Jacques Corcos
Mikolaj Przydacz

Consultation in Neurourology

A Practical Evidence-Based Guide

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ISBN 978-3-319-63909-3 ISBN 978-3-319-63910-9 (eBook)
https://doi.org/10.1007/978-3-319-63910-9

Library of Congress Control Number: 2017947903

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Foreword I

Patients impacted by neurologic injury and disease have many bothersome symptoms that can impact many facets of their life. However, it is well known that lower urinary tract symptoms secondary to a neurologic issue often have a *substantial* impact on the quality of life of these patients. The pathophysiology, evaluation, and management of patients with neurogenic bladder are well reviewed in many previously published textbooks, review articles, and chapters. In fact, I had the good fortune of being a coeditor with Dr. Corcos on the third edition of *Textbook of the Neurogenic Bladder* published in 2016. So why another book on this subject?

There are many patients in the world with neurologic issues, and many of them have bothersome symptoms related to neurogenic lower urinary tract dysfunction (NLUTD). Unfortunately, there are few physicians who truly focus on the care of NLUTD. Two physicians who truly do focus on the management of NLUTD, Dr. Jacques Corcos and Dr. Mikolaj Przydacz, have taken a unique direction with this textbook. The focus is on the clinical management of patients with neurogenic bladder. The book separates NLUTD into patients with and without spinal cord injury. Treatment options are reviewed for the various types of clinical scenarios that are seen—urinary incontinence due to detrusor overactivity, urinary incontinence due to poor sphincteric function, and urinary retention. The various complications of NLUTD are discussed (e.g., urinary tract infections, stones, autonomic dysreflexia, renal damage, etc.), followed by focused sections on patient education and current guidelines for the management of NLUTD.

I would expect this textbook to be helpful to all healthcare providers who care for patients with neurologic issues and NLUTD. For those healthcare providers who have less experience with the field, the book will provide the base of knowledge required to adequately manage these patients, and for those healthcare providers who are already experienced in the field, I suspect that there are pearls of wisdom that we can all apply to our clinical practices.

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Foreword II

Neurogenic lower urinary tract dysfunction is highly prevalent and affects the life of millions of people worldwide. It has not only a major impact on the quality of life but also imposes a substantial economic burden on every healthcare system. Nevertheless, although neurourology is becoming a more and more regarded subspecialty, bridging the fields of both neurology and urology, it is still a "stepchild" with an urgent need for well-trained and highly motivated researchers and clinicians to improve the care of patients with neurourological problems.

The control of lower urinary tract function is a complex, multilevel, central, and peripheral process with a neural network distributed across parasympathetic, sympathetic, and somatic pathways. It is therefore not surprising that many neurological disorders, such as multiple sclerosis, Parkinson's disease, stroke, spinal cord injury, spina bifida, diabetic neuropathy, Alzheimer's disease, etc., frequently result in lower urinary tract dysfunction. The location and extent of the lesion in the neurological axis determine the dysfunction pattern, which is reflected in the patient's symptoms. Indeed, the variability of neurogenic lower urinary tract dysfunction is huge and may range from a completely asymptomatic situation to end-stage renal failure requiring hemodialysis.

The prevalence and incidence of several neurological disorders are already high, and neurodegenerative disorders such as Alzheimer's disease will further increase in the course of a continuously aging population so that more and more neurological patients will require professional neurourological management. This, however, can be provided only by adequately trained clinicians and enthusiastic researchers, because many questions regarding neural control of lower urinary tract function and its alterations through the course of a neurological disorder remain unclear.

The major goal in neurourology is to protect the upper urinary tract and to achieve urinary continence and a good quality of life. Timely diagnosis and treatment are essential, and most neurourological patients need lifelong care. Clinical assessment should be comprehensive and usually includes urodynamics. Conservative and noninvasive therapies must be tested before surgical procedures are considered. Finally, an individualized, patient-tailored approach is required for the management of neurogenic lower urinary tract dysfunction.

There are several excellent books on neurourology available, but the work by Drs. Corcos and Przydacz is different: It is the joint conclusion by one of

the most experienced specialists in the field and a young enthusiastic talent—two generations provide us with an extremely helpful evidence-based guide for daily practice, a must for all interested in neurourology! Enjoy the reading—you will be thrilled!

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Thomas M. Kessler

Preface

Several good quality textbooks, books, and book chapters exist already on top of well-developed international and national guidelines to help the practice and understanding of the complex and fascinating field of neurourology. However, my personal long experience in this field compelled me to consider a new book with a different approach, one focused on our daily practice. This book is aimed to bring the reader into the heart of the action of any health professional consulted for a patient with a neurogenic bladder. This role-play idea explains the original plan of this project.

For this book, which will hopefully guide every student and physician dealing with these conditions, I had the opportunity to involve Dr. Mikolaj Przydacz, a young and bright urologist at the dawn of his practice, who quickly understood the global idea of this "real-life" book and became fully involved in its writing. Thanks to him for his full commitment to the project, for his patience, and for his excellent work.

Montreal, QC, Canada

Jacques Corcos
Mikolaj Przydacz

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Part I

Introduction

Book Presentation with Overview of Bladder Physiology

1

Book Presentation

After all these years of practice with patients presenting urinary tract symptoms secondary to many neurological diseases, we boil them down into three categories. The first group is recent spinal cord injured individuals that we see for the first time. Almost independently of the gravity of their lesion the same approach in terms of history taking and investigation plan is used. It is relatively rare to start investigating and treating their condition on this first visit except for assuring a proper bladder emptying technique.

The second group of patients is the vast majority of neurologically impaired individuals, with usually well-diagnosed neurological disease (multiple sclerosis, Parkinson disease, stroke, myelomeningocele, spinal cord injury, etc.) that we see for lower urinary tract symptoms. They have symptoms due to detrusor or sphincteric hypo or over activity. For this second group of patients diagnosis of precise dysfunction and treatment are immediately initiated.

Finally, the third group of patients are those previously diagnosed with neurological diseases and frequently initially well treated neurogenic bladder dysfunctions but who were lost to follow-up and present with a urinary complication: infection, stone, hydronephrosis with or without renal function impairment or more rarely urinary tract cancers. This last group of patients needs urgent changes in the management of their neurogenic bladder and urgent specific diagnostic and treatment approach for the complication which brought them to us.

Organization of Summaries and Recommendations

At the end of each chapter, readers will be provided with summary and recommendations. Whereas the summary part will be supported by levels of evidence (LE), the recommendation part will be enriched by grades of recommendation (GR). In supporting day-to-day clinical practice, it is highly desirable that the recommendations should follow an accepted grading system for evidence and recommendation. Thus, we decided to utilize a modified version of the Oxford System for Evidence Based Medicine as this system has already been used by the leading urological societies and consensus documents, for instance the European Association of Urology (EAU), Canadian Urological Association (CUA), or International Consultation on Incontinence (ICI). The modified version of the Oxford system can be directly "mapped" onto the original Oxford system and it is more applicable for daily practice of clinicians [1]. The employed system is presented in Table 1.1.

The modified Oxford system does not easily fit into areas of basic science, epidemiology studies, methods of assessment and investigations. Further research in evidence-based medicine is

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_1

Table 1.1 The modified version of the Oxford system can be directly "mapped" onto the original Oxford system and is more applicable for daily practice of clinicians

Levels of evidence	
Level 1	Meta-analysis of randomized controlled trials (RCTs) or a good-quality RCT
Level 2	Meta-analysis of good-quality prospective cohort studies or an individual cohort study (including low-quality RCT)
Level 3	Good-quality retrospective case–control studies or case series
Level 4	Expert opinion based on "first principles" or bench research, not on evidence
Grades of recommendation	
Grade A	Usually consistent level 1 evidence
Grade B	Consistent level 2 or 3 evidence or "majority evidence" from RCTs
Grade C	Level 4 evidence, "majority evidence" from level 2 or 3 studies, expert opinion
Grade D	No recommendation possible because of inadequate or conflicting evidence

warranted, in order to develop appropriate levels of evidence that can lead to recommendations in these important areas of medicine. Nevertheless, readers will be provided with basic knowledge and summaries of these specific areas.

Overview of the Physiology of Lower Urinary Tract

The bladder and the urethra serve two main functions: storage and periodic release of urine. These two functions are controlled by central and peripheral nervous systems (Fig. 1.1) [2, 3]. Central part includes brain and spinal cord. Peripheral part is further divided into afferent and efferent parts based on the directionality of the signal that the nerves transmit. Thus, afferent signals are sensory signals, while efferent signals are motor signals. Both afferent and efferent pathways consist of visceral and somatic pathways. Composition of visceral motor pathways are termed as the autonomic nervous system with sympathetic and parasympathetic parts.

Afferent pathways of the lower urinary tract are included in hypogastric, pelvic, and pudendal nerves, with the predominant sensory function of the second one [4, 5]. These three nerves also contain efferent pathways that transmit motor information. However, hypogastric nerve is sympathetic, pelvic is parasympathetic and pudendal is somatic. Moreover, the first arises at the upper lumbar level of the spinal cord, whereas the last two at the sacral level. Coordinated activities of the peripheral nervous system innervating the bladder and the urethra during urine storage and voiding depend on multiple reflex pathways organized in the brain and spinal cord. Special role belongs to sacral and pontine micturition centers additionally supported by the higher centres (cerebral cortex, particularly the anterior cingulated gyrus). Whereas the sacral micturition center (S2–S4) is primarily a reflex center for bladder contractions, the pontine micturition center is primarily responsible for coordinating relaxation of the urinary sphincter when the bladder contracts [6]. Cortical influence has a role in determining when and where void may be safely performed.

The neural pathways that control the lower urinary tract are organized as simple on–off switching circuits that maintain a reciprocal relationship between the urinary bladder and the urethral outlet. During urine storage, bladder distension produces low-level impulsation in bladder afferent pathways, which in turn stimulates the sympathetic outflow (via hypogastric nerve) to the bladder outlet (bladder base and urethra, with an additional detrusor inhibition) and the somatic outflow (via pudendal nerve) to the external sphincter striated muscle (Fig. 1.2a) [7]. These responses are elicited by spinal reflex pathways. Furthermore, pontine micturition center increases external urethral sphincter activity. During elimination of urine, intense bladder afferent impulsation activates spinobulbospinal reflex pathways passing through the pontine micturition center, which stimulate the parasympathetic outflow (via pelvic nerve) to the bladder and internal sphincter smooth muscle and inhibit the sympathetic and somatic outflow to the bladder outlet (Fig. 1.2b). Additionally, cortical inhibitory control, predominately located in the frontal lobe area, needs to be removed to increase bladder activity and release urine voluntarily [8–10].

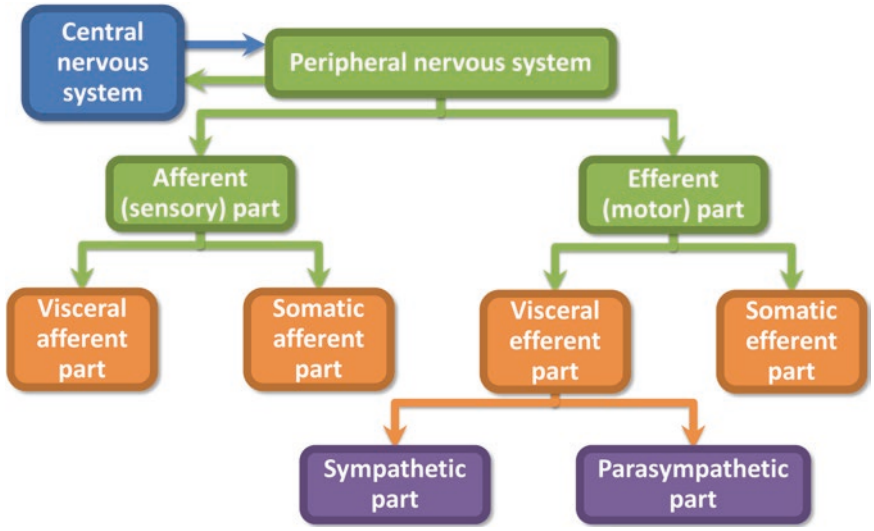

Fig. 1.1 Organization of the nervous system

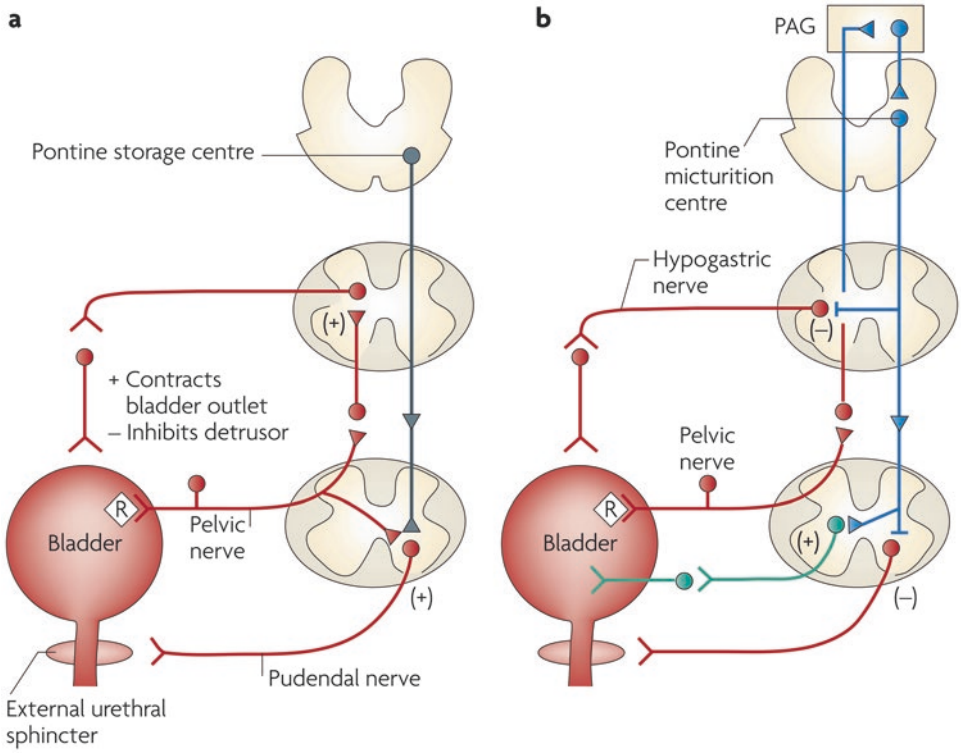

Fig. 1.2 Neural circuits that control continence and micturition. (**a**) Urine storage reflexes. (**b**) Voiding reflexes with spinobulbospinal reflex pathways shown in *blue* and parasympathetic outflow shown in *green*. Ascending afferent input from the spinal cord might pass through relay neurons in the periaqueductal grey (PAG) before reaching the pontine micturition centre. Note that these diagrams do not address the generation of conscious bladder sensations, nor the mechanisms that underlie the switch from storage to voiding, both of which presumably involve cerebral circuits above the PAG (*R* represents receptors on afferent nerve terminals) (Reprinted from Fowler et al. [7], with permission Macmillan Publishers Ltd: Nat Rev Neurosci. 2008)

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Neurogenic Bladder Pathophysiology

2

Introduction

Neurogenic bladder (NB) or neurogenic lower urinary tract dysfunction of the urinary bladder and urethra, due to central and/or peripheral nervous system diseases, is one of the most challenging problems in urology. Various disorders or injuries affecting the nervous system may cause chronic bladder dysfunction, which type depends on central or peripheral nervous system damage level and intensity. The bladder can become overactive (emptying too frequently/quickly) or underactive (not emptying completely), with urethral complex overactivity (leading to dyssynergia with partial/complete urinary retention) or underperformance (evoking incontinence). Therefore, NB pathophysiology should be described as neurogenic detrusor overactivity, neurogenic detrusor underactivity, detrusor-sphincter dyssynergia, and neurogenic sphincter deficiency. It should be noted that studies investigating pathophysiological mechanisms of NB utilize both human and animal models. As human tissues are more difficult to obtain, our current knowledge on NB pathophysiology is mainly based on animal studies and clinical observations.

Neurogenic Detrusor Overactivity

Neurogenic detrusor overactivity (NDO) is a clinical diagnosis of detrusor contractions occurring during the filling phase of urodynamics (detrusor overactivity) in the presence of relevant neurological condition [1]. However, presented definition has some limitations. Neurologically diagnosed patients may suffer from other diseases/conditions which can lead to similar symptom presentation and/or urodynamic findings. Elderly male patients with a neurological disorder may have a concomitant diagnosis of benign prostatic hyperplasia with an overactive detrusor due to bladder outlet obstruction. Both female and male patients may suffer from idiopathic overactive bladder (OAB) despite confirmed diagnosis of neurological impairment. Furthermore, uninhibited detrusor contractions can be observed in up to 30% of elderly men and women [2].

Underlying mechanism of NDO may include a lack of inhibition of motor pathway or enhancement of sensory input and/or motor output. As a consequence, pathophysiological abnormalities occur in different anatomic sites:

- Bladder urothelium/suburothelium (myofibroblasts) with afferent nerves (urothelium-afferent junction),
- Bladder detrusor smooth muscle with efferent nerves (detrusor-efferent junction)
- Spinal cord
- Brain

There is increasing evidence that bladder epithelial cells play an important role in modulation of bladder activity [3]. Bladder urothelium contains mechanosensitive and chemosensitive

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receptors and ion channels. They are mainly represented by receptors for bradykinin, purines (P2X, P2Y), neurotrophins, protease activated receptors, epithelial sodium channels (ENaC), and transient receptor potential channels (TRPC) [4]. Urothelial cells also release a wide variety of specific and non-specific transmitters like adenosine triphosphate (ATP) and prostaglandins. Suburothelial layer includes myofibroblasts with gap junction proteins (connexin 43 and cadherin-11) and are able to generate spontaneous electrical activity [5]. Afferent signals in normal bladders are carried by Aδ fibers and in lesser degree by C fibers. This chemical and structural network does allow transmission and communication between different cell types, bladder compartments, and afferent nerves. In considering the pathophysiology of NDO, special attention should be paid for urothelial ATP as it can stimulate suburothelial myofibroblasts and/or afferent nerves via purinergic receptors triggering bladder overactivity [3, 6, 7]. Of note, both myofibroblasts and afferent nerves may release ATP as well. Structural and functional changes in bladder urothelium/suburothelium have been demonstrated in patients after spinal cord injury (SCI) even in early post-trauma period [8]. Similar findings with a predominant role of ATP in NDO pathophysiology have been investigated in urothelial tissues from patients suffering from multiple sclerosis [9]. Nevertheless, studies performed by Roosen et al. stressed that increased gap junction formations (upregulations of connexin 43 and cadherin-11) in the bladder suburothelium of neurologically impaired patients has a more significant role in the pathogenesis of the neurogenic detrusor abnormality [10, 11]. In turn, de Groat et al. emphasized the role of disturbances in afferent innervation after spinal cord transection in cats and described the switching of bladder transmission from Aδ to C fibers [12]. The C-fiber afferents transmit signals of micturition reflex with a shorter latency (a condition of being temporarily inactive) than Aδ fibers, thus leading to bladder overactivity. Similar findings have been found in human bladders of patients after SCI [13]. Further studies of Yoshimura et al. on C-fiber neurons have demonstrated changes in their electrophysiologic functional properties after SCI indicating the increase in expression of TTx-sensitive sodium channels as a potential reason of short latency in micturition reflex [14]. Moreover, Apostolidis et al. have shown upregulation in the expression of P2X3 and TRPV1 receptors in suburothelial nerve fibers in NDO bladders [15]. To conclude, urothelium-afferent junction can be altered structurally and functionally in NDO and play an important role in NDO pathophysiology.

Detrusor smooth muscle with the autonomic innervation of postganglionic efferent nerves represents the main functional component in the clinical presentation of NB. One of the mechanisms leading to NDO describes postjunctional detrusor smooth muscle supersensitivity as a result of partial bladder denervation [16–18]. Due to this postjunctional pathology with reduced autonomic motor innervation, detrusor smooth muscle responses in exaggerated (supersensitive) mode to specific and non-specific neurotransmitters. Another mechanism of NDO development includes abnormalities in neurotransmitters' release and their receptors' distribution. It has been shown that after SCI the excitatory neurotransmitter mechanism changes from a purinergic to a cholinergic system [19]. In the normal bladder, the detrusor muscle mainly contains M2 and M3 cholinergic (muscarinic) receptors, with the M3 subtype playing a major role in detrusor contraction [20]. Interestingly, the proportion and role of these detrusor cholinergic receptors have recently been demonstrated to evolve after acute suprasacral SCI and chronic antimuscarinic treatment. Braverman et al. reported that total muscarinic receptor density is significantly higher in spinal cord transected rats than in normal controls [21]. M2 receptors accounted for the entire increase, with no change in M3 receptor density. Moreover, they showed a switch from M3-mediated detrusor contractions in normal rats to M2-mediated detrusor contractions in rats after spinal cord transection.

Interestingly, Biardeau et al. have recently demonstrated, in a spinal cord transected rat model, that early administration of selective muscarinic receptor antagonist could prevent NDO [22]. Another studies have shown that downregulation of calcium-activated potassium channels (BK) may lead to increased spontaneous contractile activity [23] and K_{ATP} and SK_{Ca} potassium channels are the main regulating channels of spontaneous contractile activity in neurologically impaired detrusor smooth muscle [24, 25]. Figure 2.1 presents an overview of abnormalities in bladder compartments described in pathophysiology of NDO [26].

Spinal cord represents platform between urothelium-afferent and detrusor-efferent junctions. Communication is provided by a wide network of various neurotransmitters. Among them special attention should be paid for vasoactive intestinal peptide (VIP), pituitary adenylate cyclase-activating polypeptide (PACAP), and γ-aminobutyric acid (GABA), the most important spinal cord neurotransmitters in NDO pathophysiology [27]. Whereas VIP and PACAP are pro-micturition agents with upregulation after spinal transection, GABA is an anti-micturition agent characterized by downregulation in spinally transected animals [28, 29]. Other transmitters have also been investigated. Animal studies have shown significant higher release of ATP, substance P, and neurokinin A in rats' spinal cord after transection [7, 30]. Since they are considered as excitatory neurotransmitters, their elevated concentrations can significantly contribute to NDO development. Intact communication between afferent and efferent neurons within spinal cord is supported by interneurons which modulate the micturition reflex. Their function may be altered after SCI due to the mechanism of synaptic plasticity and descending axonal degeneration after SCI may reveal axonal sprouting in interneurons [31]. This synaptic plasticity promotes more communication between afferent and efferent neurons leading to and promoting NDO. Of note, whereas presented pathophysiological abnormalities appear in various levels of the spinal cord, bladder dysfunction characterized as NDO is usually found in spinal cord damage or injury above the sacral region (further described in Chap. 3, "Pathologies Responsible for the Development of the Neurogenic Bladder").

The contribution of brain changes in NDO pathophysiology has not been well investigated. Brain plasticity after SCI has been recently descried by employing functional magnetic resonance imaging (fMRI) and neurophysiological analyses [32]. It has been shown that significant changes appear in topographical representation of different somatosensory projections within cerebral cortex after SCI. Authors hypothesized that this reorganization may have clinical consequences and proposed similar neural plasticity for bladder function. In contrast, studies utilizing middle cerebral artery occlusion animal model indicated that the forebrain augmentation contributes to the maintenance of NDO [33].

Neurogenic Detrusor Underactivity

Neurogenic detrusor underactivity (NDU) is defined as a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span during urodynamic study (detrusor underactivity) with underlying neurological pathology [34]. This definition excludes idiopathic, myogenic, and drug-induced causes of underactive detrusor [35, 36]. Within the spectrum of underactive detrusor, the condition when contractions cannot be demonstrated during urodynamics is defined as acontractile detrusor (AD). As efferent output of urine flow can be activated reflexively by both spinal and brain afferent input supported by impulsation from the pelvic visceral organs and somatic pathways from the perineal muscle and skin, underlying mechanism of NDU may include dysfunctions of sensory input (with defects in axonal conduction or synaptic transmission), decreased motor

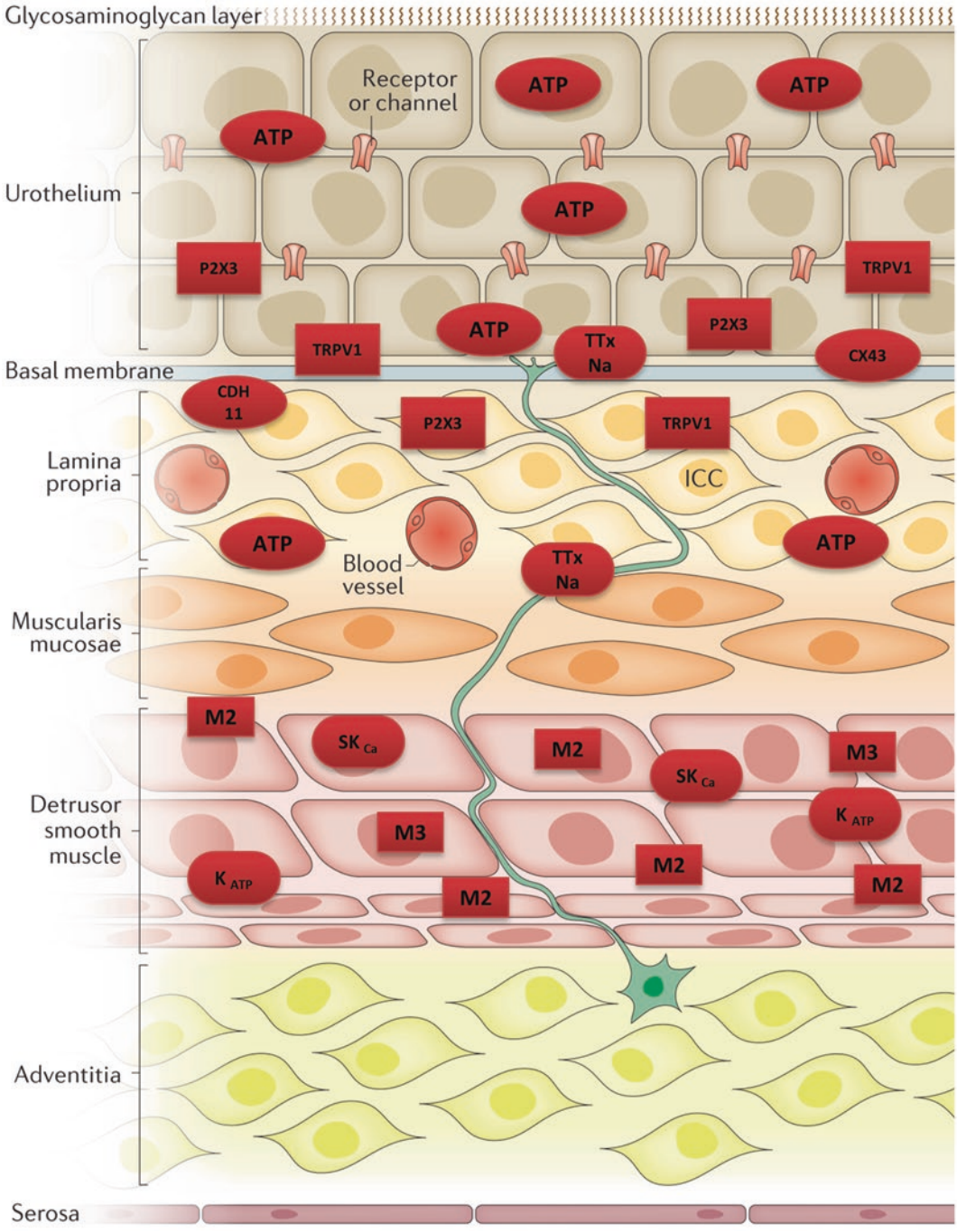

Fig. 2.1 Overview of abnormalities in bladder compartments described in pathophysiology of neurogenic detrusor overactivity. *ATP* adenosine triphosphate, *P2X3* P2X3 receptors, *TRPV1* TRPV1 receptors, *CX43* connexin 43, *CDH11* cadherin 11, *TTx Na* TTx-sensitive sodium channel, *M2* muscarinic receptors type 2, *M3* muscarinic receptors type 3, *KATP* KATP potassium channel, *SKCa* SKCa potassium channel (Adapted from Merrill et al. [26] with permission, Macmillan Publishers Ltd: Nat Rev Urol. 2016)

output, reduced central excitatory transmission, or enhanced central inhibition [37–39]. Therefore, NDU may be presented in damages of bladder peripheral afferent nerves, bladder peripheral efferent nerves, spinal cord, and brain. Whereas the disruption of the afferent tract leads to early termination of voiding reflex, the disturbances of the efferent pathway contribute to impaired activation of detrusor [40]. Brain and spinal cord play a role of integrative control centers. It should be noted that different mechanisms may occur simultaneously when NDU is diagnosed. Nonetheless, the final effect of reduced acetylcholine release from parasympathetic nerve endings to the synaptic cleft resulting in a lack of a contractile stimulus is the same for all these pathologies [38].

Underlying cause of bladder neural tract damage may be traumatic or non-traumatic. Traumatic injuries of central or peripheral bladder innervation are critical for signals circulating. In damages of bladder afferent pathways, both Aδ and C fibers may be in disrepair, leading to various intensifications of sensory disturbances. Pathophysiology of neural tract damage contains primary and secondary mechanism [41, 42]. Whereas the first is a combination of the initial impact and the subsequent persisting compression finally resulting in interruption of neural continuity, the latter includes progressive necrotization and inflammatory cell infiltration, alternations in endothelial cell function with free radical formation, ionic derangements with the largest variations in extra- and intracellular K^+ and Ca^{2+} levels, apoptosis and excitotoxin release [43–47]. These factors significantly influence on neuroplasticity. Note that bladder dysfunction characterized as NDU is usually found in damage or injury located in the sacral spinal cord or in the peripheral nervous system (discussed in Chap. 3).

In non-traumatic entities of NDU, particularly in systemic disorders causing polyneuropathy (e.g., diabetes), impaired bladder behavior described as bladder underactivity has also been documented. Studies on patients suffering from diabetic cystopathy have shown that altered metabolism of glucose, ischemia, impaired axonal transport, superoxide-induced free radical formation, and metabolic derangement of the Schwann cells have significant contribution to damage of bladder neural pathways [48, 49]. Recently published data suggest that various systemic disorders leading to NDU may also influence on other bladder compartments such as detrusor smooth muscle or urothelium [48]. Animal studies of diabetes mellitus (DM) rats have shown increased depolarization of myocytes to externally applied acetylcholine and decreased spontaneous activity, presumably related to altered purinergic transmission [50]. Changolkar et al. demonstrated that bladder underactivity related to diabetes is associated with disturbances in detrusor smooth muscle characterized as an oxidative stress, increase in lipid peroxides and sorbitol, overexpression of aldose reductase and activation of polyol pathway [51]. Other studies stressed the role of variations in neurotransmitters levels. Decreased levels of nerve growth factor (NGF) and neurotrophin-3 (NT-3) in bladder compartments and afferent nerves have been considered as the most important changes leading to detrusor underactivity [52–54]. On the other hand, Pinna et al. demonstrated that urothelial levels of endogenous prostaglandins E2 and F2α were higher in DM rats than in controls [55]. As these factors are considered as bladder relaxants, they can contribute to bladder underactivity. Similar findings were reported with regard to changes in nitric oxide synthase (NOS) and reactive nitrogen species formation [56]. NOS has been discovered as upregulated in the urothelium, lamina propria, and smooth muscle of DM rat bladders. Non-traumatic damage of bladder neural tracts may also be seen in neurological infections. The infection mechanism involves autoimmune reaction to peripheral nerves and/or roots or spreading of the infection from cutaneous nerve endings to the corresponding dorsal root ganglia. The neuropathy affecting the bladder often takes the form of an autonomic neuropathy, which may involve both the sympathetic and the para-

sympathetic, as well as afferent and efferent, innervation of the bladder and urethra [57].

NDU may also be observed in damages of the pons and the pontine micturition center (located in the dorsal pontine tegmentum) [58]. Decreased output from these structures results in a lack of a contractile stimulus. Burney et al. indicated cerebellum as a possible brain representation of NDU. They reported that patients with cerebellar infarctions are highly predisposed to detrusor underactivity with preserved function of sphincter [59] but other studies presented opposite results [60]. Studies on monkeys with medically induced Parkinson disease showed that selective destruction of striatal dopaminergic neurons which pass from the substantia nigra pars compacta to the putamen significantly contributes to detrusor underactivity [61, 62].

Detrusor-Sphincter Dyssynergia

Detrusor-sphincter dyssynergia (DSD) is defined as a detrusor contraction synchronous with an involuntary contraction of the urethral and/or peri-urethral striated muscle [63]. DSD is also known as detrusor-striated sphincter dyssynergia and detrusor-external sphincter dyssynergia [64]. This condition is caused by the interruption of the spinal pathways between the brainstem (pontine micturition center) and the sacral spinal cord (sacral micturition center) [65, 66]. In the absence of neurological disorder, impaired coordination between detrusor and sphincter during voiding is more appropriately referred to as dysfunctional voiding or pelvic floor hyperactivity [67, 68].

Presented incoordination was hypothesized to be an abnormal flexor response of the perineal musculature to bladder contraction and considered as a continence reflex exaggerated by the loss of supraspinal influence [69, 70]. Thus, current understanding of DSD includes failed inhibition of spinal guarding reflexes and incorrect excitation of Onuf's nucleus [64, 67, 71] but underlying cellular and subcellular mechanisms of this phenomenon have not been investigated. Furthermore, studies on the initial description of DSD and chronology of events present rather conflicting results. Researchers have shown that urethral sphincter may contract before, after, or at the same time as detrusor [72–74].

Neurogenic Sphincter Deficiency

Neurogenic sphincter deficiency (NSD) is a clinical diagnosis of urethral weakness or low resistance to bladder leakage due to intrinsic sphincter deficiency (ISD) caused by a neurological condition. Readers should be aware that universal agreement on this definition nor on definition of ISD has not been achieved [75]. Nevertheless, implementation of neurological contribution to the NSD term allows to exclude other non-neurogenic causes of ISD, e.g. previous pelvic surgery, aging, or hypoestrogenic state.

The pathophysiology of intrinsic sphincter insufficiency due to neurological diseases has not been well investigated. It is known that the internal urethral sphincter is under control of the autonomic nervous system, in contrast to external sphincter with somatic innervation [76]. It has been hypothesized that disorders of anterior grey column and/or anterior nerve roots with nerve fibers travelling to the sphincter may lead to the de-innervation of intrinsic sphincter and result in ISD [77]. Another hypothesis stresses that the damage of sympathetic thoracolumbar intermediolateral nuclei is responsible for clinical presentation of NSD [78]. Currently, there is no data on underlying cellular and subcellular mechanisms of NSD.

Conclusion (Table 2.1)

Table 2.1 Conclusion

Summary	Level of evidence
Neurogenic bladder (NB) pathophysiology should be analyzed based on clinical presentation described as neurogenic detrusor overactivity, neurogenic detrusor underactivity, detrusor-sphincter dyssynergia, and neurogenic sphincter deficiency	4 (Expert opinion)
Current knowledge of NB pathophysiology is based on human and animal studies, with the predominance of the latter	4 (Expert opinion)
Pathophysiological abnormalities of NB occur in different anatomic sites: bladder urothelium/suburothelium with afferent nerves, bladder detrusor smooth muscle with efferent nerves, spinal cord, and brain	4 (Bench research)
Underlying mechanism of neurogenic detrusor overactivity may include a lack of inhibition of motor pathway or enhancement of sensory input and/or motor output	4 (Bench research)
Neurogenic detrusor underactivity may be caused by dysfunctions of sensory input, decrease of motor output, reduction of central excitatory transmission, or enhancement of central inhibition	4 (Bench research)
Detrusor-sphincter dyssynergia is the result of increased motor output to the external urethral sphincter during contractions of detrusor smooth muscle	4 (Bench research)
Neurogenic sphincter deficiency is the outcome of decreased motor output to the intrinsic urethral sphincter	4 (Bench research)

Recommendation	Grade of recommendation
Understanding the basic pathophysiology of NB helps to diagnose and treat NB patients	Expert opinion

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3 Pathologies Responsible for the Development of the Neurogenic Bladder

Introduction

Neurogenic bladder (NB), also known as neurogenic lower urinary tract dysfunction, is a global and very broad term referred to acute or chronic bladder dysfunctions in neurologically impaired patients. A wide variety of neurological conditions, lesions, diseases, or injuries of central and/or peripheral nervous system may affect bladder/sphincter innervation and result in NB clinical presentation. Bladder behavior depends on extent and time-length of each specific disorder and may require close monitoring both for symptomatic control and/or potential complications. Thus, NB is not a static condition but follows its own natural history that can manifest in urological complaints and/or complications.

The clinical presentation of lower urinary tract dysfunction due to neurological disorders is determined by the site and nature of the lesion. A very simple classification system for day-to-day clinical practice, based on lesion level with expected symptoms and urodynamic findings, is presented in Fig. 3.1 [1].

In suprapontine lesions, cortical inhibition of voiding reflex is disturbed [2]. This results in clinical presentation of neurogenic detrusor overactivity with the predominance of storage symptoms. As the pontine micturition center (responsible for coordinating relaxation of the urinary sphincter when the bladder contracts) is unspoiled, urethral resistance and sphincter function with detrusor-sphincter coordination are preserved [3].

In infrapontine-suprasacral lesions, where inhibiting signals from the cortex and coordinating signals from the pontine micturition center are limited, patients present with neurogenic detrusor overactivity and/or detrusor-sphincter dyssynergia. Both storage and voiding symptoms might be reported. As the sacral micturition center (a reflex center for bladder contractions) is unspoiled, uninhibited and involuntary contractions (reflex bladder contractions) are observed.

Sacral lesions disrupt signals of the cortex, the pontine micturition center and the sacral micturition center. Infrasacral lesions, affecting afferent and/or efferent pathways, interrupt circulation of sensory and/or motor signals between the bladder and the voiding centers. Therefore, in sacral-infrasacral lesions even reflex bladder contractions are lost. This results in clinical presentation of neurogenic detrusor underactivity and/or neurogenic sphincter deficiency with the predominance of voiding symptoms.

However, clinical presentation of neurogenic lower urinary tract dysfunction may vary from that presented above. Frequent evolution of bladder behavior observed with progression of multiple diseases and multitude of lesions can elicit unexpected symptoms and findings. In presenting pathological entities that may lead to NB, special attention should be paid for traumatic

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_3

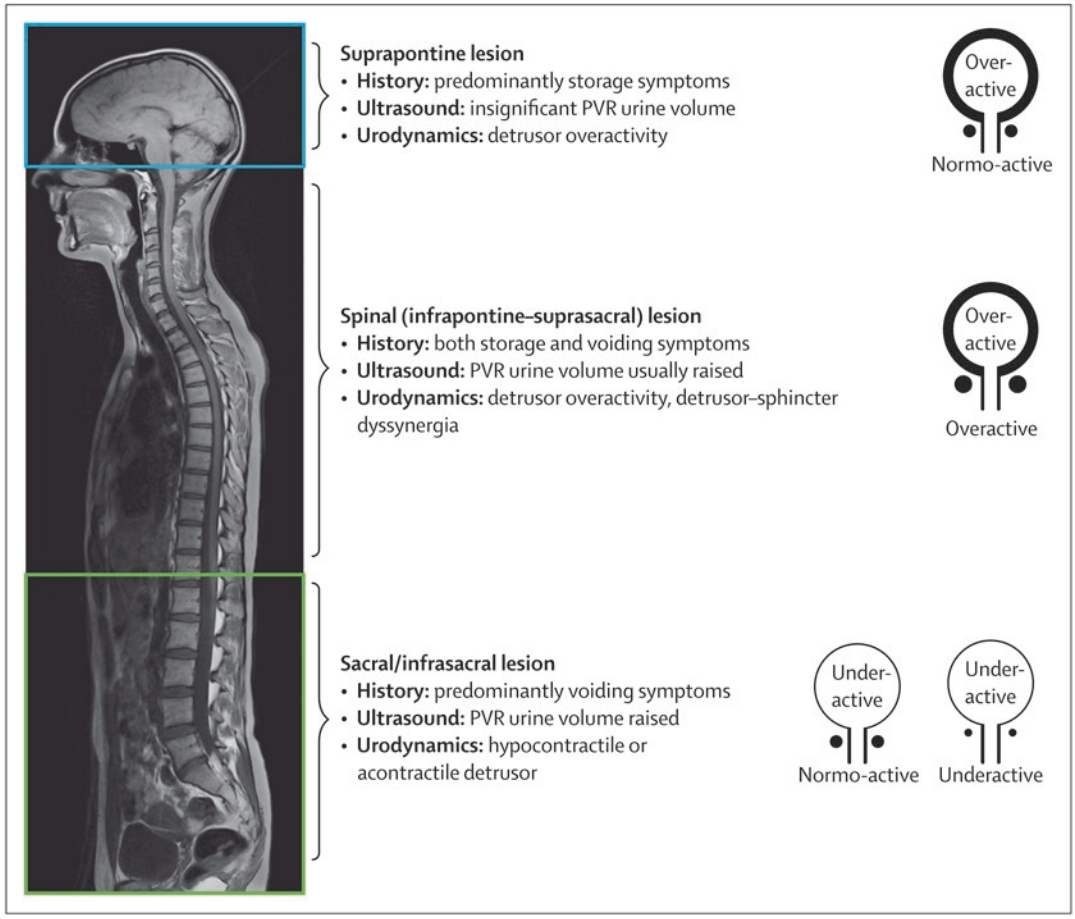

Fig. 3.1 Patterns of lower urinary tract dysfunction following neurological disease. The pattern of lower urinary tract dysfunction following neurological disease is determined by the site and nature of the lesion. The *blue box* denotes the region above the pons and that in *green* denotes the sacral cord and infrasacral region. Figures on the *right* show the expected dysfunctional states of the detrusor-sphincter system. *PVR* post-void residual (From Panicker et al. [1], with permission)

entities as patients after injuries of head and/or spinal cord represent different diagnostic and therapeutic group with specific symptom evolution. Furthermore, brain and spinal injuries often coexist as 11% of patients with spinal cord injury (SCI) have an associated head injury [4, 5]. Brain and spinal injuries may also result in different types of bladder dysfunction, making accurate neurourological diagnosis even more challenging. To make things worse, traumatic injuries may also affect cognitive and behavioral function. Taking these issues into account, organization of this chapter was designed to support physicians in their daily clinical practice.

Traumatic Entities and Their Neurourological Consequences

Head Injury

Traumatic brain injury is the leading cause of death and disability in people younger than age 45 in the United States [6]. The economic burden of this entity has been growing. It includes direct medical costs in acute and post-acute period as well as indirect costs such as loss of productivity.

As traumatic brain injuries affect supratentorial structures, patients usually present with

neurogenic detrusor overactivity (NDO). Studies suggest that NDO is more commonly associated with right-sided damage [7, 8], whereas left hemispheric injury is linked to impaired contractility [9]. Frontal-lobe injuries are more prolific to produce bladder dysfunctions than injuries of other lobes [10, 11]. Mochizuki et al. reported that unilateral right cortical lesions in the prefrontal area produce transient dysfunction, whereas bilateral lesions are inclined to make lower urinary tract (LUT) dysfunctions more permanent [12].

In the acute phase of traumatic brain injury (coma), spontaneous micturition is possible with persisted perception of bladder fullness in mild stages [13, 14]. Voiding is synergistic, with no residual. However, in up to 10% of acute patients, retention may be observed and mechanism of this dysfunction has not been well investigated [15]. This abnormality can be a result of increased cerebral inhibition, temporary pontine shock or exaggerated bladder stretching following the accident [16]. In post-acute phase, patients usually report frequency, urgency, and urgency incontinence. Symptom severity is usually in line with the extent of injury [10]. Thus, a lack of sensory or motor control of micturition reflex may also be notified in complex patients of complete lesions. Residual volume is not elevated as a result of uninhibited bladder contractions [8]. Urodynamic study usually reveals overactive detrusor with intact sphincter function [17]. In some cases, decreased detrusor compliance (ability of the bladder to accommodate to increasing volume with low pressure) may also be seen [10]. Despite the fact that etiology and mechanism of micturition disturbances due to traumatic brain injuries are complex and multifactorial, studies have shown that LUT dysfunctions in this specific group of patients have good prognosis and spontaneous resolve or improvement of bothering symptoms may be expected [8, 15, 18].

Spinal Cord Injury

The reported global prevalence of SCI is between 236 and 1009 per 1,000,000 [19]. However, epidemiological data are often limited. Whereas data on SCI prevalence are fully available from high income countries of North America, Europe and Australia; Asian, African and South American countries are not appropriately represented by reliable figures, leading to probable underestimation of overall prevalence. Traumatic SCI exacts an extensive burden on the injured individual, their family, carers, and society. In addition to the physical and psychosocial trauma, the economic burden is thought to be substantial, due to increased health care costs as well as higher rates of morbidity and premature mortality [20]. Most of these patients suffer from bladder dysfunction, which can significantly deteriorate their quality of life and have devastating complications if not managed effectively [21]. Approximately 81% of patients with SCI will have at least some degree of urinary dysfunction presenting within 1 year of the injury [22]. On the other hand, less than 1% of these patients will make a full recovery [23].

The effect of SCI on the lower urinary tract depends on cord lesion level, duration, and completeness. Therefore, clinical presentation varies in acute and post-acute phase of SCI as well as in suprasacral and sacral injuries.

Spinal Shock Following an acute phase of SCI above the sacral level, a combination of autonomic and motor dysreflexia appears and presents as flaccid paralysis and absence of reflex activity below the level of lesion [24]. This condition, known as the spinal shock, usually lasts up to 3 months. The duration of spinal shock in patients with incomplete SCI is shorter, sometimes lasting for several days [25]. Parasympathetic activation of the bladder is rendered inactive and interruption of the neuraxis below the pons eliminates the micturition reflex resulting in detrusor underactivity [26]. Of note, activity of the internal and external sphincter persists or rapidly recovers. As a result, bladder becomes atonic with disturbed filling sensations and patient presents with urine retention. It is usually followed by dribbling incontinence as a consequence of an overflow. After spinal shock, more persistent neurological changes emerge as a result of reorganization of neuronal circuitry [21].

Suprasacral Injury Following spinal shock associated with injury above the sacral region, reflex bladder function will occur as activity of the sacral micturition center is preserved. Consciousness of filling sensation might not be totally absent. Nevertheless, voluntary inhibition of the micturition reflex arc is lost. Uncoordinated and involuntary bladder contractions might occur and synergistic relaxations of the external sphincter are not usually retained. Thus, reflex bladder function can be presented as neurogenic detrusor overactivity (NDO) and/or detrusor-sphincter dyssynergia (DSD) [27, 28]. Note that, these two pathologies may often coexist. Whereas incontinence might be caused by NDO, it can also be accompanied by urinary retention owing to DSD. In both cases, the desire to void is either reduced or absent [29]. As uninhibited bladder contractions become stronger, the post-void residuals decrease. Non-specific stimuli, such as touching the skin of the lower abdomen or genitalia, can elicit reflex activity. Individuals with spinal lesions at the T10–L1/L2 level often develop an open bladder neck, with consequences of urinary incontinence due to neurogenic deficiency of the intrinsic sphincter [30].

Sacral Injury Injuries at the sacral level result in parasympathetic decentralization of the bladder detrusor and somatic denervation of the external sphincter. In cases of complete lesion, conscious awareness of bladder filling is lost and the micturition reflex is completely absent. Therefore, bladder behavior is usually characterized as neurogenic detrusor underactivity, often without demonstration of any contractions during urodynamics (acontractile detrusor). The intrinsic urethral sphincter function may also be lost contributing to incontinence. Interestingly, the external sphincter usually remains competent but with limited ability to relax and without voluntary control [26, 31]. This functional phenomenon of the external sphincter in sacral SCI patients has been explained. The pelvic nerve innervation (parasympathetic) to the bladder usually arises one segment higher than the pudendal nerve innervation (somatic) to the sphincter. Also, the nuclei are located in different portions of the sacral cord, with the detrusor nuclei located in the intermediolateral cell column and the pudendal nuclei located in the ventral gray matter [4]. In view of these various abnormalities, patients present with urinary retention and/or incontinence owing to urine overflow or a loss of urethral resistance. Moreover, patients with lesions distal to the sacrum are at risk for loss of compliance [32, 33]. It has been suggested that an altered sympathetic pathway could explain this bladder compliance decrease [34].

Spinal Cord Injury and Bladder Behavior: General Overview Multiple studies have investigated correlations between the level or the completeness of injury and bladder behavior. Table 3.1 presents results of recently published meta-analysis focusing on the level of injury, Table 3.2 analyzes the completeness of trauma, and Fig. 3.2 shows a general overview of bladder dysfunction following SCI [3, 34, 36].

To conclude, the level and the completeness of injury may help to predict and diversify bladder behavior. However, neurogenic LUT dysfunction following SCI might vary in each individual and thus requires an individually tailored management strategy, based on a specific personalized diagnosis. It should be supported by urodynamic evaluation to characterize a baseline dysfunction and to identify patients at risk for upper tract deterioration.

