecio jacobea* (common ragwort) – a common cause of pyrrolizidine alkaloid toxicity in Europe.

The intoxication typically results in the delayed onset of chronic, progressive liver failure. The onset of clinical signs is most commonly delayed 4 weeks to 12 months after ingestion of pyrrolizidine alkaloid-containing plants. There appear to be individual differences in

susceptibility, and not all horses that consume the plants develop clinical signs (Giles, 1983). Horses generally present with depression, anorexia, and weight loss for variable periods of time. Horses with areas of unpigmented skin may develop photosensitivity. The clinical course may vary from several days to several months, but when sufficient liver damage has occurred to produce functional failure, onset of profound clinical signs of hepatoencephalopathy and, in many cases, death may be abrupt. The apparent acute onset of clinical illness generally represents the end stage of a chronic, progressive disease process. Clinical signs and death may occur up to 1 year after the contaminated feed was eaten. Because all horses with access to a contaminated feed source are at risk, a history of other animals with progressive depression, weight loss, icterus, and death should alert the clinician to a possible common cause. Less commonly, clinical signs may occur more quickly after ingestion of a sufficient amount of the toxic plant (approximately 2% of body weight) and the clinical signs, laboratory findings, and even histology could appear similar to Theiler disease in those cases.

Etiology

Pyrrolizidine alkaloid toxicity is largely determined by the total dose of the pyrrolizidine alkaloid ingested. Consumption of the plants at a dose of 2–5% of the body weight of the horse, fed at once or over a period of a few days, can result in acute toxicity (Mendel et al., 1988; Stegelmeier et al., 1996). The effects of pyrrolizidine alkaloids are cumulative, and toxicity more commonly occurs after chronic low-level exposure. The alkaloids are transported to the liver via the portal circulation, and are metabolized by the microsomal enzymes into highly reactive, unstable metabolites (the dehydroalkaloids), which are potent alkylating agents (McLean, 1970). These compounds are responsible for much of the direct hepatocellular damage. Hydrolysis of the dehydroalkaloid yields the dehydroamino alcohol, which can be both antimitotic and carcinogenic. The toxic agents are capable of alkylating nucleic acids and protein, thereby inhibiting cellular replication and protein synthesis. Hepatocytes surrounding the central vein are most severely affected because that is where the pyrrolizidine alkaloids are metabolized to produce the toxic pyrroles. The affected cells cannot divide, and the hepatocytes enlarge, forming megalocytes. These cells are a characteristic histopathologic feature of this disease (Figure 51.14A and B), but may be sparse with more acute disease. When the megalocytes die, fibrosis follows and the liver shrinks (Figure 51.15). Fibrosis around the central vein may result in veno-occlusive disease. Periportal fibrosis with evidence of nodular regeneration is common.

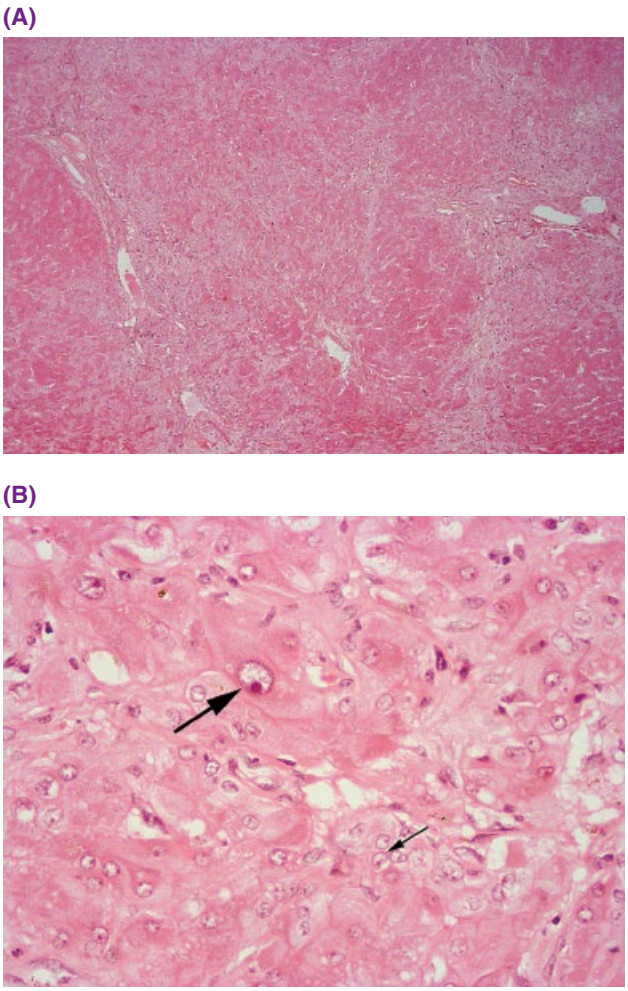
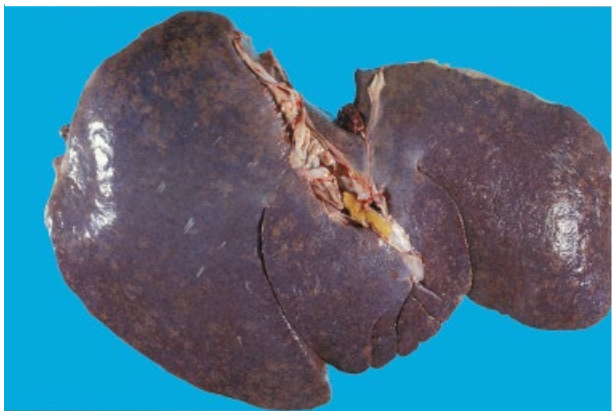


Figure 51.14 Photomicrographs of the liver showing typical histological features of pyrrolizidine alkaloid toxicity. **(A)** The liver parenchyma is largely replaced by fibrous tissue. Surviving areas of normal hepatocytes are present. Hematoxylin and eosin stain, ×4 magnification. **(B)** Small arrow shows a normal hepatocyte nucleus. Large arrow shows the nucleus of a megalocytic hepatocyte. Hematoxylin and eosin stain, ×40 magnification. Source: Courtesy of Dr G. R. Pearson, Comparative Pathology Laboratory, Department of Clinical Veterinary Science, University of Bristol.

Clinical Signs

Experimental feeding studies indicate that several stages exist in the development of pyrrolizidine alkaloid toxicity. Initially, modest characteristic liver lesions may develop along with associated biochemical evidence of liver damage without producing overt clinical signs. In a report of racing horses fed *Senecio*-contaminated alfalfa hay, poor performance was one of the earliest indicators of disease. Later, progressive liver damage results in compromised hepatic function, and, at this stage, clinical signs become evident with progressive development of depression, anorexia, weight loss, and variable icterus.

(A)



(B)

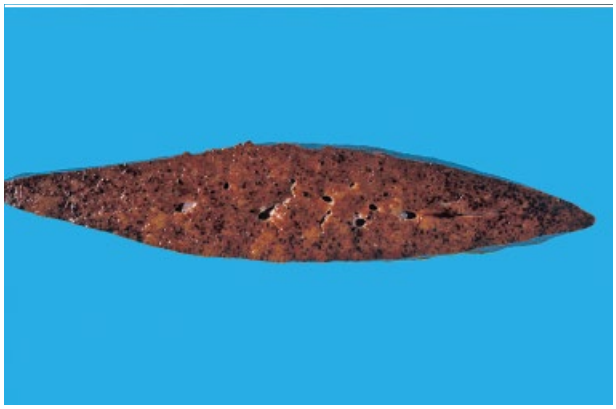


Figure 51.15 Gross pathologic appearance of the liver of a horse affected by pyrrolizidine alkaloid toxicity. The liver is mottled brown and tan, and was firm to cut. The cut surface is a mottled pale brown/tan **(A)**, and has a roughened surface **(B)**. Source: Courtesy of Dr G. R. Pearson, Comparative Pathology Laboratory, Department of Clinical Veterinary Science, University of Bristol.

The final phase of the disease process occurs with the onset of failure of function and terminal hepatic decompensation. The onset of severe clinical signs may occur suddenly and represents the end stage of a disease process that may have been developing for an extended period. Vital signs (temperature, pulse, and respiratory rate) are often within normal limits unless the horse has become agitated or convulsive. Clinically detectable icterus can be variable until the final stages of the disease process, when icterus may be moderate to severe. Central neurologic signs range from moderate depression to compulsive walking, excessive yawning, ataxia, apparent blindness, head pressing, maniacal behavior, convulsions, coma, and death. Self-inflicted trauma may occur in horses that become oblivious to their surroundings. Intravascular hemolysis may occur in the terminal stages of the disease with resultant hemoglobinuria. Photosensitivity may be noted in nonpigmented areas of the skin. Laryngeal paralysis and gastric impaction can also occur in a small number of cases (Milne et al., 1990; Pearson, 1991; Hughes et al., 2009). Other signs, such as edema, ascites, oral ulcers, halitosis, and diarrhea, have been reported, but they are not common features in horses with pyrrolizidine alkaloid intoxication (McLean, 1970; Mendel et al., 1988; Pearson, 1990).

A history of exposure to pyrrolizidine alkaloid-containing plants and clinical signs compatible with progressive liver failure allow a tentative diagnosis of pyrrolizidine alkaloid intoxication. This is particularly true in the context of previously confirmed cases from the same property or from other animals on the same feed.

Clinical Pathology

Increases in liver-derived serum enzyme activities (SDH, GLDH, and AST) are associated with active liver damage, but activities may decrease toward normal until the later stages of the disease process when marked increases may again be noted. Increases in GGT and alkaline phosphatase activities reflect the focus of the pathologic process in the periportal regions and the biliary system. Sustained moderate to marked increases in these enzymes provide an early and persistent indication of liver involvement (Mendel et al., 1988). Serum bile acid concentration is generally increased. Serum bilirubin concentrations may remain within normal limits until the horse reaches a state of functional liver failure. Total serum bilirubin generally remains <10 mg/dL (170 μmol/L), and the direct-reacting bilirubin rarely accounts for more than 25% of the total. The BUN level is generally below normal in horses with functional failure. Foodstuffs can be tested for the presence of pyrrolizidine alkaloids.

Pathologic Findings

Demonstration of typical liver lesions on biopsy or at necropsy is necessary for confirmation of the diagnosis (Figure 51.1 and Figure 51.15). The liver is often small and firm, and nodules of regenerating liver tissue may be noted in some long-standing cases. Typical lesions of pyrrolizidine alkaloid intoxication are megalocytosis, periportal fibrosis, biliary hyperplasia, and occlusion of the central veins. Liver lesions tend to be progressive, and as normal hepatic architecture is damaged and replaced by fibrous tissue, the prognosis becomes less favorable. Well-developed lesions of veno-occlusion are also considered an unfavorable finding. Exposure to massive doses of pyrrolizidine alkaloids may produce acute centrilobular necrosis, as has been documented experimentally in a number of species; the hepatic lesions in such cases may resemble those of Theiler disease. Megalocytes may not be seen in the liver until 30 days or more after exposure to pyrrolizidine alkaloids (Stegelmeier et al., 1996).

Treatment and Prognosis

Horses with pyrrolizidine-induced hepatic failure have a guarded to poor prognosis owing to the extensive fibrosis that occurs in most cases prior to the development of clinical signs (Divers, 2015). No specific recommendations exist for treatment of the damage produced by these toxic plants other than removal of the contaminated feed source. Complications associated with photosensitivity can be reduced if the horses are housed out of direct sunlight, and retention of appetite and maintenance of body weight are the most useful prognostic indicators. Even horses with moderate histological evidence of liver damage may survive if they maintain a normal appetite (Lessard et al., 1986). It is often recommended that horses with liver disease be put on a low-protein diet. This recommendation may not be appropriate unless signs of hepatoencephalopathy are present, and it may be better to feed something that the horses will eat, alfalfa hay for example, than to offer a lower protein feed source that the horses refuse to eat. Providing adequate caloric intake of a nutritionally balanced diet of grain and forage or hay is critical. Some horses with extensive liver damage survive, but remain unthrifty and may not be able to handle the stress of active athletic training (Lessard et al., 1986). Vigorous supportive care may be unrewarding in a horse with clinical signs of advanced liver failure and histological evidence of generalized fibrosis with loss of normal hepatic architecture. However, treatments for hepatic encephalopathy, antioxidant therapy with vitamin E, *S*-adenosylmethionine (SAMe), and milk thistle extract, anti-inflammatory/antifibrosis treatment with pentoxifylline, and supportive care with fluid therapy may be beneficial, and some affected horses may survive for several months or even make a complete clinical recovery (Lessard et al., 1986; De Lanux-Van Gorder, 2004). The addition of dietary supplements of cysteine, butylated hydroxyanisole (200 µg), vitamin B_{12}, and 5 mg/kg of folic acid to feed did not alter toxicity in ponies fed tansy ragwort (Garrett et al., 1984). Although a study in rats showed that the administration of SAMe and vitamin E before and after monocrotoline pyrrole exposure modulated the resulting hepatic oxidative stresses, the bioavailability of silymarin (milk thistle extract) in horses is poor (Hackett et al., 2013).

Cholangiohepatitis and Choledocholithiasis

Cholangiohepatitis is the most commonly encountered, clinically significant form of biliary tract disease in horses (Schneider, 1997; Johnston et al., 1989; Peek & Divers, 2000). Other forms of true biliary disease appear to be uncommon in horses, but biochemical evidence of hepatobiliary injury and dysfunction, including increases in serum bilirubin, GGT, alkaline phosphatase, and bile acids, frequently accompanies both acute and chronic hepatic diseases such as Theiler disease, Tyzzer disease, hepatic lipidosis, and pyrrolizidine alkaloid toxicity. Rarely, biochemical and clinical evidence of biliary tract disease may occur in association with the so-called "chronic active hepatitis," abscesses, granulomas, or infiltrative or obstructive neoplastic conditions, such as primary cholangiocarcinoma, hepatic adenocarcinoma, or metastatic hepatic tumors.

Although cholangiohepatitis probably begins as a cholangitis, the term cholangiohepatitis is appropriate because clinically significant inflammatory biliary disease in horses is uncommon without extension into the periportal region of the liver. It is probable that many mild cases of cholangitis/cholangiohepatitis are undiagnosed because horses are asymptomatic, but the condition predisposes horses to chronic, active, inflammatory hepatobiliary disease and the formation of biliary calculi. Chronic cholangiohepatitis may frequently be associated with significant intra- or extrahepatic calculus formation. Discrete calculi can often be identified ultrasonographically (Figure 51.6) or at postmortem examination (Figure 51.16 and Figure 51.17), but some horses with cholangiohepatitis develop a more sonolucent "sludge-like" material within the biliary tract. With severe suppurative cholangiohepatitis, particularly if the condition is long-standing, significant periportal and bridging fibrosis can occur. Clinically significant hepatobiliary disease appears to be more common in middle-aged to older horses (Johnston et al., 1989; Peek & Divers, 2000). Because of the absence of a gallbladder, the nomenclature surrounding biliary calculi in the horse has been confusing. The term cholelithiasis broadly refers to calculi anywhere within the biliary tract, but in humans it has come to be synonymous with calculi within the gallbladder. It is perhaps more appropriate in horses to refer to intrahepatic calculi as hepatoliths and extrahepatic calculi, usually located within the common bile duct, as choledocholiths.

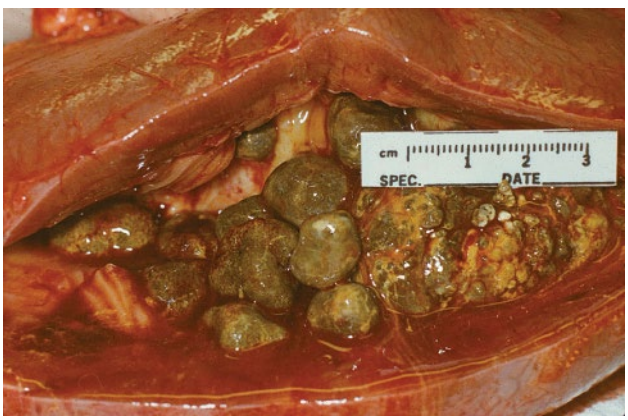


Figure 51.16 Cholelithiasis. Multiple stones in the bile duct.

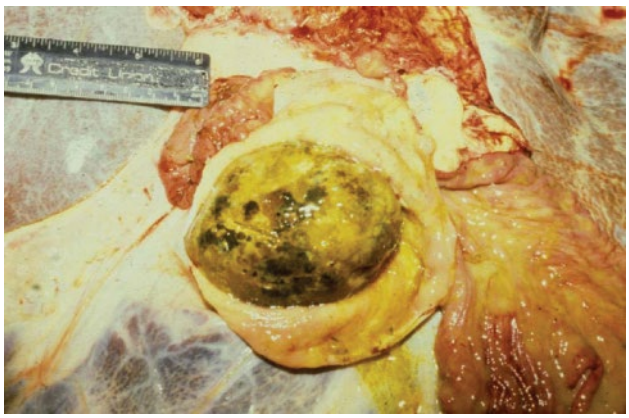


Figure 51.17 Complete obstruction of the bile duct by a single calculus may be amenable to surgical treatment.

Etiopathogenesis

Cholangiohepatitis in adult horses is presumed to develop as the result of an ascending bacterial infection from the proximal small intestine. Evidence for this comes from retrospective studies documenting the isolation of predominantly Gram-negative, enteric bacteria such as *Escherichia coli*, *Enterobacter* spp., and *Citrobacter* spp. from clinical cases (Johnston et al., 1989; Peek & Divers, 2000; Reef et al., 1990). Anaerobic enteric bacteria such as *C. pefringens* are also frequently cultured. The ascending infection is believed to predispose to calculus formation by creating a nidus around which the calculus forms. Plant material has occasionally been found in stones (Reef et al., 1990). The occurrence of enteritis or ileus before the development of cholangiohepatitis in some cases supports the theory of ascending infection (Davis & Jones, 2003; Davis et al., 2003). The composition of calculi in horses is predominantly calcium bilirubinate and calcium phosphate, analogous to infection-associated brown pigment stones in humans (Schneider, 1997; Van der Luer & Kroneman, 1982; Traub et al., 1983; Reef et al., 1990; Peek & Divers, 2000).

Clinical Signs and Diagnosis

Horses with cholangiohepatitis commonly present with the nonspecific clinical signs of fever, icterus, colic, weight loss, and, occasionally, encephalopathy and photosensitization (Traub et al., 1982; Roussel et al., 1984; Tulleners et al., 1985; Johnston et al., 1989; Peek & Divers, 2000; Reef et al., 1990; Ryu et al., 2004; Graves, 2006). Careful history taking often reveals recurrent bouts of mild-to-moderate colic coincident with fever in the preceding days to weeks. Significant weight loss commonly accompanies more chronic cases. Occasionally, signs of hyperammonemic hepatic encephalopathy can be seen when complete calculus obstruction to biliary outflow occurs or the disease process has progressed to cirrhosis.

Serum biochemical abnormalities include large increases in the hepatobiliary enzymes GGT and alkaline phosphatase, and moderate increases in the hepatocellular enzymes AST, GLDH, and SDH. Total serum bilirubin is increased, frequently well above the levels that typically occur with anorexia alone, with the direct-reacting or conjugated fraction representing more than 25% of the total in most cases. The ratio of direct to indirect bilirubin is a helpful parameter in the diagnosis of cholangiohepatitis because the proportionate increase in the direct-reacting fraction is fairly specific to this condition in horses. Bilirubinuria is usually observed since the water-soluble conjugated bilirubin is freely filtered into the urine. Serum bile acids are increased in many cases of cholangiohepatitis, and can reach very high levels (>100 mmol/L) in horses with significant biliary obstruction. Horses with either maniacal or depressive hepatoencephalopathy in association with complete calculus obstruction or severe cirrhosis may have increased blood ammonia levels. Typically, hematologic changes are consistent with chronic, active inflammation and include neutrophilia and hyperfibrinogenemia. If the condition is more than 2–3 weeks in duration, hyperglobulinemia may also be documented. If a horse has chronic cholangiohepatitis and globulins are not increased, common variable immunodeficiency syndrome should be considered.

Although clinical and laboratory findings can be highly suggestive of the condition, a definitive diagnosis of cholangiohepatitis requires liver biopsy. It is recommended that *in vitro* measurements of clotting function, specifically the PT and APTT, be made prior to hepatic biopsy. Frequently, these indices are normal but they may be prolonged if the biosynthetic capacity of the liver has diminished in association with advanced postinflammatory fibrosis. The biopsy procedure is best performed under light sedation and ultrasonographic guidance, using a 14-gauge biopsy needle. Sufficient biopsy material should be obtained for aerobic and anaerobic culture and also for routine histopathology. Identification of the liver via ultrasound lessens the risk of inadvertent colonic, diaphragmatic, or pulmonary injury that can occur when the procedure is performed blindly using traditional anatomic landmarks. Histologically, the liver tissue should be evaluated for both the severity of inflammation and the presence and extent of any periportal and bridging fibrosis. Advanced bridging fibrosis indicates a more guarded prognosis, particularly when it is accompanied by biochemical evidence of liver failure such as hypoalbuminemia, hypoglycemia, and altered clotting times. Bile duct hyperplasia is invariably reported but represents a nonspecific response to liver injury.

In healthy horses, the liver can best be identified ultrasonographically between the 11th and 16th intercostal spaces on the right side, and between the 9th and 11th spaces on the left side. In horses with cholangiohepatitis, the liver image can frequently be identified over a much greater area owing to hepatomegaly. The degree of hepatomegaly, increased hepatic echogenicity, bile duct dilatation, and the presence of significant hepatoliths should be evaluated ultrasonographically (Johnston et al., 1989; Reef et al., 1990; Schneider, 1997) (Figure 51.6). It is not possible to identify bile ducts via ultrasound in healthy horses; however, significant bile duct dilatation and discrete calculi may be detected in many clinical cases. Finding two parallel fluid-filled structures (parallel sign) is indicative of the portal vein and distended bile duct. Calculi can often best be identified in the 7–10th intercostal spaces on the right side, just ventral to the lung border, and are seen in approximately 50–75% of horses with cholangiohepatitis (Reef et al., 1990). The echogenicity of calculi and degree of acoustic shadowing vary with the extent of mineralization and are generally not as hyperechoic as nephroliths. With experience, it may be possible to characterize the hepatic parenchyma as being diffusely more echogenic than normal, particularly when significant hepatic fibrosis has occurred.

Medical Management

Long-term antimicrobial therapy is essential in the successful treatment of cholangiohepatitis and choledocholithiasis/hepatolithiasis in adult horses (Peek & Divers, 2000). In certain situations where biliary obstruction is complete, or the horse is in uncontrollable abdominal pain, surgery may be necessary. The choice of specific antibiotics should ideally be based on both aerobic and anaerobic cultures of liver biopsy material. If biopsy culture results are either unavailable or negative, broad-spectrum antibiotics such as potentiated sulfonamides, third-generation cephalosporins, or fluoroquinolones would be appropriate choices. Although the spectrum of activity of the aminoglycosides is limited to aerobic, Gram-negative bacteria, a good clinical response to this family of antibiotics is often observed, likely because of the high frequency of Gram-negative enterics as etiologic bacteria. Metronidazole (7.5–15.0 mg/kg every 8 h) should also be considered, especially if penicillin is not being administered, as anaerobic organisms are the second most common type of organism found (Gram-negative enteric bacteria are the most common). The duration of antimicrobial therapy will vary on a case-by-case basis, but experience suggests that weeks to months of therapy are necessary. Treatment failure can commonly be associated with premature antibiotic withdrawal, and it is worth considering that both clinical and biochemical resolution should be confirmed before treatment is stopped. Many horses show substantial clinical improvement in terms of appetite, absence of fever, and weight gain while still demonstrating significant biochemical evidence of hepatobiliary disease. Antibiotic treatment is recommended to be continued until serum GGT and alkaline phosphatase levels have been normal for 2–4 weeks. Repeated ultrasonographic evaluation of the liver during the course of therapy can be useful in assessing improvements in hepatomegaly, bile duct dilatation, and the resolution of any identifiable calculi. Some horses may have complete clinical and biochemical recovery, yet stones (presumably nonseptic and nonobstructing) may be seen in bile ducts on ultrasound examination. Intravenous polyionic fluid therapy can be a useful adjunct to antimicrobial therapy both in cases of acute cholangiohepatitis and during long-term therapy when an individual horse has signs of clinical deterioration.

Although bile salt therapy using chenodeoxycholic acid and ursodeoxycholic acid (ursodil or ursodiol) has no direct effect on calcium bilirubinate calculi, it may be helpful in horses with cholelithiasis by virtue of the anti-inflammatory and choleretic actions that increase bile production and may make bile more liquid and easier to excrete (Divers, 2015). DMSO may also be of benefit (Divers, 2015). Specific evidence supports the intravenous administration of DMSO in the medical management of brown pigment stones in humans (Igimi et al., 1994) and, by analogy, its use is justifiable in cases of equine choledocholithiasis and hepatolithiasis. DMSO can be administered intravenously at a dose of 1 g/kg daily for 5–7 days, diluted to a 5% solution in fluids.

Individuals that present with hyperammonemic hepatic encephalopathy may be treated with products to reduce both the production and absorption of ammonia in the large intestine. The oral administration of either neomycin (20–30 mg/kg four times daily) or metronidazole (10–15 mg/kg four times daily) has been recommended to alter cecal and colonic bacterial flora and thereby reduce ammonia production. Lactulose (90–120 mL PO four times daily) can be given as an acidifying agent to alter luminal pH and increase the conversion of ammonia to nonabsorbable ammonium ions. Adult horses with hepatic encephalopathy can vary from somnolent to violent and maniacal and often require chemical restraint for both their own protection and that of people around them. If the hepatic encephalopathy accompanies fulminate liver failure, the prognosis is extremely guarded. Intensive intravenous fluid therapy to correct and maintain hydration and electrolyte and acid–base status are essential parts of the therapy of horses with cholangiohepatitis that present with concurrent fulminate liver failure.

Surgical Management

Surgical management of cholangiohepatitis and biliary calculi should probably be reserved for cases of complete biliary obstruction (Figure 51.17) with severe, unrelenting abdominal pain that is unresponsive to conventional analgesics. Horses with complete obstruction can present with hyperammonemic encephalopathy and, therefore, benefit from intensive supportive medical management in addition to surgical relief of the obstruction. Both anecdotal and published reports claim success using surgical management by either manual lithotripsy or calculi removal via cholangiotomy. Manual lithotripsy is often successful by simple palpation and fracturing the stone, or by manually advancing the stone into the duodenum. Cholangiotomy is more likely to result in bile peritonitis, which lowers the prognosis. Recurrent obstruction is possible because most horses have additional intrahepatic calculi that are inaccessible to the surgeon, and these may continue to obstruct biliary outflow partially or completely postsurgically.

Other Biliary Conditions

Hepatic abscesses, neoplasia, and parasitic granulomas are documented, but rare, causes of obstructive hepatobiliary disease in horses. Cholangiocarcinoma and hepatoblastoma are the most common forms of primary hepatic neoplasms (Beeler-Marfisi et al., 2010), but liver metastases may be seen in association with primary tumors such as lymphoma, squamous cell carcinoma, and melanoma. Clinical and biochemical evidence of biliary tract disease is often absent, even with significant parenchymal infiltration, unless biliary drainage is obstructed. This is most commonly associated with space-occupying masses that impede extrahepatic biliary flow through the right and left hepatic ducts and the common bile duct.

Occasionally, increases in GGT, alkaline phosphatase, and bilirubin are seen in association with colonic and proximal small intestinal disease in adult horses and foals; these changes are common in horses with right dorsal displacement and/or 180° volvulus of the large colon (Gardner et al., 2005). Furthermore, horses with colonic displacement or volvulus may have increases in the hepatobiliary enzymes, probably because of abnormal extrahepatic biliary drainage rather than true hepatobiliary disease. It is worth remembering that donkeys, mules, and asses have a higher (up to three times) normal level of GGT than horses.

Chronic Active Hepatitis

Chronic active hepatitis is not a specific disease entity, but is a descriptive term for a group of conditions characterized by active, progressive, inflammatory liver disease of some duration (Carlson, 1989). The history is often one of depression, weight loss, photosensitivity, and variable icterus. Signs are often intermittent and may be associated with fever. Some horses have a history of previous or active intra-abdominal disease. Thus far, no clear evidence exists of association with advancing age, viral disease, or drug administration. The disease can progress to the point of liver failure with major CNS involvement and death. Unusual cutaneous manifestations such as moist lesions at the coronary bands may be present. Liver lesions tend to be located in the periportal region, and the histopathologic diagnosis is often a mixture of periportal fibrosis and cholangiohepatitis. In some cases, lymphocytes are the predominant inflammatory cell in the biopsy. The cause of chronic active hepatitis has not been determined, although autoimmune disease is possible. Alternatively, some cases may be a manifestation of chronic cholangitis.

Clinical Signs

Clinical signs vary with the degree of liver damage and the presence of any underlying disease process. The onset of signs is usually insidious. Horses often present with anorexia, weight loss, variable icterus, and moderate to marked depression. Neurologic signs may progress to convulsions, coma, and death. Some horses have increased rectal temperature, pulse, and respiratory rates. The moderate to high fever noted in some horses with chronic active hepatitis is not a common feature of many of the other causes of liver failure, unless complications have occurred. Petechial or ecchymotic hemorrhages may be noted in the visible mucous membranes. Intra-abdominal problems such as an enlarged anterior mesenteric artery, thickened bowel, or mass lesion may be noted. Some horses develop a moist exfoliative dermatitis at the coronary bands and in some cases this may be the presenting complaint (Carlson, 1989).

Clinical Pathology

Laboratory evaluation provides evidence of liver damage and allows an assessment of the degree of functional failure. Initially, liver-derived serum enzyme activities may be slightly to moderately increased. Later in the disease process, substantial increases in liver-derived serum enzyme activities and of the enzymes that reflect biliary damage, GGT and alkaline phosphatase, will be noted. Serum bilirubin may be increased, with direct-reacting bilirubin comprising up to 40% of the total. The urine is strongly positive for bilirubin, and serum bile acids are greatly increased. The BUN is often low, and hypoglycemia will be noted in some horses. The hemogram may show evidence of an inflammatory response with a leukocytosis, left shift, and monocytosis. The total

plasma protein concentration is generally increased, largely because of an increase in globulins. Culture of liver biopsy specimens is recommended because bacterial agents may contribute to hepatitis or cholangitis.

Pathologic Findings

Histopathologic lesions are most prominent in the periportal region, with hepatocyte damage and loss, variable fibrosis, and an inflammatory infiltrate (neutrophils or lymphocytes). The cellular component of this infiltrate tends to be mononuclear cells, except those cases with suppurative hepatitis that may have a marked neutrophilic response. Evidence often exists of cholangitis with biliary hyperplasia and bile stasis. Bacteria may colonize the liver during bacteremia via portal drainage from damaged bowel or as an ascending process from the common bile duct. Viral agents, idiosyncratic reactions to drugs, or immune reactions to diseased liver cells are thought to be major factors in the development of chronic active hepatitis in other species. The pathogenesis of the skin lesions is unclear, but they appear to represent an immune-mediated vasculitis associated with liver disease.

Treatment

Intensive supportive care is indicated until horses regain their appetite. A usually consistent favorable response to corticosteroids can be anticipated (Carlson, 2002). Initial treatment should consist of 20–40 mg of dexamethasone given by injection. This dose rate is maintained for 3–5 days (depending on the response) and is then gradually decreased over the next 7–10 days. At this time, the horse may be placed on oral prednisolone at 400–600 mg/day. Azathioprine (2–3 mg/kg PO q 24 h) could be used instead of corticosteroids if there is concern about laminitis (i.e., metabolic syndrome). Immunosuppressive therapy may be especially indicated if lymphocytes are the predominant inflammatory cell type found on the biopsy. Conversely, antibiotics are generally recommended if neutrophils predominate. Treatment may be necessary for 4–6 weeks or longer with careful monitoring of clinical signs and biochemical parameters. Bacterial infection may play a role, especially in horses with fever and a neutrophilic inflammatory infiltrate on liver biopsy, and long-term (4–6 weeks) systemic antibiotic therapy is indicated. Improvements in attitude and appetite are among the earliest and most consistent indicators of response to therapy. The above treatments are often used in combination with pentoxifylline. If there is progressive fibrosis, colchichine (0.03 mg/kg PO q 24 h) and zinc supplementation should be considered. Likewise, if there is biochemical or histological evidence of biliary obstruction, ursidiol (10–15 mg/kg PO q 24 h) should be considered.

Klein Grass (*Panicium coloratum*) Toxicity

Chronic liver disease has been reported in horses in Texas grazing pasture planted in Klein grass and also horses fed Klein-grass hay (Cornick et al., 1988). Icterus, anorexia, and progressive weight loss were the principal signs, with some horses developing colic signs. Increased GGT activity, total and direct bilirubin, blood ammonia, and bromsulfalein (bromosulfophthalein) clearance times were noted. Typical liver lesions included bridging hepatic fibrosis, cholangitis, and hepatocellular regeneration. The toxic principal is thought to be a saponin. Although death losses were reported in horses with advanced liver lesions, most horses recovered after Klein grass was removed from the diet. The sporadic nature of the disease suggests individual susceptibility, variability in the amount of feed ingested, and, perhaps, seasonal or maturational variation in the content of the toxic principal. A similar but more rapidly progressive disease has been seen in horses eating fall *Panicum* hay.

Alsike Clover Toxicity

Horses grazing alsike clover or ingesting alsike clover (Figure 51.18) in hay may develop signs of liver failure, especially photosensitization, anorexia, and icterus (Nation, 1991; Colon & Jackson, 1996; Talcott, 2000). Several horses on a farm may be affected at one time. Generally, these horses are on a clay-soil pasture containing large amounts of alsike clover. The disease appears to have yearly fluctuations in areas where alsike clover is common (eastern United States and Canada), suggesting that environmental factors contribute either to the toxicity of the plant or to the growth of a hepatotoxin

Figure 51.18 Alsike clover.

on the plant. Removal of affected horses from the pasture and supportive care treatments result in complete recovery in most cases. If the horses are not removed from the alsike clover, the disease may progress to hepatic fibrosis, fulminant hepatic failure, and death.

Hepatic Neoplasia

Primary liver tumors are rare in horses. Cholangiocarcinoma occurs mainly in older horses, which may present with anorexia, weight loss, icterus, edema, and abdominal distention (Mueller et al., 1992; Pizzigatti et al., 2011; Wong et al., 2015). This tumor tends to produce multiple masses within the liver. Extrahepatic metastasis may occur with involvement of the peritoneal and pleural cavities, intestine, spleen, and lung. Cholangiocarcinoma has been reported in combination with hepatocellular carcinoma in one horse and in another horse with concurrent septic cholangiohepatitis.

Hepatocellular carcinoma (hepatoma) has been reported primarily in horses younger than 3 years (Jeffcott, 1968; Robey et al.1990). These tumors are often solitary and may be multilobulated. Clinical signs include depression, anorexia, weight loss, abdominal distention, intermittent diarrhea, and hyperemic mucous membranes. Modest increases in liver enzyme activity may be observed. Polycythemia or erythrocytosis as indicated by a marked increase in the hematocrit has been noted in these patients; this may be a result of secretion of an erythropoietin-like substance by the tumor. In one patient, hepatocellular carcinoma was associated with an increase in serum alpha-fetoprotein, a globulin normally produced by fetal liver cells. However, it is not proven that this protein is a consistent indicator of hepatocellular carcinoma in horses.

Malignant hepatoblastoma has been rarely reported (Prater et al., 1989; Lennox et al., 2000; Axon et al., 2008; Beeler-Marfisi et al., 2010). This is an embryonic tumor of the liver with a range of histological patterns, including epithelial and mesenchymal elements. Clinical signs include anorexia, pyrexia, and pleural effusion; polycythemia has also been noted.

Other rare primary liver tumors include bile duct carcinoma (Habershon-Butcher et al., 2008).

The liver is frequently involved with metastatic lesions from primary tumors arising from other sites. These tumors include lymphoma, hemangiosarcoma, mammary carcinoma, bronchogenic carcinoma, melanoma, squamous cell carcinoma, granulosa cell tumor, and Sertoli cell tumor. In most instances, these lesions do not result in massive or generalized liver damage, and the only biochemical indication in some horses may be modest elevation of liver-derived serum enzyme activities. Most affected horses do not manifest clinical or biochemical evidence of liver failure, although depression, anorexia, weight loss, and edema may be features of an invasive and generalized neoplastic process. Ultrasonic evaluation of the liver may provide evidence of focal neoplastic lesions within the liver parenchyma. Portal vein thrombosis and hepatic encephalopathy have been reported in association with metastasis of gastric adenocarcinoma (Patton et al., 2006).

Hepatic Amyloidosis

The liver and spleen are the organs most commonly affected by systemic amyloidosis in horses (Andel et al., 1988). Two forms of systemic amyloidosis exist. In reactive or secondary systemic amyloidosis, the precursor protein is serum amyloid protein AA, which is an acute-phase protein produced by hepatocytes in response to chronic infection or inflammation (Vanhooser et al., 1988). In systemic primary, immunocytic, or idiopathic amyloidosis, amyloid light-chain fibrils are deposited (Hawthorne et al., 1990). Hepatic amyloidosis may result in liver rupture and acute death from hemoperitoneum.

Iron Overload, Hemochromatosis

Iron is a highly reactive element that plays an essential role in oxidation–reduction reactions. Iron balance is largely regulated by intestinal absorption as no mechanism exists for excretion of excessive iron stores. Newborn foals given an oral intestinal inoculum containing ferrous fumarate during the first day or two of life developed acute liver failure as a result of iron overload (Mullaney & Brown, 1988). This was probably associated with an inability of the newborn animal to regulate intestinal absorption of iron effectively and the absence of colostral glutathione prior to the iron administration. Additionally, newborn foals normally have high serum iron and high percentage transferrin saturation at birth, rendering them less able to deal with a sudden massive iron intake. Clinical signs developed within a few days, with rapid progression of anorexia, depression, icterus, collapse, and death. Liver lesions included massive necrosis, bile ductule proliferation, inflammatory infiltrate, and bile stasis. Deficiencies of vitamin E and selenium may play a permissive role in the tissue damage of iron toxicity. Vitamin E and selenium are thought to exert protective effects because of their antioxidant properties. Acute iron overload with liver damage has also been reported in a few adult horses given iron supplements orally.

Iron overload or hemochromatosis causing liver failure in horses is rare; it has been reported in adult horses with

chronic hepatic cirrhosis (Lavoie & Teuscher, 1993; Pearson et al., 1994). Clinical signs in these horses included depression, anorexia, weight loss, icterus, ventral edema, and terminal hepatic encephalopathy. Liver-derived enzyme activities and serum bilirubin were increased. Histological lesions included disruption of hepatic architecture, bridging fibrosis, and bile duct hyperplasia. Iron accumulation was noted within hepatocytes, macrophages, and Kupffer cells, as indicated by Prussian blue staining. Liver iron concentrations, measured in two horses, were high (6700 and 18,437 ppm wet weight), about 20–100 times those measured in the liver of control horses. Iron accumulation was not noted in other tissues in these horses. Serum iron was high in one of these horses and within the normal range in the other.

This condition in horses has some similarities to familial idiopathic hemochromatosis, an inherited disorder of humans, in which excessive intestinal absorption of iron leads to hepatic cirrhosis associated with iron accumulation in the liver and other tissues. This disorder of humans is associated with high serum iron and nearly complete saturation of transferrin. The few published reports in horses suggest a sporadic occurrence, although multiple cases of liver failure in horses with high serum iron were reported on a farm in Europe. At present, no evidence exists that the disorder in horses is inherited. Because excessive dietary iron has not been a consistent feature in these horses and reproduction of hemochromatosis by feeding very large amounts of iron have mostly failed, it has been suggested that, for unknown reasons, in some horses excessive intestinal iron absorption may occur with resultant accumulation of iron in the liver. High serum iron concentrations have been measured in some horses with chronic liver failure, although a causal relationship to liver damage could not be established. It is possible that the accumulation of iron in the liver and the serum is the result of liver failure, and may not be the cause of liver failure. Secondary iron overload occurs in humans with alcoholic cirrhosis. In one study of excessive dietary iron administration to adult ponies, the concentration of iron in the liver was increased, but this did not result in disease (Pearson & Andreasen, 2001).

Right Hepatic Lobe Atrophy

Atrophy of the right hepatic lobe is a rare and often unnoticed condition of horses. The condition has been reported in adult horses with colic resulting from major gastrointestinal abnormalities and is also an incidental finding at necropsy (Jakowski, 1994). Although the pathophysiology of this condition is unresolved, it has been suggested that it may result from compression of the liver associated with chronic distention of the right dorsal colon. High-grain, low-fiber diets may contribute to this condition.

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Diseases of the Small Intestine

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Introduction

Primary disease of the small intestine is common in adult horses and foals, representing 27–49% of colic cases managed surgically in different referral hospital populations (Phillips & Walmsley, 1993; Vachon & Fischer, 1995; Cable et al., 1997; Mair & Smith, 2005; Muñoz et al., 2008; Wormstrand et al., 2014). Small intestinal lesions may be broadly classified into strangulating and nonstrangulating groups, and strangulating lesions account for the majority of small intestinal lesions requiring surgical intervention. The prevalence of strangulating small intestinal lesions varies between different hospital populations and age groups, from 18–28% of all horses undergoing exploratory laparotomy (Mair & Smith, 2005; Voigt et al., 2009), to 40% of horses >20 years old admitted for assessment of colic (Brosnahan & Paradis, 2003), to 73% of neonates (<30 days old) undergoing exploratory laparotomy for assessment and treatment of colic (MacKinnon et al., 2013).

The diagnosis of small intestinal disease is covered more fully in Chapters 20 and 23, but some key features are important. The degree of abdominal pain and findings on clinical examination, including evaluation of peritoneal fluid, will be variable, depending on the nature and duration of the small intestinal disease. The presence of nasogastric reflux and palpation of distended loops of small intestine per rectum increase the suspicion of small intestinal disease (Vachon & Fischer, 1995) but may not be evident in the early stages of disease. Abdominal ultrasonography is more accurate than rectal examination for the detection of abnormal small intestine (Klohnen et al., 1996). Even if small intestinal distention is not palpable, evidence of a secondary large colon impaction should increase the suspicion of a primary small intestinal lesion being present (Klohnen et al., 1996). Transcutaneous and/or transrectal ultrasound examination can be valuable in identifying abnormal small intestine and in distinguishing between various forms of small intestinal disease, or may occasionally enable the primary lesion to be visualized, which can assist in decision making to perform surgery and facilitate surgical planning (Klohnen et al., 1996; Le Jeune & Whitcomb, 2014).

Strangulating pedunculated lipoma, epiploic foramen entrapment (EFE), primary small intestinal volvulus, and herniation in a mesenteric rent are the most frequent forms of small intestinal strangulation, but their prevalence varies between different clinic populations (Phillips & Walmsley, 1993; Morton & Blikslager, 2002; Mair & Smith, 2005). The affected portion of small intestine is variable but the ileum has been reported to be involved in 26–44% of small intestinal lesions (Edwards, 1981; Kersjes et al., 1988). Epidemiologic studies have identified risk factors for the development of different small intestinal lesions, and rates of survival also vary between different forms of small intestinal disease. Key features relating to specific lesions are detailed in each section. This information can assist the clinician when determining the likelihood of a specific small intestinal lesion being present and in determining the likely prognosis following treatment.

Strangulating Lesions

Pedunculated Lipoma

Intestinal obstruction by a pedunculated lipoma is a common cause of small intestinal strangulation, representing 3–7% of all colic cases admitted for hospital assessment (Blikslager et al., 1992; Abutarbush et al., 2005), 7–13% of all horses undergoing surgical management of colic (Phillips & Walmsley, 1993; Edwards & Proudman, 1994; Garcia-Seco et al., 2005; Mair & Smith,

The Equine Acute Abdomen, Third Edition. Edited by Anthony T. Blikslager, Nathaniel A. White II, James N. Moore, and Tim S. Mair.

Companion website: www.wiley.com/go/blikslager/abdomen

2005; Van der Linden et al., 2003), and 3–27% of small intestinal lesions (Phillips & Walmsley, 1993; Freeman & Schaeffer, 2001; Garcia-Seco et al., 2005; Mair & Smith, 2005; Wormstrand et al., 2014).

This form of colic is significantly more likely to occur in older individuals with a mean age of 16.6–19.2 years at diagnosis reported, and horses under 8 years of age are rarely affected (Blikslager et al., 1992; Freeman & Schaeffer, 2001; Edwards & Proudman, 1994; Garcia-Seco et al., 2005). In horses >20 years of age admitted for hospital assessment in one study, pedunculated lipomas accounted for 18% of all colic cases and 44% of small intestinal lesions (Brosnahan & Paradis, 2003). Geldings have also been reported to be significantly more likely to develop this form of colic (Blikslager et al., 1992; Edwards & Proudman, 1994; Garcia-Seco et al., 2005), as have pony breeds (Edwards & Proudman, 1994), Standardbreds, and Arabians (Garcia-Seco et al., 2005), whereas it is less common in Thoroughbreds and Thoroughbred crossbred horses (Edwards & Proudman, 1994).

A pedunculated lipoma is a benign, smooth tumor composed of adipose tissue that is suspended by a mesenteric pedicle of variable length that wraps around intestine and its mesentery (Figure 52.1). Additional lipomas may be found in some individuals, and 90% of lipomas are found in the small intestine (Garcia-Seco et al., 2005). Mesenteric lipomas can cause intermittent simple obstruction, resulting in recurrent colic episodes, but this is uncommon (Blikslager et al., 1992; Downes et al., 1994; Verwilghen et al., 2013). In most strangulating forms of small intestinal obstruction by a lipoma, the pedicle is usually based away from the intestine, whereas in nonstrangulating obstructions, lipomas appear more likely to have a base or pedicle that is close to the junction of the mesentery and intestine (Edwards & Proudman, 1994). Rarely, an infiltrative form of lipomatosis within the mesojejunum has been reported as a cause of recurrent colic (Linnenkohl et al., 2013). At present, there is no evidence of an association between current or prior obesity and development of a pedunculated lipoma or whether certain individuals are predisposed to these forms of adipose tissue abnormalities. This is an area that requires further research.

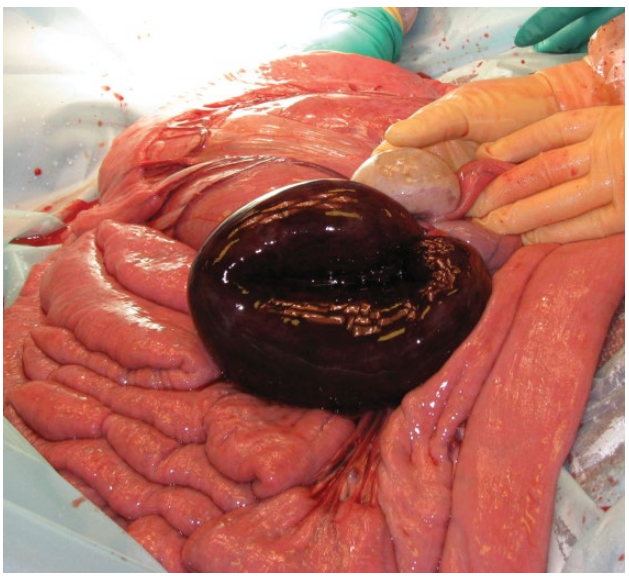


Figure 52.1 Pedunculated lipoma strangulating a portion of jejunum.

At surgery, the lipoma can be found wrapped in the jejunal mesentery. The pedicle most commonly forms a loop around a variable portion of intestine or occasionally may involve two separate small intestinal loops, which can make surgical management challenging. The degree of intestinal compromise may also be variable depending on the degree of intestinal strangulation caused by the lipoma pedicle and duration of disease. In cases where the affected portion of small intestine cannot be exteriorized, careful transection of the lipoma stalk may need to be performed within the abdomen, which carries the risk of causing a mesenteric rent and mesenteric hemorrhage (Blikslager et al., 1992). Incidental lipomas with distinct pedicles should be removed by ligation of the stalk and transection so that strangulating obstruction does not occur in the future. Spontaneous correction of a pedunculated lipoma is reported but is rare (Jansson, 2000).

Horses with this form of colic were reported in one study to be around three times more likely to develop postoperative ileus than horses that had other types of intestinal lesions (French et al., 2002). Overall rates of short-term survival for horses following surgery for pedunculated lipomas (including all horses undergoing anesthesia and those that die or are euthanased on the operating table) vary between 48 and 69% (Blikslager et al., 1992; Edwards & Proudman, 1994), with a short-term survival rate of 79% reported for horses with a pedunculated lipoma that stood following anesthesia (Blikslager et al., 1992).

Epiploic Foramen Entrapment

The epiploic foramen is an approximately 4–6 cm wide slit-like opening into the vestibule of the omental bursa through which small intestine, and rarely large colon (Foerner et al., 1993; Steenhaut et al., 1993) or cecum (Scheidemann, 1989), can become entrapped. The dimensions of the foramen vary between individual horses, and whereas there is a significant correlation between increased body weight and epiploic foramen circumference, there is no correlation between foramen size and increased age (Scheidemann, 1989; van Bergen et al., 2015). Recent studies have reviewed the three-dimensional (Van Bergen et al., 2015; Freeman & Pearn,

2015) and laparoscopic anatomy (Van Bergen et al., 2015) of the foramen and adjacent structures. There are minor differences in descriptions of the anatomic structures that border the foramen (Van Bergen et al., 2015; Freeman & Pearn, 2015), but key structures include the caudate lobe of the liver, the hepatic artery, portal vein, hepatoduodenal and hepatogastric ligaments, and the gastropancreatic and hepatopancreatic folds (Figure 52.2).

EFE can occur in a wide age range of horses, and contrary to older reports in the literature, age is not a risk factor for disease (Freeman & Schaeffer, 2001). Epidemiologic studies have also identified a strong association with cribbing (crib biting/windsucking stereotypic behavior) (Archer et al., 2004a, 2004b). In a large, multicenter study (Archer et al., 2008b), 48% of EFE cases were known to exhibit this form of behavior and horses that displayed cribbing behavior were 72 times more likely to develop EFE than horses that did not. Other factors that increase the likelihood of EFE include horses of greater height, a history of colic in the previous 12 months, and increased time spent in a stall in the previous 28 days (Archer et al., 2008a, 2008b). In the United Kingdom, EFE has been shown to have a seasonal pattern, with increased prevalence in the winter months (Archer et al., 2004b, 2006b).

The length of entrapped small intestine and degree of intestinal strangulation can be variable, and intestinal resection following correction of the entrapment may or may not be required. Infrequently, parietal herniation of a short portion of small intestine into the foramen may occur (Walmsley, 1991; Hammock et al., 1999). Most frequently small intestine becomes entrapped in a left-to-right direction (Vachon & Fischer, 1995; Archer et al., 2004b) and the ileum may be involved in up to 66% of cases (Archer et al., 2004b). Correction of the entrapment must be performed carefully to avoid tearing of any of the vascular structures bordering the foramen, which may result in fatal intraoperative hemorrhage (Livesey et al., 1991; Engelbert et al., 1993; Vachon & Fischer, 1995). Dilation of the foramen is contraindicated (Livesey et al., 1991) and traction on small intestine should be performed in a direction that does not draw intestine sharply against the edge of the portal vein (Freeman & Pearn, 2015).

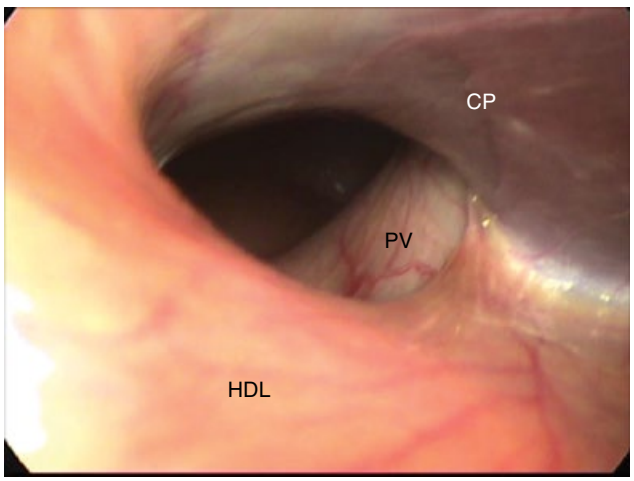


Figure 52.2 Laparoscopic view of the epiploic foramen using a right-sided approach into the abdomen in which the caudate process of the liver (CP), portal vein (PV), and hepatoduodenal ligament (HDL) can be visualized. Source: Van Bergen et al., 2016a. Reproduced with permission of John Wiley & Sons.

Postoperative survival rates vary from 66–74% survival to hospital discharge for all horses undergoing surgery to 79–95% survival of horses that recovered following anesthesia to hospital discharge (Vachon & Fischer, 1995; Freeman & Schaeffer, 2001, 2005; Archer et al., 2004b). EFE has been identified as a factor associated with a significantly reduced likelihood of postoperative survival in some studies (Proudman et al., 2002a, 2002b), which may be explained by lower preoperative total protein values and longer duration of surgery in these cases (Proudman et al., 2005). In an international, multicenter study, short-term survival for all horses undergoing surgical management of EFE was 67%, and of horses that recovered following anesthesia 78.5% survived to hospital discharge and 51% were alive at 1 year following surgery (Archer et al., 2011). Reduced likelihood of survival was significantly associated with increased preoperative packed-cell volume, length of intestine resected, and development of postoperative ileus (Archer et al., 2011).

Recurrence of EFE may be observed (Vachon & Fischer, 1995; Archer et al., 2004b). The true prevalence of this may be underreported owing to lack of postmortem data in horses euthanased for recurrence of colic following hospital discharge, but was documented in three of 71 cases of EFE in one study (Archer et al., 2004b). In these three cases, initial obstruction was nonstrangulating in nature. Adhesions may form spontaneously across the epiploic foramen following surgical correction of EFE, which may prevent recurrence in some cases. A recent study identified that spontaneous closure of the epiploic foramen had occurred in around 40% of horses following laparotomy for EFE that underwent subsequent laparoscopy from 4 weeks postoperatively (Van Bergen et al., 2016b). Current investigations into ways in which the epiploic foramen may be closed in horses at high risk of EFE include laparoscopic placement of titanium coils to stabilize the gastropancreatic fold against the caudate lobe of the liver (Munsterman et al., 2014) and laparoscopic placement of a diablo-shaped expandable construct within the foramen consisting of two preformed knitted polypropylene meshes (Van Bergen et al., 2016a) to promote adhesion formation (Figure 52.3). Further validation of these techniques in clinical cases is required before further recommendations can be made regarding their use.

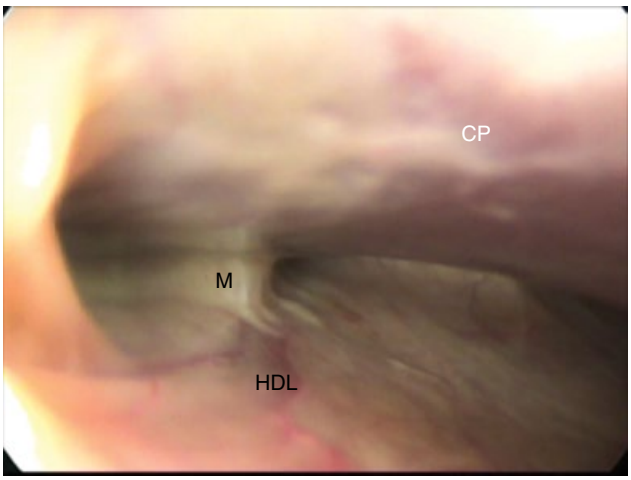


Figure 52.3 Fibrous tissue can be seen covering a mesh construct (M) placed in the epiploic foramen 1 month previously in order to obliterate the space. The caudate process of the liver (CP) and hepatoduodenal ligament (HDL) are also visualized. Source: Van Bergen et al., 2016a. Reproduced with permission of John Wiley & Sons.

Small Intestinal Volvulus

Volvulus has been defined as a >180° (Stephen et al., 2004b) or 360° or greater (Mair & Edwards, 2003) rotation of a segment of jejunum or ileum about its mesentery (Figure 52.4). Volvulus may develop as a primary lesion or may be secondary to another lesion such as an acquired inguinal hernia (Moll et al., 1991), ileal impaction (Little & Blikslager, 2002), a mesodiverticular band (Freeman et al., 1979), a Meckel diverticulum and vitelloumbilical bands (Grant & Tennant, 1973), strangulation in mesenteric rents (Gayle et al., 2000), and adhesions (Baxter et al., 1989).

Volvulus can affect a horse of any age and there is no age or breed predisposition (Stephen et al., 2004b). It is common in foals with severe colic requiring surgical intervention, representing 9% of foals undergoing abdominal surgery (Cable et al., 1997), 15–60% of foals that required surgical treatment of colic (Vatistas et al., 1996; MacKinnon et al., 2013; Bartmann et al., 2002), and 61% of foals with small intestinal lesions (Bartmann et al., 2002). It is a common cause of colic in endurance horses, representing 87% of horses that developed colic signs following a race (Alexander & Haines, 2012). Small intestinal segmental volvulus has also been reported as a rare cause of colic that developed 10 min–3 h following gastroscopy (Bonilla et al., 2014).

Volvulus nodosus is a less common form of small intestinal volvulus, and is caused by a 360° torsion of the ileum and jejunum so they form a mesenteric pouch in which prestenotic jejunum becomes entrapped. Distention of the entrapped bowel draws the ileum into the mesenteric pouch to form a tight loop that knots the entrapment (Huskamp & Toth, 1998). In one study,

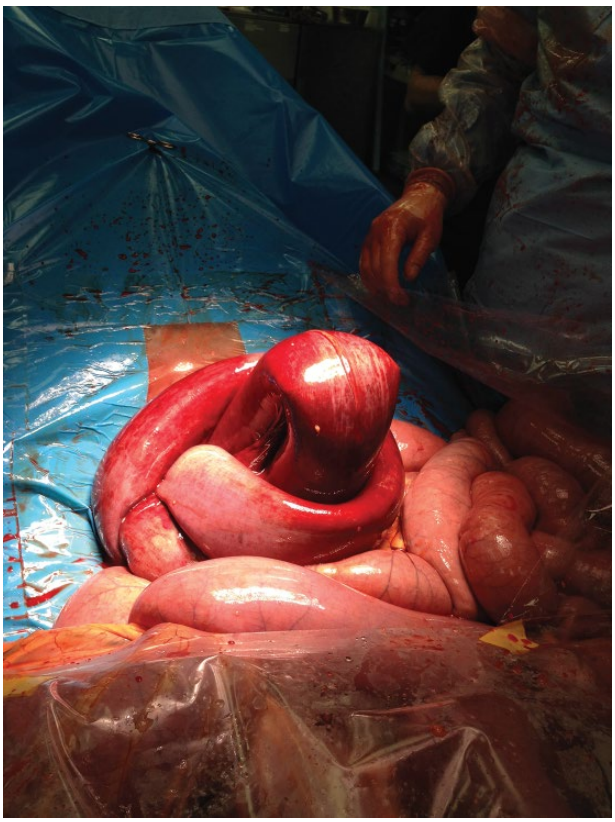


Figure 52.4 Primary volvulus of the jejunum and ileum in an adult horse.

volvulus nodosus was found in 27% of small intestinal lesions in foals <6 months old undergoing surgery for acute abdominal pain and represented 44% of the cases of primary volvulus (Bartmann et al., 2002).

Clinical signs of volvulus are typical of acute small intestinal strangulating obstruction. In one study, 74% of horses demonstrated signs of intermediate to severe abdominal pain, distended small intestine was palpable per rectum in 69%, and nasogastric reflux was obtained in 66% of affected horses (Stephen et al., 2004b). Correction of volvulus nodosus can be difficult but can be accomplished by massaging the contents of the entrapped loop into the proximal segment, thereby allowing the bowel to be pulled through the ring formed by the ileum (Huskamp & Toth, 1998). If the bowel involved in a volvulus nodosus is necrotic, time can be saved by resecting the entire lesion without reduction (Huskamp & Toth, 1998). In a study of 115 horses with primary small intestinal volvulus, 58% of all horses that were admitted to the hospital survived to hospital discharge. Of the 84 horses that were taken to surgery and recovered following general anesthesia, 79.8% survived to hospital discharge (Stephen et al., 2004b). Reduced survival was associated with increased p volume at hospital admission, postoperative colic and relaparotomy (Stephen et al., 2004a).

Intussusception

Intussusception of the small intestine is a relatively uncommon cause of colic, representing 0.8–5.2% of horses undergoing exploratory laparotomy for treatment of colic and 3.4–5.2% of small intestinal lesions found at surgery (Edwards, 1986; Van den Boom & Van der Velden, 2001; Morton & Blikslager, 2002; Mair & Smith, 2005; Wormstrand et al., 2014). Intussusception can occur in horses of all ages, but most cases described in the literature are in foals and young adult horses (Edwards, 1986; Ford et al., 1990; Greet, 1992). Rates reported for foals of different ages undergoing surgical management of colic vary from 0 to 17% (Vatistas et al., 1996; Cable et al., 1997; Bartmann et al., 2002; MacKinnon et al., 2013). Intussusception may be jejunal (Figure 52.5), ileoileal, or ileocecal and may be a cause of acute, chronic, or recurrent episodes of colic (Scott & Todhunter, 1985; Edwards, 1986).

In this form of intestinal obstruction, one intestinal segment invaginates into the lumen of another segment and continues to move aborally in the direction of peristalsis (Edwards, 1986). Predisposing factors that have been suspected include changes in intestinal motility related to enteritis, high burdens of *Parascaris* spp. or *Anoplocephala perfoliata* parasites, mesenteric arteritis, and abrupt dietary changes (Edwards, 1986; Barclay et al., 1982). Any intramural mass or focal area of intestinal thickening may also form the leading edge of a jejunojejunal intussusception, and was considered to be the predisposing factor in 45% of adult horses that developed a jejunal intussusception (Gift et al., 1993). Intussusceptions have been associated with a transverse enterotomy (Lowe, 1968), functional (stapled) side-to-side anastomosis (Frankeny et al., 1995), handsewn end-to-end jejunojejunostomy (Boswell et al., 2000), cryptococcal granuloma or granuloma of unknown cause (Boulton & Williamson, 1984; Gift et al., 1993), pedunculated papilloma (Edwards, 1986), leiomyoma (Collier & Trent, 1983; Gift et al., 1993), intestinal carcinoid (Gift et al., 1993), a persistent vitelline duct cyst (Jones et al., 2004), and multiple acquired diverticula (Southwood et al., 2010).

Clinical findings vary depending on the location of the intussusception, degree of luminal obstruction or vascular compromise, and length of intestine involved (Edwards, 1986). In adult horses, rectal examination may reveal distended loops of small intestine, and the intussusception may be palpated as a firm, painful, tubular structure (Edwards, 1986; Ford et al., 1990). On transabdominal ultrasonography, a cross-sectional view of a jejunojejunal or ileocecal intussusception can be seen as concentric rings with a "bull's-eye" appearance (Bernard et al., 1989; Le Jeune & Whitcomb, 2014). Although the strangulated intussusceptum is partly sequestered within the intussuscipiens, peritoneal fluid can reflect changes consistent with strangulation (Ford et al., 1990; Gift et al., 1993). A recent study reported asymptomatic intussusception evident ultrasonographically in 55.5% of healthy neonatal Standardbred foals (Abraham et al., 2014). Therefore, interpretation of the relevance of ultrasonographic evidence of a small intestinal intussusception in a neonatal foal should take into account other clinical and laboratory findings.

Jejunal intussusceptions accounted for 44% of small intestinal intussusceptions in one study and are less frequent than those that involve the ileum (Edwards, 1986). Jejunojejunal intussusceptions can occur in a wide age range from neonates up to 18 years of age (Edwards, 1986; Gift et al., 1993; Cable et al., 1997; MacKinnon et al., 2013), and most frequently present with acute onset moderate to severe signs of pain (Edwards, 1986).

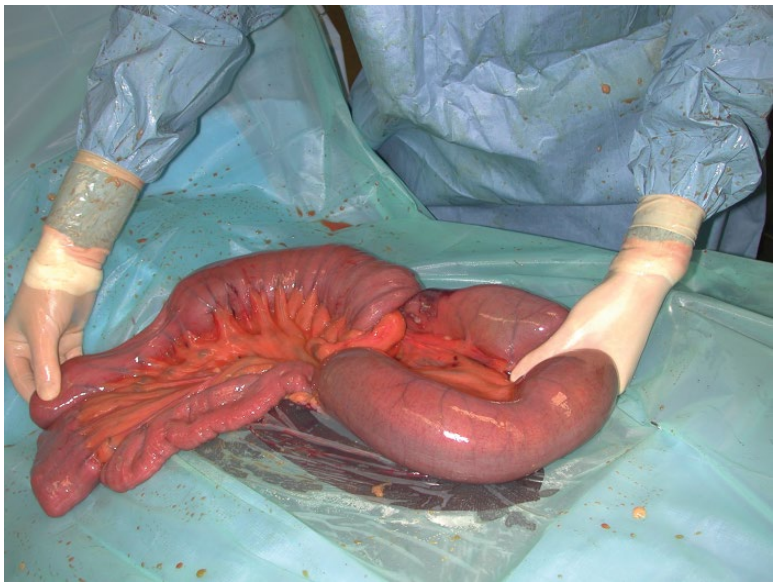


Figure 52.5 Jejunojejunal intussusception in an adult horse. Source: Courtesy of Ann Martens.

Occasionally, short jejunojejunal intussusceptions can also cause recurrent colic (Scott & Todhunter, 1985; Gift et al., 1993). Distended small intestine is usually palpable on rectal examination in adults, and was palpable as a tubular mass in 9% of horses in one case series (Gift et al., 1993). Gastric reflux is a frequent finding and peritoneal fluid changes may be variable, being reportedly normal in 38% of cases in one study (Gift et al., 1993). The length of jejunum involved can vary from 0.4 to 9.1 m and the intussusception may or may not be reducible (Gift et al., 1993; Edwards, 1986). Jejunojejunal intussusception is reduced by slow traction on the intussusceptum and gentle massage of the distal end of the intussuscipiens (Collier & Trent, 1983). If it is nonreducible, the entire intussusception can be removed by resection only (Gift et al., 1993), although this can make ligation of mesenteric vessels difficult (Edwards, 1986). Resection and anastomosis, either following reduction or without prior reduction, was required in all cases in two case series (Edwards, 1986; Gift et al., 1993).

Ileal intussusceptions are more common, with ileoileal and ileocecal intussusceptions accounting for 59% of all intestinal intussusceptions and 74% of all small intestinal intussusceptions in one case series (Ford et al., 1990). These can occur in a wide age range, from 2 weeks to 19 years (Ford et al., 1990), but in most cases occur in younger horses (Barclay et al., 1982; Edwards, 1986; Ford et al., 1990; Greet, 1992; Scott & Todhunter, 1985) at a median age of 1 year (Ford et al., 1990), with all cases in one study reported to be <24 months of age (Greet, 1992). Ileoileal intussusceptions usually form a short, doughnut-like ring close to the ileocecal junction (Edwards, 1986; Greet, 1992; Scott & Todhunter, 1985). Short ileocecal intussusceptions may result in mild, intermittent colic signs that are usually postprandial and may result in reduced appetite and fecal output, fever, weight loss, and failure to thrive (Ford et al., 1990), whereas intussusception of long segments of ileum can cause signs of severe small intestinal obstruction (Ford et al., 1990; Edwards, 1986). Ileocecal intussusceptions were palpated in the right dorsal quadrant of the abdomen in 31 and 50% of horses in two reports (Ford et al., 1990; Edwards, 1986). Peritoneal fluid may or may not be normal, being reported to be normal in most acute ileal intussusceptions in one study (Ford et al., 1990). With chronic intussusceptions, repeat episodes of intestinal obstruction can result in marked jejunal dilatation (even when empty) and muscular hypertrophy (Ford et al., 1990).

Ileocecal and ileoileal intussusceptions have been treated successfully by reduction only and by reduction and myotomy (Greet, 1992). Chronic intussusceptions of short segments of ileum may be impossible to reduce (and may rupture during attempted reduction) because of intestinal wall hypertrophy at the leading point of the intussusception and adhesion formation between intussuscepted segments (Ford et al., 1990; Greet, 1992), and may require incomplete bypass by ileocecostomy, with or without reduction (Ford et al., 1990; Maclean et al., 1991). A handsewn technique is preferable to stapling instruments because the ileal wall is so thick, and hypertrophied jejunum oral to the obstruction should recover over time. Rare long-term complications include stomal impaction, stomal constriction, ileal hypertrophy, and rupture (Ford et al., 1990; Mair & Lucke, 2000; Edwards, 1986). In acute ileocecal intussusception, the intussuscepted ileum and jejunum can be too edematous and hemorrhagic to reduce, and bypass by a jejunocecostomy without reduction can cause postoperative hemorrhage (Ford et al., 1990).

The prognosis for jejunal intussusceptions is reasonably good, with short-term survival rates for all horses undergoing general anesthesia of 43–67% and for horses that stood following general anesthesia of 60–75% (Edwards, 1986; Gift et al., 1993). Short-term survival for all horses with ileoileal or ileocecal intussusceptions is better, with short-term survival rates for all horses that underwent general anesthesia of 65–100% and for those that recovered following general anesthesia of 92–100% (Edwards, 1986; Ford et al., 1990; Greet, 1992). Some horses can have a protracted recovery after surgery for chronic ileocecal intussusception, with slow weight gain and episodes of mild colic (Ford et al., 1990). The inciting cause of the intussusception should be determined to prevent recurrence, including testing for *A. perfoliata* in horses that presented with ileoileal or ileocecal intussusceptions and appropriate anthelmintic treatment (see also the later section Ileal Impaction).

Inguinal Herniation and Rupture

Inguinal hernias and ruptures (Figure 52.6A–C) are a relatively uncommon but important cause of colic in entire males of all ages, accounting for 1.7–4.4% of horses undergoing exploratory laparotomy for colic (Mair & Smith, 2005; Wormstrand et al., 2014; Van der Linden et al., 2003) and 3.4–12.5% of those with small intestinal lesions (Mair & Smith, 2005; Wormstrand et al., 2014; Morton & Blikslager, 2002). The use of terms such as direct and indirect inguinal hernias, which are based on classifications used in humans, do not accurately describe the anatomy of hernias that occur in the horse and should be avoided (Cox, 1988). Inguinal herniation is the more common of the two forms and occurs when intestine passes through the vaginal ring into the vaginal tunic. Where intestine herniates through a rupture in the parietal layer of the vaginal tunic or the fascia of the vaginal ring, and comes to lie outside the vaginal tunic in the subcutaneous tissues, this is more correctly termed inguinal rupture (Cox, 1988). Where inguinal herniation occurs following

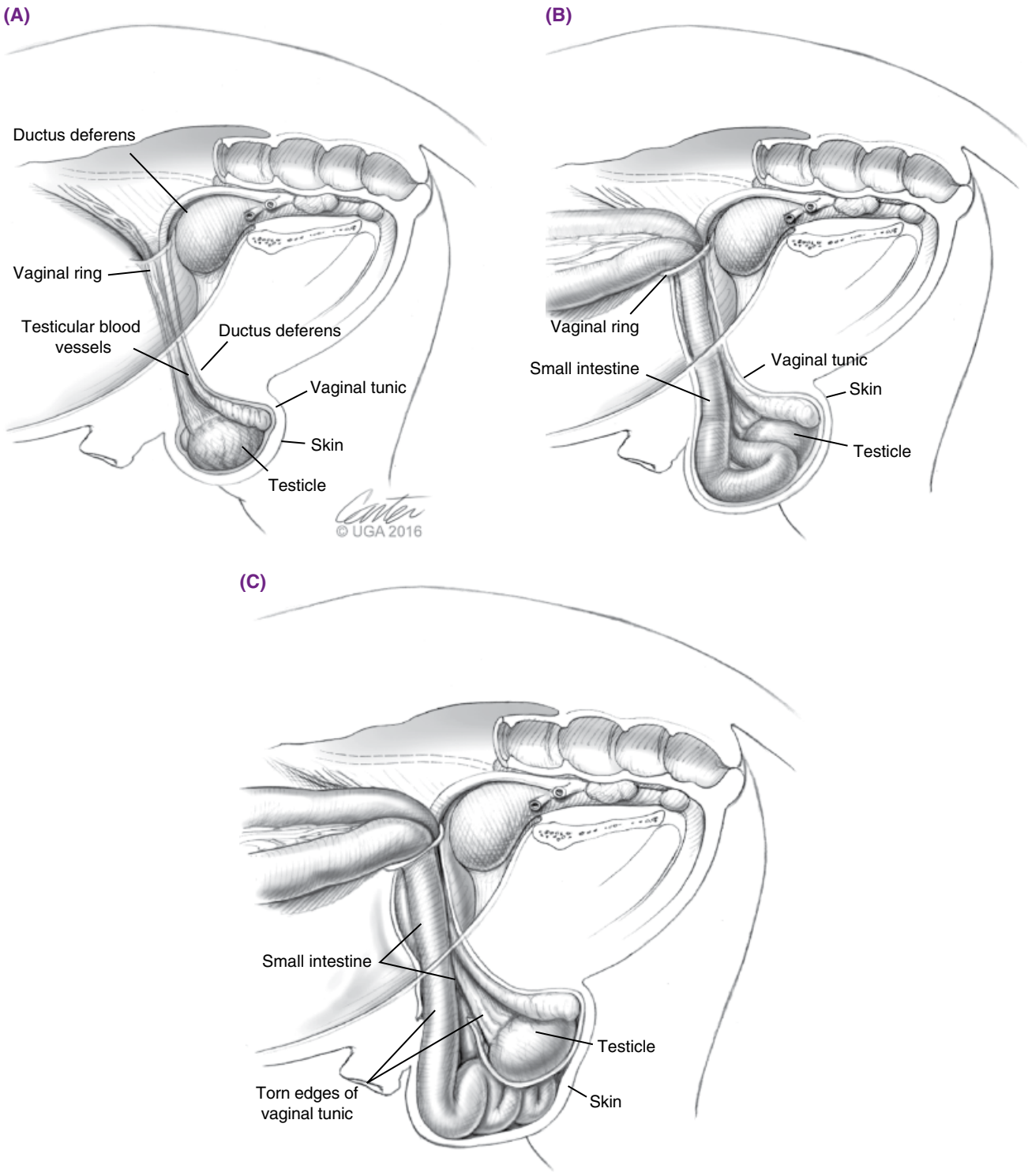


Figure 52.6 **(A)** Normal inguinal structures that are relevant to inguinal herniation and rupture in the horse. Note that the vaginal ring is the point of entry from the abdomen to the vaginal tunic. **(B)** Inguinal hernia formation with passage of small intestine through the vaginal ring into the vaginal tunic. **(C)** Inguinal rupture with herniation of intestine through a rupture in the parietal layer of the vaginal tunic and subcutaneous positioning of herniated small intestine. Source: Courtesy of the University of Georgia College of Veterinary Medicine.

castration, it is usually termed "evisceration" and most frequently occurs within 24 h following castration (Weaver, 1987; Shoemaker et al., 2004), but has been reported to occur up to 12 days later (Boussauw & Wilderjans, 1996). Evisceration occurred in 4.8% of cases following castration in one study (Shoemaker et al., 2004), and in horses with a prior history of scrotal or inguinal herniation, ligation of the vaginal tunic as close to the external inguinal ring as possible is recommended to reduce this risk (Shoemaker et al., 2004; Boussauw & Wilderjans, 1996).