Non-traumatic Entities and Their Neurourological Consequences

Suprapontine Lesion (Brain)

Cerebrovascular Accident (Stroke) Cerebrovascular accident (CVA, stroke) is one of the leading causes of morbidity and mortality, especially among the elderly. Stroke incidence ranges from 41 to 316 per 100,000 persons per year [37]. Although age-adjusted rates of stroke mortality have decreased worldwide in the past two decades, the absolute numbers of people who develop a stroke every year and live with the consequences or die from it are increasing. Of the stroke survi-

Table 3.1 Results of meta-analysis on the associations between the level of injury and bladder behavior in spinal cord injury patients

Level of injury	Neurogenic detrusor overactivity	Detrsuor-sphincter dyssynergia	Neurogenic detrusor underactivity	Normal bladder function	Number of patients
Cervical	65%	63%	9%	1%	259
Thoracic	78%	72%	9%	2%	215
Lumbar	49%	33%	39%	2%	137
Sacral	22%	13%	70%	9%	46
P value	<0.001	<0.001	<0.001	0.002	

Table 3.2 Correlation between the completeness of injury and bladder behavior in suprasacral SCI patients

	Weld et al. [35]			Rapidi et al. [36]		
	NDO/DSD	NDU (%)	Number of patients	NDO/DSD	NDU (%)	Number of patients
Complete trauma	100%	0	35	93%	7	126
Incomplete trauma	93%	3.7	161	93%	7	28
P value	0.282			0.649		

The completeness of injury was defined based on the American Spinal Injury Association (ASIA) Impairment Scale. Complete trauma (ASIA A in both studies [35, 36]). Incomplete trauma (ASIA B–D in the study by Weld et al. [35], ASIA B in the study by Rapidi et al. [36])
NDO neurogenic detrusor overactivity, *DSD* detrusor-sphincter dyssynergia, *NDU* neurogenic detrusor underactivity

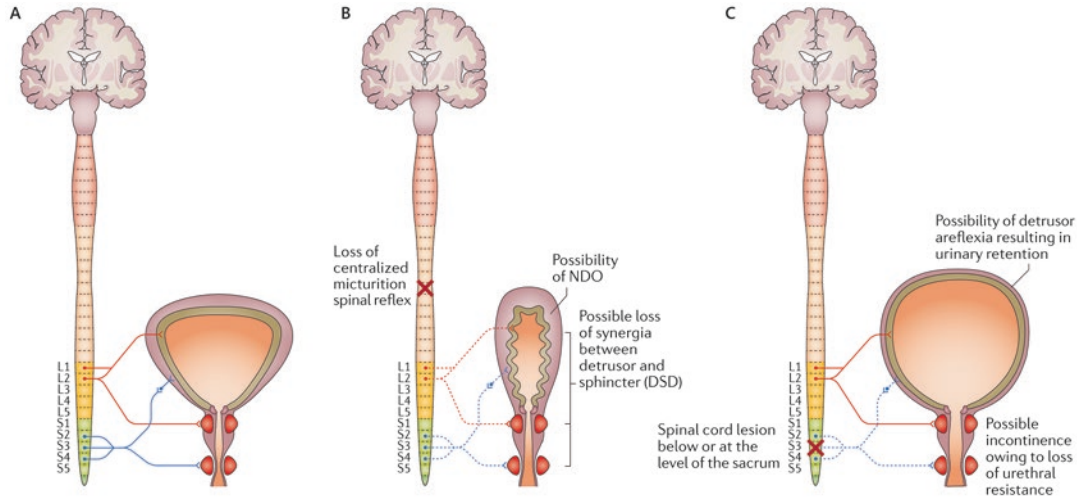

Fig. 3.2 Types of bladder dysfunction typically observed after spinal cord injury. (**a**) Intact innervation of the bladder. (**b**) Innervation of the bladder in patients with spinal cord injury (SCI) above the sacral level. Patients with such lesions often have neurogenic detrusor overactivity and detrusor-sphincter dyssynergia. If the sympathetic nerves are affected, this might result in an open bladder neck. Bladder filling sensation might be lost. A spinal micturition reflex will be present in patients with intact parasympathetic nerves. The symptoms of each patient are likely to vary, based upon the exact position and extent of SCI. (**c**) Innervation of the bladder in patients with SCI at the sacral level or below. Patients with such lesions are more likely to have urinary retention, owing to a loss of the spinal micturition reflex. Bladder filling sensations might be lost. An increased risk of incontinence, owing to a loss of urethral resistance, also exists. Again, the symptoms of each patient are likely to vary depending upon the exact position and extent of SCI. *Red line* = sympathetic innervation (via hypogastric nerve), arising at the upper lumbar level of the spinal cord. *Blue line* = parasympathetic and somatic innervation (via pelvic and pudendal nerves, respectively), arising at the sacral level of the spinal cord (Reprinted from Wyndaele et al. [30], with permission, Macmillan Publishers Ltd: Nat Rev Urol. 2016)

vors only 10% have no residual effects, whereas 40% have mild disability, 40% have significant disability, and 10% require nursing home care [38].

Impaired bladder function is considered as one of the most affecting factors on health-related quality of life in post-stroke patients [39]. Prevalence of urological complaints after CVAs ranges from 11% to almost 80% [40]. Urinary incontinence is the most common sequela of stroke affecting more than a third of stroke patients admitted to hospital with up to a quarter of these patients remaining incontinent at 1 year [38, 41]. Post-stroke urinary incontinence is a strong predictor of higher rates of mortality, greater institutionalization and increased disability [41]. Patients may also report nocturia (36–79%), frequency (17.5–36%), urgency (19–29%), difficulty in voiding (25%), straining (3.5%), and pain (2.5%) [42–44]. It should be emphasized that symptom presentation depends on a stroke phase.

In the acute phase of CVAs patients often present with urinary retention and mechanism of this condition has not been well established. Retention can be a neural representation of brain infract (called as a "cerebral shock") and presents as neurogenic detrusor underactivity (NDU) or DSD [38]. Of note, DSD is a rare finding after a cerebrovascular accident as true dyssynergia usually implies a contemporaneous spinal cord lesion occurring with the cortical lesion. Post-stroke DSD is usually confused with pseudodyssynergia [45]. Overdistension of the bladder resulted in inability to void may also be caused by impaired consciousness, restricted mobility, and an inability to communicate [46]. Prevalence of urinary retention in early phase of stroke has been estimated as 29% up to 67% within 2 weeks of the incident [47–50]. The higher percentages of retention are observed within the first 3 days of brain injury. Retention usually resolves within 2 months after discharge, correlating with urodynamic data where evolution of bladder behavior from acontractility to overactivity have been described [51]. Possible related risk factors of retention were reported as diabetes, cognitive impairment, aphasia, decreased functional status, hemorrhagic type of stroke, and injury in the frontal lobe [50, 52].

Early recovery period may also be characterized by urinary incontinence due to NDO. Brittain et al. identified rates of this condition ranging from 32 to 79% based on data from hospital admissions [53]. Thomas et al. reported that up to 25% of incontinent patients may still have problems on hospital discharge [54]. Pizzi et al. analyzed underlying urodynamic pathology in 106 ischemic stroke patients at admission, and repeated in 63 patients after 30 days [55]. Results of this study are presented in Table 3.3. To conclude, in early post-stroke period a wide spectrum of LUT symptoms (from retention to incontinence) may be demonstrated.

In the post-acute (chronic) phase of stroke, normal bladder function can return or impaired bladder function may evolve to a more fixed dysfunction, usually manifested by incontinence, frequency, and urgency [38]. Patel et al. reported that urinary incontinence can be detected in 15% of post-stroke patients at 1 year and in 10% at 2 years [56]. Brocklehurst et al. presented similar results with 12% prevalence of incontinence several months after CVA [57]. It is noteworthy to stress that data for incontinence in the current literature greatly vary. Due to different definitions of urinary incontinence, assessment methods and analyzed populations, some studies report that up

Table 3.3 Underlying urodynamic pathology of voiding problems in stroke patients (Data from Pizzi et al. [55])

	Normal bladder function (%)	Neurogenic detrusor overactivity (%)	Neurogenic detrusor overactivity with impaired contractility (%)	Neurogenic detrusor underactivity (%)
Admission	15	56	14	15
30 days after admission	30	48	6	16

to 70% of patients may suffer from urinary incontinence after 1 year of stroke [58, 59]. Nonetheless, majority of researchers agree that the incidence of urinary incontinence among stroke patients decreases with time. Possible related risk factors of urinary incontinence in post-stroke patients include increasing age, female sex, frontal lobe injury, and stroke severity characterized by stroke size [43, 44].

The presence of LUT dysfunction following stroke has been strongly associated with increased mortality rates, poor functional outcomes, and worse health-related quality of life. Therefore, accurate diagnosis and specific care for these patients should be provided. Multiple studies have found that stroke outcomes are better in patients who regained continence or remain continent [60]. Continent patients are characterized by lower rates of institutionalization and disability. Furthermore, those patients are more inclined to participate in stroke rehabilitation therapy and return to self-care activities of daily living.

Degeneration

Parkinsonian Syndrome The "parkinsonian syndrome" encompasses a number of nosologic entities that are grouped together on the basis of their shared clinical features but are separated on the basis of their different pathologies [61]. A simple classification system for use in daily clinical practice splits this syndrome into Parkinson disease (75–80% of Parkinsonian syndrome) and non-Parkinson disease entities (20% of Parkinsonian syndrome with the greatest prevalence of multiple system atrophy) .

Parkinson Disease Parkinson disease (PD) is a chronic and progressive movement disorder but extensive recognition of this disease described many non-motor symptoms reflecting to multifactorial origin and multisystemic clinical presentation [62]. In the early stages, it manifests as tremor, rigidity, bradykinesia, gait difficulty, and postural instability. Dementia, depression, cognitive and emotional problems may also occur, especially in the advanced stages of the disease.

The prevalence of PD in Western countries has been estimated to be 17–150 per 100,000 population [63, 64]. Importantly, the majority of these patients suffer from bladder dysfunctions, present in up to 70% of all such cases [65]. Bladder symptoms are more predictably troublesome as the disease advances. A multinational survey of 545 patients with a mild PD showed that patients usually report nocturia (62%) and urgency with or without incontinence (56%) [66]. Interestingly, urinary complaints were the most frequently reported non-motor symptoms. Although less common than storage problems, voiding symptoms also occur. Patients may report hesitancy, straining to void and poor urinary stream, particularly in advanced stages of the disease. Nevertheless, post-void residuals are typically low [67]. Presence of voiding symptoms has been explained as increased urethral pressure due to medications, levodopa, and its metabolites, such as norepinephrine [68]. Clinicians should also remember about possible coexistence of benign prostatic hyperplasia (BPH) in elderly PD patients. There is a paucity of data on correlation between the severity of neurological deficit in the early stages and the onset of bladder symptoms due to PD [62]. Some studies suggest that urinary symptoms begin approximately 5–6 years after the onset of parkinsonian motor symptoms [69, 70]. This leads to considerable diagnostic difficulties in differentiation of impaired bladder function between advanced PD or BPH. Moreover, urologists should be aware of possible incontinence exacerbation after prostatic surgery in patients with parkinsonism and poor voluntary sphincter contractions [71]. Of note, this does not mean that prostatic surgery should be avoided. Nowadays, it has been suggested that the risk of de novo urinary incontinence seems to be minimal in cases of refractory voiding symptoms. Preoperative assessment with urodynamically confirmed bladder outlet obstruction should be conducted before prostatic surgery as a suitable treatment option in a carefully selected population [72].

NDO with preserved bladder sensation is the most common urodynamic finding in patients

with PD, presents in 36–93% of all cases [65]. NDU or acontractile detrusor may also be found (0–48%). Some studies demonstrated evolution of bladder behavior from overactivity to impaired contractility with disease progression [73]. There is no agreement on urethral function in PD patients. Majority of studies have not reported DSD but others suggested that impaired or delayed relaxation of the striated sphincter might exist [63, 74]. Readers should keep in mind that presented discrepancy may be caused by misinterpretation of DSD as pseudodyssynergia or inclusion of patients with other neurological disorders that may lead to true DSD (e.g., multiple system atrophy) [65]. Furthermore, animal studies have demonstrated that levodopa, commonly used medication in PD, may significantly affect activity of the external urethral sphincter [75]. Until now, intrinsic urethral sphincter deficiency has not been reported in patients with PD.

Multiple System Atrophy Multiple system atrophy (MSA), similarly to PD, is a degenerative neurological disease but depicts a group of disorders previously called striatonigral degeneration, sporadic olivopontocerebellar atrophy, and Shy–Drager syndrome characterized by the same underlying pathology [76]. To confirm a diagnosis of MSA, autonomic failure, described as postural hypotension and/or urinary dysfunction, has to be demonstrated. Poorly levodopa-responsive parkinsonism or occurrence of cerebellar syndrome may also support identification of the underlying disease [77]. On the basis of the major motor deficits, MSA can be classified as MSA-P (parkinsonism-predominant) and MSA-C (cerebellar-predominant). Clinical differential diagnosis between MSA-P, the most common clinical form of MSA, and PD is difficult even for specialists, and usually requires strong concerted efforts of multiple clinicians. A limited response to dopamine receptor agonists, a lack of one-side dominance and resting tremor, and rapid disease progression are more apparent in patients with MSA than in those with PD [78]. Prominent and early dementia, hallucinations, postural instability occurring early in the course of disease, severe and early autonomic dysfunction and involuntary movements other than tremor are also more characteristic for non-Parkinson disease entities.

There is a paucity of data on MSA prevalence. A nationwide study in Iceland estimated the prevalence of MSA as 3 per 100,000 population [79]. Epidemiological study from France showed concurrent results with prevalence 2 per 100,000 population [80]. Analysing presented data, it can be speculated that MSA is a rarer finding than PD.

Up to 96% of patients with MSA may report urinary symptoms [81]. In comparison, 43% of MSA patients report orthostatic problems. The most frequently reported urinary symptom is voiding difficulty (79%), followed by nocturia (74%), urgency (63%), incontinence (63%), frequency (45%), nocturnal enuresis (19%), and urinary retention (8%). Patients may also present with a combination of these symptoms. Importantly, urinary symptoms often precede the emergence of orthostatic or motor symptoms. Up to 50–60% of patients with MSA develop urinary symptoms either before or around the time of presentation with orthostatic symptoms or motor disorders [78]. Importantly, urinary dysfunction is never the initial presentation of PD. Similarly, erectile dysfunction may often become the first presentation of MSA. These data stress that urologists may often overlook underlying neurological pathology of reported symptoms, in particular at early stages of the disease or in male patients with comorbid BPH. Male patients with MSA may even undergo surgery for bladder outlet obstruction before the correct neurological diagnosis.

NDO can be detected in 33–100% of patients with MSA, whereas NDU may be observed in approximately 60% [78]. Interestingly, a subset of patients with MSA may have bladder overactivity during storage and underactivity during voiding. This symptom composition has been termed as detrusor hyperactivity with impaired contractile function (further described in Chapter 8 Retention) [82]. Note that weak detrusor contraction is a more common finding in patients with MSA than in those with PD. Since MSA affects multiple brain regions, even the pons and lower regions, it can present with true DSD in 47% of MSA

patients [83, 84]. Another interesting finding in MSA individuals is an open bladder neck in 46–100% of patients reflecting to the intrinsic sphincter deficiency with clinical presentation of urinary incontinence [83]. Uninhibited relaxation of the external sphincter may also be occasionally found during the filling phase and results in exacerbation of urinary incontinence.

As the clinical presentation of PD and MSA (especially MSA-P) may often seem similar, Table 3.4 [78] summarizes key differences of those disorders.

Dementia Dementia is a general term for a decline in mental ability which interferes with daily life. The various causes of dementia are categorized by their neuropathology, clinical features, and/or presumed etiology [85]. Among them, Alzheimer's disease (AD) is the most common irreversible cause of dementia and accounts for an estimated 60–80% of cases.

Dementia in AD is characterized by loss of memory, intellectual dysfunction, disturbances in speech, various types of apraxia and agnosia. Pathological changes have been mainly described in the temporal, parietal, and medial frontal cortices [86]. Urinary symptoms may also occur but are very uncommon at an early stage. Urinary incontinence is the most common urological finding with 11–90% prevalence [87] and readers should keep in mind that etiology of incontinence in elderly is multifactorial and includes cognitive and physical disabilities, impaired conscious willingness, comorbidities, surrounding environment, and underlying neurological disorders. Due to AD pathophysiology, cortical inhibition of voiding reflex may be disturbed and neurological contribution to bladder dysfunction in AD patients may result in NDO. Mori et al. examined 31 institutionalized AD patients and found detrusor overactivity in 58% of them [88]. Sugiyama et al. described detrusor overactivity in 40% of 20 patients with AD. Interestingly, overactive detrusor was found in 8 of 13 incontinent patients and in 0 of 7 continent individuals [89]. Some studies presented that detrusor overactivity may also be accompanied by impaired contractile function presented as elevated post-void residuals [90] (detrusor hyperactivity with impaired contractility, further described in Chap. 8 Retention).

Brain Tumors Intracranial tumors are less prevalent than stroke with a worldwide incidence rate of 10.82 per 100,000 individuals [91]. Similarly to stroke, patients with intracranial tumors may report urinary complaints.

Table 3.4 Key differences of Parkinson disease and multiple system atrophy (Reprinted from Ogawa et al. [78], with permission, Macmillan Publishers Ltd: Nat Rev Urol. 2017)

Feature	Parkinson disease	Multiple system atrophy
Pathophysiology	Dopamine depletion in the substantia nigra	Glial cytoplasmic inclusions in various lesion
Prevalence in the USA	17.4 per 100,000 persons aged 50–59 years; 93.1 per 100,000 persons aged 70–79 years	3.0 per 100,000 persons aged 50–99 years
Onset of LUTS	Several years after onset of motor symptoms	Often precedes other non-motor or motor symptoms
Typical symptoms	OAB symptoms, voiding difficulty	OAB symptoms, voiding difficulty, urinary retention
Findings of urodynamic investigations	Detrusor overactivity, mild BOO, impaired urethral relaxation, delayed striated sphincter relaxation	Detrusor overactivity, uninhibited urethral sphincter relaxation during filling, bladder-neck opening during filling, insufficient bladder contractions
Dopaminergic drug therapy	Effective	Minimally effective
Prostatectomy	Effective	Not effective

BOO bladder outlet obstruction, *LUTS* lower urinary tract symptoms, *OAB* overactive bladder

Brain tumors disrupt central voiding regulation. Pathophysiological mechanisms include destruction of brain tissue by a rapidly growing tumor, neural pathways infiltration, and mass effect with displacement of cerebral structures and increased intracranial pressure. Therefore, tumors in the frontal lobe may cause a loss of the central inhibitory output and lead to detrusor overactivity with urge incontinence. Voluntary control of voiding may also be impaired.

Urological complaints are not the leading symptoms in clinical presentation of brain tumors. The incidence of LUT symptoms among patients with frontal lobe tumors has been estimated as 14–28% [92]. Those with brain tumors in other locations report bladder problems in less than 2%. Patients typically report storage symptoms like urgency, frequency, nocturia, and incontinence but symptom presentation can vary. Patients with pontine tumors are more likely to present with voiding difficulties and retention.

Data on urodynamic findings in patients with intracranial tumors are scant and limited to single studies or case reports. When storage symptoms occur, the most common finding in patients with frontal lobe tumors is NDO [38]. Among patients with pontine tumors, involving pontine micturition center, DSD is a more frequent dysfunction.

Cerebral Palsy Cerebral palsy (CP) is a group of permanent nonprogressive brain disorders resulting in a variety of motor abnormalities often accompanied by intellectual impairment, convulsive disorders, or other cerebral dysfunctions. Spinal cord involvement is excluded. CP is a condition beginning in early childhood and persisting through the lifespan.

Recently published meta-analysis has shown that an average of 55.5% of subjects with CP experience one or more lower urinary tract symptoms [93]. Urinary incontinence is the most frequently observed symptom with prevalence ranging between 20 and 94%. Urgency and frequency are also reported in 38.5% and 22.5% of patients, respectively. Voiding symptoms are less prevalent than storage problems. Prevalence rate of hesitancy varies between 2 and 51.5%, with an average of 24%. Quadriplegic children, those with low intellectual capacity or those with spastic manifestation have a higher prevalence of urinary dysfunction.

NDO is the most commonly observed urodynamic abnormality, with an average prevalence rate of 59% but it has been shown that up to 44% of CP patients with a diagnosis of NDO do not report lower urinary tract symptoms [94, 95]. Approximately 70% of subjects with CP also exhibit a reduced bladder capacity compared to the expected bladder capacity for age. Interestingly, several studies report DSD with an average prevalence rate of 11% [93]. As CP definition includes only suprapontine insult, some patients may have concomitant spinal lesions and suffer from related abnormalities. Another theory stresses that investigated DSD is in fact a pseudodyssynegria resulting from pelvic floor overactivity as a voluntary reaction to bladder overactivity.

Infrapontine-Suprasacral Lesion (Spinal Cord)

Demyelination Demyelinating disorders are a subgroup of white matter disorders characterized by the destruction or damage of normally myelinated structures. This impairs the signal conduction in the affected nerves and may lead to deficiency in sensation, movement, cognition, or other functions depending on which nerves are involved. Considering neurological contribution of these diseases to bladder behavior, two demyelinating disorders should be taken into special consideration.

Multiple Sclerosis Multiple sclerosis (MS) is the most common autoimmune, chronic, progressive, demyelinating disease with a median prevalence of 80 per 100,000 in Europe and 135 per 100,000 in the USA [96]. It is often first diagnosed in young individuals, with a mean age at onset of 30 years, and disproportionately affects more women than men [97].

Chronic autoimmune T-cell-mediated inflammation of the central nervous system with disruption of myelin sheaths is the pathological hallmark of this disorder. Importantly, demyelination culminates in slowdown or loss of conduction in axonal pathways, in both spinal cord and cerebral cortex. As a consequence, clinical presentation, including urological symptoms, is strongly diversified. While the main cause of MS is unknown, genetic, immunological, and environmental factors are thought to be major contributors to the disease's evolution.

Although urological symptoms at first presentation of MS are rare (3–10%), almost two-thirds of MS patients will suffer from moderate to severe urinary disturbances related to their disease [98]. Whereas MS lesions can be disseminated in various parts of the central nervous system, clinical data suggest that bladder symptoms most often result from spinal cord lesions with a disconnection between centers in the brainstem and the sacral region [99]. Physicians should keep in mind that symptoms from the lower urinary tract might also result from cognitive problems (memory loss, amotivation, apraxia, language dysfunction), related comorbidities (benign prostatic hyperplasia, urinary tract infection, stress incontinence), functional disabilities (reduced mobility, general debilitation), or medications (opioid analgesics, tricyclic antidepressants) [100]. Bladder symptoms generally appear after a mean of 6 years of MS diagnosis [101]. Symptoms of the storage phase are more frequently reported than those related to voiding. Urinary urgency is observed in 38–99% of MS patients, frequency in 26–82% and urge incontinence in 27–66% [100]. It is important to note that stress urinary incontinence may also be detected in up to 56% of MS patients, thus symptoms of mixed urinary incontinence might often be reported [102]. Symptoms of the voiding phase are less frequent with a prevalence of 6–49% [100]. Up to 50% of MS patients may report symptoms of both storage and voiding phase [103, 104]. Symptoms of the lower urinary tract usually progressively worse and become more difficult to manage with longer disease duration and greater physical disability [105].

Detrusor overactivity is the most common urodynamic finding with a prevalence of 34–91%, followed by DSD in 5–60% and detrusor underactivity reported in less than 37% [100]. Low bladder compliance may be discovered in 2–10% of patients with MS. Interestingly, normal detrusor activity can be revealed in 3–34% of MS patients who complain of urinary symptoms. On the other hand, urodynamic abnormalities can also be identified in patients who are asymptomatic. Studies have shown that different urodynamic findings may often coexist. DSD can be combined with either detrusor overactivity in 43–80% of patients or with detrusor underactivity in 5–9% [106]. Evolution of urodynamic abnormalities during course of the disease has also been described. Ciancio et al. evaluated 22 MS patients who underwent at least two urodynamic studies with a mean follow-up interval of 42–45 months [107]. They reported that 55% of examined patients had changes in their urodynamics including changes in capacity, contractility, pressure, or detrusor compliance. During follow-up periods, 64% of MS patients had the same symptoms with possible deterioration and 36% reported new complaints. Patients from both groups demonstrated significant variations in their urodynamic patterns as 43% of patients without new symptoms and 75% with new complaints demonstrated urodynamic changes in comparison to previous urodynamics. Another data stressed that prevalence of DSD may increase with the disease duration. Whereas DSD is present in 13% of MS patients after 48 months of the disease evolution, it may be demonstrated in up to 50% of patients 109 months after diagnosis [103].

Transverse Myelitis Transverse myelitis is a clinical parainfectious syndrome with immune-mediated damage of the spinal cord. Thus, its etiology can be viral, bacterial, parasitic, tuberculosis or idiopathic [108]. Transverse myelitis may exist as a part of a multifocal disease of the central nervous system (e.g., multiple sclerosis), multisystemic disease (e.g., systemic lupus ery-

thematosus), or as an isolated, idiopathic entity. Both grey and white matter of the spinal cord are involved. In rare cases, peripheral nervous system may be disrupted as well.

Acute transverse myelitis has an incidence of one to four new cases per million people per year affecting individuals of all ages with bimodal peaks between the ages of 10 and 19 years and 30 and 39 years [109, 110]. When the maximal level of deficit is reached, virtually all patients have bladder dysfunctions.

Patients usually present with a combination of storage and voiding symptoms and residual bladder dysfunction usually has a tendency to persist for a long time [111] but in the onset of the disease patients typically complain of urinary retention or voiding difficulties [112].

Data on urodynamic findings in patients with transverse myelitis is scant. Recently published study reported that detrusor overactivity is the most common urodynamic abnormality (in up to 76% of patients), followed by DSD and decreased compliance (in 48% and 33%, respectively) [113]. Another study indicated DSD as the most frequent urodynamic abnormality (in 48% of patients), followed by detrusor overactivity (35%) and hypocompliant bladder (4%).

Spina Bifida Spina bifida, also known as myelodysplasia, is a birth defect due to an incomplete closure of the neural tube in the caudal region resulting in protrusion of part or all of the content of the spinal canal through this dorsal defect. It is the first cause of congenital urological disability and the most common cause of neurogenic bladder in children [114]. It occurs in approximately 1 in 1000 births per year in developed countries with a prevalence of 8–9/10,000 in the population aged 10–69 years [115]. All levels of the spinal column can be involved, including the cervical 2%, thoracic 5%, lumbar 26%, lumbosacral 47%, and sacral region 20% [116].

Bladder function is impaired in up to 96% of patients with spina bifida [117]. Due to diversity of involved locations and relations between vertebrate and spinal cord segments, clinical presentation can significantly vary. Moreover, the differential growth rates between the vertebral bodies and the elongating spinal cord may result in dynamic changes of bladder behavior. As a result, patients may complain of storage or voiding symptoms or a combination of both of them, with a tendency to evolve. Symptoms usually start in infancy or childhood, but sometimes might be delayed until adulthood because of spinal cord tethering. Those patients should be monitored as they are at higher risk of upper urinary tract deterioration [118, 119].

A full spectrum of urodynamic bladder dysfunctions can be revealed, including NDO, DSD, NDU, and bladder acontractility. As lumbar and lumbosacral defects are the most common, majority of patients present with detrusor overactivity and/or DSD.

Sacral-Infrasacral Lesion (Spinal Cord and Peripheral Nervous System)

Intervertebral Disk Prolapse Intervertebral disk degeneration leading to disk prolapse significantly impairs patient's quality of life and may lead to serious chronic disability. Clinical symptoms of disk prolapse can vary depending on the location of the herniation. The frequency of disk prolapse is highest at L4/L5 and L5/S1 levels and represents approximately 90% of symptomatic cases. As the relation between vertebrate and spinal cord segments at the distal region of the vertebral column is most pronounced, protrusions or extrusions (more extreme extension of the disk beyond the interspace) at these levels mostly affect sacral segments of the spinal cord [120]. Underlying mechanism includes also compression of spinal nerve roots running in the subarachnoid space with dysfunction in afferent and efferent pathways. In some cases, a large central or posterolateral disk prolapse migrating medially may lead to widespread compression of nerve roots arising from multiple spinal cord levels and present with cauda equina syndrome (unilateral

or bilateral sciatica, saddle sensory disturbances, bladder and bowel dysfunction, lower extremity weakness, and sensory loss) .

The true incidence of neurogenic LUT dysfunction in patients with disk prolapse is difficult to estimate. The prevalence of urological symptoms in candidates for surgical treatment ranges from 20 to 68% [120]. Those who present with LUT symptoms usually complain of voiding problems, including intermittency, hesitancy, straining to urinate, or incomplete bladder emptying. Incontinence is a rare finding and if occurs usually indicates severe extrusion.

Majority of neurological complaints related to the intervertebral disk prolapse, including impaired bladder behavior, are slowly progressive and depend on nerve compression. Approximately 40% of patients with disk prolapse have urodynamic abnormalities [120]. Whereas an early stage prolapse may result in nerve irritation and detrusor overactivity, further progression may lead to impaired bladder sensation and results in detrusor underactivity or detrusor acontractility [121]. Among patients with abnormal urodynamic pattern, the most common finding is detrusor underactivity with prevalence of 26–74% [120]. In cases of strong acute compression of nerve roots when neural pathways are interrupted, detrusor underactivity may coexist with dysfunctional sphincter.

Peripheral Neuropathies Peripheral neuropathy is a general term for a series of disorders that result from damage of the peripheral nervous system. Depending on the type of nerve affected, it may present with impaired sensation, movement or organ function, thus be classified as sensory, motor, or autonomic. Various diseases or injuries may lead to peripheral neuropathy and present with impaired bladder behavior: systemic diseases (diabetes, sarcoidosis, amyloidosis, porphyrias), infections (lumbosacral herpes zoster, genitourinary herpes simplex, tabes dorsalis), immune system diseases (AIDS, vasculitides, Guillain–Barré syndrome), medication (chemotherapy), radiation therapy, pelvic surgery, excessive alcohol consumption. Within them, special attention should be given for diabetes and iatrogenic causes like pelvic surgery and radiation therapy.

Diabetes Diabetes mellitus (DM) is the most common cause of peripheral neuropathy worldwide and almost one-third of all patients with DM have evidence of peripheral neuropathy. The prevalence of neuropathy increases with disease duration from 21% in those with duration <5 years to 37% in those with duration >10 years [122].

Up to 80% of diabetics complain of urinary symptoms [123]. Note that some of these symptoms can be a result of metabolic disturbances (particularly polyuria) or urological comorbidities (particularly BPH or urinary tract infection). It has been reported that diabetic cystopathy (diabetic neuropathy involving bladder innervation) can occur silently and early in the course of diabetes [124]. The prevalence of diabetic cystopathy is estimated to be 43–87% in insulin-dependent diabetics with no sex or age differences [125]. As diabetic neuropathy involves both afferent and efferent pathways of the peripheral nervous system, diminished sensation of bladder filling and impaired transmission of contracting signals lead to decreased frequency of voiding (with increased bladder capacity) and poor stream (with incomplete bladder emptying). Therefore, patients typically present with elevated post-void residual and/or chronic retention.

Urodynamic study usually reveals detrusor underactivity with desire to void at large volume but other dysfunctions may also be investigated. Bansal et al. reported NDU in 79% of symptomatic DM patients, detrusor overactivity in 39%, impaired first sensation in 23%, increased bladder capacity in 25%, and bladder outlet obstruction in 29% of the men [126]. Kaplan et al. presented even higher incidence of detrusor overactivity (55%) and lower rate of underactive or acontractile detrusor (33%) [127]. This phenomenon can be explained by detrusor instability, cerebrovascular involvement, or concomitant

BPH [128, 129]. In these cases, patients more often report storage problems.

Iatrogenic Causes

Pelvic Surgery Extensive pelvic surgery, such as abdominoperineal resection for rectal cancer, radical hysterectomy or prostatectomy and aortoiliac surgery, is all likely to damage the pelvic innervation of the bladder and result in neurogenic LUT dysfunction [125]. The manifestation and the mechanism of dysfunction vary and depend on the specific type of surgery and the preoperative pathology. Diagnosed neuropathy can be described as sensory, motor, and/or autonomic. Neural injury may also coexist with structural injury of the bladder, urethra, or sphincter.

Iatrogenic neural bladder dysfunction can resolve during the early postoperative period (weeks/months) or stabilize and persist for years. Clinical manifestation depends on affected nerves [130]. Damage to the parasympathetic pathways (responsible for detrusor contraction and urethral relaxation) will result in detrusor underactivity or acontractility with or without relaxation of the urinary sphincter (denervated or underactive). Damage to the sympathetic pathways (responsible for inhibition of bladder contraction and enhancement of bladder outlet resistance) will result in impaired compliance and bladder outlet incompetence. Damage to the somatic pathways (responsible for controlling of the external urethral sphincter) will result in impaired function of bladder outlet. Damage of the all presented tracts also impair afferent pathways and lead to impairment in bladder sensation.

Patients after pelvic surgery typically suffer from combined parasympathetic, sympathetic, and somatic denervation. Classical clinical presentation includes a noncontractile bladder (underactive or acontractile detrusor) with or without impaired urinary sphincter [131] leading to elevated post-void residual and incomplete emptying.

The rate of urinary dysfunction after rectal cancer surgery ranges from 30 to 70% and usually is a result of a combination of parasympathetic and sympathetic denervation [132]. Impaired bladder behavior in patients after radical rectal excision via abdominoperineal resection can be observed for 2 weeks to 4 months and within this period 75% of incontinent patients regained passive continence [125]. By contrast, symptoms which persist 6 months after surgery are mainly permanent and long-term dysfunction can be expected in 31% of patients [133]. Radical hysterectomy may lead to neurogenic LUT dysfunction in up to 86% of patients and parasympathetic denervation is more common than sympathetic [134, 135]. Impaired bladder behavior due to damage of neural tracts following radical prostatectomy is difficult to establish. In majority of patients, urinary incontinence following surgery is a result from direct damage to the intrinsic urethral sphincter and presents as stress urinary incontinence [136]. However, some patients have concomitant detrusor dysfunction described as overactivity or impaired compliance [137]. Available data suggest that enhanced attention to nerve preservation at the time of radical prostatectomy may significantly improve bladder control [138].

Radiation Therapy Confined organization of pelvic organs imposes simultaneous radiation to different areas, including peripheral innervation. Bladder dysfunction after radiation therapy is mainly attributed to nerve damage. Moreover, chemotherapeutic agents may sensitize neural tissues to the effects of radiation [139]. Pathophysiological mechanism may also include direct radiation damage to microvascular, epithelial, and muscular components of bladder and urethra resulting in fibrosis and ischemia. Symptoms of radiation-induced neuropathy may occur months to years after radiation due to the slow reproductive cycles of glial and Schwann cells. Neurogenic lower urinary tract symptoms have been reported after pelvic radiation therapy for the treatment of prostate, bladder, rectal, cervical, and uterine cancers [125].

Conclusion (Table 3.5)

Table 3.5 Conclusion

Summary	Level of evidence
The pattern of bladder dysfunction following neurological disease is determined by the location and nature of the lesion	3
Patients with suprapontine lesions usually present with neurogenic detrusor overactivity with the predominance of storage symptoms. Infrapontine-suprasacral lesions may result in neurogenic detrusor overactivity and/or detrusor-sphincter dyssynergia, thus either storage and/or voiding symptoms may be reported. In sacral-infrasacral lesions, neurogenic detrusor underactivity is the most frequent finding and patients are more inclined to report voiding symptoms than storage problems	4 (Expert opinion)
Traumatic entities are often characterized by specific symptom evolution. Injury to the central nervous system (brain or spinal cord) may be followed by the "shock" phase with detrusor underactivity. Further bladder behavior can be predicted by cord lesion level and completeness, but clinical presentation of each patient is likely to vary	3
Approximately 81% of patients with SCI will have at least some degree of urinary dysfunction presenting within 1 year of the injury. On the other hand, less than 1% of these patients will make a full recovery	3
In non-traumatic entities bladder behavior is not a static condition either. However, instead of symptom evolution, initial bladder dysfunction may progress following progression of underlying neurological disease. Similarly to traumatic entities, clinicians may try to foresee lower urinary tract dysfunction	4 (Expert opinion)
Prevalence of bladder dysfunction in patients with non-traumatic suprapontine lesion greatly varies, even in patients with the same underlying pathology. After stroke, urological complaints may be reported by 11% to almost 80% of patients. In those with Parkinson disease and multiple system atrophy, bladder dysfunction can be found in up to 70% and 96%, respectively. More than half of subjects with cerebral palsy experience one or more lower urinary tract symptoms. Among patients with brain tumors, frontal lobe lesions are more inclined to produce urological symptoms than tumors in other locations. Etiology of urological complaints in dementia is multifactorial and includes cognitive and physical disabilities, impaired conscious willingness, comorbidities, surrounding environment, and underlying neurological disorders	3
In a group of non-traumatic infrapontine-suprasacral lesions, demyelinating diseases are the most common cause of bladder dysfunction. Almost two-thirds of patients with multiple sclerosis suffer from moderate to severe urinary disturbances related to their disease. In individuals with transverse myelitis, when the maximal level of deficit is reached, virtually all patients have bladder dysfunctions. In pediatric patients, the most common cause of neuropathic bladder is spina bifida where bladder function is impaired in up to 96% of cases.	3
Bladder dysfunction related to sacral-infrasacral lesions is a common finding in diabetic patients. Up to 80% of them complain of urinary symptoms and diabetic cystopathy may be diagnosed in 43–87% in insulin-dependent diabetics. Pelvic surgery or radiation therapy may significantly affect afferent and efferent bladder innervation and lead to neurogenic lower urinary tract impairment. The manifestations and the mechanisms of dysfunctions vary and depend on the specific type of surgery and the preoperative pathology	3

Recommendation	Grade of recommendation
The pattern of lower urinary tract dysfunction following neurological disease can often be predicted by the location, nature, and extent of the lesion. However, clinical presentation may significantly vary and physicians should be aware of these disparities.	Expert opinion

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Part II

First Consultation of Patients with Spinal Cord Injury

Medical History and Physical Examination

4

Introduction

There is universal agreement that taking a medical history and performing a physical examination should be the first step in the assessment of bladder dysfunction in patients after spinal cord injury (SCI). Thorough history and precise exam are the cornerstones of initial and long-term evaluation in patients with neurological impairment who are suffering from lower urinary tract symptoms.

Medical History

Medical history should be started with an assessment of the patient's general condition and should investigate age, sex, ethnicity, cognitive abilities (perception, thinking, reasoning, remembering), behavioral functions (interaction between the person and the environment, social attention), mobility, ability to communicate, cooperation, and psychological status (depression, anxiety, other mood disturbances). The clinician should also assess the influence of SCI on patient's self-care activities, quality of life, and day-to-day chores.

A more detailed history should document the specific details of time as well as the level and completeness of SCI. It should be conducted with validated methods and standards. The American Spinal Injury Association (ASIA) Impairment Scale (AIS) is a clinician-administered widely used classification to assess the severity (completeness) of injury in individuals with SCI (Table 4.1) [1, 2]. Questions regarding the mechanism of injury may help to identify damaged level. Interview should elicit information regarding extremity weakness, numbness, or paresthesia. Furthermore, patients should be asked about the presence of spine stabilization hardware implanted in the acute phase of injury.

As the first urological consultation of SCI individuals is usually conducted within 2 months of the traumatic accident, the majority of patients are in the stage of spinal shock. This condition appears after suprasacral SCI and usually lasts from 6 to 12 weeks but sometimes can be extended to 1 or 2 years [3]. The duration of spinal shock in patients with incomplete SCI is shorter, sometimes lasting for several days. Muscles are in a flaccid state because of loss of neurological reflexes [4]. Similarly, bladder becomes underactive with disturbed filling sensations and no voluntary control. Therefore, patients present with urine retention managed with intermittent or indwelling catheterization. As spinal shock is not a stable condition and bladder dysfunction will usually evolve to neurogenic detrusor overactivity and/or detrusor-sphincter dyssynergia, only basic urological history should be obtained. Bladder emptying technique and presence of filling sensation should be carefully questioned and documented. The patient should be queried about and then informed regarding the symptoms indicating the end of spinal shock. These include reappearance of

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_4

Table 4.1 American Spinal Injury Association impairment scale [1, 2]

A—Complete No sensory or motor function is preserved in the sacral segments S4–S5
B—Sensory incomplete Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4–S5 (light touch, pin prick at S4–S5 or deep anal pressure), *AND* no motor function is preserved more than three levels below the motor level on either side of the body
C—Motor incomplete Motor function is preserved below the neurological level and more than half of key muscle functions below the single neurological level of injury (NLI) have a muscle grade less than 3
D—Motor incomplete Motor function is preserved below the neurological level and at least half (half or more) of key muscle functions below the NLI have a muscle grade of 3 or greater
E—Normal If sensation and motor function as tested with the International Standards for Neurological Classification of SCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial SCI does not receive an AIS grade

SCI spinal cord injury, *AIS* ASIA impairment scale

bladder sensation, leakage around urethral catheter, or episodes of urinary incontinence between clean intermittent catheterizations, as well as new onset of lower extremity spasms [5]. Patients should be educated about intermittent catheterization (if this has not yet occurred), or catheterization technique should be reassessed. If a urologist presumes terminated spinal shock phase in a patient with suprasacral SCI or consults a patient with sacral/infrasacral injury who presents with urine retention (these patients do not develop spinal shock and usually maintain neurogenic detrusor underactivity), more in-depth evaluation can be conducted at the initial appointment.

Baseline and more in-depth urological investigation is generally performed 3–6 months after the initial injury, by which time spinal shock would have resolved [6, 7]. Questions about urinary symptoms should be subdivided into storage problems (frequency, urgency, nocturia, incontinence), voiding symptoms (hesitancy, straining, poor and intermittent flow), and post-micturition symptoms (sensation of incomplete emptying, post-micturition dribble). The onset and duration of symptoms with severity and degree of bother should also be determined. Patient should be asked about urinary function before SCI, and the information obtained need to be compared with current complaints. In order to maintain professional communication between clinicians, standardized terminology developed by the International Continence Society should be used [8]. Specific urinary history should evaluate bladder sensation and mode of voiding. Interview should elicit information regarding initiation of micturition (normal, precipitate, reflex, strain, Credé) and investigate whether performed by patients themselves or with caretakers. Interruption of micturition (normal, paradoxical, passive) should be revealed. In catheterized patients, the duration of each catheter use before change and the cleaning technique performed (for those using clean rather than sterile intermittent catheterization) should be recorded. Accurate reassessment of catheterization technique is also important. In the presence of urinary incontinence, a thorough history should distinguish stress incontinence, which occurs with increases in intra-abdominal pressure and is usually associated with physical activity, coughing, or straining. Severity of incontinence, both urgency and stress, can be assessed by asking about pad usage, including pad weight, size, number of used pads, and number of urinary incontinence episodes per day. Careful assessment of symptoms indicating possible complications (hematuria, dysuria, fever) should be conducted to rule out comorbid pathology such as malignancy, urolithiasis, or urinary tract infection. It should be noted that SCI individuals may present with other symptoms and signs of urinary tract infection than non-neurogenic patients. In this group, infection within the urinary tract can be manifested by new onset or increase in incontinence; leaking around an indwelling catheter; cloudy urine with increased urine odor; and increased spasticity, malaise, lethargy, anxiety or exacerbation of autonomic dysreflexia [9–11].

Of note, clinicians should be aware that the symptoms of lower urinary tract pathology are subjective and that the perception of their severity is influenced by many factors. Importantly, the severity of symptoms does not always correlate with the magnitude of disease affecting the urinary tract [5, 12, 13]. SCI patients may also lack symptoms because of impaired or altered bladder sensation. Patients might find symptoms difficult to define, such as timing of incontinence and describing whether leakage is associated with urinary urgency or with stress maneuvers like transferring in and out of a wheelchair [5]. Moreover, patients may not be able to reach the toilet in time due to their neurological deficits or poor toilet accessibility. These issues should be investigated.

Patient self-completed and interviewer-administered questionnaires can be a suitable method for assessing the patient's perspective of bothersome symptoms and their impact on the patients' quality of life. The utilization of validated questionnaires helps to establish baseline measurements and to quantitate the patient's response to treatment. Thus, questionnaires should be incorporated in day-to-day clinical practice of SCI individuals. Furthermore, the type of bladder management, considered as the pinpoint of neurourological treatment, has been shown to affect health-related quality of life in patients with SCI [14]. Among a wide variety of questionnaires utilized in patients with neurogenic lower urinary tract dysfunction [15, 16], seven were designed with special attention to SCI individuals (Table 4.2) [17–26] and three instruments (Rick Hansen Spinal Cord Injury Registry Questionnaire, Tetraplegia Hand Activity Questionnaire, Franceschini Questionnaire) are specifically validated in the SCI population [16]. Patients can also be assessed by other generic questionnaires, such as King's Health Questionnaire (KHQ) or the Short Form 36-item and 12-item Health Survey Questionnaires (SF-36, SF-12) [15]. It is important that the questionnaire of choice should have been validated in the language that it is going to be used. There is no evidence as to which validated questionnaires are the most appropriate for daily practice, therefore each questionnaire can be used alone or in combination with other questionnaires to improve assessment or monitoring of treatment outcomes. Similarly, no evidence was found whether use of these questionnaires has an impact on outcomes from treatment.

Table 4.2 Questionnaires for spinal cord injury patients with covered domains

Questionnaire	Bladder function	Bowel function	Sexual function
Qualiveen/ SF-Qualiveen [18–20]	X		X
NBSS [21]	X		
IQOL [22]	X		X
RHSCIR [23]	X	X	X
Franceschini [24]	X	X	X
THAQ [25]	X		
QoL-BM [26]		X	

SF short form, *NBSS* Neurogenic bladder symptom score, *IQOL* Incontinence-quality of life questionnaire, *RHSCIR* Rick Hansen spinal cord injury registry questionnaire, *THAQ* Tetraplegia hand activity questionnaire, *QoL-BM* Quality of life related to bowel management questionnaire

Bowel and sexual history is also important because patients with neurourological symptoms may also have related neurogenic bowel and sexual dysfunction [27, 28]. Bowel history should elicit information regarding pattern and frequency of defecation, rectal sensation, desire to defecate and possible episodes of fecal incontinence, constipation, or defecation initiation (digitation, suppository use) [17]. Sexual history should investigate symptoms of genital or sexual dysfunction, presence of sensation in genital area, lack of desire (loss of libido), difficulty in achieving orgasm, possible erectile dysfunction or ejaculation problems (premature, delayed, retrograde, anejaculation) in male or dyspareunia in female.

A wide variety of comorbidities may worsen reported symptoms. Possible related comorbidities include other neurological diseases that may lead to neurogenic bladder (see Chap. 3, "Pathologies Responsible for the Development of the Neurogenic Bladder"), endocrine disorders (i.e., complicated and uncontrolled diabetes,

diabetes insipidus), urological conditions (i.e., benign prostatic hyperplasia), respiratory dysfunctions with chronic cough (i.e., chronic obstructive pulmonary disease), fecal motility disorders (i.e., constipation or fecal incontinence), chronic pelvic pain, mobility deficits, prior pelvic surgeries, pelvic cancers, and pelvic radiation. Other details of the medical history should include information of any prior neck or back injuries or surgeries, and history of extensive pelvic procedures (abdominoperineal resection, radical hysterectomy, radical prostatectomy). As SCI-related bladder dysfunction may significantly impair renal function, patients should be carefully asked about previous and present renal disorders, including kidney stones, vesicoureteral reflux, recurrent urinary tract infections, and chronic kidney disease. In women, a thorough obstetric and gynecological history may help to identify concomitant stress urinary incontinence as a consequence of damage of the ligamentous support of the urethra. Patients should be asked about previous surgery for pelvic organ prolapse or incontinence, labor duration, mode of delivery, birth weights of children, year of delivery, intrapartum complications (e.g., obstetric anal sphincter injury, peri-urethral lacerations, wound breakdown), as well as de novo post-partum urinary symptoms.

A carefully conducted medical history is important to ensure that there are no contraindications or risk factors for potential complications with the introduction of future pharmacotherapy (anticholinergics). Conditions to consider include cardiac history, in particular a prolonged QT interval; uncontrolled hypertension; functional gastrointestinal pathology; myasthenia gravis; uncontrolled narrow angle glaucoma; and renal and liver impairment.

The patient should also be asked for the details of current medications, both prescribed and over the counter, as these may worsen reported symptoms. Diuretics and sympathomimetics can cause urgency, frequency, and urgency incontinence [29]. Voiding difficulties can also be caused by drugs with anticholinergic properties (antipsychotics, antidepressants, antihistamines, and anticholinergic respiratory agents), α-adrenoceptor agonists or opiates further described in Chap. 8, "Retention" [30]. Potential allergies, particularly for latex, should be investigated.

The history is completed only when the patient's social situation has been assessed. SCI individuals can be dependent on caregivers for their basic activities of daily living. Accessibility to care, toileting, and supplies may be limited by financial constraints or other social factors. Home health support systems as well as access to school/work/recreation should be evaluated. Strong concerted efforts with social workers may sometimes be required to improve these patients' prognosis.

Patients after high spinal cord injuries (above T6) may additionally suffer from autonomic dysreflexia. These patients should be questioned regarding episodes of headache, flushing, sweating, bradycardia, seizures, spasms, and hypertension. A detailed discussion of this life-threatening complication is presented in Chap. 15, Autonomic Dysreflexia.

For the collection and reporting of a minimal amount of information on the lower urinary tract in SCI patients, clinicians can also use the International Lower Urinary Tract Function Basic SCI Data Set (Fig. 4.1) [31, 32].