Inguinal hernias and ruptures have been reported in a wide range of ages and breeds of entire intact males. Standardbreds, Draft breeds, Warmbloods, and Tennessee Walking Horses (Schumacher & Perkins, 2010; Wilderjans et al., 2012) have been suggested to be predisposed, owing to the high incidence of herniation in these breeds, but only Andalusian stallions have been shown to be significantly more likely to develop this form of colic than other breeds (Muñoz et al., 2008). There is some evidence that intestinal herniation may develop in horses with abnormally wide vaginal rings (Ivens et al., 2009; Marien, 2001), but the vaginal ring in normal horses is wide enough to accommodate small intestine. Based on the fact that some horses developed herniation and colic signs immediately following jumping exercise or mating, it has also been suggested that deformity of the vaginal ring, trauma, or changes in intra-abdominal pressure may play a role, but this is a subject of debate (Schneider et al., 1982; Weaver, 1987). Inguinal herniation rarely occurs in geldings (Schneider et al., 1982), thought to be because the vaginal rings reduce in size soon after castration (Schumacher & Perkins, 2010), and is rare in mares (Umstead et al., 1986; Cousty et al., 2010). Acquired inguinal hernias and inguinal ruptures usually result in compromise to the vascular structures contained within (Schumacher & Perkins, 2010). Horses usually present with signs of acute onset and severe colic, and the scrotum on the affected side is usually firm, enlarged, and painful on palpation (Fischer et al., 1995). Rectal examination usually confirms evidence of small intestine entering the vaginal ring on the affected side (Schneider et al., 1982) and transcutaneous ultrasonographic examination of the inguinal region and scrotum can be useful to confirm the presence of small intestine within the scrotum (Schumacher & Perkins, 2010).

In foals, congenital inguinal hernias are interchangeably referred to as scrotal hernias. These are evident shortly after birth and most frequently contain small intestine or occasionally portions of colon. These hernias usually resolve spontaneously within 3–6 months and are unlikely to result in intestinal strangulation (Cox, 1988; Schumacher & Perkins, 2010). Manual replacement of the hernia contents into the abdomen is recommended on a daily basis, and bandaging techniques to maintain reduction of the hernia may be undertaken (Schumacher & Perkins, 2010). Surgical correction is indicated if the hernia does not resolve spontaneously, the owner is concerned because of an apparent increase in size of the hernia, or if the vaginal tunic ruptures (Klohnen & Wilson, 1996). Inguinal rupture is less common and usually occurs within 48 h of birth if it is going to happen (Spurlock & Robertson, 1988; Van der Velden, 1988a). Affected foals present with signs of colic, depression, edema of the prepuce and scrotum, and herniated intestine that is irreducible, and the scrotal skin may feel cold and moist (Van der Velden, 1988a). Immediate surgical management is indicated in these cases, although intestinal resection is usually not required (Van der Velden, 1988a). Rates of postoperative survival for all foals with inguinal ruptures that undergo surgery range from 50 to 100% (Van der Velden, 1988a; Spurlock & Robertson, 1988).

Acquired inguinal hernias are more common in entire adult males, and inguinal ruptures are less common, the latter occurring in 4–8% of horses in two case series (Schneider et al., 1982; Van der Velden, 1988b). Most inguinal hernias are unilateral, but cases of bilateral inguinal herniation (Alves et al., 2010) and concurrent acquired inguinal hernia and inguinal rupture (Vasey, 1981) have been reported. Herniated intestine can be identified once a scrotal incision has been made and the vaginal tunic entered (Figure 52.7), but may occasionally return spontaneously into the abdomen during induction of anesthesia and positioning (Van der Velden, 1988b). Nonsurgical reduction of the hernia may be performed by external compression under general anesthesia (Wilderjans et al., 2012). However, this may not be successful in returning entrapped intestine into the abdomen and does not allow direct visual assessment of the affected intestine for vascular compromise, or decompression of small intestinal proximal to the entrapment. The latter may result in the development of small intestinal volvulus (Moll et al., 1991). Where abdominal exploration is not performed, these cases should be monitored carefully and subsequent laparotomy to remove nonviable intestine or to correct an intestinal volvulus may be required (Van der Velden, 1988b). Survival to hospital discharge for all cases undergoing general anesthesia is 67–71% and for horses that recovered from general anesthesia is 77–86% (Schneider et al., 1982; Weaver, 1987).

Diaphragmatic Herniation

Diaphragmatic hernias are relatively rare in adult horses, and did not occur in any cases undergoing laparotomy in some large case series (Phillips & Walmsley, 1993; Wormstrand et al., 2014; Mezerova et al., 2008; Van den Boom & Van der Velden, 2001), but were diagnosed in 0.3% of all horses undergoing exploratory laparotomy for

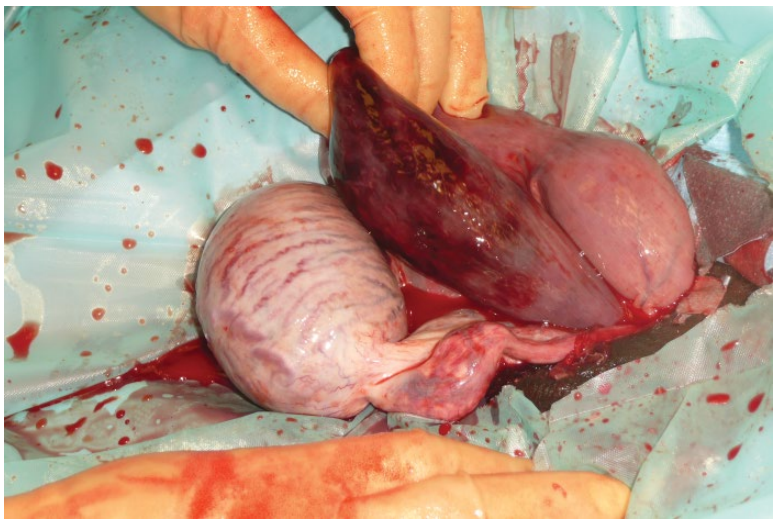


Figure 52.7 Acquired inguinal hernia in a mature Standardbred stallion. On opening the vaginal tunic, a loop of strangulated jejunum is evident lying adjacent to the testicle on the affected side.

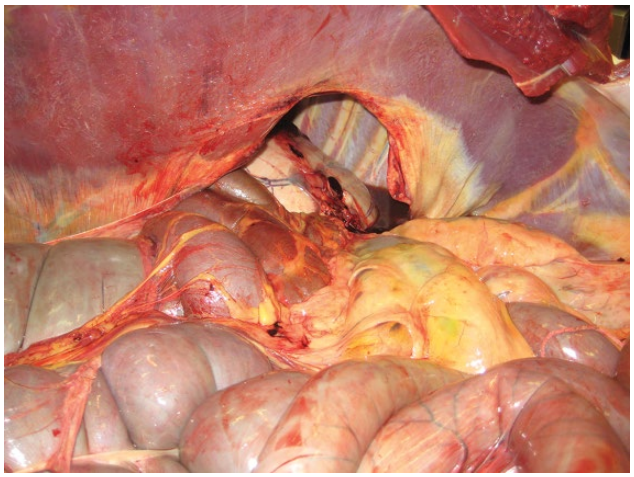


Figure 52.8 Necropsy specimen of a large, acquired diaphragmatic tear that had resulted in herniation of intestine in an adult horse. Source: Courtesy of Fernando Malalana.

colic in one series (Mair & Smith, 2005). They may also be seen in association with fractured ribs in neonates, representing 7% of neonatal foals undergoing surgery for colic in one study (MacKinnon et al., 2013). Hernias may be congenital or acquired in nature and there is no age, sex, or breed predisposition (Hart & Brown, 2009; Romero & Rodgerson, 2010). Congenital hernias usually have smooth edges and lack evidence of hemorrhage and fibrosis, whereas acquired defects have ragged edges and involve tearing of a variable portion and length of diaphragm (Figure 52.8), but definitive diagnosis is based on histology of the tissue (Hart & Brown, 2009; Romero & Rodgerson, 2010). Although herniation of any abdominal viscera may occur, herniation of small intestine is the most common (Romero & Rodgerson, 2010) and is more likely where smaller defects in the diaphragm are present (Edwards, 1993). Presenting clinical signs can be highly variable and include colic, tachypnea, dyspnea, exercise intolerance, epistaxis, lethargy, reluctance to move, and weight loss (Edwards, 1993; Hart & Brown, 2009; Romero & Rodgerson, 2010). Acquired hernias may be associated with a history of traumatic parturition in foals, pregnancy and parturition in mares, moderate to heavy exercise, and external trauma (Hart & Brown, 2009). Ultrasonographic and radiographic assessment of the thorax and abdomen is recommended in cases that have a history and clinical signs consistent with possible diaphragmatic herniation, and in the cases in which this was performed in one study (Hart & Brown, 2009), 82% of horses had changes consistent with a diaphragmatic hernia. Careful examination for concurrent injuries such as fractured ribs in foals (Palmer, 2012) or evidence of hemothorax/pneumothorax should be performed and managed appropriately, as death during anesthetic induction is not uncommon and respiratory complications can also occur intraoperatively (Hart & Brown, 2009; Romero & Rodgerson, 2010; MacKinnon et al., 2013).

At laparotomy, initial enlargement of the defect may be required to reduce herniated intestine (Edwards, 1993) and careful anesthetic monitoring is required, including the ability to perform mechanical ventilation where necessary (Clutton et al., 1992). Attempts should be made to perform closure of the diaphragmatic defect as repeat herniation can occur (Hart & Brown, 2009; Romero & Rodgerson, 2010). Closure may be performed by direct suturing or stapling of a polypropylene mesh over the defect (and combinations of both), using either hand or laparoscopic stapling equipment (Dabareiner & White, 1999; Hart & Brown, 2009; Romero & Rodgerson, 2010). Extension of the incision and placing the horse in a reverse Trendelenberg position may assist this. Alternatively, closure of the defect can be performed using hand-assisted thoracoscopic approaches in the standing horse immediately following anesthetic

recovery, or this may be delayed for a few days to weeks (Malone et al., 2001; Hart & Brown, 2009).

The prognosis for survival is poor, with two recent case series reporting overall short-term survival rates for all horses/foals presented with a diaphragmatic hernia of 16–23% (Hart & Brown, 2009; Romero & Rodgerson, 2010). In both series, a number of animals died during induction or recovery from anesthesia or were euthanased intraoperatively based on the quantity and degree of viscera involved. Postoperative monitoring for pneumothorax and hemothorax is important in these cases (Malone et al., 2001). For horses that recovered following surgery and general anesthesia, 73–77% survived to hospital discharge (Hart & Brown, 2009; Romero & Rodgerson, 2010). In the study by Hart & Brown (2009), horses were more likely to survive if they were younger (<2 years old), had small defects in the diaphragm, or had <50% of small intestine strangulated, and were less likely to survive if peritoneal fluid was serosanguinous in color.

Herniation Through the Gastrosplenic Ligament

The gastrosplenic ligament is a broad, thin portion of greater omentum that attaches the greater curvature of the stomach to the cranial edge of the spleen (Budras et al., 2011). A detailed visual description of the structure in a cadaver specimen was provided by Hunt et al. (2013). Entrapment of small intestine through a defect in the gastrosplenic ligament is an uncommon cause of colic necessitating surgical management, representing 0.3–1.5% of all horses undergoing exploratory laparotomy and 0.68–4.5% of all small intestinal lesions (Mair & Smith, 2005; Jenei et al., 2007). This lesion may develop in a wide range of ages and breeds and several studies have identified geldings to be significantly more likely to develop this lesion than mares and stallions, although the reasons for this are not clear (Jenei et al., 2007; Bergren et al., 2015). No significant difference in presentation between this lesion and other small intestinal strangulations has been reported and diagnosis is typically made at exploratory laparotomy. One case report (Hunt et al., 2013) described multiple loops of immotile, distended, and thickened small intestine located between the spleen and body wall on abdominal ultrasonography. While small intestine may normally be located along the ventral axial surface of the spleen (Klohnen et al., 1996), the former ultrasonographic findings may increase suspicion of this form of small intestinal strangulation.

In gastrosplenic entrapment (Figure 52.9), small intestine usually passes in a caudal-to-cranial direction through a defect in the ligament, resulting in entrapped intestine being found abaxial to the stomach and cranioabaxial to the spleen (Yovich et al., 1985). Entrapped intestine is usually freed relatively easily by traction, and enlarging the rent does not appear to cause problems or predispose to recurrence. Ligation of the gastroepiploic vessels within the ligament using commercial vessel sealing devices can be useful (Hunt et al., 2013). Suturing the defect closed is usually not possible (Yovich et al., 1985; Jenei et al., 2007) but it could potentially be accessible for laparoscopic closure (Jenei et al., 2007), although this is unlikely to be needed as recurrence has not been reported. Alternatively, the ligament could be partially transected to the nearest free border (Marien & Steenhaut, 1998). Postoperative survival is reasonably good, with overall rates of short-term survival in two case series reported to be between 73 and 81% (Jenei et al., 2007; Bergren et al., 2015).

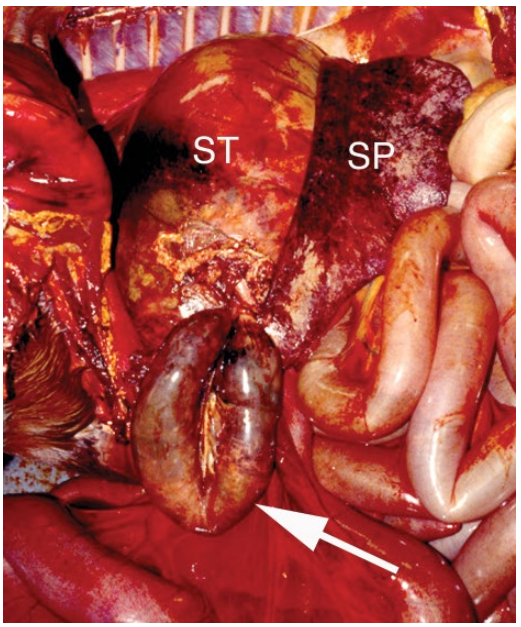


Figure 52.9 Necropsy specimen of incarceration in the gastrosplenic ligament. A segment of small intestine (arrow) has become strangulated after passing through a defect in the gastrosplenic ligament between the stomach (ST) and spleen (SP).

Mesenteric Rents

Mesenteric rents are a relatively uncommon cause of colic, resulting in small intestinal herniation in 2–8% of horses undergoing exploratory laparotomy for colic (Phillips & Walmsley, 1993; Gayle et al., 2000; Mair & Smith, 2005; Wormstrand et al., 2014) and 4–12% of small intestinal lesions diagnosed at surgery (Phillips & Walmsley, 1993; Morton & Blikslager, 2002; Mair & Smith, 2005; Wormstrand et al., 2014; Van den Boom & Van der Velden, 2001). This form of colic can occur in a wide range of age and breeds, and it is proposed that tears identified in broodmares may have been related to parturition (Gayle et al., 2000; Dart & Pascoe, 1994), which may also result in segmental ischemic necrosis of affected small intestine (Zamos et al., 1993). Mesenteric tears may be primary

lesions or congenital defects, or may develop secondary to another lesion such as ascarid impaction, ileal impaction, or mesodiverticular band, distant to or associated with a previous anastomosis (Gayle et al., 2000) or as a consequence of abdominal teratoma that resulted in a mesenteric tear (Arensburg et al., 2012).

There are few descriptions of cases in the literature, but in one case series of 15 horses with mesenteric rents causing small intestinal strangulation, small intestinal distention was palpable in 73% of horses that had rectal examination performed and nasogastric reflux was obtained in 53% (Gayle et al., 2000). Variable amounts of small intestine had herniated through the mesenteric defect (up to 12 m), and 87% of rents were located in the mesentery of the small intestine. Euthanasia was performed intraoperatively in 47% of horses due either to inability to reduce the intestinal obstruction, severe uncontrolled hemorrhage, inability to close the defect, or an extremely poor prognosis for survival based on the large amount (12 m) of intestine involved. Of the horses that recovered from surgery, 77% required a resection and anastomosis. Survival to hospital discharge was 47% for all horses undergoing surgery and 87.5% for horses that recovered following general anesthesia.

Closure of the entire mesenteric defect can be difficult or impossible through a conventional ventral midline abdominal incision and reherniation of small intestine may occur (Witte et al., 2013). Laparoscopic repair of mesenteric defects can be performed as a standing procedure in the early postoperative period (Sutter & Hardy, 2004). In another case report, a hand-assisted laparoscopic approach was used to reduce recurrence of small intestinal entrapment and enabled a large, radial rent in the small intestinal mesentery to be repaired (Witte et al., 2013).

Strangulating Umbilical Hernia

Despite the fact that umbilical hernias in foals are a common congenital defect, reported in 4.8% of a cohort of Thoroughbred foals in one study (Wohlfender et al., 2009), complications are uncommon. Intestinal strangulation, umbilical abscessation, and enterocutanous fistula formation was reported in 8.8% of horses treated at a referral hospital for umbilical hernias in one study (Freeman et al., 1988). Strangulated umbilical hernias represented 12% of horses admitted to a referral hospital with an umbilical hernia in another case series. Of horses undergoing exploratory laparotomy for treatment of colic, strangulating umbilical hernias are rare, representing 0–0.3% of horses undergoing exploratory laparotomy for treatment of colic (Mair & Smith, 2005; Phillips & Walmsley, 1993; Wormstrand et al., 2014; Van den Boom & Van der Velden, 2001), and 0–1.2% of foals undergoing abdominal surgery (Bartmann et al., 2002; Vatistas et al., 1996; Cable et al., 1997; MacKinnon et al., 2013).

In one case series (Markel et al., 1987), affected individuals varied from 1 day to 30 months of age (mean age of 11.5 months) and colic signs were not always evident, depending on the degree of luminal obstruction and compromise to the vascular supply (Markel et al., 1987). Small intestinal strangulation can develop in two ways. Most commonly, a parietal, or Richter, hernia develops, in which only a portion of the antimesenteric wall of the small intestine is entrapped and the lumen is not compromised (Freeman et al., 1988; Markel et al., 1987). This causes the umbilical hernia to become nonreducible, swollen, firm, edematous, and painful to palpation (Figure 52.10). Less frequently, a loop of small intestine may rupture through the hernial sac and dissect subcutaneously in a caudal direction (Freeman et al., 1988).

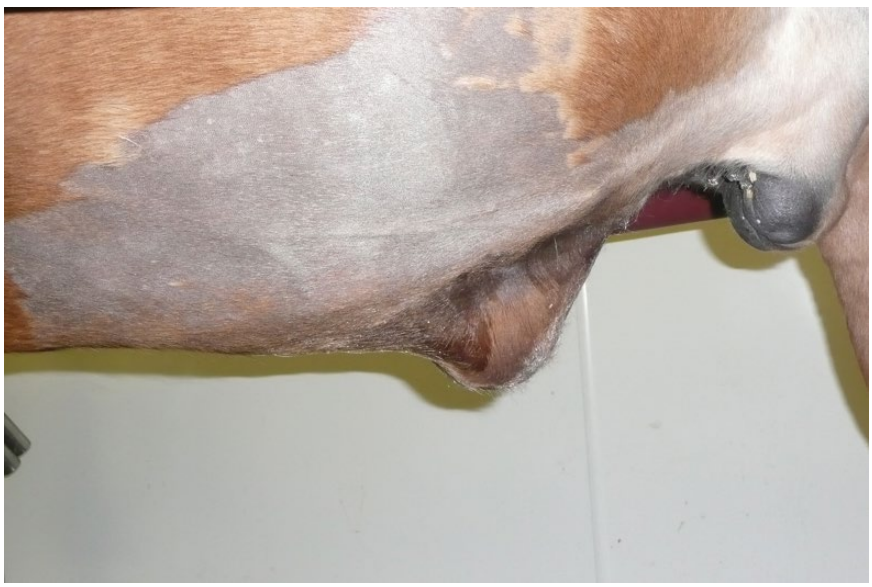


Figure 52.10 Acute onset of colic signs associated with swelling an umbilical hernia in a 2-year-old Warmblood filly. At surgery a Richter hernia of a portion of ileum was found that did not require resection.

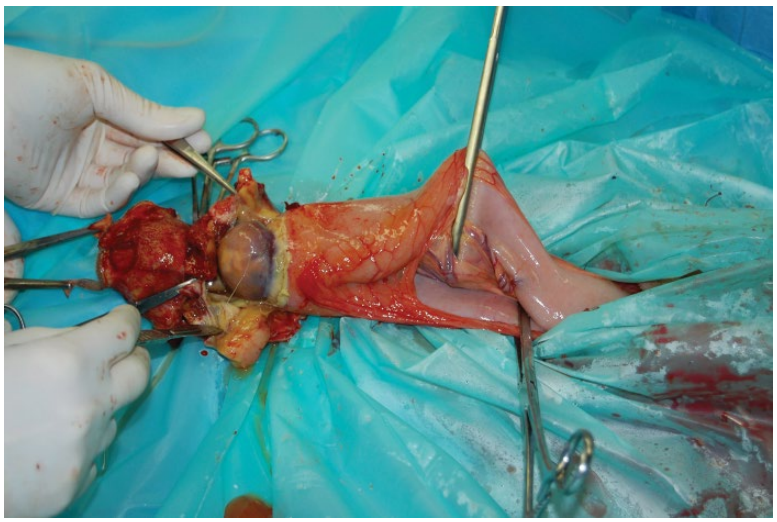


Figure 52.11 Richter hernia and subsequent adhesion of small intestine in an umbilical hernia requiring en bloc removal. Source: Courtesy of Ann Martens.

Umbilical abscessation can develop in some cases, which can lead to rupture of the hernia and formation of an enterocutaneous fistula (Freeman et al., 1988; Markel et al., 1987).

Surgical correction of strangulating umbilical hernias is performed by creating an initial ventral midline incision immediately cranial and caudal to the hernia sac to allow assessment of the strangulated portion of intestine and identification of any adhesions. The umbilical ring may then be incised, to allow open closure of the hernia following assessment and resection of intestine as required (Markel et al., 1987). Alternatively, where adhesions are present (Figure 52.11), en bloc excision of the hernial ring and intestinal resection, followed by closure of the abdominal wall, may be indicated (Orsini, 1997b). In cases with enterocutaneous fistula formation, horses should be fasted preoperatively and en bloc excision of the hernia ring performed to isolate the fistula from the abdominal incision during resection (Orsini, 1997b; Markel et al., 1987). The prognosis for survival is good (Markel et al., 1987; Freeman et al., 1988).

Vitelline Abnormalities

Failure of the vitelline (omphalomesenteric) duct, which connects the primitive yolk sac to the developing midgut, and its paired arteries and veins to atrophy normally during early fetal development can result in the formation of a congenital band, diverticulum, or cyst that may result in small intestinal strangulation. Mesodiverticular bands and Meckel diverticulum are a relatively rare cause of colic and, in two case series in which they were identified, represented 1.1–2.2% of small intestinal lesions causing colic (Mezerova et al., 2008; Van den Boom & Van der Velden, 2001). Although these are congenital defects, they can cause colic in a wide range of ages and breeds of horse. Because they can result in small intestinal strangulation, their presence is significant and emphasizes the need for thorough examination of all of the gastrointestinal tract that can be exteriorized in horses undergoing laparotomy for treatment of colic (Robert et al., 2008; Southwood, 2008). Even if not the primary cause of colic, identification and removal of these congenital abnormalities are recommended to prevent them resulting in a future colic episode (Southwood, 2008).

A mesodiverticular band is formed when either the right or more frequently the left vitelline artery and associated mesentery fail to atrophy during early embryonic development (Freeman et al., 1979). The band is usually found in the distal jejunum, approximately 1.5 m from the ileocecal junction. It extends from one side of the mesentery, usually the left, to the antimesenteric surface of the small intestine to form a triangular space (Figure 52.12). Small intestine can become entrapped in that space, resulting in stretching or tearing of adjacent mesentery, and resultant strangulation in the mesenteric rent that is formed. Of 17 horses in which mesodiverticular bands were evident at laparotomy, in only five (29%) was it the cause of colic (Edwards, 2004). Even if not the primary cause of colic, they can result subsequently in colic episodes (Robert et al., 2008). Mesodiverticular bands that are an incidental finding at laparotomy can be carefully dissected from the mesentery and serosal surface of the intestine, removing the potential for small intestine to become entrapped in the mesenteric pouch that is created by these bands. Occasionally, the band may not have an associated mesentery (Abutarbush et al., 2003), and a remnant of a vitelline vein has also been reported as a cause of small intestinal strangulation in a neonatal foal (De Bosschere et al., 1999).

Failure of the vitelline duct to atrophy normally can result in the formation of a Meckel diverticulum (Sprinkle et al., 1984) or rarely a persistent vitelline duct cyst (Jones

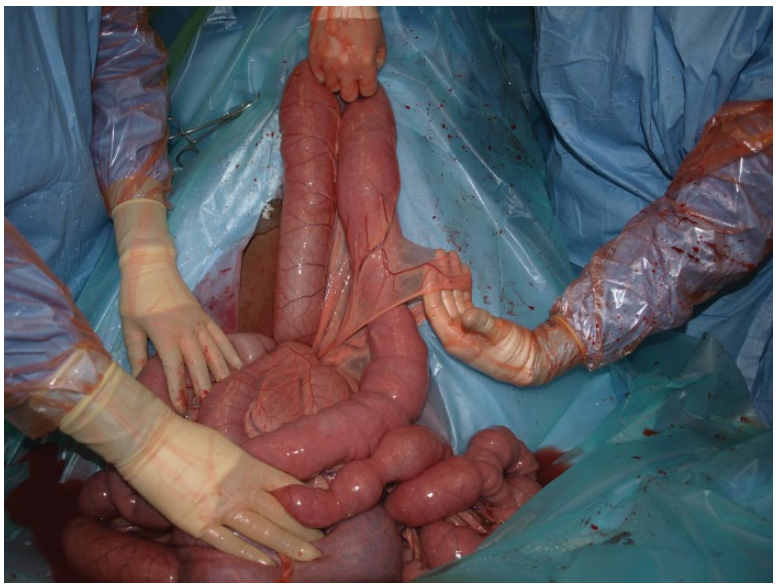


Figure 52.12 Intraoperative visualization of a mesodiverticular band that was a cause of colic in an adult horse.

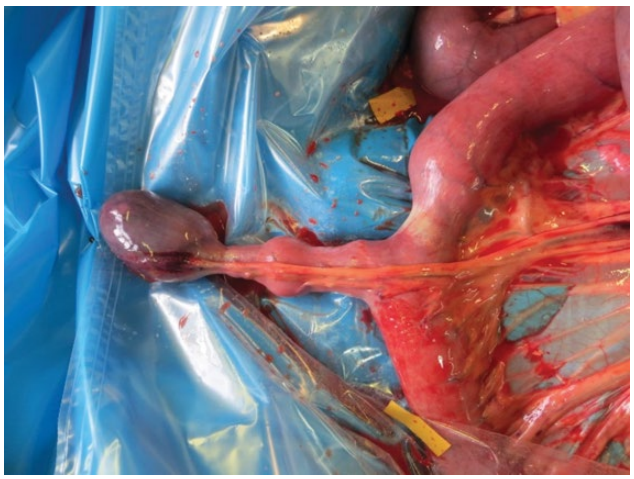


Figure 52.13 Intraoperative visualization of a Meckel diverticulum in a horse. Source: Courtesy of Ceri Sherlock.

et al., 2004). A Meckel diverticulum is a blind-ended tubular extension from the antimesenteric surface of the distal jejunum (Figure 52.13), approximately 120 cm from the ileocecal junction (Hooper, 1989; Sprinkle et al., 1984). It can be up to 35 cm long and 5–10 cm in diameter (Sprinkle et al., 1984). Occasionally, a fibrous band will persist from the apex of a Meckel diverticulum to the umbilicus to form a vitelloumbilical band, which can create an axis for small intestinal volvulus (Grant & Tennant, 1973). A Meckel diverticulum can cause colic by strangulating small intestine (Hooper, 1989; Barakzai et al., 2003), forming an axis for volvulus nodosus (Rocken et al., 1989), becoming strangulated in an umbilical hernia (Littré's hernia) (Hilbert et al., 1981), or by becoming impacted (Barakzai et al., 2003) to the point of necrosis and rupture (Sprinkle et al., 1984). In a review of 15,000 necropsies, Meckel diverticulum caused the death of all five horses (0.03%) in which it was found (Sprinkle et al., 1984), and in all four cases in which a Meckel diverticulum was identified at laparotomy it was the cause of small intestinal strangulation (Edwards, 2004). A persistent vitelline duct cyst was the cause of small intestinal intussusception in a single case reported (Jones et al., 2004). In cases of Meckel diverticulum, resection of the affected portion of intestine and anastomosis is indicated (Barakzai et al., 2003).

Miscellaneous Causes of Strangulating Obstruction

A number of other congenital and acquired lesions can result in small intestinal strangulation. Adhesions may develop after any intra-abdominal procedure and can form an axis around which attached small intestine can form a volvulus, or they can form fibrous bands through which small intestine can become strangulated (Baxter et al., 1989). Omental adhesions can also result in small intestinal strangulation (Phillips & Walmsley, 1993). Small intestine can become strangulated in anomalous congenital bands (Dearo et al., 2014) or through rents that develop in the omentum (Kelmer et al., 2008), mesometrium (Becht & McIlwraith, 1980), gastrohepatic ligament (Huskamp, 1982), small or large colon mesentery (Gayle et al., 2000), lateral ligament of the urinary bladder (Hawkins et al., 1993), cecocolic fold (Gayle et al., 2001), and components of the spermatic cord (Moll et al., 1999). Small intestine can also prolapse through the femoral canal (Torre et al., 2013), a vaginal laceration or defect in the bladder and urethra (Tulleners et al.,

1985), or through congenital (Hill & Story, 2014) or acquired hernias in the lateral abdominal wall. Entrapment of small intestine has also been reported in a mare with a uterine torsion (Ruffin et al., 1995) and within the nephrosplenic space in two horses (Goodrich et al., 1997). Mesenteric hematomas of unknown cause, and which can be difficult to access, can cause colic and ischemic necrosis of affected intestine (Van Hoogmoed & Snyder, 1996).

Nonstrangulating Obstructions

Ileal Impaction

Impaction of the ileum (Figure 52.14) is relatively uncommon but is one of the more common causes of nonstrangulating obstruction of the small intestine, accounting for 2–4.6% of horses that underwent laparotomy for treatment of colic and 4.1–11% of small intestinal lesions (Phillips & Walmsley, 1993; Mair & Smith, 2005; Mezerova et al., 2008). It is usually a primary condition, but can be secondary to other forms of ileal disease, and results in a doughy-to-solid, tubular mass of impacted ingesta of variable length that extends proximally from the ileocecal junction (Embertson et al., 1985; Hanson et al., 1998; Little & Blikslager, 2002).

Feeding Coastal Bermuda grass hay was associated with a three-fold increase in the likelihood of ileal impaction, as was failure to administer pyrantel within 3 months of hospital admission, implying an association with *Anoplocephala perfoliata* (tapeworm) infection, compared with unaffected horses (Little & Blikslager, 2002). Of ileal impaction cases in one study, 81% were demonstrated to be tapeworm related, and ileal impaction was more likely to occur in horses with increased infection intensity of *A. perfoliata* (Proudman et al., 1998). Ileal impaction may occur in horses with high tapeworm burdens due to intraluminal constriction and impaired intestinal motility at the ileocecal junction. The degree of mucosal damage and edema was proportional to the number of *A. perfoliata* present in one study (Proudman et al., 1998), and in another, horses with tapeworm infections had evidence of increased circular muscle hypertrophy and reduced numbers of myenteric plexi and neuronal cells at the ileocecal junction compared with parasite-free horses (Pavone et al., 2011). Ileal impaction occurs over a wide geographic area, but in the United States it occurs more commonly in the southeast, possibly related to feeding Coastal Bermuda grass hay, and was significantly more likely to occur in the months of September, October, and November (Hanson et al., 1998).

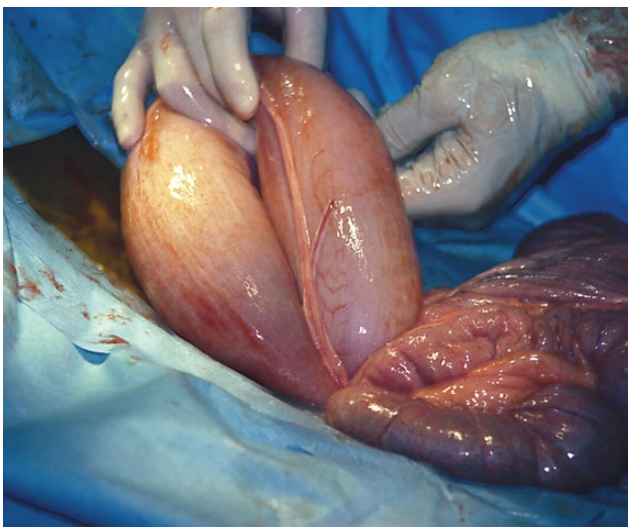


Figure 52.14 Intraoperative visualization of an ileal impaction due to Coastal Bermuda hay.

It can be difficult to differentiate ileal impactions from other forms of nonstrangulating small intestinal obstructions. Most horses present with moderate signs of abdominal pain (49–64%), with pain reported to be mild in 14–23% or severe in 19–21% (Hanson et al., 1998; Little & Blikslager, 2002; Fleming & Mueller, 2011). A specific diagnosis of an ileal impaction was made on rectal examination in 9–39% of horses (Hanson et al., 1998; Little & Blikslager, 2002; Fleming & Mueller, 2011) and generalized small intestinal distention was palpable in 87% of horses (Little & Blikslager, 2002). Nasogastric reflux was obtained in 46–62% of horses that had ileal impactions confirmed at laparotomy (Hanson et al., 1998; Little & Blikslager, 2002; Fleming & Mueller, 2011). Medical treatment may be undertaken in some cases, consisting of intravenous administration of polyionic fluids and frequent nasogastric decompression (Hanson et al., 1996; Fleming & Mueller, 2011), which may be followed by nasogastric administration of mineral oil once reflux has ceased (Hanson et al., 1996). Indications for surgical management include signs of persistent or uncontrollable pain despite analgesia, increased small intestinal distention, increased volumes of nasogastric reflux, deterioration in cardiovascular status, or changes in peritoneal fluid values (Hanson et al., 1998; Fleming & Mueller, 2011). Surgical treatment consists of extraluminal massage of the impaction, softening of the contents with intestinal fluid oral to the impaction, and decompression of the intestinal contents into the cecum. Infusion of saline and dioctyl sodium sulfosuccinate solution by injection into the lumen of the ileum using a 18-gauge needle can be utilized to assist softening of the impaction (Hanson et al., 1998). Sodium carboxymethylcellulose (SCMC) solution may be used to facilitate intestinal manipulation and minimize serosal trauma (Fleming & Mueller, 2011). Enterotomy, surgical bypass, or resection is rarely required or recommended (Hanson

et al., 1998; Little & Blikslager, 2002). Postoperative reflux has been reported to develop in 33–50% of cases (Little & Blikslager, 2002; Fleming & Mueller, 2011) and relaparotomy was required in 7% of cases in one study owing to persistent reflux, intestinal displacement, or adhesions (Fleming & Mueller, 2011).

In one case series, 54% of suspected or confirmed ileal impactions were managed medically and 92% survived to 1 year (Fleming & Mueller, 2011). The prognosis for postoperative survival in these cases is good, with 86–96% of all horses undergoing surgery for management of an ileal impaction and 91–96% of those that stood following general anesthesia surviving to hospital discharge (Hanson et al., 1998; Little & Blikslager, 2002; Fleming & Mueller, 2011). Long-term survival is also good, with 83–100% of horses alive at 1 year following hospital discharge (Hanson et al., 1998; Little & Blikslager, 2002; Fleming & Mueller, 2011), and has been shown to be better than that for other forms of small intestinal lesions managed surgically (Proudman et al., 2002b).

Recurrence is rare, occurring in 1.6% of cases in one study (Fleming & Mueller, 2011), but prevention should be based on making dietary changes if necessary, eliminating existing burdens of *A. perfoliata* and preventing high burdens of tapeworm developing in affected horses and other horses on the premises that might be at increased risk. Colic and diarrhea have been observed in a small number of horses 8–12 h following administration of praziquantel, which may be associated with killing of large numbers of tapeworms (Barrett et al., 2005). Although these clinical signs were transient and could be managed medically, in horses with known high tapeworm burdens, administration of 19 mg/kg pyrantel may be recommended as an initial treatment. Pyrantel at this dose has less efficacy against tapeworms and may be used to kill a small number of parasites, followed by administration of praziquantel or 38 mg/kg pyrantel to kill any remaining tapeworms a few weeks later (Barrett et al., 2005).

Ascarid Impactions

Large numbers of ascarid worms (*Parascaris* spp.) can cause acute small intestinal obstruction (Southwood et al., 1998). These parasites are virtually ubiquitous in foals worldwide and although the literature has predominantly referenced *Parascaris equorum*, *Parascaris univalens* is actually more prevalent, so the term *Parascaris* spp. should be used (Nielsen, 2016). Despite the widespread prevalence of this parasite, ascarid impaction is a relatively uncommon cause of colic, representing 0.5% of colic cases presented to one referral hospital and 0.4% of colic surgeries performed on horses <1 year of age (Cribb et al., 2006). Ascarid impactions usually occur in horses <12 months old but have been reported up to 5 years of age (Tatz et al., 2012). Cases were four times more likely to occur between the months of September and November in one study (Cribb et al., 2006) and 72–80% of affected individuals had received anthelmintic treatment within 24 h of colic signs developing (Cribb et al., 2006; Tatz et al., 2012).

Diagnosis is based on clinical signs consistent with a nonstrangulating small intestinal obstruction in at-risk foals, and ascarids may be obtained on nasogastric intubation (Cribb et al., 2006). Transabdominal ultrasonography is useful in identifying small intestinal distention and ascarids may be visualized (Tatz et al., 2012). Ultrasonographic examination has been validated as a means of detecting >10 ascarids within the small intestinal lumen (Nielsen, 2016). In this study, the ventral midline was imaged at three separate locations and ascarids were most reliably imaged when loops of small intestine were visualized within 5 cm of the abdominal wall. Careful ultrasonographic evaluation is required to visualize the ascarids that are visible as parallel hyperechoic lines within the intestinal lumen (Figure 52.15).

Ascarid impactions may result in simple obstruction of small intestine only or may be complicated by secondary volvulus or intussusception, occurring in 36% of foals in one study (Cribb et al., 2006), and can result in intestinal rupture (Cribb et al., 2006; Tatz et al., 2012). Small intestinal enterotomy or resection and anastomosis has been associated with significantly reduced survival (Tatz et al., 2012) and, where possible, manual evacuation of the

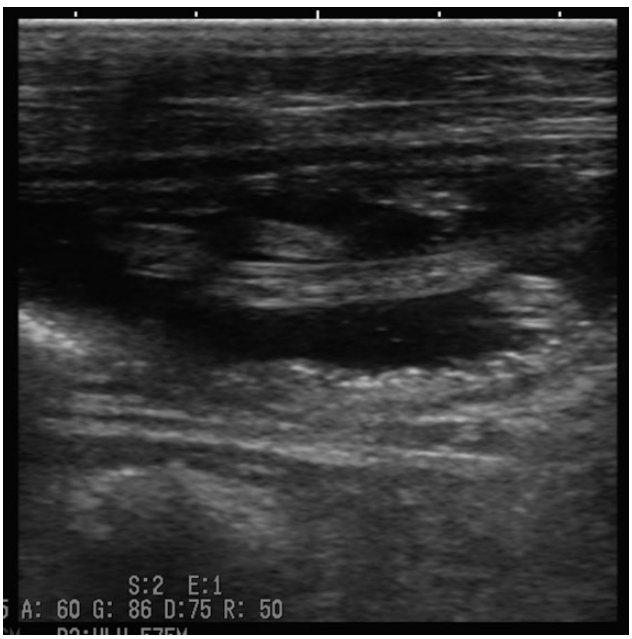


Figure 52.15 Ultrasound image of small intestine viewed transabdominally. An intraluminal ascarid (*Parascaris* spp.) can be seen as parallel hyperechoic lines ("train tracks") due to the ascarid cuticle being orientated perpendicular to the ultrasound beam. Source: Courtesy of Dr Martin Nielsen.

impacted ascarids into the cecum (rather than enterotomy) is recommended, using an appropriate lubricant such as SCMC to reduce trauma to the small intestine (Tatz et al., 2012). In contrast to a study that reported 92% mortality (Southwood et al., 1998), survival to hospital discharge in two separate case series was 79–80% (Cribb et al., 2006; Tatz et al., 2012) and was better in foals that had simple obstructions (79%) than in those that had impactions involving volvulus or intussusception (38%). Survival to 1 year was reported to vary from 27% (Cribb et al., 2006) to 60% (Tatz et al., 2012).

All foals should be considered to be exposed to infection until around 8 months of age, when immunity to the parasite develops, and the priority is to prevent large ascarid burdens developing (Nielsen, 2016). There is evidence of widespread resistance of *Parascaris* spp to commonly used classes of anthelmintics (Lyons et al., 2008, 2011; Armstrong et al., 2014) and anthelmintics that have a paralytic mode of action may predispose to impaction formation as large numbers of parasites are killed (Nielsen, 2016). Ascarid control should be prioritized in foals of 2–5 months of age, and benzimidazole-based treatments given every 2–3 months in foals together with fecal egg count reduction tests are recommended (Nielsen, 2016). Current diagnostic techniques cannot estimate the magnitude of ascarid burden, so ultrasonographic assessment of high-risk foals may be warranted (Nielsen et al., 2016).

Idiopathic Focal Eosinophilic Enteritis

Idiopathic focal eosinophilic enteritis (IFEE) is a rare cause of simple obstruction of the small intestine, but occurs with greater frequency in particular geographic regions (Archer et al., 2006a, 2014; Olmos et al., 2006), representing 3% of all colic admissions in a UK equine hospital (Archer et al., 2014) and 5% of all horses undergoing exploratory laparotomy in an Irish hospital population (Olmos et al., 2006). First identified in the late 1990s (Southwood et al., 2000), the lesions are characterized by visibly striking, hyperemic circumferential bands (Figure 52.16) or antimesenteric plaques (Figure 52.17) that are palpably thickened (Archer et al., 2006a) and result in functional and physical obstruction. These lesions have also been variously termed inflammatory bowel disease (Scott et al., 1999), idiopathic eosinophilic enteritis (Stanar et al., 2002), multifocal eosinophilic enteritis (Swain et al., 2003), and circumferential mural bands (Olmos et al., 2006). IFEE should be differentiated from focal small intestinal lesions characterized by

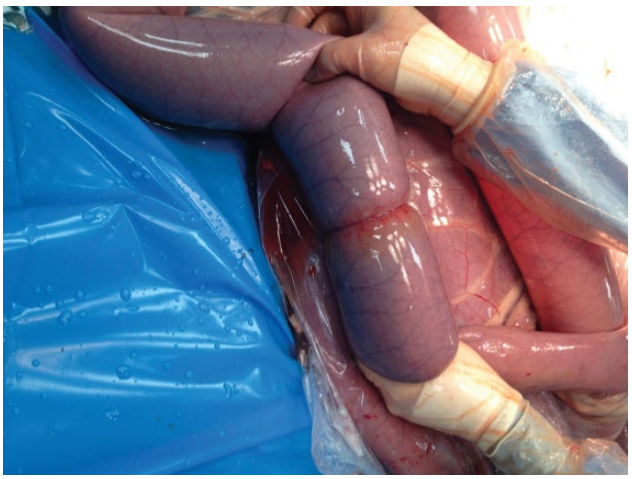


Figure 52.16 Circumferential idiopathic focal eosinophilic enteritis (IFEE) lesion resulting in impaction of ingesta oral to the site of mural thickening.

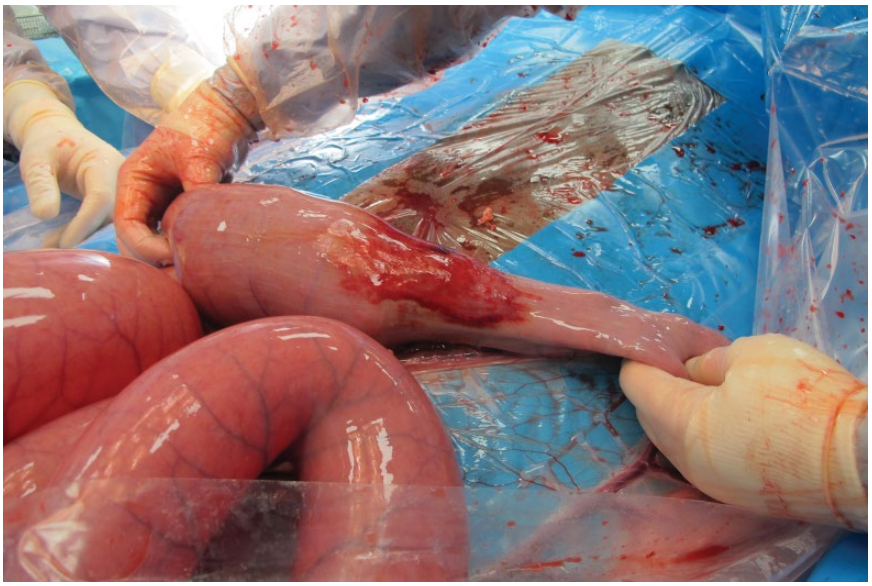


Figure 52.17 Antimesenteric plaque-like idiopathic focal eosinophilic enteritis (IFEE) lesion that resulted in simple obstruction of small intestine oral to the site.

eosinophilic infiltration that occur secondary to localized infiltration by the fungus *Pythium* spp. (Allison & Gillis, 1990) or encapsulated nematodes (Cohen et al., 1992).

The cause of IFEE is currently unknown and it appears to be sporadic or very rare in many hospital populations, being reported in a wide range of ages and breeds. An epidemiologic study in the United Kingdom demonstrated a consistent increase in cases over time (2000–2010) and significantly increased risk of IFEE in younger horses (0–5 years of age), in the months of July–November, and in specific geographic regions within the hospital catchment area (Archer et al., 2014). IFEE is difficult to diagnose preoperatively (Southwood et al., 2000) as horses may present with varying degrees of pain, and the presence of palpable small intestinal distention on rectal examination or nasogastric reflux can be variable depending on the location of any lesions and duration of disease (Archer et al., 2006a; Olmos et al., 2006).

Surgical management is usually indicated, based on pain, evidence of small intestinal distention and to diagnose definitively the cause of intestinal obstruction. One or more (up to 44) lesions may be present, but intestinal obstruction is usually due to impaction of ingesta at one lesion (Archer et al., 2006a; Olmos et al., 2006). Occasionally, gastric rupture may have already occurred (Archer et al., 2006a). Treatment consists of manual decompression of the impaction and small intestinal contents proximal to the obstruction into the cecum. Previously, surgical resection of lesions was described (Archer et al., 2006a; Southwood et al., 2000; Swain et al., 2003), but there is evidence that it is not required unless there is some form of marked intestinal stricture (Olmos et al., 2006). The lesions appear to resolve quickly and dexamethasone administration (0.08–0.1 mg/kg IV) either intraoperatively or immediately postoperatively may assist resolution of these lesions (Archer et al., 2006a; Olmos et al., 2006). Horses should be monitored carefully for the development of postoperative reflux and reimpaction, which may result in gastric rupture if frequent nasogastric decompression is not performed (Archer et al., 2006a; Olmos et al., 2006). Postoperative survival is considered to be good, with 91–100% of horses that recovered following general anesthesia surviving to hospital discharge (Archer et al., 2006a; Olmos et al., 2006). Recurrence of IFEE lesions in affected horses has not been reported.

Muscular Hypertrophy

Muscular hypertrophy is an uncommon cause of colic, accounting for 0.3–2% of horses undergoing exploratory laparotomy for treatment of colic and 0.7–4.7% of those with small intestinal lesions (Phillips & Walmsley, 1993; Mair & Smith, 2005; Mezerova et al., 2008). It is usually considered to be idiopathic but may occasionally develop secondary to obstruction or stenosis of the intestinal lumen, resulting in muscular hypertrophy of the small intestine oral to the lesion (Mair & Lucke, 2000).

Idiopathic muscular hypertrophy usually occurs in horses >5 years old (Edwards, 1981; Lindsay et al., 1981; Chaffin et al., 1992) but has been reported in foals (King, 1994) and has no breed predilection (Chaffin et al., 1992). Most horses present with a history of recurrent, low-grade colic of variable duration, with a duration of 2.4 years in one case. Horses may also present with or without anorexia and weight loss (Chaffin et al., 1992; Dechant et al., 2008). In one case series, 36% of horses commonly exhibited colic signs 1 h after eating (Chaffin et al., 1992). Clinical examination may be unremarkable between colic episodes (Chaffin et al., 1992), but when signs of colic are evident, small intestinal distention, and occasionally portions of thickened small intestine, may be palpable (Chaffin et al., 1992). Muscular hypertrophy can result in the formation of acquired diverticula and intestinal wall rupture can also occur (Lindsay et al., 1981; Mair & Lucke, 2000). Transabdominal and/or transrectal ultrasonographic examination is particularly helpful in identifying thickening of the small intestine and hypertrophy of the muscular layer (Dechant et al., 2008) and can assist identification of diverticula formation (De Solis et al., 2015), facilitating surgical planning.

The ileum is most commonly affected (Lindsay et al., 1981; Chaffin et al., 1992), but cases that involve only the duodenum (Toth & Hollerrieder, 2005) or multiple segments of jejunum, with normal intestine interspersed between (Dechant et al., 2008), have been reported. Treatment includes surgical bypass or intestinal resection (Chaffin et al., 1992; Dechant et al., 2008), but in cases involving the duodenum, surgical access may not be possible (Toth & Hollerrieder, 2005). Where surgical resection or bypass is possible, in idiopathic forms of the disease, complete recovery has been reported, including cessation of colic episodes and regaining of normal body condition (Dechant et al., 2008).

Diverticula and Pseudodiverticula

Diverticula are outpouchings of all layers of the intestinal wall (Figure 52.18) and are usually congenital, solitary lesions located on the mesenteric border. Pseudodiverticula are most frequently acquired and are usually multiple in nature, and result from disruption or weakening of the tunica muscularis, forming outpouchings of mucosa and submucosa (Southwood et al., 2010; Mair et al., 2011). The most common form of congenital diverticula is Meckel diverticulum (see the earlier section Vitelline Abnormalities), but other congenital jejunal diverticula have been described (Yovich & Horney, 1983; Riccaboni et al., 2000; Cook et al., 1996). Acquired diverticula and pseudodiverticula are uncommon and can develop

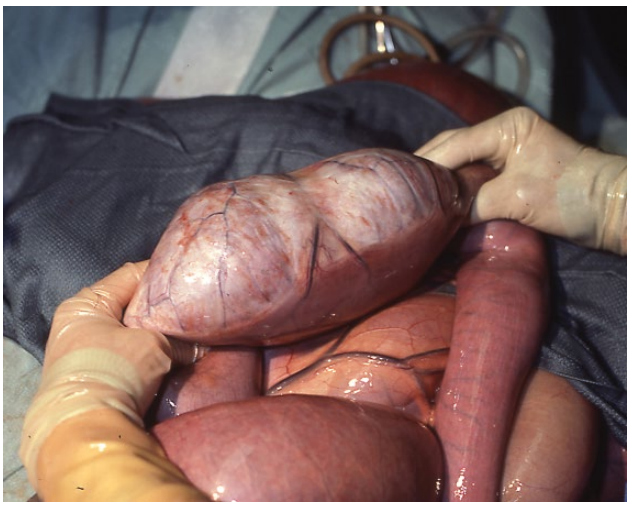


Figure 52.18 Ileal diverticulum that became impacted and caused obstruction of the ileum.

secondary to idiopathic muscular hypertrophy (De Solis et al., 2015) or lymphoma (Mair et al., 2011), and may be a cause of recurrent colic (Mair et al., 2011; Madison et al., 1991). They are usually located on the mesenteric border of the intestine (Southwood et al., 2010), but pseudodiverticula that developed secondary to lymphoma were located on the antimesenteric border (Mair et al., 2011). Transabdominal and/or transrectal ultrasonography may assist the identification of these lesions (De Solis et al., 2015) and rupture of these may occur. Surgical bypass or resection may be curative depending on the nature and location of the diverticula (Southwood et al., 2010; De Solis et al., 2012; Madison et al., 1991), but the prognosis for pseudodiverticula associated with lymphoma is very poor (Mair et al., 2011).

Neoplasia

Intestinal neoplasia is relatively uncommon in horses (Baker & Ellis, 1981) (see Chapter 62). It may affect a wide range of ages and breeds, with Arabian horses overrepresented in one study (Taylor et al., 2006) and no apparent sex predisposition. The alimentary form of lymphoma is the most common form of intestinal neoplasia (Figure 52.19), representing 56% of intestinal neoplasia cases in one study, of which 74% involved the small intestine (Taylor et al., 2006). Adenocarcinoma was the next most common cause of small intestinal neoplasia followed by smooth muscle tumors including leiomyosarcoma and leiomyoma (Figure 52.20) (Taylor et al., 2006). Ganglioneuroma (Allen et al., 1989), intestinal carcinoid (Orsini et al., 1988), and peripheral nerve sheath tumors (Kirchhof et al., 1996) have also been identified in the small intestine. In one study, lymphoma was a cause of formation of multiple pseudodiverticula in the small intestine (Mair et al., 2011).

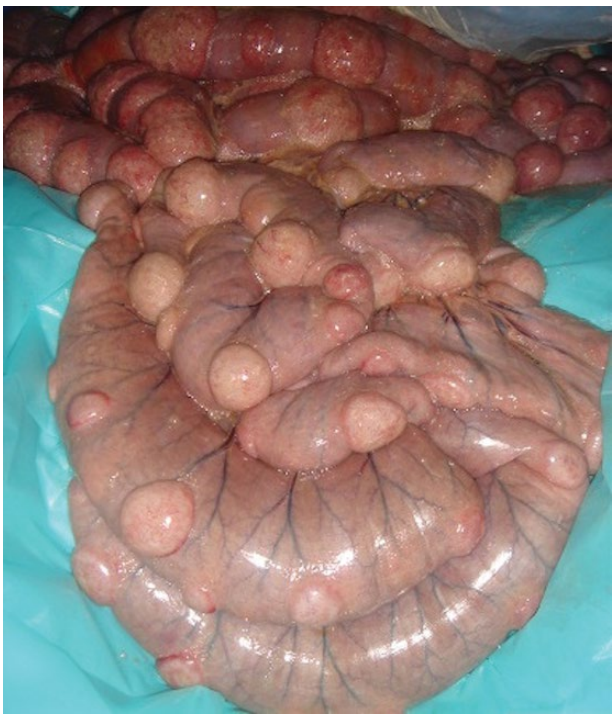


Figure 52.19 Alimentary lymphoma in a 10-month-old Spanish sports horse. Source: Courtesy of Dr Maria Luisa Rodriguez Pozo.

Clinical signs of intestinal neoplasia include weight loss, acute or recurrent colic, anorexia, and fever. The most consistent clinical signs in one study were poor body condition, tachycardia, tachypnea, fever, and diarrhea (Taylor et al., 2006). Investigation is based on rectal examination, routine blood analyses, abdominocentesis, ultrasonographic examination of the abdomen, rectal biopsy, and exploratory laparotomy (Taylor et al., 2006). Intestinal neoplasia was diagnosed antemortem in 13 of 34 horses (38%) in the study by Taylor et al (2006). Surgical removal of a discrete, focal, and accessible tumor may be successful (Hanes & Robertson, 1983; Allen et al., 1989; Livesey et al., 1986) but the prognosis for horses with multifocal or diffuse lymphoma lesions is grave (Mair et al., 2011). In the series of cases by Taylor et al (2006), the median time from onset of clinical signs to death or euthanasia was 1.9 months and only 15% of horses survived to hospital discharge.

Duodenal Ulceration and Stricture

Duodenal ulceration and stricture can develop in foals as a sequel to gastroduodenal ulcer disease and can result in delayed gastric outflow due to either functional or mechanical obstruction (Coleman et al., 2009; Zedler et al., 2009). Duodenal lesions were present in 80% of a series of foals requiring surgical management for gastric outflow obstruction (Zedler et al., 2009). Typically, gastroduodenal obstruction occurs in foals <4 months of

Figure 52.20 Pedunculated leiomyoma that had resulted in small intestinal strangulation (intraoperative view following transection of the pedicle).

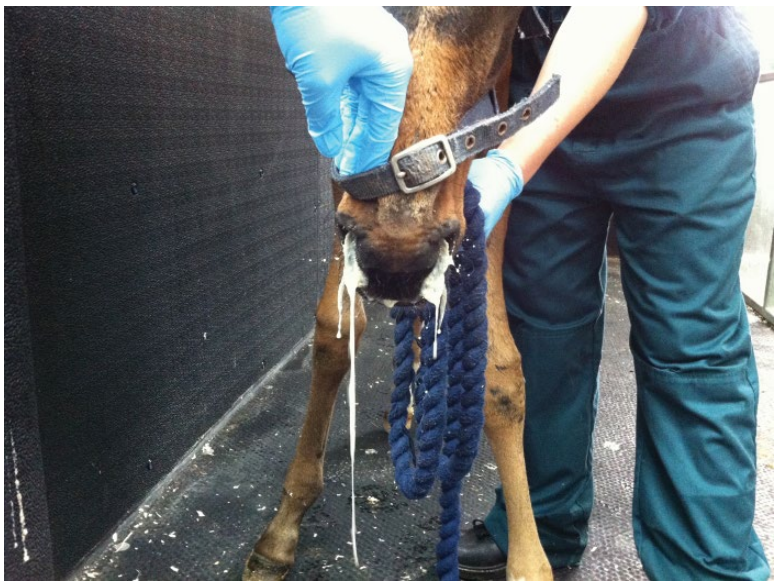


Figure 52.21 Spontaneous regurgitation of milk in a 4-week-old foal that had been treated for diarrhea 1 week previously. Source: Courtesy of Harry Carslake.

age (Orsini & Donawick, 1986; Coleman et al., 2009) and it is usually acquired in nature. Affected foals frequently have a history of recent illness such as diarrhea (Zedler et al., 2009), and administration of nonsteroidal anti-inflammatory drugs (NSAIDs) and stress have been implicated in the pathogenesis of this condition (Acland et al., 1983). Rarely, congenital strictures (Kol et al., 2005) or acquired strictures in older foals or adult horses have been reported (Ettlinger et al., 1990; Ross et al., 1989). Affected foals may present with a variety of clinical signs, including weakness, anorexia, bruxism, ptyalism, fever, diarrhea, and regurgitation of milk (Figure 52.21), and colic signs may be seen, particularly after suckling (Orsini & Donawick, 1986; Zedler et al., 2009). Esophagitis from reflux and subsequent megaesophagus, aspiration pneumonia, peritonitis secondary to rupture of ulcers, pancreatitis, and cholangiohepatitis (due to reflux of duodenal contents into the bile and pancreatic ducts) can develop as sequelae to disease or can occur postoperatively in foals that require surgical management (Acland et al., 1983; Orsini & Donawick, 1986; Zedler et al., 2009) (see Chapter 34).

Diagnosis is based on history and clinical findings, endoscopy, ultrasonography, and radiography (plain and contrast studies) (Zedler et al., 2009; Orsini, 1997a; Sprayberry, 2015). Endoscopy enables ulcers to be directly visualized, but where pyloric stricture develops the duodenum cannot be fully assessed (Figure 52.22). Ultrasonography of the stomach and duodenum can provide useful adjunctive information, such as impending perforation of an ulcer (Sprayberry, 2015), but diagnosis is usually confirmed by radiography. Plain

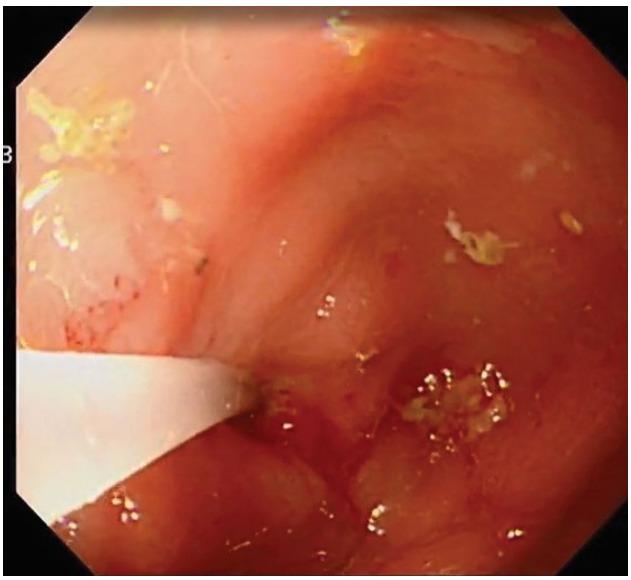


Figure 52.22 Endoscopic examination of the foal in Figure 52.21. Stricture of the pylorus had resulted in a gastric outflow obstruction. Source: Courtesy of Harry Carslake.

radiographs may reveal evidence of aspiration pneumonia, a dilated fluid-filled esophagus, and gastric distention, and gas may be evident in the hepatic duct (Orsini, 1997a). Diagnosis of gastric outflow obstruction is usually confirmed if minimal or no contrast material is observed aboral to the stomach or duodenum 30–90 min following nasogastric administration of barium (10 mL/kg) (Zedler et al., 2009), and cholangitis or cholangiohepatitis should be suspected where there is evidence of contrast agent in dilated bile ducts (Orsini, 1997a) (see Chapter 37).

Surgical management is indicated in cases where medical management is unsuccessful and gastric outflow obstruction persists. In a series of 119 foals that underwent abdominal surgery, gastroduodenal ulceration represented 5.8% of cases (Cable et al., 1997). Surgical management is based on bypass of the obstructed section of stomach or duodenum (Campbell-Thompson et al., 1986; Orsini & Donawick, 1986; Zedler et al., 2009; Coleman et al., 2009) and a variety of procedures have been described, including gastroduodenostomy and gastrojejunostomy with or without jejunojejunostomy (see Chapters 34 and 44 for a more detailed description of these). Two studies have demonstrated that survival to hospital discharge following surgery is very good (97–100%) but that the long-term prognosis is fair, with 69% surviving to 2 years in one study (Zedler et al., 2009) and 50% surviving to 3 years in a separate study (Coleman et al., 2009).

Miscellaneous Simple Obstructions

Duodenal obstruction in horses can cause severe pain, voluminous gastric reflux, and, in some horses, spontaneous gastric reflux through the nostrils (Mair, 2002).

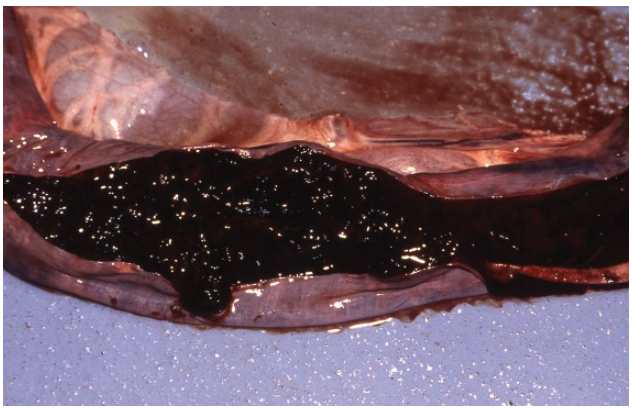


Figure 52.23 Intramural hematoma that caused obstruction of the jejunum by extraluminal compression.

Impactions of the duodenum and jejunum are rare, and causes include impacted feed material (Durham, 1998), compressed cracked corn (Bohanon, 1988), trichophytobezoar (Turner, 1986), compacted wood fragments (Green & Tong, 1988), persimmon fruit (Kellam et al., 2000), molasses-based horse licks (Mair, 2002), baling twine (Baker et al., 1974), and a cholelith (Laverty et al., 1992). Extraluminal causes of simple obstruction include intra-abdominal abscesses (Phillips & Walmsley, 1993), intramural hematoma (Figure 52.23) (Kobluk & Smith, 1988), and adhesions (Figure 52.24) (Baxter et al., 1989). Diffuse or localized peritonitis and localized intestinal necrosis can follow small intestinal perforation by wire (Davies, 1983; Dobson & Lopez, 1981), a porcupine quill (Modransky et al., 1983), ulcers (Hunter, 1975; White & Mair 2008), and unidentified materials (Elce et al., 2003). Localized lesions can be resected (Davies, 1983; Clutton et al., 1992).

Congenital segmental aplasia of jejunal lymphatics in foals (Campbell-Beggs et al., 1995; May & Good, 2007) (Figure 52.25) or tearing of postsurgical mesenteric adhesions resulting in rupture of mesenteric lymphatic vessels (May et al., 1999) may cause chyloperitoneum and colic. Surgical resection of affected intestine has been reported in four foals (Edwards et al., 1994), but the affected small intestine may be too extensive to resect (May & Good, 2007). Conservative treatment of congenital chyloabdomen, which is performed in humans, has not been reported in foals but might be an option in some cases (Campbell-Beggs et al., 1995). Neonatal prematurity, asphyxia-related injury, and septicemia can result in functional failure of the gut blood–mucosal barrier and failure of intestinal motility (Sprayberry, 2015). A syndrome of acute gastric and small intestinal ileus has been reported as a cause of acute colic in the post-parturient mare, and recurred in two mares following subsequent parturition (Hillyer et al., 2008). In this series of 15 mares, 17 episodes of ileus occurred and medical management alone was successful in six episodes, nine

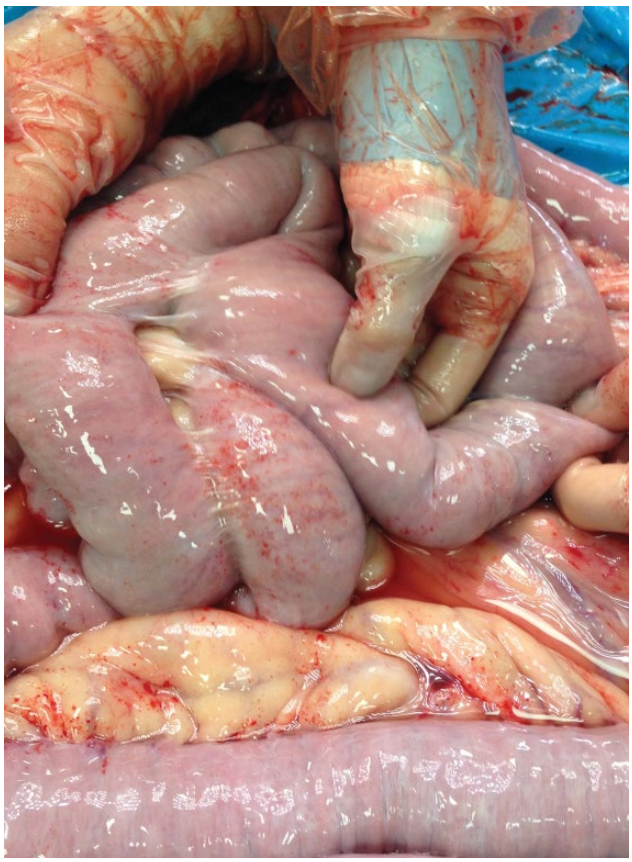


Figure 52.24 Adhesions that had formed between adjacent loops of small intestine and resulted in simple obstruction of small intestine, causing acute signs of colic. The gelding had undergone laparotomy and resection of small intestine 4 years previously.

episodes required surgical decompression of the small intestine, and two episodes required euthanasia due to gastric rupture (Hillyer et al., 2008).

Inflammatory and Infiltrative Disease

Duodenitis–Proximal Jejunitis (See Chapter 30)

Duodenitis–proximal jejunitis (DPJ), also termed gastroduodenitis-jejunitis, hemorrhagic fibrinonecrotic duodenitis, proximal jejunitis, proximal enteritis, and anterior enteritis, is an acute and sporadic disease that results in severe inflammation of the duodenum and proximal jejunum and is characterized by small intestinal ileus, abdominal pain, dullness, and profuse nasogastric reflux (Johnston & Morris, 1987; Freeman, 2000; Edwards, 2000; Cohen et al., 1994; Underwood et al., 2008). The prevalence of DPJ is difficult to determine from existing evidence in the published literature, but appears to vary between different geographic regions. It is reported to be less frequently seen in California than in other parts of the United States (Klohnen et al., 1996) and to be more severe in nature in the southeastern United States (White et al., 1987) than in the northeast (Johnston & Morris, 1987). There does not appear to be an age, breed, or sex predisposition to disease. The etiology is unknown but current evidence suggests some association with *Clostridium difficile* based on the fact that toxigenic strains were cultured from the reflux of 100% of DPJ cases and only 6.25% of the controls in one study (Arroyo et al., 2006). This study also found no evidence that *Clostridium perfringens* or *Salmonella* is involved in the pathogenesis. DPJ has been reported to be more likely to occur in horses that receive increased amounts of concentrates or horses that grazed pasture compared with control horses (Cohen et al., 2006), which was hypothesized potentially to result in disruption of the gastrointestinal microflora with consequent *C. difficile* colonization and overgrowth.

It can be challenging to differentiate DPJ from a small intestinal strangulating or nonstrangulating lesion. The clinical hallmark of DPJ is reflux of a large volume of fluid through a nasogastric tube (usually >48 L in the first 24 h), and this can be red–brown in color or may be normal in appearance (Cohen et al., 1994; Edwards, 2000). The degree of abdominal pain is variable and may range from mild to severe (Johnston & Morris, 1987; White et al., 1987). In contrast to horses with strangulating lesions, horses with DPJ may present with fever, leukocytosis, or a greater volume of gastric reflux, and their behavior may become more normal and a reduction in tachycardia may occur following gastric decompression (Johnston & Morris, 1987; White et al., 1987). The degree of small intestinal distention and the wall thickness are variable on palpation per rectum and ultrasound examination (Johnston & Morris, 1987; Le Jeune & Whitcomb, 2014). Most horses with DPJ have tachycardia, prerenal azotemia, dehydration, hypotension, and electrolyte abnormalities (Freeman, 2000). Peritoneal fluid from horses with DPJ may occasionally be serosanguinous, and the nucleated cell count and total protein concentration increase to a lesser extent than with a strangulating obstruction (Johnston & Morris, 1987). Concurrent complications may include laminitis, cardiac arrhythmias, and hepatic injury (Cohen et al., 1994; Cornick & Seahorn, 1990; Davis et al., 2003). Enteritis can also result in the development of hyperammonemia (Dunkel et al., 2011). Horses with DPJ have been shown to have significantly greater serum gamma-glutamyl transferase (GGT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) activities than horses with strangulating obstruction, which may be due to ascending infection from the common bile duct, absorption of endotoxin or inflammatory mediators from the portal circulation, or hepatic hypoxia caused by systemic inflammation and endotoxemic shock (Davis et al 2003).

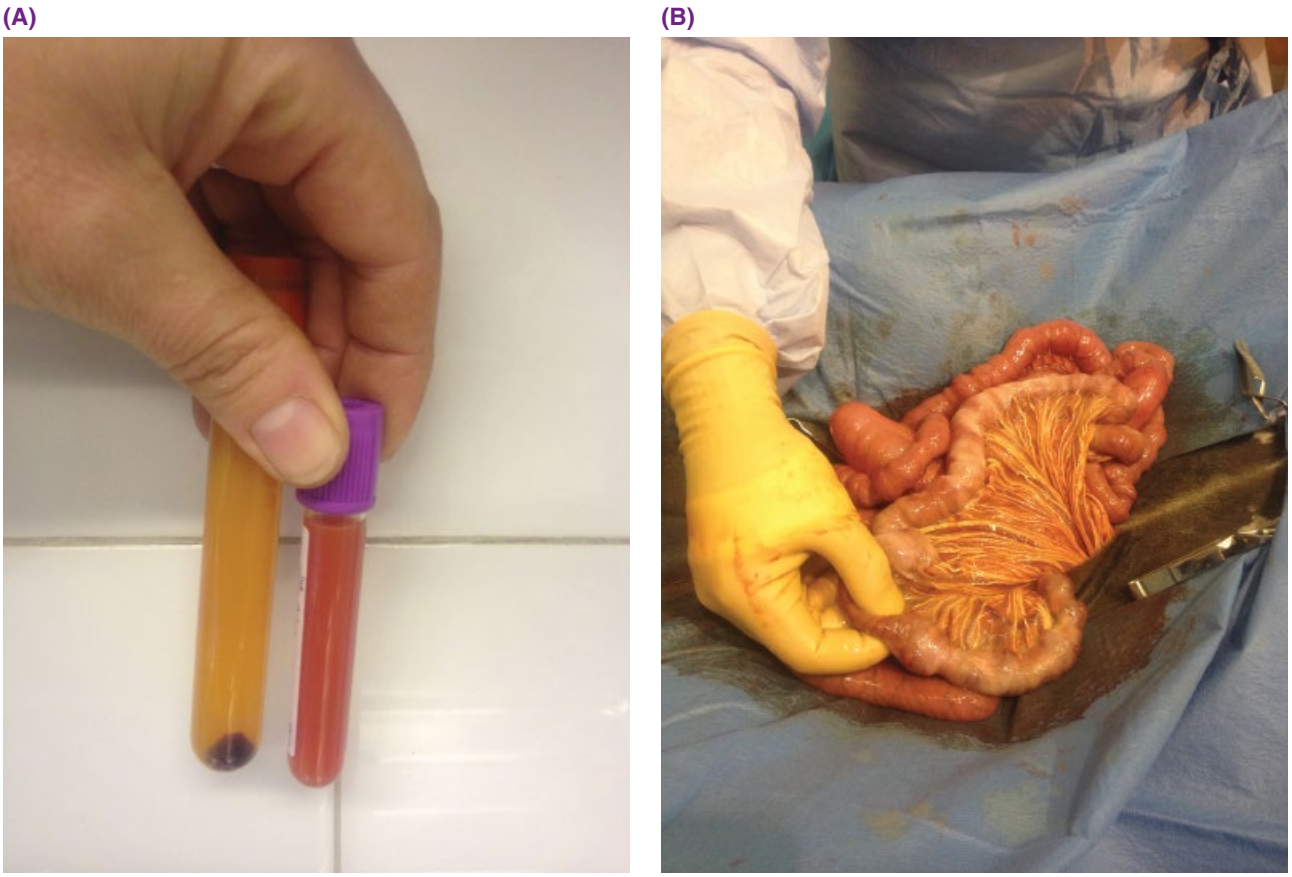


Figure 52.25 Congenital lymphangectasia and chyloabdomen in a neonatal foal. The foal had presented with acute colic shortly after parturition and characteristic opaque peritoneal fluid was obtained **(A)**. At laparotomy, dilation of the lymphatics in the affected segments of jejunum is evident **(B)**. The foal was euthanased at the owner's request. Source: Courtesy of Richard Tyler.

Laminitis was more likely to develop in horses with DPJ weighing ≥550 kg and in horses in which hemorrhagic reflux was obtained (Cohen et al., 1994).

DPJ can be managed medically but in some cases, particularly those exhibiting more severe signs of abdominal pain, surgical management is indicated in order to rule out a strangulating lesion of the small intestine (Freeman, 2000; Edwards, 2000; Underwood et al., 2008). Lack of response to medical therapy and the associated costs of prolonged medical therapy may result in surgery being performed to obtain a definitive diagnosis or may result in euthanasia (Underwood et al., 2008). In one study, 73% of cases were managed medically and in the remainder (27%) surgical exploration was undertaken (Underwood et al., 2008). At surgery, the proximal jejunum is diffusely hyperemic (Figure 52.26) and management consists of decompression of the small intestinal contents into the cecum followed by supportive medical therapy (Edwards, 2000). Medical management consists of frequent gastric decompression, replenishing fluid and electrolyte losses, combating endotoxemia, and restoring normal gastrointestinal motility (Feary & Hassel, 2006). Diarrhea, thrombophlebitis, pneumonia, and laminitis can develop (Underwood et al., 2008), requiring additional appropriate preventive and supportive therapy.

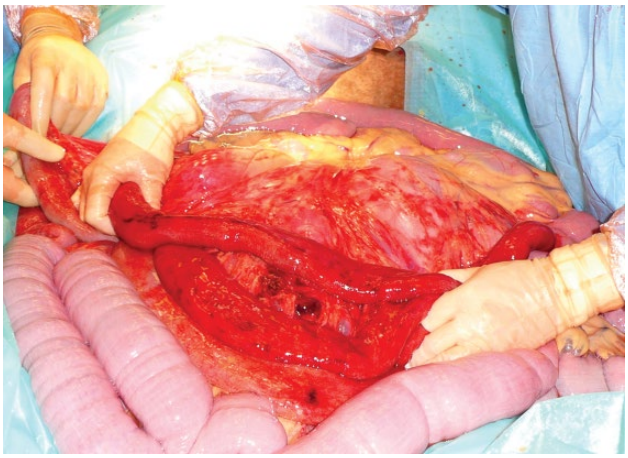


Figure 52.26 Intraoperative appearance of duodenitis–proximal jejunitis in an adult horse that had presented with severe signs of colic.

Survival is variable, reported to be 25–94% to hospital discharge (Johnston & Morris, 1987; White et al., 1987),

and in one study was reduced in horses that developed laminitis, with short-term survival rates of 45.4% compared with 69% in horses that did not develop laminitis (Cohen et al., 1994). In one study, overall survival to hospital discharge was 87% and there was no significant difference between these rates in horses managed medically (91%) and those managed surgically (75%). As horses were not randomly assigned to medical or surgical treatment, it is not possible to compare the two groups directly as surgical cases represented those with more severe forms of DPJ. Euthanasia was due to visual evidence of severe small intestinal compromise, laminitis, pneumonia, and persistent nasogastric reflux (Underwood et al., 2008).

Neonatal Enteritis (See Chapter 30)

Enteritis and enterocolitis are common in neonates, representing 43% of neonates presented to a referral hospital with colic, and may be caused by bacterial or viral pathogens (MacKinnon et al., 2013). However, differentiation between enteritis/enterocolitis and strangulating small intestinal disease can be challenging (MacKinnon et al., 2013). Diagnosis is based on assessment of physical status, results of hematology, biochemistry, and peritoneal fluid analysis, findings on ultrasonography and/or radiography, response to medical therapy and administration of analgesia, and serial changes that occur in these over time (see Chapter 31). Foals with enteritis usually present with leukopenia, neutropenia, and fever, but fever is not reliable in foals in differentiating between enteritis and other lesions (Sprayberry, 2015). Neonates with strangulating obstructions of the small intestine and those with necrotizing enterocolitis frequently exhibit signs of abdominal distention and altered mucous membrane color, but those with strangulating small intestinal lesions are more likely to show signs of severe abdominal pain, continuous pain, and nonresponse to analgesia compared with other causes of neonatal colic, including enteritis (MacKinnon et al., 2013).

Abdominal ultrasonography is particularly useful in differentiating between different forms of neonatal gastrointestinal disease (De Solis et al., 2012), but the ultrasonographic appearance of small intestine can be similar in enteritis and strangulating small intestinal lesions. Increased mural thickness is common to both, but identification of edema in the intestinal wall prior to development of mural thickening may be suggestive of a strangulating small intestinal lesion (Sprayberry, 2015). Foals with enteritis/enterocolitis are more likely to have evidence of fluid-filled intestine than strangulating small intestinal lesions (MacKinnon et al., 2013), and evidence of hyperechoic intramural gas echoes (pneumatosis intestinalis; Figure 52.27) is characteristic of necrotizing enteritis/enterocolitis (De Solis et al., 2012). Medical

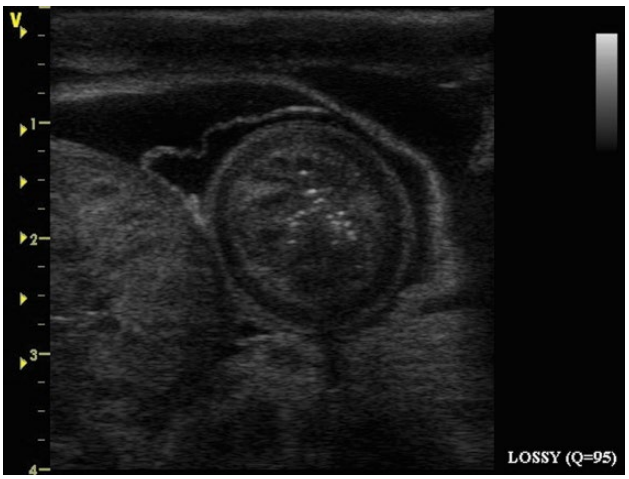


Figure 52.27 Transabdominal ultrasound image of small intestine in a neonatal foal. Hyperechoic intramural gas echoes (pneumatosis intestinalis) that are evident is virtually pathognomic for necrotizing enterocolitis. Source: Courtesy of Fernando Malalana.

therapy consists of intravenous fluids, analgesia, antimicrobials, parenteral nutrition, and plasma (MacKinnon et al., 2013). Rates of survival to hospital discharge for neonatal foals with enteritis/enterocolitis are 70–86% and are worse (33–36%) for neonates with necrotizing enteritis/enterocolitis (De Solis et al., 2012; MacKinnon et al., 2013).

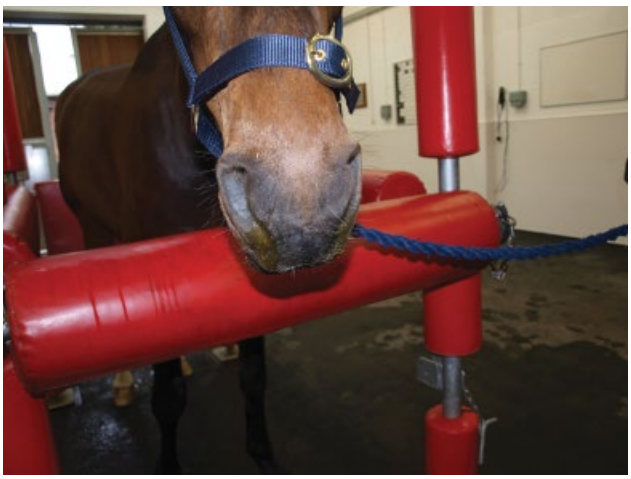
Equine Grass Sickness (See Chapter 56)

Equine grass sickness (EGS; equine dysautonomia) is a cause of functional small intestinal obstruction that occurs in certain geographic regions. First reported in Scotland in 1909, it occurs frequently in the United Kingdom and has been confirmed in cases in many countries in northern Europe and suspected in cases that have occurred in the Falkland Islands and Australia (Pirie et al., 2014), and has been diagnosed in a mule in the United States (Wright et al., 2010). An identical disease, Mal Seco, has been described in South America, predominantly in Chile (Araya et al., 2002). The definitive cause currently remains unknown (Pirie et al., 2014). The epidemiology of EGS is well characterized in the United Kingdom and a number of risk factors for the disease have been identified (Wood et al., 1998; Newton et al., 2004; McCarthy et al., 2004; French et al., 2005; Doxey et al., 1991; Wylie et al., 2014). In the United Kingdom, EGS is more likely to occur in younger horses (2–7 years of age) and in the months of April–May (Doxey et al., 1991; Wood et al., 1998).

EGS is a polyneuropathy that affects the central and autonomic nervous systems of horses and the clinical presentation will vary depending on the degree of neuronal degeneration in the autonomic and enteric nervous

systems (Pirie et al., 2014). Cases are usually defined as being acute, subacute, or chronic in nature, based on the extent of neuronal degeneration in the enteric nervous systems. Horses with the acute and subacute forms may present with signs of low-grade colic, and in acute cases small intestinal distention and spontaneous nasogastric reflux may be evident (Figure 52.28A) (Lyle & Pirie, 2009). Other characteristic clinical signs include tachycardia, bilateral ptosis (Figure 52.28B), muscle fasciculations, hypersalivation, and tucked-up abdominal appearance, and secondary impaction of the large colon may be evident on rectal examination (Lyle & Pirie, 2009). EGS should be considered as a differential diagnosis in high-risk horses in relevant geographic regions with characteristic clinical signs or where there is small intestinal distention that has no apparent etiology evident at laparotomy. Ileal biopsy should be performed in these cases as a means of antemortem diagnosis, confirming the presence of neuronal degeneration or complete loss of autonomic neurons (Scholes et al., 1993; Milne et al., 2010). Immunohistochemical staining with synaptophysin can be a useful way of confirming EGS where the findings on conventional histology are equivocal (Waggett et al., 2010). The prognosis for survival is generally hopeless in cases with ongoing reflux and evidence of small intestinal distention. More chronic cases, in which horses are able to maintain their hydration, eat, and pass feces may be candidates for nursing care and some may recover (Doxey et al., 1999; Jago et al., 2016).

(A)



(B)

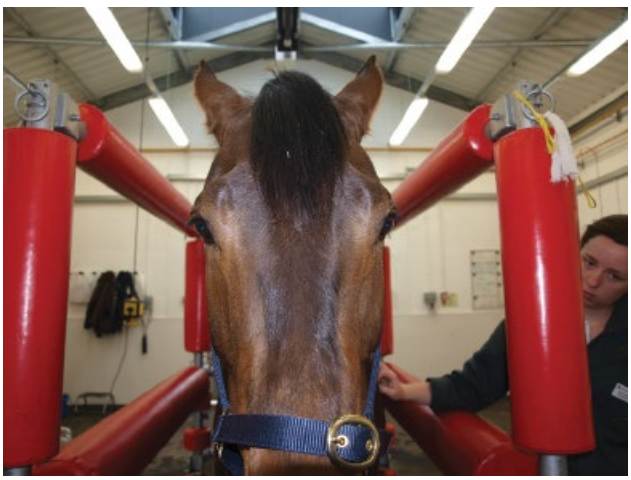


Figure 52.28 Spontaneous reflux observed at the nostrils in a horse with the acute form of equine grass sickness **(A)**. Bilateral ptosis is also evident **(B)**.

Equine Proliferative Enteropathy (See Chapter 30)

Equine proliferative enteropathy (EPE) is an emerging disease that has a widespread global distribution and may occur as a sporadic disease or may be associated with outbreaks on breeding farms (Frank et al., 1998; Lavoie et al., 2000; McClintock & Collins, 2004; Deprez et al., 2005; McGurrin et al., 2007; Merlo et al., 2009). EPE is caused by the pathogen *Lawsonia intracellularis*, which is an obligate intracellular organism (Williams et al., 1996), and infected feces from wild mammal reservoir hosts may be involved in disease epidemiology (Pusterla & Gebhart, 2013). It is primarily a disease of foals, most frequently occurring in weanling foals at around 4–7 months of age (Frazer, 2008), but infection may occur in older horses (Meyer et al., 2014). The disease is characterized clinically by fever, lethargy, peripheral edema, diarrhea, colic, and weight loss. Diagnosis can be challenging but a presumptive diagnosis is based on the age of the affected animal, clinical signs, hypoproteinemia/hypoalbuminemia, and ultrasonographic evidence of thickening of the small intestinal wall (Figure 52.29) (Pusterla & Gebhart, 2013). Antemortem diagnosis is confirmed by serology and molecular [polymerase chain reaction (PCR)] identification of *L. intracellularis* in the feces or from a rectal swab of affected foals (Pusterla et al., 2008). Treatment consists of antimicrobial therapy with macrolides alone, or in combination with rifampin, chloramphenicol, oxytetracycline, or doxycycline administered for 2–3 weeks together with concurrent supportive therapy (Sampieri et al., 2006; Pusterla & Gebhart, 2013). Use of an avirulent *L. intracellularis* vaccine should be considered in naïve and endemic farms to prevent or reduce the incidence of EPE (Pusterla & Gebhart, 2013; Lavoie, 2014). The prognosis for survival with appropriate therapy is good, with mortality rates of 13–31% reported (Pusterla & Gebhart, 2013).

Other Inflammatory or Infiltrative Disease

Enteric pythiosis is caused by *Pythium insidiosum*. This pathogen causes granulomatous disease, typically of the skin and subcutis, that is most commonly diagnosed in the Gulf Coast states of the United States, but also in the

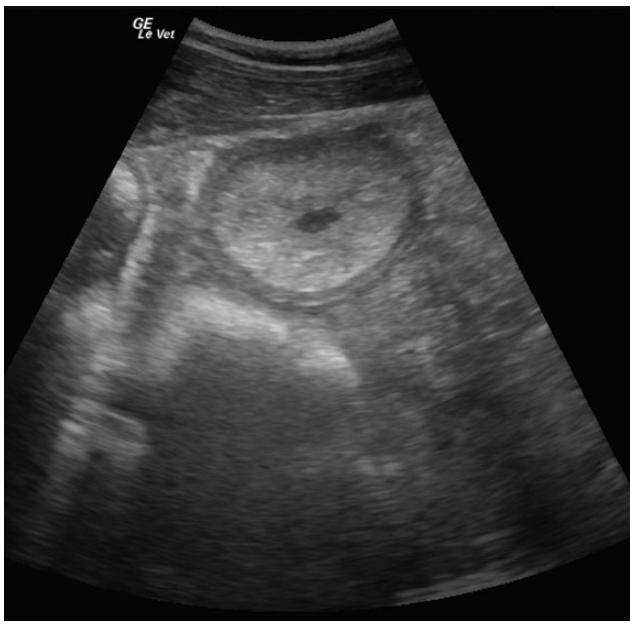


Figure 52.29 Transabdominal ultrasound image of small intestine in a foal with equine proliferative enteropathy demonstrating increased intestinal wall thickness. Source: Courtesy of Fernando Malalana.

Midwest United States (Purcell et al., 1994). *Pythium insidiosum* granuloma can cause jejunal obstruction, and clinical signs are weight loss and mild, intermittent abdominal pain (Purcell et al., 1994). Reported cases have been amenable to resection, which can be effective (Purcell et al., 1994; Allison & Gillis, 1990).

Intestinal fibrosis has been reported as a cause of weight loss and colic in horses in a small geographic distribution in Colorado, United States, possibly related to ingestion of a toxin (Traub-Dargatz et al., 1992). This lesion has also been reported in other regions of the United States and more variable clinical signs were reported (Johnson et al., 1997). Affected horses have extensive thickening of the intestinal wall, mainly in the submucosa, involving most or all of the jejunum and ileum, and with multifocal petechial hemorrhages on the serosa in some horses (Traub-Dargatz et al., 1992). The thick-walled small intestine can be palpated per rectum (Traub-Dargatz et al., 1992). Resection may be possible, but the extent of involvement can be too extensive to allow normal postoperative absorption (Traub-Dargatz et al., 1992).

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Diseases of the Cecum

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Based on studies of horses presented to university referral centers for evaluation of abdominal pain, approximately 4% of these horses had diseases that primarily affected the cecum (Campbell et al., 1984; Plummer et al., 2007). In another study of horses undergoing exploratory celiotomy for gastrointestinal disease, approximately 4% of the conditions had primary involvement of the cecum (Collatos & Romano, 1993). However, results of the former study indicate that the survival rate for horses presented with pain due to diseases of the cecum is less than 50%. Hence, although diseases of the cecum that result in abdominal pain are encountered less commonly than diseases affecting some other portions of the horse's gastrointestinal tract, diseases of the cecum should be regarded as being important by equine practitioners. The most common diseases of the cecum encountered in clinical practice are cecal tympany, cecal impaction, and cecocecal/cecocolic intussusception. This chapter reviews the important clinical aspects regarding these and other diseases that affect the cecum, their identification, methods of treatment, and prognosis for survival. Specific attention is given to complications associated with diseases affecting the cecum.

Cecal Tympany

Prevalence, Etiology, and Risk Factors

Distention of the cecum with gas occurs commonly in horses with conditions affecting the large colon, most notably colonic displacements, colon volvulus, or obstruction of the small colon. Less often, cecal tympany occurs as a primary disease, presumably due to rapid fermentation of lush pasture grasses or an abrupt change in diet (Campbell et al., 1984). In either situation, distention of the cecum causes or contributes to pain.

Clinical Findings

The most obvious clinical findings are distention of the barrel of the abdomen, taut paralumbar fossae, pain, tachycardia, and tachypnea. Simultaneous auscultation and percussion of the abdomen in the right paralumbar region will reveal a high-pitched pinging sound, characteristic of a severely distended viscus (Figure 53.1). The rectal examination will reveal a taut ventral cecal band, which courses diagonally from the right dorsal to the left ventral abdomen, and nonindentable distention of the cecum (see Chapter 20).

Treatment

Treatment of primary cecal tympany includes removal of the gas. This can be achieved by surgically preparing a site in the right paralumbar region, desensitizing it with local anesthetic, and inserting a 14–16-gauge 12.7 cm intravenous catheter into the base of the cecum. The hub of the catheter is connected to a suction device and the gas is evacuated; alternatively, the catheter is connected to an extension set with the end submerged in water so the evacuated gas can be seen bubbling in the water; this ensures correct placement of the catheter within the gas distended viscus (Figure 53.2). Gas evacuation can be facilitated by applying pressure to the cecal base per rectum. After the gas has been removed, the catheter is flushed with physiological saline solution or a broad-spectrum antibiotic during removal of the catheter to reduce the likelihood of cellulitis along the needle track in the body wall. If cecal tympany has developed secondary to other conditions, there is no need to utilize this procedure as correction of the underlying problem will resolve the tympany.

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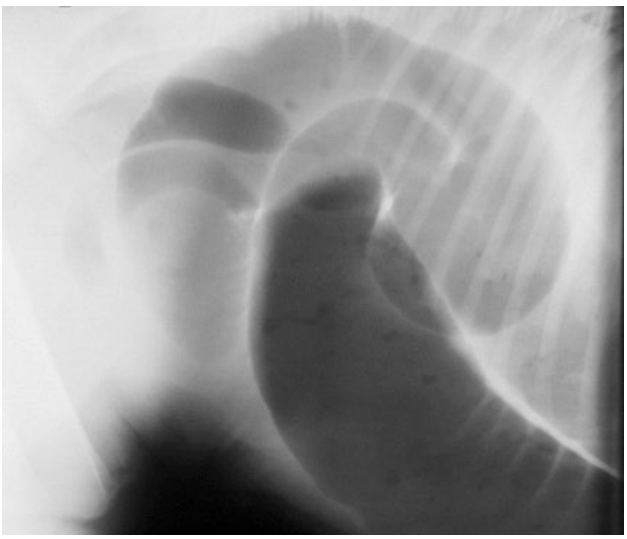

Figure 53.1 Abdominal radiograph of a horse with cecal tympany. The needle for percutaneous decompression is placed in the right paralumbar fossa in the base of the cecum.

Prognosis and Complications

The prognosis for survival from primary cecal tympany is good, whereas survival from secondary cecal tympany depends on the severity of the underlying condition. Although peritonitis can result after trocarization of the cecum to remove the excess gas, in the majority of cases the colic is resolved and the horse appears normal. Under these circumstances, the total protein concentration and number of neutrophils in the peritoneal fluid will be increased, but these findings need to be considered in light of the horse's clinical appearance and demeanor.

Cecal Impaction

Prevalence, Etiology, and Risk Factors

There appear to be two types of cecal impactions in horses, namely those in which the ingesta in the cecum is hard and dehydrated (Figure 53.3A), and those in which the contents are hydrated but the cecum fails to evacuate in a normal fashion, a condition referred to as cecal dysfunction (Figure 53.3B) (Campbell et al., 1984). Historically, the former type of cecal impaction has been associated with ingestion of coarse feed, inadequate mastication (due to poor teeth), or insufficient water supply or reduced intake of water. More recently, the condition has been associated with hospitalization, general anesthesia, and other diseases requiring prolonged treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) (Craig et al., 1987; Dart et al., 1997; Gaughan & Hackett, 1990). In one study, cecal impactions were the cause of colic in 13.9% of horses developing colic while being hospitalized for treatment of ocular disease, a much higher incidence than reported for the general population (Patipa et al., 2012). The underlying reason for the latter form of cecal impaction remains unknown, although it has been speculated that cecal muscular activity is abnormal in affected horses (Figure 53.3C). A form of this disease characterized by hypertrophy of the circular muscle layer in the cecal base and mechanical obstruction of the cecocolic orifice has been identified in horses in Germany (Figure 53.4) (Huskamp & Scheidemann, 2000; Schusser et al., 2000). Risk factors that have been associated with cecal impaction include insufficient water intake, coarse feed, hospitalization and administration of NSAIDs, and infestation with *Anaplocephala perfoliata* (Campbell et al., 1984; Collatos & Romano, 1993).

Cecal impactions have been reported to occur commonly in horses more than 8 years old, with some studies suggesting that horses >15 years old are at highest risk (Collatos & Romano, 1993; Dart et al., 1997; Plummer et al., 2007). It is important to note, however, that cecal impactions have also been reported in younger hospitalized horses (Campbell et al., 1984; Roberts & Slone, 1998). Although the results of one clinical case study suggested that Arabians, Appaloosas, and Morgans are predisposed to the condition (Dart et al., 1997), this was not corroborated in a subsequent study (Plummer et al., 2007). Cecal impactions have been associated more with abrupt rupture than are impactions involving other parts of the intestinal tract. Consequently, the fecal output of any horse being treated for other abnormalities should be assessed on a routine basis as this may help identify horses with cecal impactions earlier than otherwise would occur.

Clinical Findings

Most horses with dehydrated ingesta in the cecum exhibit mild intermittent colic signs and have minimal systemic deterioration unless the impaction has a very prolonged course. The heart rate usually is only slightly increased and intestinal sounds usually can be heard and may be associated with signs of pain, presumably as intestinal muscles contract against the obstruction. The diagnosis can be made upon rectal examination, as the impacted cecum is relatively easy to identify as the mass is situated in the right paralumbar region. The cecum can be identified by palpating the taut ventral cecal band and the fat and blood vessels overlying the medial cecal band (Collatos & Romano, 1993; Dabareiner & White, 1997).

In contrast, clinical signs of horses with hydrated cecal contents (the clinical syndrome called cecal dysfunction) are more variable, ranging from those

consistent with mild to severe abdominal pain. The first signs include mild pain, which is easily controlled with analgesics; signs consistent with severe pain only are present when cecal distention is excessive. Gas distention of the cecum occurs more commonly in horses with the latter condition, and the horse's heart rate may be normal or increased. Early in the disease, peritoneal fluid values are within normal limits, but the total protein concentration may increase as the course becomes prolonged. Horses with this type of cecal distention are likely to experience acute rupture unless the distention is relieved.

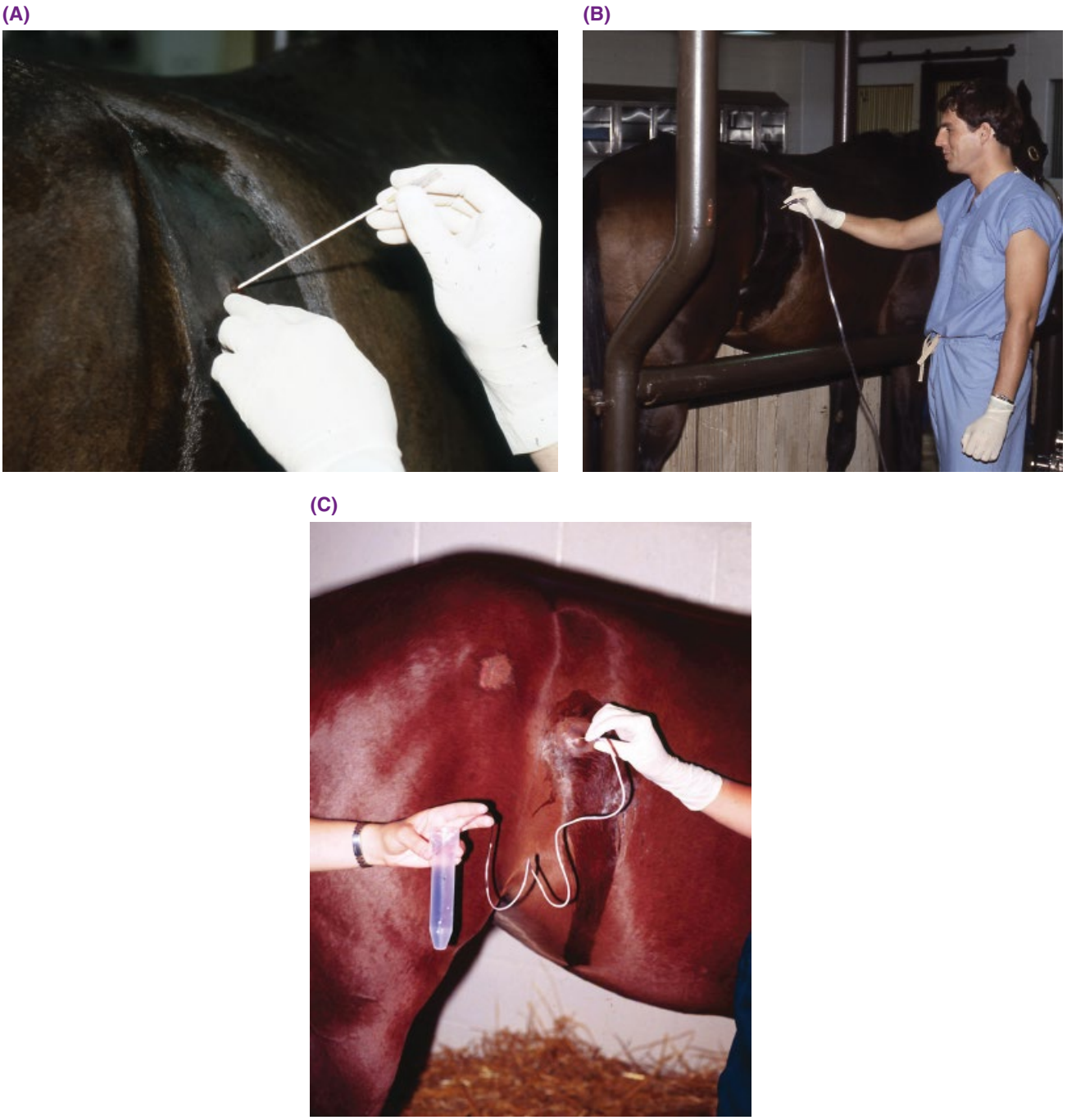

Figure 53.2 **(A)** During percutaneous cecal decompression, a catheter or needle is directed perpendicular to the skin midway between the last rib and the ventral border of the tuber coxae. **(B)** Gas can be removed rapidly by applying suction to the needle. **(C)** Alternatively, the catheter can be connected to an extension set and placed in a water container; observing the gas bubbles ensures correct placement of the catheter within the gas-distended viscus.

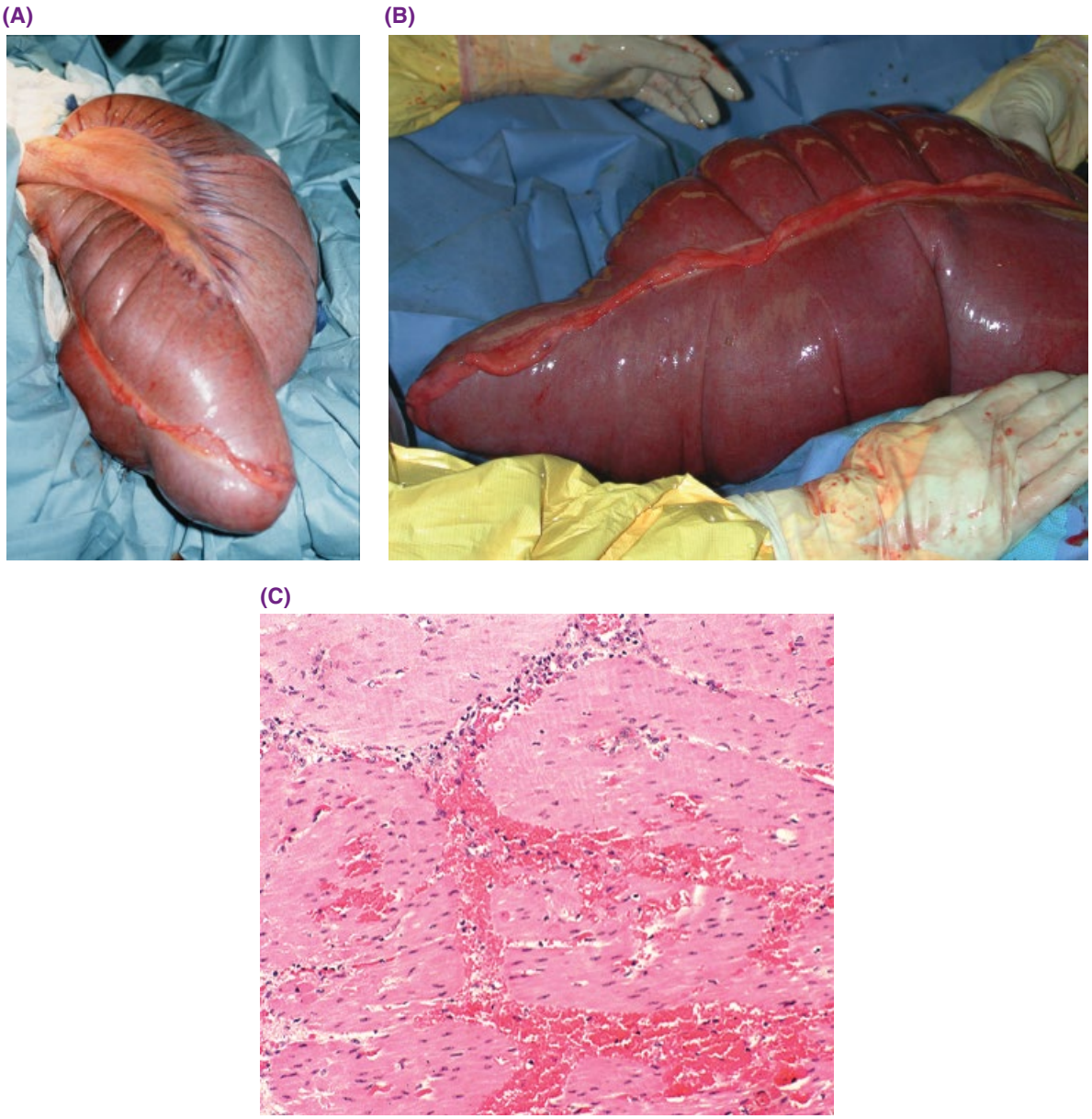

Figure 53.3 **(A)** Intraoperative photograph of the exteriorized cecum in a horse with a primary cecal impaction. **(B)** Cecal impaction (dysfunction) causing discoloration and wall thickening due to massive cecal distention in a horse. **(C)** Photomicrograph of the cecal wall that has been injured by ischemia and vascular leakage. The cecum with this type of injury will be more prone to ileus and reimpaction if a bypass procedure is not performed during surgery.

Treatment

There is some controversy regarding the best method of treating horses with cecal impaction, as the prevalence of spontaneous cecal rupture in horses with this condition has been reported to be >50% (Campbell et al., 1984). Medical treatment of horses with cecal impaction generally involves the administration of analgesics as necessary (e.g., NSAIDs), large volumes of balanced intravenous fluids, and intragastric administration of mineral oil, dioctyl sodium sulfosuccinate (DSS), magnesium sulfate, water, or magnesium sulfate. Feed should be restricted until the impaction is relieved. Many veterinarians consider aggressive fluid therapy to be the mainstay of treatment of these impactions. Balanced electrolyte solutions are administered either IV or via nasogastric tube, and often require administration of more than 50 L of fluid daily to a 450 kg horse until the impaction is resolved. The results of studies with enteral fluid therapy in horses indicate that this is at least as effective as IV fluid therapy in hydrating colonic contents (Lopes et al., 2002, 2003). In one clinical case study, 89% of horses that survived longer than 24 h after the diagnosis was made responded positively to aggressive medical therapy (Collatos & Romano, 1993). In a similar study, >80% of affected horses treated medically were discharged from the hospital

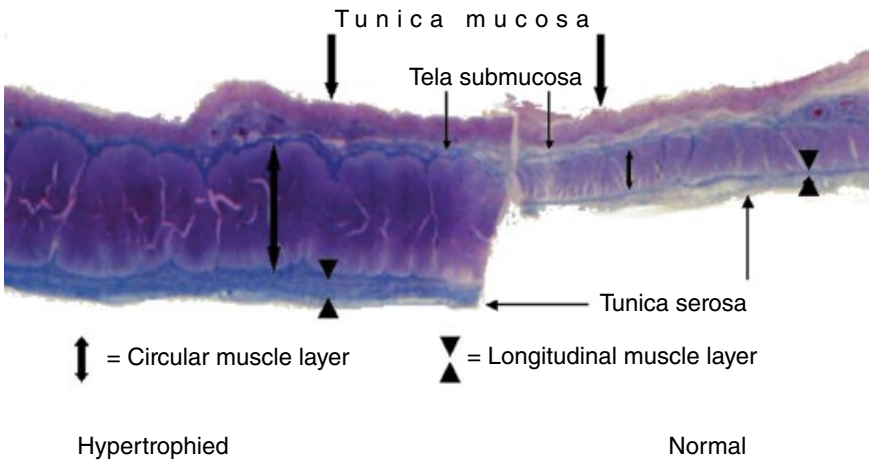

Figure 53.4 Photomicrograph of cecal wall hypertrophy from a horse with recurrent impaction compared to the cecal wall from a normal horse.

(Plummer et al., 2007). There appear to be regional differences in the clinical manifestation and outcome for horses with cecal impactions. In a recent study performed in a northern geographic location, only 61% of horses with cecal impaction managed medically survived to hospital discharge; importantly, 31% (18/59) of horses with cecal impaction managed medically developed cecal perforation (Aitken et al., 2015).

With the obvious concern about the propensity for an impacted cecum to rupture, other clinicians support surgical intervention in such cases. Surgical intervention for treatment of cecal impactions requires general anesthesia and a ventral midline celiotomy. The affected portion of the cecum is exteriorized carefully and packed off from the celiotomy site. A typhlotomy is then performed and the contents of the cecum are removed. Contamination of the tissue can be minimized by coating the serosal surface of the cecum with sterile carboxymethylcellulose. There is some controversy regarding the need for procedures other than typhlotomy, although in one study typhlotomy alone was associated with a low recurrence rate of the impaction (Plummer et al., 2007). Because simple evacuation of the impacted material has been reported by others to be followed by recurrence of cecal impaction, some surgeons elect either to anastomose the cecum and colon, enlarge the cecocolic orifice, or bypass the cecum altogether. With massive distention, the cecum can be susceptible to ischemia and reperfusion injury. When the cecal wall is thickened and discolored (Figure 53.3B), motility dysfunction should be expected after surgery. Consequently, the surgeon should consider performing a bypass procedure to prevent recurrence of the impaction.

The first of these approaches involves creating a cecocolostomy between the dorsal surface of the cecum and the right ventral colon. However, based on the results of one clinical study in which this technique was utilized, 40% of the horses treated in this fashion had recurrent abdominal pain associated with distention of the cecum or colon (Ross et al., 1986). As a result of these findings, techniques were developed to bypass the cecum by jejunocolostomy or ileocolostomy (Figure 53.5A)

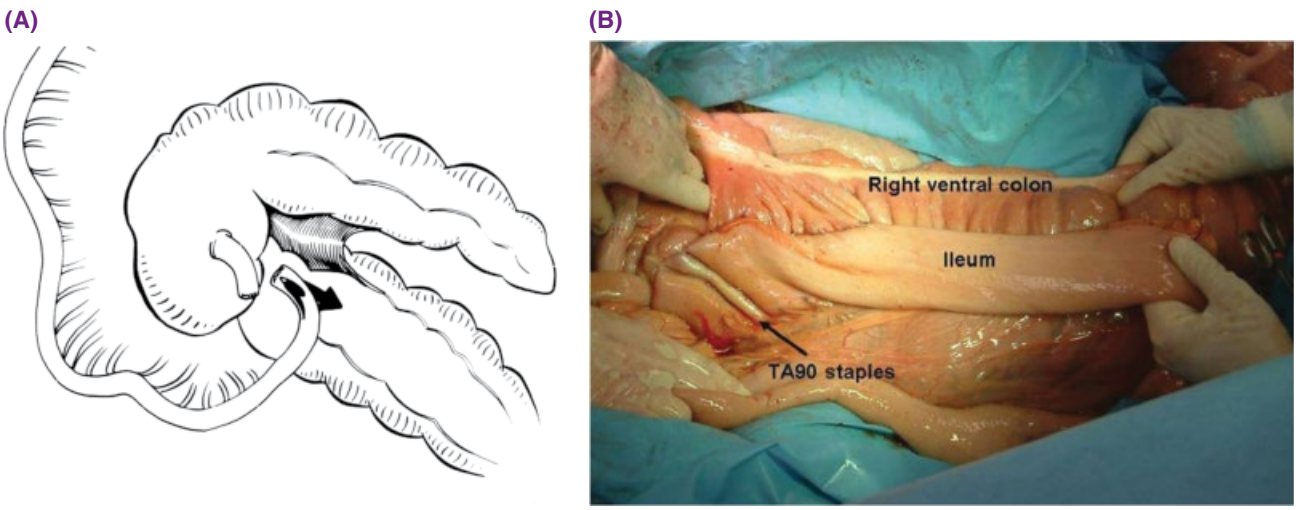

Figure 53.5 **(A)** Illustration of the ileocolostomy procedure. **(B)** Intraoperative photograph of the modified ileocolostomy procedure, where the ileum is not transected, but rather two rows of staples are applied to functionally prevent inflow of ingesta into the cecum.

(Craig et al., 1987; Symm et al., 2006). The results of a clinical case study involving nine horses treated in this manner suggest that evacuation and bypass of the cecum are effective (Gerard et al., 1996). In one study, the ileocolostomy procedure was modified to include occlusion of the more distal jejunum or proximal ileum without transecting the intestine (Figure 53.5B) (Symm et al., 2006). Results obtained using this procedure were comparable to those reported when the intestine is transected (Lores & Ortenburger, 2008; Quinteros et al., 2010). In one report summarizing treatment of 10 horses with cecal impaction due to dysfunction by typhlotomy only, all horses survived a mean of 43 months after surgery without recurrence of the impaction (Roberts & Slone, 2000). The authors recommended that anthelmintics directed against *A. perfoliata* and strongyle larvae should be administered postoperatively (Roberts & Slone, 2000). In a more extensive study of horses with cecal impaction managed surgically, 77% of horses managed with a typhlotomy alone survived to hospital discharge, whereas 88% of horses managed with a jejunocolostomy survived to discharge (Aitken et al., 2015). In that study, the type of surgical procedure did not significantly affect outcome.

Chronic recurrent impaction of the cecum can be a particularly frustrating condition. In a clinical study summarizing the response to surgical enlargement of the cecocolic orifice along the lesser curvature of the cecal base, affected horses responded positively unless the horse had pre-existing hypertrophy of the cecal musculature. The authors recommend that those horses should be treated with ileocolostomy (Huskamp & Scheidemann, 2000).

Prognosis and Complications

Owing to the propensity of the cecum impacted with hydrated ingesta to rupture, the prognosis for survival is guarded to good with aggressive therapy. In one clinical study, >80% of affected horses treated medically and 95% of horses treated surgically that were allowed to recover from anesthesia were discharged from the hospital (Plummer et al., 2007). Again, there appear to be regional differences in the outcome of horses managed medically for cecal impaction, with another study reporting short-term survival in only 61% (36/59) of horses managed medically. The majority of horses treated surgically in this study underwent typhlotomy alone. In a subsequent study of 20 horses that underwent typhlotomy and ileocolostomy, 65% were discharged from the hospital and 85% of these survived >1 year (Smith et al., 2010). More recently, 77% of horses managed by typhlotomy alone and 88% of horses managed by ileocecostomy survived to hospital discharge, with no difference in outcome observed between surgical procedures (Aitken et al., 2015). In that study, postoperative reimpaction was a complication in nine of 50 horses managed surgically; five horses had a typhlotomy alone and four horses had an incomplete jejunocolostomy procedure performed. Interestingly, there was no significant association between the type of cecal impaction, the surgical procedure performed, the use of prokinetics, the refeeding regimen, and the occurrence of reimpaction (Aitken et al., 2015).

Cecocecal and Cecocolic Intussusception

Prevalence, Etiology, and Risk Factors

Cecocecal and cecocolic intussusception are uncommon causes of colic in horses and are most prevalent in young horses (Figure 53.6 and Figure 53.7). A prevalence of 1.48% was reported in one study (Boussauw et al., 2001), and the condition affected three of 106 horses examined for chronic colic (Mair & Hillyer, 1997), and one of 151 horses with conditions requiring surgical intervention (Phillips & Walmsley, 1993). In contrast, a diagnosis of cecocecal or cecocolic intussusception accounted for 18% of horses with abdominal pain requiring surgery at a university referral center in New Zealand (Bell & Textor, 2010). The underlying cause of the development of either cecocecal or cecocolic intussusception is not known, but the conditions

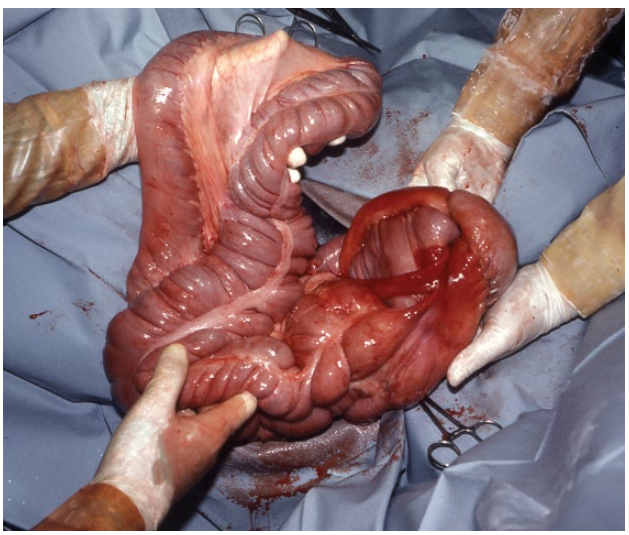

Figure 53.6 Intraoperative photograph of a cecocecal intussusception with invagination of the cecal apex into the body of the cecum.

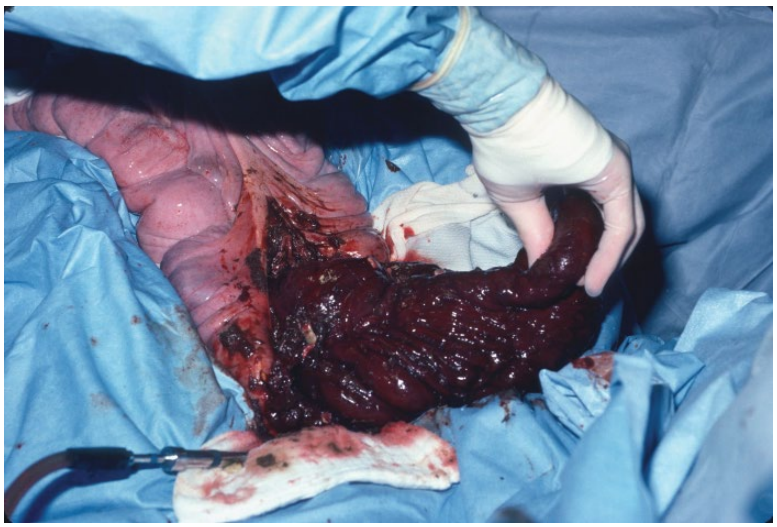

Figure 53.7 Intraoperative illustration of a cecocolic intussusception. A right ventral colon enterotomy was performed and the intussuscepted cecum is exteriorized through the enterotomy.

are thought to be associated with altered cecal motility. Some common associations include infestation with tapeworms (*A. perfoliata*) (Figure 53.8) (Gaughan & Hackett, 1990; Martin et al., 1999; Owen et al., 1989) or cyathostomes (Mair et al., 2000), cecal wall abscessation associated with *Strongylus vulgaris* (Pearson et al., 1971) or *Eimeria leukarti* (White, 1988), deworming with organophosphate compounds (Cowles et al., 1977), parasympathetic drug administration, and typhlocolitis, particularly salmonellosis. Young horses between 2 and 3 years of age appear to be at greatest risk for developing these conditions, with more than 60% of affected horses in a retrospective study of 30 cases being 3 years of age or younger (Martin et al., 1999). In the more recent study of these conditions in horses in New Zealand, the median age of horses with cecocecal or cecocolic intussusceptions was 2 years (Bell & Textor, 2010).

Clinical Findings

With cecocecal intussusception, signs of mild chronic colic, scant feces, intermittent fever and weight loss, or severe unrelenting abdominal pain can be observed. In horses with cecocolic intussusception, where the invaginated cecum is located in the lumen of the right ventral colon, signs of acute colic predominate. Variable abnormalities may be identified during the physical examination and abdominocentesis depending on the severity and duration of the intussusception. Rectal palpation will usually reveal a firm mass at the cecal base. A presurgical diagnosis can be made by ultrasound examination of the right abdominal quadrant using either the transabdominal or transrectal approach (Figure 53.9) (Bell & Textor, 2010; Boussauw et al., 2001; Smith et al., 2013; Taintor et al., 2004). Although peritoneal fluid samples obtained from horses with the chronic form of the

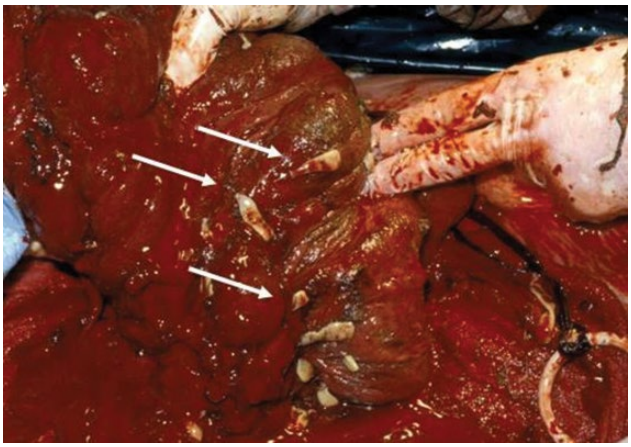

Figure 53.8 Intraoperative photograph of a cecocolic intussusception exteriorized through a ventral colon enterotomy. Tapeworms are seen on the exposed cecal mucosa (arrows).

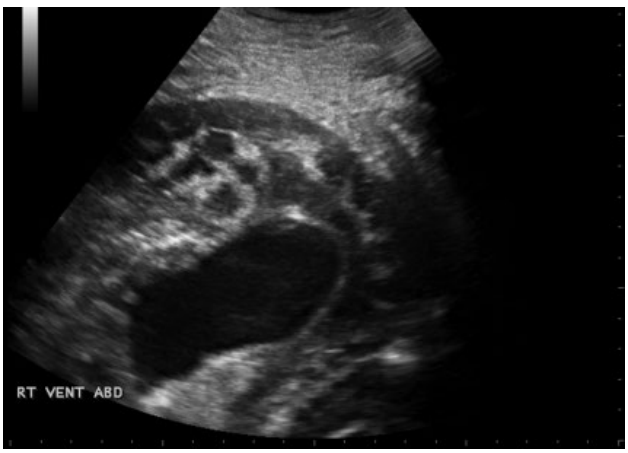

Figure 53.9 Transabdominal ultrasound of a horse with a colic intussusception as seen through the right ventral abdomen window. The double layer of the intussusceptum within the intussuscipiens is seen.

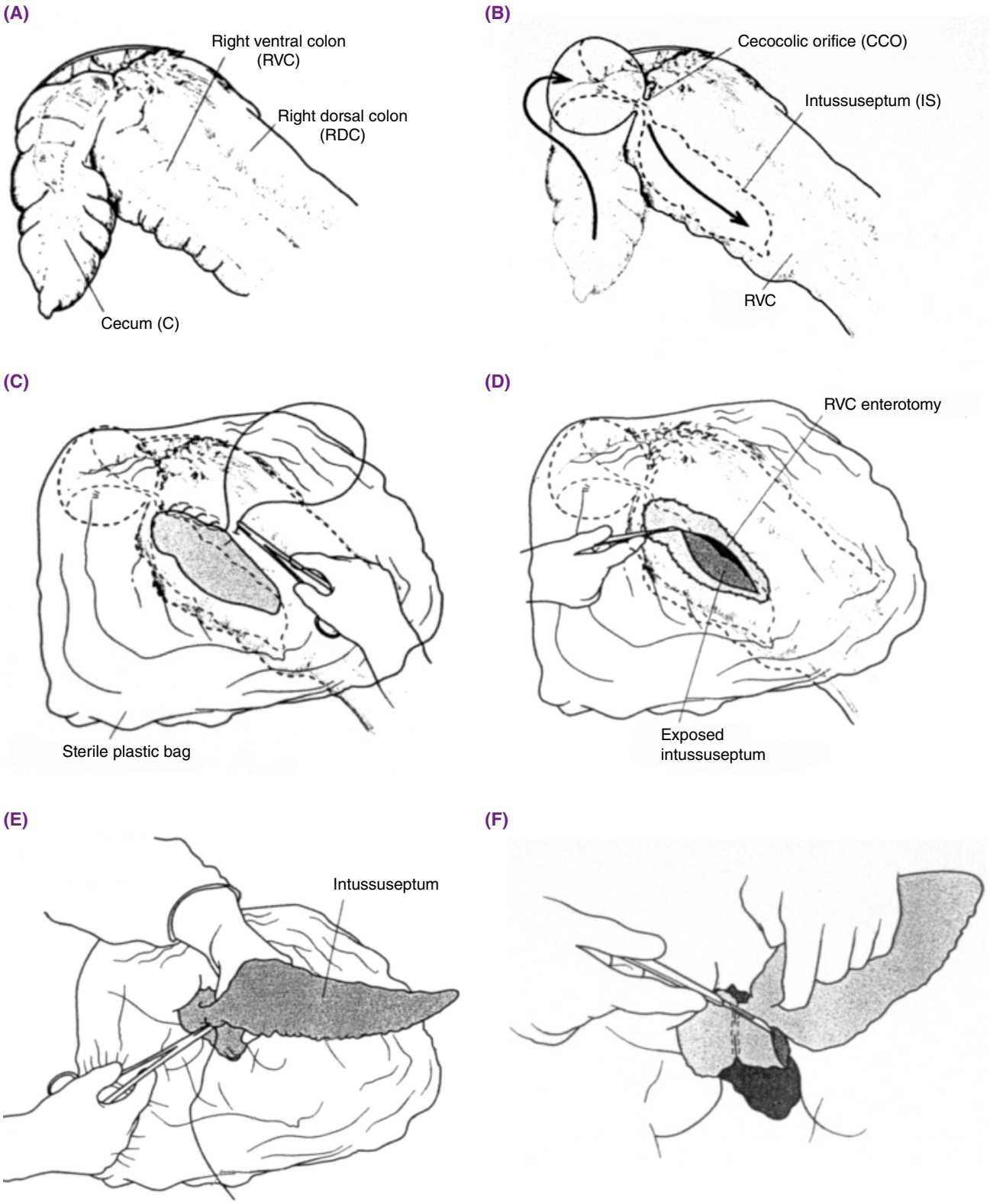

Figure 53.10 Cecum intussuscepted into the right ventral colon through the cecocolic orifice. **(A)** The normal anatomy of the cecum in relation to the right ventral colon. **(B)** The dashed line represents the outline of the invaginated cecum. **(C)** A window is made in the base of a sterile plastic bag that is sutured to the seromuscular layer of the right ventral colon before colotomy to help contain contamination. **(D)** Right ventral colotomy exposing cecal intussusceptum. **(E)** Occluding mattress sutures are placed in the inverted cecum to facilitate removal of as much cecum as possible, thus allowing reduction of remaining invaginated tissue. **(F)** Amputating the intussusceptum through the right ventral colon.

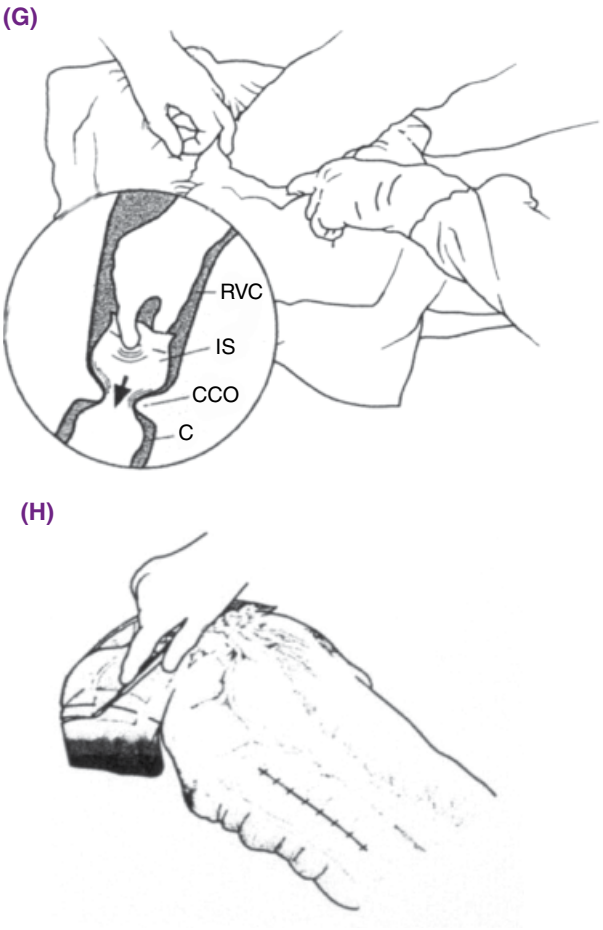

Figure 53.10 (Continued) **(G)** Careful manual reduction and repositioning of remaining invaginated cecum through the cecocolic orifice. Secure closure of the cecal stump is critical to prevent abdominal cavity contamination. **(H)** A second typhlectomy is performed to ensure that only viable tissue remains. Source: Hubert et al., 2000. Reproduced with permission of John Wiley & Sons.

disease tended to have higher total protein values and white blood cell counts than horses with the acute form of the disease in one retrospective study, the differences were not significant (Ross, 1989).

Treatment

Surgical correction is indicated in all cases. A ventral midline approach is commonly used (see Chapter 42). An alternative approach for cecocecal intussusception uses the right flank (17th or 18th rib resection) or paracostal incision to provide better access to the cecal base and body. In horses in which the cecal apex has inverted into the cecal base, it may be possible to reduce the intussusception manually. An attempt at manual reduction of the intussusception is made by inserting the hand into the intussusception and attempting to reduce it by gentle traction. In some cases, this procedure may take as long as 30 min. If successfully reduced, the cecum is examined for evidence of devitalization and, if indicated, a partial typhlectomy is performed to resect the affected portion of the cecum. In cases of irreducible cecocolic intussusception, there are two options available to restore continuity of the gastrointestinal tract: right ventral colon enterotomy and partial amputation of the intussuscepted cecum within the right ventral colon, and complete cecal bypass by ileocolostomy (Boussauw et al., 2001; Gaughan & Hackett, 1990; Hubert et al., 2000; Martin et al., 1999; Ward & Fubini, 1994; Wiemer & Van der Veen, 1999). For the first procedure, the large colon is exteriorized, preferably on a colon tray, and draped off. A sterile plastic drape is sutured circumferentially onto the colon at the site of the proposed enterotomy, in order to minimize contamination (Figure 53.10A–H) (Hubert et al., 2000). A right ventral colon enterotomy is performed between the lateral and medial free bands of the ventral colon. The intussuscepted cecum is exteriorized through the enterotomy. Reduction can be attempted then, but usually is not successful. Large, overlapping mattress sutures are placed across the invaginated cecum and a section of the cecum is amputated. It is not necessary to remove all of the affected cecum – amputation of the most accessible portion is sufficient to allow reduction of the intussusception. The right dorsal ventral colon enterotomy is then closed using a double-layer inverting pattern, with the first layer being full thickness. The intussusception can then be reduced, and the remainder of the devitalized cecum amputated.

Prognosis and Complications

The long-term prognosis for survival is variable, with reported rates ranging from 27 to 100% (Bell & Textor, 2010; Ross, 1989). The prognosis for horses with a reducible intussusception is excellent, even if a typhlectomy needs to be performed (Martin et al., 1999). Although results of the colotomy and partial typhlectomy were associated with poor results in early reports, more recent studies have reported good to excellent results with this procedure, with six of six horses and seven of eight horses surviving long term (Hubert et al., 2000; Martin et al., 1999). Postoperative complications included ileus, peritonitis, incisional infection, and colic (Hubert et al., 2000; Martin et al., 1999; Wiemer & Van der Veen, 1999). As an alternative for management of irreducible cecocolic intussusception, a jejunocolostomy or ileocolostomy can be performed, and the intussuscepted cecum is left in place. In the reported cases, the intussuscepted cecum was not oversewn. Early reports of this procedure were associated with a poor outcome, with two of two horses euthanized owing to peritonitis. Subsequent reports were associated with a

better outcome, with four of six horses surviving long term (Boussauw et al., 2001). In the latter report and another, horses were reported to have several postoperative complications, including colic and peritonitis (Boussauw et al., 2001; Ward & Fubini, 1994). Whether the colic episodes were caused by the procedure or by the fact that the intussuscepted cecum was left within the colon is unknown. It is the authors' experience that horses affected with irreducible cecocolic intussusception treated with colotomy and partial typhlectomy have a better postoperative course than horses treated by ileocolostomy.

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Specific Diseases of the Ascending Colon

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Large Colon Tympany

Large colon tympany (gas colic, spasmodic colic) is the most commonly reported cause of colic in horses (Traub-Dargatz et al., 2001; Cohen et al., 1995; Hackett, 1983). It is thought to result from excessive gas fermentation in the colon, resulting in distention and pain. In one study evaluating risk factors for simple colonic obstruction and distention colic in horses (including large colon impaction), the following factors were associated with an increased risk for this type of colic: crib biting or wind-sucking, increasing number of hours spent in a stable, recent change in the horse's regular exercise program, absence of administration of ivermectin or moxidectin anthelmintic in the previous 12 months, and a history of travel in the previous 24 h (Hillyer et al., 2002). Other factors that increase the risk of simple colonic obstruction and distention included a history of previous colic, recent (<4 weeks) lameness, and increasing time since last dental care (Hillyer et al., 2002). An association between tapeworm infestation and spasmodic colic also has been demonstrated (Proudman et al., 1998). Horses fed a hay and grain diet containing large amounts of soluble carbohydrates and less fiber have decreased water content in ingesta and increased gas, which predispose to gas colic (Lopes & White, 2002). Although large colon tympany can be self-limiting, it is thought to precede large colon displacements; therefore, identification of risk factors in affected horses may help decrease the risk of future occurrences.

Horses examined for large colon tympany are acutely painful, and may have evidence of external abdominal distention. Although affected horses are painful, typically they are systemically minimally compromised and clinicopathologic parameters, including results obtained with abdominocentesis, remain within normal reference ranges. The challenge for the clinician is to differentiate this type of colic from other, more serious causes of abdominal pain. The differentials for gas colic resulting in large colon distention include large colon displacement, large colon volvulus, ileus (impending colitis), and aboral obstruction of the transverse or small colon. Rectal palpation will reveal moderate to severe gas distention of the large colon. Treatment includes administration of analgesics and withholding feed. The response to medication is favorable and, if the diagnosis is correct, the horse's signs of abdominal pain will resolve. Lack of response to analgesics may indicate a more serious problem. If response to treatment is unsatisfactory, early referral is recommended, considering that large colon volvulus is a differential for this condition.

Large Colon Impaction

The most critical functions of the equine large colon are storage of ingesta, microbial digestion, and fluid absorption. In a 24 h period, the large intestine must recover a volume of water approximately equal to the horse's extracellular fluid volume (approximately 20–30% of body weight or 90–135 L for a 454 kg horse) (Argenzio, 1975). The storage function of the large colon allows time for microbial digestion and absorption of volatile fatty acids, the main source of energy in the equine (see Chapter 5) (Lopes & Pfeiffer, 2000). The principal mechanism for delaying transit of ingesta is the retropulsive activity initiated in a pacemaker region near the pelvic flexure (approximately 30 cm aboral to the termination of the medial and lateral free tenia of the left ventral colon) (Sellers et al., 1979, 1982). The coordinated contractions originating at the pelvic flexure pacemaker region promote physical separation of small, well-digested particles that are propelled aborally from coarser particles that are propelled orally for further

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digestion (Sellers & Lowe, 1986). This may explain the role of poor-quality feed in the development of large colon impaction.

Large colon impaction is the second most commonly reported cause of colic in horses, and is the most frequent type of simple obstruction (Cohen et al., 1995; Proudman, 1991). It represents up to 13.4% of horses with colic examined at referral centers (White, 1990; Dabareiner & White, 1995). Large colon impactions usually affect horses greater than 1 year of age, although the condition has been recognized in Miniature horses as foals. Historically, horses presented to referral centers with large colon impactions have abdominal pain exceeding 24 h in duration (Dabareiner & White, 1995).

Risk factors identified in one study for this condition were the same as identified for large colon tympany, namely crib biting or windsucking, increasing number of hours spent in a stable, recent change in the horse's regular exercise program, absence of administration of ivermectin or moxidectin anthelmintic in the previous 12 months, and a history of travel in the previous 24 h (Hillyer et al., 2002). Similarly, other risk factors for large colon impaction identified in that study included history of previous colic, recent (<4 weeks) lameness, and increasing time since last dental care. In a subsequent hospital-based study, however, dental abnormalities were not associated with the development of large colon impaction (Gunnarsdottir et al., 2014). In another study, 79 of 147 (53.7%) of horses had a change in routine in the 2 weeks prior to development of a large colon impaction, and 17 of 147 (11.5%) developed the impaction while hospitalized for a reason other than gastrointestinal disease (Dabareiner & White, 1995). Changes in management and musculoskeletal disease are identified consistently in clinical studies of large colon impaction (Dabareiner & White, 1995; Hillyer et al., 2002; Jennings et al., 2014). Decreased water intake and parasites also are mentioned, although not well documented, as factors contributing to the development of large colon impaction. High-grain diets may predispose to colonic impactions, as grain feeding is associated with an internal fluid flux and subsequent dehydration of ingesta, setting the stage for impaction (Clarke et al., 1990). Right colon dry matter content was higher when grain was part of a free-choice hay diet (White, 2003). Low temperatures can reduce water consumption, thus contributing to large colon impaction. Water consumption was 40% greater in ponies offered warm drinking water under cold weather conditions (Kristula & McDonnell, 1994).

Hospitalization and general anesthesia have been suggested as risk factors for the development of impaction colic (Dabareiner & White, 1995; Little et al., 2001). Reduced fecal output after surgery can be associated with the development of large colon impaction, and should be monitored. In one study, 10 of 37 horses with reduced fecal output after surgery developed signs of colic (Little et al., 2001). Whereas administration of phenylbutazone decreased the risk of reduced fecal output in that study (Little et al., 2001), the results of *in vitro* studies documented a negative effect of nonsteroidal anti-inflammatory drugs (NSAIDs) on large colon intestinal smooth muscle motility (Van Hoogmoed et al., 1999, 2000b). Therefore, the benefits of NSAID administration for pain control considering their negative effects on intestinal health are still a mater of debate (Campbell & Blikslager, 2000; Cook & Blikslager, 2015; Little et al., 2001).

Several management practices are thought to be associated with reduced colonic motility and perhaps contribute to large colon impaction. Stabled horses had lower motility than pastured horses, as assessed by transabdominal ultrasound (Williams et al., 2011); stabling was also associated with reduced fecal output and increased fecal dry matter (Williams et al., 2015). Contamination of hay with young datura plants was associated with an outbreak of impaction colic in a group of horses (Naude et al., 2005). Amitraz, an acaricide, has been used to induce experimental large colon impaction in horses (Roberts & Seawright, 1983). Topical spraying of amitraz was associated with systemic illness and impaction colic in three horses (Auer et al., 1984). Amitraz, atropine, glycopyrrolate, and morphine significantly prolonged the intestinal transit time in horses (Roberts & Argenzio, 1986). Atropine (0.044 and 0.176 mg/kg IV) resulted in decreased intestinal motility and decreased appetite for 2–7.5 h after injection; signs of abdominal pain were observed in three of 10 ponies after administration (Ducharme & Fubini, 1983). Topical ocular administration of 1 mg of atropine hourly resulted in decreased intestinal motility (as assessed by auscultation) for 2–18 h after administration, and signs of abdominal pain were observed in four of six horses (Williams et al., 2000). Subconjunctival administration of 3 mg of atropine resulted in decreased intestinal sounds in three of six horses and signs of abdominal pain in one (Williams et al., 2000). Horses hospitalized for ocular disease are at increased risk for colic, whether it is because of the change in management, diet, the use of NSAIDs, the use of atropine, or a combination (Patipa et al., 2012).

Lowering the luminal temperature to 20°C (room temperature) over a 100 cm length of colon cranial and caudal to the pelvic flexure for 2 h significantly decreased conduction velocity and the amplitude and duration of pressure peaks in the intestinal wall. This finding has direct relevance to surgery of the large colon, where the colon is exteriorized from the abdomen, sometimes for prolonged periods, and where luminal lavage is performed. Minimizing the time of exteriorization and using warm water for luminal lavage may help the colon recover from the effects of low temperature.

The role of intestinal parasites on pelvic flexure motility has been evaluated. In one study, arteritis of the cranial mesenteric artery induced by inoculation of *Strongylus vulgaris* larvae resulted in a reduced relative colonic blood flow, but did not cause altered motility patterns (Sellers et al., 1982). In another study, increased motility patterns were observed in the cecum and colon at intermittent intervals for several days after infection (Lester et al., 1989).

Horses with chronic (>24 h) obstructions of the large colon or with previous obstruction had decreased neuron density in the pelvic flexure, which may predispose to future obstructions (Schusser & White, 1997). Megacolon with myenteric hypoganglionosis has been described in a 6-month-old foal with severe large colon impaction and colic (Murray et al., 1988). Recurrent impactions of the large colon were diagnosed in a mare with eosinophilic enterocolitis (Bassage et al., 1997). In that mare, diarrhea, hypoproteinemia, and weight loss characteristic of the disease were not present, and the intestine appeared grossly normal at surgery and at postmortem examination. These cases support the use of intraoperative intestinal biopsies in horses with unexplained recurrent large colon impaction.

The most common location for large colon impaction is the pelvic flexure, followed by the right dorsal and transverse colon. On physical examination, affected horses typically exhibit signs consistent with mild to moderate abdominal pain, and have decreased or absent intestinal sounds, decreased or absent fecal production, and occasionally mild to moderate abdominal distention (Dabareiner & White, 1995). Nasogastric reflux is rarely present. Although rectal palpation is diagnostic in horses with pelvic flexure impaction, impactions of the right dorsal and transverse colon can be difficult to palpate in adult horses.

When a large colon impaction is suspected on the basis of rectal palpation, it is essential to differentiate that from a large colon displacement with secondary right dorsal colon impaction (Mueller & Moore, 2000). Prolonged treatment of a horse having a large colon displacement with fluids and cathartics could result in colonic rupture. In horses with a large colon displacement, the right dorsal colon can become severely impacted, mimicking a large colon impaction. However, on rectal palpation, the impacted colon can be followed to the right of the cecum. This is in contrast to a pelvic flexure impaction where the end of the pelvic flexure can readily be identified. Transabdominal ultrasound may help to identify a large colon displacement by observing the presence of mesenteric vessels on the right side of the abdomen (Grenager & Durham, 2011; Ness et al., 2012). Although this finding has a high specificity (97.9%), the sensitivity of this finding is relatively low (67.7%) (Ness et al., 2012). With right dorsal displacement, serum glutamyl transferase activity may also be increased; this has not been documented to occur in horses with large colon impactions (Gardner et al., 2005). It also is important to recognize that dehydrated fecal contents can be palpated in the large colon in horses with a small intestinal obstruction. In contrast to large colon impaction, the tenia and haustra of the ventral colon in such cases become more prominent and distinguishable (Mueller & Moore, 2000).

Laboratory data typically obtained in horses with large colon impaction reflect mild to moderate dehydration, a normal leukogram, and normal electrolyte concentrations and blood gases. The abdominocentesis results should be within the normal range. Deteriorating cardiovascular status or peritoneal fluid changes are an indication of bowel degeneration (Dabareiner & White, 1995).

Medical treatment of horses with large colon impaction includes fluid therapy, analgesics, cathartics, and withholding of feed until the impaction is resolved (Jennings et al., 2014). Intravenous administration of fluids is reserved for horses with impactions of long-standing duration (>24 h), when there is evidence of dehydration, or when nasogastric reflux is present, precluding the use of enteral fluid therapy. Balanced electrolyte solutions are administered at twice the maintenance rate, 120 mL/kg/day, to restore circulating blood volume and allow secretion of fluid into the large colon in response to cathartics. Overhydration of affected horses in combination with an oral cathartic such as magnesium sulfate is thought to promote rehydration of ingesta (Freeman et al., 1992; Lopes et al., 2002). Systemic rehydration should be performed before administration of cathartics.

Enteral fluid therapy can complement and even supplement intravenous fluid therapy. Advantages of enteral fluid therapy include administration of fluid directly into the gastrointestinal tract, stimulation of colonic motility through the gastrocolic reflex, decreased expense, and decreased need for precise adjustment of fluid composition (Lopes et al., 2002). Enteral fluids can be administered by intermittent nasogastric intubation, or by placing an indwelling feeding tube (nasogastric feeding tube, 18Fr × 250 cm; Mila International, Erlanger, KY, USA) to allow continuous fluid administration. An isotonic electrolyte solution can be made by adding 5.27 g of NaCl, 0.37 g of KCl, and 3.78 g of $NaHCO_3$ to each liter of tap water (Lopes et al., 2002). This solution results in electrolyte concentrations of 135 mEq/L of Na^+, 95 mEq/L of Cl^-, 5 mEq/L of K^+, and 45 mEq/L of HCO_3^-, with a measured osmolality of approximately 255 mOsm/L, representing a balanced slightly hypotonic electrolyte solution compared to plasma (Lopes et al., 2002). In one study, plasma electrolyte concentrations remained within the normal range when this solution was administered, compared with the marked hypernatremia and hyperchloremia that occurred when 0.9% saline was administered enterally (Lopes et al., 2001). Although

healthy horses can tolerate up to 10 L hourly via intermittent nasogastric intubation (Lopes et al., 2001), it is the author's experience that it is usually not possible to administer more than 10 L every 2 h in horses with impactions, as those horses start to reflux when more fluid is administered. Consequently, intermittent intubation allows the administration of approximately 120 L of fluids per day to horses with large colon impactions. When continuous enteral fluids are given, horses can be given approximately 5 L/h. At a rate of 10 L/h, mild signs of abdominal pain were observed in healthy horses (Lopes et al., 2002), and in horses with large colon impaction, a rate of 5 L/h was better tolerated. Fluids used in enteral fluid therapy can be water alone, or water and electrolytes. The use of a balanced isotonic electrolyte solution is associated with improved fluid absorption and decreased electrolyte imbalances (Monreal et al., 1999; Sosa León et al., 1995). In one study, hydration of right dorsal colon ingesta was significantly increased after enteral fluid therapy compared with intravenous fluid therapy combined with enteral administration of magnesium sulfate (Lopes et al., 2002). In a clinical case series, enteral fluid therapy with or without intravenous fluid therapy was successful in resolving 99% of colonic impactions (Monreal et al., 2010).