Physical Examination

The physical examination is a continuation of a comprehensive history and should be performed at the initial and later appointments. It should consist of examining the abdomen, back, loins, as well as pelvic and genital organs [33]. Palpation of the lower abdomen may reveal an enlarged, overdistended bladder. Testing the extent of bilateral sensation (increased/normal/reduced/absent) to light touch and/or pain within each dermatome (with a special attention to the sacral neuronal pathways from S1 to S4) should be performed during the first appointment (Fig. 4.2) [30]. Assessment of spinal cord-mediated reflexes is also important (Table 4.3) [34]. There is universal agreement that the return of bulbocavernous reflex signifies recovery from spinal shock [35]. In incomplete lesions, reappearance of bladder sensation may also indicate termination of spinal shock, whereas in complete lesions, reappearance

Fig. 4.1 The International Lower Urinary Tract Function Basic SCI Data Set—form for the collection and reporting of a minimal amount of information on the lower urinary tract in spinal cord injury patients (with permission from courtesy of the International Spinal Cord Society (ISCoS) [31])

INTERNATIONAL SPINAL CORD INJURY DATA SETS

LOWER URINARY TRACT FUNCTION BASIC DATA SET - FORM

Date of data collection: YYYYMMDD

Urinary tract impairment unrelated to spinal cord lesion:
No Yes, specify_____ Unknown

Awareness of the need to empty the bladder:
No Yes Not applicable Not known

Bladder emptying: Main Supplementary
Normal voiding
Bladder reflex triggering
Voluntary (tapping, scratching, anal stretch, etc.)
Involuntary
Bladder expression
Straining (abdominal straining, Valsalva's manoeuvre)
External compression (Credé manoeuvre)
Intermittent catheterisation
Self-catheterisation
Catheterisation by attendant
Indwelling catheter
Transurethral
Suprapubic
Sacral anterior root stimulation
Non-continent urinary diversion/ostomy
Other method, specify_____
Unknown

Average number of voluntary bladder emptyings per day during the last week __

Any involuntary urine leakage (incontinence) within the last three months:
No Yes, average daily Yes, average weekly Yes, average monthly
Not applicable Unknown

Collecting appliances for urinary incontinence:
No Yes, condom catheter/sheath
Yes, diaper/pad
Yes, ostomy bag
Yes, other, specify_____
Unknown

Any drugs for the urinary tract within the last year:
No Yes, bladder relaxant drugs (anticholinergics, tricyclic antidepressants, etc.)
Yes, sphincter/bladder neck relaxant drugs (alpha adrenergic blockers, etc.)
Yes, antibiotics/antiseptics: For treatment of urinary tract infection
For prophylactic reasons
Yes, other, specify_____
Unknown

Surgical procedures on the urinary tract:

No Yes, supra-pubic catheter insertion, date last performed YYYYMMDD
Yes, bladder stone removal, date last performed YYYYMMDD
Yes, upper urinary tract stone removal, date last performed YYYYMMDD
Yes, bladder augmentation, date last performed YYYYMMDD
Yes, sphincterotomy/urethral stent, date last performed YYYYMMDD
Yes, botulinum toxin injection, date last performed YYYYMMDD
Yes, artificial sphincter, date last performed YYYYMMDD
Yes, ileovesicostomy, date last performed YYYYMMDD
Yes, ileoureterostomy, date last performed YYYYMMDD
Yes, continent catheterizable valves, date last performed YYYYMMDD
Yes, sacral anterior root stimulator, date performed YYYYMMDD
Yes, other, specify_____ , date performed YYYYMMDD
Unknown

Any change in urinary symptoms within the last year:
No Yes Not applicable Unknown

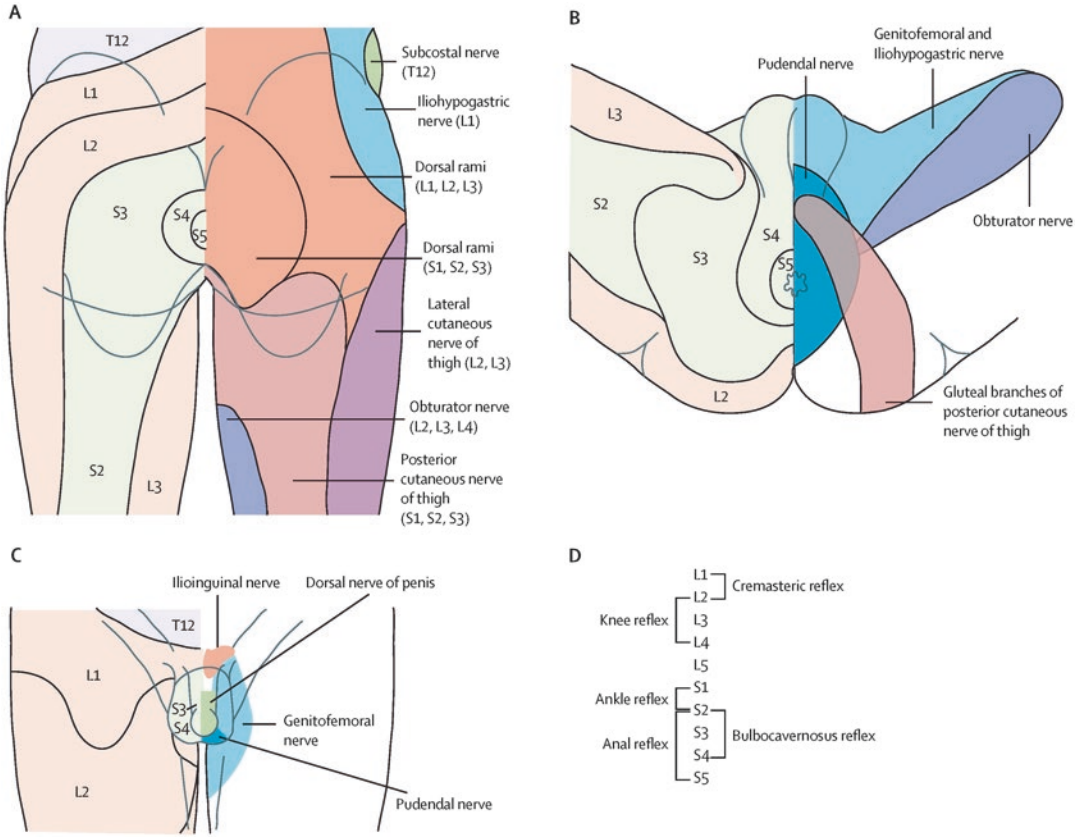

Fig. 4.2 Lumbosacral dermatomes, cutaneous nerves, and reflexes. The physical examination includes testing sensations and reflexes mediated through the lower spinal cord, and abnormal findings would suggest a lesion affecting the lumbosacral segments; mapping out distinct areas of sensory impairment helps to further localize the site of lesion. Distribution of dermatomes (areas of skin mainly supplied by a single spinal nerve) and cutaneous nerves over the perianal region and back of the upper thigh (**a**), the perineum (**b**), and male external genitalia (**c**). (**d**) Root values of lower spinal cord reflexes (with permission from Panicker et al. [30])

of osteotendinous reflexes, leakage around the urethral catheter, or episodes of urinary incontinence between clean intermittent catheterization can point out the end of this disorder [36]. Recovery of bladder function may also manifest with new onset of lower extremity spasms [5]. Further evaluation of the tone and voluntary contraction of the anal sphincter with insertion of a finger as well as assessment of the extent of voluntary contractions of the pelvic muscles should be conducted and described as increased/normal/reduced/absent. These carefully performed examinations may help to localize anatomical lesions and estimate the extent of dysfunction [34, 37].

In day-to-day clinical practice, it is highly important to maintain homogeneous communication between clinicians to reliably interpret later diagnostic and therapeutic results. As patients after SCI are under the care of multiple health care professionals, findings of physical examination should be reported with standardized methods. Thus, the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) tool should be used to properly document clinical findings (Fig. 4.3) [1, 38].

Further examination should also assess pelvic floor supports/pelvic organ prolapse and stress incontinence (spontaneous or induced by Valsalva or cough). Digital examination of the

Table 4.3 Important reflexes in neurourological assessment

Reflex	Involved segments	Method of performing	Proper (physiological) response
Bulbocavernosal reflex	S2–S4	Placing a finger in the rectum and squeezing the glans penis or clitoris. In cases of catheterized patients, can be elicited by gently pulling on the catheter	Contraction of the anal sphincter
Anal reflex	S2–S5	Pinpricking mucocutaneous junction of the anus	Contraction of the anal sphincter
Achilles reflex (ankle reflex)	S1–S2	Tapping the Achilles tendon	Dorsiflexion of the foot
Babinski reflex (plantar reflex)	L4–S2	Stroking the lateral side of the sole of the foot	Curving the toes down and eversion of the foot
Patellar reflex (knee reflex)	L2–L4	Striking the patellar ligament	Extension of the leg
Cremasteric reflex	L1–L2	Stroking the inner thigh in men	Contraction of the cremasteric muscle and elevation of the ipsilateral testis

Responses should be assessed as *normal*, *increased*, *reduced*, or *absent*

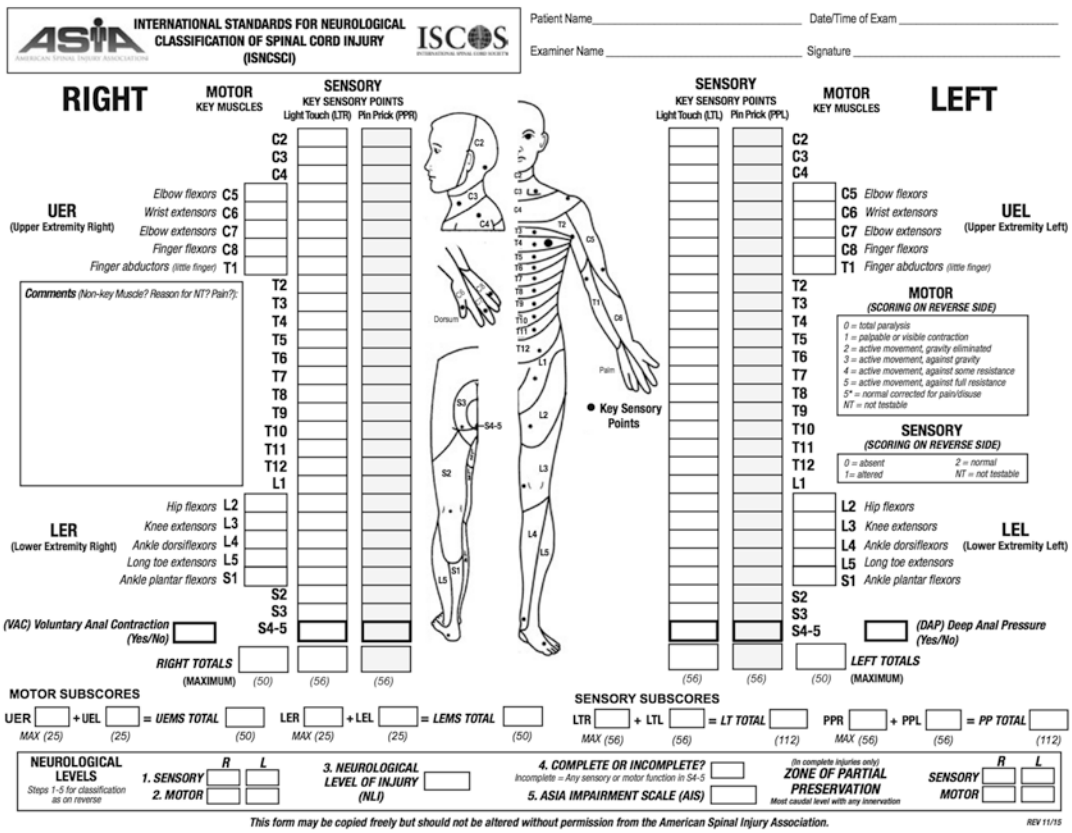

Fig. 4.3 International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) tool for physical examination (with permission from courtesy of the American Spinal Injury Association [38])

prostate (prostate enlargement indicating benign prostatic hyperplasia; areas of tenderness revealing prostatitis; fluctuance signaling prostatic abscess) or vagina (assessment of vaginal estrogenization based on lubrication, blanching of the mucosal surface) should also be performed. Fecal loading of the large intestine/rectum should be described. In patients with chronic indwelling catheters any abnormalities should be documented. These include traumatic hypospadias in men and bladder neck erosion in women.

Although careful examination can help to diagnose the specific type of the lower urinary tract dysfunction, exam conclusions should be taken with caution [39–41]. Studies have shown that prediction of neurogenic bladder type dysfunction is strongly limited, especially in patients with lumbosacral lesions, and in this group of patients it is impossible to predict the type of bladder dysfunction from physical examination alone [42]. Other comorbidities (intervertebral disk prolapse, penile and scrotal pathology, genital infection, hernias) may also significantly influence clinical findings. On the other hand, evaluation of possible comorbidities may be limited due to SCI. It is known that male patients with complete SCI are characterized by significantly smaller prostate volume than non-neurologically impaired patients [43, 44].

Additional evaluation should include assessment of cognition, mode of ambulation, mobility, balance, coordination, weakness, spasticity, hand function (particularly functional ability of the thumb and index or middle finger in patients who may require clean intermittent catheterization), skin (areas of warmth, redness, pain, presence of pressure sores, decubiti, osteomyelitis), and measurement of blood pressure.

Conclusion (Table 4.4)

Table 4.4 Conclusion

Summary	Level of evidence
Comprehensive medical history of patients after spinal cord injury (SCI) suffering from neurogenic bladder (NB) consists of assessment of their general condition, quality of life, self-care activities, complaints, related comorbidities, current medications, and social situation	4 (Expert opinion)
Urological history investigates storage problems, voiding complaints and post-micturition symptoms, as well as explores their onset and duration with severity and degree of bother. Careful assessment of alarm symptoms (hematuria, dysuria, fever) may indicate possible NB complications. Patients after SCI might also suffer from neurogenic bowel and sexual dysfunction	4 (Expert opinion)
Possible related comorbidities include other neurological diseases, endocrine disorders, urological conditions, respiratory dysfunctions, fecal motility disorders, chronic pelvic pain, mobility deficits, prior neck/back/pelvic injuries or surgeries, pelvic cancers, and pelvic radiation	4 (Expert opinion)
Current patient's medications may worsen reported symptoms and increase the risk of drug interactions	4 (Expert opinion)
Qualiveen/SF-Qualiveen, NBSS, IQOL, RHSCIR, Fransceschini and THAQ are currently available questionnaires designed with special attention for SCI individuals. Utilization of generic questionnaires in SCI patients (SF-36, KHQ) has also been reported	1
The physical examination is a continuation of a comprehensive history and may reveal abnormalities of sensation, reflexes and functions of anal sphincter and pelvic floor	4 (Expert opinion)
Carefully performed examination may help to localize anatomical lesions and estimate the extent of dysfunction; nevertheless, studies have shown that prediction of the type of bladder dysfunction from physical examination is strongly limited	2

(continued)

Table 4.4 (continued)

Recommendation	Grade of recommendation
An extensive medical history must be performed in order to appropriately diagnose and treat NB patients after SCI	Expert opinion
Validated specific or generic questionnaires should be incorporated in day-to-day clinical practice of SCI individuals	B
The physical examination should consist of examining the abdomen, back, loins, as well as pelvic and genital organs	Expert opinion
Special assessment of sensations and reflexes associated with urogenital area with description of anal sphincter and pelvic floor functions should be performed	Expert opinion
To properly document clinical findings, standardized methods and assessment tools should be employed	Expert opinion

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Testing

5

Introduction

A comprehensive medical history and specialized physical examination should be followed by other tests. During the first appointment of patients after spinal cord injury (SCI) who suffer from neurogenic bladder (NB) some additional tests are highly suggested. This includes urinalysis or urine culture, blood chemistry, voiding diary, measurement of post-void residual, and urinary tract ultrasound. Other specific tests (urethrocystoscopy, computed tomography, magnetic resonance imaging, uroflowmetry, urodynamics, video-urodynamics, specialist uro-neurophysiological tests) are elective procedures, depending on the indications.

Recommended Tests

Urinalysis/Urine Culture

Urinalysis and urine culture (if appropriate) are an integrated part of basic neurourological evaluation. If not already done by the referring physician, they should be performed as soon as reasonably possible, as SCI patients are at risk of urinary tract infection (UTI) and bacterial colonization, potentially contributing to the clinical presentation of patient's overall condition. Furthermore, reported symptoms may not clearly indicate the presence of UTI [1].

Urine analysis may reveal leukocyturia, proteinuria, glycosuria, or hematuria, indicating relevant comorbidities or complications of NB requiring further assessment. Negative results for nitrite and leucocyte esterase in reagent strip (dipstick) analysis or absence of pyuria/bacteriuria on microscopic examination reliably exclude UTI in people without additional risk factors for infections of uncommon etiology [2]. As NB patients may be colonized by strains of resistant bacteria, a dipstick test may be more useful to exclude than to prove urinary tract infection in SCI patients [3]. Thus, urine culture with antibiotic sensitivity should be performed when any evidence of infection is detected [4, 5]. Physicians should also be aware that due to bacterial colonization, urine dipstick testing and bacterial culture may sometimes be unreliable for diagnosing active infection [6]. Of note, asymptomatic bacteriuria ($>10^5$ CFU/mL), highly prevalent in individuals with SCI and NB, in older persons, and in diabetic and catheterized patients, should not be routinely treated except in pregnant women and before urological procedures within the urinary tract [7–9].

The interpretation of obtained results should also analyze bladder-emptying technique and the presence of an indwelling catheter [10]. The results should be interpreted in the context of previous urological history and treatment, as well as presence of confounding diseases and/or

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_5

comorbidities. Appropriate urine samples include clean-catch midstream samples, samples taken from a freshly inserted intermittent sterile catheter, and samples taken from a catheter port [6]. Samples from leg bags should not be analyzed.

Blood Chemistry

Blood tests allow physicians to assess the patient's general condition, kidney function, and the presence of systemic inflammation [11, 12]. As patients after SCI are at higher risk of developing renal failure than individuals suffering from non-traumatic NB, measurement of serum creatinine levels and calculation of glomerular filtration rate (GFR) is significantly useful in the baseline evaluation of overall kidney function [13]. Of note, in patients after SCI who may be characterized by low muscle mass, lower upper limits for normal range of creatinine values are appropriate [14]. The blood urea nitrogen (BUN test), along with the creatinine test, also helps to assess renal function and diagnose kidney disease. Electrolyte disorders described as abnormalities in levels of potassium, sodium, chloride, bicarbonate, phosphate, magnesium, and calcium may indicate advanced stages of renal failure [15].

Voiding Diary

The voiding diary is a simple, non-invasive method to semi-objectively quantify voiding behavior and fluid intake habits. The International Consultation on Incontinence describes three variants of voiding diaries [16]:

- Micturition time chart (includes only frequency of voiding and incontinence episodes)
- Frequency-volume chart (includes the frequency of voids along with the voided volumes)
- Bladder diary (includes frequency of voiding, incontinence episodes, voided volumes, and type and quantity of volume intake) (Fig. 5.1)

There is a paucity of studies evaluating optimal diary duration in patients with neurogenic lower urinary tract dysfunction [14, 17]. Nevertheless, data from studies investigating diary duration in patients with idiopathic overactive bladder stress that a voiding diary observation with 3–7 days duration should be recommended [18]. Researchers agree that the precision of data obtained from the diary is proportional to its length in days. However, opposite correlation exists between the length of the diary and the patient's compliance with its completion. Patients should be motivated by clinicians to faithfully conduct the test.

To date no consensus exists on reference values for voiding diary parameters, as all of these quantities are strongly influenced by multiple factors [19]. Patients might also modify their behavior to obtain optimal results, leading to invalidation of the test. Nonetheless, the voiding diary still supports clinicians in their day-to-day clinical practice. It has been shown that more than 50% of patients may overestimate daytime urinary frequency when comparing subjective symptoms to objective findings obtained from bladder diaries [20]. The voiding diary also helps to identify polyuria and nocturnal polyuria as well as to calculate 24-h and nocturnal total urine volume [14]. Divergence between diary recordings and the patient's rating of symptoms can be useful in patient counselling [20–23]. The bladder diary might help to identify dietary bladder irritants, abnormal voiding intervals, and abnormal volume intake. Presented factors can be successfully treated with behavioral and lifestyle changes [24]. The voiding diary can also be used to follow the effectiveness of treatment. Comparison of the first diary with subsequent records can help in quantifying the success of therapy. The voiding diary can help to properly conduct future urodynamic study. Decreased filling rates should be considered in patients who

24 Hour Bladder Diary			Date ___/___/_____				
Time	**Intake/Fluids**		**Urinated in the toilet**		**Accidental leakage of urine**		
	Amount (ml)	Type	Number *(how many times did you "pee" during the hour)*	Urine amount (ml)	Intensity (1-4)*	Presence of urgency (yes/no)	Activity *(what were you doing at the time of leakage)*
Please indicate the time when you woke and slept							
6 am							
7 am							
8 am							
9 am							
10 am							
11 am							
12 am							
1 pm							
2 pm							
3 pm							
4 pm							
5 pm							
6 pm							
7 pm							
8 pm							
9 pm							
10 pm							
11 pm							
12 pm							
1 am							
2 am							
3 am							
4 am							
5 am							
* **1** – few drops; **2** – soaked pad; **3** – soaked pad and underwear; **4** – soaked clothing							

Fig. 5.1 24-Hour bladder diary (sample)

show low urine volumes during each void or catheterization, as well as consistent leakage between each micturition [25]. The accurate record of diary variables can allow for estimation of functional bladder capacity and may help to reveal variations in voided volumes, indicating detrusor overactivity [26].

Note that estimation of functional bladder capacity from voided volume is usually limited to patients with neurogenic detrusor overactivity. In those suffering from neurogenic detrusor underactivity or detrusor-sphincter dyssynergia, who usually present with elevated post-void residual or retention, the catheterization diary should be implemented [19]. It is used in the same manner as the voiding diary. Recorded parameters include time and volume of urine obtained at catheterization, as well as the same values obtained for any voids between catheterizations. When sensation is preserved, episodes of urgency may also be

noted. Obtained quantities may help in the estimation of urodynamic results. When catheterization volumes exceed the volume at which filling pressures become unsafe for the upper urinary tract, appropriate management needs to be implemented [19]. The catheterization diary may also help to answer the question whether a full bladder elicits sensation in the patient. Moreover, careful record of catheterizations can show fluctuations in diuresis and could be used to determine the optimal catheterization frequency to adopt [10].

Concluding, although there is a paucity of reliable data investigating the usefulness of voiding diaries in neurologically impaired patients, it should be included in the initial patient's evaluation as a diagnostic, management and outcomes assessment tool.

Post-void Residual

Post-void residual (PVR) urine volume should be assessed during the first appointment of SCI patients suffering from neurogenic lower urinary tract dysfunction. Where the bladder fails to empty completely, PVR is elevated and may predispose to incontinence, UTIs, bladder stones, and renal dysfunction [14]. An elevated PVR indicates dysfunctional voiding, but it cannot be used to discern whether this is caused by poor detrusor contractility (underactive detrusor) or by obstruction (detrusor-sphincter dyssynergia). However, measurement of PVR during the first appointment may detect patients at high risk of upper urinary tract complications and demand immediate introduction of bladder catheterization (if not already implemented) [6]. The PVR volume at which the patient's bladder-emptying technique should be changed is related to the overall bladder capacity and remains a matter of dispute [27]. Nowadays, it is recommended to introduce patients to catheterization techniques when a PVR volume consistently exceeds 100 mL and patients present with related symptoms [10, 28]. Implementation of PVR measurement during the initial evaluation of SCI patients may also help in future evaluation of potential changes in bladder behavior. Currently available data suggest that ultrasound measurement of PVR is preferable to catheterization; portable scanners can be easily used in daily clinical practice [29–33].

Urinary Tract Ultrasound

As patients after SCI are at high risk for upper urinary tract deterioration by secondary reflux, hydronephrosis, ascending infection, and stones, baseline kidney evaluation with ultrasound should be performed during the first appointment [6, 34–36]. It is important to rule out any concomitant disorders or already developed complications at the start of management. Clinicians should also perform ultrasound as a benchmark for potential changes that may be found during future follow-up. Furthermore, ultrasound is considered a very safe procedure with minimal known adverse effects and no radiation exposure. Ultrasound gives information about renal size as well as position, cortical thickness, collecting system dilation, abnormal masses, scarring, stones, and other structural changes affecting the parenchyma (Fig. 5.2) [37]. Healthy adult kidneys commonly measure between 9 and 12 cm in length and have a cortical thickness measurement >1.5 cm [38]. Abnormal findings may indicate a wide variety of renal parenchymal disorders that can affect renal function, including end-stage renal disease (Fig. 5.3) [39, 40]. No consensus exists regarding a standardized definition of hydronephrosis. In daily clinical practice, when hydronephrosis presents, it is usually classified as mild, moderate, or severe (Fig. 5.4) [41]. As intra-observer variations in ultrasound assessment are well known, obtained results can significantly vary among clinicians. Nevertheless, severe hydronephrosis has characteristic ultrasound image, consisting of collecting system dilatation extended into renal parenchyma with cortical loss in long-standing cases [42]. Utilization of Doppler function with measurement of blood flow and resistance in the intrarenal arterial waveforms can also be used to assess the impact of hydronephrosis on renal function [42].

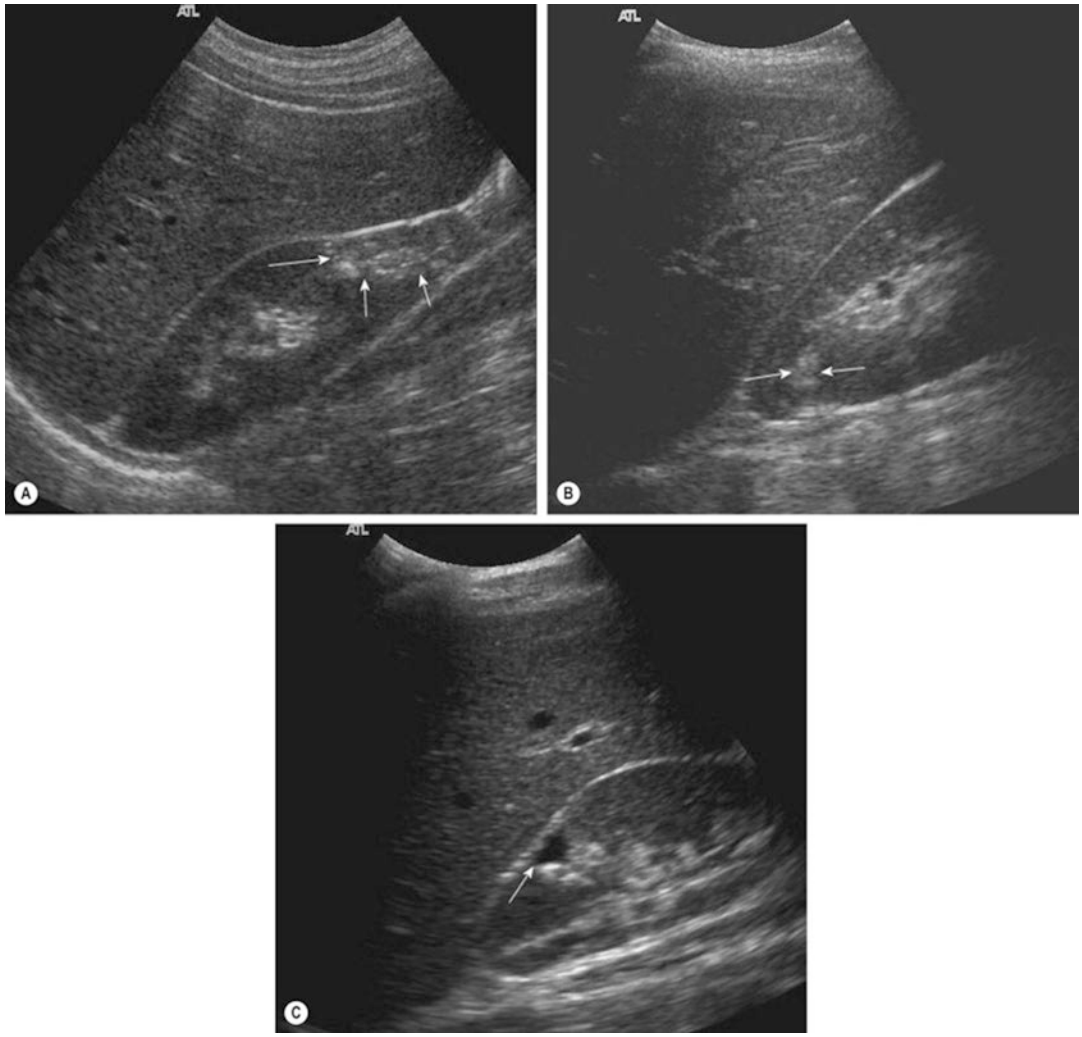

Fig. 5.2 Renal scarring. (**a**–**c**) Three examples of renal scarring (*arrows*) (From Allan [37], with permission)

Besides, Doppler ultrasonography can help in differentiation between acute and chronic hydronephrosis [43, 44]. Color flow Doppler ultrasound may also support and eventually replace retrograde cystography in the detection of vesicoureteral reflux. It has been shown that color Doppler ultrasonography can diagnose all grade IV and V refluxes, almost 90% of grade III, more than 80% of grade II, and almost 60% of grade I [45].

Bladder ultrasound helps to detect bladder stones, which are reported in almost 30% of patients with indwelling catheters (Fig. 5.5) [46, 47]. Of note, the National Institute for Health and Care Excellence (NICE) recommends referral for cystoscopy in patients with NB and suspected bladder stones on the basis that cystoscopy is the most reliable investigation for detecting bladder calculi (which can be small and poorly calcified in some cases) [6]. Bladder ultrasound may also support in the detection of bladder tumors (Fig. 5.6) [47]. It has been hypothesized that frequent detrusor contractions may increase detrusor/bladder wall thickness (DWT/BWT). Therefore, DWT/BWT and ultrasound-estimated bladder weight are being investigated as noninvasive tests in the assessment of patients suffering from NB (Fig. 5.7). However, recently

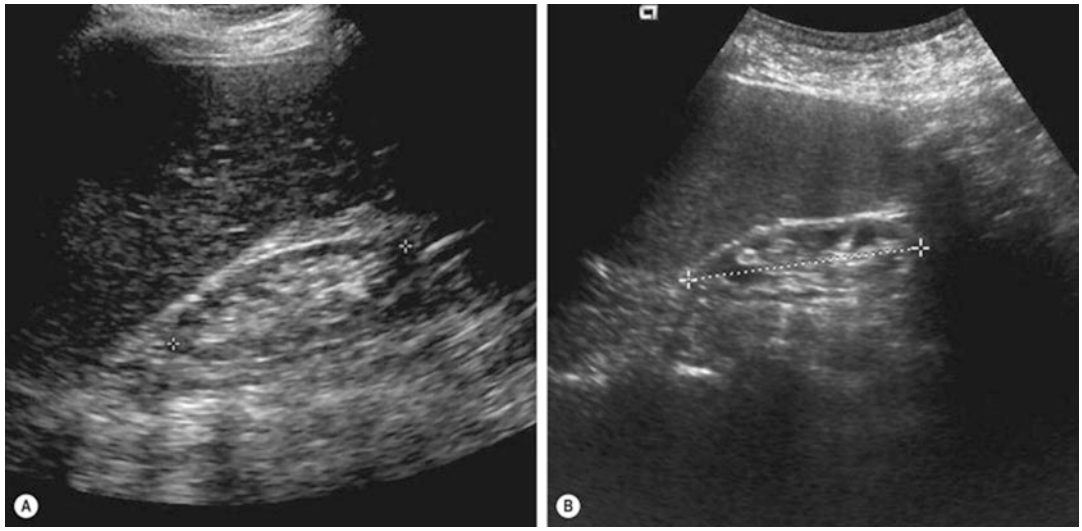

Fig. 5.3 End-stage renal disease. (**a**, **b**) Two examples of small contracted kidneys (6 cm) in patients with end-stage renal disease (From Allan [40], with permission)

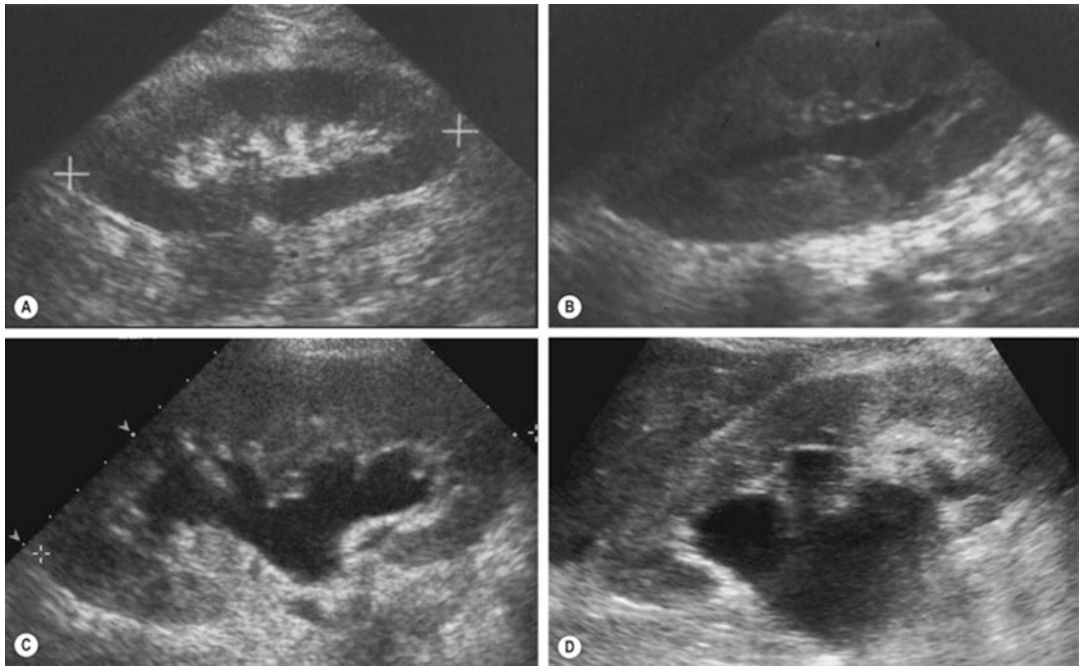

Fig. 5.4 Longitudinal ultrasound shows the grading of hydronephrosis. (**a**) Non-dilated pelvicalyceal system. (**b**) Mild hydronephrosis. (**c**) Moderate hydronephrosis. (**d**) Marked hydronephrosis (From Wah [41], with permission)

published data suggest that routine clinical assessment of BWT for monitoring the effects of treatment of detrusor overactivity is not clinically useful [48, 49] and standardization of the technique has not been demonstrated [50]. In view of these findings, DWT/BWT should not be included in the initial assessment or as a follow-up screening tool for SCI patients.

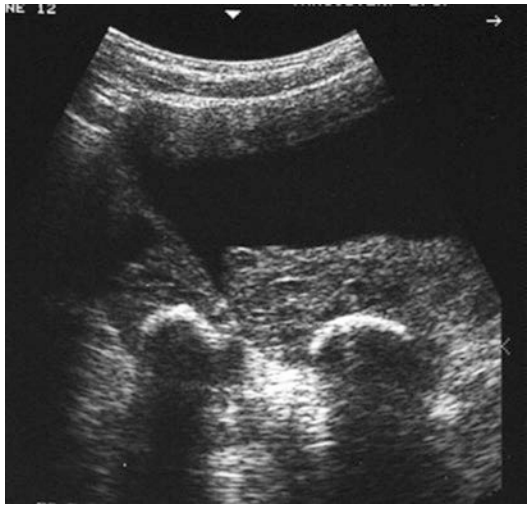

Fig. 5.5 Bladder stones. Two large (>1 cm) stones and debris settling out in a dependent fashion in the bladder. The stones are echogenic and cast acoustic shadows. On real-time imaging, the stones were mobile (From Richenberg [47], with permission)

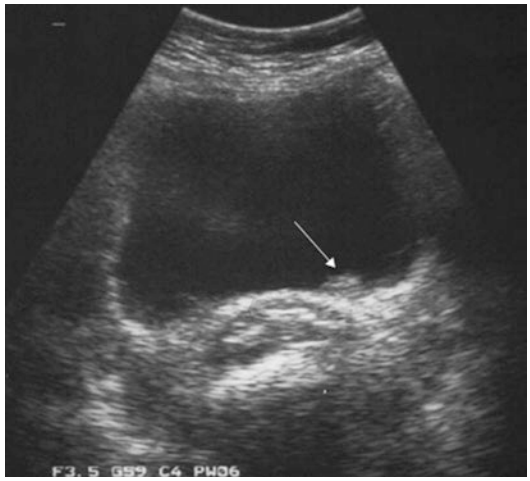

Fig. 5.6 Sessile tumor lies on the posterior bladder wall to the left of the midline (*white arrow*) (From Richenberg [47], with permission)

Elective Tests

Urethrocystoscopy

Urethrocystoscopy may be part of the initial evaluation of SCI individuals with NB. It is required in patients with unexplained or alarm symptoms, such as hematuria, chronic or recurrent UTI, and recurrent catheter blockages, usually indicating complications of NB. These include urethral strictures, trabeculations, bladder stones, bladder cancer, and diverticula. Indwelling catheters, intermittent catheterizations, and multiple endoscopic procedures may lead to urethral strictures and false passages with difficult catheterization. Bladder wall trabeculations may indicate high bladder pressure related to overactivity or infravesical obstruction [51]. As patients with NB are at higher risk of UTI, bladder stones can also be found, particularly in patients who present with recurrent UTI, bladder pain, or microscopic hematuria. Bladder cancer in patients after SCI was the subject of several studies that concluded that SCI may increase the risk of bladder neoplasm [52, 53]. The exact pathomechanism of this phenomenon is still unknown and includes not only the utilization of chronic indwelling catheterization. Moreover, proper evaluation of bladder mucosa in chronically catheterized patients may be challenging. Local irritative effect of the catheter and the balloon, usually within bladder trigone, can be difficult to distinguish from an early carcinoma. Therefore, urethrocystoscopy should sometimes be combined with bladder washing cytology or biopsy. Iatrogenic (e.g., sutures, pieces of Foley catheter) and non-iatrogenic (e.g., hairs) foreign bodies are rare findings in NB patients. In patients with a suprapubic tube, endoscopic bladder examination can be performed per the urethra or through the suprapubic tract [51].

It should be noted that urethrocystoscopy should not be used for functional evaluation of the lower urinary tract. Voluntary contractions of the external urethral sphincter or status of the bladder neck (degree of opening), both assessed during endoscopic examination, cannot replace functional studies [51]. Well-conducted urethrocystoscopy should also assess ureteral orifices. As a result of high bladder pressure and changes in bladder wall thickness, they can become widely open. Similarly, vesicoureteral reflux cannot be diagnosed based on

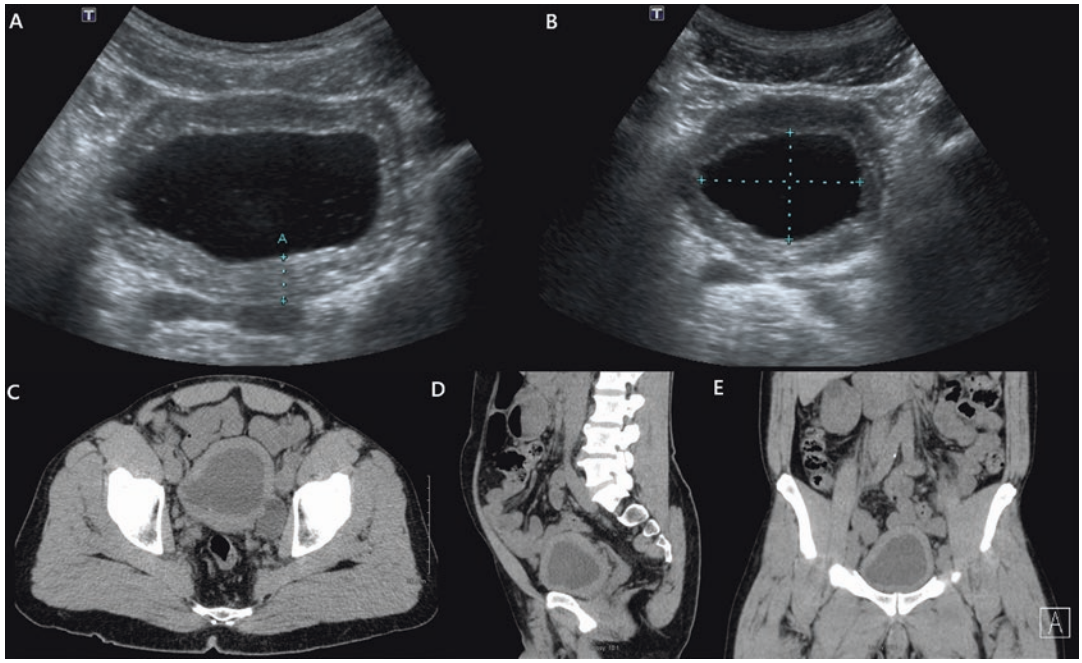

Fig. 5.7 Circumferential and diffuse wall thickening of the bladder measuring up to 15 mm. (**a**, **b**) Ultrasound. (**c**) Axial view (with one large bladder diverticulum arising from the left lateral wall), CT scan. (**d**) Sagittal view, CT scan. (**e**) Coronal view, CT scan

endoscopic examination but requires a voiding cystourethrogram.

Computed Tomography, Magnetic Resonance Imaging, Others

Advanced imaging techniques should not be included in the initial evaluation of patients with NB. Computed tomography or magnetic resonance imaging may be required in those reporting worrisome symptoms such as hematuria, suprapubic pain, or recurrent UTI [54]. The use of these advanced diagnostic tests as well as other imaging techniques (e.g., X-ray of the urinary tract, intravenous urography, cystogram/voiding cystogram, nuclear scans) should be based on patient history and physical examination, and definitely considered in patients after bladder reconstructions [55]. The imaging techniques for investigating the upper and lower urinary tracts can be documented with the International Urinary Tract Imaging Basic SCI Data Set (Fig. 5.8) [56, 57].

Uroflowmetry

Non-invasive uroflowmetry can be used as a screening test for voiding dysfunction. This technique involves measuring the speed, volume, and duration of release of urine and provides with objective information. Possible pathological findings include a low flow rate, intermittent flow, hesitancy, and low voided volume. It may help to select patients who require more sophisticated urodynamic studies. However, uroflowmetry is non-specific and may indicate bladder outlet obstruction, detrusor-sphincter dyssynergia, or bladder underactivity. Uroflowmetry does not allow for evaluation of bladder compliance, a critical component in the assessment of SCI patients [58]. Furthermore, the test requires voluntary control of voiding, making utilization of this test limited or even unfeasible in patients after SCI [10]. Finally, the results obtained describing flow pattern and rate may be modified by inappropriate positions during voiding, a significant issue in SCI patients.

URINARY TRACT IMAGING BASIC DATA SET (Version 1.0)

Intravenous pyelography / Urography or CT urogram, or Ultrasound of the urinary tract

Date performed: YYYYMMDD
Method used: ☐ Intravenous pyelography / Urography
☐ CT urography
☐ Ultrasound of the urinary tract
☐ Normal
Stasis/dilatation in upper urinary tract: ☐ Right side ☐ Left side
Kidney stone: ☐ Right side ☐ Left side
Stone in ureter: ☐ Right side ☐ Left side
☐ Bladder stone
☐ Other findings:_____

X-ray of the urinary tract – Kidney Ureter Bladder (KUB)

Date performed: YYYYMMDD
☐ Normal
Kidney stone: ☐ Right side ☐ Left side
Stone in ureter: ☐ Right side ☐ Left side
☐ Bladder stone
☐ Other findings:_____

Renography

Date performed: YYYYMMDD
Method used: ☐ DMSA (Technetium-99m dimercaptosuccinic acid)
☐ DTPA (Technetium-99m diethylenetriamine pentaacetic acid)
☐ Mag 3 (Technetium-99m mercaptoacetyltriglycine)
☐ Normal
Excretory function: Right side ___% Left side ___%
Stasis/dilatation in upper urinary tract: ☐ Right side ☐ Left side
☐ Other findings:_____

Clearance

Date performed: YYYYMMDD
_____mL/(min. x 1.73 m^2)

Cystogram

Date performed: YYYYMMDD
☐ Normal
☐ Bladder stone
Vesicoureteric reflux: ☐ Right ☐ Left
☐ Bladder diverticulum
Bladder neck at rest: ☐ Open ☐ Closed
☐ Other findings:_____

Voiding cystogram / Micturition cystourogram (MCU) / Videourodynamic

Date performed: YYYYMMDD
☐ Normal
Vesicoureteric reflux: ☐ Right ☐ Left
Bladder neck during voiding: ☐ Normal ☐ Closed (dyssynergia)
Striated urethral sphincter during voiding: ☐ Normal ☐ Closed (dyssynergia)
☐ Other findings:_____

Fig. 5.8 The International Urinary Tract Imaging Basic Data Set (Version 1.0) for documenting the imaging techniques for investigating the upper and lower urinary tracts in spinal cord injury patients (Courtesy of the International Spinal Cord Society (ISCoS) [57], with permission)

Urodynamic Testing

Urodynamic study is the cornerstone of evaluation in patients with neurogenic lower urinary tract dysfunction. It provides objective data of the effect of neurological lesion on lower urinary tract function during bladder filling and eventual controlled voiding. As patient's symptoms and signs and level of SCI do not always correlate with bladder dysfunction, urodynamic study helps to investigate the underlying dysfunction and consequently allows for the initiation of

proper treatment [59]. Urodynamic results can significantly help to assess the patient's prognosis and the risk of deterioration to the upper urinary tract, resulting in adequate follow-up monitoring. It is generally agreed that urodynamic study should be conducted to provide a precise diagnosis for each patient [60]. Multiple studies have demonstrated the clinical value of urodynamics, independent of factors relating to the spinal cord lesion [58, 61].

The urodynamic evaluation consists of several components. To properly perform this complex diagnostic procedure, it should be conducted with validated methods, recommendations, and standards. Technical points on how to undertake urodynamic testing and how to report findings have been set out and recently updated by the International Continence Society in their "Good urodynamic practices" document [62]. This data synthesis should be employed in the daily practice of clinicians who treat neurourological patients.

In individuals suffering from neurogenic lower urinary tract dysfunction, particularly after SCI, special consideration needs to be given to filling cystometry, pressure-flow study, and electromyography.

The technique of the filling cystometry, described as continuous fluid filling of the bladder via a transurethral catheter or other route (e.g., suprapubic, mitrofanoff), is used to mimic the bladder's filling and storage as well as to record the pressure–volume relationship within the bladder. Therefore, cystometry allows for the evaluation of intravesical pressure, bladder wall compliance (ability of the bladder to accommodate the increasing volume with low pressure), bladder sensation, and involuntary detrusor contractions. The results obtained may include detrusor overactivity, low bladder compliance (leading to high bladder storage pressure), abnormal bladder sensation, incontinence, and incompetent or relaxing urethra [63]. Some technical aspects should also be considered. The bladder should be empty at the start of filling. As fast filling and room-temperature saline may provoke bladder instability, a physiological filling rate should be used with body-warm saline [63]. Bladder compliance also seems more reproducible using slower fill rates [14, 58]. Currently, it is advised to start filling at a low rate of 10 mL/min or less [25]. Then, the bladder filling can be maintained at a rate of 20–30 mL/min if no increase in detrusor pressure has been seen [58, 63]. Filling rates greater than 20% of estimated bladder capacity have been shown to artificially raise detrusor pressures [64]. If the detrusor pressure continues to increase with filling, decreasing the filling rate or stopping the infusion may be required [25]. This method can help to evaluate whether increased pressure has been induced by detrusor contraction or impaired compliance. Evaluation of the detrusor leak point pressure should be analyzed with caution due to low sensitivity in the estimation of the risk for upper urinary tract deterioration or secondary bladder damage [63]. Detrusor leak point pressure of 40 cm H_2O is considered as a cut-off value for upper urinary tract failure [65]. Similarly, urethral pressure profiles are seldom used in patients with SCI [10].

During pressure-flow study, when intravesical pressure is measured with and at the same time as urine flow, coordination of detrusor muscle and urethral sphincter can be assessed. This phase of urodynamic study is used to mimic the bladder-sphincter behavior during voiding. Obtained results may include detrusor underactivity, bladder outlet obstruction, detrusor-sphincter dyssynergia (DSD), high urethral resistance, and residual urine [63]. Note that pressure-flow analysis can be conducted in those who are able to void. Furthermore, pressure-flow study mostly evaluates the amount of mechanical obstruction, thus it might have limited value in patients with underlying neurological pathology [63].

To overcome this issue, electromyography, evaluating the striated sphincter function during micturition, should be included in urodynamic evaluation of SCI patients with neurogenic lower urinary tract dysfunction. DSD represents a functional obstruction with an involuntary contraction of the urethral and/or peri-urethral striated muscle concurrent with a detrusor contraction [66]. Phasic detrusor contractions with associated increase in electromyographic activity of the external sphincter on attempted voiding are typi-

cal findings of DSD. The described mechanism leads to high intravesical pressure, which may result in vesicoureteral reflux and severe impairment of renal function. As true DSD is caused by lesions located between the brainstem and the spinal cord (see Chap. 2, "Neurogenic Bladder Pathophysiology"), patients after SCI are at high risk to develop this abnormality. Electromyography also reflects the activity of the striated pelvic floor muscles, so can be used in general evaluation of the patient's ability to control the pelvic floor [63]. Electromyography is not free from limitation. Obtained results may be disrupted by numerous artifacts caused by patient motion, leakage of urine, and movement of equipment [10]. Both the presence of a urethral catheter and abdominal straining may influence findings of electromyography [67]. Therefore, data from electromyography should be interpreted with cautions.

The International Urodynamic Basic Spinal Cord Injury Data Set has been established and includes assessment of bladder sensation, detrusor function, compliance during filling cystometry, detrusor function during voiding, detrusor leak point pressure, maximum detrusor pressure, cystometric bladder capacity, and post-void residual [68].

The time-place of urodynamics in the evaluation of neurogenic lower urinary tract dysfunction in patients after SCI is a topic of ongoing debate. The use of urodynamics is of high importance, as it has the potential to guide management. This results in preservation of renal function and in improvement of continence and quality of life. Baseline urodynamics also provide objective evidence of initial lower urinary tract function, which is important when changes of previously described dysfunction appear. Clinicians should keep in mind that bladder dysfunction in SCI patients varies according to time-dependent changes that occur after SCI (see Chap. 3, "Pathologies Responsible for the Development of the Neurogenic Bladder"). Timing of the initial urodynamic study in patients with SCI depends on the return of spinal reflexes. Following resolution of the spinal shock period, evaluation of the patient with SCI is crucial. Thus, the first urodynamic study should follow the end of the spinal shock phase when a more fixed bladder dysfunction emerges as a result of reorganization of neuronal circuitry (Fig. 5.9) [69]. Spinal shock usually lasts from 6 to 12 weeks after suprasacral SCI but sometimes can be extended to 1 or 2 years [70]. There is a universal agreement that the return of bulbocavernous reflex signifies recovery from spinal shock [71]. Furthermore, in incomplete lesions, reappearance of bladder sensation may also indicate termination of spinal shock, whereas in complete lesions, reappearance of osteotendinous reflexes, leakage around urethral catheter, or episodes of urinary incontinence between clean intermittent catheterization can point out spinal shock end [69]. Recovery of bladder function may also manifest with new onset of lower extremity spasms [25].