Cathartics are administered to increase the amount of water in the large colon or promote ingesta transit. Mineral oil is a mixture of aliphatic hydrocarbons obtained from petrolatum that is indigestible and absorbed to a limited extent. It is an intestinal lubricant that can also serve as a marker of intestinal transit. Administration of 5–10 mL/kg is usually recommended, and oil should be evident in the feces 12–24 h after administration. When mineral oil was administered to healthy horses, unformed feces were apparent 18–24 h later (Schumacher et al., 1997), and it reduced both glucose absorption and intestinal transit time (Rodrigues, 1998; Macoris & Gandolphi, 1998). However, chronic usage can result in a foreign body reaction in the intestinal mucosa (Stryker, 1941). Careful administration is necessary, as inadvertent administration into the lung results in severe and potentially fatal lipid pneumonitis (Bos et al., 2002; Scarratt et al., 1998). Mineral oil should not be confused with propylene glycol, a solution used in the treatment of ketosis in cattle; inadvertent administration of propylene glycol was the cause of death in a horse (Dorman & Haschek, 1991).

Dioctyl sodium sulfosuccinate is an anionic surface-active agent that by lowering surface tension may facilitate penetration of the fecal mass by water and fats. Effects on motility and secretion are also attributed to this product. The recommended dose range is 16.5–66 mg/kg, and the maximal recommended dose is 200 mg/kg; death due to circulatory shock can occur at a dose of 1 g/kg (Moffat et al., 1975). In one study in healthy horses, toxic signs were observed at a dosage of 50 mg/kg (Freeman et al., 1992). Therefore, it is important to label containers containing dioctyl sodium sulfosuccinate correctly to avoid overdosing. Although the small volume of dioctyl sodium sulfosuccinate that has to be administered is an advantage, its low margin of safety and lack of efficacy at low dosages make its use questionable. Concurrent administration with mineral oil can result in emulsification and subsequent systemic absorption of oil. The significance of this is unknown, but because of this the use of the combination is discouraged.

Osmotic or saline cathartics, such as magnesium sulfate or sodium sulfate, are the most effective products used to increase colonic water content (Freeman et al., 1992; White, 2003). Because of their efficacy in increasing colonic water content, these products should be used after systemic rehydration. Recommended dosages are 0.5–1 g/kg. Absorption of magnesium resulting in signs of toxicity was reported in two horses that had received a combination of dioctyl sodium sulfosuccinate and magnesium sulfate (Henninger & Horst, 1997).

Raw linseed oil produced from flaxseed was a commonly used laxative for the treatment of impactions. The addition of metallic salts during preparation of the oil enhances its properties as a wood preservative but the product is highly toxic. Therefore, only raw linseed oil should be administered to horses. Administration of raw linseed oil at 2.5 mL/kg to healthy horses resulted in watery diarrhea, anorexia, mild signs of colic, and neutropenia (Schumacher et al., 1997). Although raw linseed oil has greater laxative effects than mineral oil, the toxic effects may preclude its use, particularly in horses with compromised intestinal mucosa (Schumacher et al., 1997).

Polyethylene glycol 3350 is an effective osmotic laxative that is used in humans for the treatment of constipation or for colonic cleansing (Cleveland et al., 2001; Beck et al., 1985). This product has not been evaluated rigorously in horses, although the present author has used it successfully to treat horses with large colon impactions. The cost of this product is much greater than that of the other cathartics mentioned. Castor oil has been used as an experimental model for colitis in ponies (Roberts et al., 1989). Its use for the treatment of impaction colic is not recommended.

Analgesics are indicated as part of the management of horses with large colon impactions; NSAIDs are commonly used. The use of low-dose flunixin meglumine can help control pain without affecting large colon motility. In the course of treatment of severe impactions, some horses may require intermittent dosing with xylazine to relieve intestinal spasms (Lowe et al., 1980). The use of α_2-adrenergic drugs or spasmolytic agents, such as hyoscine *N*-butylbromide or propantheline, should be limited in horses with impactions because of their negative effect

on intestinal motility (Gomaa et al., 2011; Merritt et al., 1998). Alternatively, a constant-rate infusion of lidocaine can be used to modulate pain.

Most horses respond well to medical therapy. In one study, only 24 of 147 horses with large colon impaction required surgery (Dabareiner & White, 1995). Indications for surgery included uncontrollable pain, deteriorating cardiovascular status, or peritoneal fluid changes indicating bowel compromise. Surgical management of large colon impaction involves evacuation of the colon by pelvic flexure enterotomy. Of the horses in one study that were treated surgically, five were euthanized after tearing of the colon occurred during exteriorization from the abdomen (Dabareiner & White, 1995). Complications of surgery include intraoperative rupture of the colon, postoperative diarrhea, incisional drainage, and, rarely, septic peritonitis (Dabareiner & White, 1995).

The prognosis for horses with large colon impactions is excellent, and the majority of horses respond to medical therapy (Monreal et al., 2010). The prognosis is better for horses treated medically than surgically. In one study, long-term outcome for horses treated medically was 95.1%, compared with 57.8% for horses that required surgical intervention (Dabareiner & White, 1995). Because the most common complication encountered was jugular vein thrombophlebitis, catheter sites should be monitored carefully.

In the management of horses with large colon impaction, it will be important to avoid risk factors that predispose these animals to reimpaction if the same conditions are present. A small number of horses will require permanent dietary modifications to avoid reimpaction.

Sand Impaction

Accumulation of sand in the equine large colon can result variables signs, including colic, diarrhea, weight loss, and poor performance. Sand should be considered in the evaluation of foals and adult horses with chronic diarrhea (Ramey & Reinertson, 1984; Bertone et al., 1988). Risk factors for sand impaction include insufficient roughage in the diet, access to sand, and mineral composition of the soil. Sand impaction has been diagnosed in horses that were exposed to sand 3–8 weeks before examination (Specht & Colahan, 1988). Higher incidences of sand colic are reported in California, Florida, Michigan, and coastal regions. Although most horses with sand impaction are >1 year old (Specht & Colahan, 1988), sand accumulation has been documented in foals (Keppie et al., 2008; Ragle et al., 1989; Ramey & Reinertson, 1984; Ruohoniemi et al., 2001); Miniature horses may also be predisposed to sand impaction, because of environmental and management practices (Ragle et al., 1992).

Horses with sand impaction manifest similar signs to those with large colon impaction, unless a concurrent large colon displacement or volvulus is present. Large colon displacements or volvulus were identified in 10 of 40 (25%) and 26 of 48 (54%) horses with sand impaction (Specht & Colahan, 1988; Ragle et al, 1989). These clinical signs include mild to moderate abdominal pain, reduced fecal production, and decreased intestinal sounds. The sound of sand may be heard when the ventral abdomen is auscultated behind the xyphoid. Affected horses are responsive to analgesics, and signs can be present for several weeks. Cardiovascular status should be normal unless dehydration or intestinal devitalization has occurred. Occasionally, horses with sand impaction may show signs of endotoxemia, presumably as a result of mucosal or intestinal damage associated with the weight and abrasiveness of the sand (Ruohoniemi et al., 2001). Diagnostic procedures that are used to detect the presence of sand include examining the feces for sand, sand obtained or palpated during abdominocentesis, abdominal auscultation, rectal palpation of sand-filled viscus, abdominal radiography, and abdominal ultrasound (Korolainen et al., 2003; Ragle et al., 1989; Ruohoniemi et al., 2001). In one study, 23 of 40 horses (58%) were diagnosed with intestinal sand before surgery by one or more methods (Ragle et al., 1989). Fecal sedimentation is performed by adding water to a handful of manure, which is allowed to sediment usually in a rectal sleeve (Figure 54.1). The presence of sand on sedimentation, however, may be incidental, and horses with sand impaction may not have sand in their feces at the time of examination. The appearance of sand in the feces during treatment is considered a sign of clearance of the sand (Ruohoniemi et al., 2001). Abdominocentesis results are often normal, or include an increased total protein concentration.

Figure 54.1 Accumulation of sand in a finger of a rectal sleeve in a horse with a sand impaction of the large colon.

Abdominocentesis is not diagnostic for sand colic, but rather indicates the degree of intestinal compromise. However, the weight of the colon makes it easy to perform an unintentional enterocentesis during the procedure, and sand can be palpated with the tip of the needle or cannula (Specht & Colahan, 1988).

In one study, 13 of 23 horses correctly diagnosed with sand impaction before surgery were identified by the presence of sand obtained or palpated during abdominocentesis (Ragle et al., 1989). Abdominal auscultation for the detection of sand is performed on the ventral abdomen, with emphasis on the area caudal to the xiphoid process (Ragle et al., 1988). The sound produced has been described as similar to that produced by slowly rotating a paper bag partially filled with sand (Ragle et al., 1988). The intensity of sound is loudest with larger accumulations of coarse as opposed to fine sand (Ragle et al., 1988). In an experimental study of sand impaction in horses, all horses had at some time point auscultable sand sounds, typically after several doses of sand and several repeated 5 min auscultation periods (Ragle et al., 1988). Rectal palpation of horses with sand impaction most commonly reveals distention of the cecum and/or large colon. The impaction is seldom palpated on rectal examination. If coarse sand is present, it may be palpated through the intestinal mucosa.

Abdominal radiography provides the best method to evaluate the amount of sand accumulation, and provides a tool for monitoring the disappearance of sand with treatment (Figure 54.2) (Ruohoniemi et al., 2001). Imaging of the cranioventral abdomen is the most useful projection (Ruohoniemi et al., 2001). The magnitude of sand accumulation and the likelihood of sand being the cause of colic can be subjective. Therefore, an objective scoring system has been proposed to provide a more uniform and accurate method to assess sand accumulation (Keppie et al., 2008).

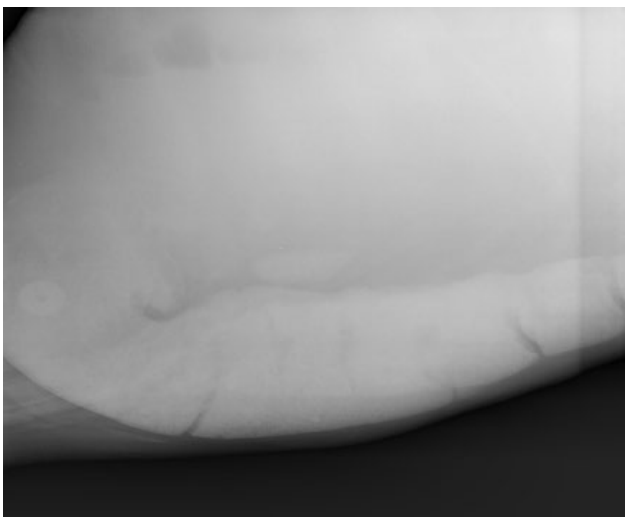

Figure 54.2 Lateral projection of the ventral abdomen of a horse showing impaction of the ventral colon with coarse sand.

Abdominal ultrasound can be used in an attempt to diagnose sand impaction, but is best used in combination with abdominal radiography to monitor clearance of the sand (Korolainen et al., 2003). Ultrasonographic evidence of sand accumulation is more subjective, and includes close and increased contact of the large colon with the ventral body wall, decreased or absent intestinal motility, and hyperechoic acoustic shadowing. In one study, radiography and ultrasound outcomes were similar in only 50% of cases (Korolainen et al., 2003). Because ultrasound is more readily performed and can be easily repeated, it is purported to be a useful tool for monitoring once a diagnosis has been made, although repeated radiographs may be indicated when results of the ultrasound are equivocal (Korolainen et al., 2003).

Medical treatment of sand impaction includes removing the horse from access to sand, rehydration by intravenous and/or oral methods, and the use of laxatives. Mineral oil is usually not effective, as it will pass around the sand. Magnesium sulfate and/or psyllium are used to promote evacuation of sand. In one study, psyllium failed to increase evacuation of sand in an experimentally induced model of sand impaction (Hammock et al., 1998). However the number of animals in the study was small and the model may not reflect naturally occurring disease. In a clinical study, horses that were refractory to treatment with psyllium were responsive to administration of magnesium sulfate and mineral oil (Ruohoniemi et al., 2001). In another study, resolution of sand impaction was improved when using a combination of psyllium and magnesium sulfate compared with either constituent alone (Niinisto et al., 2014).

Horses with sand impaction can develop abnormal motility patterns and subsequent large colon displacement. These horses are more painful, and develop gas distention of the large colon. Surgical intervention is indicated when a displacement is suspected or diagnosed, when abdominal pain is uncontrolled, when there are deteriorating cardiovascular parameters, or when there is evidence of intestinal devitalization (Ragle et al., 1989; Specht & Colahan, 1988). Standing flank laparotomy does not allow sufficient access to the large colon for evacuation of sand, and injection of the impaction is not successful in providing relief. Therefore, a surgical approach through a ventral midline is recommended. At surgery, the sand is evacuated through a pelvic flexure enterotomy (Figure 54.3). The most common location for accumulation of sand is the right dorsal colon, but any location, from the ileocecal junction to the small colon, is possible, and multiple impaction sites are commonly encountered. Care must be exercised during exteriorization of the large colon, as the weight of the sand

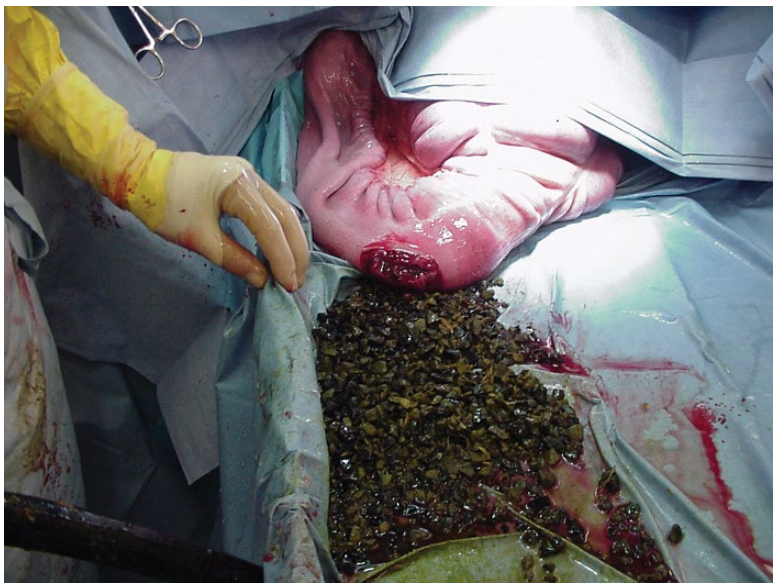

Figure 54.3 Intraoperative illustration of evacuation of gravel through a pelvic flexure enterotomy in a horse.

predisposes the colon to rupture. To facilitate exteriorization, the horse may be tilted toward the left side of the abdomen. In addition, only the minimum length of large colon necessary to perform a colotomy safely should be exteriorized; as the colon is evacuated, more of its length can be carefully exteriorized from the abdomen.

Results of surgical treatment of sand impaction are indicative of good long-term survival (Ragle et al., 1989; Ruohoniemi et al., 2001). The most common complication is postoperative diarrhea, but this complication is commonly reported after surgical evacuation of the large colon for any reason. Other complications include peritonitis associated with intestinal devitalization from pressure necrosis.

Prevention of sand impaction includes the provision of adequate roughage, feeding off the ground, and provision of additional roughage when pastures are insufficient. The use of different formulations of psyllium (pellets or flakes) has been advocated at different dosage regimens (once per day for 3 weeks then 1 week off to twice per day for 2 weeks then 1 week off), but there is no documentation of the efficacy of these different dosage regimens in preventing further sand accumulation. There is concern that long-term use of psyllium results in alterations in colonic microflora with subsequent bacterial digestion of the psyllium and decreased efficacy; this is the rationale behind interrupted administration of psyllium (Hammock et al, 1998).

Enterolithiasis

Obstruction of the large or small colon by enteroliths is a well-documented cause of intestinal obstruction in horses. Risk factors include geographic location, with California and Florida having high prevalences for this cause of colic, breed predisposition such as Arabians and Arabian crosses, Morgans, American Saddlebreds, donkeys, and Miniature horses, feeding alfalfa hay, and less than 50% of the time spent outdoors (Cohen et al., 2000; Hassel et al., 1999). However, there are other as yet unidentified factors to explain why other horses fed the same diet in the same geographic area do not develop enteroliths.

Enterolithiasis can result in acute severe luminal obstruction or can cause intermittent mild signs of colic, depending on the location of the enterolith. Those in the large colon are usually localized in the right dorsal colon and cause mild signs of intestinal discomfort. Once they migrate into the transverse or small colon, signs of acute luminal obstruction develop, with progressive abdominal distention. Although this condition causes a simple colonic obstruction, transmural pressure necrosis can occur. Critical attention to results of the abdominocentesis is important for the detection of intestinal compromise. An increase in total protein concentration above the normal range and an increase in white blood cell count can alert toward such occurrence.

Physical examination parameters will also vary accordingly, depending on the location of the enterolith and whether intestinal devitalization has occurred. Rectal palpation findings can be normal or reveal large colon distention. The enterolith can rarely be palpated. Results of the abdominocentesis are often normal, although an increased total protein concentration is an early sign of intestinal devitalization. Radiographs are a useful diagnostic method for the detection of enteroliths (Figure 54.4A and B), although the sensitivity and specificity will vary depending on the location of the enterolith and the prevalence of the disease for the hospital

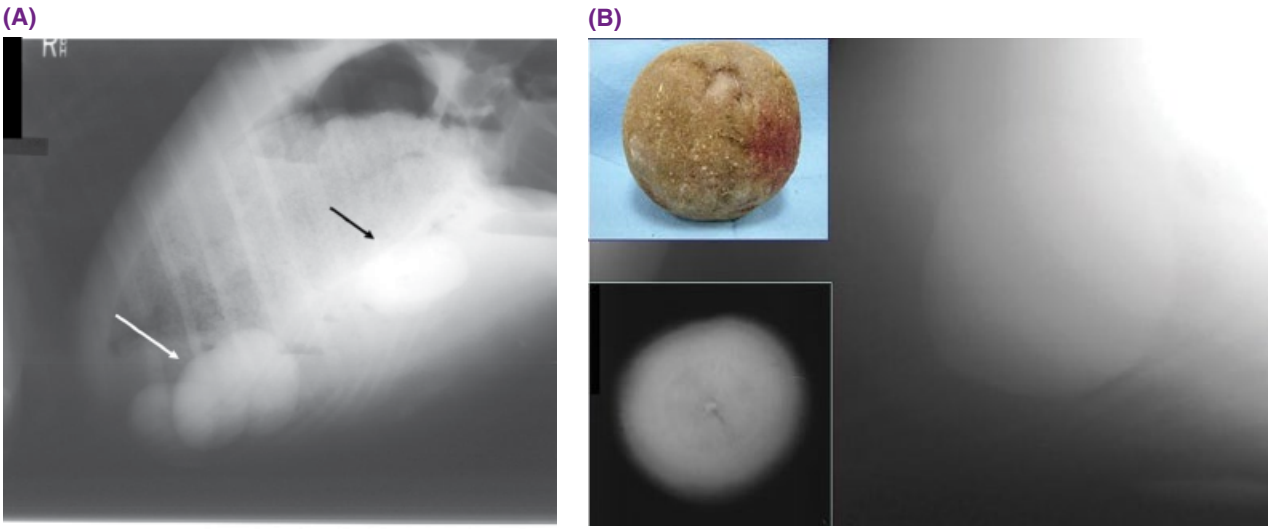

Figure 54.4 **(A)** Lateral projection of the abdomen of a Miniature horse with several enteroliths in the dorsal colon and small colon (arrows). **(B)** Lateral projection of the abdomen of a horse with a large enterolith in the right dorsal colon. The enterolith is pictured after removal in the left upper quadrant. Radiography of the enterolith is illustrated in the left lower quadrant, and shows a small central metal opacity (nidus).

population (Yarbrough et al., 1994). In one study performed in a high-prevalence area for enteroliths (Yarbrough et al., 1994), the sensitivity of radiographic diagnosis of enterolithiasis was 84.3% for those located in the large colon, compared with 50.0% for those located in the small colon. The mean overall positive predictive value for radiographs was 96.4% and the negative predictive value was 67.5% (Yarbrough et al., 1994). Similar results were obtained with computed radiography, with overall sensitivity and specificity of 85 and 93%, respectively, with large colon sensitivity (94.5%) being greater than small colon sensitivity (50%) for the detection of enteroliths. With digital radiography, the overall sensitivity and specificity were 84 and 96%, respectively, with large colon sensitivity (88.9%) being greater than small colon sensitivity (61.5%) for the detection of enteroliths (Kelleher et al., 2014). In all studies, gas distention negatively affected the detection of enteroliths.

Surgical removal of enteroliths is indicated. If the enterolith is located in the large colon, the latter is evacuated via a pelvic flexure enterotomy. A second enterotomy may be required in the right dorsal colon if the enterolith is too large to be evacuated through the pelvic flexure enterotomy. If the enterolith is lodged in the transverse colon, retrograde flushing by enema can facilitate its movement back into the dorsal colon. If the enterolith is in the small colon, it is removed by a small colon enterotomy. A partial thickness enterotomy can facilitate movement of the enterolith to a more accessible portion of the small colon (Hassel & Yarbrough, 1998). If there is pressure necrosis of the intestinal wall at the site of the obstruction, a resection may be required.

The prognosis for horses with enterolithiasis is usually excellent. However, necrosis of the intestine in an area that cannot be exteriorized, such as the transverse colon, is associated with a grave prognosis. Of 236 horses undergoing surgery for enterolith removal in the ascending colon ($n = 97$) or descending colon ($n = 139$), overall survival to discharge was 94% for ascending colon enteroliths and 88% for descending colon enteroliths, and long-term survival was 89% for ascending colon and 85% for descending colon enteroliths (Pierce et al., 2010). Although there was no significant difference in outcome based on location, more horses with descending colon enteroliths were euthanized on the table owing to inaccessibility or significant intestinal damage. In one study, bypass of the transverse colon by end-to-side anastomosis of the ventral colon to the small colon was successful in a Miniature horse with a intestinal necrosis following obstruction by a fecalith in the transverse colon (Dowling et al., 2000). The recurrence rate of enteroliths is unknown, but dietary modification such as avoidance of alfalfa hay is usually recommended.

Large Colon Displacement

Because of its lack of mesenteric attachment to the body wall, the equine large colon is freely mobile and prone to displacement. In addition, normal longitudinal shortening of the left colon promoted by contractions of the longitudinal layers move the pelvic flexure toward the diaphragm, followed by backward movement toward the pelvis during relaxation; alterations in

this motility pattern, initiated at the pelvic flexure pacemaker, could result in displacements and volvulus (Sellers & Lowe, 1986).

The normal equine diet is composed of soluble and insoluble carbohydrates. Insoluble carbohydrates are digested by microbial fermentation, resulting in the production of volatile fatty acids that are absorbed for energy production. When excess soluble carbohydrates are fed, alterations in the microbial population of the large colon can result in excessive fermentation, gas distention, and subsequent displacements (Harlow et al., 2015). The importance of the intestinal microbiota for equine intestinal health and relationship to colic is receiving increased interest (see Chapter 7). In one study, changes in the fecal microbiota preceded the development of post-partum colic in mares (Weese et al., 2015).

Large colon displacements have been classified into left dorsal displacement of the large colon, also referred to as nephrosplenic or renosplenic entrapment, right dorsal displacement of the large colon, retroflexion of the large colon, and nonstrangulating volvulus.

Nephrosplenic Entrapment

Nephrosplenic entrapment (also termed renosplenic entrapment or left dorsal displacement of the large colon) is a form of nonstrangulating large colon displacement in the horse, in which the left dorsal and ventral colons migrate lateral to the spleen in a dorsal direction until entrapped in the nephrosplenic space (Figure 54.5A and B). Some clinicians refer to left dorsal displacement when the left colons are between the spleen and the body wall, and entrapment when the left colons are in the nephrosplenic space. The depth of the nephrosplenic space appears important for entrapment, and is determined by the dorsal extent of the dorsal border of the spleen in relation to the attachment of the nephrosplenic ligament (Röcken et al., 2005). This condition has been reported in horses of any age, as early as 9 months old (Hardy et al., 2000). In one study, Warmbloods were overrepresented (Lindegaard et al., 2011). Although one report mentions an increased prevalence in male horses, others have not substantiated that finding (Baird et al., 1991; Hardy et al., 2000; Sivula, 1991). The condition has not been reported in either Miniature horses or pony breeds.

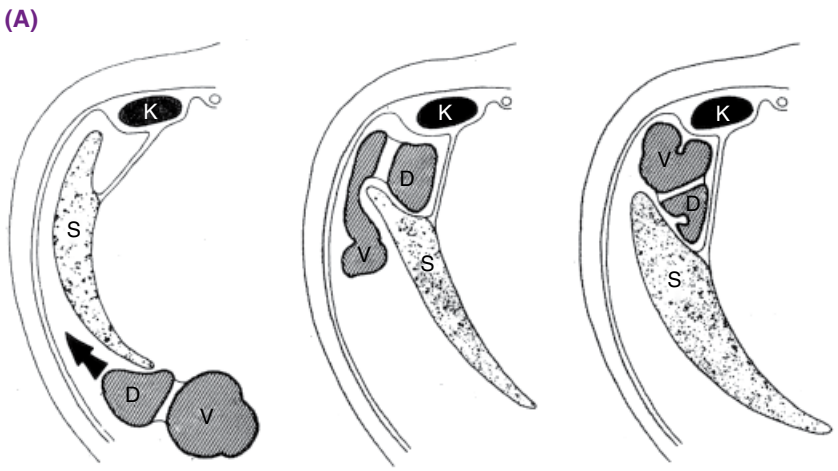

Figure 54.5 **(A)** Illustration of the proposed pathogenesis of left dorsal displacement of the large colon into the nephrosplenic space. S, spleen; K, kidney; D, dorsal part of the large colon; V, ventral part of the large colon. Source: Robinson, 1987. Reproduced with permission of Elsevier. **(B)** Laparoscopic appearance of a left dorsal displacement of the large colon in a horse. S, spleen; C, colon.

It is theorized that excessive gas formation within the left colon, perhaps in association with abnormal motility, causes the left dorsal and ventral colons to displace lateral to the spleen and dorsally into the nephrosplenic space; alternatively, the colon may displace during rolling episodes (Testa & Hilbert, 1987; Hackett, 1983; Deen, 1984; Markel et al., 1985). In most cases, there is also ventromedial rotation of the left colons, such that the left dorsal colon is rotated ventral to the left ventral colon. The weight of the colon causes the spleen to displace medially and ventrally, and to become congested. Because of impaired flow of ingesta over time, impaction of the left dorsal colon develops concurrently (Figure 54.6). With continued gas formation, the sternal and diaphragmatic flexures can migrate cranial and dorsal to the stomach between the stomach and the left liver lobe (Milne et al., 1977; Livesey et al., 1988), a displacement classified as type II in one publication (Livesey et al., 1988). Nephrosplenic entrapment is a nonstrangulating lesion of the large colon; however, when the duration of the condition exceeds 24 h, colonic congestion and edema can develop, and mural damage can occur (Testa & Hilbert, 1987). Obstruction to gastric outflow occurs because of pressure of the colon on the duodenum, or tension on the mesentery. Entrapment of the small colon or small intestine in the nephrosplenic space has been described, but these conditions are rare (Goodrich et al., 1997; Dart et al., 1992).

Horses with nephrosplenic entrapment show variable degrees of pain, depending on the location of the colon, the severity of gas distention, and the presence of secondary gastric distention. Location of the colon lateral to the spleen is associated with minimal to no discomfort, and is found in the resolving stages of the displacement. In contrast, entrapment of the colons within the nephrosplenic space with the spleen in a relatively normal position is a very painful condition. Affected horses will crouch, want to lie down, and often lean to the left. When the spleen is pushed away from the body wall and displaced ventrally, effectively opening the nephrosplenic space, there is less pressure on the colon and horses show milder signs of abdominal pain.

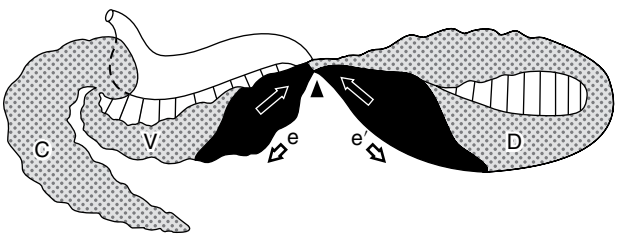

Figure 54.6 Illustration of accumulation of ingesta that occurs during left dorsal displacement of the large colon. There is an impaction of the prestenotic area in the ventral colon and dorsal colon. Proximal to these two impactions there is gas accumulation. C, cecum; V, ventral part of the large colon; D, dorsal part of the large colon. The black arrows show the direction of peristalsis. The white arrows (e and e′) show the effects of peristalsis on the intestinal tube. Source: Robinson, 1987. Reproduced with permission of Elsevier.

The diagnosis of nephrosplenic entrapment is based on the presence of several findings. Abdominal pain can be mild to severe, depending on the location of the colon and the degree of gas distention, and cardiovascular parameters are relatively normal, consistent with a simple obstruction. The complete blood count and chemistry values should be normal or consistent with mild dehydration. A low packed cell volume (PCV) in the face of dehydration has been reported as an indication of red blood cell sequestration in the spleen. The abdominocentesis results should be within the normal range; collection of splenic blood (characterized by having a PCV higher than the peripheral blood) is supportive of a diagnosis of nephrosplenic entrapment, and was obtained in 25% of affected horses in one study (Baird et al., 1991). Horses with increased peritoneal fluid white blood cells were more likely to have a long-standing duration of the condition, and to require surgical intervention (Baird et al., 1991). Nasogastric reflux is commonly obtained in horses with nephrosplenic entrapment as a result of pressure on the duodenum or mesenteric tension. Up to 43% of horses with nephrosplenic entrapment were reported to have nasogastric reflux (Hardy et al., 2000). In one study, resistance to nasogastric intubation was encountered in horses with displacement of the sternal and diaphragmatic flexures dorsal to the stomach (Livesey et al., 1988).

Ultrasound examination of the abdomen can serve as an adjunct to the diagnosis of nephrosplenic entrapment, and was diagnostic in 36 of 41 (88%) horses with nephrosplenic entrapment (Santschi et al., 1993). A 2.5 or 3.5 MHz ultrasound probe is placed over the 15th to 17th intercostal space in a direction parallel to the ground and the spleen is imaged. In the normal horse, the left kidney is imaged deep to the spleen (Figure 54.7A). In horses with nephrosplenic entrapment, the presence of gas-filled colon dorsal to the spleen precludes imaging the kidney (Figure 54.7B). Finding ventral displacement of the dorsal aspect of the spleen is also consistent with nephrosplenic entrapment. If the colons are displaced lateral to the spleen, then imaging of the spleen is also obscured. It is important to direct the probe in a horizontal direction; if the probe is angled in a dorsoventral direction, the kidney can occasionally still be imaged, giving a false negative diagnosis. It is important to realize that the inability to image the left kidney is only *supportive* of a nephrosplenic entrapment, and should be used in conjunction with rectal palpation findings. Nonspecific large colon distention or the normal presence of small colon in the nephrosplenic space can impair imaging of the left kidney (Reef, 1998). In addition, if the colon is

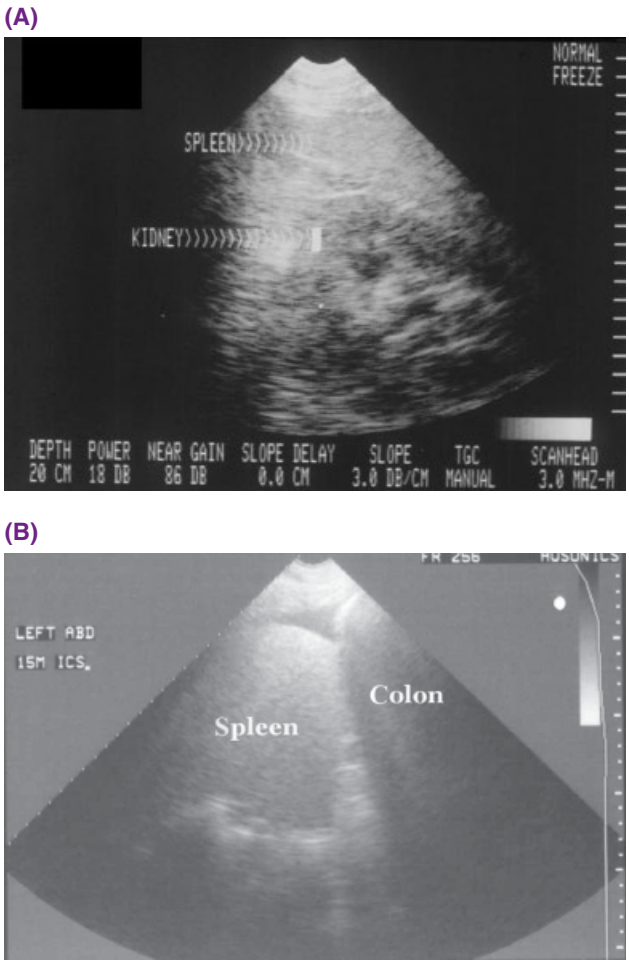

Figure 54.7 **(A)** Normal ultrasonographic appearance of the left flank of a horse, taken in the 17th intercostal space. **(B)** Ultrasonographic appearance of the left flank of a horse with left dorsal displacement of the left colon. Note that the left kidney cannot be imaged.

fluid filled, imaging of the left kidney is still possible, but the entrapped bowel is also seen (Santschi et al., 1993).

Rectal palpation remains the mainstay of diagnosis of nephrosplenic entrapment. On palpation, the left colons will most often be gas distended and the ventral colon will be dorsal to the left dorsal colon; an impaction of the left dorsal colon will often be palpated. The colons can be followed into the nephrosplenic space. It is important to palpate the colons into the nephrosplenic space as in other conditions, ranging from gas colic to large colon volvulus, the colon can assume a dorsal position within the abdomen, leading to a false diagnosis of nephrosplenic entrapment (Johnston & Freeman, 1997). This could be disastrous if nonsurgical management is attempted for a horse that has a large colon volvulus. Rectal palpation correctly identified left dorsal displacement of the large colon in 61.2, 68.7, and 72% of cases (Baird et al., 1991; Hardy et al., 2000; Sivula, 1991). This is in contrast to an earlier study that reported a correct identification rate of only 18% (Livesey et al., 1988). Rectal palpation can be impaired by patient size or temperament or in the presence of severe large colon distention.

Thorough physical examination, rectal palpation, and abdominal ultrasound should be performed in horses diagnosed with nephrosplenic entrapment, as a small number of horses will have another primary lesion involving another segment of the gastrointestinal tract. For example, gastric rupture, small intestinal volvulus, ileal impaction, large colon displacement, large colon volvulus, cecal torsion, small colon obstruction, and inguinal herniation have been documented in association with nephrosplenic entrapment (Baird et al., 1991; Hardy et al., 2000; Sivula, 1991; Santschi et al., 1993; Kalsbeek, 1989; Burns et al., 2011).

Once a diagnosis of nephrosplenic entrapment has been made and the clinician is confident that there are no other abnormalities present, options for treatment are considered. These include medical therapy with intravenous fluids and withholding of feed, exercise with or without the use of a pressor agent, rolling under general anesthesia with or without the use of pressor agents, standing flank laparotomy, and ventral midline celiotomy.

Medical and Nonsurgical Management

Administration of IV fluids supplemented with calcium gluconate is indicated when the colons are located lateral or dorsal to the spleen, but not entrapped in the nephrosplenic space. This approach is more likely to be successful if the duration of pain is ≤24 h (McGovern et al., 2012). In one study, medical therapy was successful in 38 of 50 horses (76%) (McGovern et al., 2012).

When the colons are localized in the nephrosplenic space and the horse is painful, nonsurgical management can be attempted. In one study, horses that were successfully treated nonsurgically had a shorter duration of clinical signs, a lower peritoneal fluid white blood cell count, and a higher blood lymphocyte count than horses treated surgically (Baird et al., 1991). In that study, failure of nonsurgical management was related to the severity of gas distention, which can increase with duration. It is important to emphasize that the diagnosis must be certain before attempting this option.

With all nonsurgical options, phenylephrine (Neo-Synephrine®, phenylephrine·HCl, 10 mg/mL; Winthrop Pharmaceuticals, New York, USA) commonly is used to cause splenic contraction as an adjunct to facilitate correction. Although bleeding the horse was described in the early literature to reduce splenic size (Boening & Von Saldern, 1986), this seems unnecessary and potentially detrimental. Phenylephrine is an α_1-adrenergic receptor agonist that causes vasoconstriction in most vascular

beds, and splenic contraction. In one study, the splenic area in horses was reduced to 28% of baseline and thickness to 48% of baseline after administration of phenylephrine at 3 μg/kg/min over 15 min (Hardy et al., 1994). The author has also observed the spleen with laparoscopy in standing horses being administered phenylephrine, and noted that the dorsal border of the spleen (which is responsible for maintaining the colons entrapped) is significantly reduced with phenylephrine administration. Side effects of phenylephrine are minimal at that dose, and include hypertension and reflex bradycardia. Currently, the author uses a total dose of 10 mg for horses weighing 450 kg or less and 20 mg for larger horses; the drug is diluted in 50 mL of saline and given slowly IV over 5 min. It is important to note that phenylephrine has caused significant hemorrhage in older horses (≥15 years old); in one report, four of five horses of that age died of hemorrhage after phenylephrine administration (Frederick et al., 2010). The use of phenylephrine is not universally accepted and although some studies have shown benefit in resolving nephrosplenic entrapment (Fultz et al., 2013; Hardy et al., 2000), others have failed to show improved results with its use (Baker et al., 2011).

Controlled exercise is an option for treatment of nephrosplenic entrapment provided that the horse is not lame. This procedure is more successful when performed early in the course of the disease, before the large colon becomes distended with gas (Hardy et al., 2000; Johnston & Freeman, 1997; McGovern et al., 2012; Van Harreveld et al., 1999). If there is significant distention of the left colons, the colons can be decompressed by trocarization before exercise. For percutaneous decompression, an area over the left flank is clipped and prepared aseptically. A 14-gauge over-the-needle IV catheter with a catheter extension is used to puncture the flank in a perpendicular direction. The end of the catheter extension is placed in a water container to facilitate observation of gas exiting the colons. Once in place, the trocar portion of the catheter is withdrawn a few millimeters to avoid laceration of the bowel. The trocar is replaced within the catheter if it needs to be inserted further as the colon is deflated. When doing so, care must be taken not to lacerate the tip of the catheter with the trocar. Rectal palpation can help manipulate the colon to facilitate gas evacuation. When the excess gas has been removed, the trocar portion of the catheter is removed and 1–2 mL of gentamicin are injected as the catheter is withdrawn. Removal of gas from the colon is useful before an attempt is made to use exercise for the correction of nephrosplenic entrapment; otherwise, if the colon is gas distended, it will remain in a dorsal position. Once the decompression is completed, phenylephrine is administered intravenously and the horse is exercised either on a lunge line or in a small paddock for 15–30 min. Rectal palpation is performed to ascertain the position of the colon. Exercise can be repeated if correction is not achieved. This method was successful in 11 of 12 horses (Van Harreveld et al., 1999) and 24 of 38 horses (63.2%) (Fultz et al., 2013).

Rolling the horse under general anesthesia is another nonsurgical option for correction of this disorder (Figure 54.8) (Boening & Von Saldern, 1986; Kalsbeek, 1989). This procedure has also been reported to be useful in a small number of horses with other large colon displacements (Kobluk, 1988). This option is preferred if the horse is lame or if there is large colon distention. Previous abdominal surgery may preclude the use of this procedure, as splenic adhesions may prevent successful correction of the displacement (Moll et al., 1993). For this procedure, the colon is not decompressed unless the distention is severe, as gas translocation is used to achieve correction of the displacement.

The horse is prepared for short-term intravenous anesthesia. An α_2-agonist is administered for sedation, followed by phenylephrine infusion, if desired, as described earlier. Although several techniques have been described, it is the author's opinion that a combination of techniques is preferable. The horse is anesthetized and positioned in right lateral recumbency. Using a knee or two-handed fist, the clinician then vigorously shakes the abdomen in the region of the left flank, as the horse's hind legs are being hoisted. If a hoist is not available, the horse is slowly rolled into dorsal recumbency while abdominal compressions are performed. Using the hoist, the hind legs are elevated until the horse's body reaches a 60° vertical position, while the clinician continues to shake the abdomen vigorously. The hind limbs are then lowered and all four limbs are attached to the hoist. The horse is then flipped back and forth from left to right recumbency. A third technique can then be performed in which the horse is hoisted by all four limbs, and with the clinician on the horse's left side the abdomen is shaken using the clinician's knee. After 1–2 min, the horse is repositioned in right lateral recumbency. At this stage, some clinicians prefer to place the horse in left lateral recumbency, roll it into a sternal position, and then to right lateral recumbency. The procedures are repeated two more times. After the last manipulation, the horse is returned to left lateral recumbency for recovery. Between manipulations, the clinician can attempt to verify the position of the colon. It is the author's experience that it is difficult to determine successful correction of the entrapment, either by ultrasound or rectal palpation, with the horse under general anesthesia. Therefore, the author always recovers the horse to determine if correction was achieved. Some clinicians prefer to follow immediately with surgical correction without recovery if it is felt that correction was not achieved (Baker et al., 2011; Johnston & Freeman, 1997).

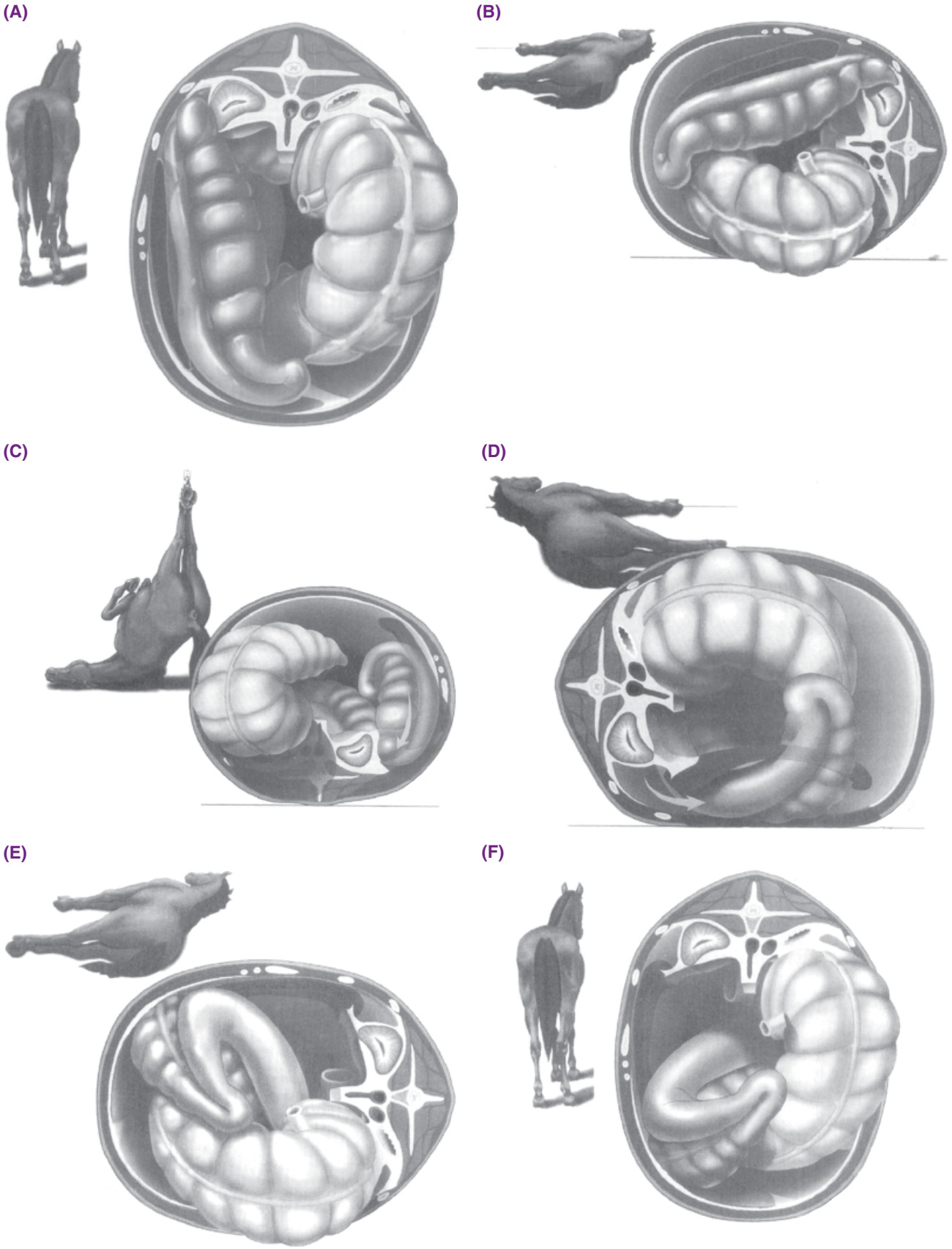

Figure 54.8 Nonsurgical correction of a left dorsal displacement of the large colon. **(A)** Caudal view of the standing horse with the left ventral and dorsal colons entrapped over the nephrosplenic ligament. **(B)** The patient is anesthetized and placed in right lateral recumbency. **(C)** Hobbles are placed on the hind limbs, and the patient is positioned in dorsal recumbency. The hind limbs are lifted to raise the hind end off the ground. The large colon falls cranially, laterally, and to the right (arrow). **(D)** The patient is then positioned in left lateral recumbency. This allows the colon to continue to fall ventrally and laterally to the spleen. **(E)** The 360° rotation is completed by rolling the individual into sternal recumbency (not shown) and then back to right lateral recumbency. (This step is omitted by some clinicians.) The colon comes to rest in a position medial to the spleen. **(F)** The patient is allowed to recover. If the procedure is successful, the colon assumes a position ventral and medial to the spleen. Rectal palpation is performed to assess the position of the colon.
Source: Adapted from Orsini & Divers, 2003. Reproduced with permission of Elsevier.

One author described manipulation of the colons per rectum. With the horse in right lateral recumbency, the hand lifts the colons off the spleen as the horse is being turned to left lateral recumbency. The use of muscle relaxants is recommended when this procedure is used to relax the rectum. Rectal manipulation must be performed with extreme caution, as rectal tears are a definite risk of the procedure (Kalsbeek, 1989).

Rectal palpation after manipulation will often reveal that the colon is lateral to the spleen and has not completely returned to its normal position. Administration of IV fluids supplemented with calcium will often result in complete correction within a few hours. Some horses may show mild abdominal pain after manipulation even though it is felt that correction was achieved. Presumably, this is a result of residual large colon distention or impaction, and it is usually responsive to analgesics.

Complications and Prognosis

Complications of nonsurgical correction most often relate to an inaccurate diagnosis, thereby delaying surgical intervention in a horse having another condition, either as the only cause for the horse's abdominal pain or in addition to nephrosplenic entrapment. The presence of other physical examination abnormalities, such as signs of cardiovascular compromise, abnormal peritoneal fluid findings, or other rectal palpation findings, such as small intestinal distention, should alert the clinician to the presence of other abnormalities that would favor surgical correction.

Complications of needle decompression can also occur; these include peritonitis, intestinal laceration, and abscess formation at the site of trocarization. The prevalence of these complications has not been documented.

Overall, medical therapy for left dorsal displacement had a success rate of 76% (38/50) (McGovern et al., 2012). Nonsurgical management with exercise had a success rate of 63.2% (24/38) and nonsurgical management by rolling under anesthesia had success rates ranging from 58% (50/87) to 84% (42/50) (Baker et al., 2011; Fultz et al., 2013). There have been no randomized clinical trials evaluating the use of phenylephrine as an adjunct to nonsurgical management of nephrosplenic entrapment. Interestingly, one study mentions that in young horses, the spleen acts more as a hematopoietic organ than a reservoir, which may lead to reduced efficacy of phenylephrine in young horses (Baker et al., 2011).

Surgical Treatment

If medical or nonsurgical treatment options are unsuccessful, or if the degree of pain and gas distention preclude the use of these approaches, surgical intervention is indicated, using either a standing flank laparotomy or ventral midline celiotomy. Standing flank laparotomy allows correction of a nephrosplenic entrapment, provided that the diagnosis is correct (Krueger & Klohnen, 2015). The advantages of the standing flank approach are avoidance of general anesthesia, direct access to the problem, access to the nephrosplenic space for closure as an option for prevention of recurrence, and more rapid return of the horse to its intended use. The major disadvantage of this approach, as is the case for nonsurgical treatment, is that if an incorrect diagnosis was made, it precludes correction of the underlying problem. Horses that are refractory to pain medication are also poor candidates for a standing surgical procedure.

For the standing flank approach, the horse is restrained in stocks with the tail bandaged and tied to avoid contamination of the incision. Sedation with xylazine or detomidine with or without butorphanol is sufficient for most horses. The left paralumbar fossa is clipped and surgically prepared. After standard preparation of the surgical site, local anesthesia is performed. This can be accomplished with a paravertebral block (Moon & Suter, 1993), an L-block, or a line block, taking care to add local anesthesia for placement of towel clamps. In the author's experience, the paravertebral block often requires additional local block in the distal aspect of the planned incision. The standard surgical approach for a flank laparotomy is midway between the last rib and the cranial aspect of the tuber coxae, starting approximately 2 cm above the palpable internal oblique muscle. In the standing horse, the modified grid is the preferred approach. In this approach, the external oblique muscle is incised, but the internal oblique and transverse abdominal muscles are bluntly divided parallel to their fiber direction in grid fashion. Additional topical application of anesthetic may be required before penetrating the peritoneum.

After the abdomen has been entered, the spleen and large colon are located. In the author's experience, it is easier to push the spleen down and under the large colon then it is to lift the large colon over the spleen. Phenylephrine may be administered to reduce the size of the spleen and facilitate correction of the displacement (Krueger & Klohnen, 2015). Once the colon is lateral to the spleen, it is gently pushed down into the ventral abdomen and repositioned medial to the spleen. The rest of the abdomen is explored. If indicated, closure of the nephrosplenic space can be performed at this time (Munoz & Bussy, 2013; Zekas et al., 1999). Carboxymethylcellulose may be instilled into the abdomen before closure (Moll et al., 1991). Closure is performed routinely.

A ventral midline celiotomy is recommended for correction of nephrosplenic entrapment if nonsurgical management is unsuccessful, if there are clinical or clinicopathological findings that indicate loss of intestinal integrity, if the presence of another lesion is suspected,

if the diagnosis is uncertain, or if the horse is too painful to withstand a standing procedure. This approach is also used when a presurgical diagnosis is not possible because the small size of the patient precludes rectal palpation, or because excessive large colon distention prevents palpation of the nephrosplenic space. The advantages of the ventral midline celiotomy are that it ensures correction, particularly in cases where the colons are dorsal and cranial to the stomach, and allows correction of other undiagnosed problems. The disadvantages include the need for general anesthesia, longer postoperative recovery, and increased cost. A routine ventral midline approach is performed. To facilitate the approach to the nephrosplenic space, the horse may be tilted slightly to the right. In the presence of excessive splenic congestion or excessive weight of the colon, phenylephrine may be given to reduce splenic size and facilitate correction. The base of the spleen is grasped and the spleen is lifted and pushed medial to the colon, thus freeing the colon from the nephrosplenic space. The colon is then cradled over the forearm and lifted out of the abdomen. If a significant impaction is present, the colon may be evacuated. The colon is assessed for signs of devitalization. Rarely, a large colon resection will have to be performed (Testa & Hilbert, 1987).

Prevention of Recurrence

The reported recurrence rates of nephrosplenic entrapment are 3.2–21%, with a higher rate of recurrence reported in Warmbloods (Baird et al., 1991; Hardy et al., 2000; Rocken et al., 2005). The recurrence rate of 21% was from a large review of medical records of horses presented to a clinic in Germany over a 16 year period and included more than 300 cases of nephrosplenic entrapment (Rocken et al., 2005). Surgical intervention procedures for prevention of recurrence are not recommended after a first incidence. However, feeding and management practices should be carefully reviewed to minimize the risk of gas formation in the large colon and subsequent displacement.

Procedures that have been advocated for prevention of recurrence of nephrosplenic entrapment of the large colon include closure of the nephrosplenic space, large colon colopexy, and large colon resection. The reader is referred to other sections for reference to large colon resection and colopexy procedures.

Closure of the nephrosplenic space will not prevent migration of the large colon lateral to the spleen or the occurrence of other forms of large colon displacement (Munoz & Bussy, 2013; Röcken et al., 2005). The procedure can be performed through a flank laparotomy, hand-assisted laparoscopy, or a minimally invasive laparoscopic approach (Marien et al., 2001; Röcken et al., 2005; Zekas et al., 1999). The flank approach is performed in the standing or laterally recumbent horse. The abdomen is entered either through a modified grid or laparotomy approach. The spleen and nephrosplenic ligament are identified and the nephrosplenic space is verified to be free of intestine. Cruciate sutures are then placed between the ligament and the tip of the spleen, using a nonabsorbable suture such as #2 polypropylene in a cruciate pattern. The abdomen is closed in a routine fashion. Alternatively, laparoscopic ablation of the nephrosplenic space can be performed in the standing horse using sutures or a mesh (Epstein & Parente, 2006; Marien et al., 2001; Munoz & Bussy, 2013; Röcken et al., 2005). In one large study, 44 horses treated by laparoscopic suturing of the nephrosplenic space had no recurrence of nephrosplenic entrapment, compared with 21% recurrence in the same hospital without closure of the nephrosplenic space, although four horses had displacement of the ascending colon between the spleen and body wall (Röcken et al., 2005).

Right Dorsal Displacement of the Large Colon

This type of displacement is thought to be initiated by retropulsive movement of the pelvic flexure, with subsequent migration of the left colon cranially, and then to the right abdominal quadrant, until the right ventral and dorsal colons are located between the cecum and the body wall. The colon can also rotate on its long axis, resulting in variable degrees of venous congestion.

The location of the colon at the time of examination is related to the clinical signs. When the colon is displaced cranially, all parameters are within normal limits, and abdominal pain is mild and intermittent. These horses may be comfortable when held off feed, with abdominal pain recurring when feed is reintroduced. These horses continue to pass small amounts of manure. On rectal palpation, there is no abdominal distention, but the examiner is unable to locate the pelvic flexure. As the colon continues to migrate in a clockwise direction, the flow of ingesta is impaired, and a secondary impaction of the right dorsal colon can develop. Gas distention also becomes more significant as is the associated abdominal pain. When a dorsal colon impaction develops, it is important not to mistake this for a pelvic flexure impaction, as continued medical treatment may result in rupture of the colon. This condition can be differentiated from a pelvic flexure impaction by the fact that the colon travels cranially to the right, and that the pelvic flexure cannot be identified. In right dorsal displacements, the cecum can be enlarged and fluid filled.

Horses with right dorsal colon displacements present with mild to moderate abdominal pain. Depending on the degree of displacement, rectal palpation will reveal absence of the pelvic flexure, presence of large colon lateral to the cecum, large colon distention, and right dorsal colon impaction. Nasogastric reflux may be

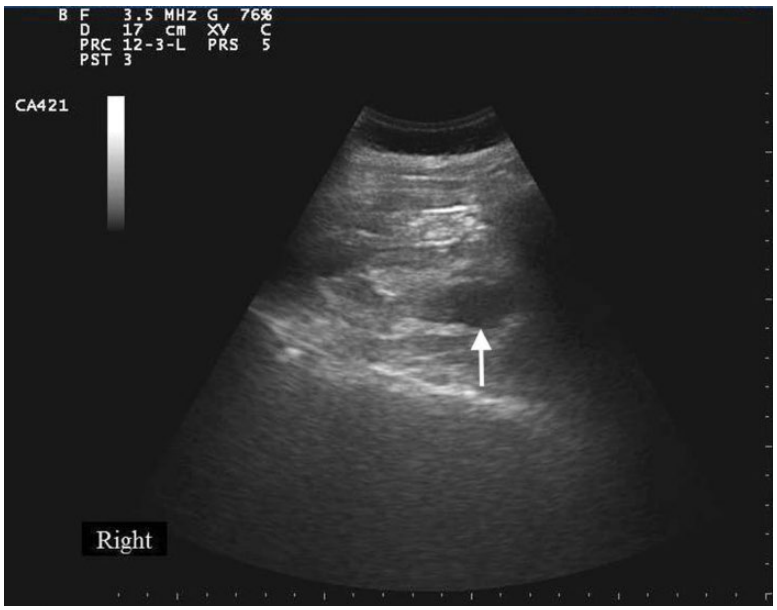

Figure 54.9 A transabdominal ultrasound image obtained in the right mid-abdominal window in a horse with a surgically confirmed right dorsal displacement of the large colon showing prominent colonic vasculature (arrow).

present if there is large colon distention. Transabdominal ultrasonographic identification of the colonic vasculature on the right side of the abdomen is often possible in horses with right dorsal displacement or 180° volvulus (Figure 54.9). Ultrasonographic visualization of colonic vasculature (as an indicator of large colon right dorsal displacement or 180° volvulus) had a sensitivity of 67.7% and specificity of 97.9%, a positive predictive value of 95.8%, and a negative predictive value of 81% in a population with a prevalence of disease of 29% (24 of 82 horses undergoing exploratory celiotomy) (Ness et al., 2012). Laboratory data are usually unremarkable, although a significant number of horses will present with increased gamma-glutamyl transferase activity, presumably related to partial obstruction of the duodenum (Gardner et al., 2005).

When horses are presented early, with normal parameters, mild abdominal pain, and minimal to moderate large colon distention, medical therapy may be attempted. Intravenous fluids are administered and the horse is monitored for resolution of the distention and relocation of the large colon. In one study, 49 of 77 horses (64%) with right dorsal displacement of the large colon responded to medical therapy (McGovern et al., 2012). However, as mentioned by the authors, a definitive diagnosis of right dorsal displacement is difficult to make without surgery; in that report, a diagnosis of right dorsal displacement was made when a gas-distended colon oriented horizontally was rectally palpated, a finding that is fairly nonspecific.

In cases where the pain is severe, there is severe large colon distention, or there is a severe secondary impaction, surgical intervention is recommended. Although in some specific circumstances the author has successfully corrected right dorsal colonic displacements via a standing flank laparotomy, a ventral midline celiotomy is preferred because of ease of exposure and correction.

At surgery, the pelvic flexure is identified, the large colon is exteriorized, and the displacement is corrected. In cases where a severe large colon impaction coexists, the large colon is exteriorized at the pelvic flexure but an attempt to correct the displacement is not made until the large colon has been evacuated, to avoid rupture during colonic manipulations. Although there is one report of successful treatment of a horse following intraoperative rupture during surgery (Schumacher, 2001), most of these cases are fatal.

The prognosis for horses with large colon displacement is excellent. Recurrence is possible, and the author has had horses redisplaced within 48 h of the first procedure. In the author's opinion, it is important not to evacuate the large colon completely, but to leave some bulk in the colon. The author also returns these horses to feed within 8 h of surgery, again to try to maintain bulk in the large colon. In one study, horses that underwent surgery for correction of a right dorsal displacement were more likely to experience recurrent episodes of colic than other types of displacements (Smith & Mair, 2010).

Nonstrangulating Volvulus of the Large Colon

Nonstrangulating volvulus of the large colon is identified when the colon is rotated from 90 to 270° on its long axis, a step that precedes the 360° large colon volvulus. Horses with this type of displacement have a clinical presentation very similar to that of other simple large colon displacements: minimal cardiovascular compromise, mild to moderate abdominal pain, normal abdominocentesis,

and mild to moderate large colon distention on rectal palpation. As is the case for horses with other displacements, medical management may be attempted. Horses that remain painful or that have worsening of abdominal distention are candidates for surgical intervention. At surgery, the colon is replaced in its normal position.

As in all forms of large colon displacements or volvulus, prevention of recurrence should be considered. Colopexy and large colon resection are two procedures that are performed in an attempt to prevent recurrence. Usually these procedures are not recommended on a first-time occurrence, but should be discussed for horses that have two or more displacements.

Other Simple Obstructions of the Large Colon

Congenital malformation of the large colon (T-shaped colon) has been reported as a cause of colic, and has been identified by the author in several horses (Figure 54.10) (Suann & Livesey, 1986; Trope & Steel, 2010). Resection and anastomosis of the colon oral to the malformation can successfully resolve the problem.

An abnormally short colon was also reported as a cause of recurrent colic in a foal; no pelvic flexure or dorsal colon was identifiable, and four teniae were present all the way through the length of the colon. The colt continued to have episodes of mild colic that were responsive to medical therapy (Koenig et al., 2007).

Fibrosis and stricture of the large colon caused by focal fibrosis at the pelvic flexure was identified in three horses and corrected by transverse closure of a pelvic flexure enterotomy made at the site of the fibrosis (Rose et al., 1991).

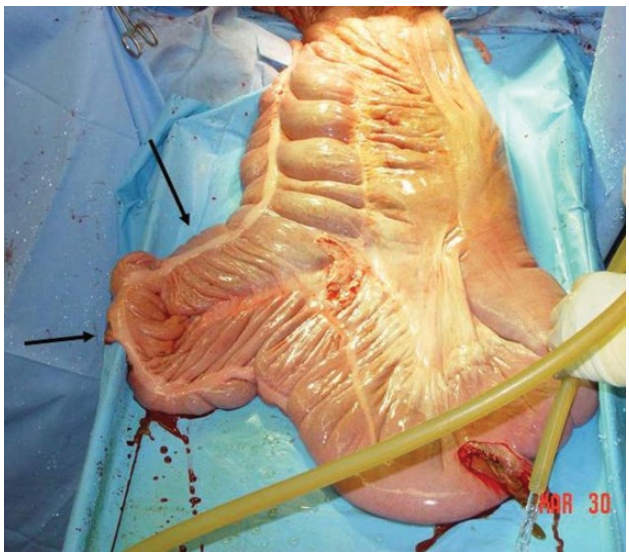

Figure 54.10 A congenital malformation of the ventral colon in an 8-month-old filly that had suffered several bouts of colic (arrows). Large colon resection and anastomosis resolved the problem.

Pelvic flexure adhesion resulting in impaction was reported in a filly with peritonitis. Laparoscopic adhesiolysis was successfully performed to allow return of transit (Boure et al., 1998).

A massive duplication cyst of the ascending colon was reported in a 27-year-old mare with a history of recurrent colic and a pendulous abdomen. The cyst was successfully removed and the mare made an uneventful recovery (Bassage et al., 2000).

Although typically reported as small intestinal strangulations, epiploic entrapment of the large colon and inguinal herniation of the large colon have been reported (Foerner et al., 1993; Steenhaut et al., 1993; Ivens et al., 2009; Robinson & Carmalt, 2009).

Defects in the mesentery of the large colon have been observed by the author in several horses (Figure 54.11). The presence of the defect allows displacement or torsion of the colon upon itself, as it is no longer confined by the mesentery. Closure of the defect allowed correction of the problem.

Large Colon Volvulus

Large colon volvulus is one of the most painful and life-threatening gastrointestinal conditions in the horse. Successful management is dependent on rapid referral and prompt surgical intervention. Without intervention, death occurs in a matter of hours.

Large colon volvulus accounts for 10–20% of horses presented for colic that undergo an exploratory celiotomy (Gonzalez et al., 2015). The prevalence of large colon volvulus is increased in geographic areas with a high concentration of broodmares. Risk factors include recent parturition, recent dietary changes, and recent access to a lush pasture. In one study, the following factors were associated with an increased risk of large colon volvulus: being a broodmare, having multiple colic episodes in the previous 12 months, receiving medication in the previous 7 days, exhibiting quidding behavior, increased hours of stabling in the previous 14 days, increasing number of horses on the premise, three or more people involved in the horse's care, feeding hay, feeding sugar beet, a change in pasture in the previous 28 days, and a change in forage in the previous 7 days (Suthers et al., 2013a).

The history of horses with large colon volvulus can vary depending on the rapidity and completeness of the volvulus. Some horses will present with a history of chronic (>24 h) colic that suddenly worsens to intractable pain; others will present with an acute onset of uncontrollable pain. Initially, despite the severe pain, horses will maintain normal cardiovascular parameters, and rectal palpation can be unremarkable. As time elapses, these horses will develop progressive large colon

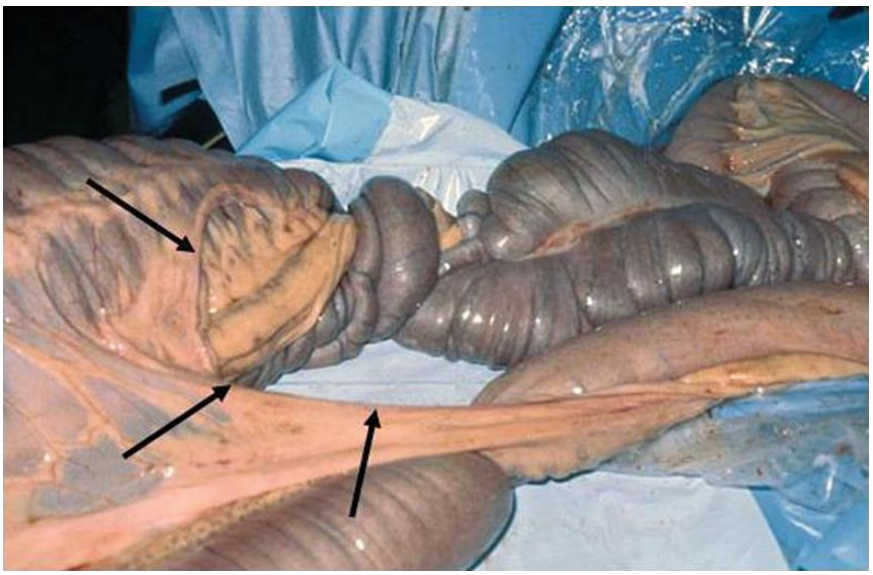

Figure 54.11 The large colon of a horse with a mesenteric defect (arrows) in the large colon mesentery, which resulted in a partial large colon volvulus.

distention and accompanying signs of cardiovascular collapse. In mares, the color of the vaginal mucosa changes and reflects the degree of compromise of the large colon (Figure 54.12A and B). If untreated, horses with large colon volvulus die of hypovolemic shock caused by abdominal compartment syndrome associated with the severe abdominal distention, and by pooling of blood in the strangulated large colon.

Treatment of horses with large colon volvulus is surgical. However, during preparation for surgery, resuscitative measures should be initiated to increase circulating blood volume and decrease abdominal pressure. Intravenous fluid therapy, including administration of hypertonic saline, colloids, and crystalloids, needs to be initiated. Trocarization to relieve abdominal distention can improve lung expansion and improve venous return, and can help support the horse during induction, until the colon can be exteriorized and decompressed. Ultrasound has been used in the diagnosis of large colon volvulus by evaluating the thickness of the large colon, with a wall thickness ≥9 mm being diagnostic (eight of 12 horses, sensitivity 67%) (Pease et al., 2004) or by the ventral location of the dorsal colon (four horses) (Abutarbush, 2006). Both studies included a limited number of horses. In the present author's experience, ultrasound can be difficult to perform in a painful horse, and colonic thickening may not be present in the early stages of the disease.

A ventral midline celiotomy approach is used, centered more cranially to facilitate the approach to the colonic base; if the colon is severely distended, a long incision may be required to facilitate exteriorization of the colon. The direction of the volvulus is best described in relation to the position of the ventral colon, to obviate the need

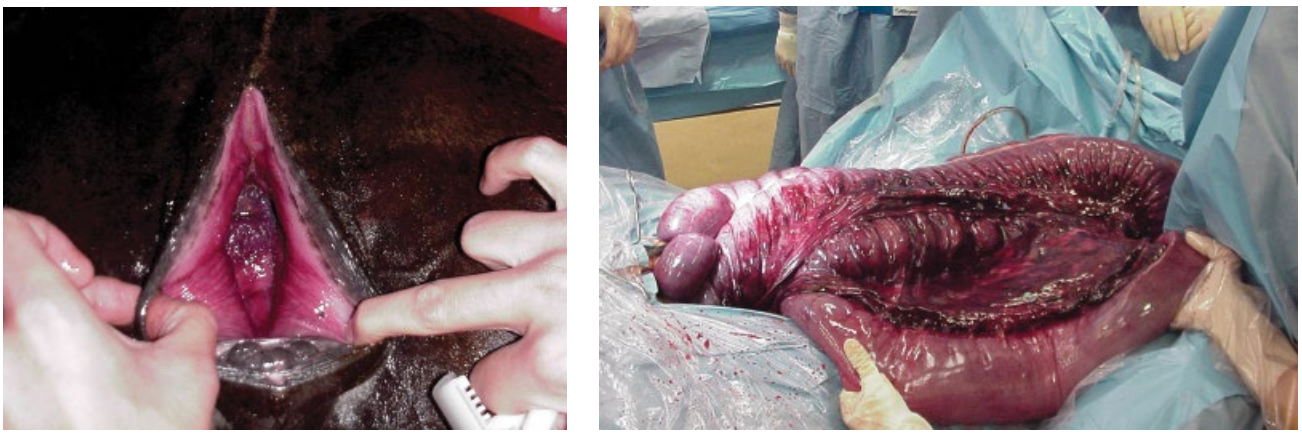

Figure 54.12 **(A)** Preoperative appearance of the vaginal mucosa in a mare with large colon volvulus. **(B)**. Appearance of the large colon in the same mare at surgery.

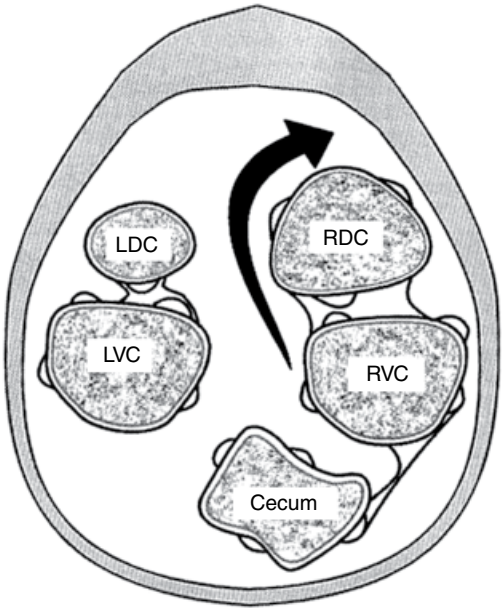

Figure 54.13 Illustration of a large colon volvulus depicting the terminology for describing the direction of the volvulus.

for describing the observer's position. Therefore, a dorsomedial volvulus indicates rotation of the right ventral colon medially and dorsally (Harrison, 1988). Most often the colon rotates in a dorsomedial direction, and the location of the volvulus is at or proximal to the cecocolic ligament (Figure 54.13). Occasionally, a volvulus involving the sternal and diaphragmatic flexures will be encountered. Volvulus of 270–720° have been described (Snyder et al., 1989).

Correction of the volvulus can be difficult, particularly if the colon is full and/or edematous; this places the colon, particularly the right dorsal colon, at risk for rupture during surgical manipulation. The ascending colon is exteriorized; if the colon is full or edematous and friable, a pelvic flexure enterotomy can be performed to empty the colon and decrease the weight of the intestine prior to correction of the volvulus. To correct the volvulus, the surgeon, positioned on the left side of the horse, places both hands in the abdomen around the base of the colon, and gently manipulates the colon in a clockwise direction (Hughes & Slone, 1997). The surgical assistant can facilitate manipulation by rotating the exteriorized portion of the colon in the same direction. Gas translocation and return of serosal color are indications that the colon is being manipulated correctly. Once a 360° rotation has been achieved, the surgeon must then ascertain that the volvulus is corrected, and that another rotation of the colon is not needed. This is accomplished by examination of the normal position of the cecum, normal position of the cecocolic ligament, and ensuring by palpation that the mesenteric attachment of the right dorsal colon to the dorsal body wall is straight. Once the colon has been returned to its normal position, the surgeon must decide on euthanasia, recovery of the horse without further intervention, colopexy for prevention of recurrence, or large colon resection. It is essential to involve the owner in the decision-making process, particularly if the colon is compromised, as the cost of further intervention or postoperative care can be significant. The surgeon must also understand that if the colon is left in place and the horse recovers, it is unlikely that a second laparotomy will be an option. By the time clinical signs indicate that a second laparotomy with the possible need for a large colon resection is required, the horse's condition will have deteriorated to the extent that survival after a resection would be unlikely. Several factors are useful to help the surgeon reach a decision. A critical factor is the horse's systemic condition both pre- and intra-operatively. A PCV that is above 50% and increases during surgery, associated with a decreasing total protein concentration, is a poor indicator of survival (Kelleher et al., 2013). In one study, plasma lactate concentration <6.0 mmol/L at admission had a sensitivity of 84% and a specificity of 83% for predicting survival (Johnston et al., 2007). An inability to maintain mean arterial blood pressure despite the use of pressor agents, persistent hypoxemia, and persistent tachycardia during surgery are also factors associated with poor survival. Examination of the colon can provide some additional information. Return of a normal pink serosal color after volvulus correction is a positive indicator, but does not indicate mucosal viability; severe postoperative endotoxemia may still occur if the mucosa is devitalized. Visual examination of the mucosa through a pelvic flexure enterotomy provides additional information. The presence of dark-red or black mucosa with no active bleeding is a poor prognostic indicator. The use of frozen sections and calculation of the interstitial-to-crypt (I:C) ratio and percentage loss of epithelium correlate well with survival; an I:C ratio of 3:1 or greater or loss of >95% of the epithelium was associated with 95% death in one study (Van Hoogmoed et al., 2000a). However, this requires the presence of personnel able to perform this evaluation. In a subsequent study in a small group of horses, pelvic flexure biopsies did not accurately predict short-term survival in 20–22.4% of horses. However short-term survival in that group was better than typically reported (86%). In a multicenter study, histomorphometric parameters, including digitally quantified measurement of hemorrhage, were predictors of short-term survival (Gonzalez et al., 2015). Unfortunately, for practical reasons, the information provided by histomorphometric assessment is limited to the postoperative period, and the surgeon must base the decision on pre- and intraoperative parameters such as heart rate, PCV, and plasma lactate (Gonzalez et al., 2015).