Some technical aspects of urodynamic study in patients with SCI should be stressed. As these patients often have concomitant neurogenic bowel dysfunction, related abnormalities may affect urodynamic findings. If the patient is not on a bowel regimen, bowel evacuation before urodynamics may be necessary. If the patient is on a bowel regimen, enemas or rectal suppositories are indicated to avoid bowel movements during the procedure. It should be remembered that prescribed medication should be administered in a timely manner before the study [25]. The majority of SCI patients have limitations in mobility, not allowing them to sit or stand. Therefore, it is acceptable to do the study in the supine position. Patients should be comfortable and protected from skin breakdowns. In those who voluntarily void, the pressure-flow phase should be performed in the position in which they usually void (standing or sitting) to allow for optimal measurement [25]. Multiple patient positions might sometimes be required, especially when expected results are not achieved in the supine position. As SCI patients often lack sensation, needle instead of surface patch electrodes can be used for electromyography, providing more reliable results regarding sphincter function [75]. Specific tests performed during urodynamics, for instance the ice-water test and

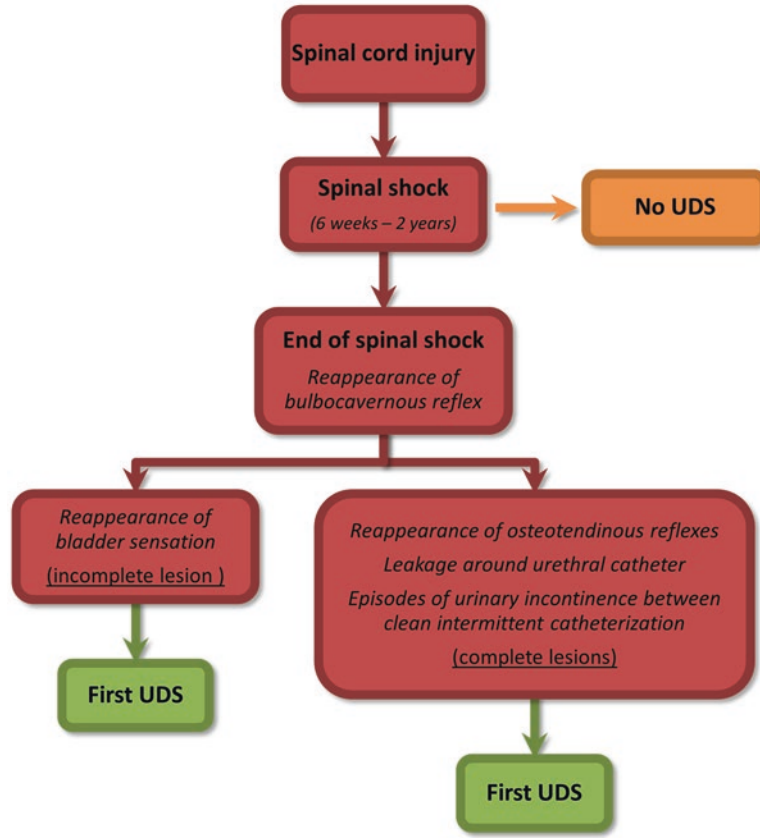

Fig. 5.9 Initial urodynamic evaluation in patients with spinal cord injury

the bethanechol supersensitivity test, have limited clinical value in SCI patients [10]. It has been reported that clinicians sometimes omit urodynamic studies in incomplete SCI patients with mild neurologic deficit monitored in the outpatient settings [60]. This practice should be avoided, as up to half of patients with mild, incomplete injuries could develop bladder dysfunction at a later date [72].

Video-Urodynamics

Video-urodynamics is a combination of urodynamic study with imaging and is considered the optimum procedure for urodynamic investigation in patients suffering from neurogenic lower urinary tract dysfunction [63]. This imaging identifies anatomical and functional abnormalities of the urinary tract and, when combined with multichannel urodynamics, provides the most comprehensive assessment of the lower urinary tract in SCI patients [54].

During filling cystometry, the radiographic assessment of the internal urethral sphincter (bladder neck) helps to determine the level of continence. If the bladder neck is open, it may indicate disorders of the sympathetic bladder innervation resulting in neurogenic sphincter deficiency. Video imaging also supports in identification of bladder and urethral diverticulae and fistula, vesicoureteral reflux, incontinence, cystocele, or ureterocele (Fig. 5.10). Fluoroscopic monitoring during urodynamics helps to assess pelvic floor muscles. Whereas the bladder base lies on the level of pubic symphysis in healthy individuals, it may drop below when the pelvic floor innervation is impaired or ligamentous support is damaged (as a result of previous pregnancy and childbirth) [14]. Consequently, video imaging can be used to differentiate the cause of incontinence between urethral hypermobility (as

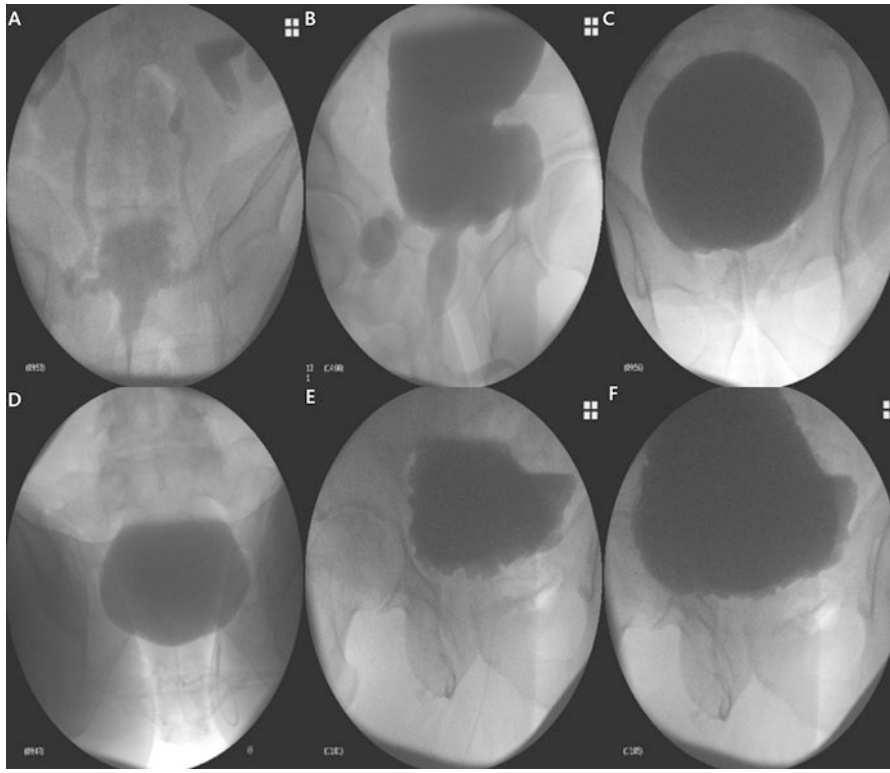

Fig. 5.10 Video-urodynamics. (**a**) Vesicoureteral reflux. (**b**) Bladder diverticula. (**c**) Hypotonic bladder (bladder capacity 700 cc). (**d**) Close bladder neck during voiding phase. (**e**, **f**) Abnormal bladder contours (trabeculated bladder)

the result of a poorly supported pelvic floor) or intrinsic sphincter deficiency. Moreover, leakage of urine can be detected at earlier time points and at smaller volumes using fluoroscopy rather than the standard uroflow sensor.

During pressure-flow study, video-urodynamics is immensely helpful in localization of the site of obstruction when high pressure/low flow state exists [58]. In patients suspected of DSD, evaluation of external sphincter behavior during voiding substantially helps in making an accurate diagnosis. In presented discoordination, video imaging shows contrast being held up at the external urethral sphincter. In rare cases, discoordination between the internal sphincter and detrusor muscle presenting as the lack of opening the bladder neck may be investigated [73]. As vesicoureteral reflux exaggerates during voiding, video imaging can substantially contribute to proper diagnosis of this condition.

At present, video-urodynamics is strongly considered in patients with impairment of renal function, structural change in the upper urinary tract (i.e., hydronephrosis or scarring), high PVR (of note, professional consensus has not been achieved on an acceptable range of PVR), and for assessment of refractory symptoms [14]. The test should be done at baseline and might be incorporated into follow-up for individual cases. NICE guidelines recommend that the use of radiological screening in conjunction with urodynamic studies is required in patients who are known to have a high risk of renal complications, particularly in those with SCI [6]. The reasoning is that several significant abnormalities commonly seen in patients with neurogenic bladder cannot be diagnosed without the additional anatomical information that X-ray screening provides. These abnormalities mainly include vesicoureteral reflux and detrusor-sphincter dyssynergia.

In SCI patients with mobility deficits, examination in multiple positions may be necessary, particularly when expected results are not achieved in the initial position [25]. Limitations of video-urodynamics include proper training of the investigator and possible related complications such as hematuria, edema of the urinary bladder wall, and bladder spasm following use of this technique [10].

Specialist Uro-neurophysiological Tests

Specialist neurophysiological tests investigating NB dysfunction have been mainly used as part of the neurological work-up or for research purposes [74]. Nerve conduction studies have been evaluated in small studies and are not routinely performed. If proper assessment of neurogenic lower urinary tract dysfunction is required, the pudendal nerve is usually investigated [63]. Other tests include reflex latency measurements of bulbocavernosus and anal reflex arcs, evoked responses from the clitoris or glans penis, and sensory testing on the bladder and urethra [63]. More recently, somatosensory evoked potentials have been used as predictive factors for effective therapy with tibial nerve stimulation [14]. The utilization of these techniques depends on specific indications and sometimes may need consultation with other clinicians.

Conclusion (Table 5.1)

Table 5.1 Conclusion

Summary	Level of evidence
Urine analysis may reveal leukocyturia, proteinuria, glycosuria, or hematuria, thus indicating relevant comorbidities or complications of neurogenic lower urinary tract dysfunction requiring further assessment	3
SCI patients may be colonized by strains of resistant bacteria, therefore a dipstick test has been shown to be more useful to exclude than to prove urinary tract infection. If infection is suspected, urine culture with antibiotic sensitivity may help to detect underlying pathology	3
Blood tests, consisting of measurement of serum creatinine, urea nitrogen, and electrolytes, as well as calculation of glomerular filtration rate, allow to assess kidney function	4 (Expert opinion)
The voiding diary is a simple, non-invasive method to semi-objectively quantify voiding behavior and fluid intake habits	4 (Expert opinion)
Post-void residual describes the volume of urine left in the bladder at the end of micturition and may indicate voiding dysfunction	4 (Expert opinion)
Urinary tract ultrasound in SCI patients may reveal upper urinary tract deterioration, hydronephrosis, and stones showing relevant comorbidities or complications of neurogenic lower urinary tract dysfunction requiring further tests	4 (Expert opinion)
Urethrocystoscopy helps in assessment of unexplained or alarm symptoms, usually indicating complications of NB such as urethral strictures, trabeculations, bladder stones, bladder cancer, and diverticula	4 (Expert opinion)
Advanced imaging techniques (computed tomography, magnetic resonance imaging) may help to identify underlying pathology of other worrisome and atypical symptoms	4 (Expert opinion)
Uroflowmetry can support in diagnosing voiding dysfunctions such as a low flow rate, intermittent flow, hesitancy, and low voided volume. This test requires voluntary control of voiding and obtained results may vary depending on positions during micturition	4 (Expert opinion)
Urodynamic study helps to properly diagnose bladder dysfunction in SCI patients as investigated symptoms and findings from physical examination as well as level of injury do not always correlate with underlying bladder abnormality	2
Video-urodynamics is a combination of urodynamic study with imaging and supports in identifying anatomical and functional abnormalities which includes mainly vesicoureteral reflux and detrusor-sphincter dyssynergia	4 (Expert opinion)
Specialist uro-neurophysiological tests include nerve conduction studies, reflex latency measurements, evoked potentials, and skin responses	4

(continued)

Table 5.1 (continued)

Recommendation	Grade of recommendation
During the first appointment of SCI patients suffering from neurogenic lower urinary tract dysfunction following tests should be conducted: urinalysis/urine culture, blood chemistry, voiding diary, measurement of post-void residual, and urinary tract ultrasound	Expert opinion
Other tests including urethrocystoscopy, computed tomography, magnetic resonance imaging, uroflowmetry, urodynamics, video-urodynamics, specialist uro-neurophysiological tests are elective procedures depending on the indication and the time of consultation	Expert opinion
The initial urodynamic study should be delayed until after the spinal shock phase has passed. It is usually indicated by the reappearance of spinal reflexes	B
Management of SCI patients should be mainly based on urodynamic findings rather than on findings from other tests. Urodynamics is the only diagnostic tool that allows functional evaluation of the urinary tract	B
Urodynamic study should be conducted with validated methods, recommendations, and standards	Expert opinion
Video-urodynamics is considered as the optimum procedure for urodynamic investigation in SCI patients	Expert opinion

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Bladder Management and Follow-Up Plan

6

Introduction

First consultation of patients with spinal cord injury (SCI) should include bladder management counselling and follow-up planning. Both activities depend on the time of consultation and the previous clinical findings.

Bladder Management

Urological care is an important part of the holistic care of SCI patients, as urological complications of SCI can be devastating and develop silently. Counselling in terms of bladder management is of utmost importance for these patients' prognosis and future quality of life. However, there is a paucity of high-quality evidence in this area [1]. To overcome this serious issue, the Spinal Cord Injury Think Tank Group from the United Kingdom developed a specific SCI management guideline to support clinicians in their day-to-day clinical practice. Table 6.1 summarizes these recommendations [1]. Due to a lack of reliable data, the recommendations presented have been mainly based on expert opinion and divided into four stages.

Patients after SCI should be educated regarding bladder management at the time of discharge. This helps to avoid complications and results in improvement of long-term care. Unfortunately, available data suggest that less than 50% of these patients have proper knowledge regarding bladder management after being discharged [2]. Therefore, it seems to be necessary to adequately inform and educate clinicians and other community health professionals in terms of the impact of bladder management on these patients' prognosis and future quality of life [3]. It has been shown that systematic teaching and learning strategy based on educational booklets directed to caregivers can be a substantial support in reaching the goals of treatment [4]. Patient education has been further described in Chap. 17, "Patient Education."

Follow-up Plan

Proper follow-up monitoring of SCI patients suffering from neurogenic lower urinary tract dysfunction has multiple goals. This helps to prevent irreversible changes within the urinary tract and includes, but is not limited to [5, 6]:

- upper urinary tract protection
- absence or control of infection
- restoring lower urinary tract function with low storage and voiding pressures for adequate bladder capacity and emptying ability
- treating incontinence
- avoidance of indwelling catheter or stoma
- social and vocational acceptability and adaptability of bladder management
- improving quality of life

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_6

Table 6.1 The Spinal Cord Injury Think Tank Guideline for the urological management of patients with spinal cord injury—Summary (data from Abrams et al. [1])

Stage	Recommendation
Immediate management (first few days from the accident)	• An indwelling catheter is almost always necessary to monitor urine output and assist in fluid management
Early management (0–2 weeks)	• The indwelling catheter should be removed as soon as possible with intermittent catheterization commenced by the care team • Clean intermittent self-catheterization can be commenced by the patient once the fracture site is stable • Indwelling catheterization may be extended in some patients, for instance in women with tetraplegia and frail elderly
Intermediate management (2–12 weeks)	• In most instances clean intermittent catheterization will be continued by a carer or clean intermittent self-catheterization by the patient will be established • Straining/Credé maneuver should be avoided • Those patients who require continuous indwelling catheterization should be converted to a suprapubic catheter as soon as possible
Long-term management (>12 weeks)	• Management should follow one of three broad options described as continence, contained incontinence, and indwelling catheters/urostomy (see Chaps. 7–9)

The outcomes of SCI patients with neurogenic bladder (NB) dysfunction have improved in the past decades. During that time urological complications, in particular renal failure and urosepsis, were the leading cause of death in SCI [7, 8]. Improvements in follow-up monitoring, bladder management strategies, and treatment of complications have virtually eliminated neurogenic bladder-related mortality in developed countries and significantly contributed to increasing the lifespan of these patients [9]. Nowadays, leading causes of death in a group of SCI patients have been reported as pneumonia and influenza, septicemia, cancer, ischemic heart disease, and suicide [10].

Nonetheless, no consensus exists on the optimum frequency of follow-up evaluation in SCI patients with NB [11]. Furthermore, there is no agreement on the specific type of tests that should be performed [9]. Currently available recommendations vary and they are mainly based on expert opinion. There is a paucity of high-quality evidence to support an optimal long-term follow-up protocol. Additionally, there is a lack of evidence on clinical outcomes when different guidelines had been strictly followed [12].

The Spinal Cord Injury Think Tank Group proposed yearly ultrasound assessment of upper and lower urinary tract with measurement of post-void residual volume when possible [1]. Kidney function should be assessed with creatinine clearance and serum creatinine levels at about 12 months, when body muscle mass has been stabilized. Then, renal evaluation should be performed annually based on the serum creatinine level as a single test. Urodynamic study should be repeated as clinically indicated. These include jeopardy of upper urinary tract, recent occurrence of incontinence, previous diagnosis of detrusor-sphincter dyssynergia with sustained raised vesical pressure or low compliance (signifying a rise in pressure with ongoing bladder filling), change in bladder management (before and after introduction of the treatment modification), onset of urinary tract infections (UTIs) or stones, and presence of vesicoureteral reflux or high post-void residual. The Group did not support regular urine testing, as the results are confusing and lead to overtreatment of clinically unimportant bacteriuria. Authors also stressed that urologists who take care of SCI patients should be aware of all responsibilities related to the patient's overall care, including bowel and sexual dysfunctions, pressure sores, pain, muscle spasms, and deteriorating neurological status.

The Veterans Health Administration Group [13] proposed that the annual evaluation of the genitourinary system needs to include urinalysis, culture with sensitivity, serum creatinine, blood urea nitrogen, assessment of upper tract function with an anatomical test (e.g., abdominal ultrasound) and/or an evaluation of function (e.g., creatinine clearance, renal scan). Diagnostic tests

such as computed tomography and intravenous pyelogram should be ordered only when clinically indicated. Surveillance using cystoscopy, cytology, and random bladder biopsy should be performed on a regular basis at the SCI center. Indications for urodynamics during follow-up include deterioration in renal function, anatomical changes in the upper tract (e.g., hydronephrosis), recurrent autonomic dysreflexia of unknown etiology, and urinary incontinence in the absence of UTI. Authors emphasized that standard medical history and physical examination (evaluating symptoms and signs) are not sensitive in screening for high intravesical pressures, thus showing the importance of urodynamic surveillance, when indicated.

The National Institute for Health and Care Excellence Guidelines recommended that lifelong ultrasound surveillance of the kidneys should be offered to people who are judged to be at high risk of renal complications (at annual or 2-year follow-up) [14]. High-risk groups have been defined as patients with SCI or spina bifida and those with worrisome findings on urodynamics (impaired bladder compliance, detrusor-sphincter dyssynergia, vesicoureteral reflux). Moreover, urodynamic investigation as part of a surveillance regimen should be considered in these groups of patients. Of note, authors did not recommend plain abdominal radiography, cystoscopy, and renal scintigraphy for routine surveillance. If an accurate measurement of glomerular filtration rate is required, it should be supported with isotopic techniques. Physicians were advised not to rely on serum creatinine and estimated glomerular filtration rate in isolation for monitoring renal function.

The expert panel of the first International Neuro-Urology Meeting concluded that noninvasive urodynamics must be part of a routine follow-up of SCI patients, as only the results of these investigations allow the timely detection of risk factors before irreversible damage has occurred [12]. Silent deterioration in bladder dysfunction is not uncommon. Retrospective data on patients with incomplete SCI have shown that more than two-thirds of ambulatory patients experienced silent deterioration of bladder function on urodynamics during long-term follow-up [15]. Changes in bladder dysfunction may also occur even though there may be no change in overall symptoms [16]. This emphasizes the importance of regular urodynamic follow-up.

Guidelines on neurourology developed by the European Association of Urology recommended regular follow-up with time intervals based on the type of neurogenic lesion and dysfunctional pattern [17]. The timespan should not be longer than 1–2 years. Special consideration of high-risk patients, particularly those with SCI, stressed that the proposed interval should be much shorter in this specific group of patients. Renal ultrasound should be performed every 6 months, whereas physical examination and urine laboratory should be conducted every year. Urodynamic investigation was recommended at regular intervals but authors did not specify precise time spans. Any significant clinical changes should be further investigated with adequate methods and recommendations.

Other proposals include 6-month follow-up monitoring during the first 2 years with the full range of clinical tests, in particular with urodynamics and ultrasound [18]. Over the subsequent 5 years, 1-year follow-up monitoring should be conducted. After that, in the following 8 years, 2-year follow-up monitoring should be employed. The utilization of specific tests depends on the current clinical situation, previous findings, and presented risk factors. Regular urodynamic checkup of SCI patients can detect changes in compliance and pressures resulting from increase in detrusor-sphincter dyssynergia before symptoms occur. Therefore, presented abnormalities can be diagnosed in time before possibly irreversible changes in the urinary tract have occurred. After 15 years, clinical and ultrasound-based assessment should be conducted every 2–5 years.

When discussing urological surveillance of SCI patients suffering from NB, special attention should be given for cystoscopic evaluation. As the exact mechanisms of increased risk of bladder cancer in SCI patients have not been well analyzed, strong recommendations cannot be provided. One proposal includes follow-up

monitoring every year in patients who have one or more of the following risk factors: smoking and age >50 years, enterocystoplasty or any augmentation cystoplasty over 10 years, any neurogenic bladder over 15 years [18]. Evaluation should be performed with urethrocystoscopy and biopsy, if required. Another proposal stated that urethrocystoscopic monitoring in high-risk patients with indwelling catheter is essential to diagnose and manage complications at an early stage [19]. Importantly, this study has shown that endoscopic findings do not significantly differ between symptomatic and asymptomatic groups. This reinforces the hypothesis that patients with indwelling urethral catheters or suprapubic tube require regular cystourethroscopic surveillance in order to diagnose and manage complications at an early stage. Interestingly, similar findings between symptomatic and asymptomatic patients have been reported with regard to ultrasound surveillance [20].

Readers should be aware that proposed schedules can be modified by presentation of other risk factors, emerging complications, or the patient's compliance with treatment.

A recently published systematic review, analyzing long-term urological follow-up strategies for patients with NB, reported 13 studies related to individuals after SCI [12]. Apart from their recommendations, the review mentions other methods of investigation that may be included in urological surveillance of SCI patients: urography, computed tomography, magnetic resonance imaging, 24 h endogenous creatinine clearance, and 99 mTc-DTPA clearance of creatinine (renal scintigraphy). The utilization of these tests depends on clinical indications. However, the majority of included studies were retrospective, without a control group, and with different time intervals and primary/secondary outcomes. To make matters worse, some of the included studies described interventions that were performed only once, and thus did not form an established surveillance program. As a result, reliable conclusions and recommendations have not been made due to the low quality of the evidence.

Another systematic review, solely focused on urological follow-up of patients after SCI, presented concurrent results [21]. Based on the available data, no definitive recommendations for screening can be made. Cameron et al. revealed that patient signs and symptoms used to predict UTI showed mixed results. Some studies demonstrated that nitrite and leukocyte esterase dipstick testing of urine was sensitive and specific for predicting infection. The authors recommended that healthy, asymptomatic SCI patients monitored annually should not undergo routine urine culture if urinalysis is normal. Cameron et al. found that serum creatinine was not sensitive for detecting early deterioration of renal function. Thus, they recommended that creatinine clearance determined by a 24-h urine sample should be employed to assess the glomerular filtration rate and the applied equation should use the proper correction factors. The authors revealed that only routine renal ultrasound has been shown to have sufficient evidence for recommendation. If ultrasound is positive, renal scan may be a good method for further testing. Ultrasound has also demonstrated good sensitivity for urinary tract stones, and there is enough evidence that ultrasound of the kidneys and urinary tract can detect urinary tract stones adequately. The authors also recommended that plain X-ray of the kidneys, ureters, and bladder should not be routinely performed to evaluate for urinary tract stones. The systematic review also revealed that urodynamics is an important part of screening, but the frequency is unclear and optimal intervals could not be determined. Similarly, the optimum bladder cancer screening method has not been defined. Annual cystoscopy and biopsy did not fit the criteria for a screening test. Consequently, Cameron et al. did not recommend this procedure even in high risk groups.

In view of these discrepancies, it seems reasonable to recommend that the time schedule for neurourological checkups and the extent of the investigations required depend primarily on risk factors (Fig. 6.1). SCI patients without worrisome findings from medical history, physical examination, and additional tests can be evaluated on an annual basis. As bladder behavior may still evolve, urodynamic study should be performed yearly during the first 3 years and thereafter every 2–3 years. Wyndaele proposed that

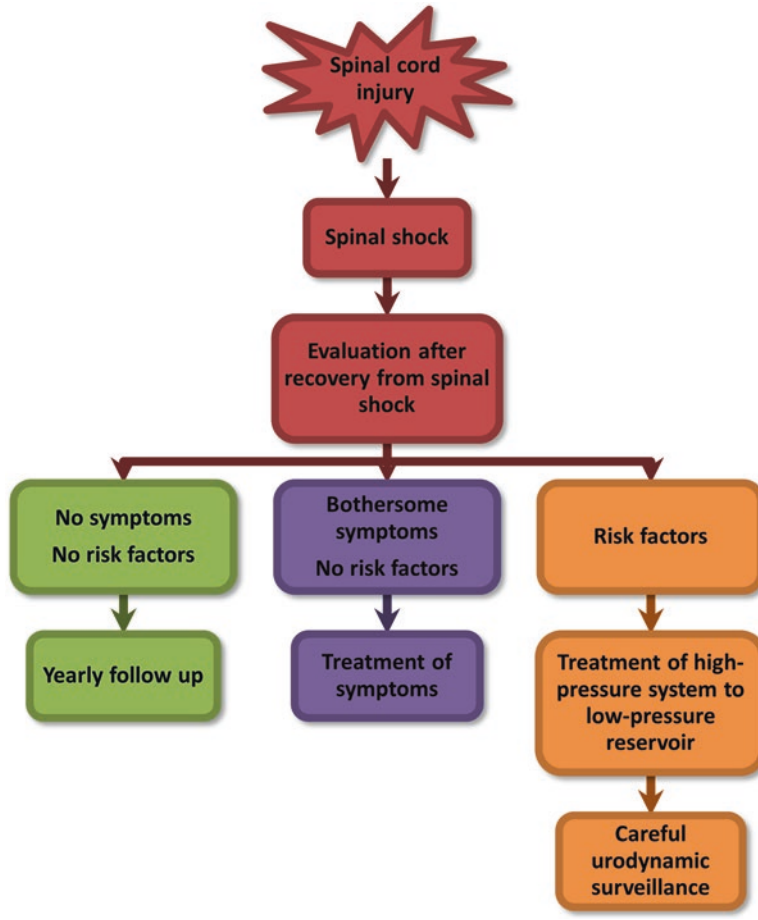

Fig. 6.1 General overview of follow-up planning after consultation with patients after spinal cord injury

urodynamic study may be necessary to repeat if the results of the initial testing were inconclusive, if the outcome of patient re-education was not successful, if results of a treatment need to be evaluated, or even as a routine evaluation 4–6 months after treatment [22]. Furthermore, clinical decision making should not be based on a single urodynamic investigation because repeat measurements may yield completely different results [23].

The German working group has proposed a list of risk factors imposing more careful follow-up monitoring. These include: febrile UTI, recurrent UTI (more than two episodes per year), increased post-void residual (on multiple measurements), increase or new occurrence of urinary incontinence and/or voiding problems, hydronephrosis (investigated with ultrasound), change of bladder morphology (trabeculations, pseudo-diverticulae), and persistent abnormal laboratory findings (elevated levels of C-reactive protein/leucocytes, or any findings indicating deterioration of kidney functions) [12]. The group also indicated urodynamic risk factors for renal deterioration and detailed high pressures during the filling phase (maximum detrusor pressure in men of >80 cm H_2O and in women of >60 cm H_2O), low compliance of <20 mL/cm H_2O, high leak-point pressure, prolonged detrusor contraction and low reflex volume with high post-void residual (>100 mL or more than 30% of functional bladder capacity). Clinicians and researchers should be aware that presented urological surveillance patterns have to be implemented with caution because of low reproducibility. Until now most studies have followed recommendations produced by Wang et al., who reported that detrusor leak-point pressure >40 cm

H_2O is significantly correlated with renal deterioration [24]. A group of British researchers recently suggested that there is a paucity of studies on correlations between detrusor storage, and/or voiding pressures and upper urinary tract changes [12].

Urodynamic study should also be considered before and after surgical interventions. Urodynamics is especially useful in patients who failed sphincterotomy [25, 26].

As different recommendations exist, practice patterns also vary around the world. Reported variations in monitoring SCI patients are presented in Table 6.2 [27–31]. These findings clearly indicate the need for consensus guidelines and recommendations.

Another issue includes patient compliance with treatment. It has been shown that follow-up monitoring, particularly with urodynamic study, may not be performed for practical reasons and owing to fear of complications [22].

Table 6.2 Variations of practice patterns in spinal cord injury patients

Country	Surveillance of upper urinary tract (% physicians who agree with proposed follow-up plan)	Surveillance of lower urinary tract (% physicians who agree with proposed follow-up plan)
Canada (Blok et al. [27])	1-year ultrasound (80%)	1-year urodynamic study (80%)
Japan (Kitahara et al. [28])	1-year ultrasound (71.8%)	1-year cystometry (52.3%)
Netherlands (Rikken and Blok [29])	1-year ultrasound (60%)	1-year urodynamic study (12%)
United Kingdom and Ireland (Bycroft et al. [30])	1–3-year ultrasound (100% of investigated centers)	1–3-year ultrasound (50% of investigated centers)
United States (Razdan et al. [31])	1-year ultrasound (85%)	1-year video-urodynamics (65%)

Of note, the study from the Netherlands evaluated patterns for all neurourological patients

Conclusion (Table 6.3)

Table 6.3 Conclusion

Summary	Level of evidence
Bladder management within the first few days from the accident includes indwelling catheterization to monitor urine output and to assist in fluid management	4 (Expert opinion)
Early management (0–2 weeks) encompasses intermittent catheterization commenced by the care team or by the patient once the fracture site is stable	4 (Expert opinion)
Intermediate management (2–12 weeks) comprises achieving permanent acceptance of intermittent catheterization	4 (Expert opinion)
Long-term management (>12 weeks) depends on patient clinical presentation	4 (Expert opinion)
The goal of continued follow-up is to preserve the upper urinary tract and prevent complications. However, complications may still occur despite an efficient bladder management program	2
Patterns of urological surveillance of patients with spinal cord injury (SCI) have been developed by multiple organizations	4 (Expert opinion)
The time schedule for neurourological checkups and the extent of the investigations required depend primarily on risk factors	4 (Expert opinion)
The majority of existing recommendations prefer annual monitoring of upper and lower urinary tract function in patients after SCI who do not present with additional risk factors	4 (Expert opinion)

(continued)

Table 6.3 (continued)

Recommendation	Grade of recommendation
Patients with SCI should be counselled in terms of bladder management during the first consultation	Expert opinion
Patients should be encouraged to perform intermittent catheterization and provided with necessary information	Expert opinion
In SCI patients without risk factors, 1-year follow-up schedule should be employed. Medical history, physical exam, urinary tract ultrasound, and urine and blood laboratory should be included. Regular urodynamic monitoring should be taken into consideration	Expert opinion
If the patient reports a change in bladder behavior or worrisome symptoms, or if routine studies show any significant abnormalities, the follow-up plan should be modified. Urodynamic study should be repeated and employed into routine monitoring	Expert opinion
When the risk factors or complications have been discovered during the first appointment, follow-up intervals should be tailored to presented abnormalities. In these patients, regular urodynamic follow-up should be employed	Expert opinion
Urodynamic study should be used to monitor patients before and after surgical interventions	Expert opinion
Clinicians should balance between the patient's compliance with treatment and follow-up intervals	Expert opinion

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Part III

Consultations for Main Complaints in Neurogenic Bladder

Incontinence Due to Neurogenic Detrusor Overactivity

7

Introduction

Detrusor overactivity is a urodynamic observation characterized by involuntary detrusor contractions during the filling phase, which may be spontaneous or provoked [1]. In patients with relevant neurological condition, the presented pathology can be termed as neurogenic detrusor overactivity (NDO) and typically occurs when neurological lesions affect suprapontine and/or suprasacral pathways regulating functions of the lower urinary tract (see Chap. 3, "Pathologies Responsible for the Development of the Neurogenic Bladder"). Patients with NDO usually report varying degrees of storage symptoms, such as urinary urgency, frequency, nocturia, and incontinence. A sensation of urinary urgency is felt as the detrusor muscle starts to contract, and if the pressure rise continues, urinary incontinence may occur [2]. In neurologically impaired patients, detrusor overactivity is the most common cause of urinary incontinence. From a patient's perspective, the incontinence is often the most bothersome effect of neurogenic lower urinary tract dysfunction because it leads to more immediately recognizable effects such as poor hygiene, skin breakdown, and social isolation [3].

Epidemiology

A recently published systematic review of the epidemiology of urinary incontinence and detrusor overactivity among patients with neurogenic lower urinary tract dysfunction emphasized that currently available data are strongly limited [4]. Authors revealed that researchers have not been using homogenous terminology. Analyzed studies used various terms to describe NDO, including neurogenic bladder, neuropathic bladder, neuropathic bladder dysfunction, and detrusor hyperreflexia. To make matters worse, several studies considered only specific symptoms of NDO such as incontinence or urgency. Although the International Continence Society (ICS) has provided physicians with standardized terminology that should be used in this area [1], it has been shown that the terminology has not been used consistently in research of lower urinary tract dysfunction. Furthermore, as NDO can be induced by a wide variety of neurological conditions, different baseline characteristics of the patient populations have been discovered, thus strongly limiting data analysis. It is well known that clinical presentation of NDO usually depends on disease stage and severity [5–7]. What's more, clinical diagnosis of NDO can be made only by urodynamic investigation. The meta-analysis emphasized that patients are usually assessed with urodynamic study only if they complain of bothersome symptoms. Therefore, estimation of NDO epidemiology is likely to be biased, and most of analyzed studies were characterized by small sample size. The study reported that 39 out of the 52 identified trials included less than 100 patients. Finally, patient-based studies suggest that those suffering from lower urinary tract symptoms are often reluctant to discuss their symptoms with health care professionals [8].

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_7

In view of these limitations, the frequency of NDO in neurologically impaired populations can be reliably estimated only in four disorders [4]. The random-effect meta-analysis found that the prevalence of detrusor overactivity was 58.2% (50.5–65.9) in patients with multiple sclerosis, 58.6% (34.3–83.0) in patients with Parkinson disease, 49.7% (37.3–62.2) in patients after spinal cord injury, and 64.7% (54.2–75.3) in patients after stroke. Of note, authors did not identify any data on the incidence of NDO in patients with presented diseases. The prevalence of urinary incontinence due to NDO has been estimated as 50.9% (36.7–65.0) in patients suffering from multiple sclerosis, 33.1% (21.3–44.8) in those with Parkinson disease, 52.3% (23.8–80.7) in individuals after spinal cord injury, and 23.6% (18.5–28.8) in those after stroke.

Results have shown that a substantial proportion of neurologically impaired patients experience urinary symptoms. Nonetheless, readers should keep in mind that clinical presentation and frequency of urological complaints vary, depending on the stage of the disease. Lower urinary tract dysfunction has been shown to correlate with disability status in patients suffering from multiple sclerosis [5], and prevalence of urological symptoms increases with the disease duration [9]. Lower urinary tract symptoms generally appear after a mean of 6 years of evolution of this neurological disease [10]. Symptoms may also occur at early stages and sometimes might be reported at the initial presentation [11]. Similarly, bladder dysfunction develops gradually with progression of the disorder in patients suffering from Parkinson disease [6]. It has been shown that the prevalence of urinary symptoms in these patients may increase from 39.3% (mean disease duration of 4.9 years) to 64.0% (mean disease duration of 17.1 years) [12, 13]. Studies suggest that urinary symptoms begin approximately 5–6 years after the onset of parkinsonian motor symptoms [14, 15]. Of note, in individuals with atypical parkinsonism (non-Parkinson disease entities with the greatest prevalence of multiple system atrophy) urological complaints often precede other non-motor or motor symptoms (see Chap. 3).

While the correlation between bladder dysfunction progression and disease duration is well documented in patients with multiple sclerosis and Parkinson disease, this trend is less evident in those after spinal cord injury or stroke. Both of them are considered as acquired and stable conditions. Whereas some patients with spinal cord injury may experience deterioration of bladder dysfunction [16], but mainly those with initial diagnosis of detrusor-sphincter dyssynergia, stroke patients do not usually report progression of micturition disturbances and may even notify symptom relief as patients regain neurological functioning [17–20]. The majority of researchers agree that the incidence of urinary incontinence among stroke patients decreases with time (see Chap. 3). In patients after spinal cord injury or stroke, clinical presentation of bladder dysfunction depends more on the location and severity of damage, as well as the presence of relevant risk factors before injury. The individual patient's ability to recover from the incident of neural injury plays an important role as well.

Incontinence resulting from NDO may also be found in patients with spina bifida, cerebral palsy, AIDS, dementia, and intracranial tumors. However, reliable reports on urodynamically confirmed detrusor overactivity in these patients are few and far between. In general, existent data are limited to single studies or case reports.

Regardless of the underlying pathology, NDO leads to a negative impact on health-related quality of life. Importantly, this influence is independent of the impact of the primary condition. Urological complaints elicited by NDO may impair emotional health, ability to perform household chores, and physical recreation [21]. Urinary symptoms with underlying neurological disease have been shown to more negatively impact the patient's quality of life than the same complaints in individuals with idiopathic overactive bladder [22]. Among storage symptoms, urinary incontinence has been demonstrated as the most bothersome. Patients with urinary incontinence report impairment of physical functioning, mental health, and social life [23].

Diagnosis

History and Physical Examination

The clinical history and physical examination are the basis of clinical practice and considered as the starting point for the assessment process. The urinary tract should be evaluated in detail. Reported storage symptoms (urgency, frequency, nocturia, incontinence) should be carefully documented. The ICS defined increased daytime frequency as the complaint by the patient of urinating too often during the day [1]. Note that frequency of time voids in the healthy population usually ranges between four and seven per day [24, 25]. The symptom of urgency as defined by the ICS is the complaint of sudden compelling desire to pass urine that is difficult to defer. However, described feelings are highly subjective and difficult to quantitate. Urgency urinary incontinence has been described as a complaint of involuntary leakage of urine either concurrently with, or immediately after, a sense of urgency. Nocturia was set as the number of voids recorded during a night's sleep with each void preceded and followed by sleep. Patients should also be asked about other urological complaints, for instance, voiding problems (hesitancy, straining, poor and intermittent flow); post-micturition symptoms (sensation of incomplete emptying, post-micturition dribble); and other complaints. Bladder sensation and onset of urological history should also be queried. Careful assessment of symptoms indicating possible complications (hematuria, dysuria, fever) should be conducted to rule out comorbid pathology such as malignancy, urolithiasis, or urinary tract infection. Neurological symptoms related to underlying neurological pathology should also be documented with onset, evolution, and any treatment.

The clinician should assess the severity of bladder symptoms and their influence on the patient's quality of life and daily activities. Severity can be assessed by asking about pad usage, including pad weight, size, number of pads used, and number of urinary incontinence episodes per day.

The bladder function can be affected by inadequate fluid intake. Storage symptoms may be exacerbated by excessive drinking. Thus, fluid intake habits should be investigated and patients should be asked how much fluid they drink each day, what type of fluids they prefer (with a special consideration for caffeine intake as an exacerbating factor for urgency and frequency), and how many times they void over a 24 h period. Assessment of other potential bladder irritants (alcohol, carbonated drinks) is also important and provides an opportunity to educate patients about modifiable habits [26–29].

As patients with neurourological symptoms may also suffer from neurogenic bowel and sexual dysfunction, bowel and sexual histories are important [30, 31]. Bowel history should elicit information regarding pattern and frequency of defecation, rectal sensation, desire to defecate, and possible episodes of fecal incontinence, constipation, or defecation initiation (digitation, suppository use) [32]. Sexual history should investigate symptoms of genital or sexual dysfunction, presence of sensation in genital area, lack of desire (loss of libido), difficulty in achieving orgasm, possible dyspareunia in the female or erectile dysfunction or ejaculation problems (premature, delayed, retrograde, anejaculation) in the male.

Incontinence and other storage symptoms may be aggravated by different comorbidities. These include endocrine disorders (i.e., complicated and uncontrolled diabetes, diabetes insipidus), urological conditions (i.e., recurrent urinary tract infections, urolithiasis, bladder/prostate cancer), respiratory dysfunctions with chronic cough (i.e., chronic obstructive pulmonary disease), fecal motility disorders (constipation or fecal incontinence), chronic pelvic pain, mobility deficits, prior pelvic surgeries, pelvic cancers, and pelvic radiation. Incontinent patients should be evaluated for stress urinary incontinence, described as the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing [1]. Therefore, in women, a thorough obstetric and gynecological history should be conducted. Pelvic organ prolapse or previous pelvic surgery for both prolapse and incontinence may influence the success of future treatment [33]. A general obstetric history with labor duration, mode of delivery, birth weights of children, year of delivery, intra-partum complications (e.g., obstetric anal sphincter injury,

peri-urethral lacerations, wound breakdown), as well as de novo post-partum urinary symptoms (e.g., urinary retention requiring prolonged catheterization or stress urinary incontinence), which may be precipitated by cesarean section, epidural block, or prolonged labor, may be necessary for evaluation [34–37]. Continuous incontinence may also be caused by ureteral ectopy, fistula formation, bladder neck erosion (from long-term catheter use), or a scarred, fixed urethra from multiple previous procedures [38]. Those patients will report constant urinary drainage (either at night while supine) and infrequent voids due to the lack of urine storage in the bladder. Psychiatric disorders such as depression, dementia, and anxiety should also be considered, as they may influence voiding patterns [39]. Accidents and operations, particularly those involving central or peripheral nervous system, should be elicited.

A carefully conducted patient history is important to ensure that there are no risk factors for potential complications or contraindications for the introduction of pharmacotherapy (anticholinergics). Conditions to consider include cardiac history, in particular a prolonged QT interval; uncontrolled hypertension; functional gastrointestinal pathology; myasthenia gravis; uncontrolled narrow angle glaucoma; and renal or liver impairment.

The patient's current medication should also be evaluated. Both prescribed and over-the-counter drugs may worsen incontinence and other storage symptoms. Diuretics and sympathomimetics can induce storage symtpoms including urgency, frequency, and urgency incontinence [40]. Antipsychotics, antidepressants, antihistamines, and anticholinergic respiratory agents may have anticholinergic properties and contribute to voiding problems (see Chap. 8, "Retention"). There is evidence that cumulative use of agents with anticholinergic properties is associated with increased risk of cognitive impairment [41].

A well-conducted medical history should be completed with assessment of the patient's social situation. Accessibility to care, toileting, and supplies may be limited by financial constraints or other social factors. Family or caregiver support should be ascertained and the patient's independence should be evaluated.

A proper history should not only aim to diagnose the cause and nature of bladder dysfunction but also to identify associated complications (see Chaps. 10–15).

Clinical examination ought to be a part of the assessment of incontinent patients suspected of NDO. It should begin with a general evaluation of mental status, cognitive impairment, obesity, physical dexterity, mobility, balance, and coordination. Special attention should be paid to mobility. Patients with impaired mobility may not have enough time to reach the toilet before incontinence occurs. Abdominal examination needs to be routinely performed. Pelvic and genital examination should assess tissue quality and sensation (see Chap. 4, "Medical History and Physical Examination," Fig. 4.1), urethra, pelvic floor supports/pelvic organ prolapse, and stress incontinence (spontaneous or induced by Valsalva or cough). In incontinent patients, skin quality should be assessed with special attention because chemical irritation from urinary or fecal incontinence as well as impaired sensation may substantially contribute to skin damage. Digital examination of the rectum with assessment of anal sphincter tone and voluntary contraction should be performed [33, 42–44]. Fecal loading of the large intestine and rectum should be described. Evaluation of spinal cord-mediated reflexes (bulbocavernosal, anal, ankle, plantar, patellar, cremasteric) is also important (see Chap. 4, Table 4.4). In patients with chronic indwelling catheters any abnormalities should be documented. These include traumatic hypospadias in men and bladder neck erosion in women.

Bladder Diary and Questionnaires

The bladder diary is useful because it provides a real-time, semi-objective, patient-reported measure of micturition frequency, fluid intake habits, and bothersome symptoms (see section "Voiding Diary" in Chap. 5, "Testing"). Accurate record of a voiding diary can allow for estimation of functional bladder capacity, calculation of 24-h/nocturnal total urine volume, as well as help in patient counselling and treatment monitoring [45].

Bladder diaries are especially useful in behavioral therapies and bladder training programs. In voiding diaries, NDO patients are usually characterized by small and frequent voids with possible incidents of urinary incontinence preceded by urgency. Physicians should motivate their patients to complete such a diary accurately during 3–7 consecutive days.

Currently there is a wide variety of patient-completed and physicians-administered questionnaires that can be used in the assessment of patients with neurogenic bladder. A number of them have been designed with a special consideration for neurologically impaired individuals. Whereas special questionnaires for SCI patients are presented in Chap. 4, individuals with multiple sclerosis can be examined with other specific questionnaires [32, 46]:

- the Functional Assessment Of Multiple Sclerosis (FAMS)
- the Functional Index For Living With Multiple Sclerosis (FILMS)
- the Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS)
- the Incontinence Quality of Life (IQOL)
- the Mean Disability Scale (MDS)
- the Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ-15/MSISQ-19)
- the Multiple Sclerosis Quality of Life Inventory (MSQLI)
- the Multiple Sclerosis Quality of Life (MSQoL-54)
- the Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ)
- the Neurogenic Bladder Symptom Score (NBSS)
- the Qualiveen/SF-Qualiveen
- the Patient Determined Disease Steps (PDDS)
- the RAYS Scale (RAYS)

Among them, HAQUAMS, MSISQ-15/MSISQ-19, MSQLI, and MSQoL-54 are the three-condition-specific (bladder, bowel, sexual function) questionnaires. Patients can also be evaluated by generic questionnaires, such as King's Health Questionnaire (KHQ) or the Short Form 36-item and 12-item Health Survey Questionnaires (SF-36, SF-12). However, such forms may be less sensitive to detect symptom change than more specific questionnaires detailed above [38]. Urge incontinence related to NDO may also be assessed by questionnaires designed for idiopathic overactive bladder (OAB). The International Consultation on Incontinence has developed specific criteria for questionnaires currently in use and has designed a recommendation grading system [47]. Questionnaires with a Grade A recommendation (highly recommended) include:

- the Overactive Bladder Questionnaire (OAB-q)
- the Overactive Bladder Satisfaction Questionnaire (OAB-S)
- the Overactive Bladder Symptom Scores Questionnaire (OABSS)
- the Incontinence Impact Questionnaire (II-Q)
- the Urogenital Distress Inventory (UDI)

The questionnaire selected should have been validated in the language that it is going to be used. Of note, each questionnaire can be used alone or in combination with others in order to improve assessment or monitoring of treatment outcomes [48]. Currently available data are insufficient to answer the question of whether or not the use of these questionnaires has an impact on treatment outcomes.

Urinalysis and Urine Culture

Existing storage symptoms, including incontinence caused by neurogenic bladder, may worsen during urinary tract infection. Moreover, presented symptoms may not reflect the presence of infection within the urinary tract [49]. Therefore, a dipstick urinalysis can be used to screen patients but it should be noted that individuals with neurogenic bladder may be colonized by strains of resistant bacteria, thus a dipstick test may be more useful to exclude than to prove urinary tract infection [50]. If any evidence of infection is detected, urine culture with antibiotic sensitivity is required [51, 52]. Note that asymptomatic bac-

teriuria (>10^5 CFU/mL), highly prevalent in individuals suffering from neurogenic lower urinary tract dysfunction, older persons, diabetic, and catheterized patients, should not be routinely treated except in pregnant women and before urological procedures within the urinary tract [53–55]. Patients should be counselled in terms of proper urine collection. Appropriate urine samples include clean-catch midstream samples, samples taken from a freshly inserted intermittent sterile catheter, and samples taken from a catheter port [56]. Samples from leg bags should not be analyzed.

Pad-Weighing Test

The pad test is a non-invasive, inexpensive tool in the diagnosis of incontinence and assessment of its severity. It has been defined by the International Consultation on Incontinence (ICI) as a diagnostic method to detect and quantify urine loss based on weight gain of absorbent pads during a test period under standardized conditions [57]. The Committee stressed that the pad test is not diagnostic for the cause of the incontinence. Furthermore, there are few data on its utility in neurologically impaired patients [58]. Several different standards have been developed, and tests can be divided into four groups, according to test length: <1, 1, 24, and 48 h. Despite the test duration, pad weighting tests can also be divided into two groups: quantitative and qualitative. The quantitative variant is used to determine the presence of urinary incontinence if the diagnosis is not clear or requires objective confirmation. This method may be improved with a colored dye, administered orally, parentally, or directly into bladder. The quantitative variant is used to measure the amount of urine leakage after executing a standardized set of activities or a normal daily routine. The amount of leakage is calculated from the formula:

$$\text{Total leakage} = \text{Total weight of pad}(\text{s}) - \text{Total weight of dry pad}(\text{s})$$

Because defining continence is difficult and not universally well-understood among patients, the ICI Committee defined the result of the test to be positive when pad weight gains >1.3 g during 24 h or >1 g during 1 h [57]. The ICI investigation concluded that a 24 h test correlates well with symptoms of incontinence and is characterized by good reproducibility. A test lasting longer than 24 h has been proved to have little advantage with poorer compliance and a test lasting shorter than 24 h may lack the ability to quantify the amount or volume of incontinence. Thus, the 24 h pad test is recommended. The ICI Committee qualified the pad test as an optional investigative tool in routine evaluation of urinary incontinence. The major limitations include the fact that the pad test cannot distinguish between urodynamic stress incontinence and detrusor overactivity. Moreover, false positives can be caused by excessive vaginal secretions or menstrual flow, particularly in younger women.

Renal Evaluation

Renal evaluation considers both function and structure. Measuring serum creatinine, blood urea nitrogen, and electrolytes levels, as well as calculating the glomerular filtration rate, helps to assess renal function. Creatinine clearance provides more precise data but requires a 24 h urine collection to assess creatinine excretion. Incomplete collection can result in underestimation of renal function. Renal scintigraphy with assessment of glomerular filtration rate is recommended when renal function is poor, muscle mass reduced, if function for each kidney has to be assessed separately, and in high-risk patients [2]. A renal ultrasound is commonly used for general assessment of kidney structure and may reveal hydronephrosis, abnormal masses, scarring, stones, and other structural changes affecting the parenchyma (see Chap. 5, Figs. 5.2, 5.3, and 5.4). Functional and structural renal evaluation should be considered especially in patients who are at risk of upper urinary tract deterioration and incorporated into baseline assessment and routine follow-up plan with proper regularity.

Other Investigations

Post-voiding residual (PVR) volume, free flowmetry, bladder ultrasound, cystoscopy, computed tomography, and magnetic resonance imaging (MRI) should be performed when clinically indicated, based on patient history as well as relevant symptoms and signs. Uninhibited detrusor contractions in NDO patients provoke incontinence and lead to small PVR. PVR should be evaluated in patients with obstructive symptoms, as NDO may coexist with detrusor-sphincter dyssynergia. PVR measurement can also be considered in patients with history of either prostatic or incontinence surgery. Ultrasound measurement of PVR is preferable to catheterization, and portable scanners can be easily used in daily clinical practice [59–63]. Elevated PVR should raise attention regarding the existence of other possible pathologies. When PVR measurement is indicated, it should be supported with free flowmetry. Bladder ultrasound and cystoscopy may be considered to exclude other causes for storage symptoms (bladder tumor, carcinoma in-situ, ulcers, bladder stones, foreign bodies, cystitis) and should be conducted in patients with recurrent urinary tract infection, persistent pyuria, hematuria, bladder pain, history of stress incontinence or pelvic surgery; and those with suspected fistula, urethral diverticulum, or urinary tract malformation. Cystoscopy should also be considered in patients with possible obstructive pathology. Ultrasound measurement of detrusor/bladder wall thickness is not currently recommended (see section "Urinary Tract Ultrasound" in Chap. 5). Advanced imaging techniques (computed tomography and MRI) should be performed when clinically indicated.