Colonic pressure has been used to predict outcome. In one study, a colonic pressure >38 cmH_2O was significantly associated with nonsurvival (Moore et al., 1996), but a more recent study failed to identify a good association between colonic pressure and survival (Mathis et al., 2006). However, in the latter study more horses underwent large colon resection and anastomosis, which may have improved the survival of horses with a nonviable colon. An unknown factor when using colonic pressure as a predictor is the duration for which the colon was subjected to the high intraluminal pressure. Other research tools that have been used to evaluate colonic viability include surface oximetry, fluorescein dye, and Doppler flow; none of these tools has gained popularity in a clinical setting.

The decision to perform a colon resection should also be based on the location of the volvulus. If the line of devitalized bowel is located distal to the cecocolic ligament, the outcome of a large colon resection is much more favorable, as resection of the affected bowel is possible. If the line of devitalization is located at the base of the colon oral to the cecocolic ligament, resection must be performed in a compromised portion of the bowel, which places the resection site at risk for dehiscence. Surgeons who are advocates of large colon resection for the treatment of large colon volvulus suggest that removing the majority of the diseased colon decreases the endotoxic load and therefore increases the likelihood of survival; in addition, removal of the large colon prevents recurrence of the condition. Surgeons who do not routinely perform large colon resections for large colon volvulus indicate that the procedure in itself has a high risk of complications, and does not in most cases result in removal of the entire diseased colon; in addition, the increased anesthesia time may be detrimental to the animal. These debates emphasize the complexity of the decision-making process in these cases, and the importance of experience, familiarity with surgical techniques, and the influence of types of cases on this process. For example, horses that are referred quickly and have a short duration of illness may seldom require a large colon resection (Hackett et al., 2015). In one study, mares with colic for 2–4 h prior to admission were three times more likely not to survive, and mares with colic for >4 h were nearly 12 times more likely not to survive than mares with colic duration <2 h (Hackett et al., 2015).

Preoperative parameters indicative of poor survival include PCV >50%, rectal temperature >102 °F (38.9 °C), and heart rate >80 bpm (Hughes & Slone, 1994; Suthers et al., 2013b). Intraoperative factors associated with a poor survival include black mucosal color, poor return of perfusion after correction of the volvulus, an increasing PCV, and a decreasing total protein concentration during surgery (Hughes & Slone, 1994). Abdominocentesis is usually normal in horses with large colon volvulus; an increase in total protein concentration in the abdominal fluid is associated with decreased survival (Snyder et al., 1989). It is the author's experience that abdominal fluid lactate concentration can increase dramatically and precede other cytologic changes. When horses are severely painful, abdominocentesis does not provide information that will alter the decision for surgical treatment, and has an increased risk of enterocentesis or injury to personnel.

Postoperative parameters associated with survival included decreasing heart rate at 48 h and decreasing plasma lactate concentration at 24 h (Suthers et al., 2013b). In contrast, nonsurvivors had a significantly decreased total protein concentration and increased blood lactate in the postoperative period (Sheats et al., 2010). A shorter time to colonic involution as determined by measuring colonic wall thickness with ultrasound was observed in horses with decreased postoperative morbidity (Sheats et al., 2010).

The reported mortality rate for large colon volvulus varies from 56 to 65%. However, in two studies, short-term survival rates were 84% (Cook et al., 1994) and 88% (Hackett et al., 2015); these higher survival rates were purported to be related to a shorter duration of illness and faster intervention time. Although short-term mortality can be high after surgical correction of large colon volvulus, a long-term probability of survival of 80% has been reported once horses have been discharged from the hospital (Proudman et al., 2002).

Right Dorsal Colitis

Right dorsal colitis is a specific type of ulcerative colitis that affects the right dorsal colon of the horse, specifically the aboral segment of the dorsal colon as it joins the transverse colon. This condition is recognized in association with administration of NSAIDs, and has been reproduced experimentally by administration of phenylbutazone. Horses with a nervous predisposition seem more prone to the development of the disease even when appropriate dosages of NSAIDs are given. Although NSAID administration is commonly associated with this condition, it also has been documented in absence of NSAID administration.

Clinical signs of right dorsal colitis can manifest as acute colic, endotoxemia, diarrhea, and even death; the disease is more common in its chronic form, when horses are presented because of weight loss, hypoproteinemia, intermittent signs of colic, and intermittent diarrhea.

The diagnosis of right dorsal colitis is based on historical findings, particularly those of NSAID administration, and ruling out other causes of weight loss, hypoproteinemia, and diarrhea. Diagnostic ultrasonography of the right dorsal colon can help identify the thickened colon (Figure 54.14) (Jones et al., 2003). Scintigraphy with

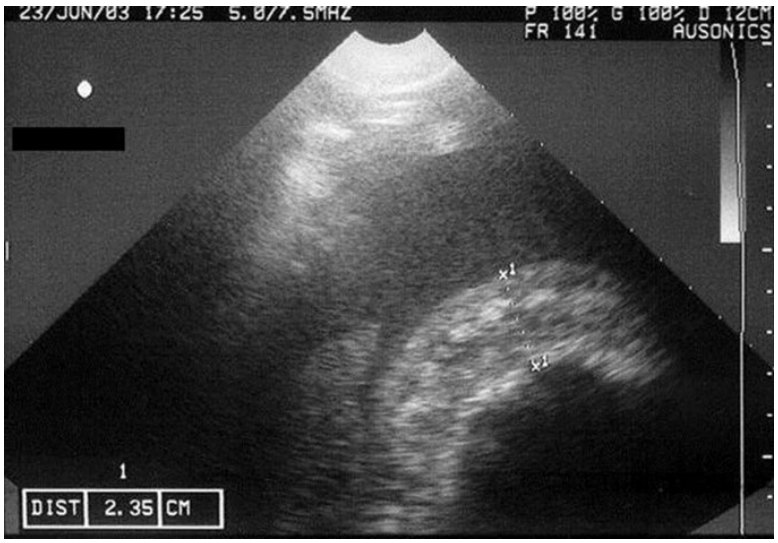

Figure 54.14 Ultrasonographic image of the right dorsal colon performed at the 11th intercostal space using a 3.5 MHz probe illustrating the marked thickening of the intestinal wall.

radiolabeled white blood cells has also been used to diagnose the condition (East et al., 2000).

Medical management is initially recommended for the treatment of right dorsal colitis, including discontinuation of NSAIDs, dietary modifications, intestinal protectants, misoprostol (as a prostaglandin E_1 replacement), and metronidazole. Dietary modifications are important to help control the signs of colic.

In cases of protracted colic, or when intermittent colic episodes are so frequent as to prevent the horse from maintaining itself, surgical exploration can be recommended. At surgery, the right dorsal colon will feel markedly thickened, and may be strictured with scar tissue (Figure 54.15). Once the disease has been identified at surgery, treatment options include right dorsal colon bypass, resection of the affected portion of the colon, large colon resection, or large colon resection and large colon bypass.

Bypass of the affected area of the large colon is performed by exteriorizing the large colon on a colon tray.

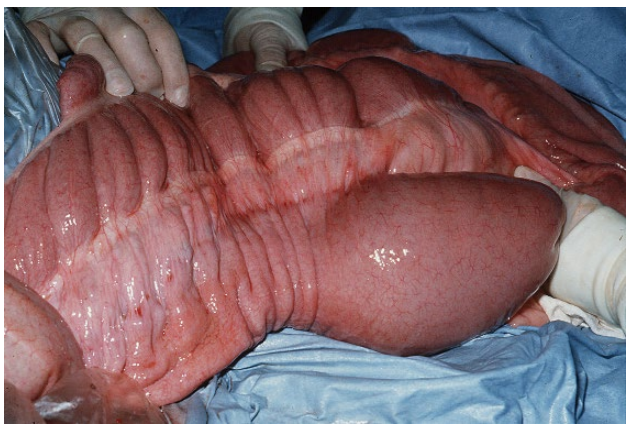

Figure 54.15 Intraoperative illustration of the right dorsal colon of a horse with severe stricture secondary to ulcerative colitis.

The small colon is then exteriorized and a 20–30 cm side-to-side anastomosis between the right dorsal colon oral to the lesion and the small colon approximately 1 m distal to the transverse colon is performed (Andrews & Robertson, 1988). When this procedure is performed, transient diarrhea has been observed postoperatively. This procedure does not remove the affected portion of the colon. Therefore, the patient can continue to suffer from continued weight loss and hypoproteinemia, until the colitis has resolved. Resection of the affected colon through a 16th rib resection has been reported in one horse (Simmons et al., 1990). This approach requires either prior knowledge of the disease or a second celiotomy approach once the diagnosis has been made. Resection and end-to-end anastomosis will be possible only if the lesion does not extend too far aborally. In cases of severe right dorsal colitis with stricture of the right dorsal colon, large colon resection and anastomosis in a side-to-side fashion can be performed to restore intestinal transit. However, complete removal of the ulcerated area would not be possible with this approach. Another approach, which has not been described for the treatment of this condition, would be to amputate the large colon, particularly the dorsal colon as far aboral as possible, and to perform an end-to-side anastomosis between the right ventral colon and the small colon. This approach has been reported for the management of nonfunctional dorsal colon lesions in two horses (Dowling et al., 2000; Freeman & Richter, 1998).

Mural Infarction (Thromboembolic Colic)

Compromise to the mesenteric vasculature without evidence of strangulation has been described in association with arteritis resulting from *Strongylus vulgaris* larval

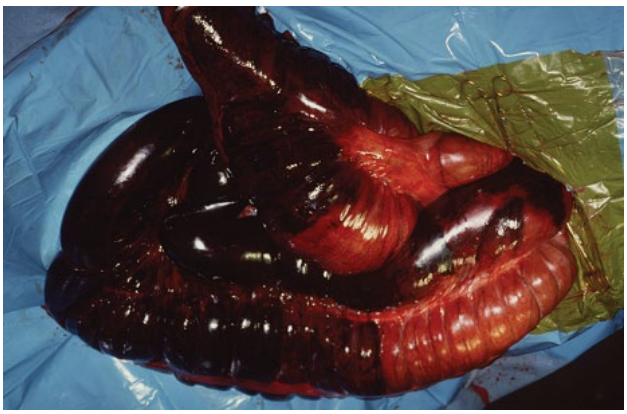

Figure 54.16 Intraoperative illustration of a horse with necrotizing enterocolitis showing venous infarction of the cecum and large colon.

migration, or in horses with severe colitis and coagulopathies (Figure 54.16).

Cases of larval arteritis can be acute, with signs of ischemic bowel disease and peritonitis, or chronic, with signs of recurrent colic and weight loss. Horses with acute thromboembolic colic will have significant changes in peritoneal fluid parameters, consistent with peritonitis; horses with recurrent colic will often have normal peritoneal fluid.

In acute cases, surgical intervention is indicated based on the signs of colic and peritonitis. At surgery, mural infarction is identified and, if possible, resection of the affected segment of intestine is performed. Careful palpation of the cranial mesenteric artery should be performed; identification of severe enlargement, aneurysm, or abscessation is an indication for a guarded to poor prognosis. A regular systematic deworming program should be instituted as part of the postoperative care of affected horses.

Horses with colitis that show acute signs of abdominal pain and abdominal distention should be suspect for thromboembolic colic and necrotizing colitis. Many of these horses will have extensive lesions that preclude surgical intervention. In addition, their systemic status, as a result of the primary colitis, makes them poor surgical candidates.

Other Strangulating Lesions of the Large Colon

Other strangulating lesions of the equine large colon have been reported; these include incarceration in the epiploic foramen (Foerner et al., 1993) or the gastrosplenic ligament (Trostle & Markel, 1993), large colon intussusception (Dyson & Orsini, 1983; Robertson & Tate, 1982), and volvulus associated with abnormal mesenteric bands or defects (Ross & Bayha, 1992; Mogg et al., 1992). Surgical intervention is dictated in these cases by the increasing degree of abdominal pain, abnormal rectal palpation findings, and peritoneal fluid parameters indicative of intestinal compromise. Resection and anastomosis of the affected colon are required to correct these conditions.

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Diseases of the Descending Colon

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Introduction

Of the horses referred to tertiary care facilities with abdominal diseases, 3–18% are evaluated because of abnormalities involving the descending colon. The frequency of obstructive disorders of the descending colon requiring abdominal surgery is approximately 4% (Parry, 1983; Dart et al., 1992b, 1999; Edwards, 1997; Beard et al., 1989a). Successful diagnosis and treatment of descending colon diseases depends on a thorough understanding of its anatomy and physiology (see Chapters 1 and 5). The mid-section of the descending colon is relatively mobile within the caudal abdomen; however, its most oral and aboral segments are fixed in position. These anatomic features facilitate transrectal palpation of the majority of the descending colon and are advantageous in the diagnostic approach to descending colon disease. In contrast, these same features hinder surgical access to the entire length of the descending colon, making visual inspection of the proximal and distal aspects of the descending colon impossible during a ventral midline celiotomy. These and other distinctive physiologic characteristics are important because they affect the approach to common diseases affecting the descending colon.

Surgical Considerations Affected by Anatomic Features of the Descending Colon

The small colon is sometimes referred to as the descending colon, a term that more accurately describes the corresponding portion of the gastrointestinal tract in humans. Details regarding the anatomy and physiology of the equine descending colon are included in Chapters 1 and 5. However, there are some specific points that require mention here as they have important implications regarding the surgical approach to diseases of the descending colon. For example, the transition between transverse colon and descending colon occurs at a fixed point adjacent to the left kidney. The descending colon is suspended from the sublumbar body wall by the mesocolon, which is the caudal continuation of the root of the mesentery. The duodenocolic fold is a narrow extension of the peritoneum and attaches the descending colon to the terminal duodenum. This important anatomic landmark is used during exploratory celiotomy to identify the cranial-most portion of the jejunum. Because of these anatomic features, the most oral and aboral portions of the descending colon cannot be exteriorized during a ventral midline celiotomy. During colic surgery, it is important, however, to palpate carefully the transition between the transverse colon and descending colon as this is a frequent site of obstruction, particularly in horses with enterolithiasis.

The vascular anatomy of the equine descending colon has been described in detail (Beard et al., 1989a). Vascular arcades, which originate from the cranial and caudal mesenteric arteries, are concealed within the mesocolon by large amounts of mesenteric fat. The cranial mesenteric artery gives rise to the middle colic artery, which supplies the cranial portions of the descending colon; the caudal mesenteric artery is responsible for the majority of the descending colon blood supply via anastomosing branches of the left colic artery and the cranial rectal artery (Edwards, 1997). A marginal artery can be found 1–2 cm away from the serosal surface coursing parallel to the longitudinal axis of the descending colon. From the marginal artery, a secondary arcade of blood vessels arises to form a hemicircumferential arterial rete that forms anastomoses on either side of the bowel (Edwards, 1997). It is often reported that survival after descending colon resection and anastomosis may be complicated by

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a relatively poor blood supply (Dart et al., 1992a, 1992b; Stashak, 1982). It would instead appear that the merging cranial and caudal mesenteric vascular supplies and the presence of three communicating intramural plexuses derived from the marginal artery allow the formation of an effective collateral blood supply (Archer et al., 1989).

The microvasculature of the descending colon may become compromised when obstructive conditions such as mural compression or intraluminal distention occur. There is evidence that progressive intraluminal distention can cause a significant reduction in total microvascular perfusion, resulting in ischemia of all layers of the descending colon with the exception of the mucosa (Faleiros et al., 2002). This may account for the reported slow progression of disease in horses with descending colon obstruction. In fact, the mean duration of colic signs (from onset of clinical signs to admission) for horses with descending colon conditions can be significantly longer than in horses undergoing exploratory laparotomy for other causes (De Bont et al., 2012).

Motility patterns of the equine descending colon have not been elucidated in detail. There is, however, clinical evidence that horses possess a well-developed gastrocolic reflex. After feeding, signals from the stomach follow the extrinsic innervation of the autonomic nervous system and cause evacuation of colonic contents. Clinicians can take advantage of this physiologic mechanism to stimulate evacuation of the colon by offering small amounts of feed to horses receiving aggressive medical treatment for obstruction of the descending colon. Mixing and propulsive movements occur in the colon but are less active than those that occur in the small intestine (Guyton & Hall, 1996). The slower transit time of colonic contents allows absorption of water and electrolytes, which leads to progressive fecal dehydration (see Chapter 5). This may be compounded in dehydrated animals, facilitating fecal accumulation and obstruction such as occurs with descending colon impactions.

The mentioned anatomic and physiologic details form the basis for a few principles that should be observed when considering the surgical approach to the descending colon. In horses with descending colon abnormalities that require surgical intervention, it is commonly necessary to evacuate the colonic contents or to remove foreign bodies via an enterotomy, which is best performed along the midportion of the wide antimesenteric band. Compared with an incision through the sacculations of the descending colon, an enterotomy through the tenia is associated with less hemorrhage, edema, and surgery time and, at 96 h from surgery, the incisional strength is superior to that with an enterotomy through the sacculations (Archer et al., 1988; Beard et al., 1989b). The antimesenteric band also can be partially incised to facilitate aboral advancement of an enterolith lodged within the most proximal aspect of the descending colon. Because this segment of the descending colon cannot be exteriorized through a ventral midline celiotomy, it is helpful to perform a seromuscular teniotomy that effectively widens the diameter of the bowel and allows enteroliths to be moved aborally up to 15 cm for safe removal (Hassel & Yarbrough, 1998). Closure of enterotomies and teniotomies is usually performed with #2-0 synthetic absorbable monofilament, such as polydioxanone, in a single-layer inverting suture pattern. It appears from one study that separate mucosal apposition does not have a significant effect on healing time and effectiveness of closure (Beard et al., 1989b).

Strangulation obstruction of the descending colon may necessitate resection and anastomosis, which, in this location is usually performed with an end-to-end technique. A stapled anastomosis technique can reduce surgery time and has been used experimentally in the descending colon; however, the handsewn technique is preferred because the intricate mesenteric vasculature can be more carefully preserved, larger luminal diameters are achieved, better healing is accomplished, and postoperative adhesion formation is minimized (Bristol & Cullen, 1988; Hanson et al., 1988). Although several anastomosis techniques are available, a few important principles of intestinal surgery should be followed in order to preserve the vascular supply, avoid compromising the luminal diameter, and minimize adhesion formation. If a two-layer closure is chosen, care should be taken to avoid excessive cuff formation, which would considerably reduce the luminal diameter, particularly in the first 7–10 days after surgery when edema formation may further restrict the size of the lumen (Witte & Barbul, 2003; Sido et al., 2004; Thornton & Barbul, 1997). In order to minimize adhesion formation, mucosal exposure of the peritoneal surfaces should be avoided by utilizing an inverting suturing technique such as a Cushing or Lembert pattern. Adhesions can be further minimized by covering the anastomotic site with a bioabsorbable hyaluronate membrane, which has been successfully used in adhesion prevention both clinically and experimentally (Mueller et al., 2000; Eggleston et al., 2001). A common anastomosis technique includes an initial simple interrupted layer oversewn with a Cushing pattern interrupted at 180° at the mesenteric and antimesenteric edges. Suture bites should be placed with great care in the area of the mesenteric attachment because the small arterial rete, concealed by the large amount of adipose tissue, may be inadvertently damaged.

Knowledge of the distribution of the intestinal flora plays an important role in the decision-making process after descending colon surgery. Compared with the small intestine, the microflora of the cecum and colon is rich in aerobic and anaerobic bacteria (Cummings et al., 1989; Rastall, 2004). The colonic microflora is dominated by strict anaerobic bacteria, including *Bacteroides* spp., and *Clostridia*. Facultative anaerobes occur in numbers

1000-fold lower and include lactobacilli, enterococci, streptococci, and Enterobacteriaceae (Rastall, 2004). These bacterial populations warrant the perioperative use of broad-spectrum antimicrobials, including metronidazole, which is specific for the prevention and treatment of anaerobic infections. The short descending colon mesentery compels the surgeon to perform resection and anastomoses or enterotomies in close proximity to the celiotomy incision, thereby increasing the risk of inadvertent abdominal contamination.

Descending colon obstruction often causes stasis of fecal material in the colon and cecum. For this reason, evacuation of the contents of the ascending colon via a pelvic flexure enterotomy should be performed in order to minimize the stresses of fecal passage on a newly created descending colon anastomosis or on a descending colon enterotomy. The rationale for evacuation of these contents is supported by the fact that the fecal material undergoes progressive dehydration in the descending colon, a process that may further stress incisions that initially depend solely on the holding power of the suture material.

In addition to the high bacterial content of the distal intestine, descending colon anastomotic healing is thought to be hindered by the relatively high activity of collagen-degrading enzymes such as matrix metalloproteinases (MMPs) (Dart et al., 1992b). Although specific studies addressing the effect of MMPs on healing of the equine colon are lacking, there is evidence that an abnormal regulation of these enzymes may lead to delayed anastomotic dehiscence in people (Stumpf et al., 2002; Agren et al., 2004; Savage et al., 1998). Increased levels of collagenase, a specific collagen-degrading enzyme that is part of the MMP family, have been documented after venous strangulation obstruction of the descending colon in ponies (Ruggles et al., 1993). Despite these findings, the major determinants of a successful outcome after descending colon resection in the horse appears to be related more to the inability to exteriorize the proximal and distal ends of the descending colon and to the presence of mesenteric fat, which does not allow an unobstructed view of the intricate vasculature at the interface between the bowel and the mesentery.

Short-term survival of horses undergoing surgical treatment of descending colon obstructions appears to be good. In a retrospective study of 300 abdominal surgery cases in the United Kingdom, the most common reasons for death/euthanasia in the postoperative period were persistent pain/colic, postoperative ileus, and grass sickness. Horses with lesions involving the small intestine and cecum had lower survival rates (75.2 and 66.7%, respectively) than those with large colon or descending colon lesions (89.9 and 100%, respectively) (Mair & Smith, 2005). Attesting to the relatively low frequency of descending colon disease, nine horses with descending colon abnormalities were included in this study, most of which had impactions or fecaliths, and all survived. However, postoperative pain and shock occurred more often in horses with descending colon rather than large colon obstruction, and in those that had an ischemic rather than a simple obstruction (Mair & Smith, 2005).

A multicenter retrospective study evaluated the outcomes associated with 43 horses undergoing resection and anastomosis of the descending colon (Prange et al., 2010). There was substantial variability in intra- and postoperative strategies used to manage these cases at the various institutions, making it difficult to identify factors associated with complications and survival. Nevertheless, lipoma was identified as the most common reason for descending colon incarceration and postoperative diarrhea as the most frequent complication. In that study, postoperative diarrhea occurred in 70% of cases, with only two affected horses culturing positive for *Salmonella* spp. Although many surgeons are concerned about the potential development of an impaction after resection and anastomosis of the descending colon, this complication was identified via rectal palpation in only five horses. In that study, 28 of 30 horses available for follow-up were alive 6 months after surgery.

Another more recent study in the United Kingdom evaluated postoperative outcomes for horses treated at a referral center for impactions, strangulating lipomas, and focal eosinophilic colitis. Resection and anastomosis was performed in 23 (27.4%) cases, 14 (60.9%) of which were due to a pedunculated lipoma (De Bont et al., 2012). In contrast to the earlier study (Prange et al., 2010), diarrhea occurred postoperatively in only 10% of the cases, none of which cultured positive for *Salmonella* spp. This finding potentially was due to the relatively low prevalence of salmonellosis in the United Kingdom. This study confirmed the overall positive outcome seen with horses treated surgically for descending colon disease. Short-term survival was, in fact, 91% for horses that recovered from anesthesia, with 90.4% of horses discharged from the hospital reported to be alive 1 year later (De Bont et al., 2012).

Obstructive Lesions

Obstructive diseases of the descending colon have been associated with specific breed, sex, and age predispositions (Dart et al., 1992b; Ruggles & Ross, 1991; McClure et al., 1992; Gay et al., 1979). According to retrospective studies, the Arabian, American Miniature horse, and pony breeds are prone to descending colon disease and the female gender appears to be overrepresented. The descending colon may be predisposed to obstructive disease owing to the nature of its function and location, but specific reasons for breed and gender predisposition are difficult to determine.

Descending Colon Impaction

Factors that may predispose to diffuse impaction of the descending colon include poor quality or inadequate ingestion of hay, poor dentition or inadequate mastication, decreased water intake, and lack of consistent exercise (Dart et al., 1992b, 1999; Keller & Horney, 1985).

Of the descending colon diseases, impaction is the most common condition requiring veterinary intervention and has been reported to be common in American Miniature horses (Ragle et al., 1992). Impaction seems to be more prevalent in the cold months of the year and may be associated with colonic dysfunction or parasitism (Ruggles & Ross, 1991). Feces obtained from horses with the condition, especially horses requiring surgical intervention, have a tendency to yield positive culture for *Salmonella* spp. Therefore, horses with the disease should be dealt with according to the appropriate infectious disease protocols (Ruggles & Ross, 1991).

Factors associated with descending colon impaction are listed in Table 55.1.

Horses with descending colon impactions are often evaluated for mild signs of colic associated with the voiding of a scant amount of loose feces. Rectal examination findings are helpful in the diagnostic process and in one study the condition was correctly diagnosed via transrectal palpation in 87% of cases. The presence of impacted fecal material in the descending colon may not allow thorough examination of the remainder of the abdomen and, in case of extensive impaction, the descending colon may be drawn over the pelvic brim into the caudoventral abdomen.

In one study, horses with descending colon impaction were compared with those with large colon impaction, as a "colic comparison group" (Frederico et al., 2006). No seasonal predisposition for descending colon impactions was identified, which differs from results of previous studies in which descending colon impaction occurred more often in the fall and winter (Dart et al., 1992b; Ruggles & Ross, 1991; Edwards, 1997). In the more recent study, diarrhea was more prevalent at the initial examination in horses with impactions of the descending colon than of the large colon (41 and 5%, respectively). Diarrhea may be a risk factor for development of descending colon impaction, as diarrhea was the only factor significantly more common in horses with descending colon impaction than in horses with large colon impaction. Descending colon impactions were confirmed by rectal palpation in 35 of the 44 horses (80%). In this study, surgical intervention was required more frequently than medical management alone (24% versus 4%), and the decision to perform surgery was based on the development of abdominal distention (Frederico et al., 2006). This study confirmed the overall positive outlook for horses requiring treatment for descending colon impactions as 21 of 23 horses (91%) treated medically and 20 of 21 horses (95%) treated surgically survived to discharge from the clinic (Frederico et al., 2006).

Table 55.1 Factors reported to be associated with small colon impaction (Ragle et al., 1992; Tennant, 1975; Huskamp, 1984; Dart et al., 1992b; Edwards, 1997; Ruggles & Ross, 1991).

Signalment	Possible etiology	Predisposing factors
American Miniature horse	Colon dysfunction	Fall and winter months
Shetland pony	Submucosal edema	Decreased water intake
Female		Poor dentition
Horses older than 15 years		Inadequate mastication
		Poor-quality roughage
		Parasitism
		Lack of regular exercise or turnout

Horses with descending colon impactions may be successfully treated with medical therapy that includes the judicious use of nonsteroidal anti-inflammatory drugs (NSAIDs) (flunixin meglumine at 1.1 or 0.5 mg/kg), intravenous fluid therapy, and oral rehydration therapy, including a balanced electrolyte solution, and fecal softening compounds such as magnesium sulfate or mineral oil. The medical treatment of horses with descending colon impaction may not be straightforward because affected horses often exhibit signs of abdominal discomfort during the course of therapy, which may be caused by the peristalsis of the bowel working to clear the impaction. In these cases, the clinician should carefully evaluate the use of analgesic medications, which may include the intravenous administration of 2% lidocaine at a loading dose of 1.3 mg/kg, followed by a constant-rate infusion at 0.05 mg/kg/min. Lidocaine has been shown to have an effect on gastrointestinal motility and may also provide analgesia by decreasing inflammation in the bowel through inhibition of prostaglandin synthesis (Nieto et al., 2000; Rimbäck et al., 1986, 1990).

Surgery may be necessary when horses do not respond to medical therapy and is accomplished via a ventral midline celiotomy. Following exposure of the impacted segment, the descending colon is gently massaged while an assistant performs an enema with lubricated warm water (J-Lube; Jorgensen Laboratories, Loveland, CO, USA) aimed at softening the impaction. A stomach tube is passed into the rectum and carefully guided to the impacted segment while the surgeon controls the progress of the tube via transmural palpation. In instances in which the descending colon is edematous and hyperemic or when there is concurrent rectal damage, it may be necessary to perform an enterotomy along the antimesenteric

band to evacuate impacted fecal material. The location of the enterotomy should be as close to the midpoint of the descending colon as possible because this section can be exteriorized away from the celiotomy incision to prevent inadvertent contamination of the abdomen.

The results of studies comparing medical and surgical treatments indicate that horses undergoing surgery tend to have longer hospitalization times and a tendency to yield postoperative fecal cultures positive for *Salmonella* spp. (Rhoads et al., 1999; Ruggles & Ross, 1991). Two studies reported a high success rate with medical treatment; in one of the studies, the long-term survival was significantly lower for horses treated surgically versus those treated medically (Ruggles & Ross, 1991), whereas in the other study the long-term survival was similar regardless of medical or surgical treatment (Rhoads et al., 1999).

The prognosis associated with medical management of descending colon impaction is favorable (approaching 100%), whereas the outcome of surgery may be complicated by the trauma induced during bowel manipulation and a relatively higher concentration of anaerobes found in the distal intestine. For these reasons, perioperative broad-spectrum antimicrobial therapy should include the use metronidazole as a preventive measure against anaerobic infection (Dart et al., 1992b; Edwards, 1997).

Focal Intraluminal Obstructions

The most frequent discrete obstructions of the descending colon are fecaliths, enteroliths, and ingested foreign bodies (McClure et al., 1992; Gay et al., 1979; Ragle et al., 1992; Blue, 1979; Boles & Kohn, 1977; Van Wuijckhuise-Sjouke, 1984; Yarbrough et al., 1994). Fecaliths are hardened masses of fecal material and result from poor mastication or digestion of hay. They are commonly diagnosed in yearling horses, particularly American Miniature horses, transitioning to a forage diet or in older horses with abnormal dentition. Similarly to other similar obstructive masses, phytobezoars and trichobezoars are formed from magnesium ammonium phosphate and contain poorly digested plant material or hair, respectively.

Enteroliths are a common cause of colonic obstruction in specific geographic areas, such as the west and southwest regions of the United States (see Chapter 54) (Hassel et al., 1999, 2001, 2004; Pierce, 2009; Feige et al., 2000; Maher et al., 2011; Kelleher et al., 2014). Smaller sized enteroliths are more likely to move through the large colon and commonly become lodged at the transition point between the transverse and descending colons. This area is particularly vulnerable to obstruction owing to narrowing of the bowel lumen that occurs at this location.

Although uncommon, foreign body obstruction of the descending colon has been reported to occur especially in younger, inquisitive-natured horses, which are prone to ingesting items such as rope halters, hay nets, and baling twine (Boles & Kohn, 1977). Over time, the irregular contour of these synthetic objects becomes encrusted with ingested fiber materials and minerals and can compromise the integrity of the bowel wall, increasing the likelihood of septic peritonitis.

The diagnosis of an isolated obstruction can occasionally be made by identifying the obstruction on transrectal palpation. More often, however, the clinician will suspect this type of lesion due to the signalment of the patient, the history, and the clinical signs. An example of a clinical picture that may lead to suspect fecalith obstruction would be that of a yearling American Miniature horse with colic-like symptoms, progressive abdominal distention, and lack of fecal output (Hughes et al., 2003). Abdominal radiography is a sensitive ancillary diagnostic test used to identify enteroliths in the large and descending colons (Hassel et al., 1999; Lloyd et al., 1987).

Medical treatment is unlikely to be successful in localized obstructions and the treatment of choice is an exploratory celiotomy aimed at the removal of the cause. The most successful approach is through an enterotomy placed along the mid-portion of the antimesenteric band of the descending colon. However, on occasion, the obstruction may be located in the oral or aboral portion of the intestine, hindering exteriorization of the mass. For orally located obstructions, the surgeon can attempt retropulsion of the mass into the right ventral colon and then proceed with removal via a pelvic flexure enterotomy (Edwards, 1997). In case of enterolith obstruction, the teniotomy technique described earlier may lead to safe removal, allowing further advancement of the obstructing concretion (Hassel & Yarbrough, 1998).

Vascular and Strangulating Lesions

Strangulation obstruction of the descending colon is an uncommon condition. However, the literature includes reports of several clinical cases in which the descending colon was either affected by mural vascular lesions or entrapped in a variety of tissues, including ovarian pedicle, teratomas, mesenteric rents, and the stalk of strangulating lipomas (Pearson & Waterman, 1986; Speirs et al., 1981; Evard et al., 1988; Parks et al., 1986; Rhoads & Parks, 1999; Edwards & Proudman, 1994; Dart et al., 1991b; Blikslager et al., 1992). Lipomas may be predisposed to form in the descending mesocolon because of the large amount of fat in that mesentery and are often encountered as incidental findings during celiotomy. Other than strangulating lipoma, polyps and leiomyomas have been associated with descending colon vascular compromise. In one horse a leiomyoma within the lumen of the descending colon had subsequently formed the lead point of an intussusception (Mair et al., 1992). Other lesions that rarely affect this segment of the bowel

include volvulus, herniation, and intussusception (Ross et al., 1988).

The clinical signs consistent with vascular and strangulating lesions are associated with an acute obstruction of the descending colon and lead to acute fecal stasis, progressive abdominal distention, and severe colic. Typical rectal examination findings include large colon tympany and difficulty in examining the entire abdomen owing to a sudden obstruction of the descending colon. The diagnosis of strangulating lesions may be aided by the use of transrectal ultrasound examination (Freeman et al., 2001). Compromised intestine leads to the development of toxemia, which increases heart and respiratory rates, causes progressive dehydration, and eventually cardiovascular derangement and shock. Key to the successful resolution of these conditions is prompt surgical intervention preceded by aggressive fluid therapy aimed at restoring intravascular volume and stabilizing blood pressure.

Mural Lesions

Submucosal hematomas have been speculated to occur as a result of parasitism (*Strongylus vulgaris* larvae) (Pearson & Waterman, 1986; Speirs et al., 1981). Submucosal hemorrhage can be extensive and leads to secondary obstruction because the hematoma interferes with the lumen of the descending colon. Importantly, descending colon hematomas may rupture the mucosal lining, causing obvious intraluminal hemorrhage (Speirs et al., 1981). This may be detected on the sleeve of the veterinarian after a rectal examination and should not be mistaken for bleeding associated with rectal tearing, a more typical cause of bleeding from the distal intestine after transrectal palpation. Treatment of choice for mural hematomas is surgery, which usually requires evacuation of the hematoma and resection and anastomosis of the affected descending colon segment. When the hematoma can be completely exteriorized, the procedure is usually successful, although this depends on the length of intestine involved and the location of the hematoma.

Lesions Associated with the Reproductive Tract and Pregnancy

Strangulation of the descending colon attributable to ovarian structures may be caused by an ovarian pedicle or entrapment of the colon between a granulosa cell tumor and the ovarian ligament (Wilson et al., 1989). Strangulation of the descending colon has also been reported to result from a testicular teratoma whereby the bowel was partially obstructed by the spermatic cord (Evard et al., 1988; Parks et al., 1986). Owing to straining that occurs during delivery, mares in the second stage of labor may incur severe abdominal trauma that may affect the viability of the descending colon either by compromising the bowel directly or by damaging the mesocolon and associated vasculature (Dart et al., 1991a; Booth et al., 2000). The present author has also seen two cases of uterine torsion complicated by concurrent entrapment of the descending colon in the twisted broad ligament. Foaling injuries that may compromise the descending colon are also associated with severe rectal prolapse (types II and IV), which causes rupture of the mesocolon, intussusception, and disruption of the arterial supply, leading to ischemic necrosis of the bowel (Edwards, 1997).

Surgical intervention is necessary in these cases and is often performed as a true exploratory celiotomy as, in most cases, a preoperative diagnosis is rarely obtained. Careful evaluation of intestinal viability during surgery is important when the vasculature is only partially compromised and the lesion has not caused a clear line of demarcation between viable and nonviable intestine. An additional complicating factor to consider pertains to the removal of damaged reproductive structures such as ovaries or masses, thereby requiring a modification of the initial celiotomy approach. In cases in which involvement of the female reproductive tract is suspected, the surgeon may elect to perform a laparoscopic evaluation of the caudal abdomen prior to selecting the most appropriate laparotomy approach.

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Equine Grass Sickness

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Introduction

Equine grass sickness (EGS, equine dysautonomia) is a dysautonomia/polyneuropathy affecting grazing Equidae (horses, ponies, donkeys, and exotic Equidae) with damage to neurons of the autonomic, enteric, and somatic nervous systems. The clinical signs are mostly attributable to damage to the autonomic and enteric nervous system, with disease severity varying depending on the extent of neuronal degeneration. Extensive neuronal degeneration is seen in the acute and subacute forms, resulting in severe intestinal dysmotility that is incompatible with survival. In contrast, some horses with less severe neuronal degeneration, as occurs in some chronic cases, may survive. First described in 1909, the disease occurs throughout the United Kingdom and many northern European countries, including Norway, Sweden, Denmark, France, Belgium, Switzerland, Austria, Hungary, the Netherlands, and Germany (Wylie & Proudman, 2009; Pirie et al., 2014). The disease has recently been diagnosed in a mule in the United States (Wright et al., 2010). Mal seco (dry sickness) is a similar condition that occurs in the Patagonia region of Argentina and in Chile and the Falkland Islands (Uzal & Robles, 1993; Araya et al., 2002).

Epidemiology

Equine grass sickness affects predominantly young horses with access to pasture in the springtime. Although the disease has been seen in most breeds, a recent study of cases in Scotland suggested an increased susceptibility of native Scottish breeds (Wylie et al., 2014).

All ages can be affected, but the highest incidence occurs among 2–7 year olds. Low circulating antibody levels for both *Clostridium botulinum* type C and *Clostridium novyi* type A surface antigens, and a *Clostridium botulinum* type C toxoid are associated with an increased risk of devloping EGS (McCarthy et al., 2004b). Individuals in good bodily condition may also be predisposed to developing the disease (Doxey et al., 1991a).

Although the disease can occur at any time of year, in the northern hemisphere, the highest incidence occurs in the spring and summer (April–July) (Doxey et al., 1991a; Wood et al., 1998). In the southern hemisphere, the highest incidence occurs in October–February. The disease has occasionally been reported in horses that have no access to pasture, but it usually affects grazing horses, and it often recurs on certain premises or pastures (Wood et al., 1998; McCarthy et al., 2004a). Premises-level risk factors associated with an increased risk of disease include previous occurrence of EGS on the premises (Wood et al., 1998; McCarthy et al., 2004a), increased soil nitrogen content (McCarthy et al., 2004a; Edwards et al., 2010), pasture disturbance (McCarthy et al., 2004a), and an increased number of horses on the pasture (Doxey et al., 1991a).

Recent movement to a new pasture or new premises has been shown to be a predisposing factor in several studies (Doxey et al., 1991a; Wood et al., 1998). Wood et al. (1998) reported horses to be at particular risk if they had changed pastures within the previous 2 weeks. Change of feed type or quantity during the 14 days prior to the onset of disease have also been identified as risk factors (McCarthy et al., 2004b). In one study, mechanical removal of feces from the pasture was identified as a potential risk factor (Newton et al., 2004). Occurrence of the disease has also been related to other stresses such as foaling, castration, or breaking-in. Cool (7–10 °C [46–50 °F]), dry weather tends to occur in the 10–14 days preceding outbreaks (Wood et al., 1998).

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Companion website: www.wiley.com/go/blikslager/abdomen

Pathogenesis and Pathology

The cause of EGS remains uncertain, although a natural neurotoxin, either ingested or produced within the gastrointestinal tract, is probably involved. The gross pathological features of the disease reflect the effects of dysautonomia and impaired gastrointestinal motility. Acute cases often have gastric and small intestinal distention with fluid, and reflux esophagitis (linear erosions of the mucosa of the distal esophagus), as a result of small intestinal dysmotility (Lyle & Pirie, 2009). Subacute cases frequently develop hard, corrugated impactions of the large colon, reflecting colonic dysmotility and dehydration of the intestinal contents. A characteristic black coating of the colonic contents is commonly seen (Milne, 1991; Lyle & Pirie, 2009) (Figure 56.1). Mucus-coated, hard, dry fecal balls are present in the small colon in subacute and chronic cases (Figure 56.2), reflecting the decreased feed intake due to anorexia and/or dysphagia (Milne, 1991; Lyle & Pirie, 2009), or possibly disease-associated cachexia (McGorum & Kirk, 2001). Chronic cases also often have bilateral rhinitis sicca (Figure 56.3), characterized by crusting or ulcerative lesions of the nasal mucosa (Milne, 1991; Lyle & Pirie, 2009).

Histopathologic abnormalities include degenerative neuronal changes involving the autonomic, enteric, central, and peripheral nervous systems (Barlow, 1969; Gilmour 1973; Scholes et al., 1993; Whitwell 1997; Cottrell et al., 1999; Hahn et al., 2001). Typical histopathologic findings include extensive chromatolysis, with loss of Nissl substance, eccentricity or pyknosis of the nuclei, neuronal swelling and vacuolation, accumulation of intracytoplasmic eosinophilic spheroids, and axonal dystrophy. The extent of the neuronal pathology within the enteric nervous system largely determines the severity of disease and, consequently, the prognosis for survival (Pirie et al., 2014).

Since EGS was first reported, a vast array of etiologic hypotheses have been proposed and addressed experimentally, yet to date, the definitive cause remains elusive (Pirie et al., 2014). Recently, a possible role of exotoxins produced within the intestinal tract by *Clostridium botulinum* type C has been implicated (Hunter & Poxton, 2001; McCarthy et al., 2004a, 2004b; Wylie & Proudman, 2009). As a soil-borne organism, many of the risk factors associated with EGS could theoretically support a role for *C. botulinum* in EGS (e.g., soil disturbance) (Pirie et al., 2014) and, recently, an increased body of experimental evidence demonstrating an association with *C. botulinum* C1 neurotoxin has been generated,

Figure 56.1 Black coating on the colonic ingesta in a case of subacute equine grass sickness (EGS).

Figure 56.2 Mucus-coated, hard, dry fecal balls from the rectum in a case of chronic equine grass sickness (EGS).

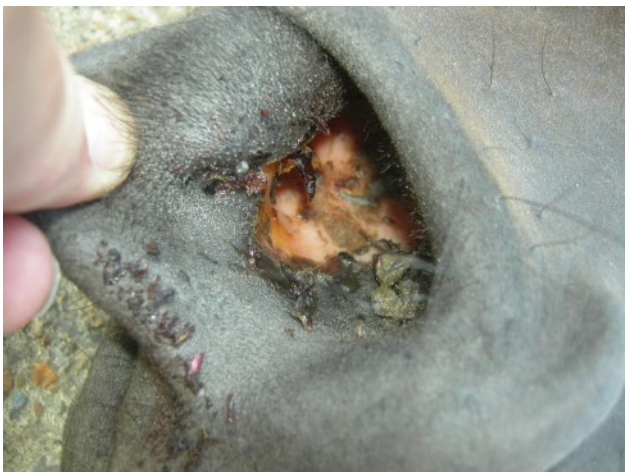

Figure 56.3 Rhinitis sicca in a case of chronic equine grass sickness (EGS).

initially via the significantly greater frequency of detection of *C. botulinum* C1 neurotoxin in the ileal contents and/or feces of EGS cases compared with healthy horses (Hunter et al., 1999; Poxton et al., 1997, 1999). However, a similar difference in detection frequency of *C. perfringens* between EGS cases and control horses, and an increase in the number of other clostridial species in EGS has also been reported (Garrett et al., 2002; Waggett et al., 2010b), thus potentially reflecting a generalized clostridial overgrowth in a dysfunctional bowel.

Clinical Signs

Three clinical forms of the disease are recognized (acute, subacute, and chronic), although there is considerable overlap between these groups. These three groups are traditionally distinguished from each other according to the duration of illness: acute 1–2 days, subacute 2–7 days, and chronic >7 days. The validity of this classification has been questioned, since the duration of illness is affected by factors other than the severity of the disease, such as treatments, supportive care, and elective euthanasia (Pirie et al., 2014). Clinical evidence suggests that the disease subcategory is predetermined at the time of disease onset, and therefore a more appropriate means of subclassification would be based on the nature and progression of clinical signs, both of which correlate with the extent of neuronal damage (Hahn et al., 2001; Pirie et al., 2014).

The clinical signs in all forms of EGS are largely reflective of dysfunction of the autonomic nervous system (including the enteric nervous system), together with somatic neuronal damage. All forms of EGS may demonstrate clinical signs of dullness, anorexia, dysphagia, and tachycardia (Hudson & Pirie, 2005; Lyle & Pirie, 2009; Wylie & Proudman, 2009), with the severity of these signs usually correlating with the subcategory of disease (Pirie et al., 2014). Ptosis (Figure 56.4), patchy sweating, and muscle fasciculations can also occur in all forms of EGS. Ptosis results from denervation of sympathetic axons innervating Müller's superior tarsal muscle, the smooth muscle underlying the levator palpebrae superioris, as opposed to somatic nerve dysfunction of the levator palpebrae superioris, or the levator angulis oculi medialis innervated by CN III and VII, respectively (Hahn & Mayhew, 2000a). The patchy sweating in EGS cases may result from denervation of sympathetic nerve fibers, either with subsequent chemical hypersensitivity of the sweat gland, as proposed in some forms of human dysautonomia (Bickel et al., 2004), and/or with vasodilatation and subsequent increased sudoriferous adrenaline arriving at the sweat glands. Additionally, the reported 10-fold increase in plasma adrenaline concentrations in EGS cases compared to control horses is also likely to cause generalized hyperhidrosis (Hodson et al., 1986).

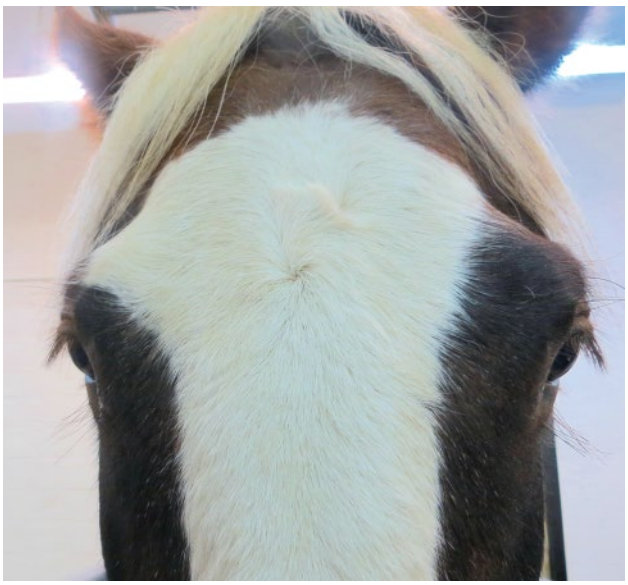

Figure 56.4 Bilateral ptosis in a case of chronic equine grass sickness (EGS).

Acute EGS

Typical clinical signs associated with acute EGS include the following:

- Depression and somnolence
- Inappetence
- Colic – mild to moderate pain
- Tachycardia (heart rate up to 100 beats/min)
- May be pyrexic (up to 40 °C [104 °F])
- May have bilateral ptosis (see Figure 56.4)
- Muscle fasciculations of the triceps and quadriceps muscle groups
- Sweating, generalized or localized to the flank, neck, and shoulder regions
- Dysphagia
- Drooling/dribbling of saliva
- Dehydration
- Small intestinal distention
- Gastric reflux – this may be spontaneous with nasal discharge of malodorous green or brown fluid
- Reduced or absent bowel sounds
- Abdominal distention.

Most patients with acute EGS die or require humane destruction within 2 days. The prognosis is hopeless.

Subacute EGS

The clinical signs of subacute EGS are similar to but less severe than those of acute cases. Signs include:

- Dysphagia
- Persistent tachycardia
- Patchy sweating on the flanks, neck, and shoulder
- Muscle tremors (triceps and quadriceps)

- Weight loss and development of marked "tucked-up" abdomen
- Ptosis (see Figure 56.4)
- Nasogastric reflux and episodes of colic possible.

Most patients with subacute EGS die or require humane destruction within 7 days. The prognosis is hopeless.

Chronic EGS

The clinical signs in the chronic form are insidious in onset. Survival of chronic grass sickness is possible in some appropriately selected and managed cases. Signs of chronic EGS include:

- Severe weight loss with the development of a "tucked-up" abdomen
- Base narrow stance and adoption of an "elephant on a tub" posture (Figure 56.5)
- Weakness and toe dragging
- Ptosis (see Figure 56.4)
- Persistent tachycardia (up to 60 beats/min)
- Muscle tremors
- Patchy sweating
- Mild colic
- Mild dysphagia and accumulation of food in the mouth
- Rhinitis sicca with accumulation of dry mucoid discharge around the nares (see Figure 56.3) and the presence of a distinctive "snuffling" sound during breathing.

There are a few anecdotal, but unconfirmed, reports of recurrence in horses that have survived after the chronic form. It is postulated that subclinical disease may also occur, but this is not well documented.

Diagnosis

Epidemiologic characteristics, signalment, clinical signs, and results of rectal examination allow a tentative diagnosis. The presence of persistent tachycardia not compatible with the degree of pain or circulatory compromise is a characteristic feature of most cases. Examination per rectum commonly reveals small intestinal distention in acute EGS, and firm and corrugated secondary large colon and cecal impactions in subacute EGS (Pirie et al., 2014). Dry, mucus-coated feces are frequently found in the rectum in subacute and chronic forms. Transabdominal ultrasonography can be helpful to identify small intestinal distention; localized contractile motility may be seen, attributable to the presence of nonpropulsive segmental contractions (Pirie et al., 2014). Confirmation of EGS can be made only by demonstrating histopathologic lesions in the autonomic or enteric ganglia at postmortem examination or by ileal biopsy at laparotomy. Hematologic and biochemical analyses are unrewarding, revealing nonspecific changes such as hemoconcentration and azotemia in acute and subacute forms (Doxey et al., 1991b). An increase in the acute phase proteins, including haptoglobin, orosomucoid, serum amyloid A, and fibrinogen have been reported (Milne et al., 1991; Copas et al., 2013), but these are also nonspecific findings.

Confirmation of the presence of smooth muscle paralysis causing bilateral ptosis in EGS can be achieved by observing its temporary reversal following topical administration of phenylephrine (Hahn & Mayhew, 2000b). Phenylephrine eye drops 0.5% cause a greater increase in the size of the palpebral fissure (as measured by the change

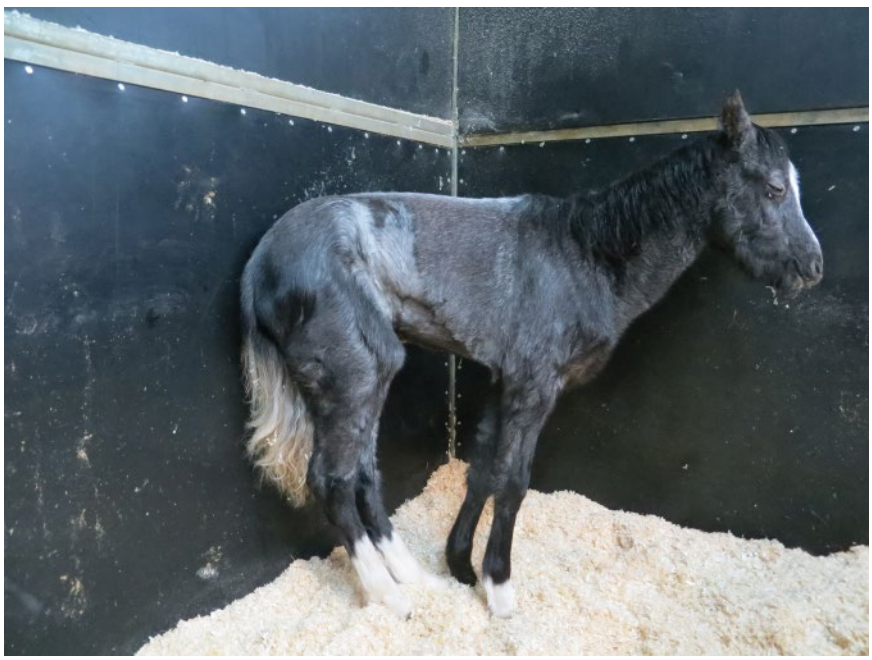

Figure 56.5 Base narrow, "elephant on a tub" stance in chronic equine grass sickness (EGS).

in the angle of the eyelashes with the head observed from a frontal view) than occurs in normal horses. This test should be performed in nonsedated horses.

Endoscopic examination of the distal esophagus of patients with acute EGS may reveal longitudinal linear ulceration of the mucosa. Esophageal dysmotility may also be appreciated endoscopically by observing retrgrade flow of fluid in the distal esophagus (Lyle & Pirie, 2009). Radiographic or fluoroscopic evaluation of esophageal dysmotility can also be identifed using a barium swallow (contrast esophography) (Greet & Whitwell, 1986). Electromyography can be used to demostrate evidence of skeletal muscle neuropathy in some EGS cases (Wijnberg et al., 2006).

Exploratory laparotomy and ileal biopsy may be needed to confirm the presence of EGS or to differentiate acute EGS from surgical diseases causing small intestinal obstruction (especially anterior enteritis, ileal impaction, and idiopathic focal eosinophilic enteritis). The ileum has the greatest neuronal loss in EGS, and therefore represents the optimal site for biopsy collection during exploratory laparotomy (Scholes et al., 1993). Histopathologic examination of formalin-fixed biopsies offer a 100% diagnostic sensitivity and specificity (Milne et al., 2010), but carry the disadvantage of a long processing time. Histopathologic examination of H&E-stained cryostat sections is associated with a faster processing time but only has a 95% sensitivity and 73% diagnostic specificity, a factor which could result in inappropriate euthanasia (Milne et al., 2010; Waggett et al., 2010a). The potential value of rectal biopsies in the diagnosis of the disease has been reported; this method was found to have a sensitivity of 71% and a specificity of 100% when two rectal biopsies were taken from 14 EGS cases and 10 control horses (Wales & Whitwell, 2006). However, the biopsies in that study were taken postmortem, and were not obtained using a standard biopsy instrument that would be utilized in the live horse. Since rectal mucosal biopsies are readily obtained from the horse (Traver & Thacker, 1979; Lindberg et al., 1996; Ricketts 1996), this technique could potentially offer a less invasive means of confirming the diagnosis of EGS in live animals without the necessity of performing an exploratory laparotomy to obtain ileal biopsies. However, subsequent assessment of the sensitivity of histopathologic examination of rectal biopsies obtained using a standard antemortem biopsy technique were disappointing (21%), owing primarily to the low density of neurons within the small samples that could be evaluated (Mair et al., 2011).

Treatment

The majority of cases of EGS do not survive. Acute and subacute EGS cases are invariably fatal and should be managed with humane destruction. However, supportive care in the form of intravenous fluid infusion, analgesic administration, and regular gastric decompression may be initiated until a more definitive diagnosis is achieved, at which point euthanasia should be recommended (Pirie et al., 2014).

Individuals with mild chronic disease may survive after prolonged treatment and nursing care; around 40% of chronic EGS cases survived in one study (Doxey et al., 1995a). Treatment should be considered in cases fulfilling the following criteria (Lyle & Pirie, 2009):

- Some ability to swallow food and water
- Some appetite present
- Some intestinal motility present
- Heart rate less than 60 beats/min
- Absence of moderate to severe colic signs.

Management of chronic EGS should include the following:

- General nursing care with frequent human contact, frequent grooming, and regular hand walking and grazing.
- Palatable high-energy, high-protein feeds offered 4–5 times a day. Grass, apples, and fresh vegetables should be offered. A variety of different compounded feeds and forages should be available (Doxey et al., 1995b).
- A deep, clean bed should be available to encourage the horse to lie down.
- Hand walking may help to stimulate appetite and intestinal motility.
- Cisapride 0.5–0.8 mg/kg PO q 8 h for 7 days may help intestinal motility; however, its efficacy is uncertain (Milne et al., 1996).
- Flunixin meglumine 0.5–1.1 mg/kg IV or phenylbutazone 2.2–4.4 mg/kg IV may be administered as necessary to control abdominal pain.
- Diazepam, 0.05 mg/kg IV q 2 h, can be administered as an appetite stimulant, although its efficacy is uncertain (Fintl & McGorum, 2002).
- Fecal output should be monitored, and enteral fluid therapy used if necessary to soften fecal consistency.
- Mineral oil may also be helpful to aid fecal transit.
- Probiotics may be helpful; their efficacy has not been evaluated.
- Antibiotics should be administered in cases with evidence of feed inhalation.

Continuous-flow enteral feeding has been used in selected cases, as have total and partial parenteral nutrition. Although there is currently insufficient evidence to suggest that such approaches will alter the ultimate outcome of the case, their use will reduce the rate of weight loss and may therefore extend the period of time available for a spontaneous improvement in appetite to occur (Pirie et al., 2014).

Although prediction of the duration of supportive care required or the success of outcome can be difficult (Doxey et al., 1999), in addition to the degree of dysphagia, appetite, and colic (cited earlier in relation to the selection of cases for treatment), the severity of rhinitis sicca has been shown to be greater in nonsurvivors (Milne et al., 1994).

Cases likely to survive generally gain weight in the first 5 weeks after diagnosis, with return to normal body weight taking an average of 9 months. A proportion of surviving horses retain residual signs including:

- Poor appetite
- Degrees of dysphagia
- Occasional colic
- Sweating
- Coat abnormalities – textural or color changes (Doxey et al., 1995a, 1998).

Histological examination of ileal samples obtained from successfully treated chronic EGS cases several years following the treatment period has revealed extensive neuronal loss, despite continued and relatively normal gastrointestinal function and motility (Doxey et al., 2000).

Prevention

Studies are currently evaluating the immunogenicity and safety of a recombinant protein-based type *C. botulinum* toxin vaccine.

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Rectal Tears

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Anatomy

The rectum extends from the pelvic inlet to the anus and is approximately 30 cm in length in the adult horse (Sisson, 1975). There is no apparent line of demarcation between the distal small colon and the proximal rectum and therefore the plane of the pelvic inlet is used as the division between these two structures (Sisson, 1975). The rectum can be divided into two segments: a cranial (peritoneal) segment, which is proximal to the peritoneal reflection, and a caudal (retroperitoneal) segment, which is caudal to the peritoneal reflection and forms a flask-shaped dilatation called the rectal ampulla. The peritoneal reflection has been estimated to be approximately 15–20 cm proximal to the anus in an adult 450 kg horse, but can vary considerably with age and the amount of body fat (Sisson, 1975; Schumacher, 2002). The peritoneal segment of the rectum is suspended by the mesorectum, a continuation of the mesocolon. As the rectum passes caudally into the retroperitoneal area of the pelvic canal, it is attached by connective tissue to surrounding structures (Sisson, 1975; Schumacher, 2002). The outer muscular layer of the ampulla has thick longitudinal muscle bundles (Arnold et al., 1978). The rectococcygeus muscle, which forms a large band on each side, originates from the longitudinal muscle and travels dorsocaudally, inserting onto the ventral surface of the fourth and fifth caudal vertebrae (Sisson, 1975).

Etiology and Prevention

The majority of rectal tears are iatrogenic, occurring during rectal palpation (Alexander & Gibson, 2002; Claes et al., 2008). Most rectal tears occur from pressure exerted by a contractile wave as it passes around the examiner's hand or from stretching of the rectal wall when attempting to palpate a structure (Baird et al., 1989; Arnold et al., 1978). Other reported causes of rectal tears include spontaneous rupture of the rectal wall, parturition, dystocia, breeding accidents, and trauma (Welland, 2003; Kay et al., 2008; Arnold et al., 1978; Schumacher, 2002; Slone et al., 1982; Guglick et al., 1996). In order to decrease the likelihood of rectal tears occurring during rectal palpation, the horse should be appropriately restrained, sedated, or otherwise medicated as/if needed, and the palpator should not advance their hand during a contractile wave, but should retract the hand as the contraction pushes it caudally.

Iatrogenic rectal tears were thought to occur more frequently in young horses (1–5 years old), stallions, and geldings who are not accustomed to rectal palpation (Stauffer, 1981; Arnold et al., 1978). Other studies, however, have shown that older horses (more than 7–9 years old) and mares are more likely to be affected (Watkins et al., 1989; Claes et al., 2008). Mares may appear to be overly affected simply because more mares are palpated per rectum than stallions or geldings for breeding purposes. Arabian horses and Miniature horses appear to be at an increased risk for rectal tears, with 20–42% of reported rectal tears occurring in Arabians (Watkins et al., 1989; Claes et al., 2008). The increased incidence of rectal tears in this breed may be due to their smaller size and/or fractious nature. Horses examined for abdominal pain may also be at an increased risk. Horses with colic often have firm feces, which may cause the rectal mucosa to be dry and friable. They are also often subjected to multiple rectal examinations, increasing the chances for repetitive trauma to the rectum. Copious lubrication, sedation, adequate restraint, and epidural anesthesia should minimize the occurrence of these iatrogenic rectal tears (Baird & Freeman, 1997). Stretching the rectal wall cranially when attempting to palpate abdominal structures should also be avoided. The palpator's hand

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should be carefully advanced cranial to the area of interest and then brought caudally, releasing tension on the bowel wall, when palpating intra-abdominal structures.

Iatrogenic rectal tears are an inherent danger during rectal palpations. Rectal tears appear to be as likely to be caused by experienced equine practitioners as by new graduates (Stauffer, 1981). It is likely that all equine practitioners will be involved directly or indirectly with a rectal tear. It has been suggested that explaining the risks and consequences of rectal tears to horse owners prior to palpation, although not required, may help avoid legal complications if a rectal tear occurs during palpation, assuming that the palpation was performed with proper technique and restraint. An information sheet that describes the risks and benefits of rectal palpation can be distributed to clients before examination of a horse, mailed with a new-client information packet, or used as a handout at colic or reproduction seminars (Blikslager & Mansmann, 1996). If the above precautions were made, the veterinarian should make no statements concerning admission of guilt or responsibility for payment. The veterinarian must contact the holder of their liability insurance policy promptly (Freeman, 2012).

Location and Classification of Rectal Tears

Rectal tears have been divided into grades I–IV predicated on the layers of the bowel wall involved (Table 57.1) (Baird & Freeman, 1997; Rick, 1989; Watkins et al., 1989; Arnold et al., 1978). Grade I tears involve only the mucosa and submucosa layers. Grade II tears involve only the muscular layers, with the mucosal and submucosal layers remaining intact. These result in a mucosal–submucosal hernia due to lack of support from the muscularis externa. Grade III tears involve the mucosa, submucosa, and muscularis. They are further subdivided into grade IIIa and IIIb rectal tears (Baird & Freeman, 1997). A grade IIIa tear involves all layers except the serosa. Grade IIIb tears involve all layers of the rectum but are in locations where there is no serosal covering (i.e., mesorectal attachment or in the retroperitoneal space). Grade IV tears involve all layers of the rectal wall and communicate with the peritoneal cavity.

Table 57.1 Rectal tear grades and descriptions.

Grade	Description
I	Mucosa and submucosa layers only
II	Muscularis only – intact mucosa and serosa
IIIa	All layers except serosa
IIIb	All layers but occur in locations where there is no serosa (i.e., mesorectal attachment or caudal to peritoneal reflection)
IV	All layers and communicate with abdominal cavity

Most grade I tears have been reported to occur ventrally or dorsally. Grade II tears are very rare (Claes et al., 2008). Most grade III and IV tears occur on the dorsal or dorsolateral aspect of the rectum parallel to the longitudinal axis of the rectum and between 5 and 55 cm (average 25–30 cm) proximal to the anus (Arnold et al., 1978). The dorsal wall of the rectum and distal small colon is characterized by a thickening of the longitudinal muscle forming the mesenteric tenia and a thinning of the circular muscle (Sisson, 1975). Blood vessels that travel in the mesocolon penetrate the muscularis externa on each side of the mesenteric tenia approximately one-fifth to one-quarter of the circumference from the mesenteric angle (Sisson, 1975). It is suggested that this is an area of inherent weakness in the bowel wall in humans (Gennaro & Rosemond, 1974). Additionally, the bowel lacks serosa dorsally between the two sheets of mesocolon attachment, further limiting its strength.

Tears involving the intraperitoneal part of the rectum or small colon are more serious than tears distal to the peritoneal reflection as they can lead directly to fecal contamination of the peritoneal cavity. However, fecal accumulation in the pelvic canal from tears distal to the peritoneal reflection can also lead to bacterial contamination of the abdomen (Freeman, 2012). Since the distance between the anus and the peritoneal reflection varies significantly between horses, it is difficult to determine if the tear is intraperitoneal based on the distance between the tear and the anus alone (Sisson, 1975).

Clinical Signs and Diagnosis

There is significant variation in whether or not the person who is performing the rectal palpation feels the tear when it occurs. In some cases, a release of pressure over the hand is felt when the tear occurs and abdominal organs can be directly palpated (Baird & Freeman, 1997). In other cases, however, the examiner is unable to appreciate the torn rectal wall (Baird & Freeman, 1997). In many cases, blood on the rectal sleeve or on the feces will be the first indication that a tear may have occurred. Although a blood-tinged sleeve may indicate mucosal damage only, any blood on the sleeve should be thoroughly investigated to determine the cause and extent of damage. In some cases, no blood is seen and clinical signs of depression, colic, anorexia, and fever are the first indication that a tear has occurred, or the tear is found at necropsy (Stewart & Robertson, 1990).

The speed of onset and progression of clinical signs depends on the severity of the tear. Horses with grade I

tears may never develop any clinical signs, especially if they are on a diet that maintains soft feces. Alternatively, horses with grade I tears may over several days begin to show signs of colic, becoming anorexic and depressed as the tear slowly progresses to a grade III or IV tear. Horses with grade III and IV tears develop clinical signs more rapidly. These horses may develop clinical signs associated with peritonitis and endotoxic shock such as fever, colic, sweating, and depression within several hours of the insult (Freeman, 2012).

Since the choice of treatment, and also the prognosis, are dependent on the type of rectal tear, an accurate classification of the tear should be made as soon as possible. The horse should be adequately restrained and sedated before examining the extent of the damage. A nose twitch should be used and preferably the horse should be placed in stocks if available. The horse should be sedated appropriately with combinations of α_2-agonists, including either xylazine (0.3–0.6 mg/kg IV) or detomidine (0.01 mg/kg), and possibly in combination with an opioid, including butorphanol tartrate (0.01–0.04 mg/kg IV). Efforts should be made to decrease rectal straining in order to facilitate examination of the tear and to prevent worsening of the tear as contractile waves pass over the examiners hand. This can be most effectively accomplished with epidural anesthesia (5–7 mL of local anesthetic including 2% lidocaine or 2% mepivacaine ± α_2-agonists). Other methods of reducing rectal straining include IV administration of the anticholinergic agent scopolamine butylbromide (Buscopan 0.3 mg/kg IV) and administration of parasympatholytic drugs (propanthelene bromide 0.014–0.07 mg/kg IV or atropine 0.044 mg/kg IM or SQ) (Schumacher, 2002). A lidocaine enema (12 mL of 2% lidocaine in 50 mL of water) may also help desensitize the rectum and aid in reducing rectal straining. Careful palpation with a bare hand covered with a water-soluble gel provides the most sensitive evaluation of the extent of the tear. A thin flap-like or undermined membrane is likely a mucosal–submucosal tear. A thick cavity-like depression lined by a thin membrane is most likely a grade III tear. Speculums and endoscopy have also been used to assist in the evaluation and visualization of the tear. Speculums may not be sufficiently long if the tear is proximal and the mucosal folds can obscure the view, preventing detection of the tear (Baird & Freeman, 1997). Endoscopy with air insufflation of the rectum can be helpful in evaluating the tear but is often not available to the referring veterinarian.

Rectal tears have been associated with as many as 13.4% of legal claims involving medical procedures in horses, but appear to have been declining in more recent years (Stauffer, 1981; Claes et al., 2008; Alexander & Gibson, 2002). Claims of negligence are probably more likely to occur because of poor management after the tear occurred rather than the creation of the tear (Freeman, 2012). It has been shown that early recognition and appropriate early intervention improve survival and therefore it is critically important that rectal tears are recognized early and treatment is initiated (Watkins et al., 1989). The owner should be informed of the potential problem as soon as a tear is suspected. The veterinarian should describe the steps they are taking to determine the extent of the tear and the importance of establishing an accurate diagnosis. Once the tear has been diagnosed and classified, the owner should be informed of the treatment options and associated complications. At this point, it is advantageous to call the referral hospital for advice on emergency treatment and transportation.

Emergency Management

Initial treatment is dependent on the severity of the tear. Grade I tears may be successfully managed medically with antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g., flunixin meglumine 1.1 mg/kg q 12 h IV), tetanus toxoid, and a laxative diet. Grade II tears usually do not present at the time of the tear. Rather, the horse presents later when the defect in the muscularis externa interferes with normal passage of feces, resulting in tenesmus and/or impaction. Grade III and IV tears require emergency management in the field to prevent further damage to the rectum leading to peritonitis, septic shock, and death. Emergency management of greater than grade 1 tears should consist of broad-spectrum antimicrobial therapy (e.g., potassium penicillin 22,000 IU/kg q 6 h IV, gentamicin 6.6 mg/kg q 24 h IV, and metronidazole 15 mg/kg q 6 h IV or PO). Flunixin meglumine (1.1 mg/kg q 12–24 h IV) is given for anti-inflammatory and antiendotoxin effects. All feed should be withheld.

Rectal packing with a "rectal tampon" is indicated to prevent feces from impacting in the tear and causing further contamination and expansion of the tear (Baird & Freeman, 1997; Taylor et al., 1987; Watkins et al., 1989). The packing is made from a doubled 3 inch stockinette filled with rolled cotton (Figure 57.1). The cotton should be moistened and the stockinette sprayed with dilute povidone-iodine and covered with lubricant prior to placement. After placement of the pack, more cotton may be added as needed to fill, but not distend, the rectum. It is imperative that the orad end of the tampon be positioned sufficiently proximal to the tear (approximately 10–20 cm) that the feces do not compress the tampon, exposing the tear to the feces. The tampon is maintained in place by closing the anus with towel clamps or with a purse-string suture. If a stockinette is not available, rolled gauze placed in accordion fashion can be used. The packing is placed after taking steps to prevent rectal straining (see above). Ideally, caudal

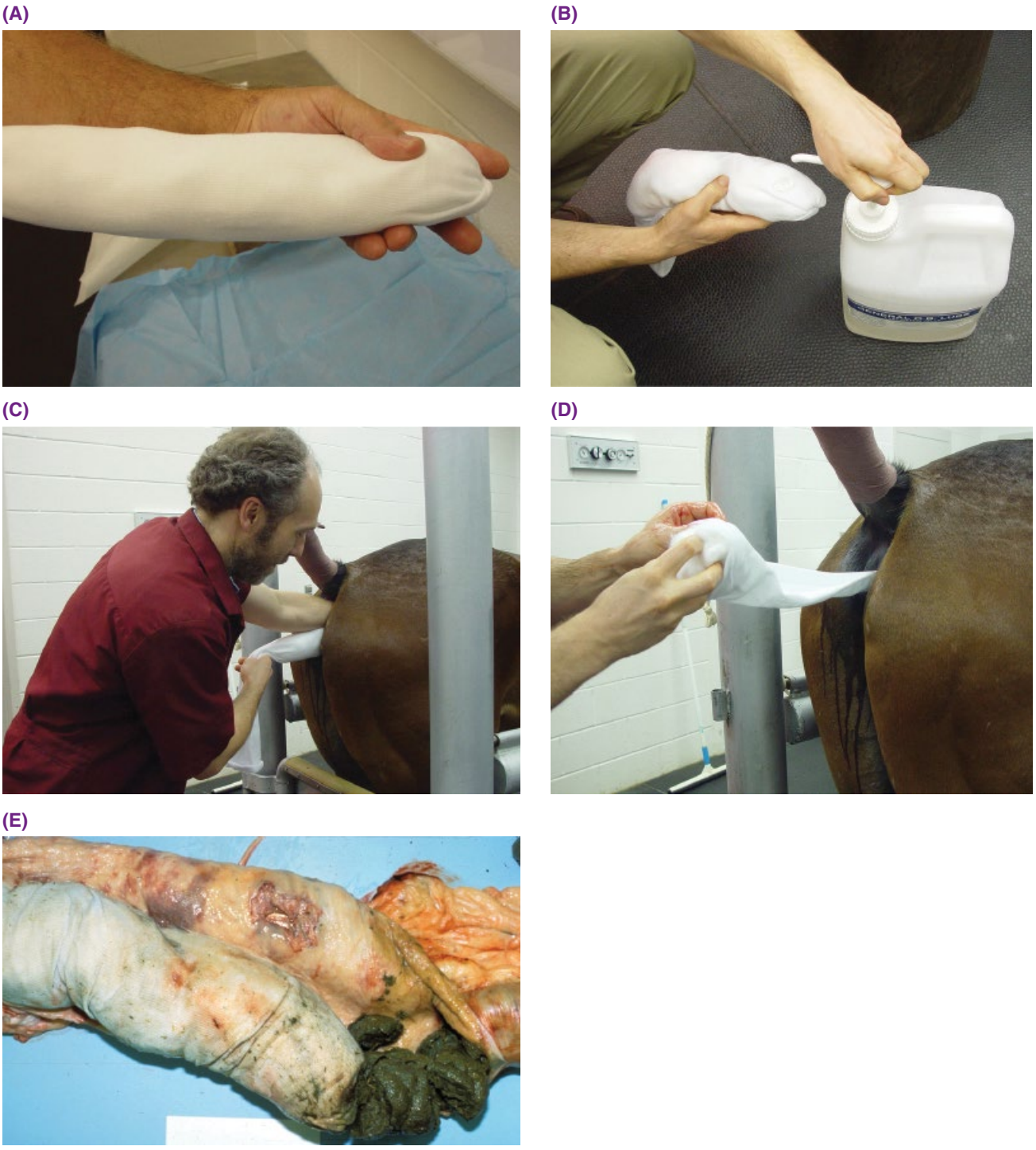

Figure 57.1 Rectal packing. **(A)** Three-inch stockinette loosely filled with cotton. **(B)** Stockinette is covered with lubrication. **(C)** Stockinette is inserted into the rectum with the proximal end positioned 10 cm cranial to the tear. **(D)** Additional cotton is added to the stockinette so that it fills the rectum. **(E)** Postmortem image depicting rectal packing appropriately positioned relative to the rectal defect with feces contained cranial to the packing.

epidural anesthesia is maintained to prevent straining until the definitive treatment is performed. Appropriate placement of the tampon will effectively prevent the feces from further damaging the tear. Inappropriate placement can potentiate further damage by diverting the feces into the tear. If effective rectal packing is not possible, one alternative strategy that has been suggested is to evacuate the rectum manually repeatedly. This can be especially helpful if the horse is more than 2 h away from the referral hospital (Katz & Ragle, 1999).