Urodynamics

As detrusor overactivity has been defined as involuntary detrusor contractions during the filling phase that may be spontaneous or provoked, urodynamic investigation is the cornerstone in the diagnosis and management of patients suffering from incontinence due to NDO [1]. The urodynamic components of NDO are isolated to the filling phase, and special attention should be paid to this portion of the test (Fig. 7.1) [64].

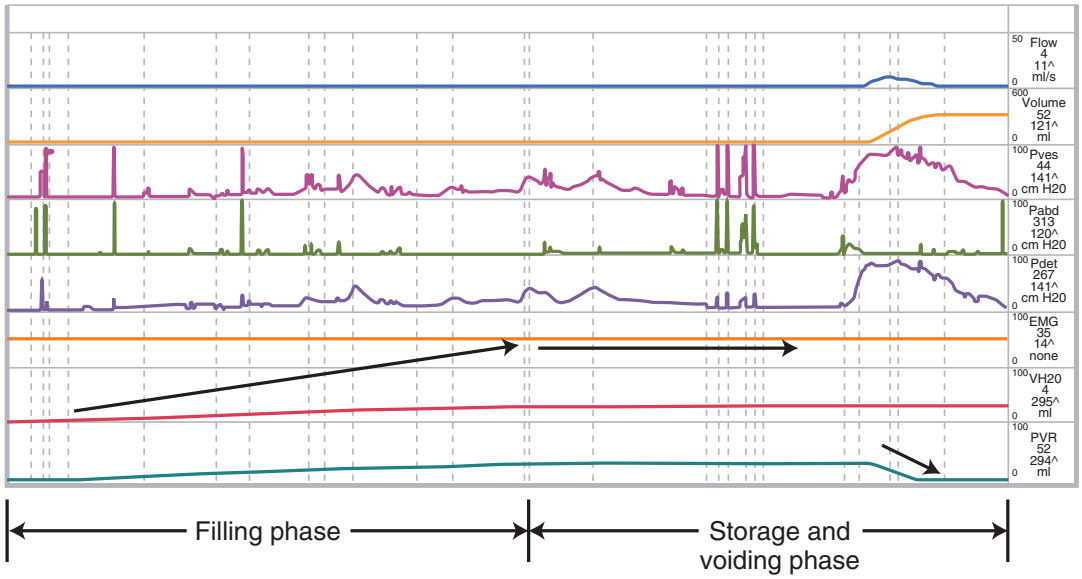

Fig. 7.1 The filling phase is indicated by the steady increase in volume in the bladder as it is being filled. The storage phase can be identified by a stable volume in the bladder. The voiding phase begins when the patient is given permission to void. Note that, in this instance, the patient is able to void successfully. There is an increase in flow with a concomitant decrease in the post void residual (PVR) volume (From Choe et al. [64], with permission)

Investigated abnormalities may include involuntary detrusor contractions, decreased compliance, increased bladder sensation, and decreased cystometric capacity.

Involuntary Detrusor Contractions The presence of involuntary detrusor contractions is necessary to diagnose detrusor overactivity (Fig. 7.2) [64]. These contractions may be spontaneous or provoked (Fig. 7.3), i.e., induced by cough, Valsalva maneuver, short phase of increased bladder filling rate, or the sound of running water (turning on the taps) [64].

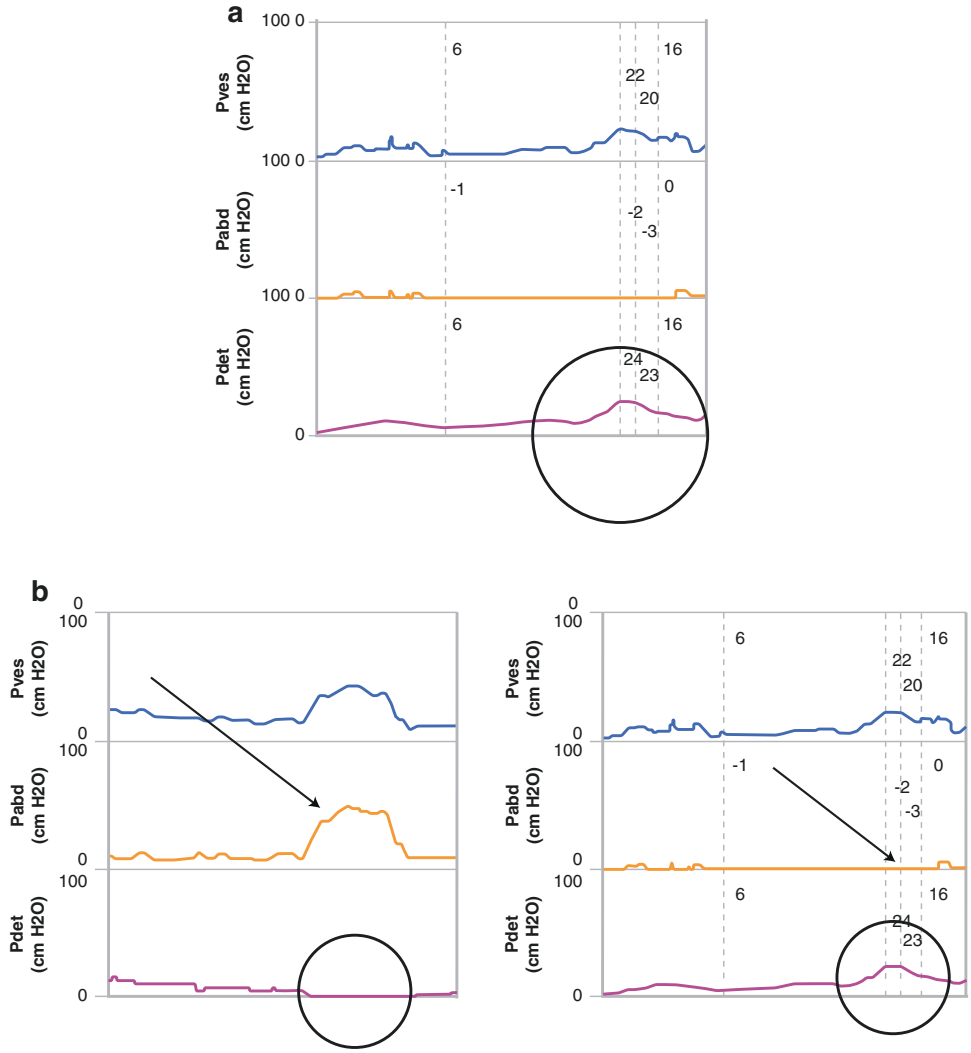

Fig. 7.2 (**a**) This is an example of detrusor overactivity (highlighted by the *circle*) during the filling cystometrogram. The detrusor pressure (Pdet) tracing is *calculated* using the intravesical pressure (Pves) and abdominal pressure (Pabd) values *measured* inside the bladder and further explained in (**b**). (**b**) Using the equation Pdet = Pves − Pabd, the calculated Pdet (*circled*) in the figure on the left is zero since the rise in Pves is associated with a rise in Pabd (highlighted by the *arrow*). This can be seen, as in this case, due to a Valsalva maneuver, which causes a slow controlled rise in the Pabd and Pves tracings for the duration of the maneuver. Conversely, the calculated Pdet (*circled*) in the figure on the *right* represents a true increase in Pdet, since the rise in Pves is not associated with a rise in Pabd (highlighted by the *arrow*). In other words, the increase in Pdet is independent of any intra-abdominal pressure activity (From Choe et al. [64], with permission)

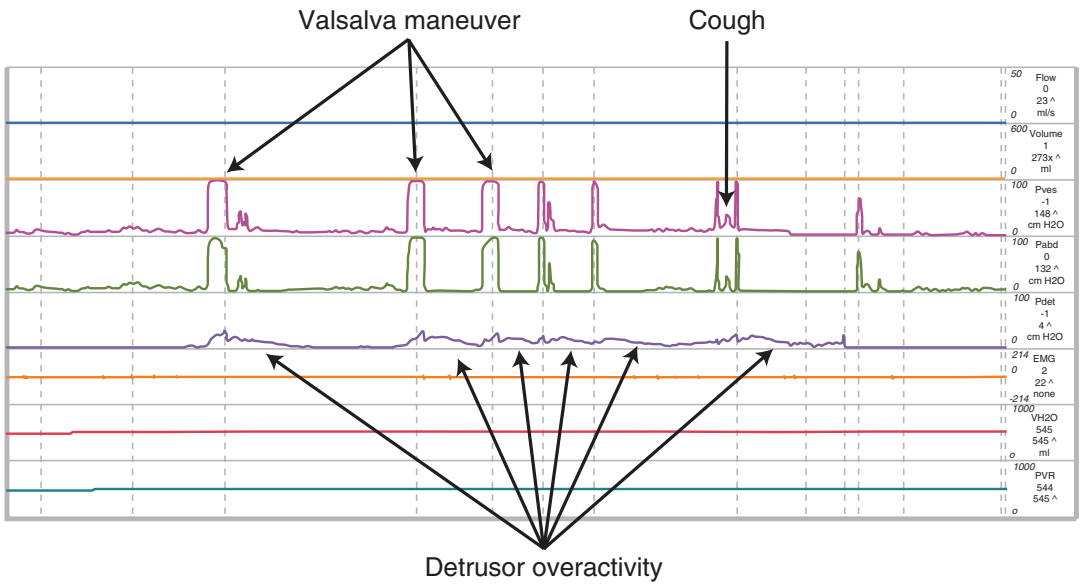

Fig. 7.3 Detrusor overactivity occurs following episodes of provocative maneuvers (Valsalva and cough) (From Choe et al. [64], with permission)

The ICS described certain patterns of detrusor overactivity [1]:

- Phasic detrusor overactivity—defined as a characteristic waveform that may or may not lead to urinary incontinence (Fig. 7.4) [64]. The term waveform has not been specified, but as the name suggests, one would expect cyclical increases and decreases in the detrusor pressure (Pdet) tracing [64].
- Terminal detrusor overactivity—defined as a single involuntary detrusor contraction occurring at cystometric capacity, which cannot be suppressed, and results in incontinence usually leading to bladder emptying (voiding) (Fig. 7.5) [64]. Currently available data suggest that terminal detrusor overactivity has a higher prevalence in neurologically impaired patients than in those without underlying neurological pathology [65–68]. Therefore, when discovered, it should arouse special attention for neurological disease.
- Detrusor overactivity incontinence—defined as incontinence due to an involuntary detrusor contraction (Fig. 7.6) [64].

Analyzing filling phase of urodynamics, clinicians may encounter two measurable leak point pressures named the detrusor leak point pressure (DLPP) and abdominal leak point pressure (ALPP). Nonetheless, the recently updated consensus document of the ICS entitled "Good Urodynamic Practices and Terms" introduced only one term—leak point pressure (LPP) [69]. It has been defined as the pressure (spontaneous or provoked) that has caused fluid to be expelled from the bladder at the moment that it is visible outside the urethra (may also be used for extra-urethral urine loss or stoma). This may refer to abdominal, cough, or Valsalva LPP or detrusor LPP. Provocation and pressure recording site ("type of LPP") should be reported. This newly introduced term is concurrent with current recommendations that DLPP should be interpreted with caution in neurogenic patients due to low sensitivity in estimating the risk to the upper urinary tract or for secondary bladder damage [32].

Some studies suggest that NDO can be distinguished from idiopathic detrusor overactivity based on findings from a filling phase of urodynamics [69, 70]. Lemack et al. reported that patients with NDO may have a greater amplitude of the first overactive contraction and maximum detrusor contraction. Using a cut-off

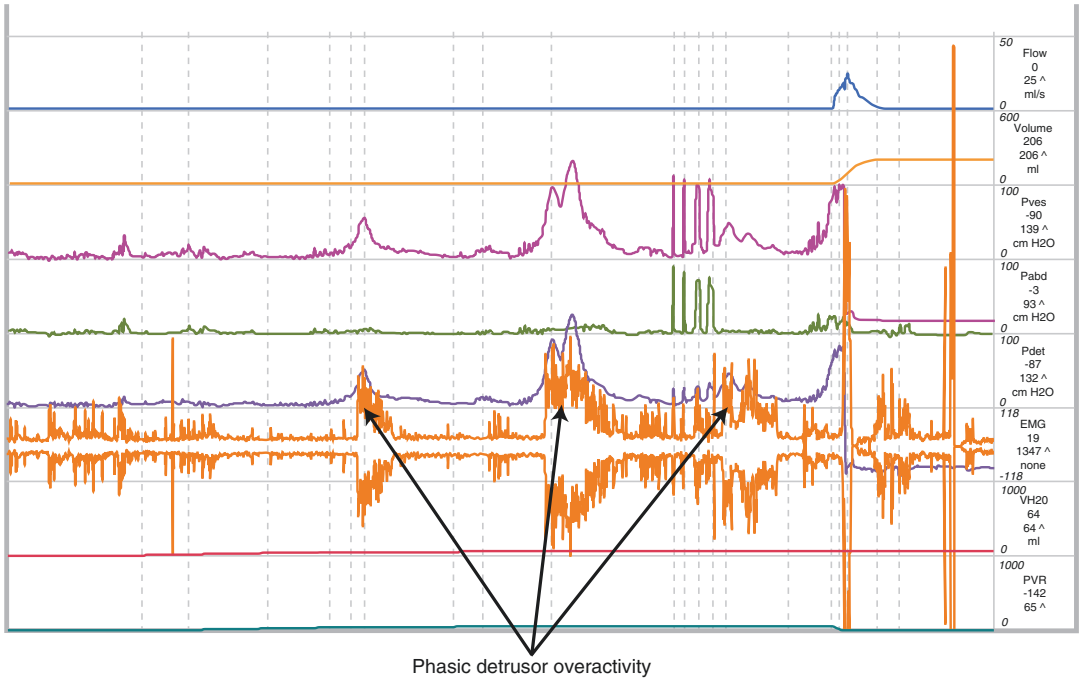

Fig. 7.4 This urodynamics test demonstrates "waveforms" in the detrusor pressure (Pdet) tracing with phasic detrusor overactivity. There is no standardization regarding the characteristics of the "waveform," but is generally recognized as cyclical increases and decreases in Pdet. Note that the abdominal pressure (Pabd) is silent, suggesting that the increases in Pdet are due to contractions arising in the bladder (From Choe et al. [64], with permission)

value of 30 cm H_2O for amplitude of the first overactive contraction, the authors achieved a positive predictive value of 88% for identification of underlying neurological disease. However, it is important to note that NDO and idiopathic detrusor overactivity may also look identical on urodynamics [71]. This emphasizes that NDO is a clinical diagnosis of urodynamically confirmed detrusor overactivity in patients with underlying neurological pathology. NDO is strictly defined by the patient's neurologic status and not by the presence of involuntary detrusor contractions on the urodynamics tracings [64].

In neurological patients, detrusor overactivity may often coexist with detrusor-sphincter dyssynergia further described in Chap. 8. Nevertheless, clinicians should keep in mind that NDO is a diagnosis derived from the filling phase of urodynamics (storage), whereas detrusor-sphincter dyssynergia occurs during the pressure-flow study (voiding) [64].

Decreased Bladder Compliance During normal bladder filling, the bladder stores increasing volumes of urine while maintaining low storage pressure. Bladder compliance describes the relationship between change in bladder volume and change in detrusor pressure measured during the filling phase of urodynamics [1]. Compliance is calculated by dividing the volume change (ΔV) by the change in detrusor pressure (ΔPdet) and it is expressed in mL/cm H_2O.

$$\text{Compliance} = \text{change in volume}\left(\Delta V, \text{mL}\right) / \text{change in pressure}\left(\Delta\text{Pdet}, \text{cm}\,\text{H}_2\text{O}\right)$$

The current recommendation is to measure compliance between the start of bladder filling and the attainment of cystometric capacity (or

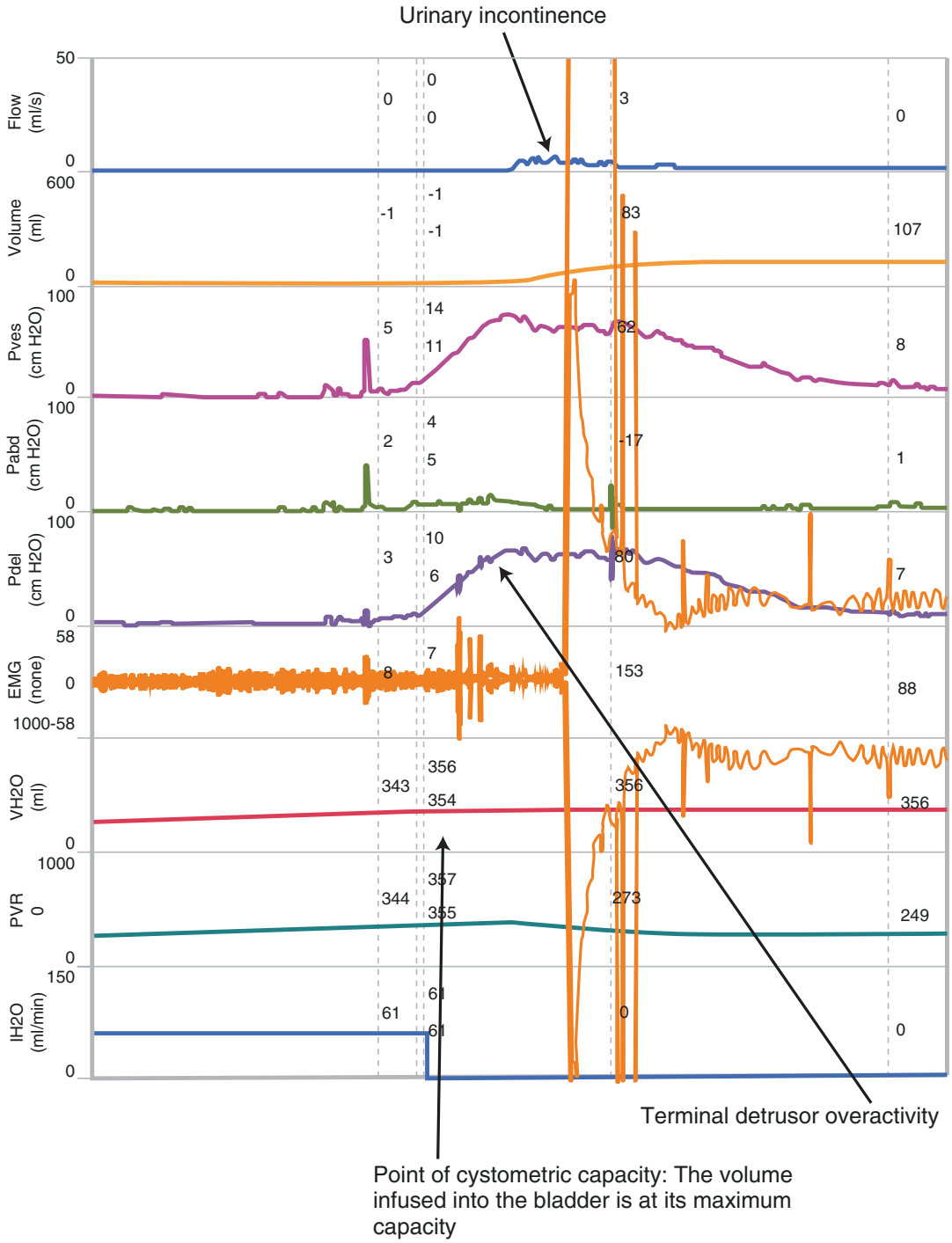

Fig. 7.5 This patient has terminal detrusor overactivity, defined as a single involuntary detrusor contraction occurring at cystometric capacity that cannot be suppressed, and results in incontinence (From Choe et al. [64], with permission)

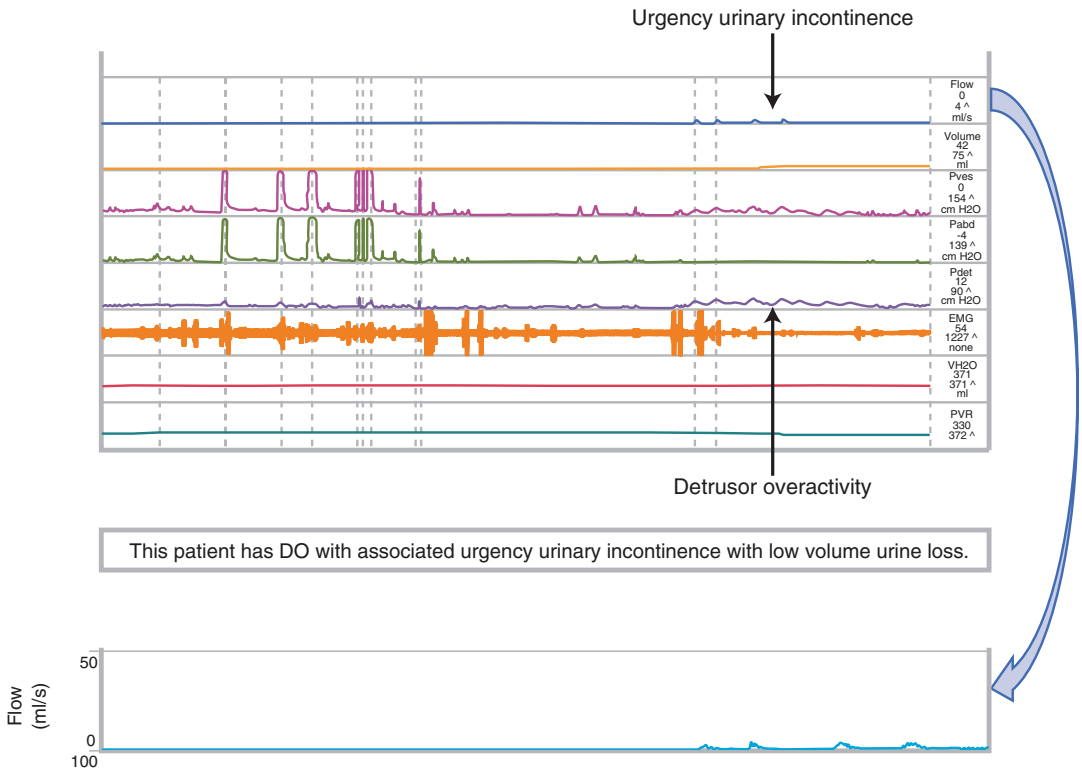

Fig. 7.6 This patient has detrusor overactivity with associated urgency urinary incontinence with low volume urine loss (From Choe et al. [64], with permission)

immediately before the start of any detrusor contraction that causes significant leakage). Both points are measured excluding any detrusor contraction. Compliance is considered to be one of the most reproducible and reliable urodynamic measurements [72].

Decreased (poor, low) bladder compliance signifies an abnormal increase in detrusor pressure between measurement points. There is no agreement on absolute value for bladder compliance. Studies suggest that compliance values below 10–15 mL/cm H_2O should be considered as abnormal [73, 74]. Decreased compliance leads to high bladder pressures that can throw the upper urinary tract into jeopardy. This may present as upper tract deterioration, vesicoureteral reflux, and pyelonephritis [73]. It is agreed that a sustained bladder pressure of greater than 40 cm H_2O can cause significant risk to the upper tracts. Poor bladder compliance can be observed in multiple neurological disorders, including stroke, spinal cord injury, multiple sclerosis, multiple system atrophy, spina bifida, transverse myelitis, or iatrogenic nerve damage from pelvic surgery. Non-neurological entities may also result in low bladder compliance, for instance bladder outflow obstruction, chronic cystitis, chronic urinary tract infection, or even chronic catheterization as a consequence of connective tissue scarring of the bladder wall [75]. Decreased compliance substantially contributes to storage symptoms, including urgency, frequency, and incontinence.

Measurement of bladder compliance can be altered by anatomic variations (e.g., bladder diverticula) or intrinsic sphincter deficiency as consequences of additional urine capacity or urine leakage, respectively [72]. Low bladder compliance can be exaggerated by high filling rate. Moreover, phasic detrusor overactivity can sometimes be misleading and confused for abnormal

compliance, particularly when it is prolonged and of low amplitude. Stopping of fluid infusion may help in proper diagnosis. If detrusor pressure returns to baseline, then the rise in detrusor pressure is caused by an involuntary detrusor contraction; if the detrusor pressure remains elevated, then the rise in detrusor pressure is caused by abnormal compliance [72].

Increased Bladder Sensation Increased bladder sensation has been defined by the ICS as an early first sensation of filling, early desire to void, and/or strong desire to void that occurs at low bladder volume and that persists [1]. During filling cystometry, the patient may also experience urgency, which is defined as a sudden compelling desire to void.

It has been proposed that the first sensation of filling in healthy individuals should appear at mean bladder volume 222.5 ± 151 mL in men and 175.5 ± 95.5 mL in women. The first desire to void should be reported at 325 ± 140.5 mL (male) and 272 ± 106 mL (female) of mean volume of the bladder. Strong desire to void can be expected at 453 ± 93.5 mL (male) and 429 ± 153 mL (female) of mean bladder volume [76]. Another proposal emphasized that the first sensation of bladder filling occurs at an average of 40% of maximal cystometric capacity, while strong desire to void occurs at an average 70% of maximal cystometric capacity [77]. In neurologically impaired patients, increased bladder sensation results from involuntary detrusor contractions and impaired compliance [78].

Decreased Cystometric Capacity Cystometric capacity is the bladder volume at the end of filling cystometrogram [1]. The end point for bladder filling should be well documented on urodynamic tracing. Normal cystometric capacity is generally defined as 300–550 mL with larger values obtained in men compared to women [79]. Yoon and Swift defined abnormally small cystometric capacity as less than 300 mL. Nevertheless, the authors advised clinicians to interpret low cystometric capacity with caution, ideally together with data obtained from a bladder diary [80]. Detrusor overactivity, impaired compliance, and increased bladder sensation may lead to leakage of urine before the patient reports the sensation of fullness (Fig. 7.7) [81]. In these situations, cystometric capacity is decreased and measured as the volume at which leakage began.

Maximum cystometric capacity is the volume at which the patient feels he/she can no longer delay micturition. At maximum cystometric capacity, patients have a strong desire to void, and they report that they cannot hold any more in their bladder. Note that according to terminology introduced by the ICS, maximum cystometric capacity should be defined only for patients with normal bladder sensation [1]. As individuals with neurogenic bladder dysfunction often have impaired bladder sensation, this parameter should not be reported in this specific group of patients.

Treatment

The main objectives for current strategies in the management of NDO are protection of the upper urinary tract, restoration of the lower urinary tract function, as well as improvement of urinary continence and the patient's quality of life [82].

Conservative Treatment

Conservative treatment is cheap, widely available, and rarely complicated. It includes behavioral techniques, lifestyle changes, and management of other medical conditions. Although there is a paucity of well-conducted studies in neurologically impaired patients, conservative treatment should be employed. This usually requires support from caregivers and health-care professionals to be successful. It is beneficial to introduce conservative treatment in conjunction with education about lower urinary tract function for the patient and/or their family members and carers [56]. Some aspects of presented techniques are described in Chap. 17, "Patient Education."

Behavioral techniques include two main treatment options: bladder training (BT) and pelvic floor muscle therapy (PFMT). BT includes the

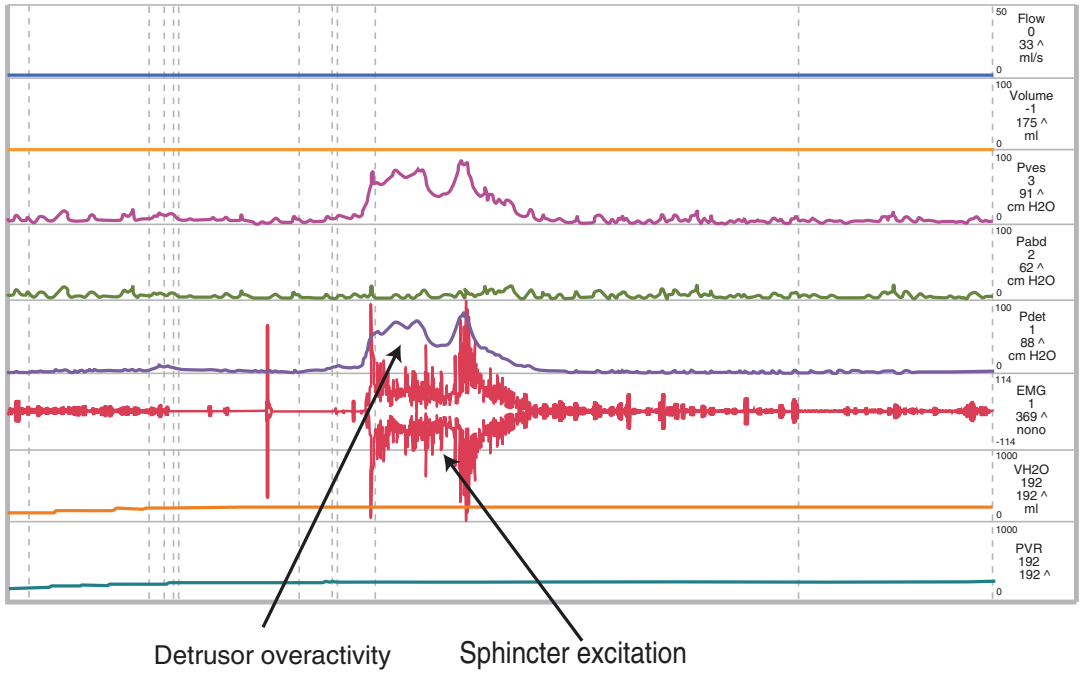

Fig. 7.7 Cystometrogram in a patient with neurogenic bladder dysfunction and severely diminished cystometric capacity. Vesical pressure and abdominal pressure were equalized at the start of the study with a corresponding detrusor pressure of zero. First sensation was reported at 20 cc, detrusor overactivity was seen at 29 cc, and first desire to void reported at 48 cc. A second involuntary contraction was seen at 78 cc with corresponding leakage of urine (From Smith et al. [81], with permission)

use of bladder diaries, bladder control strategies, timed voiding, prompted or scheduled voiding, or delayed voiding. These are all used to alter patient voiding patterns. PFMT has been shown to improve urinary frequency, number of daily incontinence episodes, and mean cystometric capacity in patients with multiple sclerosis [83]. A recently published study on patients with NDO after spinal cord injury provided evidence that a 6-week program of PFMT may have a beneficial effect on promoting voluntary control of NDO and can reduce incontinence in selected cases with a motor incomplete spinal cord lesion [84]. PFMT may also include urgency suppression, control strategies, and biofeedback. Combined treatment of PFMT, biofeedback, and neuromuscular electrical stimulation has been found to be safe and effective in women with multiple sclerosis [85].

Lifestyle changes include fluid, caffeine, diet management, and weight loss. Patients should individually identify bladder irritants. Presented strategy also includes making the toilet more accessible and improving the patient's mobility. Patients should be informed about incontinence pads and protective products. Male incontinent patients can be candidates for a condom catheter connected to a collection bag. The penile clamp is contraindicated in NDO patients because of the risk of further increase in intravesical pressure [32].

Management/treatment of other medical conditions includes optimization of bladder-related comorbidities, changes in drug intake if these influence diuresis and/or bladder function, as well as treatment of other physical and psychosocial issues such as constipation, depression, or anxiety.

Pharmacological Treatment

In neurological patients suffering from neurogenic bladder, the recommendation is to use drug treatment in conjunction with conservative modalities [86]. Pharmacological management of

neurogenic bladder is primarily aimed at controlling and alleviating bothersome symptoms of urgency, frequency, and urinary incontinence. There is currently no curative pharmacological treatment of this condition. Available literature includes several individual studies and systematic reviews. Drugs can be administered orally, transcutaneously, or intravesically.

Oral Administration These drugs include anticholinergics and beta 3 agonists, with limited data on the latter.

Antimuscarinic drugs have been widely used for many years to treat patients with NDO and they are currently recommended as the first-line choice for treatment of NDO [32]. They have an antagonistic action on muscarinic receptors throughout the body, but improve detrusor overactivity symptoms by blocking the M2 and M3 receptors in the bladder, and therefore are thought to reduce storage pressures, prevent involuntary detrusor contractions, improve bladder compliance, increase bladder capacity, and reduce episodes of storage symptoms, including incontinence [87].

A recently published meta-analysis has confirmed that anticholinergic treatment in patients with NDO is associated with better patient-reported cure and improvement of urodynamic parameters when compared with placebo [82]. Researchers have not proved the superiority of one drug over another and suggested that the only difference between drugs is their side-effect profiles. They emphasized that there is still uncertainty about which anticholinergic drugs are most effective and which doses should be chosen. An update of a systematic review of the efficacy, tolerability, and safety of oral antimuscarinics in neurogenic bladder dysfunctions has also failed to answer these questions [88].

The choice of antimuscarinic agent has been analyzed by the Expert Panel of European Association of Urology in their Neurourology Guidelines [32]. The panel reported that oxybutynin, trospium, tolterodine, and propiverine are established, effective, and well-tolerated treatment modalities for NDO, even in long-term use. Similar results have been shown in efficacy of darifenacin and solifenacin evaluated in patients with spinal cord injury and multiple sclerosis. Experts emphasized that there is a paucity of clinical data for the use of fesoterodine in treatment of NDO.

Anticholinergic therapy is frequently prescribed at higher doses than in idiopathic overactive bladder. Studies comparing standard to higher dose of different anticholinergic therapies showed that this attitude may improve outcomes [88–93]. Higher dosages or double anticholinergic therapies were regularly associated with better improvement in patient-reported outcomes and urodynamic parameters. Current data suggest that the appearance of side effects is comparable to that of normal-dosed antimuscarinics [88, 89]. Combined antimuscarinic treatment by using two different antimuscarinics with slightly different receptor profiles might also be a right option for patients affected by neurogenic bladder, particularly in those refractory to previous antimuscarinic monotherapy [94]. Proposed strategies might slow down or delay other more invasive treatments. Of note, clinicians should be aware that such practices are usually outside of the regulatory licenses for the overactive bladder [95].

Antimuscarinics are contraindicated in patients with narrow-angle glaucoma, as their anticholinergic action can induce or precipitate acute angle closure [96]. Antimuscarinic drugs contribute to the overall anticholinergic burden, adding to the polypharmacy of patients with other anticholinergic effects. Anticholinergic burden has been linked to cognitive dysfunction [41], but also with increased mortality and cardiovascular risk [97]. As neurogenic bladder dysfunctions are usually lifelong, these effects should be considered. Potential side effects include dry mouth, constipation, visual disturbance, skin reactions, cognitive impairment, and reduction in bladder emptying. Urinary retention is possible in those who void spontaneously [91, 92, 98]. Thus, the National Institute for Health and Care Excellence Guidelines recommend monitoring residual urine volume in people who are not using intermittent or indwelling catheterization after starting antimuscarinic treatment [56]. Dose titration in those individuals should be done carefully [99]. Available data

suggest that oxybutynin may be less well tolerated than other antimuscarinics [95]. Data from studies on idiopathic overactive bladder emphasize that immediate release formulations of antimuscarinics should be avoided if extended-release formulations are available [100]. The longer-acting formulations were found to be more effective and have decreased side effects, but little evidence supports the use of one long-acting agent over another [99].

It is well known that adherence and persistence with anticholinergics is poor in idiopathic overactive bladder, but there is little evidence on this subject in NDO. A retrospective analysis of 26,922 patients with neurogenic bladder revealed that 38% of patients discontinued oral therapy within 1 year [101].

Commonly used antimuscarinic drugs for management of NDO has been recently evaluated by Panicker et al. [2]. A summary of their findings with updates is presented in Table 7.1 [102].

Beta-3-adrenergic receptor agonists have recently been introduced. Mirabegron has been reliably evaluated in idiopathic overactive bladder, proving its efficacy. However, there is a paucity of data for neurological patients. Hypothetical efficacy of mirabegron in patients with spinal cord injury and neurogenic bladder has been described in one retrospective analysis [103] and one animal study with transected rats [104]. Authors of both papers stated that mirabegron therapy could be an effective treatment option, but further research is warranted.

Transcutaneous Administration Data of transcutaneous drug administration in patients with neurogenic bladder are strongly limited. Study of SCI patients with NDO found that transdermal

Table 7.1 Commonly used antimuscarinic drugs for management of neurogenic detrusor overactivity

Antimuscarinic drug[a]	Dose (mg)	Frequency	Level of evidence in studies of NB patients
Darifenacin			
Controlled release	7.5–15	Once daily	3
Fesoterodine			
Controlled release	4–8	Once daily	DNA
Oxybutynin			
Immediate release	2.5–5	Two to three times a day	1
Controlled release	5–20	Once daily	1
Transdermal patch	36 (releasing approximately 3.9 mg oxybutynin per 24 h)	Replace once every 3–4 days	1
Propiverine			
Immediate release	15	One to three times a day	1
Controlled release	30	Once daily	1
Solifenacin			
Controlled release	5–10	Once daily	2
Tolterodine			
Immediate release	2–4	One to two times a day	3
Controlled release	4	Once daily	3
Trospium chloride			
Immediate release	20	Twice daily (before food)	1
Controlled release	60	Once daily	1

Summary of analysis made by Panicker et al. with updates [2, 102]
NB neurogenic bladder, *DNA* data not available
[a]Presented in alphabetical order

oxybutynin may be an attractive option, as it was well tolerated and effective [105]. In patients with idiopathic overactive bladder, a transdermal route has shown similar efficacy and significantly improved side effect profile [106].

Intravesical Administration To minimize systemic absorption and related side effects of antimuscarinics, an intravesical route of oxybutynin delivery has been investigated by multiple studies [107–111]. A recently published randomized prospective controlled multi-center trial demonstrated the efficacy and safety of intravesical 0.1% oxybutynin hydrochloride in the treatment of NDO compared to its oral administration [106]. Another study revealed that electromotive administration may improve intravesical drug uptake and result in better urodynamic parameters [107]. It has been shown that increasing doses of oxybutynin installed intravesically improve effectiveness without a significant increase in side effects [109] and can be safely combined with oral antimuscarinics with better effectiveness [110]. Bladder installation is performed with crushed pills diluted in water or saline and instilled in the bladder after catheterization and allowed to dwell [108]. The intravesical route is not free from limitations. It is time consuming and, with the increased tolerability of extended-release oral medications, remains an infrequent route of administration [99]. It should be also stressed that there is no standard instillation protocol, and the treatment is not licensed [95].

Intravesical drug treatment has also been reported with vanilloids, capsaicin, and resiniferatoxin [112, 113]. However, the European Association of Urology recommended that currently there is no indication for the use of these substances, which are not licensed for intravesical treatment [32]. Corcos and Ginsberg stressed that no protocol has been proposed to control detrusor overactivity with these modalities [114]. Furthermore, studies have shown that botulinum toxin A injections provide superior clinical and urodynamic benefits compared to intravesical resiniferatoxin [115]. Therefore, these substances are not currently used in daily practice.

Botulinum Toxin A Injections

Not all patients achieve continence or urinary tract safety with antimuscarinics alone. Given the widespread use of botulinum toxin A (BTX-A) injections and its proven clinical efficacy, this treatment is currently considered as a second line therapy and the most effective minimally invasive strategy [32]. BTX-A inhibits acetylcholine exocytosis, an important excitatory neurotransmitter in the bladder that stimulates detrusor contractions via M2 and M3 receptors (see Chap. 2, "Neurogenic Bladder Pathophysiology") [116]. Treatment of NDO with BTX-A has been shown to significantly improve urodynamic parameters such as maximal cystometric bladder capacity and detrusor pressures, as well as clinical parameters including urinary incontinence. BTX-A also improves patient's quality of life and significantly contributes to preservation of renal function [117, 118]. Its clinical efficacy has been extensively proved in recently published meta-analyses of patients with NDO after spinal cord injury and with multiple sclerosis [119, 120]. Some case series have also reported satisfying results for other conditions, such as cerebrovascular accident, Parkinson disease, and multiple system atrophy [121–123].

BTX-A injections are recommended when anticholinergic therapy has shown to be ineffective or poorly tolerated. Patient selection involves preprocedural urodynamic study to diagnose NDO. Those with incontinence related to other causes may not benefit from detrusor BTX-A injections [119]. Currently, three different formulations of BTX-A are commercially available in Europe and the USA: onabotulinumtoxinA (Botox®, Allergan Inc., Irvine CA, USA), abobotulinumtoxinA (Dysport®, Ipsen Limited, Paris, France), and incobotulinumtoxinA (Xeomin®, Merz Pharmaceuticals, Raleigh NC, USA) [124]. However, only onabotulinumtoxinA and abobotulinumtoxinA are supported with reliable and adequate clinical data in the field of urology. Both of them have already been characterized by the level A recommendation for NDO treatment with proved safety and efficacy [124, 125]. Clinicians should also be aware that utilization of

both formulations depends on local health care authorities, and in many countries only onabotulinumtoxinA is approved for use in NDO [124]. Moreover, onabotulinumtoxinA is the only formulation approved by the U.S. Food and Drug Administration [2].

Studies report that a dosage of 200–300 U of onabotulinumtoxinA is comparable with 500–750 U of abobotulinumtoxinA [126]. The proposed dosages have proven their efficacy [118, 126–129] but both 750 U of abobotulinumtoxinA and 300 U of onabotulinumtoxinA have not shown better results compared to 500 U of abobotulinumtoxinA and 200 U of onabotulinumtoxinA, respectively [126, 130, 131]. Therefore, the recommended dose for intradetrusor injections in NDO patients is 200 U of onabotulinumtoxinA and 500 U of abobotulinumtoxinA [124, 126]. There is little evidence of the potential difference between onabotulinumtoxin and abobotulinumtoxin in terms of outcomes [119]. No recommendation can be made about formulation superiority.

There is universal agreement to perform 20 cystoscopic guided injections of 200 U onabotulinumtoxinA in the detrusor muscle (Fig. 7.8) [124, 132]. Each 100 U of onabotulinumtoxinA should be well dissolved in 10 mL saline, making the concentration equivalent to 10 U/mL. Thus, each injection contains 1 mL of solution. Following this recommendation, if 300 U of onabotulinumtoxinA is required, it should be infiltrated in 30 sites [124, 133]. Current literature recommends an ultrafine needle (22–27 gauge, 4 mm in length) for the procedure [124, 134–136]. Additional stopper helps to prevent bladder perforation and reduce leakage to the bladder lumen or extravesical tissues [135]. There is a paucity of data comparing intradetrusor, suburothelial, and bladder base injections in neurogenic patients. A small study with 23 neurogenic patients showed no differences in efficacy

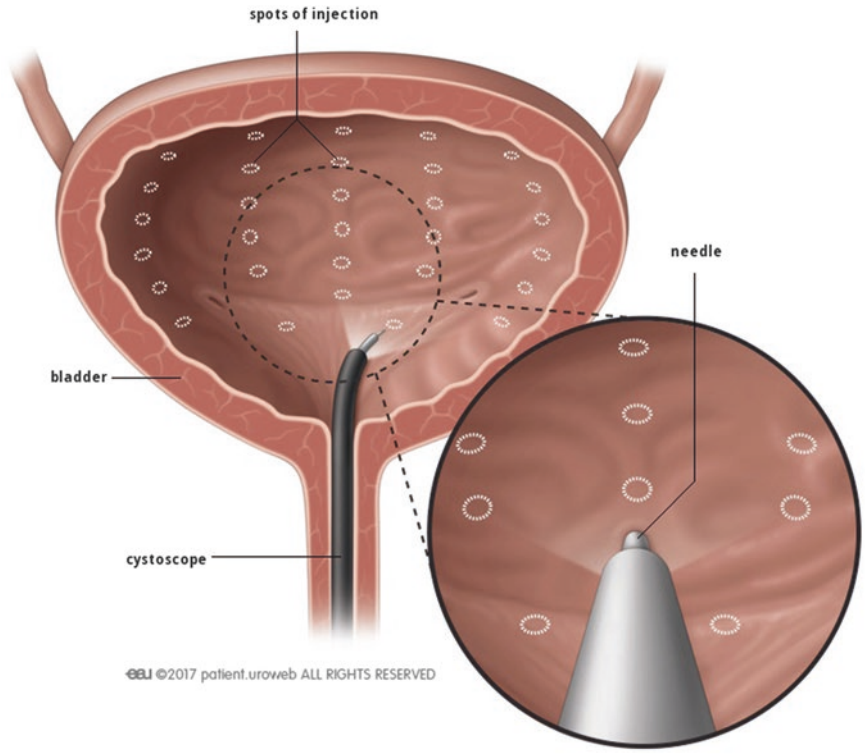

Fig. 7.8 Injections of botulinum toxin into the bladder wall (Courtesy of the European Association of Urology [132], with permission)

between the intradetrusor and suburothelial injections of 300 U of onabotulinumtoxinA [137]. It is hypothesized that intratrigonal injections can cause vesicoureteral reflux and extensive damage to the sensory nerve endings, as the trigone has a prominent submucosal nerve plexus [138]. However, studies reported that intratrigonal injections are not associated with vesicoureteral reflux, elevated post-void residual, or increased need for self-catheterization in comparison to extratrigonal injections [134, 135]. Interestingly, a study comparing onabotulinumtoxinA 300 U intradetrusor injections with 200 U intradetrusor plus 100 intratrigonal injections in 36 patients with spinal cord injury and NDO showed an increased efficacy with the trigone inclusion [139]. Studies analyzing injections with flexible and rigid cystoscopes showed no statistical differences in terms of urodynamic outcomes, symptom improvement, or patient's quality of life [129, 134]. Surgeon preference and institutional practice usually decide what technique is applied. The bladder volume is typically kept at 150–200 mL and punctures of blood vessels are avoided during injection. Both local and general or regional anesthetics can be used [140]. The local method usually involves installation of lidocaine 2% (50 mL for 10–30 min) [136]. Available data suggest that BTX-A injections can be safely performed in an outpatient setting [140] and patients can be discharged from the clinic after they have voided [141].

The safety of intradetrusor BTX-A therapy for NDO has been documented [142]. Local complications include urinary tract infection (16.7%) and hematuria (4.9%), as well as elevated post-void residual (50%) or retention (23.7%) [143]. Other side effects are nausea/vomiting (13%), depression (11%), muscle spasms (9.7%), constipation (9.3%), local or generalized muscle weakness (7%), back pain (7%), dizziness (7%), insomnia (7%), headache (4%), diarrhea (6%), flu-like symptoms (5.7%), de novo autonomic dysreflexia (5.5%), and fatigue (5%). Systemic complications of central effects of the neurotoxin involving the respiratory (paralysis of respiratory musculature) or gastrointestinal systems (dysphagia) are extremely rare and have not been reported after administrations for urological disorders [124]. The patient should be informed about all possible side effects and the potential need of self-catheterization. Therefore, assessment of hand function, mobility deficits, and general condition should be performed prior to injections. Clinicians should bear in mind that initiation of clean intermittent catheterization and side effects rates appear to increase in a dose dependent fashion [144]. Side effects have been shown to be dose-related [118, 145]. When adverse events follow the first injection, clinicians may consider decreasing the follow-up dose of onabotulinumtoxinA to 100 U [124]. As BTX-A has multiple recommendations outside of detrusor overactivity (e.g., cosmetic, muscular spasticity, ophthalmologic), the highest cumulative dose of onabotulinumtoxinA has been recommended to not exceed 360 U within a 3-month interval for multiple indications [141, 146]. Some experts recommend using the same botulinum toxin formulation and injecting within 24 h of each indication, or if this is not possible, to space injection treatments at least 3 months apart [147].

Use of antibiotic prophylaxis for botulinum toxin A injections is recommended [148]. Some clinicians suggest that 100 mg of nitrofurantoin twice daily for 10 days after the injection is sufficient therapy [124]. The manufacturer of onabotulinumtoxinA recommends that prophylactic antibiotics should be administered 1–3 days before treatment, on the treatment day, and 1–3 days after treatment [141]. In patients who already perform clean intermittent catheterization and are prone to develop urinary tract infection, a urine culture should be considered a couple of days before the procedure in order to choose an appropriate antibiotic prophylaxis based on the sensitivity. Patient preparation may also include pre-treatment withdrawal of antiplatelet therapy or anticoagulants. In the United States discontinuing antiplatelet therapy (including aspirin) and anticoagulants at least 3 days before the injection procedure is recommended [141] but these recommendations are not consistent across international regulatory documents.

The data are sparse for pregnant and breastfeeding women and BTX-A therapy should be

avoided in this specific group of patients. Other contraindications include an active urinary tract infection or acute urinary retention at the time of treatment, general muscle disorders (e.g., myasthenia gravis, Lambert Eaton syndrome, amyloid lateral sclerosis), allergy to any components of a chosen formulation, or any previous adverse effects to botulinum toxin. Treatment with BTX-A may be contraindicated in patients with insufficient hand skills or caregiver assistance, in those unwilling to start clean intermittent catheterization (if required), as well as in those who are unable to maintain a condom catheter [149]. The manufacturer also recommends that aminoglycoside antibiotics and spectinomycin should be avoided, as there is a theoretical risk of these agents potentiating the effects of onabotulinumtoxinA [141].

The first follow-up appointment is recommended after 7–10 days in spontaneously voiding patients [124]. Post-void residual measurement should be performed and clean intermittent catheterization should be employed if required (based on the amount of residual urine and the presence of symptoms). The second follow-up appointment is recommended after 2–3 months and it evaluates the efficacy of treatment. Furthermore, Guidelines of The National Institute for Health and Care Excellence recommend monitoring the upper urinary tract in people who are judged to be at risk of renal complications (for example, those with high intravesical pressures on filling cystometry) [56]. BTX-A causes a long-lasting but reversible effect for approximately 9 months [130, 150, 151]. Current data indicate that repeated injections are not less effective than the first application [144, 152]. Experts suggest that patients who received multiple injections are able to recognize by themselves when the effect of the toxin starts to decrease, and they can be advised to initiate their appointment for new injections [124]. Patient-based studies indicate that the interval between repeat injections appears to be relatively constant in a single patient [153]. Nevertheless, less experienced patients may require closer follow-up.

Some studies describe a phenomenon called "secondary failure"—satisfying results with the first injection or injections followed by decreased efficacy after subsequent applications. It has been hypothesized that underlying immunological mechanism (anti BTX-A antibodies), technical problems with subsequent injections, or progression of the underlying neurological disorder may lead to this phenomenon [154, 155]. If the "secondary failure" syndrome appears, it is suggested to repeat the injection at least 3 months after the failed injection [124]. A small, non-randomized study reported that replacement of one formulation by other formulation can be effective if treatment failure appears at first injection [156].

Neurostimulation/Neuromodulation

Neurostimulation is a term referring to electrical stimulation applied directly to a nerve fiber in order to achieve a desired function (sphincter contraction or detrusor relaxation). In turn, neuromodulation describes electrical stimulation applied indirectly in order to modify sensory and/or motor functions of the lower urinary tract [114]. The exact mechanism of action remains uncertain. It is postulated that neuromodulation works by stimulating somatic afferent nerves, artificially producing action potentials that modulate abnormal sensory input from the bladder to the brain [157]. Several sites of implantation have been investigated but only two are currently used in daily practice. Whereas sacral neuromodulation (SNM) engages the sacral nerve root (S3), tibial nerve stimulation (TNS) engages the sensory component of tibial nerve. The activation of somatic afferent nerves inhibits bladder sensory pathways and reflex bladder overactivity, which may restore normal bladder function [158]. Furthermore, plastic reorganization of cortical networks triggered by peripheral neuromodulation has been proposed [159].

Although the mechanism of action is unclear, neuromodulation remains an alternative treatment strategy reserved for patients who have failed the previously described treatment methods. Despite the fact that neuromodulation has been mainly investigated in patients with idiopathic overactive bladder, its utilization has naturally been extrapolated to treat urge urinary incontinence secondary to a neurogenic cause [158].

Sacral Neuromodulation SNM is considered as a stage procedure [160]. In a first step, a tined quadripolar lead is percutaneously inserted into the S3 foramen using bony landmarks and fluoroscopic control (Fig. 7.9). Then, electrical stimulation of the sacral nerve root is performed to assess placement of the lead. Proper placement evokes plantar flexion of the ipsilateral toes, bellows contraction of the levator ani, pulling sensation in the rectum, or tingling/vibrations in the vagina, labia, scrotum, or penis [160, 161]. When the implantation phase is completed, the lead is connected with a temporary external pulse generator. Then, the patient undergoes a 1- to 2-week trial of neuromodulation to assess the likelihood of clinical improvement and he/she is able to modify the intensity of stimulation as well as frequency and width of pulses. The patient is instructed to use a voiding diary to record symptoms and bladder function. After that, the results obtained are evaluated. If the patient has at least 50% symptom improvement, the lead will be attached to an implantable pulse generator and the device will be fixed into the upper portion of the buttock (Fig. 7.10) [132]. If not, the lead will be removed [162, 163].

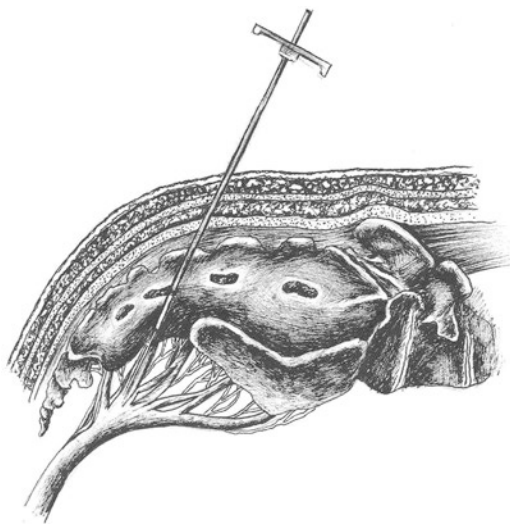

Fig. 7.9 Schematic drawing of cannulation of the third sacral foramen. The tip of the cannula will ideally be placed against the corresponding sacral nerve when the cannula is inserted at an angle of 60° to the skin over the sacrum

Data on SNM in the neurogenic population are limited to patients with stroke, Parkinson disease, multiple sclerosis, and incomplete spinal cord injury [160]. These mainly include case–control studies and case reports with heterogeneity of neurological lesions. There is a lack of randomized controlled trials with powerful sample size and long-term follow-up. To make things worse, the majority of available studies do not include descriptions or indicators of disease severity. High-grade recommendations cannot be made. Nevertheless, keeping in mind these limitations, the available literature suggests that SNM demonstrates similar efficacy among the neurogenic and non-neurogenic patients in terms of successful test phase, device implantation, clinical outcomes, urodynamic results, safety, and quality of life [160]. Patients should be carefully selected. Success rates of the test phase in neurologically impaired patients range between 50–68%, whereas success rates of permanent implantation range between 80–92%. To compare, implantation success rates in the non-neurogenic population range from 80 to 90% [161, 164–166]. Clinicians should always remember that the results obtained may be influenced by the stage of the disease and its progression [166]. It has been shown that up to 33% of patients with multiple sclerosis may not achieve successful treatment due to disease progression [157, 158, 162, 164, 167]. Patients with potentially progressive neurological disorders should be informed that SNM treatment may lose its efficacy with disease progression. Nowadays, it is generally agreed that patients with already progressing neurological disease are not candidates for SNM [2].

Peters et al. retrospectively analyzed 71 patients who underwent SNM procedure for neurogenic bladder dysfunction due to various neurological disorders. The predominant neurological diagnoses were stroke, Parkinson disease, and multiple sclerosis. They reported significant decrease in frequency and urgency episodes [166]. However, statistically significant improvements in the daily incontinence episodes and incontinence severity were not demonstrated. The authors emphasized that the lack of statistically significant changes in

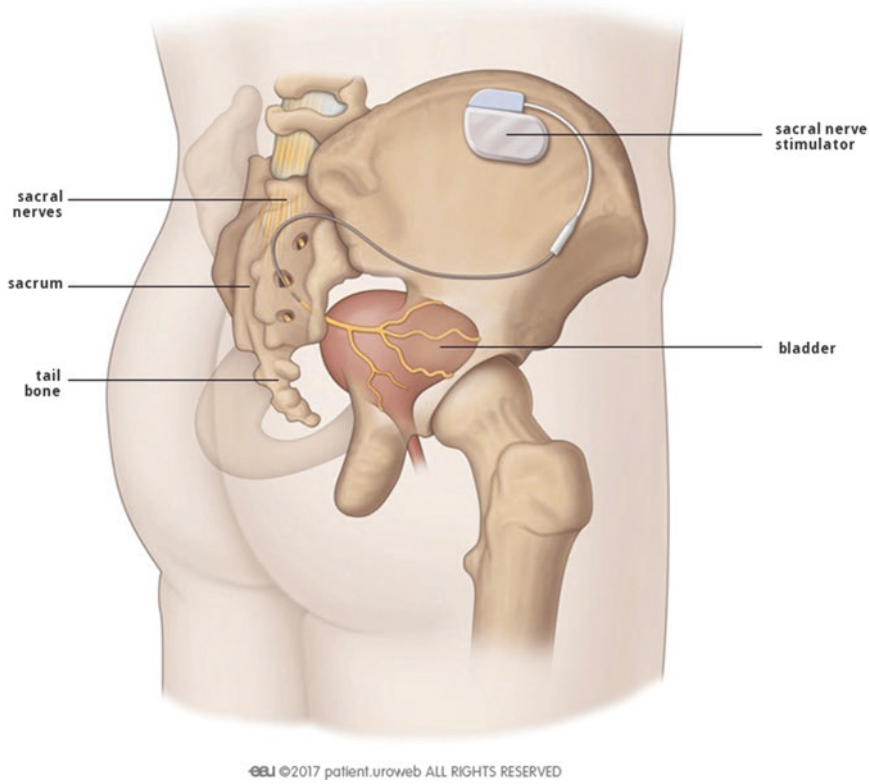

Fig. 7.10 Sacral neuromodulation after implantation of pulse generator (Courtesy of the European Association of Urology [132], with permission)

incontinence might have been caused by a small sample size. Chaabane et al. investigated 34 patients with NDO treated with SNM. They showed that SNM significantly reduced episodes of urgency, frequency, and incontinence as well as improved urodynamic parameters [168]. A recently published study analyzed 50 patients after spinal cord injury. Among them, 26 patients presented with NDO and achieved satisfying results during the test phase. At follow-up, 65% of patients did not need additional treatment for NDO and 80% reported complete continence. Both urinary frequency and frequency of pad use were significantly reduced. More than 90% of patients were satisfied with treatment outcomes. However, no significant suppression of NDO was detected on comparing urodynamic studies before and after introduction of SNM (the mean time between postimplantation urodynamics and SNM implantation was 6.6 months). The authors concluded that SNM may have limited value in patients with NDO [169]. Another study presented opposite results and indicated that SNM is a valuable treatment option for patients with multiple sclerosis [170]. Kessler et al. in their meta-analysis showed that SNM may be an effective and safe procedure for the treatment of patients with neurogenic bladder but the number of included patients was low with high between-study heterogeneity [164]. Moreover, it is unclear which neurological patients are most suitable for SNM and who can achieve the best outcomes. Also the effect of different pulse rates and its effects on clinical efficacy have not been studied. The pulse rate is generally set between 10 and 16 Hz, while the pulse width is set at 210 ms [161]. In order to make strong recommendations, a randomized placebo-controlled double-blind clinical trial investigating SNM for neurogenic lower urinary tract dysfunction is underway [171].

Adverse effects include discomfort in the area of the implanted pulse generator as well as infection and lead migration [161]. SNM is contraindicated in pregnant women due to hypothetical risk of fetal loss or preterm labor. SNM has not demonstrated efficacy in stress urinary incontinence or mixed urinary incontinence [158, 167, 170, 172]. Lower efficacy has been reported in older and non-ambulatory patients [170, 172–174]. SNM may also be contraindicated in patients with spinal abnormalities or contractures that may hinder percutaneous lead placement. Furthermore, patients after spinal cord injury with mobility deficits may be at risk for sacral decubitus ulcers resulting from the implanted pulse generator. This treatment should be carefully considered in patients with progressive disorders, as they may require MRI in the future. Therefore, some experts recommend SNM only in patients with relapsing–remitting subtype of multiples sclerosis who have not experienced any relapse for 2 years and who are not likely to require repeated MRI scans [160]. MRI of the abdomen or pelvis is contraindicated, as it may cause displacement or heating of the electrodes as well as dislodgement or reprogramming of the device. Nevertheless, a newer generation of SNM devices have made the use of 1.5 T-head MRI possible [175].

Tibial Nerve Stimulation TNS can be considered in patients with contraindications for SNM or in those who refuse SNM as a more invasive treatment. The tibial nerve is stimulated by an electrode inserted 4–5 cm cephalad to the medial malleolus (Fig. 7.11) [132]. In daily practice, clinicians can demarcate a proper place by three fingerbreadths cephalad from the medial malleolus

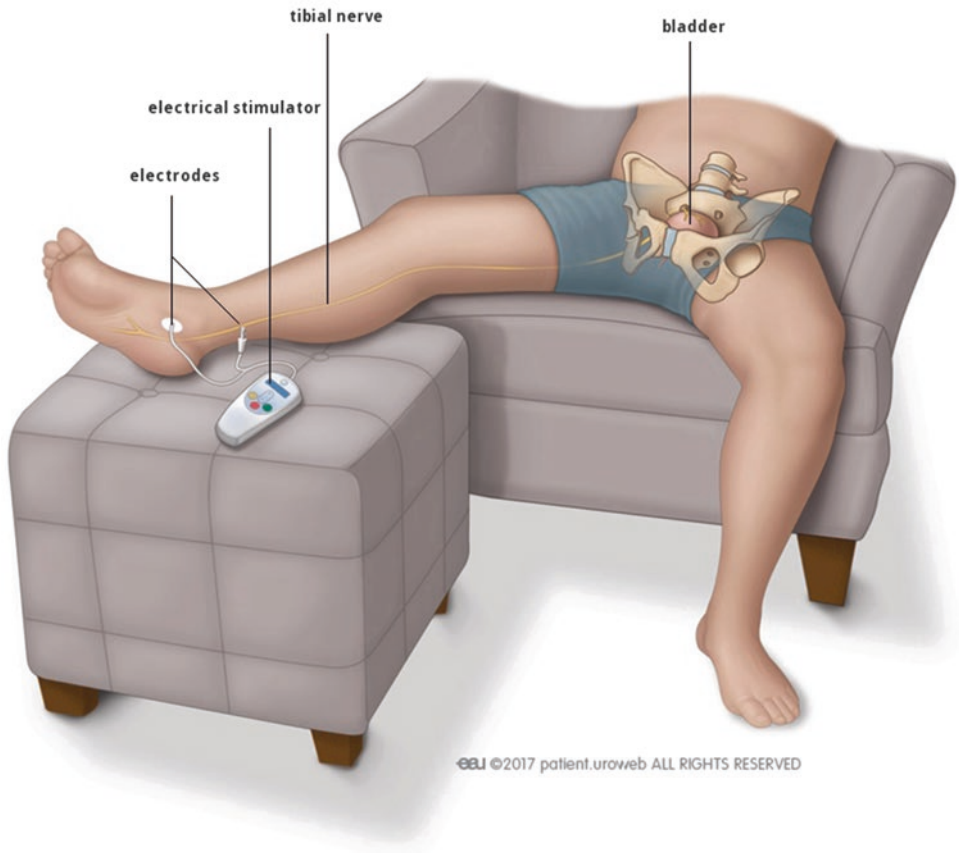

Fig. 7.11 Tibial nerve stimulation (Courtesy of the European Association of Urology [132], with permission)

and one fingerbreadth posterior to the margin of the tibia [160, 176]. The electrode is inserted at an angle of 60° to the skin and advanced 3–4 cm posterior to the tibia. Then, a stick-on electrode is placed on the medial surface of the calcaneus or on the bottom of the foot. After that, the electrodes are connected to a stimulator. The flexion of the big toe or the movement of the other toes, as well as a sensory response (tingling sensation), confirms the correct position of the needle electrode. Patient pain and sensation are used to titrate stimulation. Treatment course usually lasts 8–12 weeks with one 30-min session per week [2, 160]. When patients report satisfying results, treatment can be repeated [162, 177, 178].

TNS was found to be effective and safe for treating idiopathic overactive bladder in randomized controlled trials [179–181]. It has been shown that TNS may be a valuable treatment method of NDO in patients after spinal cord injury [182, 183] but a recently published systematic review indicated only some preliminary evidence of safety and effectiveness for TNS treatment in patients with neurogenic bladder [184]. The studies included analyzed patients with multiple sclerosis, Parkinson disease, stroke, and spinal cord injury (complete and incomplete). Urodynamic findings included increased maximum cystometric capacity, increased bladder volume at first detrusor overactivity, and decreased maximum detrusor pressure during the storage phase. Long-term treatment may also decrease the number of voids and leakages as well as post-void residual volume. Another systematic review showed that success rates of TNS range from approximately 40–100% for NDO or urinary retention [185]. Although the findings are promising, the overall quality of the evidence is low and the majority of studies were characterized by small sample size and were thus underpowered to measure the main outcomes, leading to significant risk of bias and confounding results. In addition, it is unclear which stimulation parameters and maintenance regime are most effective. Studies also suggest that the treatment effect is fairly short lived and the need to return for the next treatment courses can be particularly difficult for neurological patients [2]. More reliable data from well-designed, adequately sampled, and powered randomized clinical trials is warranted to reach definitive recommendations. TNS appears to be a promising and novel treatment for neurogenic lower urinary tract dysfunction [184]. No TNS-related adverse events have been reported. TNS also allows the performance of diagnostic measures such as repeated MRI. TNS may also be considered as a good alternative to SNM in patients with skeletal abnormalities that may lead to complicated or infeasible lead placement. Thus, physicians and patients should consider tibial nerve stimulation as safe and effective third-line treatment in a carefully selected population.

TNS treatment is contraindicated in patients with pacemakers, implantable defibrillators, coagulopathy, or in pregnant women [160].

Transcutaneous Electrical Nerve Stimulation Transcutaneous route refers to non-invasive treatment in contrast to percutaneous techniques referring to minimally invasive options [184]. Transcutaneous techniques utilize stick-on electrodes connected to a stimulator (often a small, battery-powered machine). In 1974 Sundin et al. first demonstrated that electrical pudendal stimulation inhibits bladder contraction in cats [186]. Subsequently, the technique was deeply investigated at different stimulation sites and is now used as transcutaneous electrical nerve stimulation (TENS) for the treatment of various urological dysfunctions [187]. Currently, direct pudendal nerve stimulation can be undertaken via differing anatomic and technical approaches [188]. Transcutaneous stimulation may also involve the tibial nerve, and this approach has shown its safety and efficacy in treating urgency incontinence in patients with multiple sclerosis or after stroke [189, 190].

A recently published systematic review of TENS for treating neurogenic lower urinary tract dysfunction has shown preliminary evidence indicating TENS as an effective and safe treatment option [187]. TENS was defined as *any* transcutaneous electrical nerve stimulation. The study included various sites: suprapubic, clitoral, penile, vaginal,

rectal, and sacral dermatome. Authors proposed that TENS may increase maximum cystometric capacity and bladder volume at first detrusor overactivity, as well as decrease maximum storage detrusor pressure and maximum detrusor pressure at first detrusor overactivity. Chronic treatment may also decrease the number of voids and leakages per 24 h. However, similarly to TNS data, the quality of evidence was low, especially due to a lack of well-designed, appropriately sampled, and powered randomized clinical trials. Authors stressed that their work demonstrated the potential of TENS for treating neurogenic bladder dysfunction and identified the need for more reliable data in order to make definitive conclusions.

TENS is contraindicated in patients with pacemakers, implantable defibrillators, pregnant women, those who have dermatological lesions (e.g., dermatitis, eczema) in electrode placement, or those who have an allergic response to the electrodes, gel, or tape [191].

Surgery

Bladder Augmentation and Detrusor Myectomy When less invasive procedures have failed or patients have contraindications for them, surgery should be considered. The more invasive approach may also be taken into account in patients with serious complications such as sepsis, urethral/perineal fistulae, renal failure (secondary to hydronephrosis and/or ureterovesical reflux), or severe urinary incontinence. The surgical approach is used to treat detrusor overactivity and/or poor bladder compliance. Thus, the aims of surgical therapy are to reduce the amplitude of detrusor contractions and increase reservoir capacity [192]. Surgery is also valuable option for optimizing renal preservation and the patient's quality of life. The most common surgical options are enterocytoplasty (bladder augmentation) and partial detrusorectomy (detrusor myectomy, auto-augmentation).

Enterocystoplasty, or bladder augmentation, seems to be the most valuable surgical modality. This procedure leads to the increase of bladder capacity by incorporation of a bowel segment to the bladder (Fig. 7.12) [132]. Furthermore, the augmented bowel segment has a potential to diminish detrusor contractility. A detubularized segment of the distal ileum is most commonly used (ileocystoplasty). The ileum seems to give the best results in terms of ease of use, risk of complications, and efficacy [86]. Other options also consider a detubularized colic or cecal segment as well as part of the stomach [158]. If concomitant vesicoureteral reflux has been observed before the procedure, ureteral reimplantation should be taken into account as a mean of renal function protection [193], but it remains uncertain whether reimplantation is beneficial [194]. Nonetheless, in the event of grade IV or V reflux, ureteral reimplantation may be necessary [86].

Overall, continence rates after enterocystoplasty due to NDO have been reported at 80–100% [195]. A case series of 13 individuals with neurogenic bladder dysfunction treated with enterocystoplasty showed good or moderate long-term outcomes in 92% of patients [196] with improvment of bladder capacity and compliance. Despite that, 31% of patients had persistent detrusor overactivity. More recently, long-term studies on patients after spinal cord injury have revealed that ileocystoplasty for bladder augmentation significantly reduced storage pressures and improved continence rates [197]. Augmentation ileocystoplasty is also an effective surgical approach for patients with multiple sclerosis and myelodysplasia [198–200]. Bladder substitution should also be considered in patients with fibrotic bladder walls [32].

Specific complications related to this procedure include stone formation, recurrent urinary tract infections, reoperation (cystoplasty rupture and bladder perforation due to overdistension or catheterization trauma) [149, 201, 202], impaired catheterization due to mucus production, metabolic disturbances (chronic hyperchloremic acidosis and hypocalcemia with bone demineralization, vitamin B12 deficiencies), intestinal transit disorders (postoperative ileus and small bowel obstruction or diarrhea, chronic bowel disturbances), and long-term deterioration of kidney function and malignancy [203–205]. Importantly, risk of malignancy is known to be higher with the use of the large intestine or gastric wall compared to the small intestine

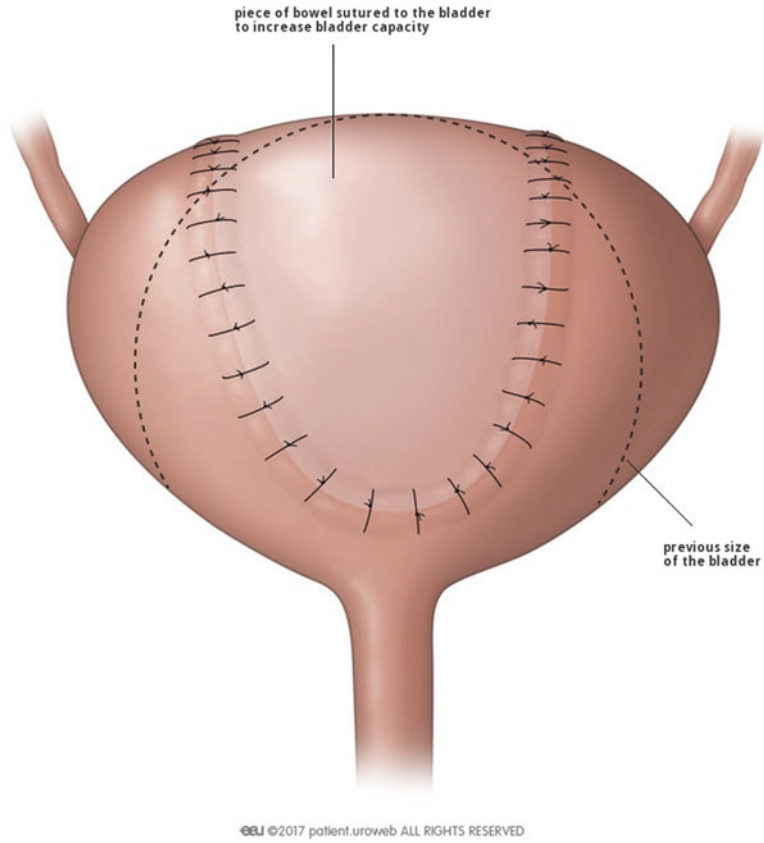

Fig. 7.12 Enterocystoplasty (Courtesy of the European Association of Urology [132], with permission)

[195, 206]. This factor in the selection of bowel segment should be carefully considered, especially in young patients. Risk factors proposed for the development of malignancy include urinary stasis, nitrosamines, infection, bladder calculi, chronic patch inflammation, and immunosuppression [195]. Tumors are generally adenocarcinomas of the bladder or bowel, most commonly located in the region of the anastomosis. Enterocystoplasty may also impair bladder emptying, thus some patients may have to start intermittent catheterization. Other residual symptoms may need adjuvant anticholinergic therapy, bladder neck reconstruction, and/or continent urinary diversion (i.e., Mitrofanoff channel) to obtain full continence [195]. Surgeons should keep in mind that patients needing bladder augmentation often have a number of additional ailments, making the postoperative recovery even more challenging [195]. The postoperative care should involve close attention to the return of bowel function, as neurologically impaired patients often have a concomitant neurogenic bowel dysfunction and may require aggressive bowel regimens [158]. In view of the presented data, it is recommended to carefully discuss complications, risks, and alternative treatments with the patient and/or their family members and carers before the procedure [56]. Patients should be offered lifelong follow-up after augmentation cystoplasty. Despite multiple complications, recently published studies have reported that quality of life of patients after augmentation cystoplasty is higher compared to those after multiple BTX-A injections [207].

Augmentation cystoplasty is currently feasible using a robot-assisted laparoscopic approach [208] but comparative studies with open route are still warranted to make reliable recommendations.

Bladder augmentation should be avoided in patients with bowel diseases (Crohn's disease, con-

genital anomalies such as cloacal exstrophy), bladder malignancy, conditions resulting in short bowel (wide bowel resections), severe abdominal adhesions from previous surgery, after pelvic irradiation, and in those with compromised renal function [149]. Significant renal impairment remains a controversial relative contraindication [195]. Studies of children with chronic renal insufficiency and neurogenic bladder who underwent augmentation cystoplasty showed no change in renal function at 1.9-year follow-up in 73% of cases and improvement in only 18% [209]. Impaired cognitive function and limited manual dexterity are relative contraindications that may lead to inability to perform clean intermittent self-catheterization [195].

Partial detrusorectomy, also known as detrusor myectomy and auto-augmentation, involves resecting a portion of the detrusor, thus creating a bladder pseudodiverticulum to increase capacity and compliance [210]. The bladder urothelium is left intact. The main advantages over enterocystoplasty are lower morbidity (the peritoneal cavity is not opened, the intestinal tract is not involved), shorter operative time, and preservation of bowel segments for potential future procedures in case of auto-augmentation failure. However, the long-term efficacy and durability of auto-augmentation does not appear to be as strong as enterocystoplasty [211, 212]. Moreover, experts indicate that patients after detrusor myectomy are at increased risk of spontaneous or traumatic bladder perforation [210]. As the evidence on detrusor myomectomy in neurological patients is controversial, this procedure should not be routinely recommended [86].

Urinary Diversion When all treatment options have failed, urinary diversion must be considered for renal protection. Indications for performing a urinary diversion include worsening hydronephrosis, progressing renal failure, and recurrent significant urinary tract infections. Urinary diversion is further described in Chap. 13, "Renal Failure."

Unfortunately, some patients are medically unfit for a number of or all the treatment options presented in this chapter. These individuals usually have to use containment methods such as permanent catheters, condom catheters, or incontinence pads.

Conclusion (Table 7.2, Fig. 7.13)

Table 7.2 Conclusion

Summary	Level of evidence
The prevalence of urinary incontinence due to neurogenic detrusor overactivity (NDO) has been estimated as 50.9% in patients suffering from multiple sclerosis, 33.1% in those with Parkinson disease, 52.3% in individuals after spinal cord injury, and 23.6% in patients after stroke	2
Evaluation of incontinent patients includes a comprehensive medical history with bladder diary and questionnaires, physical examination, urinalysis/urine culture, pad-weighing test, renal ultrasound, post-voiding residual volume, free flowmetry, bladder ultrasound, cystoscopy, computed tomography, magnetic resonance imaging, and urodynamics	4 (Expert opinion)
Urodynamic findings in patients with NDO include involuntary detrusor contractions, decreased compliance, increased bladder sensation, and/or decreased cystometric capacity	2
The main objectives for current strategies in the management of NDO are protection of the upper urinary tract and restoration of the lower urinary tract function, as well as improvement of urinary continence and the patient's quality of life	4 (Expert opinion)
Conservative treatment includes behavioral techniques (bladder training, pelvic floor muscle therapy), lifestyle changes, and management of other medical conditions. Available data suggest that these modalities may help to control symptoms	2–4
Antimuscarinic treatment in patients with NDO is associated with better patient-reported cure and improvement of urodynamic parameters when compared with placebo	1

(continued)

Table 7.2 (continued)

Summary	Level of evidence
Antimuscarinics can be administered orally, transcutaneously, or intravesically. Oral administration has been most comprehensively investigated	1
Treatment of NDO with botulinum toxin A has been shown to significantly improve clinical and urodynamic parameters as well as quality of life in patients after spinal cord injury and multiple sclerosis	1
Sacral neuromodulation and tibial nerve stimulation have been insufficiently studied in patients with neurogenic lower urinary tract dysfunction but current data suggest that such modalities may help to treat patients with incontinence due to NDO	2/3
The literature proposes two main surgical approaches to treat NDO: enterocytoplasty (bladder augmentation) and partial detrusorectomy (detrusor myectomy, auto-augmentation)	3/4

Recommendation	Grade of recommendation
An extensive medical history with carefully conducted physical examination followed by bladder diary/questionnaires, urinalysis/urine culture, pad-weighing test, renal ultrasound, urodynamic study, and other necessary tests are recommended to be performed in every incontinent patient suspected of NDO	Expert opinion
Other necessary investigations should be performed when clinically indicated, based on underlying neurological pathology, patient history, as well as relevant symptoms and signs	Expert opinion
Conservative treatment should be considered in all patients suffering from incontinence due to NDO. Patients, their family members and/or carers should be educated about lower urinary tract function and treatment goals	C
Pharmacotherapy with antimuscarinics should be employed in all patients suffering from incontinence due to NDO, if not contraindicated	A
If orally administered antimuscarinics are poorly tolerated, transcutaneous or intravesical route may be considered	B/C
Botulinum toxin A injections are recommended in patients who have had an inadequate response to or are intolerant of pharmacotherapy (B). This approach should be considered especially in patients after spinal cord injury or with multiple sclerosis when anticholinergic therapy has shown to be ineffective or poorly tolerated (A)	B, A
Sacral neuromodulation or tibial nerve stimulation should be considered after failure of the above treatment options and may be recommended in carefully selected patients. Sacral neuromodulation should be considered as a more invasive, irreversible, and higher risk modality	C
Surgery may be indicated when all other options have failed or patients present with contraindications for less invasive modalities	C

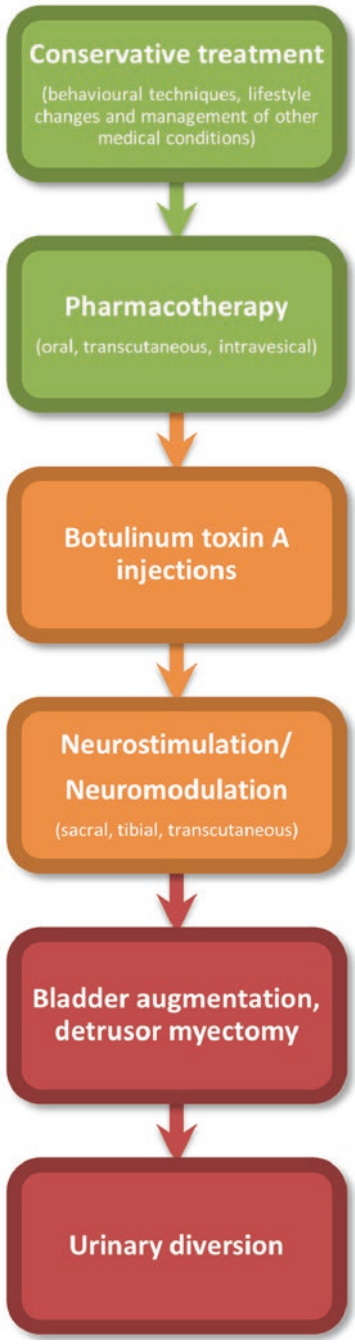

Fig. 7.13 Treatment algorithm for incontinence due to neurogenic detrusor overactivity

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Retention

8

Introduction

Patients with neurogenic lower urinary tract dysfunction may suffer from urinary retention, the inability to voluntarily void urine. This condition can be acute or chronic. Acute retention of urine is defined as a painful, palpable, or percussible bladder, with the patient unable to pass any urine [1]. Chronic retention is defined as a non-painful bladder that remains palpable or percussible after the patient has passed urine. These patients may also present with incontinence due to overflow and debilitating problems such as recurrent infections resulting from chronically elevated post-void residual.

The underlying urodynamic pathology of retention includes detrusor underactivity or detrusor-sphincter dyssynergia (DSD). Detrusor underactivity is a urodynamic observation of contractions of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span [1, 2]. In patients with relevant neurological condition, the presenting pathology can be termed as neurogenic detrusor underactivity (NDU). This term excludes idiopathic, myogenic, and drug-induced causes of underactive detrusor [3, 4]. NDU typically occurs when neurological lesions affect sacral, infrasacral, and peripheral neural pathways regulating functions of the lower urinary tract (see Chap. 2, "Neurogenic Bladder Pathophysiology," and Chap. 3, "Pathologies Responsible for the Development of the Neurogenic Bladder"). NDU may also appear in the acute phase of neural injury and in some general motor disorders (e.g., Parkinson disease) [5].The underlying pathophysiology of detrusor underactivity in these specific groups of patients is currently not well understood, although studies have correlated detrusor underactivity to the patient's overall motor function [6]. Within the spectrum of detrusor underactivity, the condition in which contractions cannot be demonstrated during urodynamics is defined as an acontractile detrusor. DSD is defined as a detrusor contraction synchronous with an involuntary contraction of the urethral and/or peri-urethral striated muscle [1]. This condition is observed when neurological lesions appear between the brainstem (pontine micturition center) and the sacral spinal cord (sacral micturition center) (see Chaps. 2 and 3). Impaired coordination between detrusor and sphincter during voiding in patients without relevant neurological disorder should not be termed as DSD. In these patients, the dysfunction is more appropriately referred to as dysfunctional voiding or pelvic floor hyperactivity [7, 8].

Epidemiology

The precise incidence and prevalence of NDU and DSD are unknown given the variability in neurological disorders [5, 9]. Lack of epidemiological data is exacerbated by the requirement that NDU and DSD can be diagnosed only with a pressure-

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_8

flow urodynamic study. Some studies consider only patient-reported voiding symptoms without concomitant urodynamic evaluation. Available data are limited to single cohort studies or case reports. To make matters worse, there is no agreed-upon consensus of what defines reduced contraction strength, prolonged bladder emptying, or normal voiding time span when detrusor underactivity is suspected [4]. Specific normative values need to be identified in future research [2].

The most common neurogenic causes of detrusor underactivity include diabetes, previous pelvic surgery and radiation therapy, infrasacral spinal cord injury (SCI), vertebral disk prolapse, multiple sclerosis, and Parkinson disease. Detrusor underactivity may also appear in the acute phase of cerebrovascular accident, traumatic brain injury and SCI.

DSD can occur after any trauma or disease below the pons and above the sacral cord. These mainly include: SCI, multiple sclerosis, multiple system atrophy, spinal dysraphism, and transverse myelitis [9]. DSD is more frequent in patients with a complete rather than incomplete spinal cord lesion and in such cases is more likely to be continuous [10].

Epidemiological data on related voiding symptoms and urodynamic findings of detailed disorders have been presented in Chap. 3.

Additionally, retention is the most common urological finding in infection-related neurogenic bladders. These include lumbosacral herpes zoster, genitourinary herpes simplex, tabes dorsalis, Guillain–Barré syndrome, Lyme disease, poliomyelitis, and acquired immune deficiency syndrome (AIDS) [11]. Among them, only AIDS-related voiding dysfunctions have been reliably estimated to affect 16–45% of patients with neurological complications of this disease [12]. Impaired bladder function becomes more common with disease progression [13, 14]. Neurogenic voiding dysfunction in AIDS patients portends poor prognosis. At the time of seroconversion, patients may present with acute urinary retention mainly by way of DSD [12, 15, 16]. If neural involvement progresses, NDU or acontractile detrusor may be found in up to 45% of cases.

Both NDU and DSD with related voiding symptoms significantly affect patients' quality of life and jeopardize renal function. Clinicians should keep in mind that DSD may have more profound effects on renal function than NDU. It has been estimated that up to 50% of patients with DSD develop serious urological complications [17, 18]. High intravesical pressures during voiding lead to elevated retrograde pressures in the ureter and pelvis, hydronephrosis, renal scarring, and, ultimately, terminal renal failure. Furthermore, DSD may often occur in combination with detrusor overactivity, particularly in patients after suprasacral SCI. DSD-related complications have been shown to occur less frequently in women and patients with multiple sclerosis, perhaps due to lower detrusor pressures [7, 19, 20].

Diagnosis

History and Physical Examination

A detailed history as part of the initial evaluation is imperative. Presenting complaints associated with urinary retention usually are attributed to dysfunctional bladder emptying. Thus, most patients complain of voiding problems (hesitancy; straining; poor, prolonged and intermittent flow; terminal dribble) and post-micturition symptoms (sensation of incomplete emptying, post-micturition dribble), terms for which have been developed and defined by the International Continence Society (ICS).

- Hesitancy—the term is used when an individual describes difficulty in initiating micturition, resulting in a delay in the onset of voiding after the individual is ready to pass urine.
- Straining to void—the term describes the muscular effort used to either initiate, maintain, or improve the urinary stream.
- Slow stream—reported by the individual as his or her perception of reduced urine flow, usually compared to previous performance or in comparison to others.
- Intermittent stream (intermittency)—the term is used when the individual describes urine

flow, which stops and starts, on one or more occasions, during micturition.
- Terminal dribble—the term is used when an individual describes a prolonged final part of micturition, when the flow has slowed to a trickle/dribble.
- Feeling of incomplete emptying—a self-explanatory term for a feeling experienced by the individual after passing urine.
- Post-micturition dribble—the term is used when an individual describes the involuntary loss of urine immediately after he or she has finished passing urine, usually after leaving the toilet in men, or after rising from the toilet in women.

The interview should elicit information regarding initiation of micturition (reflex, strain, Credé) and investigate whether performed by individuals themselves or with caretakers. Patients may also present with complete lack of voiding (usually accompanied by abdominal pain) or incontinence (due to overflow). In patients already catheterized, the duration of each catheter use before change and performed catheterization technique should be recorded. Reassessment of bladder-emptying technique is also important. Patients should be asked about other urological complaints, in particular storage problems (urgency, frequency, nocturia), as both NDU and DSD may sometimes present with mixed storage and voiding symptoms [21]. Clinician should also evaluate the presence of bladder sensation. The onset of complaints should be carefully investigated and classified as acute or chronic. In patients with chronic retention, symptom onset may be gradual and it can go unnoticed by caregivers or by patients with limited bladder sensation or who are severely cognitively impaired and cannot report symptoms [22]. Previous history of urinary retention or episodes of catheterization should be elicited. Possible progression of the voiding dysfunction should be clarified (stable or changing complaints), as it has been shown that DSD tends to worsen over time, and there is a correlation between neurological status and clinical findings [7]. Similarly, the prevalence of detrusor underactivity may increase with age, and studies report that it is more common in men. Up to 48% of elderly non-neurogenic patients may show underactive detrusor [5]. Potential myogenic causes of detrusor underactivity should also be excluded [4]. This include impaired bladder perfusion (chronic ischemia is commonly seen in patients with atherosclerosis and microvascular diseases), bladder fibrosis, and age-related degradation [21]. Special attention should be given to diabetic patients, as reported symptoms usually result from integrative mechanism, i.e., both myogenic and neurogenic damage [23]. In elderly male patients, reported voiding symptoms may be associated with bladder outflow obstruction (BOO) mainly due to benign prostatic hyperplasia. However, it is not possible to differentiate NDU, DSD, and BOO without urodynamic study [21]. Studies have shown that there is a poor correlation between symptoms and urodynamic diagnosis in this specific group of patients [24, 25]. Accurate assessment of symptoms indicating possible complications or other causes of retention (hematuria, dysuria, fever) should be conducted to rule out comorbid pathology such as malignancy, urolithiasis, or urinary tract infection. Neurological symptoms related to underlying neurological pathology should also be documented with onset, severity, evolution, and any treatment.

It is important to analyze how reported complaints affect the patient's quality of life. Patients should be asked about the degree of hardship the symptoms cause and whether they influence their daily activities, social life, and work productivity.

As patients with neurourological complaints may also suffer from neurogenic bowel and sexual dysfunction, bowel and sexual histories are important [26, 27]. Bowel history should elicit information regarding pattern and frequency of defecation; rectal sensation; desire to defecate; and possible episodes of fecal incontinence, constipation or defecation initiation (digitation, suppository use) [28]. Sexual history should investigate symptoms of genital or sexual dysfunction; presence of sensation in genital area; lack of desire (loss of libido); difficulty in achieving orgasm; dyspareunia in women; and erectile dysfunction or ejaculation problems (premature, delayed, retrograde, anejaculation) in men.

Retention and other voiding problems may be aggravated by different comorbidities. Apart from underlying neurological disorder, other causes of urinary retention can be categorized as obstructive, infectious/inflammatory, or pharmacologic [11]. The most common obstructive pathology in men is benign prostatic hyperplasia [29, 30]. Furthermore, end-stage BOO may also lead to significant detrusor underactivity. Other obstructive causes include prostate cancer, phimosis, paraphimosis, and external-constricting devices applied to the penis. In women, obstructive retention often involves pelvic organ prolapse such as cystocele, rectocele, or uterine prolapse. In both sexes, urethral strictures, stones, and foreign bodies, as well as bladder tumors with blood clots can directly block the flow of urine [31]. Benign or malignant pelvic masses as well as fecal impaction and gastrointestinal or retroperitoneal masses may lead to external compression of the bladder neck. Infectious/inflammatory causes of urinary retention include sex-specific and general pathologies. In males, acute prostatitis and prostatic abscess may cause urine retention. In females, painful vulvovaginal lesions and vulvovaginitis can vitally impair voiding. Urethritis (from a urinary tract infection or sexually transmitted infection) as well as genital herpes (with local inflammation and painful urination) may lead to urine retention in both sexes. Numerous pharmacologic agents have direct or indirect effects on the lower urinary tract and can decrease detrusor contractility [3, 30, 32]. Both prescribed and over-the-counter drugs may worsen voiding symptoms and lead to retention. Drugs with antimuscarinic properties, such as tricyclic antidepressants, may compete with acetylcholine at muscarinic receptors, resulting in bladder relaxation. Nonsteroidal anti-inflammatory drugs have shown to doubly increase the risk of urinary retention [33]. Calcium channel antagonists may also occasionally precipitate retention in individuals who have presumably been rendered more vulnerable as a result of predisposing risk factors [3]. It has been shown that polypharmacy significantly increases the risk of urinary retention [34]. Table 8.1 lists medications associated with voiding difficulties [3, 30, 32]. Other causes may include any prior urinary tract trauma or surgery, post-partum complications (e.g., obstetric anal sphincter injury, peri-urethral lacerations, wound breakdown), as well as de novo post-partum urinary symptoms.

A well-conducted medical history should be completed with an assessment of the patient's social situation. Accessibility to care, toileting, catheters, and other supplies may be limited by financial constraints or other social factors. Family or caregiver support should be queried and the patient's independence should be evaluated.

A proper history should not only aim to diagnose the cause and nature of bladder dysfunction but also to identify associated complications of neurogenic lower urinary tract dysfunction. The consequences of urinary retention depend on the chronicity of the problem and the degree of urine retention. In patients with acute complete obstruction, metabolic disturbances, including acidosis, azotemia, and hyperkalemia, can be life-threatening. Increased intravesical and intraureteral pressures can dramatically reduce the glomerular filtration rate and renal blood flow. Rupture of the urinary tract is also possible. In patients with chronic retention, hydronephrosis, renal failure, recurrent urinary tract infections, or urolithiasis may be observed during initial consultation (see Chaps. 10–15).

In addition to medical history, a comprehensive physical examination should be performed. It consists of examining the abdomen, back, and loins, as well as pelvic and genital organs. Abdominal examination should include percussion and palpation of the bladder [11]. A bladder may be percussible if it contains at least 150 mL of urine and it should be palpable with more than 200 mL [30, 35]. Bladder tone and pain should be assessed. Further exam may also reveal abdominal or flank masses or fullness, suggesting malignancy or fecal impaction. Clinicians should evaluate sensation within sacral dermatomes (special consideration for S2–S4 dermatomes) and perianal area (see Chap. 4, "Medical History and Physical Examination," Fig. 4.1), spinal cord-mediated reflexes (see Chap. 4, Table 4.3), as well as anal sphincter tone and voluntary con-

Table 8.1 Pharmacologic agents associated with urinary retention and voiding symptoms [3, 30, 32]

Class	Drugs
Antiarrhythmics	Disopyramide, procainamide, quinidine
Anticholinergics (selected)	Atropine, belladonna alkaloids, benztropine, biperdin, darifenacin, dicyclomine, disopyramide, fesoterodine, flavoxate, glycopyrrolate, hyoscyamine, ipratropium bromide, oxybutynin, propantheline, scopolamine, solifenacin, tolterodine, trihexyphenidyl
Antidepressants	Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, duloxetine, imipramine, maprotiline, nortriptyline, paroxetine
Antihistamines (selected)	Brompheniramine, chlorpheniramine, cyproheptadine, diphenhydramine, hydroxyzine, meclizine, promethazine
Antihypertensives	Hydralazine, nifedipine
Antiparkinsonian agents	Amantadine, benztropine, bromocriptine, levodopa, trihexyphenidyl
Antipsychotics	Chlorpromazine, clozapine, fluphenazine, haloperidol, prochlorperazine, quetiapine, thioridazine, thiothixene
Antiulcer agents	Cimetidine, ranitidine
Calcium channel antagonists	Amlodipine, diltiazem, felodipine, nifedipine, verapamil
Chemotherapeutic agents	Vincristine, cisplatin
Hormonal agents	Estrogen, progesterone, testosterone
Muscle relaxants	Baclofen, cyclobenzaprine, diazepam
Sympathomimetics (alpha-adrenergic agents)	Ephedrine, phenylephrine, phenylpropanolamine, pseudoephedrine
Sympathomimetics (beta-adrenergic agents)	Isoproterenol, metaproterenol, terbutaline
Miscellaneous	Amphetamines, carbamazepine, dopamine, mercurial diuretics, nonsteroidal anti-inflammatory drugs (e.g., indomethacin), opioid analgesics (e.g., morphine, hydromorphone, oxycodone)

tractions. The urethra should be examined for the presence of obstructing masses, diverticula, cysts, or breakdowns. The external genitalia are evaluated for evidence of injury, pathological masses, or local irritation contributing to painful urination or urine retention. In men, prostate size should be assessed. In women, a pelvic exam should analyze pelvic organ prolapse that can cause bladder outflow obstruction. A bimanual exam may help to evaluate uterine size, position, and support, as well as rule out any palpable pathological masses. Inspection of the vagina and surrounding perineal skin may reveal atrophy, lesions, or scars associated with prior surgery, as well as urine-related skin breakdown. Tenderness of the levator muscles may suggest pelvic floor hypertonicity associated with dysfunctional voiding. Urethral hypermobility and the presence of stress urinary incontinence (spontaneous or induced by Valsalva or cough) should be assessed.

The clinician should carefully examine hand function, in particular functional ability of the thumb and index or middle finger, as patients with retention usually require intermittent catheterization.

Clinicians should also assess the patient's mental status, cognition, mode of ambulation, mobility, gait, balance, coordination, weakness, and spasticity.

Bladder Diary and Questionnaires

Because reported complaints need to be objectively established, specific or generic questionnaires should be employed (note the discussion of questionnaires for SCI patients in Chap. 4, and the discussion of generic questionnaires and those for patients with multiple sclerosis in Chap. 7, "Incontinence Due to Neurogenic

Detrusor Overactivity"). A voiding diary can be helpful in clarifying the frequency and severity of patient's symptoms (see the discussion of voiding diaries in Chap. 5, "Testing"). In patients suffering from retention, a catheterization diary, used in the same manner as the voiding diary, may be more valuable [36]. Recorded parameters include time and volume of urine obtained at catheterization, as well as the same values obtained for any voids between catheterizations. When sensation is preserved, episodes of urgency may also be noted. Obtained quantities may help in characterizing the patient's compliance to bladder management regimes. When catheterization volumes exceed the volume at which filling pressures become unsafe for the upper urinary tract, appropriate management needs to be implemented. Moreover, careful record of catheterizations can show fluctuations in diuresis and could be used to determine the optimal catheterization frequency to adopt.

Urinalysis and Urine Culture

Infectious and inflammatory pathologies may cause or aggravate reported voiding problems in neurologically impaired individuals. Therefore, a urinalysis is recommended in patients suffering from retention [37, 38]. It may also reveal hematuria, proteinuria, or glycosuria, indicating possible complications of neurogenic bladder or important comorbidities that may lead to urine retention. As described in Chap. 5, a dipstick analysis may be more useful to *exclude* than to *prove* urinary tract infection, and if any evidence of infection is detected, urine culture with antibiotic sensitivity is required. Of note, asymptomatic bacteriuria should not be routinely treated (see Chap. 5—section "Urinalysis/Urine Culture") [17]. In already catheterized patients, samples from leg bags should not be analyzed. Well-obtained urine specimens are samples taken from a freshly inserted intermittent sterile catheter and those taken from a catheter port [39].

Uroflowmetry

In patients who still void, non-invasive uroflowmetry should be conducted to objectively document the voiding pattern and the initial ability of bladder empting. It also serves as an valuable method to monitor treatment results [17]. Obtained findings may include a low flow rate, decreased peak flow rate, prolonged and intermittent flow, hesitancy, low voided volume, and prolonged voiding time (Fig. 8.1) [40]. However, these findings are not specific, because they may also be seen in NDU, DSD, or structural abnormalities [41].

Post-void Residual

Clinicians emphasize that post-void residual (PVR) urine volume should be assessed in all patients suspected of urinary retention [22]. Elevated PVR predisposes to incontinence, urinary tract infections, bladder stones, and renal

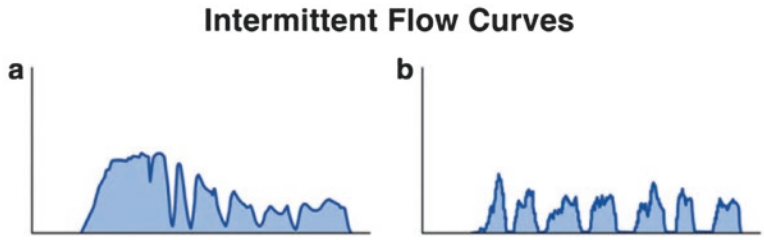

Fig. 8.1 (**a**) Detrusor-sphincter dyssynergia. (**b**) Valsalva voiding curve: patients with areflexic or hypocontractile bladder void with Valsalva maneuver that is represented as an intermittent and irregular curve (From Storme and McCammon [40], with permission)

dysfunction [42]. An elevated PVR indicates dysfunctional voiding, but it cannot be used to discern whether this is caused by poor detrusor contractility (underactive detrusor) or by obstruction (DSD, structural abnormalities). However, measurement of PVR may reveal the necessity of immediate introduction of bladder catheterization (if not already implemented). The PVR volume at which the patient's bladder-emptying technique should be changed is related to the overall bladder capacity and remains a matter of dispute [43]. It is currently recommended to introduce patients to catheterization techniques when a PVR volume consistently exceeds 100 mL and patients present with related symptoms [44, 45]. On the other hand, chronic urinary retention was traditionally defined as a PVR >300 mL [46]. Available data suggest that ultrasound measurement of PVR is preferable to catheterization, and portable scanners can be easily used in daily clinical practice as a convenient non-invasive tool [47–51].