Medical Management

Grade I and II tears rarely require surgical treatment (Arnold et al., 1978; Baird & Freeman, 1997; Freeman, 2012; Rick, 1989). Grade I tears, involving only the mucosa or mucosa and submucosa, respond in most cases to antibiotics such as trimethoprim sulfonamide (20 mg/kg q 12 h PO), and flunixin meglumine (1.1 mg/kg q 12 h IV or PO), mineral oil (1 gal q 24 h via nasogastric tube), and dietary changes such as bran mashes, moistened pellets, or grass both to reduce the volume of feces and to keep the feces from becoming firm and impacting at the tear. Although some horses with grade I tears receive no form of treatment and heal uneventfully, it is recommended that if there is any undermining of the mucosa or if the tear is longer than 2 cm, medical management should be initiated (Eastman et al., 2000a). If all or a significant portion of the submucosa layer remains intact, grade I tears should heal with medical management without complications. However, if the tear extends significantly into the submucosa, the remaining submucosa and the underlying muscularis offer a relatively weak barrier to further tearing. In these cases, the tear has an increased risk to progress to a grade III or IV tear. Consequently, a critical factor in determining whether grade I tears heal with medical therapy alone is the extent of submucosal involvement. It can be difficult, however, to assess on palpation and visual inspection. If in doubt, grade I tears can be sutured per rectum. Suturing grade I tears after careful cleaning will speed healing. Whichever method of treatment is used, the clinical response should be monitored closely using physical examination, complete blood count, and serial peritoneal fluid analysis as needed. Grade II tears often present as an incidental finding. If the diverticulum or mucosal–submucosal hernia becomes large (>5 cm), these horses may present with tenesmus or with a rectal impaction (Arnold et al., 1978; Baird & Freeman, 1997; Eastman et al., 2000a, Schumacher, 2002). Medical management involves feeding a laxative diet to prevent impaction at the defect.

Although grade III tears usually require surgical intervention, there have been several reports of successful treatment with medical management alone (Katz & Ragle, 1999; Mair, 2000). In one case series of grade IIIb rectal tears, six of eight horses were treated successfully by administration of broad-spectrum antibiotics and NSAIDs, maintenance of soft feces with a diet of grass and bran mashes, and daily administration of liquid paraffin by nasogastric tube, along with daily manual removal of feces from the rectum after sedation and epidural anesthesia (Mair, 2000). All horses presented with or developed septic peritonitis during the course of treatment. Three of the six successfully treated cases developed a rectal diverticulum at the site of the tear without any obvious clinical problems. The successful outcome in 75% of these cases was attributed to early treatment, with the use of broad-spectrum antibiotics (penicillin, gentamicin, and metronidazole) until the tear filled in with granulation tissue and the peritoneal fluid returned to normal (between 2 and 7 weeks). The authors felt that manual evacuation of feces should be done only if the tear is felt to be impacted with feces, so as to avoid further trauma to the tear.

In another report of four cases of grade IIIb tears treated medically, the authors recommended frequent manual evacuation of feces in contrast to the above report (Katz & Ragle, 1999). Manual evacuation was performed every 1–2 h for the first 72 h, every 6–8 h by days 4 and 5, with decreasing frequency to once per day as the tear healed. This approach required maintenance of caudal epidural anesthesia initially, which was subsequently replaced with lidocaine and lubricant enemas. All four horses had tears less than 10 cm in diameter. Manual evacuation was discontinued after between 9 and 21 days. All four horses were treated successfully by this approach. These results suggest that in certain cases with early initiation of treatment, manual evacuation and medical therapy may be a viable alternative to surgical treatment grade IIIb rectal tears (Katz & Ragle, 1999).

Horses with full-thickness tears into the retroperitoneal space may be treated in a similar manner with manual evacuation of feces, antimicrobial therapy, and stool softener (Mazan, 1997; Schumacher, 1999). In these cases, the tear is into connective tissue, which allows the tear to be packed with gauze soaked in antiseptic solution until the defect fills with granulation tissue. Perirectal abscesses that may result from the fecal contamination can be drained into the rectum or perianally. Rectal tears in mares that subsequently develop abscesses can be drained perivaginally with or without ultrasound guidance (Delesalle et al., 2009). In some cases, abscesses may dissect into the tissue layers of the inner thigh. Ventral drainage, broad-spectrum antimicrobials, and NSAIDs are indicated.

Surgical Management

The techniques described for surgical treatment of rectal tears are colostomy, temporary rectal liner, direct suturing, and stapling (Blikslager et al., 1995; Freeman et al., 1992; Taylor et al., 1987; Eastman et al., 2000a, 2000b, Kay et al., 2008; Stewart & Robertson, 1990). Each of these techniques can be used individually as the primary surgical repair. Both colostomy and temporary rectal liner techniques may be combined with direct suturing to decrease the stress at the suture repair (Eastman et al. 2000; Watkins et al., 1989). Another surgical approach is to evacuate the large colon and small colon through enterotomies and withhold feed for 5–7 days postoperatively,

allowing the tear to develop a good bed of granulation tissue before starting the horse on a low-residue diet. In most cases, the evacuation of the gastrointestinal tract is combined with some other surgical procedure that specifically addresses the tear.

Temporary Indwelling Rectal Liner

In this procedure, a rectal ring with attached rectal liner is sutured to the distal small colon proximal to the tear and functions to provide temporary protection of the tear from fecal contamination during the healing process (Baird & Freeman, 1997; Freeman, 2012; Taylor et al., 1987). The ring for the temporary rectal liner is made from a 5 × 10 cm plastic rectal prolapse ring that is trimmed at each end to form a 5 × 7 cm ring. Holes are then drilled 1.5 cm apart in one edge of the central groove and #5 Dacron suture material is laced through the holes to form a continuous anchor suture. The liner can be constructed from either a rectal sleeve or plastic cover from an arthroscopic camera sutured and glued to the ring.

To implant the rectal liner, a ventral midline celiotomy is made with the horse in dorsal recumbency. Although it is possible to implant the liner in the standing horse, it is considerably more difficult to evacuate the colon, potentially increasing the risk of postoperative feed impaction at the liner. At surgery, a nonsterile assistant introduces the well-lubricated rectal ring and attached sleeve into the anus and with the intra-abdominal assistance of the surgeon carefully manipulates the ring orad until it is positioned cranial to the tear but far enough caudal that the sleeve does not retract into the rectum when the horse stands (Baird & Freeman, 1997; Freeman, 2012; Taylor et al., 1987). A circumferential ligature of #3 chromic gut is placed around the small colon over the central groove in the ring. The suture is placed tightly enough to compress the tissue adequately to prevent fecal material from passing under the suture. Four to six retention sutures [#2-0 poly(glycolic acid)] are placed equidistant around the small colon to include the circumferential suture, all layers of the intestinal wall, and the anchor suture in the rectal ring. The retention sutures and the circumferential suture are oversewn with a Lembert pattern. This ensures that the continuity of the intestinal tract is maintained when the ring and circumferential ligature slough 9–12 days after surgery. In order to reduce the volume of feces passing through the area in the immediate postoperative period, the large colon is emptied through a pelvic flexure enterotomy and the small colon is carefully emptied by flushing with a hose directed through the ring and liner from the anus. In most cases, drain tubes are placed for peritoneal lavage (Baird & Freeman, 1997; Taylor et al., 1987).

Postoperative care includes continuation of broad-spectrum antibiotics, NSAIDs, and peritoneal lavage. The healing of the rectal tear is evaluated by careful digital palpation every 48–72 h. A reduced volume of soft feces should be maintained by feeding a pelleted ration and administering mineral oil by nasogastric tube until the ring and liner detach and pass through the anus. Obstructions at the ring should be removed by retrograde flushing under epidural anesthesia. To prevent retraction of the sleeve into the rectum, the horse may need to be cross-tied to prevent it from lying down. Approximately 60% of horses treated for grade III tears were reported to heal using this technique (Taylor et al., 1987). Failures were due to serosal necrosis leading to peritonitis, tearing of the sleeve, retraction of the sleeve uncovering the tear, and formation of a rectoperitoneal fistula. Direct suturing of the tear in conjunction with the temporary rectal liner is recommended in order to prevent serosal necrosis leading to peritonitis (Taylor et al., 1987; Watkins et al., 1989). The reduction in size and prevention of lesion expansion may aid in healing and reduce the potential of a grade III rectal tear converting to a grade IV tear. A temporary rectal liner will be unsuccessful if used as the sole treatment for tears involving >25% of the circumference of the rectum (Watkins et al., 1989).

Loop Colostomy

The goals of colostomy treatment for rectal tears are first to divert feces to allow the tear to heal and then to restore normal anatomic function. Therefore, colostomy techniques require two surgeries, the first to construct the colostomy and the second to reverse the colostomy after the rectal tear has healed. Both end and loop colostomy techniques have been described in horses (Blikslager et al., 1995; Freeman et al., 1992; McIlwraith et al., 1998). The end colostomy is performed by transecting the colon proximal to the tear and using this proximal end to form the colostomy stoma while the distal segment is oversewn and remains in the abdomen. The loop colostomy involves bringing an intact loop of small colon out of the flank and making a longitudinal enterotomy in the loop to construct the stoma. The end colostomy has several disadvantages compared with the loop colostomy. First, it is more difficult to construct since the colon has to be transected. Second, during the time it takes for the rectal tear to heal, the distal blind end of the colon atrophies. This makes the colostomy reversal more difficult owing to the discrepancy in size of the proximal and distal ends. Additionally, the atrophied distal segment may predispose to impaction at the anastomosis. Atrophy of the small colon distal to the colostomy occurs to a lesser extent with the loop colostomy. Concerns that the loop colostomy results in incomplete diversion of feces are

not warranted since the correct construction of the stoma allows gravity to produce complete fecal diversion (Baird & Freeman, 1997; Blikslager et al., 1995; Freeman et al., 1992). For these reasons, only loop colostomy techniques will be described.

The techniques used for constructing the loop colostomy vary depending on where the incisions are made, how many incisions are used, where the stoma is placed, and whether the procedure is performed in the standing or anesthetized horse (Baird & Freeman, 1997; Freeman, 2012). If the rectal tear occurred during a colic examination, the surgeon needs to consider whether abdominal exploration is warranted to diagnose and treat the colic further. In this case, general anesthesia with a ventral midline incision allows the best chance to explore the abdomen and surgically correct the colic. The colostomy is then constructed by placing the horse in lateral recumbency and making the stoma in the left flank, or recovering the horse and performing the colostomy in the standing horse. If the rectal tear occurred during a reproduction examination or during some other incident not requiring an abdominal exploration, the colostomy can be performed in the standing horse, through either a single or double flank incision, which avoids the costs and risks of general anesthesia.

Single-incision Loop Colostomy

In this procedure, the stoma is incorporated in the closure of a single flank incision. There are two variations of this procedure (Baird & Freeman, 1997; Freeman et al., 1992). In one technique, a 12–15 cm incision is made parallel with the costal arch (Freeman, 2012; Freeman et al., 1992). The incision is made sharply through the external abdominal oblique fascia and continued bluntly through the aponeurosis of the internal abdominal oblique, the aponeurosis of the transversus abdominal oblique, and the peritoneum. The small colon at least 1 m proximal to the peritoneal reflection is exteriorized through this incision. This distance is important because a significant number of adhesions may form between the body wall and the small colon during the healing process, necessitating a larger than anticipated segment of small colon to be resected during the reversal surgery. If the colostomy is placed too far distally, it becomes difficult to exteriorize sufficient distal small colon for resection and anastomosis during the colostomy reversal. Once the segment of small colon has been exteriorized, it is folded to form a loop. The two arms of the loop are sutured together for approximately 8 cm using absorbable suture in a continuous Lembert pattern (Freeman, 2012; Freeman et al., 1992). The sutures are placed half the distance from the mesentery to the antimesenteric tenia. As the suture line approaches the folded end of the loop, the suture line is placed closer to the mesentery so that the antimesenteric tenia is exposed (Figure 57.2). Suturing the two arms in this configuration facilitates the complete diversion of the feces at the colostomy stoma and also stabilizes the two arms of the colon, reducing the chances of herniation at the stoma. The prepared loop is then positioned so that the proximal segment is at the cranioventral aspect of the incision and the distal loop is more dorsal and caudal. The loop is exteriorized such that approximately 2–3 cm of the loop extends beyond the skin margins. The seromuscular layer of the small colon is sutured to the muscles of the body wall in an interrupted pattern with absorbable sutures. The dorsal part of the body wall incision is closed up to the loop, leaving approximately 6–8 cm of the cranioventral aspect of the incision to construct the stoma. A 6–7 cm enterotomy is made in the antimesenteric tenia and the edges of the enterotomy are sutured to the skin (Figure 57.3). A single-incision loop colostomy can be difficult to perform in the standing horse because a relatively long incision is made at the level of the fold of the flank. Therefore, general anesthesia is often used. With the two-incision colostomy, the longer incision is made in a more dorsal location, making it simpler to perform in the standing horse.

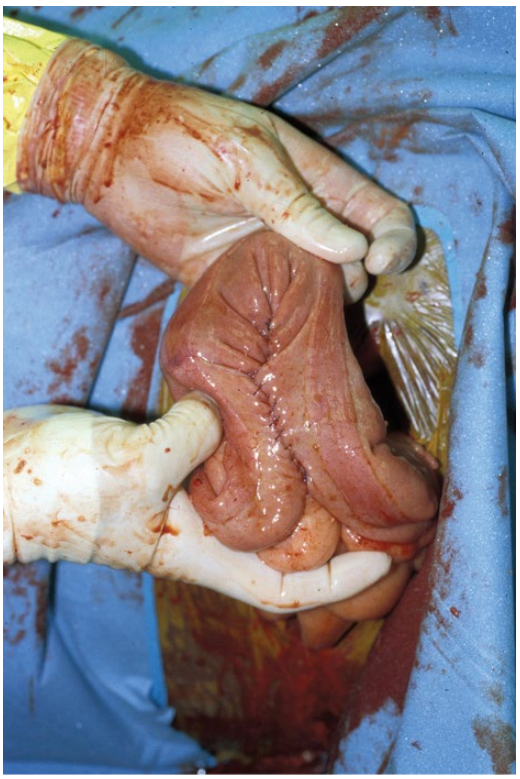

Figure 57.2 Two arms of the loop of small colon that has been prepared for a loop colostomy through a flank incision. Note how the suture line is placed to closer to the mesentery at the end of the loop to expose the antimesenteric tenia for the colostomy stoma.

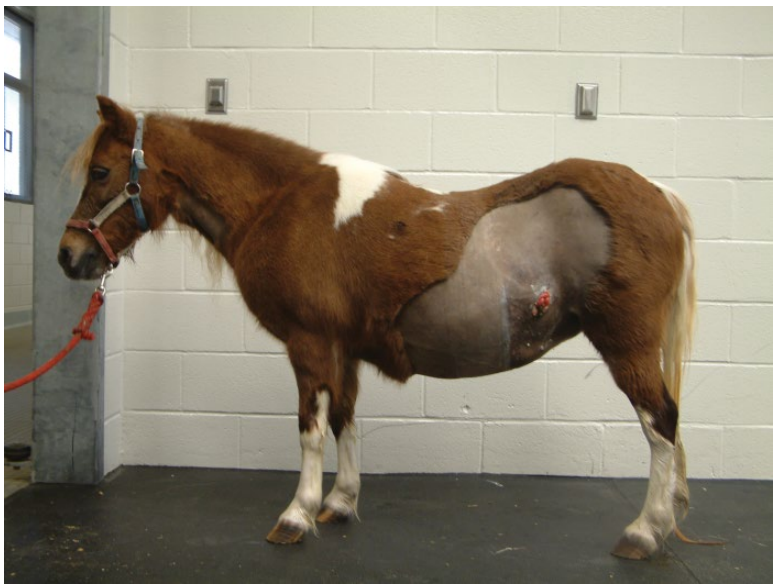

Figure 57.3 Horse with a loop colostomy constructed under general anesthesia via ventral midline laparotomy and stoma created via a single flank incision.

A variation of the described single-incision colostomy technique has been reported (Blikslager et al., 1995). In this technique, the incision is positioned midway between the level of the tuber coxae and the level of the coxofemoral joint and not centered at the level of the fold of the flank. The subcutaneous tissue and external abdominal oblique musculature are transected sharply. The internal abdominal oblique and transverse abdominal muscles are bluntly separated parallel to their muscle fibers. A loop of small colon is exteriorized in the middle of its accessible length. The authors did not suture the two arms of the small colon loop together; rather, the seromuscular layer of the small colon was sutured to the external abdominal oblique and/or to the subcutaneous tissue (Blikslager et al., 1995). An 8–10 cm antimesenteric incision was made to create the stoma and the edges were sutured to the skin. The incision in this technique is in a more dorsal position than the single incision in the fold of the flank; consequently, this colostomy technique can be performed in the standing horse.

Standing Double-incision Loop Colostomy

The first incision is made to construct the loop in the small colon that will be used for the colostomy (Freeman, 2012; Freeman et al., 1992). Under sedation and local anesthesia, a 15 cm incision is made in the left flank starting about 8–12 cm below the tuber coxae. The small colon is identified and a section that is at least 1 m proximal to the peritoneal reflection is exteriorized. The small colon loop is prepared as described previously. A second 6–8 cm incision angled dorsally 20–30° at its caudal end is made for the stoma placement at the level of the flank fold of the stifle midway between the fold and the costal arch (Figure 57.3). The incision is made through all layers, making sure to incise any potentially constricting tissue. If the incision is too small, it will constrict the proximal loop of small colon predisposing to impaction proximal to the colostomy stoma. If it is too large, it will increase the risk of prolapse or herniation of small colon. The prepared small colon loop is brought out of the lower incision aided by manipulation of the loop with the surgeon's arm in the high flank incision. Approximately 3 cm of the loop should extend beyond the skin margins with the proximal arm of the loop positioned at the cranioventral aspect and the caudal arm positioned in the more dorsal and caudal aspect of the incision (as described earlier). Interrupted absorbable sutures are placed between the seromuscular layer of the small colon and the muscle and fascia of the body wall. These sutures are important to anchor the colon loop to the body wall and to provide a seal to prevent potential peritoneal contamination that may occur from ingesta leakage between the skin and colostomy closure. A 6–8 cm incision is made through the antimesenteric tenia into the lumen of the small colon. The edges of the colostomy incision are sutured to the skin with simple interrupted nonabsorbable sutures (Freeman, 2012; Freeman et al., 1992).

Colostomy/Ventral Midline Celiotomy

In horses in which the rectal tear occurred during a colic evaluation, a ventral midline celiotomy may be required for abdominal exploration and treatment of the gastrointestinal problem. A ventral midline celiotomy also allows the large colon to be evacuated, reducing the amount of feces having to pass out of the colostomy in the immediate postsurgical period and also allows more aggressive and effective lavage of the abdomen if needed because of abdominal contamination secondary to the rectal tear.

If colostomy has been chosen as the technique to treat the tear, the loop for the colostomy should be constructed though the ventral midline incision. This will allow the colostomy incision for the stoma to be kept small. The ventral midline incision should then be closed and the stoma constructed through a small incision in the low flank as described in the two-incision technique with the horse repositioned in right lateral recumbency or constructed in the standing horse after recovery from anesthesia. Stoma construction with the horse in dorsal recumbency may lead to obstruction of the stoma as the tissue layers change when the horse recovers (Freeman, 2012; Freeman et al., 1992). Placing the horse in lateral recumbency decreases the amount of the tissue layers shifting in the body wall when it recovers, decreasing the risk of obstruction of the stoma postoperatively.

Postoperative Management

Horses are maintained on a laxative and low-bulk diet of bran mash and moistened pellets with increasing amounts of grass if available and/or alfalfa hay once the colostomy appears to be working effectively (Baird & Freeman, 1997; Freeman, 2012; Freeman et al., 1992). Antibiotics and NSAIDs are continued as necessary to treat peritonitis and any postoperative incisional infections. Placement of a drain for peritoneal lavage is predicated on the clinical condition of the horse and peritoneal fluid evaluation. Petroleum jelly is placed under the colostomy stoma to prevent scalding. Normograde flushing of the colon distal to the colostomy is recommended in order to limit atrophy of the distal segment. Flushing should be initiated only after the tear has become lined with a good granulation tissue bed, approximately 5–7 days after the colostomy (Baird & Freeman, 1997; Freeman, 2012; Freeman et al., 1992).

Colostomy Reversal

Once the tear has filled in with granulation tissue and has epithelial tissue covering the defect, the colostomy can be reversed. Times reported for reversal have been from 13 to 68 days (Freeman, 2012; Freeman et al., 1992; Blikslager et al., 1995; Eastman et al., 2000a). If the horse has been on a grass and alfalfa hay diet, it should be switched to a low-bulk diet for 3–4 days prior to surgery. Feed should be withheld for at least 24 h prior to surgery. The horse is placed on broad-spectrum antibiotics (penicillin, gentamicin, and metronidazole) and NSAIDs. The surgery is performed under general anesthesia with the horse in right lateral recumbency. To minimize contamination, the stoma is first closed using an inverting horizontal mattress pattern in the skin. An elliptical skin incision is then made around the closed stoma to allow for an "en bloc" resection (Blikslager et al., 1995; Freeman et al., 1992). One group recommends making the elliptical skin incision 1 cm from the edge of the colostomy and then inverting the skin margin over the colostomy (Blikslager et al., 1995). Careful sharp and blunt dissection is required to separate the loop of small colon and stoma from the surrounding body wall. The dissection is made difficult due to significant adhesions of body wall to small colon around the colostomy. Once the stoma and adjacent small colon are completely separated from the body wall, the stomal segment and adjacent small colon with severed adhesions are resected. The distal segment of the small colon will be smaller in diameter than the proximal segment owing to atrophy. To correct for this size disparity, the distal segment is transected at a more acute angle than the proximal segment. A two-layer, hand-sutured, end-to-end anastomosis is preferred (Hanson et al., 1988). The first layer is a simple continuous pattern that is oversewn with a Cushing pattern. The muscle and fascial layers of the flank incision are closed with a simple continuous pattern. The closure of the body wall is unavoidably under considerable tension owing to the amount of body wall and attached adhesions removed during the "en bloc" resection. Placement of Penrose drains has been recommended because incisional problems are not uncommon (Freeman, 2012; Freeman et al., 1992). The skin is closed with simple interrupted sutures with periodic placement of vertical mattress sutures if necessary to relieve tension. A stent is sutured over the incision. Postoperatively, the horse is maintained on antibiotics and NSAIDs for approximately 5 days. They are converted from the laxative diet to a normal diet very slowly, over a period of 3–4 weeks.

Complications and Prognosis of Colostomy

Peristomal herniation and small colon prolapse through the stoma are two reported complications following colostomy (Freeman, 2012; Freeman et al., 1992). Increasing the size of the stoma may increase the risk of small colon prolapse. For this reason, the stoma should be made with an opening no larger than the diameter of the colon proximal to the stoma (Baird & Freeman, 1997; Freeman, 2012; Freeman et al., 1992). The longer incision required for the single-incision colostomy may be associated with greater laxity in the peristomal body wall compared with the double-incision colostomy. For these reasons, the double-incision colostomy has been recommended over the single-incision colostomy by some surgeons (Baird & Freeman, 1997; Freeman, 2012; Freeman et al., 1992).

Impaction proximal to the stoma is another reported complication of colostomy (Baird & Freeman, 1997; Freeman, 2012; Freeman et al., 1992; Blikslager et al., 1995). Making the stoma too small or leaving constricting

bands of tissue in the body wall around the stoma may increase the risk of impaction at the stoma. Placing the stoma too high on the flank may also predispose to impaction. These should be treated by carefully breaking down the impaction digitally or with the aid of gentle lavage. Placing the horse on a laxative diet should decrease the occurrence of impactions. Partial dehiscence of the colostomy with mechanical separation of the colon and skin closure during recovery from general anesthesia is another reported complication. The dehiscence should either be treated by primary closure or be allowed to heal by second intention. Performing the colostomy in the standing horse avoids this problem. Incisional infection with abscessation and/or partial dehiscence is seen after colostomy and colostomy reversal (Blikslager et al., 1995; Freeman et al., 1992). Abscesses should be drained and partial dehiscence left to heal by second intention. Impaction after colostomy reversal should be treated with fluid therapy and laxatives and may require surgical intervention, highlighting the need for maintenance of a low-residue, laxative diet. Other complications reported are rupture of mesenteric vessels, spontaneous closure, adhesions, and laminitis.

Two of six horses having colostomies to treat grade III rectal tears survived in one report and five of seven horses survived in another report (Freeman et al., 1992; Blikslager et al., 1995). The majority of deaths in horses where colostomies have been performed to treat rectal tears have been attributed to the peritoneal contamination associated with the rectal tear, with technical difficulties less commonly implicated (Blikslager et al., 1995; Freeman et al., 1992; Watkins et al., 1989). For this reason, it is important that adequate first aid be administered to protect the tear and that the colostomy is performed as soon as possible in order to divert feces and prevent further damage and fecal contamination of the tear.

Primary Repair

Several techniques for primary repair have been described. Instrumentation specifically developed to facilitate visualization and access for suturing tears per rectum, such as a long, expandable speculum and pistol-grip needle holders, has been used successfully to repair rectal tears (Freeman, 2012). However, repairing rectal tears with the aid of these instruments is difficult and the instrumentation is not available at most facilities. Primary repair of grade IV rectal tears has been accomplished by intussuscepting the damaged segment through the anus using traction sutures placed in the tissue around the tear and stapling the tear in the standing horse (Stewart et al., 2014; Kay et al., 2008). An important point to note with this technique is that it is possible only in caudally located grade IV tears. Grade IV tears result in loss of negative pressure in the abdomen and therefore facilitate intussusception of the distal small colon. This technique can also be performed in anesthetized horses placed in lateral recumbency. Exteriorizing the damaged portion of the rectum can be facilitated by transecting the anal sphincter with either technique (Embertson et al., 1986). Intussuscepting the damaged segment through the anus by intra-abdominal manipulation through a ventral midline celiotomy has also been described (Wilson & Stone, 1990). In most cases, the tear is too far cranial to the anus and the mesocolon too short to allow exposure of the tear by these techniques. Laparoscopic techniques with sutured or stapled repair of iatrogenic tears have been described in an experimental model and clinical case (Brugmans & Deegen, 2001; Stewart et al., 2014). Tears into the dorsal mesentery would be difficult to repair with the laparoscope because mesentery would prevent access to the tear. Laparoscopic repair of rectal tears has not been evaluated in clinical cases.

Nonvisual Direct Suturing Per Rectum

An alternative technique using nonvisual direct suturing has been described in several reports with encouraging results (Eastman et al., 2000a, 2000b; Watkins et al., 1989). In this technique, the patient is restrained in the standing stocks. Caudal epidural anesthesia is administered and rectal packing, if present, is removed. Caudal epidural anesthesia is critically important as this results in anal relaxation and development of a pneumorectum, which in turn increases space for the surgeon to work in the rectum. Tying the tail in a dorsal position with the anal sphincter relaxed from the caudal epidural will aid in development of a pneumorectum. There may be some mechanical advantage in suturing tears on the left side with the right hand and tears on the right side with the left hand, but configuration and surgeon comfort will dictate this decision (Eastman et al., 2000a, 2000b). Fecal material is digitally removed from the rectum and distal colon. Careful cleaning of the defect is important prior to suture closure. Moistened 4 × 4 inch gauze sponges are used to remove manure from the lumen walls. If the tear is not full thickness, gentle gravity lavage should be used to assist in cleaning the tear. If the tear is grade IV, assessment of the degree and duration of peritoneal contamination will aid in determining whether a repair should be attempted. Assessment of the tear by video endoscopy and/or digital palpation is more informative than speculum evaluation (Figure 57.4). Digital assessment and repair are performed without gloves to improve tactile sensation.

For surgical repair, #5 Dacron on a 6–8 cm, half-circle cutting or trocar point needle in a cruciate or simple interrupted pattern is recommended. The suture length for each suture placed is 100–150 cm, with the needle placed in the middle of the suture. This suture is selected

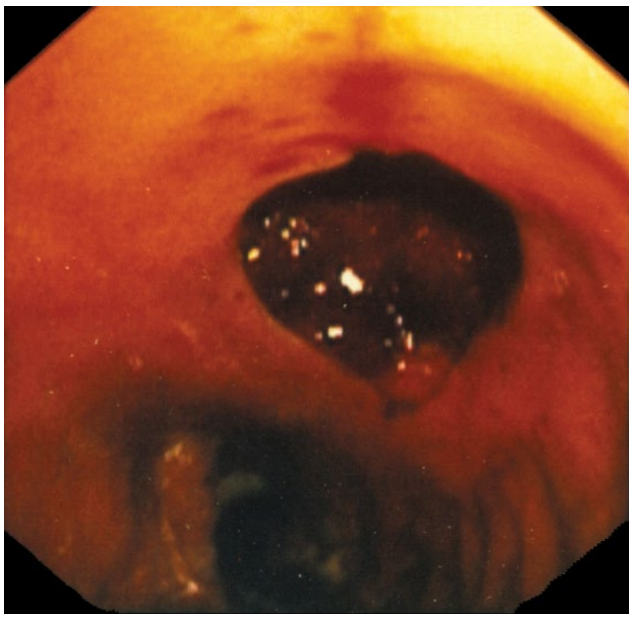

Figure 57.4 Video endoscopy of a grade IIIb rectal tear.

because it is large enough to feel easily when digitally placing and can be cut into long lengths. With both ends of the suture held outside the rectum, the digitally shielded needle is advanced manually to the tear. The first bite is positioned in the center of the caudal border of the tear, holding the needle with the thumb and first two fingers. The needle is inserted approximately 1.5 cm from the edge of the wound and guided to the center of the defect subserosally by the second and third fingers (Figure 57.5A). The needle is pulled through this tissue and again grasped with the thumb and first two fingers. Next, the needle is placed in the center of the proximal edge with the bite beginning subserosally within the defect and guided to exit 1.5 cm from the defect's edge. It is helpful to use the third finger to press the tissue onto the needle (Figure 57.5B). The needle is then withdrawn from the cranial aspect of the defect and brought out of the rectum. One side of the doubled suture is pulled through, leaving a simple interrupted strand suture in place with its distal end extending 10–15 cm distal to the anal sphincter. The distal end of the suture is clamped on the needle side with a hemostat, leaving the needle threaded on the proximal half of the suture. The clamped suture is held in place to one side by an assistant and the needle is moved near the opposite end of the suture strand and carried into the rectum. Applying traction on the placed suture will aid in closing the defect in a transverse plane. For the next bite, the suture is passed through both cranial and caudal edges of the defect without repositioning the hold on the needle if possible. The needle is grasped in the same manner as before and the third finger is placed within the defect to provide

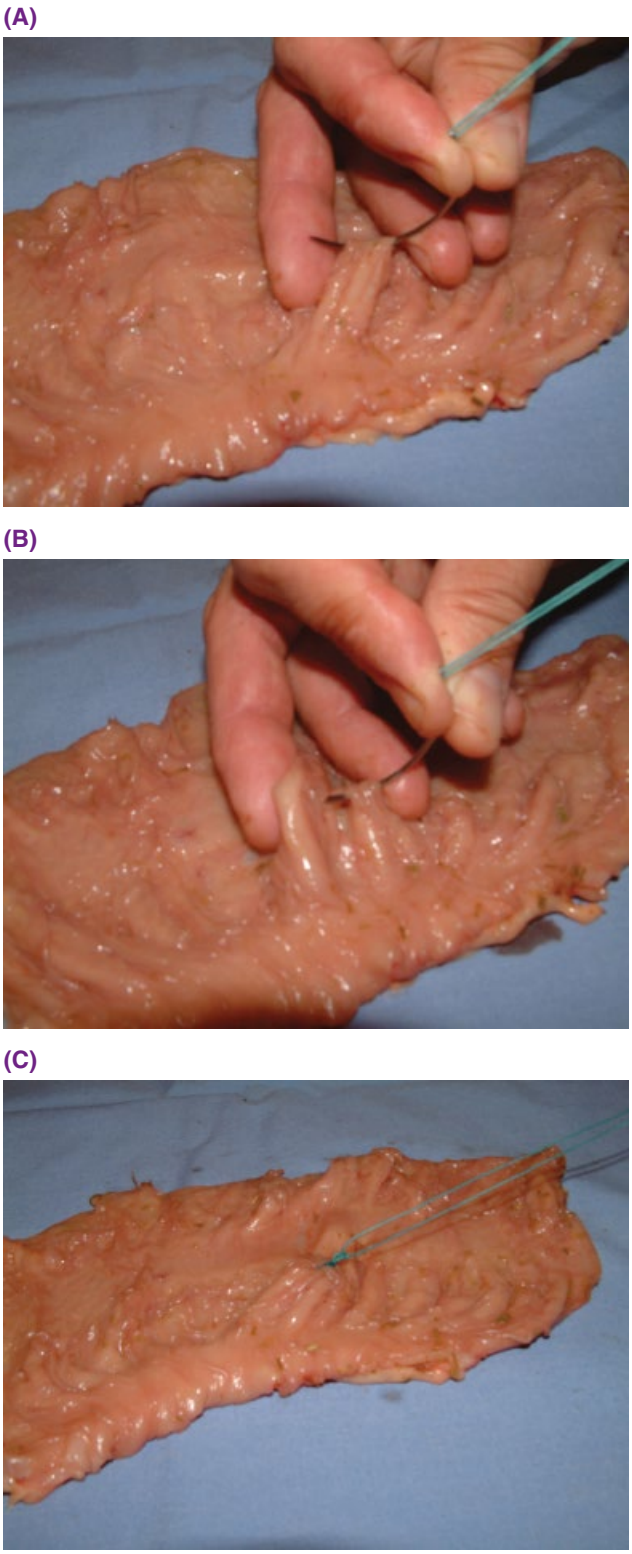

Figure 57.5 Nonvisual direct suturing technique. (A) The needle is inserted 1.5 cm from the wound edge and guided to the center of the defect subserosally by using the second and third fingers. (B) The second bite is started subserosally in the defect and exits 1.5 cm cranial to the defect edge holding the needle with the thumb and first two fingers. (C) The suture is tied by forming the knots outside the rectum and pushing them down tight with one hand in the rectum and one hand outside.

guidance of the needle from the caudal edge into the defect and then positioned to press the tissue over the point of the needle as it travels out of the cranial edge of the defect. The needle is then brought out of the rectum. Releasing the previously placed hemostat and pulling the needle end of the suture through will form the cruciate suture. The knots are tied outside the rectum, pushing them inside with one hand while maintaining pressure on the suture with the other hand (Figure 57.5C). The ends of the sutures are left intact to retract the tissue for additional knot placement (Figure 57.6). Additional sutures are placed working from the cranial portion of the defect caudally. In this way, as the rectal lumen decreases in diameter with each suture placement, the surgeon is placing subsequent sutures in areas that have not been previously narrowed. After all sutures have been placed (usually two to six), the ends are cut with tags that are long enough to aid in identification and facilitate their removal (Eastman et al., 2000b).

The horse is maintained on IV fluids and a therapeutic course of broad-spectrum antibiotics for a duration predicated on clinical and laboratory parameters. Placement of an abdominal lavage tube is determined by peritoneal fluid analysis and clinical status. The horse should be maintained on a low-bulk diet. The suture line is checked at 24–48 h intervals. If defects are felt either from loosening sutures or reduction of edema, additional sutures should be placed. The sutures are removed after 12–14 days.

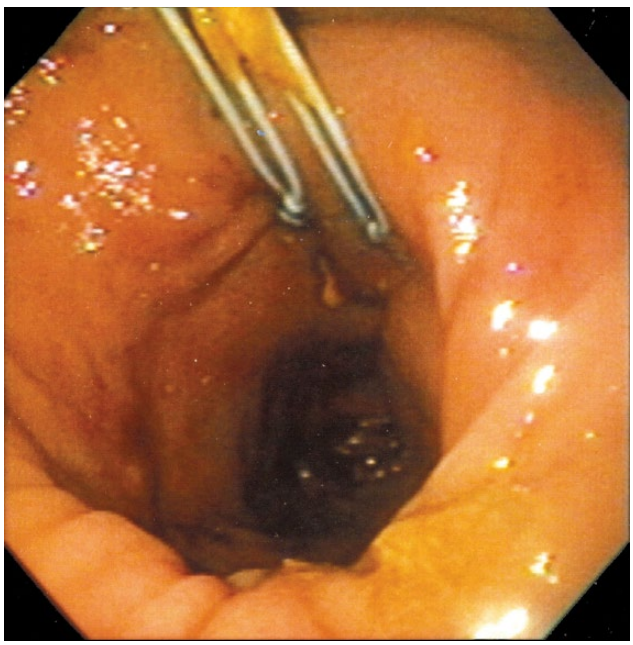

Figure 57.6 Direct suturing of a grade IIIb tear, leaving the ends of the suture long to facilitate caudal retraction of the tissue to ease completion of the suture line.

Ventral Midline Exposure and Antimesenteric Enterotomy for Suture Repair

It has been reported that tears more than 25 cm proximal to the anus may be amenable to primary closure through a ventral midline celiotomy (Freeman, 2012). In mares, the ventral midline incision can extend between the mammary glands, improving access to the tear. In geldings and stallions, a paramedian incision is necessary for caudal extension. Elevating the hindquarters may also improve surgical exposure to the tear (i.e., a Trendelenburg-like position) (Brosnan et al., 2008). If the tear is lateral or ventral, direct access for suture repair of the tear within the peritoneal cavity is possible. A glass speculum inserted in the rectum and positioned under the tear may facilitate visualization of the tear for suture placement. Placing an arm in the rectum to move the bowel segment with the tear cranial and ventral may also improve visualization (David et al., 1997). If the tear is dorsal into the mesocolon, it can be approached through an antimesenteric enterotomy (Wilson & Stone, 1990). A ventral midline incision is made as far caudally as possible. Balfour retractors are placed to facilitate caudal retraction of the body wall. The caudal portion of the small colon is exteriorized and the tear is palpated within the abdomen. If the tear is dorsal, it can be felt within the mesocolon. Traction on the small colon will bring the tear closer to the incision, but in most cases the segment of affected bowel will remain in the abdomen. Laparotomy sponges are used to pack off the surgical area, and a Penrose drain is placed to occlude the proximal small colon. An antimesenteric incision is made as close to the level of the tear as possible. The surgeon will have to decide if the enterotomy can be made far enough caudally to provide sufficient access for surgical repair of the tear. Stay sutures are placed to retract the incised edges of the bowel. Feces from the enterotomy site to the tear are removed. Deaver retractors are inserted into the bowel in a caudal direction to facilitate visualization of the tear (Wilson & Stone, 1990). The tear should be meticulously cleaned, removing any feces within the tear and from within the dorsal mesocolon (Figure 57.7). The tear is then closed in a simple continuous pattern, including the mucosa, submucosa, and muscularis using #2-0 absorbable suture. The antimesenteric enterotomy is closed routinely. Evacuation of the large colon should be performed to decrease fecal flow through the repair. Complications reported with this technique involve infection in the dorsal mesocolon leading to dorsal abscess formation. If this occurs, ventral drainage into the lumen of the bowel once the abscess is walled should be established (Wilson & Stone, 1990).

Prognosis and Recommendations

The prognosis for horses with rectal tears depends on the severity of the tear, the degree of fecal contamination

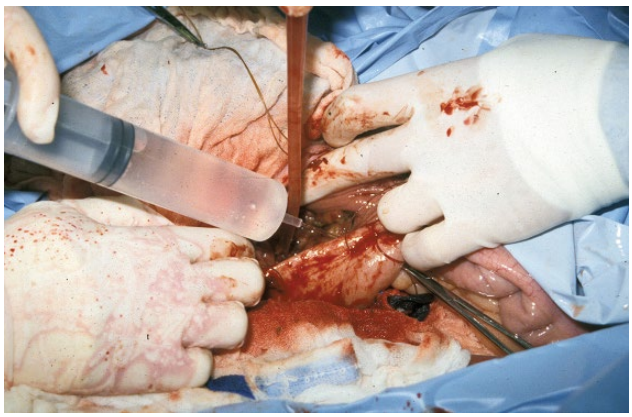

Figure 57.7 Antimesenteric enterotomy, via ventral midline incision, for primary closure of a grade IIIb tear. The space into the dorsal mesentery is meticulously cleaned prior to suturing the tear.

of the tear (strongly influenced by first aid administered), the techniques used to treat the tear, and most likely the experience and skill of the surgeon performing the repair. Most retrospective studies on rectal tears report on the outcome of a specific type of treatment for a relatively small number of cases (Blikslager et al., 1995; Freeman et al., 1992; Katz & Ragle, 1999; Mair, 2000; Mazan, 1997; Stewart & Robertson, 1990; Stewart et al., 2014; Kay et al., 2008; Taylor et al., 1987; Wilson & Stone, 1990). From those reports, recommendations have been made regarding treatment and outcome specific for that repair technique. These have been referred to in the earlier discussions of the individual treatment techniques. Owing to the small number of cases, their ability to predict prognosis accurately is somewhat limited.

There are several reports looking at the outcome of larger groups of horses treated by several different methods (Eastman et al. 2000a, Watkins et al., 1989; Claes et al., 2008). These have provided some general recommendations about treatment, permitted comparisons of different individual or combined treatment techniques, and allowed predictions to be made concerning prognosis. In one report evaluating multiple techniques used to treat 35 horses with grade III or IV rectal tears, several observations were made (Watkins et al., 1989). With regard to prognosis, in general, appropriate first aid appears to be critically important regardless of the exact nature of the tear (Watkins et al., 1989). Most horses with grade I tears do well when managed as discussed earlier (Eastman et al. 2000a, Watkins et al., 1989; Claes et al., 2008). Grade II tears are very rare but tend to do well and can even be an incidental finding. The prognosis decreases greatly as the grade of tear increases to grade III and IV regardless of how these horses are managed. Horses with grade III tears have a reported short-term survival of 38–64% (Claes et al., 2008; Watkins et al., 1989). Horses with grade IV tears have an even poorer short-term survival, with reported rates of 0–2% in these larger retrospective studies (Watkins et al., 1989; Claes et al., 2008). Deciding on which technique or combinations of techniques to use or euthanasia is determined by multiple factors such as the time elapsed since the injury occurred, the degree of contamination, surgeon experience with various techniques, and size and location of the tear. Direct suturing appears to be associated with the best prognosis and is the treatment of choice at our hospital, but may not be the best choice based on other surgeons' experience. If the direct suturing cannot be performed, the surgeon has minimal comfort with this technique, or the tear is sutured but the surgeon feels the repair is weak, then the recommendation is a standing two-incision loop colostomy with or without ventral midline celiotomy if indicated because of abdominal contamination or concurrent colic.

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58

Malabsorption Syndromes

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Malabsorption syndrome commonly refers to the group of diseases with impairment of digestive and/or absorptive processes arising from structural or functional disorders of the small intestinal tract and its associated organs (including the pancreas, liver, and biliary tract) (Roberts, 1985; Rogers & Madanick, 2005). These diseases can affect the absorption of carbohydrates, proteins, fats, vitamins, minerals, and, to a lesser extent, water and electrolytes (Roberts, 1998). Infiltrative bowel diseases, that is, diseases in which the mucosa and submucosa are infiltrated by abnormal cells – usually inflammatory or neoplastic cells – are the most common cause of malabsorption (Roberts, 1998; Schumacher, 2003; Mair et al., 2006). In the adult horse, such diseases that are confined to the small intestine usually result in chronic weight loss, whereas chronic diseases affecting the large intestine result in diarrhea and protein-losing enteropathy (Roberts, 1983, 1998). However, small intestinal diseases may result in secondary large intestinal dysfunction as a result of the abnormal amounts of carbohydrates, fats, and amino acids entering the large bowel from the ileum. In addition, many of the chronic infiltrative diseases that result in small intestinal malabsorption can affect the large bowel concurrently, causing malabsorption of volatile fatty acids, water, and vitamin K in the hind gut. Thus, in clinical cases, both small intestinal and large intestinal malfunction often occur simultaneously (Roberts, 1983, 1985, 1998). In people and small animals, disturbances in digestive processes (i.e., maldigestion), especially from exocrine pancreatic insufficiency or reduced intestinal bile salt concentration, are common causes of maldigestion and malabsorption. The rarity of pancreatic dysfunction and the herbivorous diet of the horse mean that maldigestion is less important and more difficult to diagnose. However, maldigestion almost certainly contributes to the chronic weight loss that occurs in horses with malabsorption syndromes associated with diseases that cause mucosal villous atrophy in the small intestine (Roberts, 1998).

The primary clinical sign associated with malabsorption syndromes in adult horses is chronic weight loss. If the disease process is limited to the small intestine, weight loss may be the only clinical sign, and it becomes important to eliminate other causes of weight loss. Although malabsorption syndromes affect the digestion and absorption of carbohydrates, protein, and fat, diagnostic tests in the horse usually concentrate on dysfunction of carbohydrate digestion/absorption. Inadequate fat absorption is of limited importance in the horse, although malabsorption of fat-soluble vitamins may result in dermatitis, neurologic diseases, and retinal dysfunction. Increased protein loss from the intestine (protein-losing enteropathy) is more commonly associated with large intestinal disease because of the larger surface area of the equine large intestine; however, concurrent small intestinal malabsorption and significant protein-losing enteropathy are likely to cause severe and rapid weight loss. Apart from weight loss, other clinical signs that may be identified in horses with infiltrative bowel diseases include colic, lethargy, diarrhea, and dependent edema (Scott et al., 1999; Mair et al., 2006) (Figure 58.1). Malabsorption syndromes may also predispose to other conditions, such as equine motor neuron disease.

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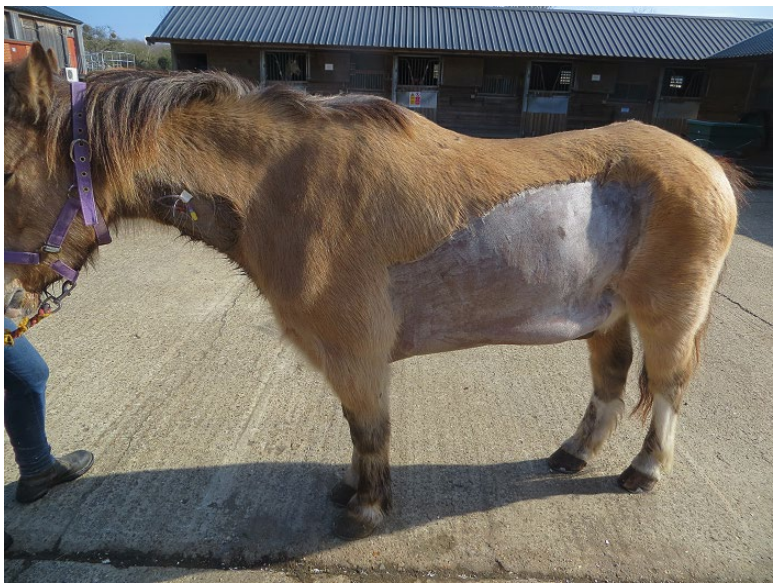

Figure 58.1 Extensive ventral edema in a pony affected by malabsorption syndrome.

Causes of Malabsorption Syndrome

The important causes of malabsorption syndrome in the horse include the following:

- extensive small intestinal resection
- chronic inflammatory bowel diseases
  - granulomatous enteritis
  - idiopathic eosinophilic enterocolitis
  - multisystemic eosinophilic epitheliotrophic disease
  - lymphocytic/plasmacytic enterocolitis
  - intestinal fibrosis
- alimentary lymphoma
- amyloidosis (Hayden et al., 1988)
- enteric infections
  - *Lawsonia intracellularis* (very rare in adults)*
  - mycobacterial infection
  - *Rhodococcus equi* (very rare in adults)*
  - enteric fungal infections
- idiopathic villous atrophy
- immune-mediated (gluten enteropathy)
- congestive heart failure
- portal vein thrombosis
- intestinal ischemia
- parasitism.

* Reported in a 26-month-old Thoroughbred with coinfection (Shimizu et al., 2010).

Extensive Small Intestinal Resection

Insufficient absorptive area is a common cause of small intestinal malabsorption. This can be caused by extensive/excessive small intestinal resection after surgery for small intestinal strangulations ("short bowel syndrome"). The greater the amount of small intestine resected, the greater is the risk of malabsorption of carbohydrates, lipids, and minerals. Removal of small sections of small intestine has no untoward long-term effects, but extensive resections may result in the horse becoming a "digestive cripple." Horses affected by short bowel syndrome develop weight loss and show poor performance.

Other problems that have sometimes been observed after extensive small intestine resection in horses and ponies include anorexia and liver disease (Tate et al.,1983; Spurlock & Spurlock, 1989). The precise amount of small intestine that can safely be removed is still a matter of conjecture and appears to vary from horse to horse. Although the remaining bowel is probably capable of compensation, there is a limit to the length of intestine needed for this to occur. One study suggested that no more than 60% of the small intestine could be safely resected (Tate et al., 1983), but other studies suggest that up to 70% can be removed without causing subsequent malabsorption (Haven et al., 1997). At the time of surgery, it should be recognized that strangulated small intestine can increase in length by up to 25% (Freeman, 1997), and this factor must be taken into consideration when assessing the amount of bowel that can safely be removed.

Chronic Inflammatory Bowel Disease

Chronic inflammatory bowel disease is the collective term for a group of infiltrative bowel diseases that produce similar clinical signs (primarily chronic weight loss) (Schumacher, 2003; Kalck, 2009). These diseases are not as well defined in the horse as they are in other species, and their etiology is generally unknown. The small and the large intestines, the regional lymph nodes (Figure 58.2), and, sometimes, other abdominal organs may be involved. The cellular infiltrate may consist of a

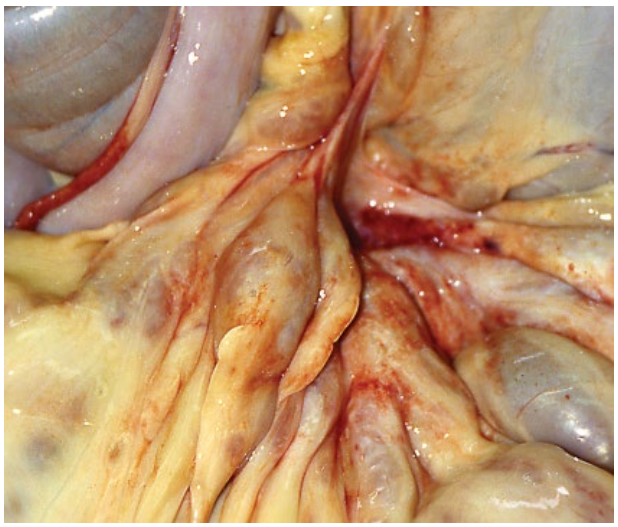

Figure 58.2 Gross postmortem appearance of enlarged mesenteric lymph nodes in a horse affected by chronic inflammatory bowel disease.

mixed cellular population or there may be a predominance of a specific cell type such that chronic inflammatory bowel disease may be classified into a number of different disease types. Although the signalment, clinical signs, clinopathologic findings, and gross pathologic changes can sometimes be characteristic for one type of disease, in most cases differentiation between these diseases requires histopathologic examination of the affected portion of intestine (Table 58.1).

Granulomatous Enteritis

Granulomatous enteritis is characterized by diffuse granulomatous lesions, predominantly in the small intestine, with lymphoid and macrophage infiltration of the lamina propria, and variable numbers of plasma cells and giant cells (Meuten et al., 1978). Villous atrophy is marked (Figure 58.3, Figure 58.4, and Figure 58.5) and lesions attributable to other forms of granulomatous change (such as mycobacterial and fungal infections) are absent. No etiologic agent has been identified in granulomatous enteritis, although it has been proposed that the disease may result from an abnormal host inflammatory reaction to intestinal bacteria or dietary components. The lesions associated with this condition have similarities to those of Johne disease in cattle and Crohn disease in people. *Mycobacterium paratuberculosis* has been implicated as a possible causative factor in the development of Crohn disease in humans, and experimental infection of horses with this organism results in microscopic granulomatous lesions similar to those identified in patients with Crohn disease. However, acid-fast organisms are rarely identified in Ziehl–Nielson-stained sections of tissue from affected horses. Structural changes of the epithelial surface in granulomatous enteritis range in severity from a slight thickening and shortening of villi to the appearance of a virtually flat mucosa, upon which crypts open directly or through shallow cavities encircled by collars of epithelial cells. Between these extremes, the mucosa shows a variety of patterns, all characterized by distinctly abnormal villus projections. Enterocytes display a flattened surface epithelium with ultrastructural abnormalities, including pronounced shortening of microvilli (Lindberg & Karlsson, 1985).

Granulomatous enteritis can occur at any age and in any breed or either sex, although it appears to be most common in young adult horses (1–5 years of age) (Merritt et al., 1976; Johnson & Goetz, 1993). It has also been most commonly reported in Standardbreds. A familial predisposition to the disease has been suggested; one report documented the occurrence of the condition in three sibling Standardbred horses (Sweeney et al., 1986). A possible association between granulomatous enteritis and exposure to aluminum has also been described (Fogarty et al., 1999). Affected horses usually present with signs of chronic and progressive weight loss and anorexia. Skin lesions, especially around the head, limbs, and coronets, occur in some horses (Woods et al., 1993). Other signs indicative of gastrointestinal disease (diarrhea and colic) are unusual. Some affected horses may respond to dexamethasone therapy (Duryea et al., 1997). Affected horses that have focal areas of intestinal damage may respond to surgical resection of the affected areas (Schumacher et al., 1990).

Table 58.1 Typical pathologic changes in the small intestine in different chronic inflammatory bowel diseases.

Disease	Pathologic changes
Granulomatous enteritis	Aggregates of macrophages and epithelioid cells
	Giant cells
	Villous atrophy
Idiopathic eosinophilic enterocolitis	Infiltration of all intestinal layers by eosinophils
Multisystemic eosinophilic epitheliotrophic disease	Infiltration of mucosa and submucosa by eosinophils, lymphocytes, and macrophages (also cutaneous, hepatic, and pancreatic lesions)
Lymphocytic/plasmacytic enterocolitis	Infiltration of lamina propria with lymphocytes and plasma cells
	Villous atrophy

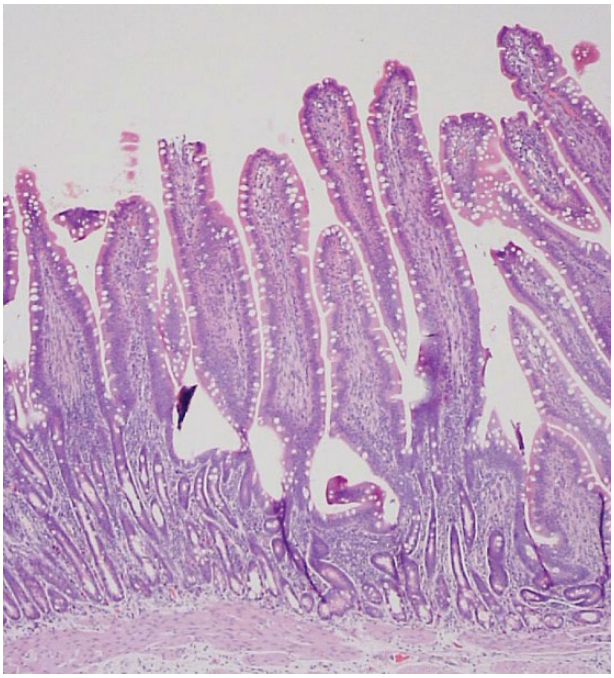

Figure 58.3 Normal mucosa of the small intestine of an adult horse showing the typical villous structure. H&E, ×10.

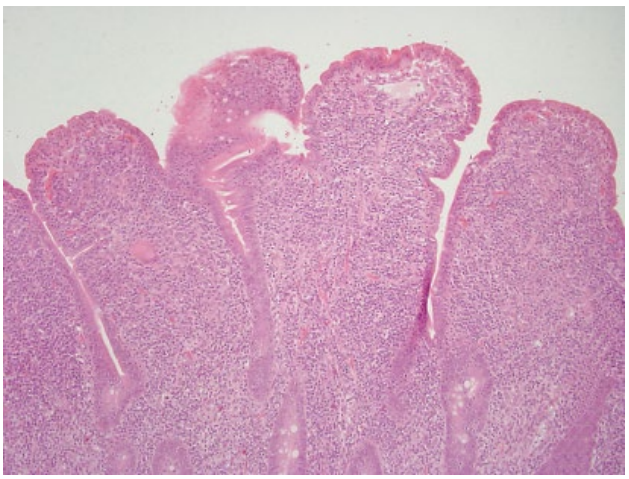

Figure 58.4 Histological appearance of the small intestinal mucosa from a horse with granulomatous enteritis. There is thickening and fusion of villi with an infiltrate of mixed inflammatory cells. H&E, ×10.

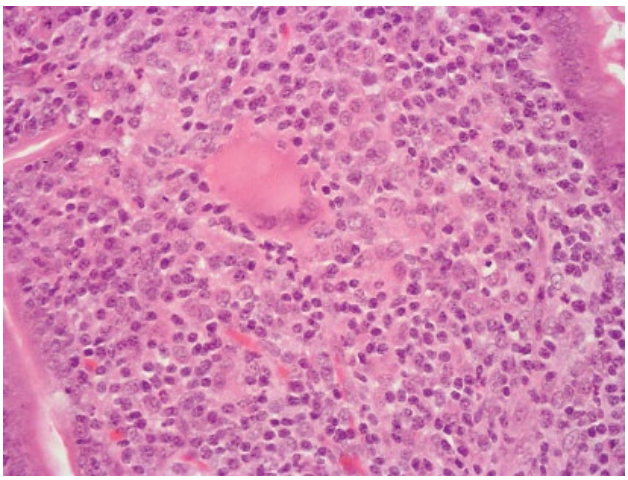

Figure 58.5 Higher power view of the lamina propria of the same horse as in Figure 58.4 (granulomatous enteritis). There is a heavy inflammatory cell infiltrate with multinuclear giant cells. H&E, ×40.

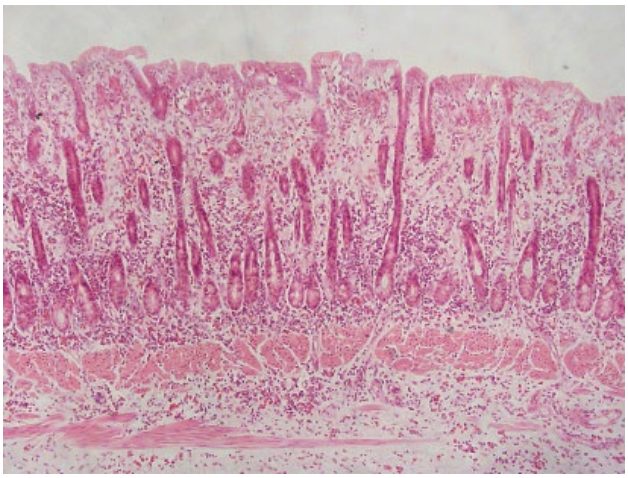

Figure 58.6 Histological appearance of small intestinal mucosa in a horse affected with eosinophilic enteritis. There is villous blunting and fusion resulting in a flat appearance to the mucosa. H&E, ×10.

Idiopathic Eosinophilic Enterocolitis

Chronic eosinophilic infiltrates may take the form of diffuse inflammatory cell infiltration of the small intestinal mucosa with eosinophils and lymphocytes, or an eosinophilic granulomatous infiltrate (Figure 58.6 and Figure 58.7) (Gibson & Alders, 1987; Schumacher et al., 2000; Merritt, 2002). Mucosal ulceration, enlargement of ileal Peyer's patches, and mesenteric lymphadenopathy are frequently present. The etiology of the condition is unknown, but the nature of the inflammatory infiltrate has led to the suggestion that it represents an immune-mediated response to parasites (Cohen et al., 1992; Archer et al., 2006).

This disease may occur as a diffuse infiltrative disease of the small intestine or as focal infiltrative lesions. In the small intestine, focal infiltrative lesions often cause circumferential mural bands that result in partial obstruction of the bowel lumen and are associated with colic (often recurrent colic) (Figure 58.8) (Scott et al., 1999; Southwood et al., 2000; Perez-Olmos et al., 2006; Archer et al., 2006, 2014). These bands purportedly are caused by mural fibrosis stimulated by the eosinophilic enzymes. The diseased segments of intestine may be amenable to surgical resection, but this is not always necessary. Idiopathic focal eosinophilic enteritis and diffuse eosinophilic enteritis

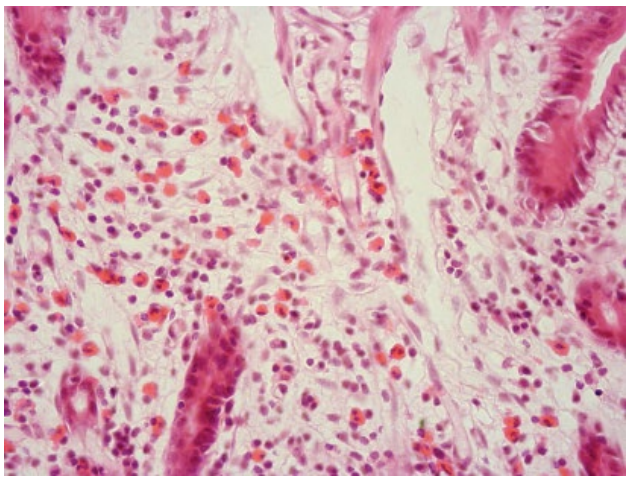

Figure 58.7 Higher power photomicrograph of the small intestinal mucosa of the same horse as in Figure 58.6 (eosinophilic enteritis). There is a heavy eosinophil infiltration in the lamina propria. H&E, ×40.

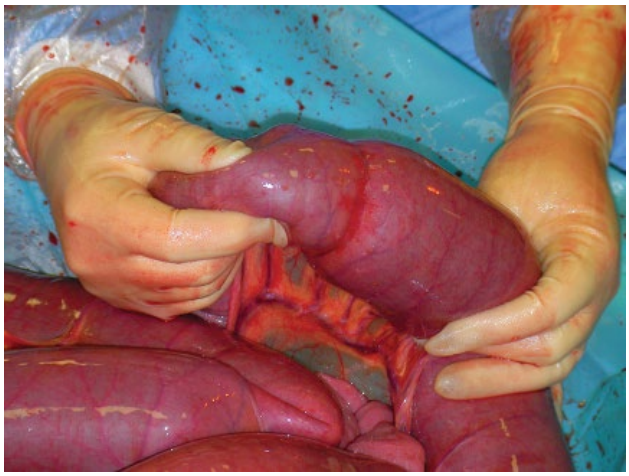

Figure 58.8 Appearance at exploratory laparotomy of annular constriction of the jejunum caused by focal eosinophilic enteritis.

have similar inflammatory cell compositions, but increased numbers of macrophages are present in the small intestine of horses with focal eosinophilic enteritis (Mäkinen et al., 2008).

Segmental eosinophilic colitis is an uncommon disease that results in a local obstructive lesion of the wall of the left dorsal colon (Edwards et al., 2000) (Figure 58.9). Affected segments of bowel show variable mucosal necrosis, submucosal edema, and eosinophil infiltration of the lamina propria and deeper layers of the colon wall. No cause has been established, although a parasite-associated etiology is suspected. Affected horses usually present with mild to moderate intermittent colic. The pain is responsive temporarily to analgesics, but recurs as the action of the analgesic wears off. There may also be varying degrees of abdominal distention for a few

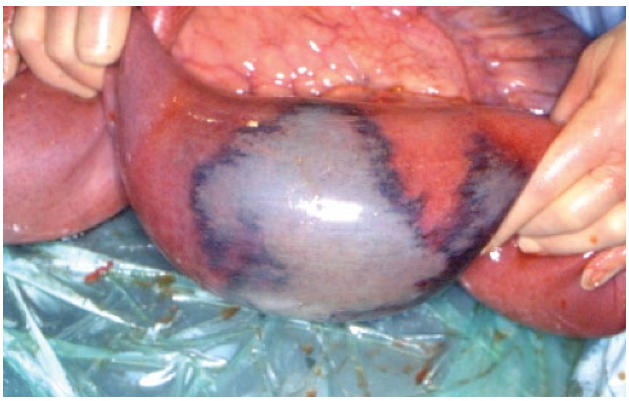

Figure 58.9 Appearance at exploratory laparotomy of segmental eosinophilic colitis, characterized by a focal area of eosinophilic inflammation at the pelvic flexure.

hours to several days. The heart rate varies depending on the duration of disease, but is usually in the range 36–75 bpm.

Rectal examination of affected horses typically reveals varying degrees of large colon and cecal distention and a relatively soft impaction of the pelvic flexure and left ventral colon. Mural edema may be evident in the pelvic flexure and left dorsal colon and, in some cases, the corresponding mesocolon may be edematous. This is sometimes accompanied by a segmental, firm enlargement (approximately 10 cm diameter) of the left dorsal colon. Peritoneal fluid analysis reveals evidence of nonseptic peritonitis. The fluid is usually turbid and yellow–orange, although in a few cases sanguinous peritoneal fluid is obtained. The total nucleated cell count in the peritoneal fluid is increased (from 10 to 250×10^9/L) and consists predominantly of neutrophils. The total protein concentration is also increased (more than >30 g/L).

Treatment consists of removal of the impaction and surgical resection of the affected segment of colon (Edwards et al., 2000). In very mild cases where the luminal obstruction is minimal, resection of bowel may not be necessary, although there is a risk of subsequent worsening of the disease postoperatively. In cases where the segment of abnormal colon is short, a wedge resection may be performed with ligation of segmental vessels but leaving the colic artery and vein intact. When resection of greater lengths of left dorsal colon is required, the colic vessels should be ligated twice and the compromised segment of bowel transected at an oblique angle. After resection, the colon is repaired by end-to-end anastomosis. The defect in the colonic mesentery should be closed with a simple continuous suture pattern.

In one review of 22 cases of segmental eosinophilic colitis, long-term follow-up information was available for 18 horses (Edwards et al., 2000). Of these horses, 16 were alive and well, with no history of colic, 3 months to

7 years after discharge from the clinic. One horse in which resection of the colon was not performed had recurrence of colic symptoms.

Multisystemic Eosinophilic Epitheliotrophic Disease

Multisystemic eosinophilic epitheliotrophic disease is characterized by cutaneous, respiratory, hepatic, and pancreatic lesions in addition to gastrointestinal lesions. The lesions usually involve infiltration by eosinophils and lymphocytes, but in some cases basophils may be the primary inflammatory infiltrate. In some reports, the condition has been variably referred to as eosinophilic gastroenteritis, eosinophilic colitis, eosinophilic granulomatosis, hypereosinophilia syndrome, and exfoliative eosinophilic dermatitis and stomatitis. It is recommended that the terms eosinophilic gastroenteritis and eosinophilic enterocolitis be used to describe cases in which the lesions are restricted to the gastrointestinal tract, although they may be variants of multisystemic eosinophilic epitheliotrophic disease.

As with granulomatous enteritis, most reported cases of multisystemic eosinophilic epitheliotrophic disease involve young horses, especially Standardbreds (Schumacher, 2003). A severe dermatitis resembling pemphigus foliaceus is commonly present, with skin lesions on the face, limbs, and ventral abdomen. Ulceration of the coronets and oral cavity is also commonly present (Pass & Bolton, 1982). Peripheral eosinophilia may be present. Involvement of the liver and pancreas results in increases in serum liver enzymes, including gamma-glutamyl transferase (GGT).

Diagnosis is achieved by biopsy of skin, rectum, and/or liver. Eosinophil infiltrates in the wall of the rectum are a common finding in normal horses (Sloet van Oldruitenborgh-Oosterbaan & Grinwis, 2014), but eosinophilic granulomas associated with vasculitis and fibrinoid necrosis of intramural vessels are considered pathognomic of multisystemic eosinophilic epitheliotrophic disease (Lindberg et al., 1985, 1996).

The etiology of this disease is unknown, although immune-mediated disease and response to parasites are often assumed to be involved. Treatment of affected horses with anthelmintics, antibiotics, hydroxyurea, and corticosteroids is usually unsuccessful, although a small number of horses may show a temporary improvement (Hillyer & Mair, 1992; McCue et al., 2003; Carmalt, 2004).

Lymphocytic/Plasmacytic Enterocolitis

Lymphocytic/plasmacytic enterocolitis is characterized by mucosal infiltration by lymphocytes and plasma cells in the absence of granulomatous changes (MacAllister et al., 1990; Kemper et al., 2000). The disease appears to affect horses of all ages and breeds and either sex. Clinically, most affected horses present with chronic weight loss, with or without diarrhea and recurrent colic. Some horses may respond to treatment with parenterally administered dexamethasone. In other species, such as the dog, lymphocytic/plasmacytic enterocolitis is thought to represent a nonspecific intestinal immune response to agents that cause intestinal damage. It may represent a prelymphomatous change in such species; it is currently unknown if a similar progression may occur in the horse.

The histopathology of equine inflammatory bowel disease suggests a disturbance in intestinal immune homeostasis. The pathogenesis of the disease remains to be established, but it has been suggested that Th17 cells are involved, possibly through recruitment of neutrophils via IL-17A, in combination with inadequate suppression of the inflammatory response by regulatory T cells (Tregs) (Olofsson et al., 2015).

Alimentary Lymphoma

Alimentary lymphoma may be a primary neoplastic disease, or it may represent part of a multicentric disease or a metastatic spread from a primary focus elsewhere in the body (Mair & Hillyer, 1992). Several distinct clinicopathologic syndromes exist, including multicentric or generalized, alimentary, mediastinal, cutaneous, and solitary tumors of extranodal sites (Neufield, 1973; Mair & Hillyer, 1992; Carlson, 1995; Savage, 1998; Schneider, 2003; Taintor & Schleis, 2011). Approximately 19% of horses with lymphoma have the alimentary form, and this type of lymphoma tends to occur in older horses (mean age 16 years in one study (Taylor et al., 2006)). The alimentary form of lymphoma most commonly affects the small intestine, and can develop as diffuse intestinal infiltrates associated with weight loss and small intestinal malabsorption, focal intestinal or mesenteric masses (Figure 58.10)

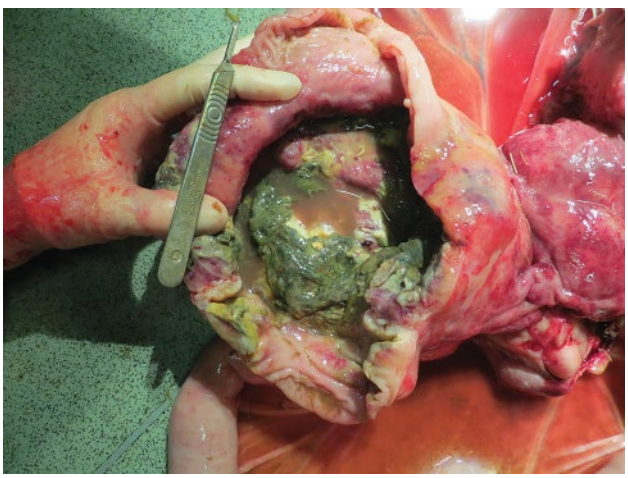

Figure 58.10 Focal area of lymphoma that resulted in a diverticulum with ulceration of the mucosa of the jejunum.

associated with weight loss and abdominal pain, or combinations of these lesion types (Roberts & Pinsent, 1975; Wilson et al., 1985; Platt, 1987; Carlson, 1995; Hillyer & Mair, 1992; East & Savage, 1998; Taylor et al., 2006). Alimentary lymphoma may on occasion occur only in the large colon, especially the right colon, where clinical findings may mimic right dorsal colitis. Diarrhea may be present, especially if the large intestine is affected (Wiseman et al., 1974; Love et al., 1992; Mitsui et al., 2007; Sanz et al., 2010). Mesenteric lymph nodes are also commonly infiltrated by malignant cells. Villous atrophy is commonly present in association with small intestinal infiltrates (Figure 58.11 and Figure 58.12). Mucosal ulcers are also commonly present, and these can contribute to loss of serum proteins and the development of hypoproteinemia. Luminal bleeding can result in blood-loss anemia in addition to the typical anemia associated with chronic inflammation or neoplasia. Pseudodiverticula formation, with subsequent mural necrosis and peritonitis, has also been described (Mair et al., 2011).