Renal Evaluation

In patients with significantly elevated post-void residual, history of previous retention, or with risk factors for chronic kidney disease, renal evaluation is recommended. Basic laboratory and imaging studies are necessary to monitor kidney function. Measuring serum creatinine, blood urea nitrogen, and electrolytes levels, as well as calculating the glomerular filtration rate, help to assess renal function. Creatinine clearance provides more precise data but requires a 24-h urine collection to assess creatinine excretion. Incomplete collection can result in underestimation of renal function. Renal scintigraphy with assessment of glomerular filtration rate is recommended when renal function is poor, muscle mass reduced, or if the function of each kidney has to be assessed separately in high-risk patients [43]. A renal ultrasound is a valuable tool for the general assessment of kidney structure and may reveal hydronephrosis, abnormal masses, scarring, stones, and other structural changes affecting the parenchyma (see Chap. 5, Figs. 5.2, 5.3, and 5.4).

Bladder Ultrasound

Bladder ultrasound helps to detect stones and any possible tumor, indicating other causes of urinary retention or already developed complications of neurogenic bladder.

Other Investigations

Additional tests may help in proper diagnosis. Their utilization depends on clinical presentation. Evaluation of serum blood glucose and prostate-specific antigen can be considered based on the patient's history, symptoms, and signs. Contrast cystourethrography may be helpful in outlining the bladder neck and urethra, as well as vesicoureteral reflux. Direct visualization of the urethra and bladder via urethrocystoscopy may be useful to detect strictures, tumors, stones, or inflammation, and should be especially considered in patients with recurrent urinary tract infections [17]. Advanced imaging techniques (computed tomography, magnetic resonance imaging) should be performed when pelvic, abdominal, or retroperitoneal mass, as well as other malignancy causing external bladder neck compression is suspected [11].

Urodynamics

Because symptoms lack adequate precision, urodynamic study is of value in the final diagnosis. It allows distinguishing between NDU (impaired contractility with *low pressure-low flow*) and DSD (functional obstruction with *high pressure-low flow*). Only urodynamic study can offer more detailed information about the underlying mechanism of neurogenic lower urinary tract dysfunction. Urodynamic study should be performed according to widely adopted and reliable recommendations. These include *Good Urodynamic Practices and Terms 2016: Urodynamics, uro-*

flowmetry, cystometry, and pressure-flow study, developed by the ICS and *Urodynamic studies in adults: AUA/SUFU guideline*, developed by the American Urological Association and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction [52, 53].

Patients with Retention Due to Neurogenic Detrusor Underactivity The main urodynamic finding is detrusor underactivity defined as a detrusor contraction of reduced strength and/or duration resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying [1]. When no detrusor contraction is noted, an acontractile detrusor may be identified. Presented abnormalities are isolated to the voiding phase of urodynamic study. Nevertheless, neurological patients suffering from retention may also present with abnormalities of storage phase, including reduced sensation and increased cystometric capacity.

Detrusor Underactivity Urodynamic investigation of detrusor underactivity is characterized by a poor maximum flow rate (Qmax) and an abnormal flow pattern, associated with a poorly sustained, low-amplitude detrusor contraction (Figs. 8.2 and 8.3) [54, 55]. However, there are currently no universally accepted urodynamic parameters to define presented abnormalities [4]. The ICS does not define specific cutoffs or state any preference for any certain method of evaluation. Standardized assessment is characterized by lack of normative data, thus highly subjective.

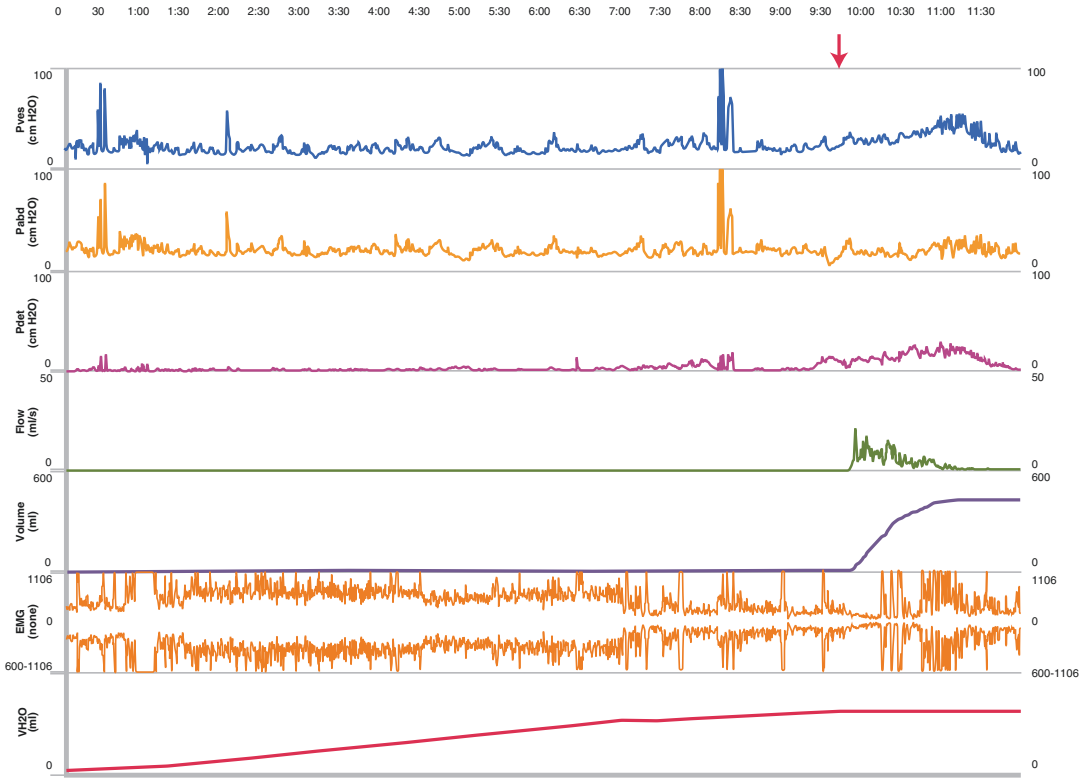

Fig. 8.2 Urodynamic tracing of a female with difficulty urinating due to detrusor underactivity. Permission to void denoted by *red arrow*. The patient was noted to apply external pressure to her suprapubic region, or Crede, to assist with voiding. Thus, a subtle rise in the abdominal pressure is noted with Crede maneuver which is also reflected in the vesical pressure tracing. Qmax of 21 mL/s is not representative of her flow curve as she does a Crede maneuver to achieve that result. Average flow rate is considerably lower and more representative of her altered voiding function. Electromyography (EMG) shows appropriate relaxation as voiding starts, though increased EMG activity during void may reflect straining (From Bacsu et al. [55], with permission)

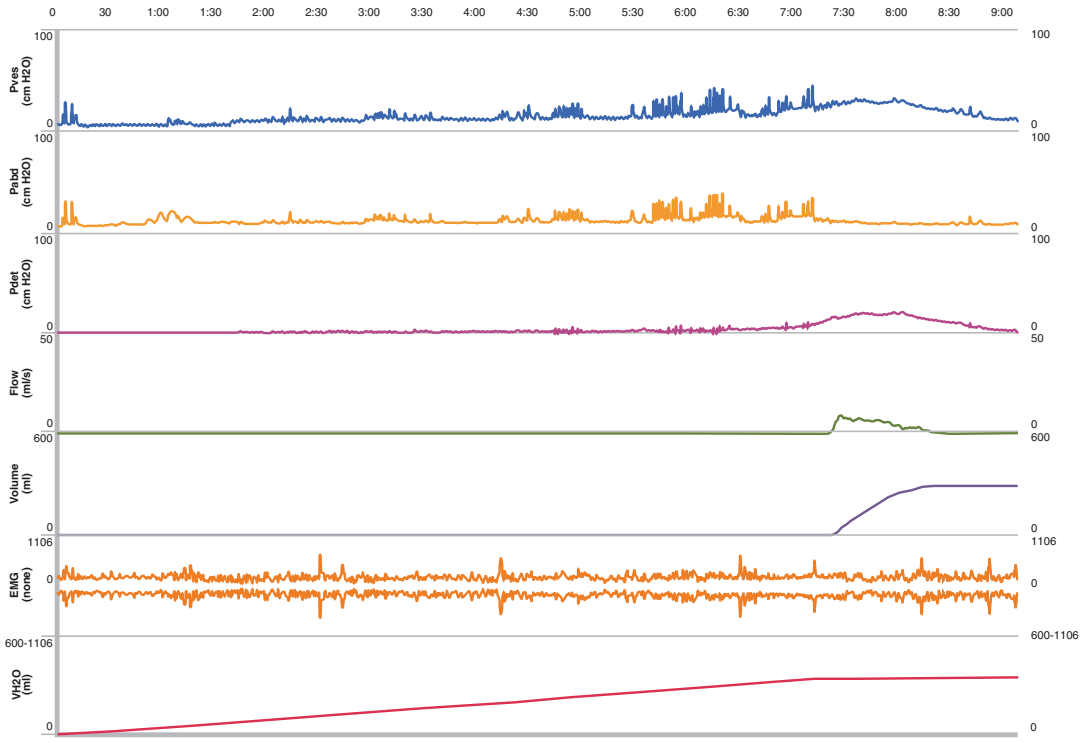

Fig. 8.3 Urodynamic tracing of a male who is 4 years post-radical prostatectomy with incomplete bladder emptying and elevated residual. Permission to void given twice, and noted with increases in both abdominal and vesical catheters and corresponding small volume voids. Detrustor pressure (Pdet) does not rise substantially with his void, and a prolonged flow curve is noted. Qmax is 10 mL/s with Pdet @Qmax of 14 cm H_2O. His BCI (PdetQmax + 5 Qmax) is 64 (<100), which represents detrusor underactivity. He also was catheterized for 90 mL at the end of the study (From Bacsu et al. [55], with permission)

Several conceptions have been proposed to describe the relationship between detrusor pressure (Pdet) and urinary flow (Q) when detrusor underactivity is suspected. For day-to-day clinical practice, some experts proposed simple criteria of detrusor underactivity defined as [46]:

$$\text{Pdet@Qmax} < 30-45\,\text{cm}\,H_2O\,\text{with}$$
$$\text{Qmax} < 10-15\ \text{mL/s}$$

Pdet @Qmax—detrusor pressure at maximum flow rate, Qmax—maximum flow rate.

As female bladders generate lower pressures during voiding, some studies consider female detrusor underactivity when detrusor pressure at Qmax is less than 10 cm H_2O [25]. To objectify bladder contractility, mathematical equations have been developed. These mainly include bladder contractility index (BCI) [56], the Watts factor [57], and the linearized passive urethral resistance relation (linPURR) [58]. Among them, BCI seems to be the most useful for daily clinical practice. It is simple, quick to calculate, and easily reproducible. BCI is based on detrusor pressure at maximum flow rate (Pdet @Qmax) and maximum flow rate (Qmax):

$$\text{BCI} = \text{Pdet@Qmax} + 5\,\text{Qmax}$$

In men, BCI > 150 suggests strong contractility; BCI 100–150 suggests normal contractility; and BCI < 100 suggests weak contractility. Complete absence of detrusor contraction may be termed as acontractile bladder (Fig. 8.4) [55, 57]. Because the equation was primarily developed for men with bladder outflow obstruction, Tan modified the BCI calculation and proposed a new formula of contraction strength for women, known as the projected isovolumetric detrusor pressure (PIP) [59]:

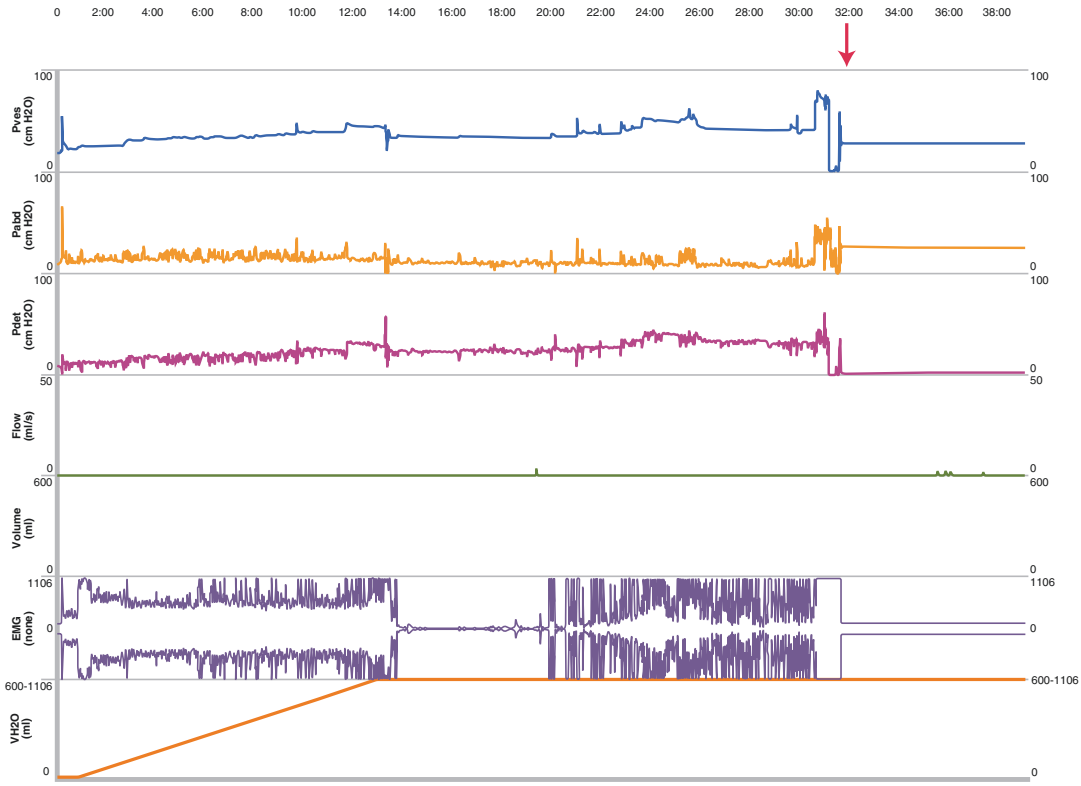

Fig. 8.4 Urodynamic tracing of a female with acontractile detrusor and inability to void due to multiple sclerosis. Urodynamics revealed delayed first sensation (537 mL) and cystometric capacity of 733 mL. No incontinence was observed during filling. Despite having large cystometric capacity and desire, with permission, to void (at *red arrow*), she did not mount any detrusor contraction. An increase in vesical pressure is noted through this long filling curve suggestive of somewhat altered compliance. Given that this occurs over a volume of over 700 mL, the impact of this pressure change can be mitigated by an appropriate catheterization schedule. Urodynamic catheters were removed after the patient was unable to void with reasonable attempts of urination. After the catheter was removed, she urinated only 11 mL. Detrusor acontractility is diagnosed during her attempt to void (From Bacsu et al. [55], with permission)

$$\text{PIP} = \text{Pdet} @ \text{Qmax} + \text{Qmax}$$

With this modified formula, normal contractility in the female was defined as PIP = 30–75 [59]. In efforts to better clarify detrusor underactivity, further calculations have been proposed that can be helpful in assessing more complicated patients; these should be studied in the professional urodynamic literature [60, 61].

Reduced Bladder Sensation Sensation of bladder filling is purely subjective and therefore depends on a cooperative and informed patient for reliability. Bladder sensation is reduced if it is diminished throughout bladder filling. Bladder sensation may also be completely absent. Many neurologically impaired patients may present with alternations of first sensation of bladder filling, first desire to void, and/or strong desire to void. It has been shown that up to 71% of patients after SCI or with myelodysplasia may experience impaired sensation compared to 30% of non-neuropathic patients [62]. Among individuals with altered sensation, up to 40% of neurological patients may report complete absence of sensation compared to 3% of non-neuropathic patients. Interestingly, further testing of non-neuropathic patients with impaired bladder sensation can reveal unrecognized underlying neurological pathology such as diabetic polyneuropathy, multiple sclerosis, or peripheral neuropathy after multiple pelvic surgery. Clinicians should bear in

mind that the assessment of bladder sensation is highly subjective and should be taken with caution, as some patients may report a sensation of bladder filling even when the bladder is not being filled [63, 64]. Proposed intervals of bladder volumes referring to normal bladder sensations are included in Chap. 7, "Incontinence Due to Neurogenic Detrusor Overactivity," in the section "Urodynamics."

Increased Cystometric Capacity Normal cystometric capacity is generally defined as 300–550 mL with larger values obtained in men compared to women [65]. Both detrusor underactivity and reduced bladder sensation significantly contribute to increased cystometric capacity. In daily clinical practice, the combination of detrusor underactivity with reduced bladder sensation and increased cystometric capacity is most often seen in patients with diabetic cystopathy (Fig. 8.5) [66].

Patients with Retention Due to Detrusor-Sphincter Dyssynergia DSD is a urodynamic observation of a detrusor contraction synchronous with an involuntary contraction of the urethral and/or peri-urethral striated muscle [1]. It is diagnosed during the voiding phase of urodynamics. DSD may lead to prolonged detrusor contractions, structural bladder damage, vesicoureteral reflux, and upper urinary tract damage. As DSD occurs in lesions between the brainstem and the sacral spinal cord, patients may also present with concomitant neurogenic detrusor overactivity (NDO) and involuntary control of micturition.

In healthy individuals, there is a slight gradual increase in sphincter electromyogram (EMG) activity during bladder filling [67]. The EMG signal should stay relatively quiet and consistent [68]. During voiding, the first recorded event of this phase is a sudden and complete relaxation of the striated sphincteric muscles, shown by complete electrical silence of the EMG [67]. This is followed almost immediately by a rise in detrusor pressure as the bladder and proximal urethra become isobaric. The EMG signal then resumes once the bladder is empty. The sphincter complex is also coordinated during sudden increases in abdominal pressure. Coughing or Valsalva maneuvers elicit reflex contraction of the sphincter manifested as an increase in EMG activity [67].

In patients with DSD, relaxation of the striated sphincteric muscles during voiding is absent and coexists with detrusor contraction (Fig. 8.6) [67]. Diagnosis of DSD by EMG requires elevated EMG activity during detrusor contraction, in the absence of Valsalva and Crede maneuvers [8, 69]. These maneuvers would be detected as a rise in abdominal pressure (Pabd). Additional fluoroscopy has proven invaluable in the

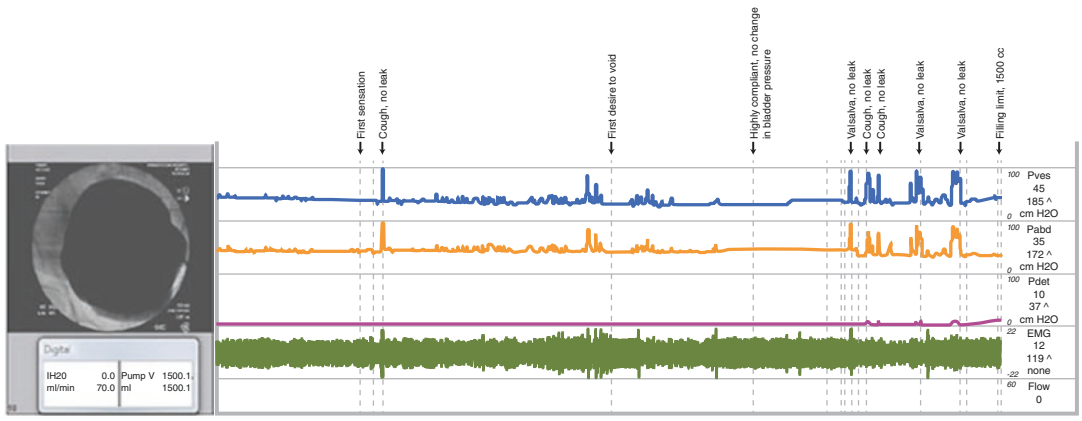

Fig. 8.5 Cystometrogram of a patient with diabetic cystopathy showing a hypocontractile large capacity bladder; maximum cystometric capacity was never reached. Vesical pressure and abdominal pressure were equalized at the start of the study with a corresponding detrusor pressure of zero. Filling was discontinued at a volume of 1500 cc. This bladder is highly compliant without evidence of detrusor overactivity (From Smith et al. [66], with permission)

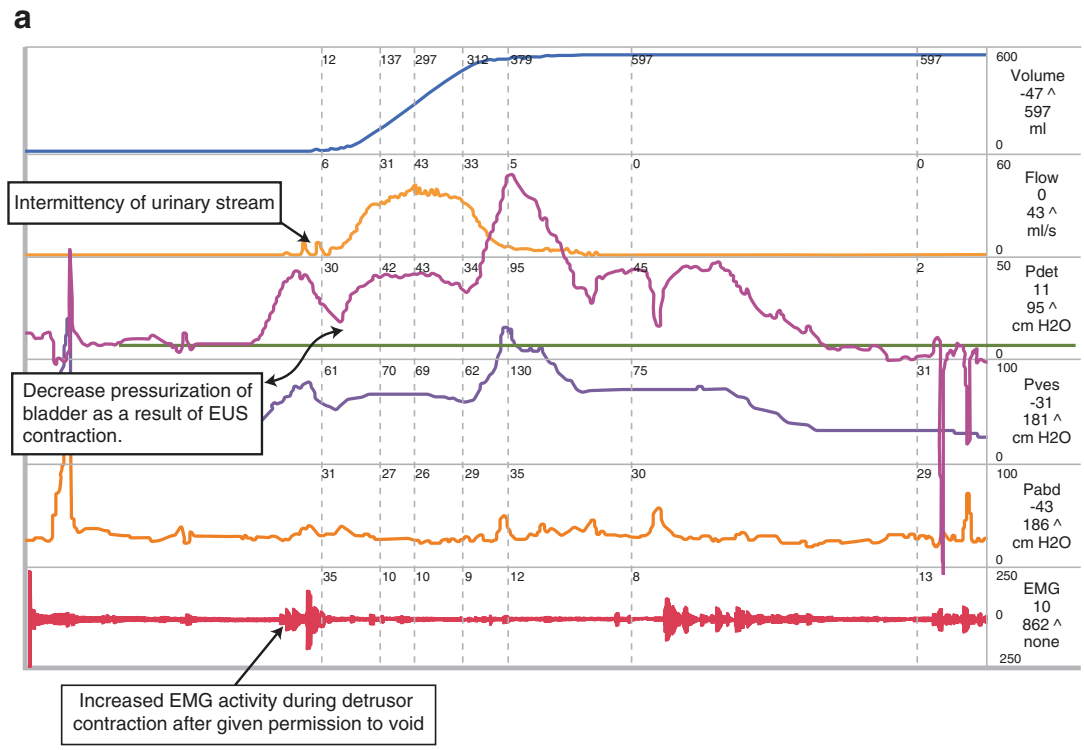

Fig. 8.6 (**a**) Increased electromyography activity causing urethral obstruction. (**b**) Open bladder neck with poor flow past-urethral sphincter (From Harris et al. [67] with permission)

diagnosis because a urodynamist can see a dilation of the urethra to the level of the striated sphincter (spinning top urethra), no passing contrast through the area of the striated sphincter, and/or intermittent contractions of the striated sphincter.

Two classifications of DSD have been proposed. Blaivas et al. suggested that DSD should be classified according to the pattern of external urethral sphincter electromyographic activity, whereas Yalla et al. proposed classification according to the bladder pressure and resulting flow [70–72]. In order to simplify this condition for daily clinical practice, DSD can also be characterized as intermittent (Fig. 8.7) [68] or continuous (Fig. 8.8) [68] according to the consistency of the sphincter contraction during the detrusor contraction [10]. The initial description of DSD and the chronology of events still remain a matter of dispute. Studies have shown that urethral sphincter may contract before, after, or at the same time as detrusor [7, 71, 73].

Readers should be aware that the diagnosis of DSD with EMG is poorly standardized with variance in the type of electrodes (needle, patch) and their placement [8, 69]. Patch electrodes are frequently used due to easier placement, better tolerance, and greater patient mobility [69].

It is important to note that some volitional behaviors such as recruitment of pelvic floor due to pain or discomfort, Valsalva/Crede maneuvers, or any other source of artifact (fluid on patch, etc.) may mimic DSD [67]. If an unexpected increase in EMG signal was noted without any identifiable artifact, video imaging should be employed. Fluoroscopy can significantly help in the diagnosis of DSD and in the determination of vesicoureteral reflux [8, 17]. Furthermore, it is more sensitive in leakage detection than direct observation. Diagnostic discrepancy between EMG and fluoroscopy ranges from 40 to 46% [8, 69]. Male patients are more often diagnosed by means of EMG, whereas female patients are more often referred to video imaging [8, 69]. It has been suggested that the diagnosis of DSD in males by video imaging may be impaired due to anatomical bladder outflow obstruction (prostate), whereas in females diagnosis by EMG may be impaired due to increased electrode artifact [9]. A combination of EMG and fluoroscopy seems to be the best option but with limited availability [8, 69]. Moreover, it has been suggested that the clinician should be present during the urodynamic study to increase the accuracy of the diagnosis [9, 69].

A rare finding in neurologically impaired patients is a discoordination between bladder neck relaxation and detrusor contraction. This abnormality is also referred to as bladder neck dyssynergia, detrusor-internal sphincter dyssynergia, smooth sphincter dyssynergia, and proximal sphincter dyssynergia [7]. Similarly to DSD, this primary bladder neck obstruction leads to high detrusor pressure with low urinary flow rate. Non-neurogenic causes of the reported discoordination include benign prostatic hyperplasia and urethral stricture in males, and obstruction from pelvic organ prolapse, urethral stricture, previous anti-incontinence surgery, or urethral diverticulum in females [67]. Pelvic floor dysfunction is another possible cause seen in both sexes. Such discoordination does not cause a significant increase in EMG activity during voiding, as seen in tracing of patients with DSD or dysfunctional voiding (the EMG only reflects changes in the external urethral sphincter). Bladder neck dyssynergia can be diagnosed only by simultaneous imaging of the bladder outlet during voiding. Fluoroscopy of the pressure-flow study will show a failure of bladder neck opening (closed bladder neck and no bladder neck funneling) with a relaxation of the striated sphincter. Just for the record, patients with DSD will present with opened bladder neck without concurrent relaxation of the external sphincter [7, 74].

Clinicians should remember that in the absence of a neurological abnormality, impaired coordination of detrusor contraction and sphincter relaxation is more appropriately referred to as dysfunctional voiding or pelvic floor hyperactivity

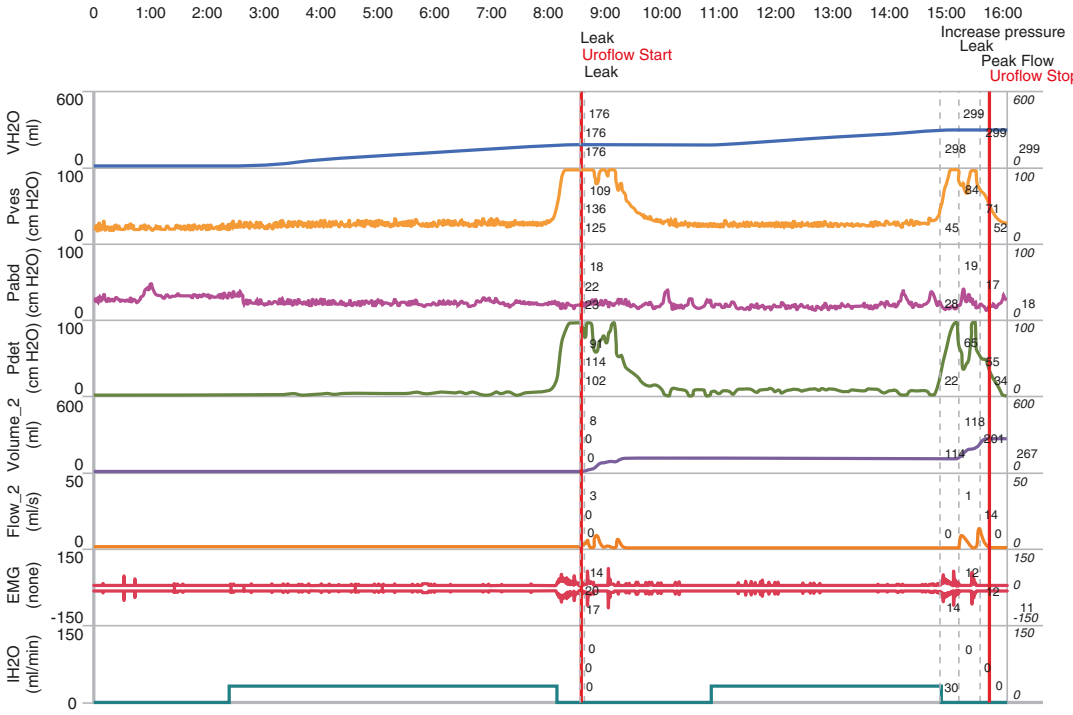

Fig. 8.7 Detrusor-sphincter dyssynergia. Intermittent involuntary contraction of the striated sphincter during the involuntary detrusor contraction (From Borawski [68], with permission)

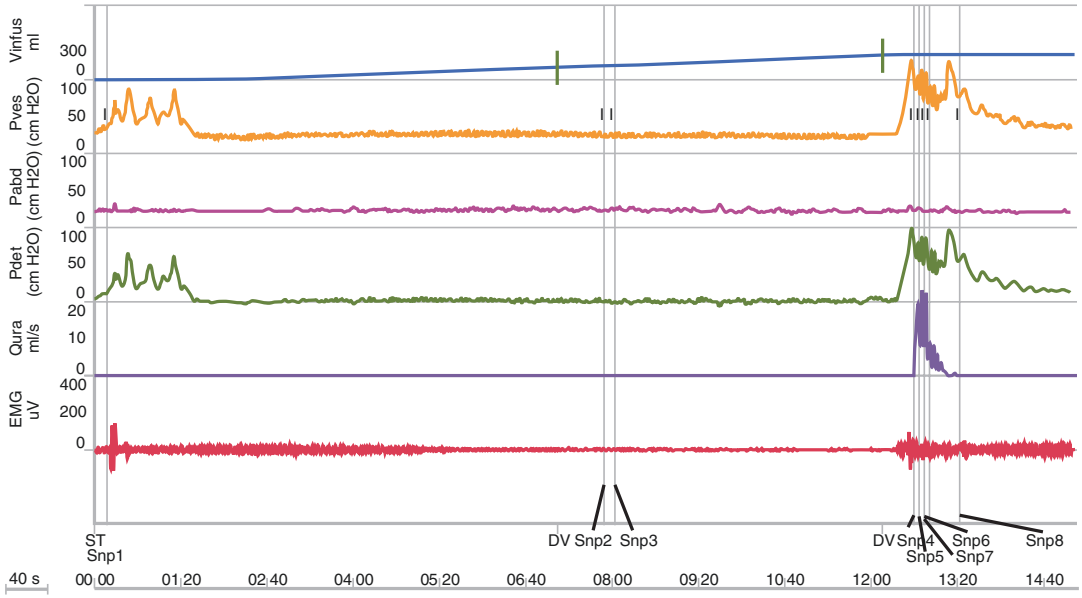

Fig. 8.8 Detrusor-sphincter dyssynergia. An involuntary contraction of the striated sphincter that continues throughout the involuntary detrusor contraction (From Borawski [68], with permission)

(see Chap. 2). Dysfunctional voiding is defined as an intermittent and/or fluctuating flow rate due to involuntary intermittent contractions of the peri-urethral striated muscle during voiding in neurologically normal individuals [1].

As patients with DSD are at high risk for multiple complications, including renal failure, and the disorder often worsens over time, routine lifelong follow-up monitoring should be offered to this specific group [7, 17, 70, 75]. It has been shown that patients with complete sensory and/or motor deficit have worse prognosis of DSD than those with incomplete deficits [75].

Treatment

Treatment of Patients with Retention Due to NDU

Intermittent Catheterization Intermittent catheterization (IC) is a method of bladder emptying at a specified time frequency by inserting a catheter into the bladder, draining the bladder, and then removing the catheter [76]. This technique does not require an intact sacral micturition reflex to be present. IC is considered to be a safe and effective treatment modality of neurogenic bladder dysfunction for short- and long-term use [77–79]. Nowadays, IC should be recommended as the first choice of treatment for those with inability to empty the bladder adequately and safely, particularly if the patient is physically and mentally willing to perform the task or has a caregiver who is able to assist [80]. Threshold volumes for initiating IC are not standardized and remain a matter of dispute [54]. Experts proposed than a PVR volume consistently more than 100 mL in symptomatic patients should prompt the start of IC [45]. IC should be immediately implemented in patients with PVR-related recurrent urinary tract infections, overflow urinary incontinence, or upper tract damage [21].

IC can be done either by the patient (intermittent self-catheterization, or ISC) or by a caregiver. Neurological disorders, including poor manual dexterity (in particular insufficient hand skills), weakness, tremor, rigidity, spasticity, disturbed perineal sensation, impaired visual acuity, cognitive impairment, or paraplegia, can affect the ability of a patient to perform self-catheterization [43]. Elderly patients should not be disqualified from self-techniques, as studies have shown that they have abilities similar to the general population in learning IC [81]. Thus, they should be offered IC preferentially over indwelling catheterization whenever possible. Furthermore, ISC is associated with reduced depression and lower discontinuation rates compared with assisted IC [82, 83]. General contraindications for IC include [54, 76]:

- abnormal urethral anatomy (strictures, false passages, bladder neck obstruction)
- small bladder capacity (<200 mL)
- little motivation or inability or unwillingness to adhere to the catheterization time schedule
- high fluid intake regimen (may require frequent catheterization, which may not be practical)
- adverse reaction to passing a catheter into the genital area multiple times a day or prohibitive body habitus or psychological lack of acceptance (patient's acceptance is required for long-term compliance)
- tendency to develop autonomic dysreflexia with bladder filling despite treatment
- caregiver who is unwilling to perform catheterization (relative contraindication)

Such limitations should be carefully assessed before starting IC.

IC can be carried out with sterile or clean technique. The sterile (non-touch) variant involves using a sterile single-use catheter along with sterile gloves, gown, and mask; disinfectant wipes or swaps; and sterile drainage tray or closed collection bag. Healthcare professionals in hospital settings mainly use this technique. Clean technique uses either a sterile single-use catheter or a clean reused catheter and a clean container with clean gloves or hands washed with soap and water. Patient population using

single-use hydrophilic catheters have an estimated incidence of urinary tract infection between 40 and 60%, compared with the observed prevalence of urinary tract infection for multiple use of 70–80% [84–87]. Clean technique has been widely adopted in community settings, as it is less time consuming and easier to perform, as well as decreases the cost of IC [88]. Nevertheless, the overall clinical evidence remains insufficient for powerful decision-making and it is not possible to state that one catheter method is better than another [77, 78, 89]. An updated systematic Cochrane review on strategies for catheter use emphasized that the evidence base is weak [90]. Currently, clean IC is most commonly used, and experts suggest that the sterile technique cannot be considered as a routine procedure [28, 91]. Sterile IC may be used in patients with recurrent urinary tract infections occurring with clean IC, and aseptic IC is an alternative to sterile IC [54, 76, 89, 92]. In addition, readers should be aware that decreased frequency of urinary tract infections with sterile technique is counterbalanced by significantly increasing cost compared with clean catheterization [89].

Suitable catheter material is an important factor for successful outcomes. Several types of catheter are currently available including [79]:

- uncoated polyvinyl chloride
- uncoated polyvinyl chloride with a separate lubricant applied manually
- gel-coated polyvinyl chloride (prelubricated with gel by the manufacturer)
- hydrophilic-coated (needing activation by manually adding water)
- ready-to-use hydrophilic-coated (coating already contains water)

There are multiple products available with different features designed to make IC easier, depending on various circumstances (Fig. 8.9) [93]. A recently published systematic review with meta-analysis demonstrated advantages of hydrophilic-coated catheters in decreasing risk of urinary tract infection and urethral trauma, as well as improving patient's satisfaction. Prelubricated catheters has been shown to be superior to conventional polyvinyl chloride catheters [89]. Moreover, it is noteworthy that catheter type may be important for patient compliance with treatment. Patient satisfaction is crucial, as it influences adherence to the IC regimen. Studies have shown greater degree of satisfaction with hydrophilic and prelubricated catheters, given their advantages of convenience, comfort, and ease of insertion when compared to conventional polyvinyl chloride [89, 94–98]. Therefore, acceptance might be maximized by starting all new patients on hydrophilic catheters [84].

In order to improve outcomes and prevent complications, proper education and support are required, both during initial teaching and future follow-up. A well-trained and experienced clinician, usually a specialized nurse, has a vital role in teaching proper self-catheterization technique, exploring possible barriers, and maintaining compliance with long-term management [99]. Well-structured training programs for patients have been shown to improve outcomes [81] and acceptance of treatment [100–102]. Patient education has been further described in Chap. 17, Proper Education of Patients Suffering from Neurogenic Bladder.

The frequency of catheterization depends on specific clinical presentation, including bladder volume, fluid intake, and PVR volume, as well as urodynamic parameters (compliance, detrusor pressure) [43]. Adequate frequency ranges from occasional IC to complete dependency on IC for bladder emptying [54]. Experts recommend that complete urinary retention should be managed with four to six catheterizations per 24 h [43]. Some individuals may need to awake from sleep at night to catheterize. If bladder volumes at catheterization consistently exceed 500 mL, it has been proposed to increase frequency of IC and adjust fluid intake, as well as to consider alternative method of bladder management [54, 76]. On the other hand, clinicians should be aware that more than six catheterizations per day is usually considered excessive and may have negative impact on patient compliance with treatment [42]. The catheter size most often used is between 12–16 Fr [28]. Patients who leak urine between

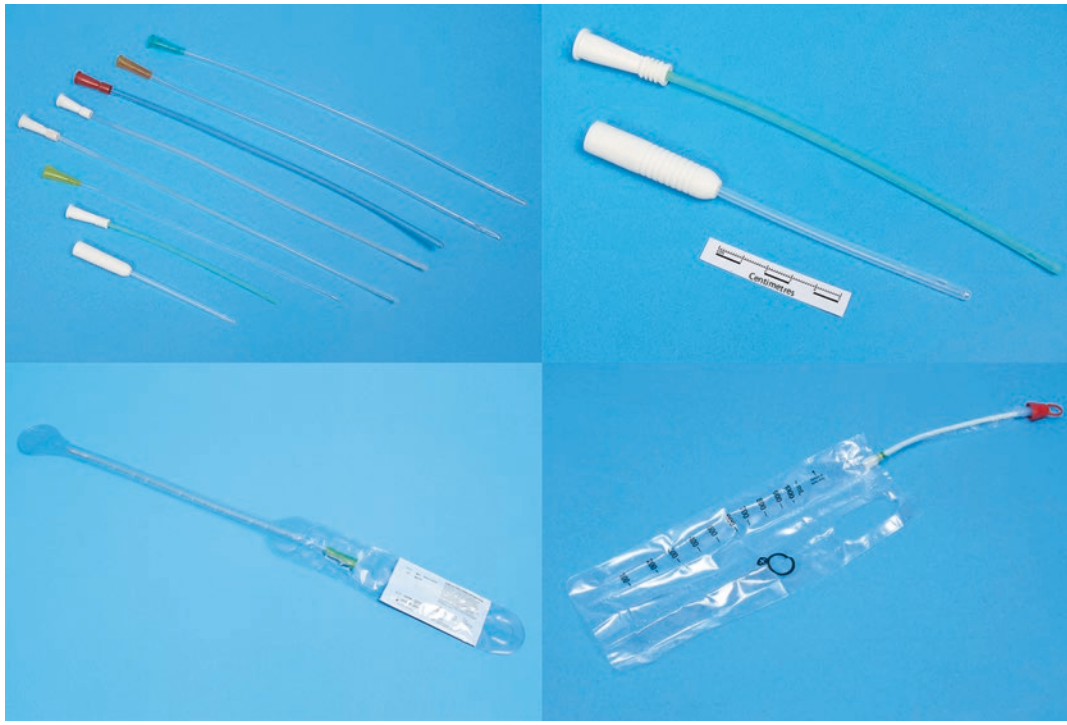

Fig. 8.9 Display of the multiple products available with different features designed to make intermittent catheterization easier, depending on various circumstances (Continence Products Advisor [93], courtesy of the International Continence Society (ICS), with permission)

catheterization require special attention. Possible causes of this situation include urinary tract infections, progression of neurological disease, emerging new problems of bladder or sphincter, as well as inadequate fluid intake. Those who are able to void but empty their bladder incompletely will need to use the catheter one to three times per 24 h after voiding [43].

Complications of IC include bacteriuria and urinary tract infection, urethritis, epididymoorchitis, epididymitis, prostatitis, urethral trauma/hematuria, urethral false passages, urethral stricture, autonomic dysreflexia (in those with injuries at T6 and above), and bladder stones [76]. Complications may increase in the long term [78]. However, it has to be emphasized that it is sometimes difficult to attribute causality because developing complications can potentially be caused by the underlying bladder dysfunction [79]. Complication rates are reduced with self-catheterization technique compared with assisted IC [86, 103, 104]. In individuals with recurrent urinary tract infections who perform IC, clinicians should reassess catheterization technique as well as consider change of catheter type, or start antibiotic prophylaxis [105]. Asymptomatic bacteriuria is a common finding in patients performing IC. It has been estimated that the incidence of bacteriuria is 1–3% per catheterization, and 1–4 episodes of bacteriuria occur for 100 days of clean IC [106]. After 30 days, almost all patients will develop this condition [107, 108]. Just for the record, asymptomatic bacteriuria should not be routinely treated except in pregnant women and individuals before surgical procedures within the urinary tract (see Chap. 10, "Urinary Tract Infection").

Indwelling Catheterization For patients in whom intermittent catheterization is not feasible, indwelling catheterization deserves consideration. It is a method of bladder emptying in which

a catheter is inserted into the bladder and maintained in place for an extended period of time. The catheter can be inserted manually through the urethra (urethral catheter) or surgically into the lower abdomen cephalic to the pubic bone (suprapubic tube). Chronic indwelling catheterization should be considered in patients with [76]:

- acute neural injury (in order to monitor urinary output and fluid balance)
- inabilities to perform IC (e.g., poor hand skills, spasticity, tetraplegia, cognitive impairment)
- limited assistance from a caregiver
- lack of success with other, less invasive bladder management methods
- incontinence episodes between IC when continence is hard to improve
- difficulties in wearing continence devices
- high fluid intake
- episodes of autonomic dysreflexia between IC
- preferences to indwelling catheterization because it offers greater expediency and compatibility with the patient's lifestyle

Whenever a transurethral route has been chosen, full silicone or hydrogel-coated catheters are preferable [78]. It is recommended to use 12–16 Fr catheters with lumen size as large as possible and small (5–10 mL) self-retaining balloons. Such an approach aims to minimize the pressure effect on the bladder neck and to maximize time to blockage by incrustation. Frequency of catheter change depends on catheter material and size of the lumen. It has been proposed to change siliconized latex catheters every 1–2 weeks and silicone or hydrogel-coated catheters every 2–4 weeks or longer [78]. In those with a history of catheter encrustation or bladder stones, catheter change every 1–2 weeks should be considered [76]. Catheter placement should be conducted with sterile materials and aseptic technique, followed by routine catheter care, to keep the closed drainage system aseptic and to minimize complications. Patients should also be educated in terms of daily cleanliness and hygiene care. Bladder irrigation and antibiotic prophylaxis are not routinely recommended [78].

In comparison with IC, the use of an indwelling transurethral catheter significantly increases the risk of complications. Whereas short-term treatment with transurethral indwelling catheterization is considered a safe modality, long-term management is controversial. Experts suggest that long-term transurethral catheterization may be safe only if a careful checkup of urodynamic bladder function, as well as upper and lower tract imaging, is performed regularly at least yearly [78]. It has been shown that chronic urethral catheterization is associated with various complications such as urinary tract infections, urethritis, epididymoorchitis, epididymitis, prostatitis, sepsis, urethral trauma and bleeding, hypospadias, fistula, bladder neck incompetence, sphincter/urethral erosion, bladder/kidney stones, bladder cancer, and allergy [109].

Some of these complications may be avoided with suprapubic catheterization. This mainly includes urethral trauma and destruction of the bladder neck. The suprapubic catheter also offers the possibility of genital activity with less preparation. Clinicians should still remember that both transurethral and suprapubic routes are inferior to IC. A unique complication associated with suprapubic catheterization is bowel perforation during catheter insertion [109]. The suprapubic route should be considered for individuals with [76]:

- urethral abnormalities (stricture, false passages, bladder neck obstruction, urethral fistula)
- urethral injury (patients after pelvic trauma with blood at the urethral meatus, perineal and scrotal hematomas, hematuria)
- difficulties with urethral catheter insertion
- recurrent urethral catheter obstruction
- perineal skin breakdown due to urine leakage secondary to urethral incompetence
- prostatitis, urethritis, or epididymoorchitis
- urethral discomfort
- psychological considerations (body image, personal preference)
- desire to improve sexual genital function.

A recently published study on quality of life after suprapubic catheter placement in patients

with neurogenic bladder has shown that suprapubic catheterization is an effective bladder management strategy in carefully selected patients who have failed other options [110]. Moreover, 80% of the patients considered the suprapubic catheterization to have improved their urological quality of life compared with previous bladder emptying methods. In another study, quadriplegic patients, regardless of gender, reported greater satisfaction with the use of a suprapubic catheter compared to clean IC [111]. Even though suprapubic catheterization is currently considered as a safe and effective short-term method to manage urinary retention, it is not routinely recommended for long-term use, and variations of clinical practice exist [78]. Some clinicians highly favor suprapubic catheterization for long-term management [111, 112], while others are concerned about complications during its long-term use [113]. If suprapubic catheterization has been employed for chronic management, less irritating catheters, improved closed drainage systems, and regular follow-ups must be implemented. A suprapubic catheter should be changed every 4 weeks [76]. In those with a history of catheter encrustation or bladder stones, catheter changes every 1–2 weeks should be considered.

Multiple studies have shown that the rate of bladder cancer is higher in individuals who manage their bladders with long-term indwelling catheters. The exact pathophysiological mechanism has not been well established. Increased risk of bladder cancer can be assigned to recurrent infections, stones, and chronic inflammation associated with catheter use. Some studies demonstrated that cystourethroscopic surveillance in patients with indwelling catheters is essential to diagnose and manage associated complications at an early stage, to minimize symptomatology, as well as to maintain good health and quality of life [114]. Interestingly, it has been shown that endoscopic findings do not significantly differ between symptomatic and asymptomatic groups. This reinforces the hypothesis that patients with indwelling urethral catheters or suprapubic tube require regular cystourethroscopic surveillance. One proposal includes annual cystoscopy (with biopsy, if required) for those chronically catheterized (both transurethral and suprapubic) for more than 5–10 years as well as in those with an episode of gross hematuria or chronic urinary tract infections refractory to therapy [78]. In patients with additional risk factors for bladder neoplasm (e.g., smoking, occupational exposures), closer follow-up schedule may be considered.

Bacterial colonization in chronic management with indwelling catheters is unavoidable. This may lead to recurrent catheter blockage and systemic infection. The risk of bacteriuria in patients with indwelling urethral catheter is about 3–10% per catheter-day, approaching 100% after 30 days of use [107, 108]. On the other hand, the incidence of febrile infections within the urinary tract occurs at a rate of only 1/100 days of catheterization [106]. Concurrent results have been shown with the suprapubic variant [115]. Nonetheless, as stated previously, asymptomatic bacteriuria should not be routinely treated.

In cases of acute urinary retention, patients must be immediately managed with complete decompression of the bladder via urethral or suprapubic route. It has been hypothesized that rapid decompression may lead to potential complications such as hematuria, hypotension, and post obstructive diuresis. However, there is no evidence that gradual bladder decompression will avoid these complications [11]. Thus, rapid and complete emptying of the bladder is recommended [116]. After urine evacuation, patients at risk for post obstructive diuresis should be monitored with serum electrolyte analyzers (two or three times per day) and encouraged to hydrate orally or intravenously until the diuresis has resolved [22]. IC should be implemented as soon as reasonably possible.

Sacral Neuromodulation Sacral neuromodulation (SNM) has demonstrated positive outcomes in individuals with urinary retention due to detrusor underactivity [22]. Rates of successful elimination of need for catheterization in patients with retention have been reported to be as high as 69–81% [117–120]. However, the data are limited for neurologically impaired patients. The

majority of available trials excluded patients with underlying neurological disorder. A study of Lombardi et al. analyzed SNM for treatment of non-obstructive urinary retention in individuals with incomplete SCI [121]. The researchers revealed that 42.4% (36 in 85) of included patients responded well to the percutaneous first stage of SNM. Of note, this study was restricted to higher functioning patients, classified as American Spinal Injury Association (ASIA) classification C or D (see Chap. 4, "Medical History and Physical Examination"). Post-surgery urodynamics showed improved bladder sensation, increased maximum urine flow, and decreased PVR. Additionally, 22 patients were able to void spontaneously. During follow-up, one third of the patients had at least one or more "failures" that required contralateral or S4 implantation. Nevertheless, permanent SNM was highly efficacious in the mean follow-up of 23 months in all 36 patients. Another study evaluated 11 highly functional SCI patients with chronic neurogenic non-obstructive urinary retention and found that 82% of subjects had a positive test phase and were able to void spontaneously after device implantation [122]. Nonetheless, the urodynamic parameters, including maximum bladder capacity, detrusor pressure, and bladder compliance, did not change significantly under SNM treatment. One study of ten individuals with multiple sclerosis and NDU found that 100% of subjects failed the test phase of SNM [123]. Severity of underlying disease was not described. On the other hand, a study of Marinkovic et al. of 14 subjects with multiple sclerosis and urinary retention due to NDU found that 86% of individuals were able to void spontaneously after placement of an implantable pulse generator [124]. The mean post-operative post-void residual was 51 mL and max flow rate was 18 mL/s.

To conclude, research findings indicate that patients with non-obstructive urinary retention have a lower success rate after SNM compared to patients treated with SNM for storage dysfunction (see Chap. 7, "Incontinence Due to Neurogenic Detrusor Overactivity"). A recently published pilot study aimed to predict SNM treatment success in men with impaired bladder emptying-time and presented a new diagnostic approach. Authors showed that SNM treatment response in this population can be predicted with the BOO-contractility (Maastricht-Hannover) nomogram [125]. Men below the 10th percentile are likely to be treatment nonresponders, whereas the majority of men above the 10th percentile are responders. Some experts suggest that SNM can be considered and offered only in a select group of patients with an intact spinal cord, micturition center, and spinal roots [3]. The data for NDU and SNM are insufficient to support clinicians in their daily practice with reliable recommendations. In addition, SNM is costly and there are concerns regarding long-term efficacy. Therefore, this modality should be considered only by well-experienced and specially trained neurourologists.