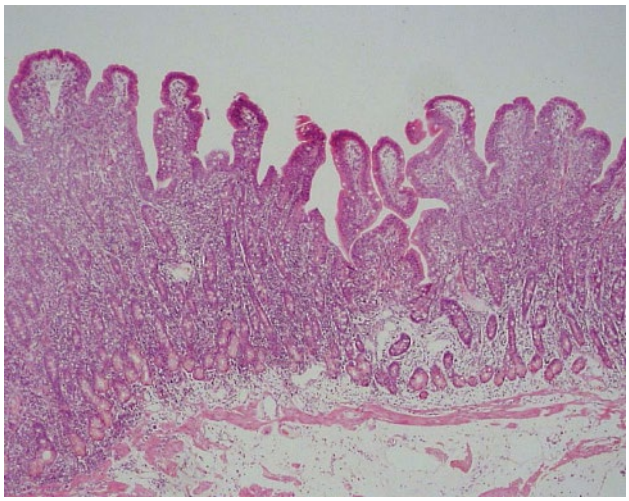

Figure 58.11 Photomicrograph of alimentary lymphoma demonstrating a sheet of neoplastic lymphocytic cells infiltrating the mucosa, resulting in blunting and fusion of villi. H&E, ×10.

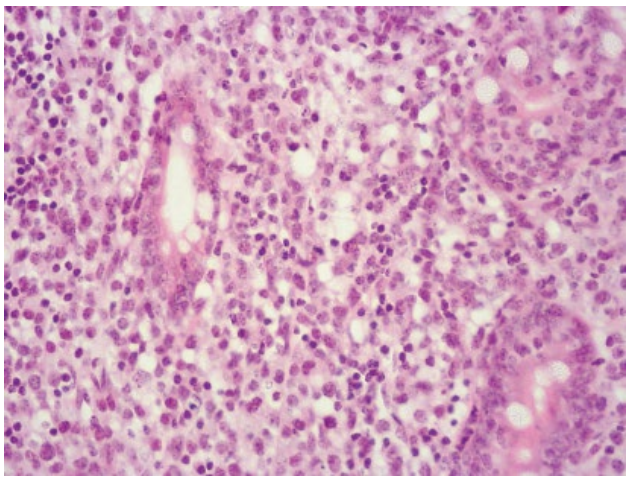

Figure 58.12 Higher power photomicrograph of the small intestinal mucosa of the same horse as in Figure 58.11 (alimentary lymphoma). There is a heavy infiltrate of lymphoma cells in the lamina propria. Mitoses are present. H&E, ×40.

Enteric Infections

Equine proliferative enteropathy was first described by Duhamel & Wheeldon (1982), and since then has been recognized in foals worldwide (Lavoie, 2014). Equine proliferative enteropathy is caused by *Lawsonia intracellularis*, a Gram-negative obligate intracellular bacterium. Infection by this bacterium is most prevalent in pigs, but a wide range of animal species, including wildlife and nonhuman primates, may also be affected. The disease is characterized by a protein-losing enteropathy and is associated with variable clinical signs, including growth retardation, lethargy, subcutaneous edema, fever, colic, and diarrhea, mainly in foals aged 4–7 months. Subclinical infections also occur. Diagnosis is based on the clinical signs, increased thickness of the small intestinal wall on ultrasonographic examination, and hypoproteinemia. Positive serology and polymerase chain reaction (PCR) analysis of the feces support the diagnosis. At necropsy, thickening of the jejunal or ileal mucosa creating an irregular and corrugated appearance is characteristic of the disease. Histological examination reveals severe hyperplasia of the crypt epithelium of the small intestine with the presence of curved, intracellular bacteria in the apical cytoplasm of these enterocytes. Most affected foals with uncomplicated infections will recover if treated with appropriate antimicrobials (tetracyclines or macrolides/rifampin). Death may occur after a few days of onset of clinical signs, although a chronic presentation is more common. Severe necrotizing enteritis leading to disseminated coagulopathy and rapid death has also been reported (Page et al., 2012; Arroyo et al., 2013). The intrarectal administration of a commercial live porcine vaccine to young foals has been shown to be safe (Nogradi et al., 2012) and to offer protection against a challenge with virulent *L. intracellularis* (Pusterla et al., 2012). Vaccination should be considered in a herd where the infection is endemic, although the extra-label use of the vaccine should be taken into account when considering this approach. Passively acquired antibodies to *L. intracellularis* do not have an effect on the occurrence of clinical or subclinical equine proliferative enteropathy (Page et al., 2015).

Mycobacterial granulomatous enterocolitis is rare, and is usually associated with avian strains of *Mycobacterium tuberculosis* or *M. intracellulare*. There are also rare reports of enteric fungal infections involving *Aspergillus*

fumigatus or *Histoplasma capsulatum*. It has been suggested that fungal infections may be most likely in horses undergoing chronic antimicrobial or corticosteroid treatments.

Intestinal Fibrosis

Fibrosis of the submucosa of the small intestine has been described as a rare cause of weight loss, recurrent abdominal pain, and progressive debility (Schultheiss et al., 1995; Johnson et al., 1997). Thickening of the small intestine may be palpable per rectum in some cases. Small intestinal malabsorption may not be demonstrated by oral glucose or xylose absorption tests. The cause is unknown.

Clinical Signs

The clinical signs associated with chronic infiltrative small intestinal diseases are generally similar regardless of the lesion (apart from horses affected by alimentary lymphoma and multisystemic eosinophilic epitheliotrophic disease, which may have primary signs related to involvement of other body systems).

The clinical presentation is characterized by chronic weight loss. Other signs are variable and may include diarrhea, intermittent or chronic colic, variable appetite, depression, lethargy, peripheral and dependent edema, pyrexia, and skin lesions (Table 58.2). Skin lesions occurring in horses with malabsorption include thin hair coat, patchy alopecia, focal areas of scaling and crusting, and coronitis (Figure 58.13). Severe, and often highly pruritic, skin lesions may be present in horses affected by multisystemic eosinophilic epitheliotrophic disease. Paraphimosis may occur in male horses associated with severe debility (Simmons et al., 1987).

Table 58.2 Clinical signs associated with malabsorption syndromes in the adult horse.

Vital signs	Usually normal; occasionally pyrexia
Mucous membranes	Sometimes pale
Appetite	Variable – poor, normal, or increased
Body condition	Usually chronic weight loss
Demeanor	Variable – normal, dull, or depressed
Fecal consistency	Variable – normal, reduced, increased, or diarrhea
Pain	Variable – none, intermittent, or chronic low-grade colic
Edema	Variable – none or ventral/limb edema
Rectal palpation	Variable – normal, thickened intestine, enlarged lymph nodes
Skin lesions	Variable – none, generalized, exudative dermatitis, coronitis

Diagnosis

A thorough clinical and clinicopathologic examination is required in horses presenting with signs of chronic weight loss. Clinicopathologic findings in horses affected by malabsorption syndrome are nonspecific, but may include some or all of the following (Sweeney, 1987):

- hypoalbuminemia
- hyperglobulinemia or hypoglobulinemia
- neutrophilia (occasionally neutropenia)
- eosinophilia (rare)
- anemia (normocytic, normochromic); hemolytic and macrocytic anemia, and thrombocytopenia have been recorded in some cases of alimentary lymphoma
- hyperfibrinogenemia
- hyperlipemia
- increased serum alkaline phosphatase
- increased serum GGT (multisystemic eosinophilic epitheliotrophic disease)
- reduced glucose absorption during oral glucose absorption test (Roberts & Hill, 1973; Murphy et al., 1997)
- reduced xylose absorption during D-(+)-xylose absorption test (Bolton et al., 1976)
- increased serum IgA concentration
- decreased serum IgM concentration (lymphoma)

Figure 58.13 Coronitis associated with malabsorption syndrome.

Horses with chronic inflammatory bowel disease experience malabsorption coupled with enteric loss of proteins of all molecular weights. Because globulins are manufactured faster than albumin, the most consistent abnormality involving serum proteins is hypoalbuminemia. Anemia is most common in horses with granulomatous enteritis (Woods et al., 1993), but has also been reported in some horses with lymphocytic/plasmacytic enterocolitis and multisystemic eosinophilic epitheliotrophic disease.

Enlarged mesenteric lymph nodes may be palpable per rectum in some affected horses (especially horses with alimentary lymphoma). Abnormally thickened bowel wall may occasionally be palpated per rectum, and this finding may be confirmed using abdominal ultrasonography. A recent study of abdominal ultrasonography (Ceriotti et al., 2016) assessed the sensitivity and specificity of ultrasonographic measurement of small intestinal wall thickness in the diagnosis of inflammatory bowel disease, using rectal biopsy as a reference standard. Thirty-five horses presented for chronic weight loss were retrospectively selected. When all patients were considered, a 5.7 mm cutoff value for wall thickness was the best compromise between sensitivity (36.8%) and specificity (87.5%). When only those patients with diffuse intestinal thickening were considered, a 5 mm cutoff value was the best compromise between sensitivity (50%) and specificity (100%). The authors concluded that ultrasonography appears to be a specific method for the evaluation of small intestinal wall thickness, and could be useful in the diagnostic protocol of inflammatory bowel disease in horses with chronic weight loss. However, it is important to note that horses with muscular hypertrophy of the small intestine have the most thickened small intestine of any equine disorder causing weight loss. The weight loss in horses with muscular hypertrophy of the small intestine is due to chronic colic and not to inflammatory bowel disease.

Abdominal paracentesis in affected horses frequently yields normal peritoneal fluid. Neoplastic cells are occasionally present in the peritoneal fluid of horses with alimentary lymphoma (Mair & Hillyer, 1992). Increased numbers of eosinophils may sometimes be present in peritoneal fluid obtained from horses with eosinophilic infiltrative disease.

Diagnosis of infiltrative bowel diseases may be facilitated by histopathologic examination of rectal mucosal biopsies (Lindberg et al., 1996). However, in many cases, the infiltrative disease is confined to the small intestine, and histological examination of the rectal mucosa fails to identify any abnormalities. Lymphoidal cells and plasma cells may be present in the rectal mucosa of horses with a variety of intestinal diseases, including cyathostominosis, granulomatous disease, and alimentary lymphoma; the identification of lymphocytic proctitis in a rectal biopsy therefore should not be interpreted as evidence of lymphocytic/plasmacytic enterocolitis. Likewise, it should be recognized that eosinophils are commonly present in the rectal mucosa and submucosa of many healthy horses, and their identification in rectal biopsies is not proof of multisystemic eosinophilic epitheliotrophic disease or idiopathic eosinophilic enterocolitis (Sloet van Oldruitenborgh-Oosterbaan & Grinwis, 2014). However, the presence of eosinophilic granulomas, associated with vasculitis and fibrinoid necrosis of intramural vessels, in rectal tissue is considered diagnostic of multisystemic eosinophilic epitheliotrophic disease. Skin biopsies or ultrasound-guided biopsy of liver, lymph node, or lung may reveal evidence of multisystemic eosinophilic epitheliotrophic disease.

A diagnosis of small intestinal malabsorption is made using a carbohydrate absorption test such as the oral glucose absorption test or the D-(+)-xylose absorption test. The oral glucose absorption test is more commonly used because of the ease of determining plasma glucose concentrations; however, the results of the oral glucose absorption test require careful interpretation. The immediate dietary history, gastric emptying rate, intestinal transit, age, and hormonal effects of the horse influence the glucose peak and curve shape. Higher glucose peaks are recorded from healthy horses eating hay or grass than from those eating concentrates. Recent changes in appetite or cachexia may affect the results. In healthy horses, administration of 1 g of glucose per kilogram body weight as a 20% solution results in a maximum plasma glucose level (at least 85% higher than baseline) at 120 min (Roberts & Hill, 1973). Horses can be divided into three groups on the basis of the results of the oral glucose absorption test (Mair et al., 1991):

1) Normal absorption – plasma glucose concentrations at 60 and 120 min are within the normal range as defined by the mean ± 2SD of the results of Roberts & Hill (1973), and the glucose concentration at 120 min is more than 85% higher than the resting value.
2) Partial malabsorption – plasma glucose concentrations at 60 and 120 min are below the normal range as defined by the mean ± 2SD of the results of Roberts & Hill (1973) and the glucose concentration at 120 min is 15–85% higher than the resting value.
3) Total malabsorption – plasma glucose concentrations at 60 and 120 min are below the normal range as defined by the mean ± 2SD of the results of Roberts & Hill (1973) and the glucose concentration at 120 min is less than 15% higher than the resting value.

Horses with total malabsorption are likely to have a diffuse infiltrative small intestinal disease, whereas horses with normal absorption are likely to have a histologically normal small intestine. Horses with a partial

malabsorption result may have evidence of an inflammatory infiltrate, villous atrophy, or bowel wall edema, but they may also have histologically normal intestine, and further diagnostic tests should be carried out. The reason why some horses with infiltrative small intestinal diseases may have only partial malabsorption results after an oral glucose tolerance test is likely to be the presence of focal intestinal lesions that only partially interfere with the absorptive function of the entire intestinal tract.

Unfortunately, the oral glucose absorption test is not definitive. Two horses affected by weight loss have been described in which an initial flat oral glucose absorption test absorption curve subsequently improved and became more normal (Church & Middleton, 1997). Intestinal biopsies were normal in both horses. It appears, therefore, that malabsorption (as determined by a history of weight loss and a flat oral glucose absorption test absorption curve) may occur in the absence of significant morphologic change in the small intestine, and the condition may be transient. In addition, abnormal oral glucose absorption test results have been recorded in a number of adult horses with chronic diarrhea, in which postmortem examination revealed that the lesions were confined to the large intestine (Love et al., 1992).

Unlike the oral glucose absorption test, the D-xylose absorption test is not affected by hormonal effects or mucosal metabolism (Bolton et al., 1976). However, gastric emptying, intestinal motility, intraluminal bacterial overgrowth, and renal clearance affect the shape of the D-xylose absorption curve. Healthy mares not fed for up to 96 h had flatter curves and a slower decrease in plasma D-xylose than when deprived of food for 12–36 h (Freeman et al., 1989). Abnormal D-xylose absorption represented by a flat curve or delayed absorption is indicative of jejunal disease, and has been recorded in horses with chronic inflammatory bowel disease, parasitism, and idiopathic villous atrophy (Brown, 1992); however, abnormal D-xylose absorption curves have also been detected in horses lacking small intestinal histopathologic abnormalities (Roberts, 1985).

In one study, the diagnostic and prognostic value of nuclear scintigraphy with technetium-99 m-labeled hexamethylpropylenamine oxime-labeled leukocytes was assessed in horses with weight loss due to gastrointestinal malabsorption by comparing the results with those obtained from healthy control horses (Menzies-Gow et al., 2003). Intestinal uptake of activity was detected in some, although not all, of the affected horses, but in none of the control horses. The technique was, therefore, specific for intestinal abnormalities, but failed to detect some horses that might have had intestinal lesions. No indications of the horses' specific diagnoses were obtained, and their prognosis or response to treatment could not be predicted.

Confirmation of the diagnosis of infiltrative small intestinal diseases and villous atrophy is made by histological examination of sections of small intestine. Full-thickness intestinal wall biopsies may be obtained at exploratory laparotomy/celiotomy for this purpose. Unfortunately, horses with malabsorption states are often not good candidates for surgical exploration of the abdomen, and wound complications are common in the postoperative period because of hypoproteinemia and the catabolic state. If surgery is to be performed, biopsies should be taken from any grossly abnormal section of bowel. If the bowel appears grossly normal, at least three small intestinal biopsies should be taken, one each in the proximal, mid-, and distal small intestine. Biopsies should also be obtained from the cecum and large colon at the same time. Biopsies of mesenteric lymph nodes often reveal similar pathologic changes to small intestinal infiltrates, and at least one lymph node should be biopsied at the same time as the bowel wall biopsies are taken. Bowel wall and lymph node biopsies can also be successfully obtained via a flank laparotomy that can be performed in the standing horse, utilizing local anesthesia (Figure 58.14). This approach greatly reduces the complications associated with healing of ventral midline incisions. Alternatively, intestinal and mesenteric lymph node biopsies may be taken via laparoscopic techniques in the standing patient, thereby eliminating the necessity for general anesthesia and significantly reducing the risk of wound complications (Schambourg & Marcoux, 2006; Bracomonte et al., 2008). However, obtaining intestinal biopsies laparoscopically requires specialized and expensive stapling equipment that may not be widely available. An alternative approach is to perform standing laparoscopy and obtain mesenteric lymph node biopsies if appropriate, followed by creation of a flank laparotomy (by joining two or more laparoscopic ports) and exteriorization the jejunum for biopsy outside the abdomen. A noninvasive biopsy of the duodenum can also be performed via gastroduodenal endoscopy (Divers et al., 2006). This may be diagnostic if the duodenum is involved, which is commonly the case with some of causes of infiltrative bowel disease (e.g., lymphocytic/plasmacytic enteritis). At least three samples of duodenal mucosa/submucosa should be collected. Mucosal bleeding at the biopsy site is an indication that an adequate sample was obtained. This procedure is most conveniently performed immediately after conclusion of the glucose or D-xylose absorption test. In view of the small sample size and superficial depth of biopsy achievable by this means, care with histopathologic examination is essential in order to avoid making incorrect diagnoses.

Even if full-thickness intestinal wall biopsies are obtained, the histological diagnosis of inflammatory bowel disease in horses and other species is subjective, and pathologic assessments vary as a result. One

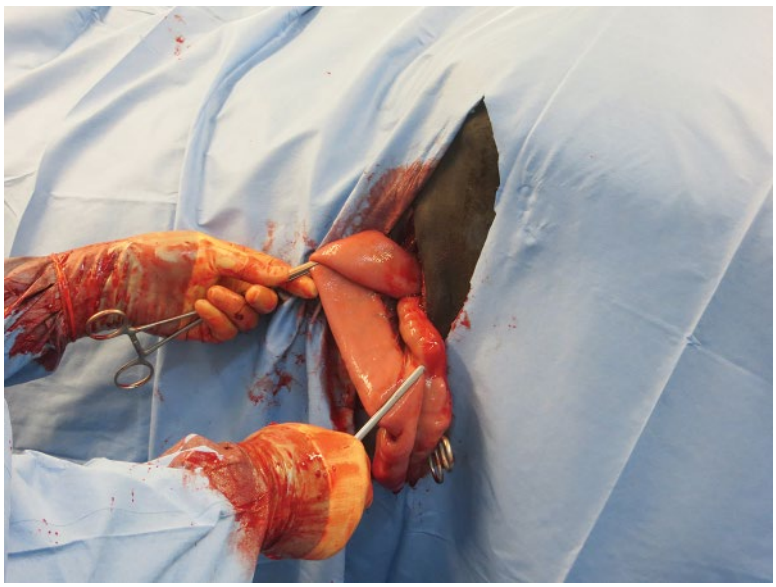

Figure 58.14 Flank laparotomy with exteriorization of a segment of jejunum in preparation for harvesting a full-thickness intestinal biopsy.

important criterion is increased infiltration of the lamina propria by eosinophils, plasma cells, lymphocytes, or macrophages, but this is difficult to assess without a knowledge of the normal immune cell populations and potential for individual variation. A study of jejunal specimens from 14 horses that had not shown clinical or postmortem signs of gastrointestinal disease counted populations of plasma cells, T lymphocytes ($CD3^+$), B lymphocytes ($CD79a^+$ cytoplasmic membranes), eosinophils, macrophages, and neutrophils in the villous lamina propria and intercryptal lamina propria (Packer et al., 2005); there were significantly higher counts of plasma cells, B lymphocytes, and eosinophils in the intercryptal than in the villous region, which accords with previous findings in dogs. This information should be used as control data for future quantitative morphometric analysis of immune cells in small intestinal specimens from horses in which inflammatory bowel disease has been diagnosed. Studies of eosinophilic enteritis and granulomatous enteritis have indicated an increase in T cells and a reduced fraction of B cells in the basal lamina propria compared with healthy horses (Olofsson et al., 2013).

Treatment

The prognosis for horses affected by malabsorption syndromes has historically been considered to be guarded to poor. Severe hypoalbuminemia, in particular, is considered a risk factor for nonsurvival (Metcalfe et al., 2013). By the time that the final diagnosis is reached, the disease is frequently well advanced. Horses affected by diffuse alimentary lymphoma have a hopeless prognosis and should be humanely destroyed, although chemotherapy may prolong survival for 6–12 months. Treatment of horses with fungal enterocolitis with systemic antifungal drugs is usually unrewarding. Horses with diffuse eosinophilic and lymphocytic/plasmacytic enterocolitis may respond well to systemically administered corticosteroids and, on rare occasions, complete recovery may occur. Surgical resection of affected intestine in horses with eosinophilic enteritis or less commonly granulomatous enteritis may be curative.

Recently, the results of treatment of 20 horses with findings consistent with inflammatory bowel disease [based on the fulfillment of one or more of the following additional inclusion criteria: hypoproteinemia, hypoalbuminemia, malabsorption (impaired xylose absorption), an increased intestinal wall thickness on ultrasonographic examination, or histopathologic changes in rectal biopsy] have been reported (Kaikkonen et al., 2014). These 20 horses were treated with a standardized larvicidal anthelmintic regime and a minimum of 3 weeks of corticosteroid therapy. The initial response to treatment was good in 75% of horses, with a 3 year survival rate of 65%. The overall 3 year survival in horses that responded to initial treatment (12/15) was significantly higher than in those that did not respond to initial treatment (1/5). The peak D-xylose concentration was significantly higher in survivors (1.36 ± 0.44 mmol/L) than in nonsurvivors (0.94 ± 0.36 mmol/L). It was concluded that the overall prognosis for long-term survival in horses with a presumptive diagnosis of inflammatory bowel diseases appears to be fair to moderate, and the initial response to anthelmintic and corticosteroid therapy could be a useful prognostic indicator.

Azathioprine is an immunosuppressive drug used in the treatment of autoimmune or immune-mediated

disease. There is anecdotal evidence that it is a useful adjunct to corticosteroid therapy in inflammatory bowel diseases (Divers, 2010). The reported dose rate is 3 mg/kg administered orally every 24 h (Hardefeldt et al., 2010), but the dosage is tapered before discontinuation.

Nutrition

Some level of digestive and absorptive capability is likely to remain in most horses with diseased small intestine. Horses with chronic inflammatory bowel disease may benefit from being fed highly digestible feeds. Provision of a palatable, easily assimilated high-energy and high-protein source is indicated. Supplementing the diet with electrolytes, minerals, and vitamins is also useful. Feeds with a high-quality fiber content (grass hay and access to pasture, complemented by commercial high-fiber diets based on beet pulp and soybean hulls) may help increase body weight by increased conversion of cellulose to volatile free fatty acids in the cecum. This high-fiber diet is especially beneficial for horses affected by chronic inflammatory bowel disease without diarrhea. Feeding more frequent meals (i.e., interval feeding) in smaller amounts may also aid in improving digestion and absorption if the horse has a good appetite. Energy intake can be increased by feeding high-fat diets (5–10% of the diet containing vegetable oils or rice bran). Changing the horse to a high-fat diet should be undertaken slowly. Enteral feeding through an indwelling nasogastric tube is rarely indicated in view of the poor long-term prognosis. There is no justification in trying to sustain a severely debilitated horse when the prognosis is very poor.

In one study, horses with extensive small intestine resection gained weight when placed on interval feeding, even though the D-xylose absorption test results indicated malabsorption (Haven et al., 1991). In contrast, horses with extensive small bowel resection fed twice daily had substantial weight loss and diarrhea in another study (Tate et al. 1983).

The potential role of gluten sensitivity has been demonstrated in a 14-year-old Warmblood stallion with inflammatory bowel disease that also had elevated serum concentrations of antibodies known to be important in the diagnosis and pathogenesis of human celiac disease (Van der Kolk et al., 2012). This horse's clinical signs and duodenal biopsy histopathology findings improved when it was fed a gluten-free diet.

Drug Therapy

Corticosteroid therapy is frequently ineffective in treating horses with chronic inflammatory bowel disease, although some cases of idiopathic eosinophilic enterocolitis and lymphocytic/plasmacytic enterocolitis appear to be responsive to corticosteroids. A small number of horses with granulomatous enteritis, multisystemic eosinophilic epitheliotrophic disease, and intestinal lymphoma may respond to corticosteroids, although long-term improvement is highly unlikely (Johnson & Goetz, 1993; Woods et al., 1993). There is a report of clinical remission of the signs of granulomatous enteritis in one horse after long-term corticosteroid administration (Duryea, 1997). Parenterally administered dexamethasone is likely to be more effective than orally administered corticosteroids in the treatment of chronic inflammatory bowel disease, and prolonged courses of therapy are required.

Other potential treatments for chronic inflammatory bowel disease might include anabolic steroids, orally administered antibiotics, iodochlorhydroxyquin, anthelmintics, salicylazosulfapyridine and methylsulfapyridine. Currently, no evidence suggests that any of these treatments is highly effective. Metronidazole, which is both an antimicrobial and an anti-inflammatory agent, is beneficial in the treatment of some humans with Crohn disease, and it might have potential value in the treatment of horses with chronic inflammatory bowel disease. Hydroxyurea, an antineoplastic drug used to treat humans with hypereosinophilia syndrome, has been shown to produce a temporary improvement in a small number of cases. Other chemotherapeutic agents, including vincristine, cytosine, and cyclophosphamide, have generally failed to have any beneficial effects in horses with malabsorption (Platt, 1986). As mentioned earlier, some horses with alimentary lymphoma respond favorably for 6–12 months during chemotherapy.

Surgery

Surgical resection of limited areas of affected bowel may produce some short-term benefits, but the diffuse nature of the lesions in many of the diseases usually precludes this therapeutic option. In some cases of alimentary lymphoma, granulomatous enteritis, and eosinophilic enterocolitis, only focal areas of the intestinal wall may be diseased, and these lesions may be amenable to surgical resection.

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Colic and Pregnant Mares

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Colic During Pregnancy

Diagnostics

Abdominal pain occurs frequently in pregnant mares, and most episodes resolve with minimal medical therapy. However, some colic episodes in pregnant mares are more severe and require intensive medical or surgical intervention. The first step in determining the appropriate therapy is to establish the cause of the pain and the necessity for supportive care. The most common sites of colic in pregnant mares are the gastrointestinal tract and the uterus. A less frequent cause of abdominal pain is damage to the abdominal tunic.

Most colic episodes originate from lesions involving the gastrointestinal tract, but abnormalities involving the uterus become a more likely source for the pain as the pregnancy progresses. Because the causes of uterine-related colic are few, and their occurrence is relatively infrequent compared with those involving the gastrointestinal tract, the easiest way to determine the source of the colic is first to eliminate uterine and abdominal wall causes. The first step is to palpate the uterus via the rectum to ascertain its shape, size, and orientation. If these findings are normal, the uterus is very unlikely to be the source of abdominal pain. Occasionally, parturition or abortion can be confused with colic, so a cervical examination by speculum or by gentle palpation can be helpful. This procedure should be performed cautiously to avoid introducing vaginal contamination, as a relaxed cervix in late-term mares is common, and not necessarily a sign of impending parturition. If the uterus is not the cause of pain, the location of colic is assumed to be gastrointestinal, as abdominal tunic disorders are readily apparent by visual observation.

The diagnostic workup for a pregnant mare with gastrointestinal colic is the same as for a nonpregnant horse. However, in the late-term mare, the usefulness of palpation of the viscera per rectum and transabdominal ultrasound can be reduced as the large uterus obscures the viscera.

Determining the best course of treatment in the pregnant mare with colic is further complicated by concerns about the health and maturity of the fetus. Transabdominal ultrasound of the fetus can provide some information about fetal heart rate and activity, and selected biochemical makers and hormonal parameters have been investigated as markers of fetal health, but are usually not available to make an emergency determination. However, decision making can be simplified by following two guidelines: (1) the best way to care for the foal is to care for the mare and (2) mares exhibiting signs of abdominal pain should have an exploratory laparotomy.

Assessment of Fetal Health and Maturity

Accurate assessment of fetal health is a challenge, but there are recommendations available (Bucca, 2006), particularly for ultrasonic examination (Reef et al., 1996). Fetal death can be easily determined by visualizing asystole via transabdominal ultrasound in the late-term fetus, but less dramatic compromise of the fetus can be difficult to detect. Daily ultrasound examinations to determine fetal heart rates, fetal movement, and an estimation of fetal fluid volume and echogenicity are the best methods to assess fetal well-being in the high-risk pregnancy. Fetal heart rates should range from 70 to 110 bpm. Repeatedly higher or lower rates are associated with fetal compromise. It is important to detect fetal death as dystocia can result from attempted delivery of a dead fetus without assistance.

Fetal maturity can be estimated by measuring electrolyte concentrations in mammary secretions, as concentrations of calcium, potassium, and sodium change as the fetus reaches maturity (Leadon et al., 1984; Peaker

The Equine Acute Abdomen, Third Edition. Edited by Anthony T. Blikslager, Nathaniel A. White II, James N. Moore, and Tim S. Mair.

Companion website: www.wiley.com/go/blikslager/abdomen

et al., 1979). Before maturity, concentrations of sodium and potassium in mammary secretions are similar to those in serum (sodium concentration higher than that of potassium), but these concentrations invert about 3 days before birth (the sodium concentration becomes lower than that of potassium), indicating accelerating fetal maturity. Although electrolyte concentrations in mammary secretions provide only an estimate of maturity, it currently is the best test available. If fetal survival is a primary goal, methods of assisting parturition, such as induction or hysterotomy, should be delayed if possible until the concentrations of the electrolytes in mammary secretions have inverted.

Gastrointestinal Colic

There have been four retrospective studies that have described the lesions that cause colic in pregnant mares and determined risk factors for pregnancy loss (Santschi et al., 1991; Boening & Leendertse, 1993; Chenier & Whitehead, 2009; Drumm et al., 2013). Table 59.1 summarizes the important findings of these studies; they do not always agree on specifics, but as a whole provide clinicians with guidance about prognosis and the factors that may impact gestation.

Medical

Mild colic occurs frequently in pregnant mares. As in nonpregnant horses, most colic episodes in pregnant mares resolve with minimal therapy. These single colic episodes appear to have little effect on either the mare or the fetus. However, when abdominal pain is accompanied by signs of endotoxemia, or is repetitive, there is risk to both mare and foal. Endotoxemia may have the greatest effect on the fetus in the last 60 days of gestation (Santschi et al., 1991; Boening & Leendertse, 1993). Retrospective studies of colic in pregnant mares provide conflicting statistical results on the impact of endotoxemia (Table 59.1), but even when unsupported by data, authors remain concerned about the effects of endotoxin on the mare and fetus (Drumm et al., 2013). It is not known if endotoxin can cross the equine placenta, but endotoxemia can cause uteroplacental perfusion abnormalities in cattle (Giri et al., 1990), and the concurrent cytokine release may be the mechanism for compromise in late-term pregnancies. Early in equine pregnancy, experimental endotoxemia can cause prostaglandin-mediated luteolysis and subsequent pregnancy loss (Daels et al., 1991). It is not known if circulating concentrations of endotoxin in clinical cases are sufficient to result in luteolysis and abortion, but that may be the mechanism for greater pregnancy loss at <40 days of gestation compared with later (Drumm et al., 2013). Sustained signs of endotoxemia are most common in mares requiring intensive medical therapy for diseases such as proximal duodenitis/jejunitis or colitis. The appropriate therapy for endotoxemia includes correction of the inciting cause, administration of cyclooxygenase inhibitors such as flunixin meglumine, and appropriate fluid support (Moore & Barton, 2003).

Surgical

When relatively small groups of pregnant and nonpregnant horses are compared, there is no significant difference between the types of lesions causing colic (Santschi et al., 1991), but there are a few intestinal lesions that are frequently associated with pregnancy. In the early stages of pregnancy, the pregnancy itself appears to have little effect on the health of the mare, but the previous pregnancy may have some residual effect. During late pregnancy, the gravid uterus occupies a very large portion of the intra-abdominal space, causes stretching of the abdominal wall, and leaves little room for colonic ingesta. After parturition, the colon has more space to move owing to the laxity of the abdominal musculature and the empty colon. Additionally, it is common for recently foaled mares to receive fermentable feedstuffs as concentrates or lush forage and pasture. The combination of an empty colon that is predisposed to tympany and has more room for movement is believed to predispose postparturient mares to colonic displacements and large colon volvulus.

Large colon volvulus is of particular concern to broodmare owners as it occurs commonly in broodmares in early to mid-gestation, recurs in some individuals, and is often fatal (Hance & Embertson, 1992; Ellis et al., 2008). Owing to the shape of the postparturient abdomen, the space for the large colon and cecum is larger and has a deeper ventral concave shape. The authors' hypothesis is that the apex of the cecum is on the midline, and the right ventral colon is pulled toward the midline via the cecocolic ligament, which attaches to the ventrolateral band. This causes a slight clockwise (as viewed from behind) rotation of the colons, and results in an axial placement of the ventral colon relative to the dorsal colon. The oblique (as opposed to a vertical stacking) orientation of the colons is also promoted by concavity of the diaphragm. When the colons are in this position, gas in the ventral colon or the apex of the cecum, or heavy feed in the dorsal colon, can promote further rotation of the colon. As the rotation continues, the colons twist tighter against the dorsal colonic attachments. This results in colic by obstructing gas and ingesta and, if severe, death by colonic vascular compromise. Keeping the colon full by providing constant access to roughage is one method proposed to reduce the development of colonic displacement and volvulus.

Surgical correction is essential to the treatment of large colon volvulus, and rapid intervention is necessary. The colon is untwisted through a ventral midline

Table 59.1 Summary of patient numbers and outcome assessments for retrospective studies of pregnant mares treated for colic.

Study	No. of pregnant mares with colic	Foal positive outcome	Mare age at colic	Stage of gestation at colic	Clinical endotoxemia negative impact	Duration of anesthesia negative impact	Hypoxia negative impact	Hypotension negative impact	PPO[a]: all (%)	PPO medical, PPO surgical (%)	Surgery negative impact
Santschi et al. (1991)	105	Born alive at >300 days of gestation	Not considered	No impact	Yes when severe	No impact	All: no >270 days: yes	No	82.0	85, 80	No
Boening & Leendertse (1993)	115	Born alive at >300 days of gestation	Not considered	No impact	Yes	Not considered	Yes	Not considered	83.6	90.2, 79.5	No
Chenier & Whitehead (2009)	153	Stand and nurse; survive 24 h	Not considered	Not considered	No	Yes, >3 h worse	No	Yes	69.9	78.2, 53.8	Yes
Drumm et al. (2013)	228	Registered with Jockey Club (>30 days of age)	≤15 years better	≤40 days worse	No	Trend for longer	No	No	66.7	All surgical	All surgical

a) PPO, positive pregnancy outcome.

celiotomy (see Chapters 42 and 54). A pelvic flexure enterotomy can be performed to evacuate the colon and inspect the mucosa for viability. If the colon is viable, it is replaced in the abdomen. If the colon is compromised, resection of 60–75% of the colon is possible (Ellis et al., 2008). Large colon resections are performed to remove devitalized tissue, reduce the absorption of endotoxins, and reduce the dramatic loss of plasma protein that can occur after surgery. Although the mares often have diarrhea and weight loss after surgery, they will gain it back in several weeks and can carry both the present and subsequent foals to term. The approximately 30% recurrence rate of large colon volvulus in Thoroughbred broodmares has led to the development of colopexy procedures to prevent colonic rotation (Hance & Embertson, 1992); these techniques have not been universally accepted. The development of large colon volvulus in mares after foaling may be reduced by feeding forage rather than fermentable feeds, so as to fill the colon with ingesta rather than gas, and by promoting exercise to improve the muscular tone of the abdominal wall and support normal gastrointestinal motility.

Two causes of colic specifically associated with pregnancy are small intestinal entrapment over the broad ligament and through rents in the proximal duodenal mesentery. Both conditions occur most commonly in mares in the latter quarter of gestation, and the jejunum becomes entrapped over the broad ligament. The distended small intestine is readily palpable per rectum, and because of concerns about small intestinal strangulation, these mares often are subjected to an exploratory celiotomy. The bowel is usually not compromised, and the colic is resolved by correcting the entrapment and decompressing the intestine.

Rents in the mesentery generally involve the short axis of the mesentery from the root to the antimesenteric attachment. Entrapment of the small intestine occurs because the available room in the abdomen is reduced by the enlarging uterus and the bowel is displaced through the rent. Owing to the large size of the rent, intestine probably moves freely in and out of the rent. Presumably, however, as the uterus enlarges, the intestine becomes entrapped, causing physical obstruction and colic. Strangulation of the entrapped intestine is rare owing to the large size of the rents. There is usually no fresh hemorrhage in the abdomen from the mesentery and the margins of the tears are healed, suggesting that the rent had occurred previously, perhaps during parturition. Mesenteric rents most commonly involve the duodenum and small colon, where the mesentery is short and perhaps more likely to be damaged; however, a distal jejunal rent has also been described (Dart & Pascoe, 1994). Correction of mesenteric rents causing small intestinal herniation requires removal of bowel from the rent, resection of any damaged intestine, and closure of the rent. Closure of the rent can be difficult as the proximal extent is deep in the abdomen and the uterus makes exposure difficult or impossible. It is generally accepted that leaving a large hole is better then a partially closed one, so if the rent cannot be substantially closed, it is left undisturbed. Owners are advised that another colic episode during this gestation is a possibility. Closure of the rent after foaling via celiotomy or laparoscopy should be considered.

Hysterotomy During Colic Surgery

If the lesion causing colic cannot be accessed because of the enlarged uterus, removing the foal may allow the colic episode to resolve. This is an uncommon approach, and should be avoided if possible. If the foal is not ready for birth, the decision to remove the foal is essentially an abortion to save the life of the mare, and should only be done on that basis. If the foal is close to term and the mare's mammary secretion electrolyte concentrations are consistent with fetal maturity, the foal is delivered and sent to intensive care, the uterus closed, and the lesion causing the colic episode corrected. Because the survival rates of these foals will be low, this procedure should not be performed if the colic lesion can be corrected otherwise.

Anesthesia

Anesthesia of the pregnant mare is not substantially different from that of nonpregnant horses. However, there is an increased risk to the mare's life if anesthesia is performed in the last trimester of pregnancy (Johnston et al., 1995). The reasons for this increased risk are unclear, but possibly involve the cardiovascular changes associated with late pregnancy, the challenge of ventilation, the weight of the mare, and perhaps some delay in therapy due to concerns about anesthesia. All anesthetic agents have an effect on the fetus (Daunt et al., 1992), so alteration to the anesthetic protocol is unnecessary. One consideration is to minimize the use of α_2-agonists, such as xylazine and detomidine, as they increase uterine tone (Von Reitzenstein et al., 2002). The author's preference is to use xylazine (0.3–0.5 mg/kg IV for sedation), and then rely on additional agents such as 5% guaifenesin (100 mg/kg IV) or diazepam (0.1 mg/kg IV) for relaxation before inducing anesthesia with ketamine (2.0 mg/kg IV).

Another anesthetic consideration in late gestation pregnancies is hypoxia, as hypoxia in the last 60 days of gestation has been associated with poor fetal outcomes in some retrospective studies (Boening & Leendertse, 1993; Santschi et al., 1991), but not confirmed by others (Chenier & Whitehead, 2009; Drumm et al., 2013). In normal pregnancies with catheterized fetuses, oxygen uptake of the uterus, placenta, and fetus increases by 2–3-fold in late gestation (Fowden et al., 2000). Therefore, arterial oxygenation should be maintained at 80 mmHg

or greater during surgery, if possible. However, it can be difficult to ventilate mares with a large uterus and distended bowel when they are positioned in dorsal recumbency. In such cases, the best way to prevent hypoxia is to diagnose the primary condition early, decompress the bowel quickly, and correct the lesion as soon as possible. Strict attention should be paid to proper padding and positioning of the late pregnant mare during general anesthesia, as the extra weight of the fetus and fluids will place extra stress on the muscles, making postoperative myopathy a possibility.

Abortion After Colic Treatment

There is little risk to the fetus in a pregnant mare that has responded well to routine medical therapy for a colic episode. The incidence of abortion increases for mares requiring surgery or intensive therapy (Boening & Leendertse, 1993; Santschi et al., 1991; Chenier & Whitehead, 2009). The increased likelihood of abortion after surgery for a nonstrangulating colonic lesion is extremely low, if no complications arise. Mares with strangulating colonic lesions or small intestinal lesions appear to have about a 10% postsurgical abortion rate that can be attributed to either the colic or the treatment. Multiple bouts of colic, particularly if they occur after surgical interventions, also seem to be associated with an increased incidence of abortion. To minimize the risk of abortion, surgical therapy for colic should be performed as soon as the need for surgical intervention has been determined.

Abortions after colic episodes occur because of fetal death. Once the fetus dies, parturition should occur within 48 h. Dystocia is frequent because the fetus cannot actively participate in parturition, thereby resulting in carpal and poll flexion. These malpositionings are readily corrected, and can be anticipated by checking fetal viability daily via transabdominal ultrasound. Mares will often deliver at night, so 24 h monitoring of a mare with a dead fetus is necessary.

Pregnancy Maintenance

There are many adjunctive strategies directed at supporting pregnancies, but evidence for their efficacy in clinical situations is mostly anecdotal. There is experimental evidence that the administration of altrenogest (44 mg/day) may have benefits (Daels et al., 1996). For mares in early gestation, exogenous progestagens can be administered if the possibility of luteal compromise exists. Therapy can be continued until sufficient endogenous production of progestagens can be demonstrated. For mares in later stages of gestation, stall confinement with light exercise such as 1–2 h turnout in a small paddock or round pen is believed to be beneficial. Strict stall confinement of the late-pregnant mare should be avoided as it can lead to accumulation of edema in the limbs and around the udder. For medical therapy, the author uses altrenogest 0.09 mg/kg orally sid and flunixin meglumine at 0.5 mg/kg IV tid or 1.0 mg/kg IV bid. The altrenogest is used as a tocolytic and the flunixin meglumine for its anti-inflammatory properties. Other clinicians use pentoxyphylline (12 mg/kg PO bid) for its anti-inflammatory and rheologic properties, and provide intranasal oxygen to the mare to improve oxygen delivery to the fetus when the mare shows clinical evidence of endotoxemia or hypoxemia.

Uterine Causes of Colic

Uterine Torsion

Torsion of the uterus occurs in mid- to late gestation (Pascoe et al., 1981; Wichtel et al., 1988; Chaney et al., 2007; Jung et al., 2008; Spoormakers et al., 2016). The primary clinical sign in affected mares is abdominal pain that is usually moderate in degree but occasionally can be severe. Uncommonly, the gastrointestinal tract can be involved in the torsion (Ruffin et al., 1995). Systemic compromise is rare and, when present, indicates uterine damage or gastrointestinal complications. The diagnosis of uterine torsion is made by palpation; one broad ligament is very taut and passes over the uterus and the other is palpated as a band under the uterus. There is no preference for the direction of rotation. The cervix is rarely open and vaginal twisting is usually not apparent.

Treatment of mares with uterine torsion requires physical detorsion of the uterus. This can be accomplished via either a standing laparotomy (Spoormakers et al., 2016), a ventral midline approach with the mare under general anesthesia (Jung et al., 2008), or a nonsurgical rolling procedure with the mare under general anesthesia (Wichtel et al., 1988. The stage of gestation when the torsion occurs has a significant impact on both mare and foal survival. When torsions occur at <320 days of gestation, mare survival is ~97% and foal survival is 72–91%. When torsions occur at ≥320 days, mare survival decreases to 65–73%, and foal survival to 32–56%. The procedure chosen is dependent on the condition of the mare and her stage of gestation when the torsion occurs, financial constraints of the owners, facilities available, and the clinician's preference. A ventral midline laparotomy is preferred because of its versatility and the ability to inspect the uterus and correct any concurrent gastrointestinal problems (Jung et al., 2008). However, there is evidence that correction of uterine torsion via a standing flank procedure will result in improved outcomes, especially when performed in pregnancies <320 days (Spoormakers et al., 2016). In later gestation, the procedure used to effect detorsion of the uterus did not have an impact on survival rates.

The nonsurgical rolling procedure should probably be reserved for situations where surgery is not possible, and

is most successful in mares in mid-gestation (Wichtel et al., 1988). The mare is anesthetized and placed in lateral recumbency on the same side as the direction of the torsion. The purpose of the rolling procedure is to hold the foal and uterus in place and roll the mare to "catch up" with her uterus and fetus. A board can be used across the flank to hold the uterus and foal still while the mare is rolled. Correction of the torsion is determined by rectal palpation. The rolling procedure can be repeated, if unsuccessful. Once the torsion has been corrected, the mare is allowed to recover from anesthesia.

Uterine torsions can be corrected by standing laparotomy at any stage of gestation, but correction can be difficult in late-term mares owing to the size and weight of the gravid uterus. Standing correction requires that the mare tolerate the procedure, and should not be performed in mares with suspected uterine damage. Sufficient sedation and analgesia are important; an inverted "L" block with local anesthetic is made in the flank on the side to which the uterus is rotated. A vertical incision is then made through the skin of the flank, and the abdomen is opened via a modified grid incision (sharp dissection through the external abdominal oblique, blunt fiber separation through the internal oblique and transversus muscles). The surgeon's arm is placed under the uterus and the uterus is gently rocked back and forth. The goal is to gain sufficient momentum to "flip" the uterus into its normal position. The surgeon should be careful to put pressure on the uterus only with the flat of the hand to avoid tearing the uterus. If detorsion is difficult, the flank incision can be enlarged to admit both arms to allow manipulation of the uterus. In difficult cases, flank incisions can be made bilaterally and detorsion performed by two surgeons.

The ventral midline approach can be used for late-term mares and for mares with suspected uterine damage. The uterus is approached through a large caudal ventral midline incision. By placing the hands and arms under and around the uterus, the uterus is untwisted. Filling the abdomen with sterile saline will reduce friction in the abdomen and facilitate detorsion. In rare cases when the detorsion of the uterus cannot be achieved, the fetus can be removed to facilitate detorsion. If the uterus is ruptured, the fetus is delivered and the uterus sutured. Mares with extensive uterine damage should be euthanized.

Uterine Artery Hemorrhage

The majority of uterine artery hemorrhages occur during parturition, but they can occur during gestation and result in signs of colic. The diagnosis is made by physical examination, which will reveal pain, hypovolemia if the hemorrhage is severe, a hematoma associated with the broad ligament of the uterus, and blood in peritoneal fluid obtained by abdominal paracentesis (Britt, 1997). Ultrasonic examination of the abdomen and uterus will reveal a uterine or broad ligament hematoma and varying amounts of free blood in the abdomen. There are many treatments for uterine artery hemorrhage, most of which focus on supporting the mare while the arterial defect seals. The most important therapy is probably gentle supportive care, mild sedation, and analgesia.

Hydrops

Hydrops refers to excessive production of fluid by the placenta. Most cases in horses are allantoic hydrops, although amniotic hydrops also has been reported (Sertich et al., 1994). Affected mares have massive abdominal enlargement out of proportion for their stage of gestation. They can develop respiratory distress, particularly when lying down, move stiffly, and have signs of mild abdominal pain. Rectal examination reveals massive fluid distention of the uterus, and the fetus usually cannot be palpated. Abortion of a hydropsical pregnancy should be strongly considered owing to the danger of uterine (Honnas et al., 1998) or abdominal wall rupture and the high likelihood of fetal abnormalities (Allen, 1986), and to protect the uterus from overstretching. With informed client consent to the risks, conservative treatment can be attempted, as there is one report of successful conservative treatment of hydrops amnion, which required intensive therapy of both mare and foal, and an assisted delivery (Christensen et al., 2006).

If abortion is performed, the massive fluid loss that occurs in mares with hydrops should be anticipated to prevent or treat hypovolemia. Mares can be administered crystalloid fluids IV preinduction to ensure a good plasma volume. Induction usually can be performed by manually dilating the cervix and rupturing the chorioallantois. Using gentle pressure, the cervix usually can be dilated but, if necessary, cervical softening with topical misoprostil can be considered. Insertion of a sterile large-bore tube, such as a nasogastric tube, can be used to attempt controlled fluid removal, but with mare contraction can result in a violent fluid release. Once the fluid begins to flow, a small fetus usually will present itself and can be delivered with gentle traction; euthanasia is frequently indicated owing to prematurity and a high incidence of fetal abnormalities. Retained placenta is common, and should be treated appropriately.

Abdominal Tunic Disorders

Damage to the abdominal tunic occurs most frequently as prepubic tendon rupture or stretching, but can also present as muscular hernias in the abdominal wall (Hansen & Todhunter, 1986; Ross et al., 2008). Damage can occur in abnormal pregnancies such as hydrops, but more commonly occurs in apparently normal pregnancies. Presenting signs in affected mares are usually colic

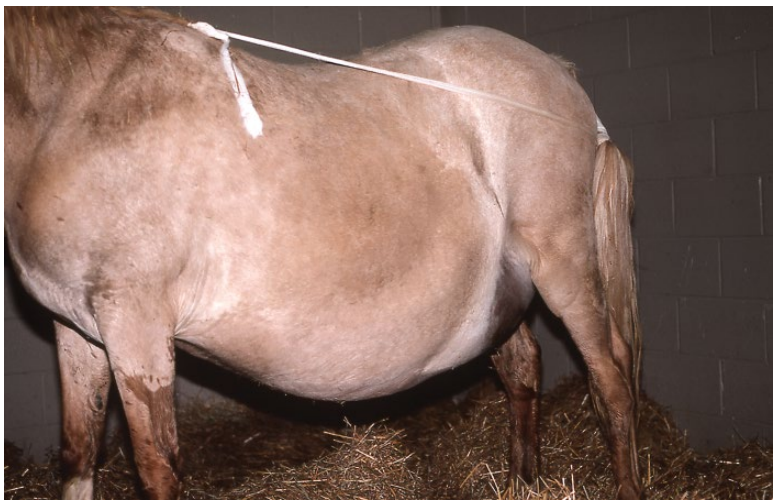

Figure 59.1 Prepubic tendon rupture in a mare. The condition hinders rear limb movement and distorts the mammary glands.

and edema of the caudal aspect of the abdomen. Diagnosis of a prepubic tendon rupture is made by observing an upward tilt of the caudal pelvis caused by a lack of tension on the pubic bone. Usually there will also be symmetric edema cranial to the mammary gland, a caudal orientation of the teats sometimes with hemorrhagic discharge (Figure 59.1). Ultrasound of the area will reveal edema and hemorrhage, and a discontinuity in the fibrous portion of the abdominal wall. Prepubic tendon ruptures rarely occur in isolation, and usually have associated muscular injuries. Muscular ruptures tend to be asymmetric and can extend dorsally into the flank. Ruptures are thought to occur most frequently in draft mares, but also are seen in light breeds of horses. The most common clinical sign seen is colic due to the pain associated with tearing of the support structures.

Mares with injuries to the abdominal tunic can be successfully managed with conservative therapy such as abdominal supports, analgesics, and stall confinement (Ross et al., 2008). However, some injuries progress and eventually require euthanasia. If a severe injury is present before the fetus is mature, the likelihood of carrying the foal to term is low. If the mare's life (without the ability to carry subsequent foals to term) is important, preterm induction with assistance during delivery may be indicated. However, it is usually not clear whether induction or continuing the pregnancy is more injurious to the mare, and one report suggests that caution be exercised when considering dramatic intervention in these cases. (Ross et al., 2008).

If the mare completes her pregnancy, foaling should be attended, as she may not be able to provide sufficient abdominal contraction to deliver the foal quickly. Carrying future pregnancies to term is unwise, but has been accomplished (Perkins & Frazer, 1994). Embryo transfer may be a reasonable option if reproductive capabilities are essential. For some abdominal hernias, surgical repair can be performed after the hernia develops a distinct fibrous border (Tulleners & Fretz, 1983).

Partial damage or stretching of the prepubic tendon can be managed successfully, and success is related to the amount of damage. Clinical signs include abdominal pain and edema in the area of the tear, but the pelvis and mammary gland remain in their normal orientations. In some cases, affected mares have what appears to be a stretched prepubic tendon, with a lengthened distance between the umbilicus and the base of the mammary gland. These mares should be stall confined and administered anti-inflammatory drugs as needed. Subsequent pregnancies can occur successfully but should be closely monitored.

Colic After Pregnancy

Diagnostics

Evaluation of colic in recently foaled mares can be complicated by normal postpartum events such as uterine pain from delivery of the placenta and uterine involution. Just as in pregnant mares, the uterus and the gastrointestinal tract should receive equal attention to determine the source of the abdominal pain. Transabdominal ultrasound should always be part of the examination of a depressed or painful postpartum mare to detect abdominal fluid accumulation and intestinal distention. If abdominal fluid is detected, abdominal paracentesis should be performed to determine if peritonitis or hemorrhage is present. If peritonitis is present, there is little need to determine the specific source of the infection for mares with a surgical option. An abdominal exploratory approach to determine the cause of the peritonitis, possibly correct it, and lavage the abdomen should be performed as soon as possible. For mares without a surgical option, sampling the abdominal fluid will provide information about the severity of infection and whether euthanasia is appropriate. Some horses with peritonitis

will respond to medical therapy only, but it can be difficult to predict success early in the course of the process. For valuable mares, an exploratory celiotomy can resolve most questions and prevent fatal peritonitis.

Gastrointestinal Colic

Medical

The majority of episodes of postparturient abdominal pain are mild to moderate in intensity and respond to medical therapy. For most postparturient mares, the specific causes of colic are speculative, but bruising of the small colon and generalized ileus are frequent occurrences. Treatment of these mares with laxatives, anti-inflammatory drugs and oral or IV fluids is generally sufficient for the resolution of abdominal pain. Colic episodes with evidence of concurrent endotoxemia can be the result of ingesta leaking from small rents in the intestine. If there is contamination of the peritoneal cavity with feed, these mares invariably die from peritonitis and adhesions. However, if peritonitis is diagnosed early and the peritoneal cavity is contaminated by bacteria but not plant material, surgical closing of the tear and lavage of the abdomen can be successful. Placement of abdominal drains at surgery allows for postoperative lavage of the abdominal cavity, which may be beneficial.

Rupture of the Small Colon Mesentery or Prolapse of the Small Colon

Rupture of the mesentery of the small colon can occur during the abdominal press of parturition (Dart et al., 1991). The presence a rectal prolapse during foaling should raise the suspicion of this injury, but rectal prolapse is not required for this condition to occur. Stretching of the mesentery during parturition tears the distal small colon mesentery from the bowel for a variable length, causing intra-abdominal hemorrhage, ileus, small colon impaction, and eventually bowel necrosis. Onset of clinical signs associated with the rupture can be delayed for 24–48 h after foaling, and the initial finding is a lack of fecal passage. A low-grade fever (102–103 °F/38.9–39.5 °C) usually develops, followed by bloating and colic. Rectal examination will reveal an impaction of the distal small colon. Differential diagnoses for mares with peritoneal effusion after foaling include tearing of the wall or the vascular supply of the uterus or intestine.

Treatment of mares with small colon mesenteric ruptures that result in compromised bowel requires surgery. Repair of the damage is limited by accessibility to the distal aspect of the mesenteric tear. If the necrotic small colon extends into the pelvic canal, euthanasia is usually necessary. If healthy bowel can be reached at the distal limit of the tear, resection and anastomosis of the damaged bowel should be performed. Access to structures in the caudal abdomen can be improved by the relaxed abdominal wall after parturition, making a large ventral midline incision, removing the large colon from the abdomen, and tilting the head of the surgery table forward. The small colon is transected at the distal limit of the damage. The compromised bowel is removed from the abdomen and is used as a conduit to relieve the impaction in the damaged section of the small colon and in the bowel oral to the damage. After a sufficient amount of ingesta has been removed to allow anastomosis, an end-to-end handsewn double inverting closure of the small colon is performed. This author prefers to use a Utrecht pattern using #000 monofilament absorbable suture. The mesentery that can be seen should be closed using a simple continuous pattern. Closure of the deeper mesentery is performed without visualization. Deep mesenteric closure is performed using absorbable suture material on a large-taper 1/2 circle needle in a simple continuous pattern. Closure of the mesentery close to the dorsal body wall is performed first. The knot is made either with a double strand of suture and looping the needle through the two strands after placing the first bites, or with a one-handed tie. By placing traction on the distal mesentery, both sides of the tear can be palpated in the abdomen and sutured using one hand. A moistened large laparotomy sponge positioned beneath the mesentery ensures that bites will grab the sponge (and be detected) rather than adjacent bowel. Before closure of the abdominal wall, the large colon should be emptied via pelvic flexure enterotomy and additional fluid added to its lumen to soften the remaining ingesta. This will reduce and soften the volume of feces that must immediately pass the anastomosis. An abdominal drain can be placed at surgery and used for abdominal lavage postoperatively.

Postoperatively, food is withheld until intestinal motility returns. Replacement fluids are given intravenously as necessary to maintain hydration. Feeding begins within 24–36 h after surgery, and low-residue processed feeds, green grass, and moistened hay are fed to soften ingesta and reduce straining. Mineral oil is administered via nasogastric tube for its laxative effects. Perioperative use of antimicrobials, such as penicillin (22,000 IU/kg IV qid) and gentamicin (6.6 mg/kg IV sid), is recommended, and metronidazole (15–20 mg/kg PO tid) can also be administered to prevent anaerobic bacterial growth. Postoperative complications are common after repair of small colon ruptures and include colic, colitis, peritonitis, and adhesions.

For mares in which an anastomosis cannot be performed, and the owners are reluctant to euthanize the horse, the distal small colon and rectum can be prolapsed through the rectum and oversewn. A permanent colostomy is then performed in the left flank, usually by a two-stage procedure wherein the colostomy is performed standing after the celiotomy. The standing procedure

allows for accurate positioning of the colostomy and avoids stressing the colostomy during recovery. This salvage procedure is aimed at mare survival to raise the foal, and subsequent breeding is not advised.

Diaphragmatic Hernia

Diaphragmatic hernias can occur after foaling and cause colic due to bowel entrapment (Auer et al., 1985). The diaphragm tears owing to high intra-abdominal pressure, and this can occur after normal foaling. Any part of the intestine can become entrapped through the tear. The most common clinical sign associated with diaphragmatic hernia is colic, but respiratory embarrassment also can occur. Diaphragmatic hernias are most often discovered during exploratory abdominal surgery, but can be identified preoperatively by ultrasound and thoracic radiographs. Surgical correction of the entrapment and closure of the tear are necessary. Closure of the diaphragmatic tear is usually very difficult owing to the size and location of the defect and the damage to the tissue margins. The poor quality of the tissue margins of a fresh tear makes recurrence of the hernia very likely either during recovery or soon thereafter. The use of a surgical mesh to support the closure is recommended.

Uterine Trauma

Uterine ruptures can occur before foaling, but most occur during parturition and become apparent in the immediate postpartum period. Clinical signs become evident within the first 24–48 h after foaling and consist of depression, low-grade fever, and often colic. Leukopenia is a common laboratory finding (Dolente et al., 2005). Some mares with uterine tears will hemorrhage sufficiently to show signs of anemia and, if the tear involves a major artery, hypovolemia will be the predominant clinical finding. The presumptive diagnosis of uterine tears that do not involve major vessels is made by clinical signs and results of abdominal paracentesis. Occasionally, uterine tears can be palpated per vaginum but most are too cranial to be detected. Abdominal fluid analysis will indicate peritonitis that worsens over time. Mares with uterine ruptures tend to have large volumes of abdominal fluid that can resemble lochia and increased concentrations of leukocytes (especially polymorphonuclear cells) and protein.

Although one study could not establish a significant survival difference (75%) between conservative and surgical treatment of uterine tears (Javsicas et al., 2010), other clinicians, including the author, believe that uterine tears are best treated by surgical correction (Hooper et al., 1993). Conservative therapy is not less expensive than surgical intervention, and in the author's experience requires a longer treatment period and results in a greater incidence of adhesions and subsequent colic episodes. A celiotomy allows the best inspection of the uterus, the most thorough peritoneal lavage, and accurate repair of the tear. Abdominal drains can also be placed for postoperative lavage. Some very caudal tears can be sutured from the endometrial side per vaginum, but surgery performed in this manner is done blindly and does not allow for abdominal lavage. Preoperative considerations should be directed at supporting the systemic circulation before anesthesia and may include administering whole blood or crystalloids. Mares that accumulate large volumes of fluid in the abdomen should have the fluid drained before anesthesia and circulating blood volume replaced. Surgical repair of the tears is straightforward, and they can be closed using either a single or double inverting suture pattern. Copious abdominal lavage is beneficial in reducing abdominal contamination, and an abdominal drain should be placed to facilitate abdominal lavage postoperatively. Postoperative care is directed at resolving the peritonitis and promoting uterine involution. Large-volume (10–20 L) abdominal lavage for 2–3 days after surgery can assist in physical removal of debris and has been shown to reduce adhesion formation in horses after colic surgery. Anti-inflammatory drugs and broad-spectrum antimicrobials are indicated to treat the peritonitis, and oxytocin (20 IU IM q 2 h) can be used to assist in uterine involution.

Conservative treatment of uterine tears is similar to postoperative care and relies on the administration of antimicrobials to treat the peritonitis while the uterine rent heals spontaneously. Standing abdominal lavage can be performed.

Urogenital Hemorrhage

Urogenital hemorrhage, which is a significant cause of referral of mares after parturition, tends to occur in older mares and is discovered soon after delivery (Dolente et al., 2005). The most common source of urogenital hemorrhage is the uterine arteries in the broad ligament, but hemorrhage can also originate from the myometrium and vagina. Definitive mechanical treatment (pressure or ligation) is rarely possible, and treatment is largely supportive.

Fatal rupture of the uterine, internal iliac, or internal pudendal arteries (Uneo et al., 2010) most commonly occurs in the peripartum period. Mares can show anxiety and depression in addition to colic usually within the first 24 h after foaling (Britt, 1997). Hemorrhage should be suspected if pale mucous membranes and subnormal rectal temperature are present. Other clinical signs seen are determined by the amount of blood lost, and whether the hemorrhage is confined to the broad ligament or uterine wall or escapes into the abdomen or uterine lumen. If the blood escapes from the broad ligament, the mare will become severely hypovolemic or can die acutely. If the arterial rupture is confined by the broad

ligament, the presenting clinical sign is abdominal pain. The hematoma can be palpated in the broad ligament and seromuscular surface of the uterus per rectum, and it is believed that stretching of these structures causes pain. Confirmation of the hematoma can be obtained using transrectal ultrasound, and intraperitoneal bleeding can be demonstrated by abdominal paracentesis. Mares with hemorrhage into the broad ligament predominantly show signs of pain, and treatment should be directed at relieving discomfort and reducing further hemorrhage.

Treatment of mares with blood loss into the peritoneal cavity or uterus can be challenging owing to the rapid, acute blood loss and is directed toward treating circulatory shock and controlling hemorrhage. Crystalloid fluids, colloids, plasma, and fresh blood can all be used to restore vascular volume. Hypertonic saline (1–2 L IV) can be used to increase the circulatory volume rapidly, but must be followed by administration of isotonic fluids. Overdiluting the blood is a concern, and it is important to note that initial determinations of packed-cell volume (PCV) are unreliable indicators of the extent of hemorrhage owing to the release of concentrated red blood cells from the spleen. The PCV and total plasma protein concentration should be monitored closely, as they can decrease dramatically during fluid therapy. If the PCV decreases to <15% and the plasma protein concentration decreases to <4.0 mg/dL, transfusion with 6–8 L of cross-matched fresh whole blood should be considered. If whole blood is unavailable, fresh-frozen plasma can be used as a source of clotting factors. Although there is a concern that restoring blood pressure can exacerbate hemorrhage, hypovolemia generally is the cause of death in mares with these ruptures, so careful restoration of fluid volume is indicated. The author believes that stall confinement, intravenous administration of plasma, and light sedation combined with analgesics are the core of therapy.

Additional medical therapies for hemorrhage include naloxone (0.8 mg IV) (Byars, 1990), aminocaproic acid (20 g in fluids IV as a loading dose followed by 10 g q 6 h) (Britt, 1997), flunixin meglumine (0.5–1 mg/kg IV bid), and butorphenol tartrate (0.03–0.07 mg/kg IV or IM prn). The opiate agonist/antagonists are used to treat hemorrhagic shock, the aminocaproic acid inhibits fibrinolysis, and the nonsteroidal anti-inflammatory drug reduces peritoneal inflammation and pain. These latter drugs should be used judiciously, as they can adversely affect platelet function and perhaps worsen hemorrhage.

Intravenous administration of 10% formalin (10 mL in 1 L or saline IV) has also been used in horses for the treatment of hemorrhage owing to its ability to decrease hemorrhage, and may have a place in the treatment of arterial ruptures associated with parturition.

Surgical therapy for uterine artery ruptures has been attempted through both flank and ventral midline approaches. Surgical therapy is complicated by the hypovolemia and the difficulty in isolating the bleeding vessels due to the extensive tearing usually present in the broad ligament. Surgical treatment has not shown any clear advantage over medical therapy. A survival rate of 84% has been reported for mares with periparturient hemorrhage (Arnold et al., 2008). A subsequent fertility rate of 49% has been documented for affected mares. Although recurrence of hemorrhage in one study was not known (Arnold et al., 2008), the author is aware of mares that have foaled without incident in subsequent pregnancies.

Urinary Bladder Rupture

Rupture of the urinary bladder is uncommon in the postfoaling mare, but should be considered when large volumes of fluid accumulate in the abdomen. Ultrasound will demonstrate the fluid, and measurement of creatinine in the abdominal fluid confirms the diagnosis if its concentration is twice that of serum creatinine. Cystoscopy of the bladder can allow visualization of the tear. Small urinary bladder tears can heal spontaneously if the bladder is kept empty using an indwelling urinary catheter, but larger tears require surgical correction. Surgical repair of urinary bladder tears can be attempted via a ventral midline incision, but this approach does not allow access to the middle and caudal aspects of the urinary bladder. Standing repair of urinary bladder tears can be performed by directly suturing the tear by inverting the bladder through the urethra (Stephen et al., 2009) or by retracting the bladder through a colpotomy (Rodgerson et al., 1996). Standing repair has the advantages of avoiding general anesthesia in a systemically compromised mare. Urine should be drained from the abdominal cavity in all cases of bladder rupture, and is a very important preoperative consideration when general anesthesia is performed.

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60

Colic from Alternative Systems: "False Colics"

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Colic is neither a specific disease nor a diagnosis, but simply represents the behavioral manifestations of abdominal pain. Although colic is generally associated with diseases of the gastrointestinal tract, conditions of other body systems can also cause pain that creates behavior similar to colic. These clinical signs can be difficult to differentiate from pain due to gastrointestinal disease. These conditions are commonly referred to as "false colics." A list of differential diagnoses of the commonest causes of "false colic" is given in Box 60.1.

Differentiation between "true" and "false" colics depends upon obtaining an accurate history and performing a careful physical examination, coupled where appropriate with further diagnostic procedures such as clinical pathology and diagnostic imaging. Although not invariably true, horses exhibiting colic caused by disorders of systems other than the gastrointestinal tract will often show mild to moderate pain (e.g., pawing the ground, lying in sternal or lateral recumbency for prolonged periods of time, or reluctance to move) or other additional signs, but rarely demonstrate signs of severe pain (e.g., rolling violently). However, distinguishing signs of mild to moderate abdominal pain from pain arising elsewhere can sometimes be a challenge to the veterinarian.

Pain Associated with the Female Reproductive Tract

Ovulation Pain

Occasionally, mares will demonstrate abdominal pain in association with ovulation during estrus (Schweizer, 2002). Affected mares typically demonstrate mild to moderate colic signs similar to those demonstrated by horses with acute, short-lived gas colic or spasmodic colic. Rectal palpation and/or ultrasonography confirms that the mare is in estrus, with a large follicle or recent ovulation present in one or both ovaries. The affected ovary is painful to palpation. It can often be difficult to be certain that colic in a mare identified during estrus is indeed caused by ovulation pain rather than a nonspecific or spasmodic colic. Further credibility is given to the diagnosis by demonstrating a low blood progesterone concentration at the time of the colic, and by documenting a cyclic recurrence of the colic episodes every 18–21 days, coinciding with the mare's estrous periods.

Affected mares usually respond well to treatment with analgesic doses of intravenous phenylbutazone or flunixin meglumine, and laxatives (e.g., mineral oil) to lessen the possible discomfort associated with defecation. Usually, the signs resolve immediately with medication or within a few hours if left unmedicated. Long-term solutions include treatment with supplemental progesterone (altrenogest 0.044 mg/kg PO sid) to prevent ovulation during the physiologic breeding season (i.e., spring and summer). In extreme cases, where chronic medication is not possible and the mare has no potential value as a broodmare, ovariectomy could be considered.

Postovulation Hematoma

Occasionally, the normal ovarian hemorrhage that occurs postovulation to form the corpus hemorrhagicum is excessive and a large hematoma forms. These structures can become fairly large (10–30 cm in diameter). The mare generally shows no clinical signs and continues to cycle normally as the hematoma slowly regresses over weeks to months (Bosu & Smith, 1993). Occasionally, however, affected mares may become acutely painful (Schweizer, 2002). Ovarian hematomas have been reported in at least one mare to cause recurrent colic. Management is aimed at alleviating the mare's pain during the acute episode (as for ovulation pain). If a recurrent problem arises, the use of altrenogest as

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Box 60.1 Common causes of "false colic"

Female reproductive tract
- Ovulation
- Postovulation hematoma
- Granulosa cell tumor
- Other ovarian tumors
- Vaginal (breeding) injuries
- Pregnancy
- Uterine torsion
- Dorsoretroflexion of the uterus and abortion
- Dystocia
- Arterial rupture and uterine hematoma
- Third-stage labor
- Perineal injuries
- Uterine rupture
- Inversion of the uterine horn
- Uterine marbles
- Other uterine disorders

Male reproductive tract
- Orchitis
- Testicular torsion
- Thrombosis of the spermatic cord vessels
- Preputial myiasis
- Balanoposthitis

Urinary tract
- Cystic calculi
- Renal calculi
- Ureteral calculi
- Urethral calculi
- Pyelonephritis
- Cystitis
- Ruptured bladder

Liver
- Acute hepatitis/hepatic failure
- Cholangiohepatitis
- Cholelithiasis

Pancreas
- Acute pancreatitis
- Chronic pancreatic disease

Spleen
- Splenic abscess
- Splenomegaly

Respiratory tract
- Pleuritis
- Pleuropneumonia

Cardiovascular system
- Aortoiliac thrombosis
- Aortic rupture
- Acute hemorrhage
- Myocardial infarction
- Pericarditis
- Aortic rupture and aortopulmonary fistulation
- Congestive heart failure

Musculoskeletal system
- Laminitis
- Acute exertional rhabdomyolysis
- Atypical myopathy
- Rupture of the prepubic tendon and ventral hernias

Nervous system
- Tetanus
- Botulism
- Seizures
- Equine motor neuron disease

Metabolic diseases
- Primary hyperammonemia
- Hypocalcemia (lactation tetany)

previously described to prevent ovulation during the physiologic breeding season may be considered.

Granulosa Cell Tumor

The granulosa cell tumor is the most common ovarian tumor in the mare. These tumors are usually benign, but often hormonally active. Clinical signs vary, depending on the hormonal pattern of the tumor, but commonly include stallion-like behavior, nymphomania (prolonged periods of estrus behavior or shortened inter-estrus periods), or anestrus. Occasionally, the presence of a large tumor may result in intermittent colic, especially associated with exercise (Sherlock et al., 2016). Some affected mares may have a history of reluctance to train and/or poor performance. It is likely that the pain associated with the enlarged ovary is the result of tension in the broad ligaments as the tumor moves with the mare's movements. Rectal palpation typically reveals the presence of one (or both) enlarged ovary(ies) that has lost its normal bean-shape, and a small, inactive contralateral ovary. Most granulosa cell tumors are 10–20 cm in diameter (although they may be larger). Ultrasonography can be helpful, although the ultrasonographic appearance of granulose cell tumors is variable depending on their structure and composition. They may be uniformly echogenic, heterogeneous with a honeycomb appearance, or largely hypoechoic/anechoic. Treatment is ovariectomy of the affected ovary. If surgery is not performed, the owner should be warned of the mare's possible future discomfort, and a small risk of hemorrhage from ruptured ovarian ligaments or the ovarian capsule. Metastasis is extremely rare.

Other Ovarian Tumors

Other ovarian tumors occur less frequently than granulosa cell tumors, and include teratomas (Catone et al.,

2004), cystadenoma and cystadenocarcinoma (Held et al., 1982; Hinrichs et al., 1989; Son et al., 2005), dysgerminoma (Meuten & Rendano, 1978; Chandra et al., 1998; Gehlen et al., 2006; Harland et al., 2009), thecoma (Raoofi et al., 2006; Azizi et al., 2014), lymphoma (Canisso et al., 2013), leiomyoma and fibroleiomyoma (Carstanjen et al., 2009; Daniel et al., 2015), and adenocarcinoma (Pauwels et al., 2012). Among other signs, these tumors may present with signs of chronic or recurrent abdominal pain.

Vaginal (Breeding) Injuries

Trauma to the vagina can result from breeding, especially in situations where the stallion's penis is long relative to the mare's vagina, or the stallion is excessively forceful and vigorous during intromission and thrusting (LeBlanc, 1999). The severity of the damage can vary from bruising to lacerations to rupture, where the stallion's penis penetrates into the peritoneal cavity through the cranial vaginal wall. Such injuries may be suspected when fresh blood is noted on the stallion's penis or draining from the vulva of the mare immediately following dismount. These findings warrant an immediate manual vaginal examination of the mare to ascertain the degree of injury. Sexual rest of the mare is indicated even if the damage is considered to be minor, since a full rupture may occur if the mare is covered again during that estrus period. Colic signs may be mild to severe, depending on the degree of damage, and are sometimes accompanied by tenesmus. Alternatively, the mare may develop signs of depression and endotoxic shock following the traumatic cover. A potentially severe peritonitis may occur after gross contamination of the peritoneal cavity by the stallion's penis, his ejaculate, or vaginal flora. Acute and severe colic signs may also develop if a portion of the mare's viscera becomes entrapped through the vaginal rent. Eventration of bowel or the urinary bladder may also occur (Richardson & Reid, 1985).

Treatment of minor injuries to the vagina includes sexual rest (30–60 days), broad-spectrum antibiotics, and a Caslick procedure to prevent further peritoneal contamination via possible pneumovagina. The rent in the vagina is usually small and dorsal to the cervix and is left to heal by secondary intention. The mare should be prevented from lying down for the first few days following the injury to reduce the risk of secondary herniation of viscera. If the rent is in the vaginal floor or if it is excessively large, an attempt to suture and close the defect should be made.

Pregnancy

See Chapter 59. Many pregnant mares show signs of abdominal pain intermittently during the course of their gestation (Frazer et al., 2002). These episodes are typically very brief and mild. Such bouts of discomfort may be attributed to vigorous movements of the foal; mild stretching of the broad ligaments upon movement of the mare or the foal, or mild digestive upsets (Schweizer, 2002). In most instances the signs resolve spontaneously.

Mares in late gestation may also be found lying down and groaning, which can be confused with colic. The large size of the gravid uterus in such late-term mares can put pressure on the diaphragm that is increased when they lie down, thereby causing some difficulty in breathing and a groaning noise.

Uterine Torsion

See Chapter 59.

Dorsoretroflexion of the Uterus and Abortion

Dorsoretroflexion of the uterus is a rare cause of colic in the gravid mare (typically occurring between 7.5 and 11 months of gestation) (Schweizer, 2002). Affected mares present with acute, moderate to severe colic signs, abdominal straining, constipation, and swelling of the vulva and perineal region. Administration of analgesics is typically ineffective in controlling the mare's pain. Diagnosis is made by rectal palpation; a tense uterus is felt within the pelvis with the fetal head and limbs in a normal birth presentation overlying and obscuring the cervix. Vaginal examination is required to differentiate this condition from abortion. In the former case, the cervix will be found to be closed in the cranial extent of the vaginal canal and ventral to the fetus, which is palpable dorsal to the vagina through the vaginal wall. In the aborting mare, the cervix will be dilated and the fetus and its membranes will be readily palpable within the vaginal canal through the dilated cervix.

Treatment of dosoretroflexion of the uterus includes the administration of uterine relaxants (200 mg IM of isoxsuprine or 200 µg slow IV or IM of clenbuterol once or repeatedly over 3–6 h intervals for 1–2 days), and repelling the relaxed uterus containing the fetus back into the abdomen via careful rectal manipulation. Resolution of colic signs usually occurs within 15 min of administration of the uterine relaxants, and it has been reported that restricting the mare's food intake and regular hand walking help to return the mare to normal within a few days.

Uterine Marbles

Insertion of marbles into the uterus of mares has been used to suppress estrous cycles. In one reported case (Freeman & Lyle, 2015), uterine marbles were considered to be the cause of recurrent colic, which resolved completely on removal of the marbles.

Pneumovagina

Damage to vestibular fold secondary to trauma of parturition may result in temporary disruption of the normal seal between the vestibule and vagina, allowing an inrush

of air into the noninvoluted uterus. The vestibule and vagina may function as a one-way valve, allowing air to pass into the uterus but not allowing it to leave, resulting in sufficient accumulation of air to cause uterine distention and the consequent activation of stretch receptors in the uterine wall (Livesey et al., 2008).

Pyometra

Mares with pyometra often show few or no systemic signs; however, some affected horses may demonstrate low-grade chronic or acute colic. The uterus may accumulate up to 60 L of exudate. Mares with pyometra frequently have a fibrosed or occluded cervix (Arnold et al., 2015).

Arterial Rupture

See Chapter 59.

Stages of Labor

See also Chapter 59. During stage I labor, the mare may act restless and show signs of colic, such as getting up and down and flank watching. These signs can be due to gastrointestinal disease, so an examination to make sure the behavior is due to labor is indicated. Stage III labor (passage of the placenta) normally causes some degree of discomfort and pain to the mare. The signs associated with the uterine contractions that occur at this time range from mild discomfort (occasional kicking at belly, stretching out and posturing as if to urinate, lying down quietly in sternal recumbency, flank watching, etc.) to more dramatic bouts of pain (agitation, frequently getting up and down, rolling, etc.). The majority of mares seem to pass their placentas within 30–60 min of the foal's delivery, but it is not unusual for signs of discomfort to persist (usually for no more than an additional hour) after passage of the placenta as uterine contractions continue as the mare's uterus begins to involute. Hand walking to provide the mare with relief and distraction from her discomfort may be helpful, but analgesic treatment is rarely necessary. Typically throughout these episodes, the mare's vital signs are stable, and she remains bright, with a good appetite and interest in her foal.

Perineal Injuries

Perineal damage (first-, second-, and third-degree perineal lacerations, vestibular bruising, hematomas, etc.) occurring during parturition can lead to a reluctance to defecate, secondary constipation, and low-grade colic. Anti-inflammatory drugs (phenylbutazone or flunixin meglumine) and also local treatment with topical anti-inflammatory ointments are indicated to relieve pain and swelling of tissues. Administration of oral laxatives (mineral oil) and laxative feeds (bran mashes, grass, etc.) may help to soften the feces and make their passage less painful to the mare so that she is more willing to defecate.

Uterine Rupture

See Chapter 59.

Inversion of a Uterine Horn and Uterine Prolapse

Inversion of a uterine horn (intussusception) during the first few hours after foaling frequently results in acute pain that is unresponsive to low-dose analgesics. Pain is the result of the ovary and tip of one horn becoming inverted and entrapped within the uterine lumen. The myometrium proceeds to spasm, resulting in an intussuscepted ring. In response, many mares will begin to strain and the condition may progress to a complete prolapse of the uterus through the vulvar lips if left uncorrected (Perkins & Frazer, 1994). Invagination of a uterine horn most commonly occurs in conjunction with a retained placenta, and may occur secondary to the weight of the placenta pulling on the horn in which it is retained, and/or being pulled on during the course of attempts at manual removal. Dystocia has also been sighted as having a predisposing association with uterine prolapse.

Diagnosis of an inverted uterine horn is based on a rectal palpation finding of a blunted uterine horn with a tense mesovarium disappearing into the center of the blunted tip (Asbury, 1993; Vivrette, 1997; Frazer, 2002). In minor intussusceptions, the ovary may not yet be entrapped and is still palpable at the tip of the blunted horn. Palpation of this area is often painful to the mare and sedation is recommended. The inverted horn can also often be palpated per vaginum within the lumen of the uterus.

If possible, any retained placenta should be gently removed if it will come away readily so as to decrease the tension on the horn. However, if it cannot be easily detached, it may be preferable to cut off the majority of the exteriorized hanging placenta at a level just below the vulva so as to decrease the strain on the invaginating horn. Direct treatment and correction of the invaginated uterine horn include controlling the mare's straining and pain (sedation, epidural anesthesia), manual reduction of the inverted horn per vaginum (may require the use of uterine relaxants such as acepromazine and clenbuterol), and full replacement of the previously invaginated horn and ovary to their normal position (manually or using intrauterine sterile saline to distend the uterine horns). Supportive therapy in the form of intravenous fluids, nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics, tetanus prophylaxis, and so on may also be indicated (especially in cases complicated by retained

placenta). Careful use of low-dose oxytocin (10–20 IU IM) once the horn has been returned fully to its normal position may also aid in rapid normal involution and prevention of a recurrence.

If the invaginated tip is not identified and left in place, necrosis may ensue. This will usually be associated with a decrease in the mare's discomfort, but with the development of septic peritonitis. Surgical intervention is necessary in such cases.

Pain Associated with the Male Reproductive Tract

Orchitis

Orchitis is an inflammation of the testis, characterized by a painful, warm swelling of the affected testicle (DeVries, 1992). It is usually traumatic in origin, resulting in sterile inflammation, and may be uni- or bilateral. Infectious orchitis is uncommon in the stallion, but may occur as a result of ascending infection (e.g., *Klebsiella pneumoniae*) or localization of systemic disease (e.g., *Streptococcus equi*). Penetrating wounds can result in localized swelling and abscessation. The affected testicle often hot, painful, and very tense due to swelling that is confined by the tunica albuginea. Superimposed edematous swelling in the scrotal skin makes palpation difficult. The stallion is likely to be febrile and may demonstrate colic-like signs of pain. Systemic antimicrobials, anti-inflammatory medication, and hydrotherapy are indicated, but often unilateral orchiectomy is necessary to minimize damage to the contralateral testis.

Testicular Torsion (Torsion of the Spermatic Cord)

Acute testicular torsion is rare (DeVries, 1992; Varner & Schumacher, 1999). The condition is caused by torsion of the spermatic cord, and results in signs similar to acute orchitis (severe colic, scrotal swelling, mild pyrexia). The condition is usually unilateral, but may be bilateral. The testicle is usually rotated by 180°, but can be rotated by 360° or more, with occlusion of spermatic vessels. The clinical signs depend on the severity of the torsion. In many cases, 180° torsions are subclinical, or the stallion may demonstrate mild, intermittent scrotal pain that becomes most pronounced during exercise. In contrast, 360° torsions, which are usually unilateral and generally cause acute severe testicular pain with scrotal edema and hemorrhage. Persistent colic and a stilted hind leg gait are observed. Obstruction of the venous drainage (pampiniform plexus) by a 360° torsion leads to hemorrhagic infarction of the testicle and severe edema. Arterial obstruction leads to ischemic necrosis of all ipsilateral scrotal contents located distal to the site of torsion.

Diagnosis of a 180° spermatic cord torsion is achieved by palpating the cauda epididymus and scrotal ligament within the cranial rather than the caudal scrotum. With a 360° torsion, these structures are located in their correct (caudal) location, but there is acute scrotal pain and unilateral swelling. The spermatic cord is thickened. The condition must be differentiated from inguinal or scrotal hernia, and palpation of the vaginal ring should be completed per rectum to establish the presence or absence of herniated intestine. Unilateral castration is indicated in most cases due to ischemic damage to the testis.

Thrombosis of the Spermatic Cord Vessels

This is a rare disease associated with thrombosis of vessels within the pampiniform plexus and the testicular artery (Horney & Milne, 1964). The cause has not been established. The clinical signs are similar to those of 360° torsion of the spermatic cord. Definitive diagnosis is only achieved during exploratory surgery. Unilateral castration with excision of the cord proximal to the site of the lesion is required.

Balanoposthitis and Preputial Myiasis

Severe balanoposthitis and preputial myiasis ("fly strike") can cause pruritus/irritation resulting in the horse kicking at his abdomen, thereby resembling colic. This behavior may not be ameliorated by the administration of analgesic drugs. Careful examination of the prepuce of male horses showing this behavior should be undertaken.

Pain Associated with the Urinary Tract

Urolithiasis

Most cases of obstructive urinary tract diseases in horses are caused by urolithiasis (DeBowes et al., 1984; Ford, 1992). Incomplete obstruction of the urinary tract can cause dysuria, incontinence, and mild abdominal pain, whereas complete urinary obstruction results in moderate to severe pain.

Nephroliths develop around a nidus associated with a variety of renal diseases, including pyelonephritis and renal papillary necrosis. Although nephrolithiasis and ureterolithiasis are painful conditions in humans, horses with these conditions often remain asymptomatic until bilateral obstructive disease leads to the development of chronic renal failure (Ehnen et al., 1990). However, specific signs of upper urinary obstructive disease (i.e., colic, stranguria, hematuria) may be present in some cases. Diagnosis is based on rectal palpation, diagnostic ultrasonography, and clinical pathology.

Cystic calculi are the commonest recognized form of urolithiasis in the horse (DeBowes et al., 1984; Laverty et al., 1992). The commonest type of equine calculus is the spherical stone composed of calcium carbonate, with either a speculated or smooth surface. Clinical signs may include hematuria, stranguria, pollakuria, urinary incontinence, and low-grade recurrent abdominal pain. Hematuria may be most obvious after exercise. Diagnosis is achieved by palpation and diagnostic ultrasonography of the bladder per rectum. Cystoscopy can also be helpful. Treatment involves surgical removal.

Urethral calculi are most commonly seen in male horses. These calculi probably originate in the bladder, and pass down the urethra until they lodge where the urethra narrows as it passes over the ischial arch. In some cases they may lodge further distally in the penile urethra. Complete urinary obstruction results, which causes signs of persistent colic with frequent straining and posturing to urinate. Rectal palpation reveals a distended, turgid bladder. The diagnosis is confirmed by passage or a urinary catheter or endoscope, which becomes obstructed by the urolith. Treatment of calculi lodged at the ischial arch involves removal via a perineal urethrotomy. Calculi lodged in the distal urethra can sometimes be grasped with forceps and crushed prior to removal. In some cases, surgical removal of the stone under general anesthesia is required.

If the bladder ruptures consequent to urethral obstruction by a calculus, signs of colic will disappear, but be replaced by progressive depression and anorexia due to postrenal acute renal failure and peritonitis (Laverty et al., 1992).

Cystitis

Cystitis is uncommon in horses (Boy, 1992). It most often occurs secondary to conditions that cause urine stasis or urinary tract trauma. Cystitis is more common in females than males, probably owing to the shorter urethral length in females. Predisposing conditions include trauma sustained at parturition, neurologic dysfunction of the bladder or urethra, and cystic calculi. Cystitis associated with phenylbutazone administration has also been reported (Aleman et al., 2011). The clinical signs include frequent urination, pollakiuria, tenesmus, and abdominal pain. Diagnosis is achieved by a combination of rectal palpation, diagnostic ultrasonography, cystoscopy, and urinalysis. Treatment involves the use of appropriate antibacterial drugs and treatment of the predisposing cause.

Pyelonephritis

Inflammation of the renal parenchyma, calyces, and pelvis due to bacterial infection (i.e., pyelonephritis) is rare in the horse (Boy, 1992). It has been described in association with urolithiasis, recurrent cystitis, and bladder paralysis. Concurrent nephrolithiasis or ureterolithiasis may be present. Affected horses generally present with signs of fever, depression, low-grade abdominal pain, inappetence, and weight loss. Hematuria or pyuria may be seen, but there is no stranguria or pollakuria unless there is concurrent lower urinary tract infection. Diagnosis is achieved by a combination of rectal palpation, ultrasonography, urinalysis, ureteral catheterization, bacteriology, and hematology and serum biochemistry. Treatment involves prolonged courses of appropriate antimicrobials and treatment of any underlying disease. In selected cases, unilateral nephrectomy may be considered.

Bladder Rupture

See also Chapter 59. Rupture of the urinary bladder is rare in adult horses, but has been associated with urethral obstruction (especially males) and foaling trauma in mares.

Ruptured bladder and uroperitoneum are more commonly recognized in neonatal foals (Hackett, 1984; Richardson, 1985). Although there are several different possible sites of urine leakage leading to uroperitoneum, including the urachus, ureter, and urethra, the commonest site is the bladder. Colts and fillies can be affected, but colts are more commonly affected (Hackett, 1984). The pathogenesis of uroperitoneum includes increased abdominal pressure during delivery, external trauma, infection within the urachus, or necrotic cystitis. Tears or defects within the bladder occur most commonly on the dorsal aspect.

Foals that develop uroperitoneum may not show clinical signs until 2–3 days of age. Clinical signs include progressive abdominal distention, tachycardia, tachypnea, depression, low-grade colic, and decreased interest in nursing. Although many foals will have stranguria or oliguria, some affected foals will appear to urinate normally.

Diagnosis of uroperitoneum is made by a combination of physical examination, diagnostic ultrasonography, abdominal paracentesis, and clinical pathology. Percutaneous ultrasonography over the caudoventral abdomen usually shows excessive peritoneal fluid; a defect in the bladder wall may also sometimes be seen. Serum electrolyte abnormalities classically include hyponatremia, hypochloremia, hyperkalemia, and azotemia. The peritoneal fluid should be evaluated by cytology (calcium carbonate crystals in the peritoneal fluid are a strong indication of bladder rupture), and comparison of the creatinine values from serum and abdominal fluid. The diagnosis can be confirmed when the creatinine concentration in the abdominal fluid is twice that in the serum.

Treatment of foals with uroperitoneum almost always requires surgical repair of the defect. However, stabilization

of the electrolyte and acid–base abnormalities must be performed prior to surgery to prevent anesthetic complications or even death due to high levels of potassium. Medical stabilization should include drainage of the excessive abdominal fluid, through either a teat cannula or small chest trocar. Intravenous fluids should be administered to correct hypovolemia and electrolyte abnormalities. Normal saline can be administered intravenously along with dextrose to combat hypoglycemia and promote movement of potassium intracellularly. Severe or nonresponsive hyperkalemia can also be treated with intravenous calcium or subcutaneous insulin.

Liver Diseases

Cholangiohepatitis, cholelithiasis, hepatic encephalopathy, and primary hyperammonemia may all present with signs mimicking colic. These diseases are described in detail in Chapter 51.

The Pancreas

Acute Pancreatitis

Acute pancreatitis is a rare cause of severe abdominal pain in horses (McClure, 1987). The cause is uncertain, and antemortem diagnosis is rarely made because the clinical signs mimic other gastrointestinal diseases producing acute colic (especially small intestinal strangulating obstructions and anterior enteritis). The pancreas is not easily visualized during routine surgical exploration of the abdomen, and may be overlooked at necropsy, especially if gastric rupture has occurred.

In many cases, the precise cause of acute pancreatitis remains undetermined. However, it can sometimes occur in association with hyperlipemia. It has been speculated that excess lipid is deposited in and around the pancreas in hyperlipemia. This lipid is subsequently hydrolyzed by pancreatic lipase, and released as free fatty acids. Free (unbound to albumin) fatty acids are cytotoxic and when the albumin binding capacity is exceeded pancreatic vascular injury occurs, resulting in necrotizing pancreatitis.

The clinical signs of acute pancreatitis in adult horses include severe abdominal pain, hypovolemic shock, tachycardia, tachypnea, pronged capillary refill time, sweating, cold extremities, and gastric distention with voluminous nasogastric reflux. Specific diagnostic features are not evident from the clinical signs or clinical pathology findings. Abdominal sounds are variable but often reduced or absent. No specific abnormalities are detected by rectal examination. Peritoneal fluid may be serosanguinous or hemorrhagic.

Most affected horses appear to die within 24 h. No specific therapy apart from symptomatic treatment for abdominal pain and hypovolemic shock has been described.

Chronic Pancreatic Disease and Insulin-dependent Diabetes Mellitus

Insulin-dependent diabetes mellitus is very rare in horses. However, adult horses and ponies may develop signs of exocrine pancreatic insufficiency, with or without associated insulin-dependent diabetes mellitus, following destruction of the pancreas by diseases, such as neoplasia (pancreatic adenocarcinoma) and chronic pancreatic necrosis. Chronic eosinophilic pancreatitis has been reported, and is assumed to be caused by parasite (*Strongylus equinus* and *S. edentatus*) migration through the gland (Bulgin & Anderson, 1983; Hamir, 1987).

The clinical signs associated with chronic pancreatic disease may include chronic weight loss despite good or increased appetite, depression, inappetence, intermittent colic, persistent or recurrent pyrexia, and jaundice. If there is concurrent insulin-dependent diabetes mellitus, polyuria and polydipsia may also be observed.

Clinical pathologic abnormalities are inconsistent, but may include the following: raised serum amylase and lipase concentrations, raised peritoneal fluid amylase levels, hypocalcemia, hyperglycemia, glucosuria, hypertriglyceridemia, raised serum gamma-glutamyl transferase (GGT), and hyperbilirubinemia. Reference values for amylase and lipase activities should be established by each laboratory (Parry & Crisman, 1991). Serum amylase activity for normal horses usually ranges from 14 to 35 U/L, and values <50 U/L are generally considered to be normal. Peritoneal fluid amylase activity is usually slightly lower than serum activity. Serum lipase activity is normally <87 U/L.

Interpretation of pancreatic enzyme activity in horses can be difficult because the enzymes are not exclusively of pancreatic origin, and may be released from other tissues such as the gastrointestinal tract. In addition, renal disease may result in decreased excretion of amylase and therefore lead to elevated serum levels. In the diagnosis of acute pancreatitis, secondary damage to the pancreas from hypovolemia or reflux of duodenal contents up the pancreatic duct can result in release of pancreatic enzymes into the circulation. Confirmation of chronic pancreatitis or pancreatic carcinoma is generally made either at exploratory laparotomy or at postmortem examination.

The Spleen

Primary diseases affecting the equine spleen are rare. The commonest clinical disease that involves the spleen is renosplenic (nephrosplenic) entrapment of the large colon (left dorsal displacement of the colon).

Other reported splenic conditions include splenic abscess and hematoma, splenic rupture, and neoplasia.

Splenic Abscess

Splenic abscesses may be confined to the spleen or arise in association with other abdominal abscesses (Rumbaugh et al., 1978). Such abscesses usually cause signs of weight loss, inappetence, fever, and variable abdominal pain. Commonly identified clinicopathologic abnormalities include leukocytosis, neutrophilia, hyperfibrinogenemia, and hyperglobulinemia. Total bilirubin levels may be elevated because of inappetence. Peritoneal fluid often shows elevated total protein concentration and an increased nucleated cell count with an increased percentage of neutrophils. Free or intracellular bacteria may also be observed. Peritoneal fluid should be submitted for bacteriologic culture; commonly identified organisms include *Streptococcus equi* subsp. *equi*, *Streptococcus equi* subsp. *zooepidemicus*, *Salmonella* spp., *Clostridium* spp., *Bacteroides* spp., and *Corynebacterium pseudotuberculosis* (the last is confined to specific geographic locations such as the western United States).

Splenic abscesses may be palpable per rectum and may be visible by ultrasonography. They may also be visualized using laparoscopy. Treatment may include long-term antibiotic therapy (based on the results of culture if possible), drainage of the abscess (surgically or using ultrasound guidance), or splenectomy. Splenectomy is usually carried out via a flank incision involving resection of the 16th or 17th rib; this approach often involves penetration of the diaphragm and the thoracic cavity (Wilson & Constantinescu, 1992).

Hemoperitoneum and Splenic Rupture

Splenic rupture is rare in horses. It may arise secondary to direct trauma (e.g., kicks or vehicular accidents) or may be associated with a primary disease involving the spleen, such as hematoma or neoplasia. Most of the reported cases have involved rupture of the visceral surface of the spleen. In many cases, the affected horse will be found dead as a result of exsanguination. Clinical signs in less severe cases include signs of hypovolemic shock (weakness, trembling, sweating, dyspnea, pale mucous membranes, tachycardia) and colic. Diagnosis is aided by the identification of hemoabdomen by abdominal ultrasonography and abdominocentesis. Treatment is supportive (i.e., therapy of hemorrhagic and hypovolemic shock), followed, if appropriate, by splenectomy. Hemoperitoneum of other causes may cause signs of abdominal pain (Dechant et al., 2006).

Splenic Haematoma

Like splenic rupture, splenic hematoma is uncommon in horses, although transient hematomas secondary to trauma may be present subclinically. Large hematomas may be associated with abdominal pain. Diagnosis may be achieved by ultrasonography, rectal palpation, or laparoscopy. Treatment is supportive care.

Pain Associated with the Respiratory Tract

Pleuritis and Pleuropneumonia

Primary pleuritis (i.e., pleuritis unassociated with underlying pulmonary disease) is unusual, but may arise from penetrating thoracic trauma. More commonly, pleuropneumonia develops secondary to bacterial pneumonia, with extension of the infection into the pleural space (Rush & Mair, 2004). The history of horses with pleuropneumonia often includes events or factors that suppress pulmonary defense mechanisms (such as viral respiratory infection, long-distance transportation, general anesthesia, and strenuous exercise) (Chaffin & Carter, 1993).

Horses with bacterial pleuropneumonia usually present with fever, depression, lethargy, and inappetence. Many horses demonstrate signs of pleural pain (pleurodynia), respiratory difficulty, and endotoxemia. Horses with pleural pain have an anxious facial expression, stand with their elbows abducted, and are reluctant to move, cough, or lie down. Affected horses walk with a stiff, stilted gait, and some will grunt in response to thoracic pressure, auscultation, or percussion. These signs may be mistaken for signs of abdominal pain. The severity of respiratory difficulty depends on the volume of effusion and the extent of pulmonary consolidation. In most cases, the respiratory pattern is characterized by rapid, shallow respiration due to pleural pain and restricted pulmonary expansion by pleural effusion. A plaque of sternal edema is observed in horses with a large volume of pleural effusion.

Auscultation of horses with pleuropneumonia reveals a lack of breath sounds in the ventral lung fields, and abnormal lung sounds (often crackles) in dorsal lung fields. Cardiac sounds may be muffled or absent, or may radiate over a wider area. Although uncommon, pleural friction rubs are most prominent at end inspiration and early expiration, and are detected in horses with peracute disease (prior to development of effusion) or after thoracic drainage. Identification of dull areas on thoracic percussion indicates pulmonary consolidation, abscessation, or pleural effusion. Horses with pleural effusion typically have a horizontal fluid line, below which all pulmonary fields are dull, and above which resonant sounds are produced. Horses with pleurodynia object to this procedure, and may grunt in response to examination.

Clinicopathologic abnormalities will vary with the stage and severity of disease. In horses with peracute

pleuropneumonia, laboratory findings will reflect bacterial sepsis or endotoxemia, and will include abnormalities such as leukopenia, neutropenia, left shift, hemoconcentration, and azotemia. Horses with more stable disease will have leukocytosis, mature neutrophilia, hyperfibrinogenemia, hyperglobulinemia, hypoalbuminemia, and anemia.

Ultrasound examination can identify gas echoes, fibrin, loculation, and fluid within the pleural space. Transudative pleural fluid (peracute pleuropneumonia, neoplastic effusion) appears anechoic, whereas more cellular exudate appears echogenic. Ultrasonographic evidence of large areas of pulmonary consolidation, in conjunction with serosanguinous suppurative pleural effusion, is consistent with pulmonary infarction and necrotizing pneumonia (Carr et al., 1997).

Thoracocentesis is performed for diagnostic and therapeutic purposes in horses with pleuropneumonia. Malodorous pleural fluid is associated with necrotic tissue and anaerobic infection, and indicates a more guarded prognosis. Serosanguinous pleural fluid has been observed in horses with necrotizing pneumonia, pulmonary infarction, thoracic trauma, and thoracic neoplasia. Thoracocentesis samples are submitted for cytologic evaluation, anaerobic/aerobic bacterial culture, and sensitivity, Gram stain, and biochemical analysis. Polymicrobial and mixed anaerobic–aerobic infections are common. Aerobic bacteria are isolated from more than 90% of the cases, and the most common organisms are *Streptococcus zooepidemicus*, *Escherichia coli*, *Actinobacillus* spp., *Klebsiella* spp., *Enterobacter* spp., *Staphylococcus aureus*, and *Pasteurella* spp. (Chaffin & Carter, 1993). Anaerobic bacteria are isolated from 40–70% of horses with pleuropneumonia, and include *Bacteroides* spp., *Clostridium* spp., *Peptostreptococcus* spp., and *Fusobacterium* spp.

Medical therapy for bacterial pleuropneumonia requires broad-spectrum antimicrobial therapy, anti-inflammatory drugs, and supportive care (Carr et al., 1997). The combination of penicillin, gentamicin, and metronidazole is often used for initial therapy. The antimicrobial regimen may require adjustment as the results of bacterial culture and sensitivity become available. Intravenous antibiotics are preferable in the early stages of treatment (14–28 days) to ensure adequate concentrations. Oral antimicrobial therapy can be instituted as the horse becomes more stable and production of pleural fluid subsides. Thoracic drainage using repeated thoracocentesis or indwelling thoracic drains is helpful in most cases.

Some horses fail to clear the pleural infection over the course of weeks to months despite antimicrobial therapy and drainage via indwelling chest tubes. Thoracotomy allows manual removal of organized fibrinous material and necrotic lung, and is sometimes needed in chronic cases that fail to respond to more conservative treatment. There are two options for creating a thoracotomy in horses with pleuropneumonia: a rib resection or dissection through the intercostal space. The intercostal approach heals more quickly and usually allows adequate drainage, but manual access to the thoracic cavity is limited and resection of necrotic lung is difficult. Rib resection creates a larger defect for more effective drainage and debridement, but heals more slowly, is more painful after surgery, and may develop a chronic draining tract. Both procedures are performed in standing, sedated horses with local analgesia. Postoperatively, debris can be removed from the pleural cavity by manual debridement and lavage (sterile, isotonic fluids) on a daily basis. After adequate granulation of the incision (7–10 days), hydrotherapy of the wound and thorax can be performed with tap water.

Pain Associated with Cardiovascular Disease

Pericarditis

Pericarditis is an inflammatory syndrome involving the parietal and visceral layers of the pericardial sac. There are three general forms of pericarditis, effusive, fibrinous, and constrictive, although various combinations of these forms also occur. Effusive pericarditis is characterized by accumulation of fluid within the pericardial sac. Fibrinous pericarditis develops when there is fibrin deposition and often accompanies fluid accumulation. If fibrin within the pericardial sac matures to fibrous tissue or progresses to fibrosis of pericardial or myocardial tissue, constrictive pericarditis may result. Infectious causes of pericarditis include bacterial and viral agents. Diagnosis is achieved by ultrasonographic evaluation of the heart (Reimer, 2013). Although not common, horses with pericarditis may present with signs of colic/pain due to pericardial pain or concomitant pleurodynia (Dill et al., 1982; Perkins et al., 2004).

Arterial Rupture

Rupture of the aorta is uncommon, but has been associated with an aneurism/rupture and aortopulmonary fistula, and aortic ring rupture (Physick-Sheard, 1999). These vascular accidents may result in sudden death or, less commonly, signs of acute thoracic pain.

Aortic Rupture and Aortopulmonary Fistulation in the Friesian Horse

A form of aortic rupture, located proximal to the ligamentum arteriosum, has been reported in Friesian horses. Some cases are found dead without prior signs, but in others signs such as recurrent colic, peripheral edema, and sustained tachycardia may be present for several weeks prior to cardiac failure (Ploeg et al., 2013).

Aortoiliac Thrombosis

Thrombosis of the terminal aorta and its major branches (the iliac arteries) is an unusual condition of unknown etiology that can result in exercise-associated pain and lameness/stiffness that disappears with rest (Azzie, 1969; Maxie & Physick-Sheard, 1985). The disease is associated with the development of a thrombus at the aortic quadrification with secondary embolization of the vascular tree of the hind limbs. The clinical signs are variable, and the course of the condition can be chronic, with initial signs of vague hind leg lameness. As larger vessels become involved, more severe clinical signs occur, including exercise-induced stiffness, weakness, and pain. Signs are usually asymmetric and resolve with rest. Clinical examination immediately after exercise may reveal a cold limb, but this sign is inconsistent. Occasionally, horses will present with an acute and severe problem with marked pain, sweating, and severe lameness. Diagnosis is aided by palpation of the peripheral pulses, rectal palpation, and ultrasonography.

Congestive Heart Failure

Chronic hepatic and mesenteric congestion and edema have occasionally been reported as causes of chronic colic (Wijnberg, 1988).

Pain Associated with the Musculoskeletal System

Severe musculoskeletal pain, such as may occur with acute laminitis, exertional rhabdomyolysis and atypical myopathy (summer pasture-associated myopathy), may all produce signs that can, at least initially, be confused with colic. However, careful clinical examination will usually reveal the musculoskeletal system rather than the abdomen to be the site of pain.

Exertional Rhabdomyolysis

Horses with exertional rhabdomyolysis usually present with stiffness, sweating, and distress during or after exercise (Hodgson, 1999). Affected horses may stretch out as if to urinate, become reluctant to move, and in severe cases become recumbent. Attempts to move affected horses may result in severe pain and anxiety. The affected muscles (commonly the back, hindlimb, and shoulder muscles) are often firm and painful when palpated. Myoglobinuria may be present in severe cases.

The diagnosis of exertional rhabdomyolysis is achieved by a combination of the history (the disease invariably follows exercise or exertion) and clinical findings. Muscle damage can be confirmed by measuring serum concentrations of creatine kinase and aspartate aminotransferase.

Atypical Myopathy (Summer Pasture-associated Myopathy)

Atypical myopathy is more likely to be confused with colic than exertional rhabdomyolysis because of the absence of any history of preceding exercise. This acute myopathy affects grazing horses, usually less than 6 years of age (Hosie et al., 1986; Harris, 1996). The causes of equine atypical myopathy include environmental toxins and fatty acid oxidative metabolism impairment. Toxicity associated with *Acer negundo* (box elder) has been identified as the cause in North America, whereas in Europe the sycamore tree (*Acer pseudoplatanus*) appears to be the cause; both plants contain the toxin hypoglycin A.

The clinical syndrome is characterized by sudden onset of stiffness, weakness, and sometimes recumbency, with passage of dark-brown urine (Votion et al., 2007). Affected horses may be found recumbent and unable to rise, and may initially look as if they are suffering from colic. However, on careful examination most will not appear to be in distress or pain. Adverse climatic conditions often occur prior to an outbreak, and clinicopathologic evaluations reveal markedly elevated levels of creatine phosphokinase (CPK) and aspartate aminotransferase (AST). Treatment is supportive, but the condition carries a high mortality rate.

Prepubic Tendon Rupture and Ventral Body Wall Hernias

Rupture of the prepubic tendon or other abdominal wall musculature is most commonly seen secondary to trauma or to the stress of the weight of a normal or abnormal pregnancy (e.g., hydrops or twins) (see Chapter 59). The pain demonstrated by the affected mare is a direct result of the tearing of the abdominal support structures and/or the possible herniation and strangulation of bowel through the rents.

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Abdominal Trauma

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The diagnostic approach to and management of abdominal trauma in horses represent a clinical challenge. Injuries can range from uncomplicated external trauma without visceral involvement to severe penetrating or nonpenetrating injuries involving major abdominal organs. Timely identification of internal damage represents the most challenging aspect of managing horses with abdominal trauma. This is particularly true in horses with blunt injury when obvious abdominal wounds are not present.

Abdominal injuries can be of different etiologies and may involve the abdominal wall alone or abdominal viscera such as the intestine and portions of the urinary and reproductive tracts. Intra-abdominal injuries commonly occur in mares during parturition. These injuries can occasionally be fatal or may result in mesenteric tears, intestinal injury, and hematoma formation, leading to colic-like symptoms (Dart et al., 1991; Hanson & Todhunter, 1986; Zamos et al., 1993). Prepubic tendon rupture and injury to the uterus also can occur in the parturient mare (Brooks et al., 1985; Jackson, 1982). Penetrating trauma may result from horses impacting sharp objects or gunshot wounds or may be iatrogenic (Lindley, 1976; Vatistas et al., 1995). As an example of such cases, injury to the blood vessels of the abdominal wall has been reported to occur during the percutaneous placement of trocars during laparoscopy (Ragle et al., 1998).

Initial evaluation and treatment of the horse depend on the mechanism of injury (i.e., penetrating or blunt) and on the hemodynamic status of the horse. The priorities for evaluating and treating horses with penetrating injuries differ from those for horses that have sustained blunt trauma because the respective patterns of injury are markedly different. Penetrating trauma typically results in an externally localized injury that may lead to massive abdominal contamination if the gastrointestinal tract is involved. Conversely, blunt trauma may result in injuries that involve several organs. Regardless of the mechanism of injury, it is critical that hypotension and hypovolemia are identified and appropriate treatments initiated promptly to increase the horse's chance of survival.

Diagnostic Approach

The diagnostic approach to horses with abdominal trauma may be facilitated by following an algorithmic approach. One of the first priorities is to determine whether or not the horse is in a stable cardiovascular condition and if the injury is open or closed (Figure 61.1). Subsequently, the type of injury will dictate further diagnostic and therapeutic decisions that must be considered.

Physical Examination

Most horses with abdominal injury exhibit varying degrees of colic-like signs, the intensity of which ranges from mild to intense. Pain may result from the injury itself or from the presence of free blood in the abdomen, which causes distention and chemical peritonitis. Hemorrhage associated with an organ, as in the case of splenic hematoma, or involving support structures (e.g., broad ligament, mesentery) will also be accompanied by signs of pain (Mehl et al., 1998). Blood losses exceeding 25% of the horse's blood volume will result in clinical signs of restlessness, recumbency, and pawing, which can be confused with colic. Inconsistencies in the clinical picture, such as marked tachycardia associated with mild and intermittent abdominal pain, should alert the clinician to the possibility that the underlying problem may not be gastrointestinal in origin.

Evidence of dehydration and hypovolemia on physical examination accompanied by tachycardia and tachypnea

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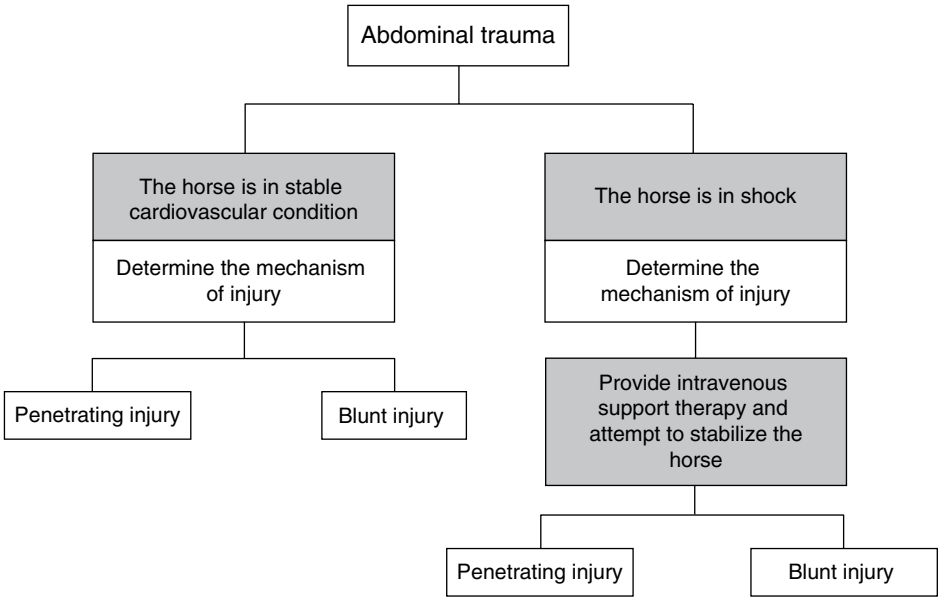

Figure 61.1 Algorithmic approach to assessing a horse with an abdominal injury prior to initiating specific trauma therapy.

indicates the presence of circulatory shock and calls for aggressive supportive therapy. Shock may result from one or more of the following: violent circumstances surrounding the injury (traumatic shock), acute blood loss (hemorrhagic shock), or visceral rupture (endotoxic shock). Catecholamine release and sympathetic stimulation result in peripheral vasoconstriction and splenic contraction, leading to pale mucous membranes and cold extremities (limbs, ears, and muzzle). As a result of splenic contraction, initial values for packed-cell volume (PCV) and plasma protein will be unreliable indicators of the severity of blood loss. In fact, within the first 24 h, the PCV may be increased transiently owing to the release of erythrocytes from the spleen. Decreased capillary hydrostatic pressure will also allow fluid to move into the vascular space, assisting in the temporary restoration of blood volume.

Wound and Abdominal Examination

A thorough assessment of the wound is critical, particularly if a penetrating abdominal injury is suspected. It is not uncommon for horses to be evaluated for gunshot wounds or impalement injuries. The diagnostic approach should be directed toward determining whether or not the abdominal cavity has been penetrated and, if so, which of the abdominal organs have been injured (Figure 61.2). Thus, if the entry point is near the diaphragmatic reflection, the horse should be examined for possible thoracic injury. With this in mind, a thoracic radiograph may be helpful in identifying either pneumothorax or hemothorax (Holcombe, 1999). Examination of the wound should be carried out via careful digital palpation using sterile technique. An abdominal wound may not necessarily correlate with abdominal penetration and care should be taken not to penetrate the peritoneum inadvertently while examining the site of injury. Although local anesthesia may facilitate the examination, ventrally located wounds can be edematous and painful to the touch, thereby complicating completion of the examination. If there is obvious evidence of abdominal penetration, the horse should be prepared for emergency celiotomy. In contrast, when the findings of the external examination are inconclusive, additional diagnostic measures are warranted.

Abdominal paracentesis is an important part of the diagnostic workup and obtaining a representative sample of peritoneal fluid may greatly facilitate the diagnostic process. The use of transabdominal ultrasound during collection of peritoneal fluid offers several advantages. Fluid can be identified ultrasonographically and sampled accurately without risking inadvertent perforation of an abdominal organ. Avoidance of abdominal organs during the paracentesis also facilitates interpretation of the laboratory results. Ultrasonography also may allow the detection of excessive free fluid (hemoperitoneum) and the identification of free-floating fibrin or fibrinous tags on serosal surfaces (peritonitis). Abdominal ultrasonography has been used to determine the size and location of splenic hematomas in horses (McGorum et al., 1996; Spier et al., 1986). The superficial location of the spleen renders this organ prone to blunt trauma, particularly in the form of kicks from other horses. More invasive diagnostic procedures may be warranted, particularly if the result of peritoneal fluid analysis is inconclusive or a sample cannot be obtained.

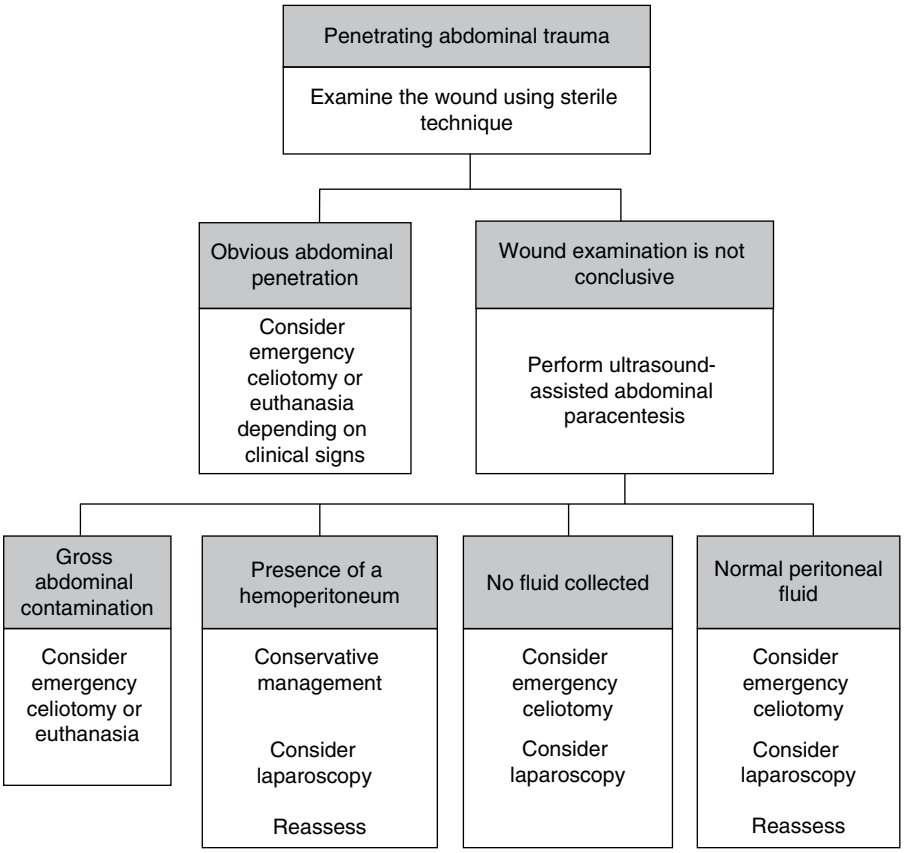

Figure 61.2 Algorithmic approach to assessing a horse with a penetrating abdominal injury.

Laparoscopy

The use of laparoscopy in horses with abdominal trauma has been reported and is becoming more popular as surgical methods are refined and more surgeons gain experience with the technical aspects of the equipment (Ragle et al., 1997). When performed in the standing horse, laparoscopy may yield conclusive information, thereby avoiding the risks of general anesthesia. This is especially useful in unstable animals. In contrast, an exploratory celiotomy may be required after laparoscopy, either because the clinician fails to recognize an abnormality or the abnormality cannot be addressed via laparoscopy.

Reports in the human literature document a decrease in hospital stay in patients with negative laparoscopic findings compared with patients with negative celiotomy findings (Salvino et al., 1993). In those studies, reduced hospitalization correlated with a significant reduction in the overall costs. This is an equally important issue in veterinary practice. The use of laparoscopy, in selected cases, can avoid the aftercare and the expenses associated with celiotomy. Furthermore, in humans, the use of laparoscopy in abdominal trauma has been advocated as either a screening, diagnostic, or therapeutic tool (Villavicencio & Aucar, 1999). Similarly, laparoscopy is a useful screening and diagnostic tool in horses to exclude or detect specific abdominal problems such as hemoperitoneum, splenic injury, and intestinal perforation and to confirm peritoneal penetration. In horses with blunt injury, laparoscopy may be useful in determining the source of abdominal hemorrhage when conservative management fails to improve the hemodynamic status of the horse and the cause of the symptoms remains unclear. When the external features of an abdominal wound are equivocal, laparoscopy can confirm or exclude peritoneal perforation. Trauma to the upper abdominal quadrants can be assessed in the standing horse.

Laparoscopy can play a useful role in the case of injuries requiring celiotomy. General anesthesia and emergency celiotomy are elected when the abdominal wall is structurally disrupted without the presence of a laceration. In such cases, the surgeon can explore the abdomen laparoscopically before using an open procedure. The laparoscopic examination of the peritoneal aspect of a wound may suggest an approach to the abdomen different from the standard ventral midline celiotomy, thereby targeting the abdominal incision to a location that best suits the individual case (e.g., away from contaminated areas). The assessment of ventrally located abdominal lacerations can be problematic because of the rapid development of dependent edema,

Box 61.1 Uses of laparoscopy in abdominal trauma

Diagnosis of hemoperitoneum
Source of hemoperitoneum
Mesenteric hematoma
Injury to the spleen, liver, and kidneys
Diaphragmatic hernia
Abdominal penetration
Intestinal perforation
Intra-abdominal assessment of the peritoneal aspect of a ventrally located wound
Screening method prior to celiotomy

which complicates the external evaluation of the wound. In addition, the planes of the subcutaneous fascia and of the abdominal musculature may ride over each when the force of impact is tangential to the abdomen. This produces a disruptive and disorganized pattern of injury, making it difficult to determine whether or not the abdomen has been penetrated. With the horse under general anesthesia, the laparoscope can be placed distant from the area of injury, allowing a safe assessment of the visceral aspect of the wound. This evaluation may help the surgeon decide whether or not an open procedure is needed. This may allow the surgeon to avoid the potential complications and extended recovery period associated with celiotomy incisions. Box 61.1 summarizes laparoscopic applications in abdominal trauma.

Therapeutic applications of laparoscopy in horses with traumatic injuries are less obvious. However, in horses, certain operations, such as diaphragmatic hernia repair, targeted abdominal drain placement, and hemostatic procedures involving the mesentery, may be easier to perform laparoscopically because of the improved visibility over open techniques (Sutter & Hardy, 2004). Laparoscopy alone does not represent the gold standard in the clinical approach to abdominal trauma in horses. Nonetheless, its use in combination with diagnostic modalities such as abdominal ultrasound and paracentesis can undoubtedly add valuable information to the diagnostic process. In addition, the use of laparoscopy prior to celiotomy in ventral abdominal trauma assessment is an interesting application as it can help the surgeon assess the peritoneal side of the injury, target the open approach, or simply avoid a celiotomy.

Treatment

Treatment of abdominal trauma should be conservative at first unless there is obvious abdominal penetration, in which case an emergency celiotomy (with or without laparoscopy) is a necessary choice. Horses should be treated for the systemic effects of trauma with intravenous fluid therapy and nonsteroidal anti-inflammatory drugs (NSAIDs). Additional resuscitative measures may be warranted, such as the administration of hypertonic (7.2%) saline solution (5 mL/kg) to correct severe dehydration and restore cardiovascular function and calcium gluconate supplementation (500 mL of a 23% solution added to 5–10 L of isotonic fluids). A tetanus booster should be administered.

Abdominal wounds need to be debrided with care to avoid inadvertent penetration of a compromised abdominal wall. Fresh wounds can be closed primarily, although in most cases wounds are heavily contaminated and are configured as skin flaps, which may be dealt with by promoting second intention healing or delayed primary closure. The judicious use of drains will promote ventral drainage of the wound, thus avoiding seroma and possible abscess formation. There is the tendency for abdominal wounds to favor the formation of subcutaneous emphysema, which can diffuse along the subcutaneous plains distant from the wound area. This condition is usually benign and resolves with wound healing and may be aided by placing a pressure bandage around the horse's abdomen.

Penetrating abdominal injuries can be fatal if the integrity of the bowel is compromised, leading to spillage of fecal material and subsequent massive peritonitis. The goals of an exploratory celiotomy are to verify the presence of injured intestine, restore its integrity and repair the abdominal defect associated with the wound. Survival of horses with penetrating trauma may depend on the intestinal segment involved. It appears that contamination resulting from small intestinal traumatic perforation is more forgiving than similar large colon wounds. Because of the low pH of the stomach and the small bowel, the stomach and the proximal portions of the small intestine (duodenum and jejunum) contain low numbers of microorganisms. In the distal small intestine (ileum) and large colon, bacterial numbers are much higher, which may lead to greater contamination in case of spillage (Hao & Lee, 2004). Based on a recent review of gunshot wounds in horses, an exploratory laparotomy would be indicated when peritoneal fluid analysis, rectal examination, and ultrasonography reveal findings consistent with peritonitis (Munsterman & Hanson, 2014). According to a case series, clinical signs of peritonitis can develop more subtly and be accompanied by varying degrees of severity when metallic wire foreign objects penetrate the bowel wall after being ingested by the horse (Lohmann et al., 2010). During a celiotomy, devitalized intestinal segments need to be removed and puncture wounds restored by oversewing with healthy serosa. Sources of hemorrhage should be located and controlled. Finally, a thorough abdominal lavage should be performed to remove contaminants and may be followed by placement of an abdominal drain. Specific techniques for treating peritonitis are described in Chapter 29.

In horses with blunt injury, the main goal should be to stabilize the horse and carefully monitor its progress. Blunt trauma may in fact be limited to only superficial bruising requiring minor local and systemic anti-inflammatory therapy, but in severe cases, the abdominal organs may suffer significant damage. Splenic, hepatic, or diaphragmatic injury and also peritonitis or hemoperitoneum may not be clinically obvious on presentation, warranting a cautious clinical approach.

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Abdominal Abscesses and Neoplasia

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Introduction

Abdominal abscesses and neoplasia are relatively uncommon causes of acute abdominal pain compared with other types of strangulating and nonstrangulating obstructions. The similarities in clinical presentation of horses with abdominal abscesses and neoplasia make preoperative diagnosis challenging (Zicker et al., 1990). This chapter presents information on the anamnesis, diagnosis, treatment, and prognosis for abdominal abscesses and abdominal neoplasia in the horse.

Abdominal Abscessation

Anamnesis

Historical findings associated with abdominal abscesses include anorexia, lethargy, depression, weight loss, acute and chronic signs of abdominal pain, diarrhea, and pyrexia (Arnold & Chaffin, 2012; Pratt et al., 2005; Pusterla et al., 2007; Reuss et al., 2009; Rumbaugh et al., 1978). Abdominal abscesses have been classified into two types, primary and secondary (Arnold & Chaffin, 2012). Primary causes of abdominal abscesses include systemic bacterial infection secondary to upper respiratory tract infections. Common bacterial species associated with primary abdominal abscesses include *Rhodococcus equi*, *Streptococcus equi* subsp. *equi*, and *Corynebacterium pseudotuberculosis* (Arnold & Chaffin, 2012; Pratt et al., 2005; Pusterla et al., 2007; Reuss et al., 2009; Rumbaugh et al., 1978). These bacteria more commonly affect younger animals, but can also affect adult horses. Horses housed in association with clinically affected horses with upper respiratory tract disease are at risk for exposure and can become infected. Owners should be questioned about the horse's exposure to clinically infected animals and whether or not there has been recent evidence of upper respiratory disease.

A variety of other bacteria can cause or contribute to the formation of abdominal abscesses, including anaerobic bacteria such as *Clostridium* spp. and *Fusobacterium necrophorum* (Aleman et al., 2003; Arnold & Chaffin, 2012). Secondary abscesses may develop secondary to penetrating abdominal trauma, ulceration or perforation of abdominal viscera, or after abdominal surgery (Arnold & Chaffin, 2012).

Diagnosis

All horses suspected of having an abdominal abscess based on historical information should have the following diagnostic tests performed: complete physical examination, complete blood count (CBC) including fibrinogen, biochemical profile, abdominocentesis, abdominal palpation per rectum, and abdominal ultrasonography. Additional diagnostic tests that can be considered include nuclear scintigraphy (labeled white blood cell scan) and laparoscopy (Koblik et al., 1985; Klohnen, 2012).

Physical examination abnormalities associated with abdominal abscesses include hyperemic mucous membranes (with or without a toxic line), dehydration, lameness secondary to laminitis, inguinal masses, limb edema, thin body condition, diarrhea, abdominal distention, painful abdomen (abdominal stenting), and ventral abdominal edema.

CBC and fibrinogen abnormalities associated with abdominal abscesses include leukocytosis or neutropenia, mature neutrophilia with or without a left shift, and hyperfibrinogenemia (Arnold & Chaffin, 2012; Pratt et al., 2005; Pusterla et al., 2007; Reuss et al., 2009; Rumbaugh et al., 1978). Biochemical abnormalities include increases in blood urea nitrogen (BUN) and creatinine concentrations (typically associated with prerenal azotemia), hyper- or hypoproteinemia, hypoalbuminemia, hyperglobulinemia, and electrolyte disturbances (e.g., hypocalcemia).

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Abdominocentesis is crucial for making a diagnosis of peritonitis, which is frequently associated with abdominal abscessation (Bach & Ricketts, 1974; Hawkins et al., 1993). Peritoneal fluid is usually copious in quantity and has an abnormal gross appearance. Peritoneal fluid can range from opaque to grossly purulent. Peritoneal fluid samples can range cytologically from transudate, modified transudate, exudative, to suppurative. Nucleated cell counts frequently exceed 25,000 nucleated cells/μL (25×10^9/L) and total protein concentrations are typically increased above 2.5 g/dL (25 g/L). Peritoneal fluid cytologic abnormalities include neutrophilia with a left shift and intracellular or extracellular bacteria. In instances of gastrointestinal rupture, food material, bacteria, and protozoa may be identified in the peritoneal fluid. Peritoneal fluid obtained from horses with suspected peritonitis should be submitted for both aerobic and anaerobic culture.

Abdominal palpation per rectum is indicated in all horses suspected of having an abdominal abscess. Rectal examination abnormalities associated with abdominal abscesses include identification of firm masses within the mesentery or adjacent to other abdominal viscera (spleen, urogenital tract, kidneys), adhered loops of intestine, thickened loops of intestine, small intestinal distention, increased fluid accumulation within the abdomen, and roughened peritoneal surfaces.

Masses that are palpable per rectum should be examined with transrectal ultrasonography, as this approach will allow the ultrasound probe to be positioned closer to the abscess than is possible using the transcutaneous approach. This will result in obtaining a better quality ultrasound image. Abdominal ultrasonography should be performed in all horses with suspected intra-abdominal abscessation. Transcutaneous ultrasound can be used to characterize the size and character of the exudate within the abscess. Abdominal abscesses have a characteristic ultrasonographic appearance (Arnold & Chaffin, 2012; Reuss et al., 2011). Typical findings include a thick (2–4 cm capsule) containing hyperechoic fluid and fibrin strands. Gas echoes may also be observed in horses with anaerobic infection. In some circumstances, viscera may be observed adhered to the mass. Other ultrasonographic findings associated with abdominal abscesses include peritoneal effusion, small intestinal distention, edematous small or large intestine, masses within the spleen, liver, or involving the kidneys and urogenital tract, and enlargement/abscessation of umbilical remnants (Arnold & Chaffin, 2012; Cypher et al., 2015; Nogradi et al., 2013; Sellon et al., 2000; Squinas & Britton, 2013). Ultrasound-guided aspirates are sometimes possible and can be useful in obtaining samples for microbial culture and cytology. A complete ultrasound examination must include both sides and the ventrum of the abdomen.

The diagnosis of an abdominal abscess is frequently made using a combination of the aforementioned techniques. However, a small percentage of horses (<20%) may require exploratory celiotomy or necropsy to make a definitive diagnosis.

Treatment

The most difficult decision regarding management of horses with suspected abdominal abscessation is whether to treat conservatively or with surgery. In the author's experience, the primary determining factor is the degree of abdominal pain. Some authors feel that surgical intervention is more effective than medical management (Mair & Sherlock, 2011). Horses unresponsive to analgesics and medical treatment should have an exploratory celiotomy performed. Numerous authors have documented successful management of abdominal abscesses with medical management only (Arnold & Chaffin, 2012; Berlin et al., 2013; Elce, 2006; Pratt et al., 2005; Pusterla et al., 2007; Reuss et al., 2009; Rumbaugh et al., 1978). An evaluation of the available literature regarding the success of surgical management reveals a poor to guarded prognosis in many instances (Arnold & Chaffin, 2012; Elce, 2006; Mair & Hillyer, 1997; Prades et al., 1989; Rigg et al., 1987; Taylor et al., 1981). The present author's experience in treating horses with abdominal abscessation has been less than favorable.

Medical Management

Horses diagnosed with an abdominal abscess in the absence of severe abdominal pain should be managed conservatively. Conservative management should include the administration of systemic broad-spectrum antimicrobials and anti-inflammatory drugs (Arnold & Chaffin, 2012; Berlin et al., 2013; Elce, 2006; Pratt et al., 2005; Pusterla et al., 2007; Reuss et al., 2009; Rumbaugh et al., 1978). The antimicrobials most commonly used include penicillin G, gentamicin sulfate, metronidazole, and trimethoprim sulfamethoxazole. Metronidazole is indicated for treatment of anaerobic bacteria. If at all possible, peritoneal fluid or aspirates from the abscess should be submitted for culture and sensitivity to guide antimicrobial therapy. It is the author's preference to treat intravenously initially (7–10 days), followed by long-term administration of oral antimicrobials. Chronic administration of antimicrobials can range from weeks to months before resolution of the abdominal abscess. Flunixin meglumine is the preferred nonsteroidal anti-inflammatory drug (NSAID). However, some veterinarians favor preferential COX-2 inhibitors to prevent the development of gastrointestinal secondary side effects associated with nonselective classical NSAIDs such as flunixin meglumine. Resolution of the abdominal abscess can be assessed with abdominal palpation per rectum, ultrasonography, and resolution of clinical signs.

Horses diagnosed with septic peritonitis in conjunction with abdominal abscessation should be treated with peritoneal lavage (Hawkins, 2003). Peritoneal lavage can be performed with the horse standing. A large-bore chest tube can be inserted percutaneously into the abdominal cavity to facilitate instillation of a balanced polyionic solution (Figure 62.1). The present author routinely infuses up to 20 L of fluid at a time for abdominal lavage. After the fluid has been infused, the horse is walked and then the fluid is drained. It is not unusual not to obtain full recovery of the infused fluid. Peritoneal lavage is performed for a minimum of 3–5 days or until clinical signs of peritonitis have resolved. Ideally, the decision for discontinuation of lavage is guided by cytologic analysis of subsequent peritoneal fluid samples. Declining nucleated cell counts and total protein concentration are indications that medical management is being effective. Neutrophilic inflammation should gradually decrease and mononuclear cell concentrations should increase within the peritoneal fluid.

Abscesses that are adhered to the abdominal wall may be candidates for percutaneous drainage. Abscess adherence is often subjective, but ultrasonography may be the best method of determining this. Laparoscopy can be used to define the size and adherence of the abscess capsule to the body wall. Drainage may be accomplished by implanting a chest tube or Foley catheter. Alternatively, a stab incision can be made through the full thickness of the abdominal wall and the abscess capsule. Chest tubes, Foley catheters, or small-diameter stomach tubes can be used to lavage the abscess cavity and facilitate drainage.

Surgical Management

Horses with suspected abdominal abscesses that are refractory to analgesics and aggressive medical management are candidates for surgery (Arnold & Chaffin, 2012; Elce, 2006; Mair & Sherlock, 2011; Prades et al., 1989; Rigg et al., 1987; Taylor et al., 1981). A variety of approaches have been described to evaluate and manage abdominal abscesses. These include, but are not limited to, standing, ventral midline, paramedian, and laparoscopic procedures. The decision regarding which approach to use is dependent on the location of the abscess. If it is not possible to define completely where the abscess is or what it involves, the present author generally prefers to perform a ventral midline celiotomy.

A complete abdominal exploration should be performed to determine the full extent of the abscess and the structures it involves. If possible, abscesses should be aspirated to obtain samples for microbial culture and sensitivity testing. Small, focal areas of abscessation (<10 cm) and those secondary to castration or involving umbilical structures may be amenable to removal (Arnold & Chaffin, 2012). Abscesses involving the mesentery or segments of the gastrointestinal tract may require resection and anastomosis of small or large intestine and/or descending colon. Large, diffuse areas of abscessation are more difficult to manage. Treatment options will vary depending on the structures that are involved with the abscess. For example, extensive intestinal adhesions (Figure 62.2) and/or involvement of the spleen, liver, kidneys, and urogenital tract all influence treatment options. Horses with extensive adhesions that are not amenable to bypass procedures and that manifest preoperative moderate to severe signs of abdominal pain are candidates for euthanasia (Arnold & Chaffin, 2012). Likewise, financial constraints for the owner may contribute to decision making for euthanasia (Arnold & Chaffin, 2012).

If the owner elects to treat the horse, four options exist: surgical drainage of the abscess, bypass procedures of

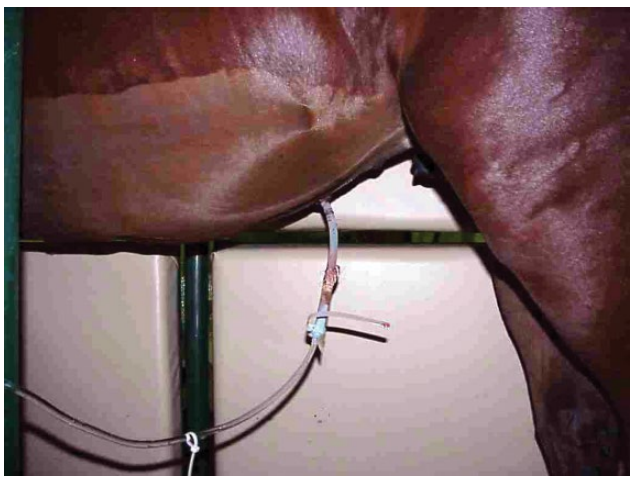

Figure 62.1 A large-bore chest tube has been inserted through the abdominal wall in order to perform abdominal lavage with the horse standing.

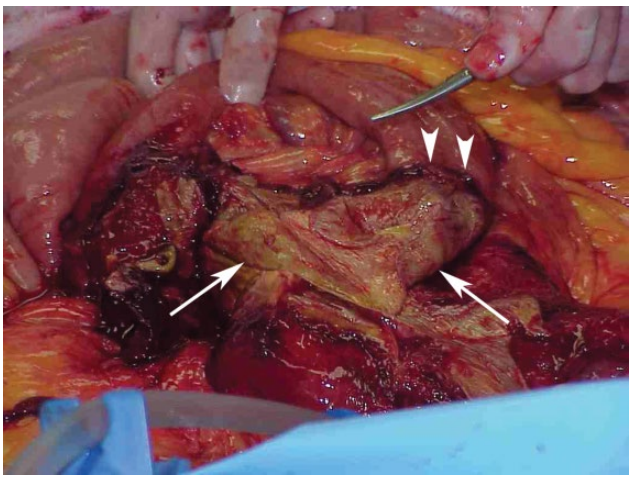

Figure 62.2 Abdominal abscess within the mesentery of the small intestine (arrows), with small intestinal adhesions (arrowheads).

the abscess in combination with medical management, marsupialization of the abscess to the body wall, and continued medical management (Arnold & Chaffin, 2012; Elce, 2006; Mair & Sherlock, 2011; Prades et al., 1989; Rigg et al., 1987; Taylor et al., 1981).

In select cases (horses with well-defined abscesses and minimal adhesions), the abscess can be drained surgically (Mair & Sherlock, 2011). This could include large-bore needle (14 gauge or greater) aspiration and suction and/or small surgical incision to remove purulent exudate from the abscess cavity. An indwelling, percutaneously positioned Foley catheter or chest tube can be inserted into the abscess cavity for postoperative lavage (Mair & Sherlock, 2011). The major risk for intra-abdominal surgical drainage is a predisposition to turning a focal infectious process into a diffuse process by contaminating the abdominal cavity and adjacent viscera with purulent abscess drainage. These cases would require postoperative peritoneal lavage through an indwelling tube to manage postoperative peritoneal inflammation and potentially diffuse peritonitis.

Bypass procedures are generally limited to horses with adhesions of the small intestine to the abscess (Taylor et al., 1981). For a bypass procedure to be effective, the loop of small intestine leading into the mass of adhesions and the loop of small intestine exiting the mass must be sutured together using a side-to-side anastomosis. A hand-sutured or -stapled anastomosis can be performed at the discretion of the surgeon.

Marsupialization has been used as a successful method of managing nonresectable abdominal abscesses (Prades et al., 1989; Rigg et al., 1987). For this method to work, the abscess must be close enough to the abdominal wall that the cavity of the abscess can be sutured to the abdominal wall so the capsule can be incised. The edges of the capsule are then sutured to the skin. The abscess can be left to drain on its own or a chest tube or Foley catheter can be inserted into the center of the abscess for postoperative lavage.

Horses in which abdominal pain can be managed with NSAIDs may be candidates for aggressive medical management, as described previously.

Decision making for treatment must entail an honest and open discussion with the owner regarding a realistic prognosis and the expense of long-term medical treatment even after the abscess has been managed surgically.

Prognosis

The prognosis for horses with abdominal abscesses is generally regarded as poor to guarded. Regardless of the treatment method used, the prognosis for abdominal abscesses has ranged from 25 to 100%. The reported success rate for medical management has ranged from 25 to 100% and for surgical management from 50 to 67%. However, it is important that each horse be considered on a case-by-case basis as some horses can have a good to favorable outcome with appropriate therapy (Arnold & Chaffin, 2012).

Abdominal Neoplasia

The most common neoplasm in the equine abdomen is the pedunculated lipoma (Garcia-Seco et al., 2005), which is covered in depth in Chapter 52. This discussion focuses on the other less common forms of abdominal neoplasia, which tend to be associated with chronic signs of abdominal pain far more often than with acute signs of pain (Hillyer & Mair, 1997; Mair & Hillyer, 1997; Pearson et al., 1975; Zicker et al.1990). There have been multiple case reports and retrospective studies detailing various forms of neoplasia in the abdominal cavity (Hillyer & Mair, 1997; Mair & Hillyer, 1997; Pearson et al., 1975; Zicker et al., 1990). Most of these neoplasms were diagnosed on postmortem examination, although there are case reports of successful surgical treatment for abdominal neoplasia (Boyle et al., 2004; Cribb & Boure, 2010; Harland et al., 2009; Janicek et al., 2004; Muravnick et al., 2009; Parks et al., 1986; Rambags et al., 2003; Santschi et al., 1995; Schneeweiss et al., 2015). This section concentrates on the anamnesis, diagnosis, treatment, and prognosis of abdominal neoplasia in the horse.

Anamnesis

Most horses with abdominal neoplasia present with a history of anorexia, lethargy, weight loss, chronic signs of abdominal pain, diarrhea, and occasionally acute signs of abdominal pain when intestinal obstruction develops secondary to the neoplasm. In fact, some of the clinical signs of abdominal neoplasia are similar to those associated with abdominal abscessation (Zicker et al., 1990). In rare instances, horses may present with a primary complaint of abdominal distention or a mass visible externally. Some horses may have a history of weight loss despite an apparently good appetite.

Diagnosis

All horses suspected of having abdominal neoplasia based on historical information should have the following diagnostic tests performed: complete physical examination, CBC including fibrinogen, biochemical profile, abdominocentesis, abdominal palpation per rectum, and abdominal ultrasonography. Laparoscopy can also be considered (Klohnen, 2012).

Although CBC and fibrinogen abnormalities associated with abdominal neoplasia are often nonspecific, they may be normal or include leukocytosis or neutropenia, mature neutrophilia with or without a left shift, and

hyperfibrinogenemia. Biochemical profiles can be normal or have some of the following abnormalities: increases in BUN and creatinine concentrations (typically associated with prerenal azotemia), hypoproteinemia, hypoalbuminemia, and electrolyte disturbances (e.g., hypocalcemia).

Abdominocentesis should be performed in all horses suspected of having abdominal neoplasia (Meyer et al., 2006; Ricketts & Peace, 1976; Tarrant et al., 2001; Zicker et al., 1990). A variety of fluid types can be obtained in the horse with abdominal neoplasia and can include transudate, modified transudate, and exudative. Peritoneal fluid can be copious in quantity and its gross appearance can range from clear to opaque to grossly purulent. Nucleated cell counts can be normal or be >5000–10,000 nucleated cells/μL ($5–10 \times 10^9$/L) and total protein concentrations can be increased (>2.5 g/dL; 25 g/L). Peritoneal fluid cytologic abnormalities include neutrophilia with a left shift and increased numbers of mononuclear cells, including mesothelial cells, and in some instances abnormal neoplastic cells can be observed (Meyer et al., 2006; Ricketts & Peace, 1976; Tarrant et al., 2001; Zicker et al., 1990).

Abdominal palpation per rectum is indicated in all horses suspected of having abdominal neoplasia. Rectal examination abnormalities associated with abdominal neoplasia include identification of firm masses within the abdominal mesentery or adjacent to other abdominal viscera (e.g., spleen, urogenital tract, or kidneys), adhered loops of intestine, thickened loops of intestine, and roughened peritoneal surfaces. Masses that are palpable per rectum should be examined with transrectal ultrasonography.

Abdominal ultrasonography should be performed in all horses suspected of having intra-abdominal neoplasia (Janvier et al., 2016). Transcutaneous ultrasound can be useful in characterizing the size and character of the mass. In some circumstances, viscera may be observed adhered to the mass. Ultrasound-guided biopsy samples can sometimes be obtained using core-type biopsy needles (De Clerq et al., 2004). A complete ultrasonographic examination must include evaluation of both sides and the ventrum of the abdomen. Transrectal ultrasonography should be performed when masses are palpable per rectum, as the probe can be positioned closer to the mass than transcutaneously. Using this approach, a better quality ultrasound image may be obtained. In the present author's experience, a diagnosis of abdominal neoplasia is not often made in horses admitted for evaluation of acute abdominal pain until an exploratory celiotomy has been performed.

Laparoscopy or an exploratory celiotomy may provide the only means to diagnose an abdominal neoplastic mass. The choice of laparoscopy or traditional exploratory celiotomy is at the discretion of the surgeon, but laparoscopy is preferred when the goal is diagnosis rather than definitive treatment. The primary advantages of laparoscopy include the fact that it can be performed with the horse standing, general anesthesia can be avoided, and it allows easy access to both sides of the abdomen. Biopsy samples can also be obtained under direct visualization, thereby allowing for precise tissue sampling. The main disadvantage of standing laparoscopy is that definitive treatment cannot always be accomplished, thus requiring a ventral midline celiotomy.

Treatment

The majority of cases of abdominal neoplasia are not amenable to treatment by the time they are definitively diagnosed. Frequently, abdominal exploration is performed to provide a definitive diagnosis but not necessarily to achieve a "cure." However, focal masses with minimal intestinal or organ involvement may be suitable for surgical resection. This could include urogenital neoplasia (ovary, testicle, and uterine masses), splenic neoplasia (Figure 62.3), and focal masses involving small intestine, large intestine, or descending colon (Boyle et al., 2004; Cribb & Boure, 2010; Harland et al., 2009; Janicek et al., 2004; Muravnick et al., 2009; Parks et al., 1986; Rambags et al., 2003; Santschi et al., 1995; Schneeweiss et al., 2015). The present author has successfully treated horses with leiomyoma of the uterus, adenocarcinoma of the small colon, and myxosarcoma involving a single loop of jejunum. Therefore, the present author prefers to make a definitive diagnosis via abdominal exploration to obtain the most information for the owner to use in deciding whether or not to proceed further, and to be able to provide an accurate prognosis.

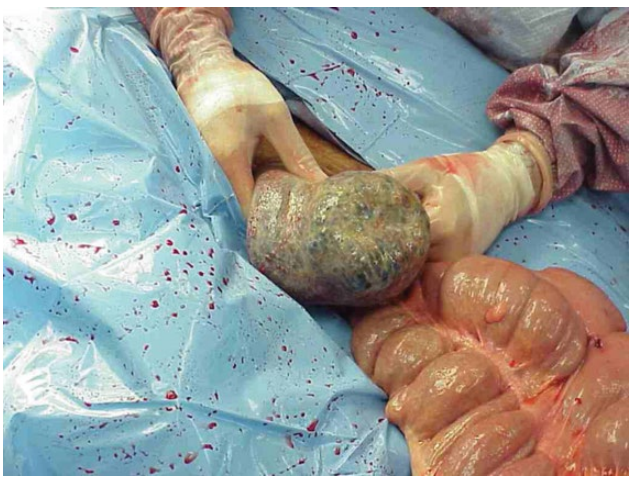

Figure 62.3 Splenic tumor in a horse with chronic intermittent colic.

Prognosis

The prognosis for most horses with abdominal neoplasia is poor to guarded, with the majority of cases being candidates for euthanasia. Although this is supported by the many case reports of abdominal neoplasia diagnosed on postmortem examination, some horses can be treated surgically with a successful outcome. Determining factors in the decision for euthanasia include systemic disease such as lymphoma, extensive involvement of multiple segments of intestine or other abdominal organs, severe intestinal adhesions, metastatic disease, and masses so large that they are not suitable for surgical resection.

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