The implantation technique and related complications are presented in "Neurostimulation/Neuromodulation" section in Chap. 7.

Other Modalities Assisted bladder-emptying techniques (triggered reflex voiding, Valsalva or Credé maneuvers) are not currently recommended [28]. Such techniques could be associated with a rise in intravesical pressures and bladder outlet resistance, thus putting in jeopardy the upper urinary tract [83, 126]. The maneuvers may further impair pelvic floor function and lead to concomitant stress urinary incontinence [78]. In SCI patients, triggered reflex voiding may also induce autonomic dysreflexia [127].

Pharmacological management of NDU has been investigated and very little success has been achieved. There is no rationale for use α-adrenoceptor blockers without concomitant bladder outflow obstruction [43]. α-blockers are not expected to improve NDU and may be considered only for decreasing bladder outlet resistance in patients with a non-relaxing bladder neck or benign prostate enlargement [45]. Parasympathomimetic drugs such as bethanechol to stimulate cholinergic receptors and potentially augment detrusor contraction did not show efficacy in clinical practice [128, 129]. Studies on inhibitors of acetylcholinesterase (e.g., distigmine, pyridostigmine, neostigmine) showed concurrent results [130]. Furthermore, multiple side

effects such as nausea, vomiting, diarrhea, abdominal cramping, bronchospasm, flushing, headache, visual disturbance, salivation, sweating, and rarely cardiac arrest limit the clinical use of presented agents [130].

Surgical interventions for NDU have become increasingly uncommon. Reduction cystoplasty (partial cystectomy to decrease bladder volume and increase detrusor contractility) and bladder wall strengthening by striated muscle flap (transposition of the latissimus dorsi muscle around the bladder) are performed only at individual specialized centers [131–136]. These techniques involves extensive surgery and might be associated with major morbidity. To make things worse, the risk-to-benefit ratio has not been established, as such techniques have been validated on only small groups of patients. The long-term outcome of these procedures is still unknown. As less invasive options are currently widely available, a surgical approach should be considered only by specially trained and well-experienced neurourologists in patients for whom all other treatments have failed.

Fig. 8.10 summarizes available treatment of NDU.

Treatment of Patients with Retention Due to DSD

Intermittent Catheterization + Pharmacotherapy The principles of DSD management are to aid bladder emptying and reduce intravesical pressure. Therefore, IC combined with anticholinergic drugs (see Chap. 7) is the most common treatment modality for DSD [9]. Individuals with DSD should be instructed to pass the catheter to the level of sphincter and wait for spasms to reduce before continuing to pass the catheter [137]. Other medications such as α-blockers and anti-spasticity drugs (benzodiazepines, baclofen, dantrolene) have been investigated and have been found to have a limited role in the management of DSD [7, 138, 139]. Although several studies of neurogenic patients indicated that α-blockers (including alfuzosin [140], prazosin [141], silodosin [142], tamsulosin [143–145], terazosin [146], urapidil [147, 148], and phenoxybenzamine [149]) may decrease urethral resistance and improve flow rate and reported voiding symptoms, overall data quality is low (except from one study with tamsulosin [143]), with a limited number of included patients and statistically significant results, as well as a lack of detail regarding underlying neurological disorders or urodynamic dysfunctions. Furthermore, these studies were performed only on carefully selected patients who maintained their ability to void; thus, the results obtained cannot be directly mapped onto patients in retention [150]. When voiding is not possible, treatment with α-blockers does not appear to change this condition [141, 144, 150]. In view of these findings, some urologists use α-blockers only empirically (in higher recommended doses) for the treatment of voiding symptoms of neurogenic origin, an approach supported by favorable side effect profile [150]. As stated previously, α-blockers may be rationally considered in patients with a non-relaxing bladder neck or concomitant benign prostate enlargement. The latter group of medication (anti-spasticity drugs) may produce troublesome adverse reactions, including general muscle weakness and gait disturbances, additionally minimizing their overall usefulness [17].

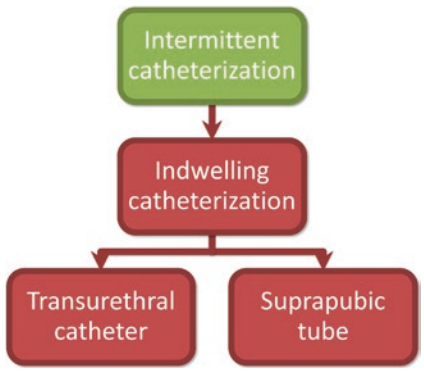

Fig. 8.10 Treatment of urinary retention due to neurogenic detrusor underactivity

Botulinum Toxin A Injections Intrasphincteric injection of botulinum toxin type A (BTX-A) may be considered in patients with DSD who are not able to perform IC. The patient's cognitive and visual impairment as well as manual dexterity

does not affect their eligibility for treatment [151]. This option aims to decrease urethral resistance. It has been investigated in quadriplegic men unable to perform IC and in patients of both genders with multiple sclerosis [17]. Dykstra et al. demonstrated that intrasphincteric injection of BTX-A decreased PVR urine volume in 8 of 11 SCI patients and reduced urethral pressure in 7 individuals [152]. Interestingly, symptoms of autonomic dysreflexia were also reduced in 5 patients. Schurch et al. reported a significant reduction of maximum urethral pressure in 88% of patients (21 out of 24) and decreased PVR in 71% [153]. Nevertheless, in eight patients the PVR remained high. No improvement of autonomic dysreflexia was noted. De Sèze et al. conducted a randomized, double-blind, lidocaine-controlled study on 13 patients with DSD and SCI. The authors used 100 U of BTX-A vs. 4 mL of lidocaine. They found a significant decrease in maximal urethral pressure and PVR at 1 month follow-up [154]. A study by Chen et al. prospectively evaluated 20 patients after SCI who were injected with a single dose of 100 U BTX-A [155]. After treatment, the authors reported significant reductions in integrated EMG and static and maximal urethral pressure, but not in maximal detrusor pressure and detrusor leak point pressures. PVRs were significantly decreased during 6-month follow-up and no adverse effects were noted. In view of these findings, it has been proposed that patients with DSD and concomitant detrusor overactivity should be injected simultaneously into external urinary sphincter and bladder detrusor. A recent Cochrane meta-analysis of BTX-A treatment for DSD has shown that this treatment option improves some urodynamic parameters such as voiding pressures and PVR after 30 days, although the authors emphasized that the studies included have risk of bias due to inconsistent description of outcome measures [156].

BTX-A is usually injected into the urinary sphincter under EMG or cystoscopic control [17]. With EMG technique, physicians locate the external urinary sphincter with a needle. In males, the needle is usually inserted into the perineal raphe at equal distance between scrotum and anus. Then, the needle is directed towards the prostatic apex palpated rectally [153]. In females, the needle is inserted into the anterior vaginal wall, once medially or twice paramedially, underneath the mid-urethra and approximately 2 cm proximal to the urethra opening [157]. Of note, no difference has been found between a single median injection and two para-median injections in each hemisphere of the sphincter [158]. After needle placement, the correct location of the needle is confirmed by typical tonic activity of the external urinary sphincter or reflex activity elicited by glandular or clitoral squeezing (bulbocavernous reflex). With cystoscopic technique, 2–4 injections are performed at 12, 3, 6 and/or 9 o'clock of the sphincter. The needle has to be inserted deeper (1 cm) than in the injection of bulking agent, as the needle needs to reach the muscle, not the suburothelial space [159]. BTX-A can also be injected into the external sphincter via an ultrasound-guided transperineal approach, but this technique has not been widely adopted.

Studies report that a dosage of 80–100 U of onabotulinumtoxinA and 150–250 U of abobotulinumtoxinA are effective [17]. The total dose is usually diluted in 2–4 mL of 0.9% saline. The procedure is usually performed under local anesthesia (10 mL of lidocaine gel, injected into the urethra, 10 min before injection) in an outpatient setting. Patients with autonomic dysreflexia need blood pressure monitoring during the procedure [151].

An overall satisfaction rate of 60.6% was reported with this treatment [160]. Nonetheless, BTX-A causes a short-lasting and reversible effect for approximately 1–4 months, thus requiring frequent procedures [17]. It has been proposed that the duration may be increased up to 12 months with two consecutive monthly reinjections after the initial treatment success [153].

Even though BTX-A could be useful for managing DSD, there is lack of definitive proof and good quality data. Available studies are characterized by different protocols, variable BTX-A dosage, and small sample size. No study has provided long-term data nor evaluated the role of repeated injections [161]. Concluding, intrasphincteric injection of BTX-A should be considered with

caution. It has been proposed that onabotulinumtoxinA injected into the sphincter may serve as a temporary solution for patients who may be considering surgical sphincterotomy [7].

At this time other minimally invasive techniques such as intraurethral stents, transurethral balloon dilatation, or overdistention of the female urethra with Credé maneuver have been abandoned [162]. Moreover, intraurethral stents are no longer commercially available [163].

Sacral Neuromodulation SNM is a treatment option for DSD but remains poorly supported with rather conflicting results. A recently published study analyzed 24 SCI patients suffering from NDO with DSD [122]. In 16 (66.7%) of them the test phase was successful (defined as symptom improvement of >50%) but the urodynamic parameters did not differ significantly between patients with sufficiently treated DSD compared with those with persistent DSD. Concurrent results have been presented by Lombardi et al. who did not find any improvement if NDO was combined with DSD [164]. On the other hand, the second arm of this trial, consisting of patients with pure NDO, has been characterized by a significant decrease in incontinence and in urodynamic parameters. Interesting results have been shown by Chaabane et al., who treated eight of nine patients with DSD successfully [165]. Besides SCI patients, this study also included individuals with multiple sclerosis. Further study of 25 individuals with multiple sclerosis found that all patients with retention due to DSD (n = 9) showed a significant increase in the voiding volume as well as significant decrease in the residual volume and mean number of catheterizations [123]. Moreover, patients reported significant increase in their quality of life.

These studies conclude that SNM may be considered in incomplete SCI patients with DSD without concomitant detrusor overactivity or in patients with multiple sclerosis suffering from chronic retention due to DSD. Nonetheless, readers should note that stimulation parameters and placement locations have not been established [166]. As a reasult, SNM should not be routinely recommended and may be considered only in carefully selected patients.

External Sphincterotomy In male patients who are noneligible for or who failed treatment described previously, external sphincterotomy is an option of surgical management. It prevents complications related to indwelling catheterization and those resulting from DSD. External sphincterotomy eliminates the resistance of the external sphincter and leads to the management of incontinence by means of an external urinary appliance such as a condom catheter. Following a successful sphincterotomy, improvement in bladder emptying and stabilization of the upper urinary tract can be achieved in 70–90% of patients [167]. The procedure is primarily performed in individuals with increased residual urine and high pressure voiding who failed conservative treatment [168]. Other candidates are tetraplegics with poor hand function and repeated episodes of autonomic dysreflexia; patients with repeated urinary tract infections; those difficult to catheterize because of urethral false passages and/or secondary bladder neck obstruction; as well as individuals with complications of DSD such as decreased renal function, vesicoureteral reflux, stone disease and genitourinary infections, including urosepsis [7].

Currently a sphincterotomy with a Collings electrocautery knife is the most established technique [168]. An anterior incision (11, 12, or 1 o'clock) beginning at the level of the proximal part of the verumontanum and ending in the corpus spongiosum of the bulbar urethra is the flashpoint of the procedure. Incisions at 3 or 9 o'clock of the sphincter should be avoided, as they may lead to excessive bleeding [17]. A loop electrode may also be used for the resection [169].

External sphincterotomy is the most invasive treatment for symptomatic DSD. Possible complications include excessive bleeding (up to 25% of patients, sometimes with subsequent clot retention) [139], impotence (7%) [170, 171], and urethral stricture (3–13%) [171–173]. Hemorrhage with blood transfusion has been reported in 0–23% of patients, depending on the location of the incision [139]. A large catheter of >20 Fr is usually required for several days to apply transurethral pressure at the resection site [137]. To minimize operative and perioperative

blood loss, particularly in patients who are at risk for excessive bleeding, sphincterotomy with a contact neodymium:yttrium-aluminum-garnet (Nd:YAG) laser should be considered. Studies have shown that laser sphincterotomy has similar efficacy and significantly decreases blood loss in the majority of patients [174, 175]. Free beam laser leads to coagulative necrosis; therefore, it is not suitable for this procedure [7].

Failure of this treatment may present as a continuation of recurrent urinary tract infections (25%) as well as persistence of hydronephrosis (33%), vesicoureteral reflux (10–60%), elevated PVR (20–25%), or episodes of autonomic dysreflexia (5–10%) [161, 167]. The reasons for failure may include inadequate sphincterotomy with persistent DSD or impaired detrusor contractility with poor bladder emptying. Management of failed sphincterotomy consists of either repeat sphincterotomy or catheter drainage. It has been estimated that 15–40% of patients subsequently require a repeat procedure [139]. In patients who additionally present with bladder neck obstruction, a trial of α-blockers or bladder neck incision/resection may be considered [139].

Indwelling Catheterization, Urinary Diversion, and Advanced Surgery Failure of the described DSD therapies may require long-term indwelling catheterization, urinary diversion, or dorsal root rhizotomy with sacral anterior nerve root stimulation (available only in specialized centers) [17, 139].

Fig. 8.11 presents treatment algorithm of DSD.

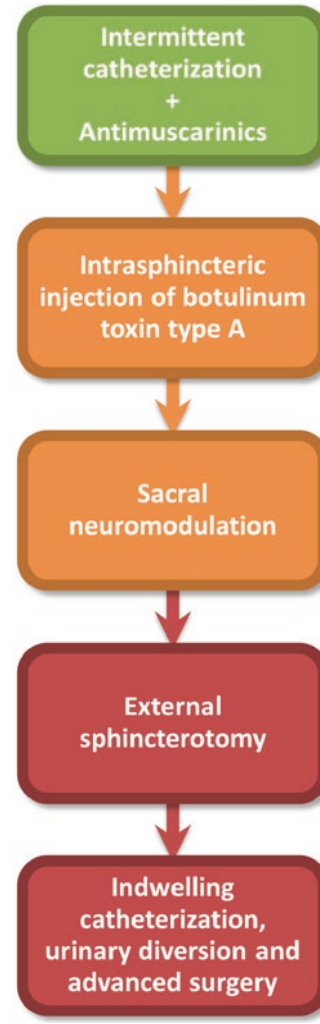

Fig. 8.11 Treatment of urinary retention due to detrusor-sphincter dyssynergia

Special Consideration for Patients with Detrusor Hyperactivity and Impaired Contractility

Detrusor hyperactivity with impaired contractility (DHIC) is characterized on urodynamics by low-amplitude involuntary detrusor contractions during filling and impaired bladder contractility during emptying (Fig. 8.12) [55, 176]. Thus, patients tend to develop high PVR volumes and chronic urinary retention but incontinence may also be reported [177]. This abnormality occurs predominantly in the elderly population, and the pathophysiology of this paradoxical voiding dysfunction remains unclear [178–180]. It has been hypothesized that DHIC is a direct consequence of long-standing detrusor overactivity or a coincidental association of two separate etiologies, with each one contributing independently to the two different components of DHIC [176]. DHIC has been described in patients with stroke, Parkinson disease, multiple sclerosis, myeloneuropathy, sacral/infrasacral SCI, and peripheral neuropathy.

The clinical presentation varies, and DHIC can often mimic other voiding dysfunctions.

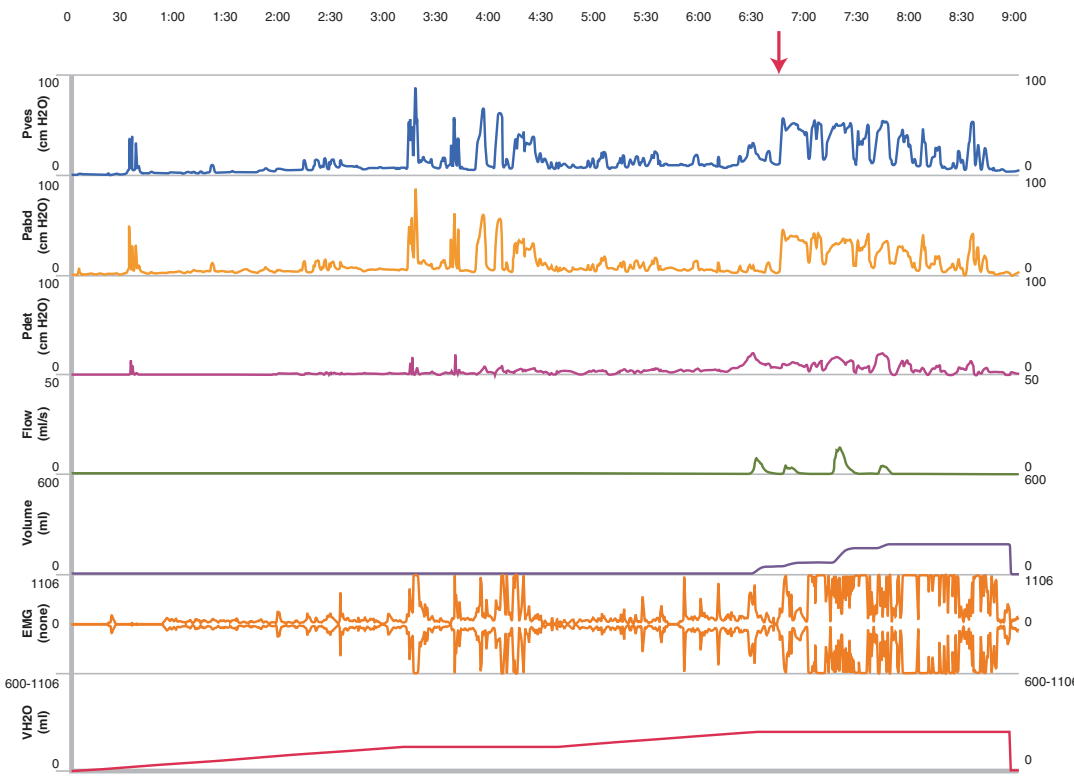

Fig. 8.12 Urodynamic tracing in an elderly female with detrusor hyperactivity and impaired contractility consistent with detrusor hyperactivity with impaired contractility. Note terminal detrusor overactivity just prior to permission to void. After permission (denoted by *red arrow*), she voids primarily by straining and does not generate very high detrusor pressures (From Bacsu et al. [55], with permission)

DHIC may often be misdiagnosed as incontinence resulting from benign prostatic hyperplasia with outlet obstruction, underactive detrusor with chronic retention, and stress urinary incontinence due to intrinsic sphincter deficiency, particularly in women [176]. Incontinence may result from both detrusor overactivity and overflow. Patients present with concomitant storage and voiding symptoms, and predominance of storage or voiding problems is often seen. Accurate diagnosis requires awareness of this condition, careful medical and pharmacological history, with elimination of other disorders that can confound DHIC (e.g., outlet obstruction), physical examination, bladder diary, and video-urodynamics. As DHIC tends to appear in frail individuals living in nursing homes, special attention should be paid for assessment of the patient's mental status and cognitive function in order to plan an appropriate bladder rehabilitation regimen. Simple cystometry may not recognize subtle involuntary detrusor contractions during filling associated with urgency and leakage because of underactive component (poor contractility) of DHIC [176]. Video imaging helps to rule out intrinsic sphincter deficiency (see Chap. 9, "Incontinence Due to Neurogenic Sphincter Deficiency"). Clinicians should also bear in mind that comprehensive diagnostic assessment may become unnecessarily burdensome for these subjects and should balance between accurate diagnostic procedures and patient compliance.

Treatment of DHIC is a challenge for urologists. Management depends on symptom presentation, degree of bother, and urodynamic findings [176]. A conservative approach with behavioral techniques (pelvic floor muscle therapy), lifestyle changes (fluid intake adjustments, prompted

voiding), and management of other medical conditions may help to control reported symptoms. In patients with predominant storage complaints, low dose anticholinergics, or a beta-3 agonist may be initiated with careful monitoring of residual urine [55]. As DHIC affects mainly the elderly, antimuscarinics may substantially impair cognitive function [181]. Anticholinergic burden has also been linked with increased mortality and cardiovascular risk [182]. These effects should be considered in the potential use of a medication for a prolonged duration of time. If predominant symptoms are due to reduced bladder emptying, α blockers may help reduce outlet resistance and improve emptying, particularly in males [150]. In patients with continued high PVR volumes and imminent urinary retention, IC is recommended. However, extremely frail incontinent patients living in nursing homes with irreversibly compromised quality of life are often disqualified from IC and managed with indwelling catheters. Mixed symptoms can be treated with a combination therapy of α blockers and anticholinergics or a beta-3 agonist. A recently published study evaluating SNM in patients with DHIC has shown promising results with satisfactory success rates in treatment of both detrusor overactivity and impaired contractility [183]. At the first stage of SNM implantation, 14 of 20 patients (70%) had a significant treatment response. Among them, 9 patients had a response to both elements of DHIC, 4 had a response to the detrusor overactivity alone, and 1 had a response to the voiding component alone. Despite the results are encouraging, SNM may be less available because most patients suspected of having DHIC are often frail elderly. Another study investigated the efficacy and safety of intravesical onabotulinumtoxinA injection as a minimally invasive treatment option for DHIC [184]. Twenty-one individuals with urodynamically-proven DHIC and 21 age-matched patients with idiopathic overactive bladder with urodynamic detrusor overactivity were treated with intravesical injections of 100 U of onabotulinumtoxinA. The subjective symptom scores improved significantly in both groups with no statistical difference between groups but DHIC patients did not demonstrate a decrease in episodes of urgency and urgency urinary incontinence. The therapeutic efficacy lasted for a mean of 4.9 ± 4.8 months in DHIC patients and 7.2 ± 3.3 months in patients with idiopathic overactive bladder. Even though the incidence of adverse events was comparable between the groups and did not increase in DHIC individuals, authors concluded that the efficacy of intravesical onabotulinumtoxinA injection in DHIC is limited and short-term. When all presented strategies have failed or patients have been disqualified from them, indwelling catheterization or incontinence devices should be considered.

Conclusion (Table 8.2)

Table 8.2 Conclusion

Summary	Level of evidence
Retention due to neurogenic detrusor underactivity (NDU) may be observed in patients with diabetes, previous pelvic surgery or radiation therapy, sacral/infrasacral spinal cord injury (SCI), intervertebral disk prolapse, multiple sclerosis, and Parkinson disease. This condition might also be seen in the acute phase of cerebrovascular accident and traumatic brain/spinal cord injury	2/3
Detrusor-sphincter dyssynergia (DSD) can occur after any trauma or disease below the pons and above the sacral cord. These mainly include: SCI, multiple sclerosis, multiple system atrophy, spinal dysraphism, and transverse myelitis	2/3
Evaluation of neurological patients who present with urinary retention includes a comprehensive medical history, physical examination, bladder/catheterization diary, questionnaires, urinalysis/urine culture, uroflowmetry, post-void residual, renal ultrasound, bladder ultrasound, cystoscopy, computed tomography, magnetic resonance imaging, and urodynamics	4 (Expert opinion)
Urodynamic findings in patients with NDU include detrusor underactivity, reduced bladder sensation, and increased cystometric capacity	2/3
During urodynamics, patients with DSD present with detrusor contractions synchronous with involuntary contractions of the urethral and/or peri-urethral striated muscles	2/3
Treatment of retention due to NDU includes intermittent or indwelling catheterization (transurethral or suprapubic)	1/2
Intermittent catheterization with hydrophilic-coated catheters decreases the risk of urinary tract infection and urethral trauma as well as improves patient satisfaction. Prelubricated catheters have been shown to be superior to conventional polyvinyl chloride catheters	1
Indwelling catheterization is associated with higher risk of complications	3
Although the care and related complications of transurethral and suprapubic indwelling catheters are similar, a suprapubic variant is less traumatic to the urethra and offers the possibility of genital activity with less preparation and fewer complications	3
Sacral neuromodulation has demonstrated its efficacy in treatment of NDU in highly functional spinal cord injured patients	3
Other assisted bladder-emptying techniques (triggered reflex voiding, Valsalva or Credé maneuvers) may deteriorate renal function	4
α-adrenoceptor blockers and parasympathomimetic drugs have demonstrated little success in NDU treatment	3
Intermittent catheterization combined with anticholinergic drugs to reduce detrusor pressures is the most common treatment modality for DSD	2/3
Other medications such as α-blockers and anti-spasticity drugs (benzodiazepines, baclofen, dantrolene) have shown a limited role in the management of DSD	3
Intrasphincteric injection of botulinum toxin type A has been investigated in quadriplegic men unable to perform IC and in patients with multiple sclerosis of both genders. Positive outcomes with reduced bladder outlet obstruction has been shown, but with temporary efficacy	2/3
Sacral neuromodulation has been demonstrated as an effective treatment modality of DSD in incomplete SCI patients without concomitant detrusor overactivity and in individuals with multiple sclerosis	3/4
External sphincterotomy has demonstrated improvement in bladder emptying and stabilization of the upper urinary tract in a majority of operated patients	3

(continued)

Table 8.2 (continued)

Recommendation	Grade of recommendation
An extensive medical history with carefully conducted physical examination followed by other necessary tests and urodynamic study needs to be performed in every neurological patient suffering from retention	Expert opinion
Other necessary investigations should be performed when clinically indicated, based on underlying neurological pathology and patient history, as well as relevant symptoms and signs	Expert opinion
Intermittent catheterization should be employed as a standard treatment for all patients who are unable to empty their bladder	A
Hydrophilic-coated and prelubricated catheters should be used	B
In patients with DSD, intermittent catheterization may be combined with antimuscarinic drugs	C
Patients must be well instructed in how to perform intermittent catheterization	Expert opinion
Indwelling transurethral and suprapubic catheterization should be avoided and considered only in patients with contraindications for intermittent catheterization	B
Other assisted bladder-emptying techniques (triggered reflex voiding, Valsalva or Credé maneuvers) should be avoided	C
Sacral neuromodulation may be considered in highly functional SCI patients with NDU, incomplete SCI patients suffering from DSD without concomitant detrusor overactivity, and in individuals with multiple sclerosis reporting chronic retention due to DSD	C
Intrasphincteric injection of botulinum toxin type A may be considered in quadriplegic DSD men unable to perform intermittent catheterization and in DSD patients of both genders with multiple sclerosis	C
More invasive surgical interventions can be considered only for patients who cannot or do not want to do intermittent catheterization, when other treatment options have failed, or patients present with contraindications for less invasive modalities	C
Although external sphincterotomy using a cold knife has traditionally been a surgery of choice for patients with DSD, laser sphincterotomy may be an appropriate alternative that carries less morbidity with similar efficacy, and thus should be considered	C
External sphincterotomy is contraindicated in women and in men with difficulty in maintaining a condom catheter	C

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Incontinence Due to Neurogenic Sphincter Deficiency

9

Introduction

In the normal healthy lower urinary tract, urinary continence is maintained because the pressure in the urethra exceeds that of the bladder. Intrinsic urethral sphincter deficiency has been proposed as a urethral weakness or low resistance to bladder leakage [1]. Currently, standardization in defining intrinsic sphincter deficiency is lacking, as is a technique with which to measure it; therefore, identifying and comparing different effective treatments for this condition is challenging [2]. Intrinsic sphincter deficiency is usually associated with refractory urinary incontinence and includes neurogenic and anatomical varieties. With underlying neurological disease, this condition can be termed as neurogenic sphincter deficiency (NSD). The treatment for NSD is extremely challenging for urologists and involves methods to improve bladder outlet resistance, such as artificial urinary sphincter, slings, injection of a bulking agent, bladder neck reconstruction, or bladder neck closure. Because each of these methods has its own merits and drawbacks, and no single one is effective for all patients or considered as a real gold standard, clinicians need to carefully analyze which method will be most suitable for the patient.

Epidemiology

The most common cause of incontinence in patients with neurogenic lower urinary tract dysfunction is neurogenic detrusor overactivity (see Chap. 7, "Incontinence Due to Neurogenic Detrusor Overactivity"). NSD is a less common cause of incontinence, so the patient group discussed in this chapter is highly selected. NSD is observed when neurological lesions or injuries appear below the sacral spinal cord leading to denervation of the intrinsic sphincter. These are typically individuals with myelodysplasia, sacral agenesis, sacral/infrasacral spinal cord injury, laminectomy complications, vertebral disk disease, severe pelvic fractures, and nerve injury from resection of low colorectal cancers [3]. Reliable data on incidence and prevalence of NSD in detailed conditions are sparse.

In neurologically impaired patients, intrinsic sphincter deficiency may also occur in non-neurogenic mechanism. Direct injury of the urethral sphincter may derive from chronic indwelling catheterization. An indwelling catheter erodes and damages the bladder neck and/or the external sphincter. As a result, little or no sphincteric function remains [3].

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_9

NSD may also emerge with appearance of complications of neurogenic bladder. In male patients managed with self-intermittent catheterization, membranous urethral stricture that involves the external sphincter can appear during the long-term follow-up. Repair of the stricture with a urethroplasty can damage the external urethral sphincter and reveal latent NSD.

Diagnosis

Medical History

NSD should be suspected based on a careful medical history followed by a precise physical examination. Whereas neurogenic detrusor overactivity presents as urge urinary incontinence, NSD usually appears as stress incontinence. Stress urinary incontinence (SUI) is a condition of involuntary loss of urine on effort, physical exertion, sneezing, or coughing that is often bothersome to the patient and frequently affects quality of life [4]. Patients with SUI related to NSD usually report severe incontinence, often occurring with minimal changes in position [5]. Nevertheless, total incontinence should also raise the suspicion of other concomitant pathology, e.g., urinary-vaginal fistula or an ectopic ureter [6]. Patients should be asked about precipitating events, because any activity with an increase in intra-abdominal pressure can lead to involuntary loss of urine. Incontinence can occur with minimal activity such as walking or rising from a chair. Clinicians should be aware that the amount of urine loss may be out of proportion to the stress [7]. Severity of urinary incontinence, frequency of occurrence, and volume of urine lost should be carefully evaluated. This can be assessed by asking about pad usage, including pad weight, size, number of pads used, and number of urinary incontinence episodes per day. Onset and duration of reported complaints need to be documented. Fluid intake habits should be investigated and patients should be asked how much fluid they drink each day, what type of fluids they prefer, and how many times they void over a 24 h period. Patients should also be questioned about other urological complaints, including storage symptoms (urgency, frequency, nocturia); voiding problems (hesitancy, straining, poor and intermittent flow); post-micturition symptoms (sensation of incomplete emptying, post-micturition dribble); and impaired bladder sensation. Thus, negative responses to queries regarding symptoms of predominant urgency, incomplete emptying, incontinence associated with chronic urinary retention (referred to as overflow incontinence), functional impairment, and continuous leakage in patients with underlying neurological disorder may indicate NSD. Careful assessment of symptoms indicating possible complications (hematuria, dysuria, fever) should be conducted to rule out comorbid pathology such as malignancy, urolithiasis, or urinary tract infection.

After the urologic history, thorough neurologic and medical histories should be obtained. Neurological symptoms related to the underlying neurological pathology should be documented with onset, evolution, and any treatment. Storage symptoms including incontinence may be aggravated by different comorbidities. Furthermore, intrinsic sphincter deficiency may also be caused by non-neurogenic damage to structures that constitute the urethral sphincter mechanism (direct sphincter injury resulting from urethral catheter trauma or previous surgical interventions related to non-neurogenic causes). Stress incontinence may also result from weakness in the supporting tissues of the urethra and leads to urethral hypermobility [8]. Therefore, a carefully conducted medical history should elicit information regarding endocrine disorders (i.e., complicated and poorly uncontrolled diabetes, diabetes insipidus); cardiovascular diseases (volume status or diuretic therapy can increase urine flow and cause incontinence); urological conditions (i.e., urolithiasis, bladder/prostate cancer); respiratory dysfunctions with chronic cough (i.e., chronic obstructive pulmonary disease, chronic bronchitis); fecal motility disorders (constipation or fecal incontinence); chronic pelvic pain; mobility deficits; pelvic cancers; pelvic radiation; mental health disorders; dementia; inability to ambulate; and cognitive impairment. Special attention should be paid to previous extensive or radical pelvic surgery (e.g., radical hysterectomy or prostatectomy), as well as anti-incontinence surgery or

complex urethral procedures (e.g., urethral diverticulectomy or urethrovaginal fistula repair). In women, a thorough obstetric and gynecological history must be obtained to exclude other potential causes of SUI. A general obstetric history with labor duration, mode of delivery, birth weights of children, year of delivery, intrapartum complications (e.g., childbirth-related injuries, obstetric anal sphincter injury, peri-urethral lacerations, wound breakdown), as well as de novo post-partum urinary symptoms (e.g., urinary retention requiring prolonged catheterization or SUI) that may be precipitated by cesarean section, epidural block, or prolonged labur may be necessary for evaluation [9–12]. Pelvic organ prolapse or previous surgery may influence the success of future treatment [13]. Factors that suggest a history of prolapse include prior use of a pessary, dyspareunia, and sensation of vaginal pressure or fullness.

As patients with neurourological symptoms may also suffer from neurogenic bowel and sexual dysfunctions, bowel and sexual histories are important [14, 15]. Bowel history should elicit information regarding pattern and frequency of defecation; length of time to evacuate; rectal sensation; desire to defecate; and possible episodes of fecal incontinence, constipation or defecation initiation (digitation, suppository use) [16]. Sexual history should investigate symptoms of genital or sexual dysfunction, presence of sensation in genital area, lack of desire (loss of libido), difficulty in achieving orgasm, possible dyspareunia in females and erectile dysfunction or ejaculation problems (premature, delayed, retrograde, anejaculation) in males.

In addition, a complete list of the patient's medications (including over-the-counter drugs) should be obtained to determine whether individual drugs might influence the function of the bladder or urethra leading to urinary incontinence. Agents that can exacerbate incontinence include diuretics, alpha-adrenergic blockers, caffeine, and alcohol [7]. Angiotensin-converting enzyme inhibitors (ACEI) may increase coughing, leading to more frequent episodes of incontinence [17]. When appropriate, these agents should be stopped or changed to help manage the patient's incontinence.

A well-conducted medical history should be completed with an assessment of the patient's social situation. Accessibility to care, toileting, and supplies may be limited by financial constraints or other social factors. Family or caregiver support should be determined and the patient's independence should be evaluated.

A proper history should aim not only to diagnose the cause and nature of bladder dysfunction but also to identify associated complications (Chaps. 10–15).

Although medical history is important and useful in screening for those with NSD, it has been shown that patient history is strongly limited in diagnosing this specific pathology [18].

Physical Examination

A comprehensive medical history should be followed by thorough examination. It should begin with a general evaluation of mental status, cognitive impairment, obesity, physical dexterity, mobility, balance, and coordination. Special attention should be paid for mobility, as patients with impaired mobility may not have enough time to reach the toilet before incontinence occurs. Abdominal examination should be carefully and routinely performed. It should rule out diastasis recti, masses, ascites, and organomegaly, which can influence intra-abdominal pressure leading to incontinence [19]. Examination of the back may reveal skin dimples, scar, or hair tuft indicative of spinal dysraphism or the tethered cord syndrome [5]. Pelvic examination should include an evaluation for inflammation, infection, and atrophy, as chemical irritation from urinary or fecal incontinence as well as impaired sensation may substantially contribute to skin damage. Because the urethra and trigone are estrogen-dependent tissues, estrogen deficiency may also contribute to sphincter dysfunction [5]. The most common finding in patients with inadequate estrogen levels is atrophic vaginitis presented as thinning and paleness of the vaginal epithelium, loss of rugae, disappearance of the labia minora, and presence of a urethral caruncle [19]. Pelvic organ prolapse (with cystocele, urethral polyps, or rectocele) often accompanies

atrophic vaginitis [17, 20–22]. The prolapse can also produce a relative obstruction of the urethra that can impair bladder emptying, thus masking or reducing the severity of symptoms. This is referred to as occult, potential, masked, or hidden SUI [23]. With reduced prolapse, SUI may become apparent or worsen [24]. When organ prolapse occurs, it should be documented with recommended methods and standards. In day-to-day clinical practice, it is currently recommended to employ the simplified pelvic organ prolapse quantification system (S-POP-Q) [25, 26]. Sensation within the genitourinary area should be assessed and documented (see Chap. 4, "Medical History and Physical Examination," Fig. 4.1). Digital examination of the rectum with assessment of anal sphincter tone and voluntary contraction should be performed. Evaluation of bulbocavernosal (and other spinal cord-mediated, see Chap. 4, Table 4.4) reflexes is also important. Fecal loading of the large intestine and rectum should be described. Examination of the urethra may reveal diverticula, usually identified as a distal bulge under the urethra. Gentle massage of the area frequently produces a purulent discharge from the urethral opening. In patients with chronic indwelling catheters any abnormalities should be documented. These include traumatic hypospadias in men and bladder neck erosion in women.

As NSD patients typically complain of SUI, this condition should be carefully investigated and documented. Cough stress test objectively demonstrates leakage from the urethra simultaneously with a cough and it is diagnostic of SUI [25, 27]. Of note, negative result of the test (absence of leakage) does not exclude presence of stress incontinence [25, 27]. Delayed fluid loss is considered a negative cough stress test result and should elicit attention of cough-induced detrusor overactivity (see Chap. 7) [23]. The cough stress test is usually performed when the patient has a comfortably full bladder or following retrograde filling to a volume of at least 300 mL [28, 29]. The test can be performed in the supine or standing position. However, if done supinely and the result is negative, the test must be repeated in the standing position with the bladder filled to at least 300 mL [30]. The patient stands while wearing a pad or with his or her legs shoulder-width apart over a cloth or paper sheet on the floor to see the leakage [17]. If no leakage is observed despite patient symptoms of stress incontinence, the health care provider needs to ensure that the patient had a full bladder by measurement of voided urine volume and post-void residual [23]. Moreover, false-negative results may occur if the cough is not forceful enough, if the pelvic floor muscles contract to override urethral sphincter incompetence, or if severe prolapse masks the leakage [25, 31]. In patients with prolapse, the reduction of the prolapse should be performed [24, 27]. Nowadays, it is recommended to perform a cough stress test in all patients initially suspected for stress incontinence [30]. A modification of the cough stress test is the supine empty stress test. After voiding, the patient is placed in the supine position and asked to perform cough and Valsalva straining maneuvers. A positive test is recorded if urethral leakage is observed from the meatus coincident during any maneuver [32]. Although this test has not been found to be reliable nor validated in neurogenic patients, available data suggest that when the result is negative (no leakage), intrinsic sphincter deficiency is less likely to exist [30, 33].

Although NSD has been associated with a fixed, well-supported urethra, in some patients NSD can be present in association with urethral hypermobility. Thus, SUI due to NSD may be additionally aggravated. Urethral hypermobility refers to the excessive downward displacement of the urethra during Valsalva [25]. The Q-tip (cotton swab) test has been proposed to quantitate objectively the degree of urethral hypermobility. It is performed by inserting a lubricated cotton tipped swab into the urethra to the level of the urethrovesical junction of a patient in the lithotomy position (Fig. 9.1) [34]. Then, the angle of the swab compared with horizontal is assessed. Next, the patient coughs or strains, and the change in the angle of the swab is noted [25, 35]. Hypermobility is defined as a Q-tip angle of more than 30° from horizontal [35]. Clinicians should be aware that Q-tip test is not standardized or reproducible, since there is no control of the

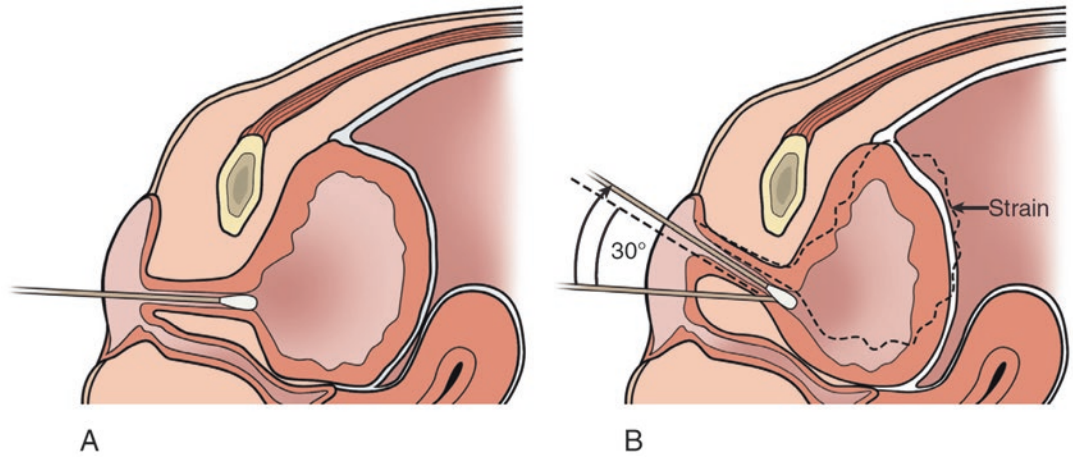

Fig. 9.1 Cotton swab test to assess urethrovesical junction mobility. (**a**) Cotton swab at rest. (**b**) Cotton swab with strain (Valsalva). The urethrovesical junction descends, causing upward deflection of the Q-tip (From Dell [34], with permission)

Fig. 9.2 The Bonney test

amount of pressure generated when the patient strains [5].

Manual urethral support may help to distinguish between intrinsic sphincter deficiency and urethral hypermobility (descent of the bladder neck). The test, known as the Bonney test, manually supports the anterior vaginal wall, correcting urethral hypermobility (Fig. 9.2) [5]. The goal of the test should not be to elevate the anterior vaginal wall but to prevent its descent. The index and middle fingers are placed on both sides of the urethra to support the bladder neck. If no urine leaks on stress, incontinence seems to be caused by descent of the bladder neck. If urine still leaks, incontinence due to intrinsic sphincter deficiency is highly suspected. However, there is a tendency to occlude the urethra simultaneously with correction of urethral hypermobility. The use of a ring forceps instead of fingers may lower the risk of this occlusion. Similarly to the Q-tip test, the Bonney test is not standardized or reproducible, and absence of urine leakage does not exclude intrinsic sphincter deficiency.

More recently, Thubert et al. have described a simple clinical test that involves gentle downward traction of the posterior vaginal wall provided by a split speculum performed with the bladder filled with 400 mL of saline in a supine position [36]. A positive test (leakage demonstrated during the procedure) was shown to correlate with intrinsic sphincter deficiency (defined as maximal urethral closure pressure <20 cm H_2O) with a positive predictive value of 94.67%. Note that the test has not yet been validated in neurological patients.

In neurologically impaired patients who present with SUI, assessment of pelvic floor muscle strength should also be conducted. It can easily be performed by instructing the patient to squeeze (contract) their pelvic floor muscles and then vaginally palpating the effect [30, 33].

Clinicians should not forget about pulmonary and cardiovascular assessment in patients suspected of SUI due to NSD. The pulmonary examination should rule out any possible cause of chronic cough. The cardiovascular examination should look for evidence of volume overload (edema) that might lead to increased urine flow and aggravate incontinence.

Other Recommended and Elective Tests

A bladder diary can provide an accurate record of urinary output, average voided volume, frequency of voiding, frequency and nature (precipitating events) of incontinent episodes, as well as type and volume of fluid intake. Evaluation of symptoms and assessment of impact on quality of life can be facilitated by the use of validated questionnaires, both condition-specific instruments and general validated questionnaires. Urinalysis and/or urine culture are vital to assessing the incontinent patient with neurogenic lower urinary tract dysfunction and should be obtained to rule out urinary tract infection, hematuria, proteinuria, and glycosuria. Blood chemistry, including assessment of serum creatinine level, helps to evaluate the patient's overall condition. The pad-weighing test helps to assess the severity of incontinence. Upper tract studies must also be considered in high-risk patients, specifically those with spinal cord injuries and spina bifida. Post-voiding residual volume, free flowmetry, bladder ultrasound, cystoscopy, computed tomography, magnetic resonance imaging, nuclear renogram, and voiding cystourethrography should be performed when clinically indicated, based on patient history as well as relevant symptoms and signs. Details regarding discussed tests are presented in Chap. 7.

Urodynamics

Urodynamic testing provides objective data of NSD. Low maximal urethral closure pressure (MUCP) (<20 cm H_2O) and low abdominal leak point pressure (ALPP) (<60 cm H_2O) are commonly used as indicators of intrinsic sphincter deficiency [8, 37–40]. Physicians should bear in mind that it is difficult to make these values absolute cutoffs, thus discrepancies in the literature do exist [38]. Furthermore, there is a lack of true consensus on methodologies for measuring MUCP and ALPP [40]. The value of MUCP depends on the type, size, and rigidity of the urethral catheter, patient position, bladder volume, withdrawal speed, and rate of infusion if fluid-perfused catheters are used, and orientation of urethral sensor(s) if micro tip catheters are used [41]. The measurement of ALPP depends on patient position, bladder volume, size of any catheter in the urethra used to measure intravesical pressure, baseline pressure used, speed of response in detecting leakage from the meatus, and how the patient increases abdominal pressure [42].

The high-pressure zone of the mid-urethra produces MUCP. If this area is deficient, incontinence may occur. MUCP is the maximum difference between the maximum urethral pressure and the intravesical pressure [4]. Typically, MUCP is measured at rest, as opposed to ALPP, which is measured during an increase in intra-abdominal pressure and simulates the real world scenario that leads to leakage [38].

ALPP is the intravesical pressure at which urine leakage occurs due to increased abdominal pressure in the absence of a detrusor contraction [4]. ALPP can be induced either by cough (cough leak point pressure) or by Valsalva (Valsalva leak point pressure). It has been shown that cough leak point pressure is typically larger than the Valsalva leak point pressure, and the latter parameter demonstrates less variability in provoking SUI [43, 44]. Therefore, some experts suggest that Valsalva maneuver is more reliable for assessing intrinsic sphincter deficiency than cough [8]. Of note, a recently published update of *Good Urodynamic Practices and Terms* by the International Continence Society introduced the single term "leak point pressure" [45]. The leak point pressure (LPP) is the pressure (spontaneous or provoked) that has caused fluid to be expelled from the bladder at the moment that it is visible outside the urethra (may also be used for extra-

urethral urine loss or stoma). This may refer to abdominal, cough or Valsalva leak point pressure. Provocation and pressure recording site ("type of LPP") should be reported. Intravesical volume can affect the LPP measurement if it is either too high or too low. It is recommended to assess the LPP for the first time at a bladder volume of 150 mL and then re-test at volumes of 200–300 mL [39, 46]. Re-testing can be performed every 50–100 mL until SUI is elicited and a combination of cough and Valsalva can be used to reproduce signs of urinary leakage [47].

As SUI can also be caused by urethral hypermobility, urodynamics may help to distinguish between intrinsic sphincter deficiency and urethral hypermobility. It has been proposed that ALPP of 60 cm H_2O or less indicates a significant degree of intrinsic sphincter deficiency, whereas ALPP of 90 cm H_2O or more is usually associated with pure urethral hypermobility. ALPP values between 60 and 90 cm H_2O form a gray area in which hypermobility and intrinsic sphincter deficiency usually coexist [48].

Video-urodynamics gives a more precise view of the bladder neck during filling and voiding. Many authors consider video-urodynamics as an optimum method for the diagnosis of intrinsic sphincter deficiency (leakage without urethral hypermobility), particularly in neurological patients [8]. Observation of an open bladder neck and proximal urethra seen on video imaging may be of value for proper diagnosis of NSD [40, 49]. Fluoroscopy can also be used to capture images during urinary leakage of small amounts, undetectable with conventional urodynamics. However, additional costs and the requirements of radiological equipment make this test impractical or even unavailable at some centers.

Figure 9.3 presents an example of urodynamics in a patient with NSD [47].

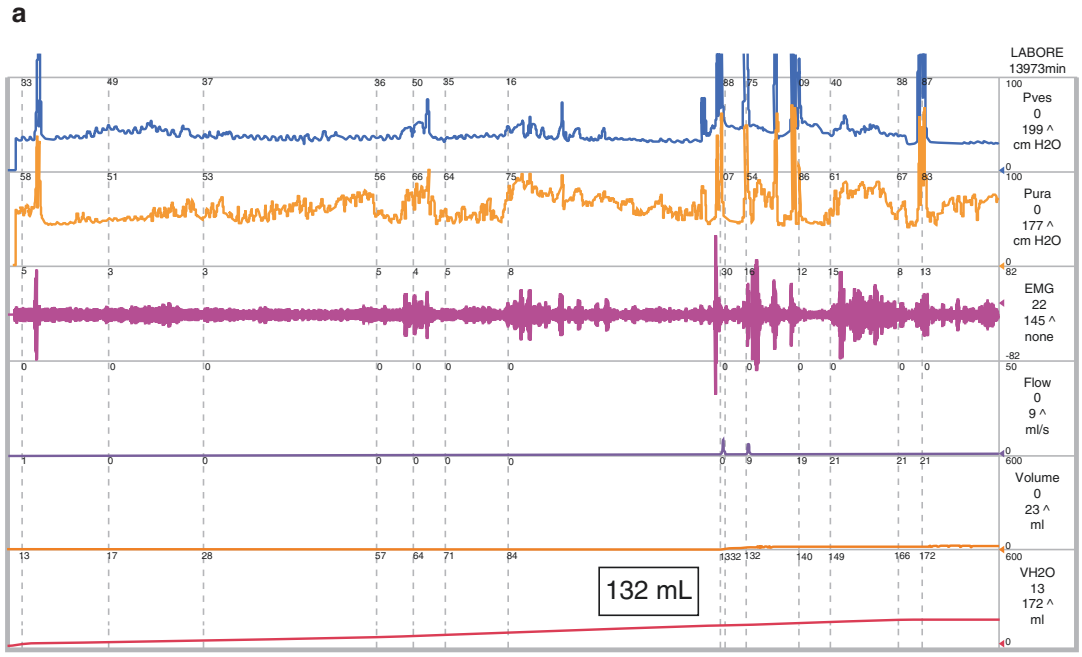

Fig. 9.3 Urodynamics of a patient with persistent urinary incontinence due to neurogenic sphincter deficiency. (**a**) The tracing shows stress urinary incontinence with provocative maneuvers at a volume of 132 mL. At this volume, the patient has a Valsalva leak point pressure (LPP) of 44 cm H_2O and a cough LPP of 102 cm H_2O [(**b**) portion of urodynamics tracing from (**a**) showing stress urinary incontinence]. There were no involuntary detrusor contractions. Fluoroscopy images showed an open bladder neck, both at rest and during leakage [(**c**) an open bladder neck during leakage of urine] (From Suskind and Clemens [47], with permission)

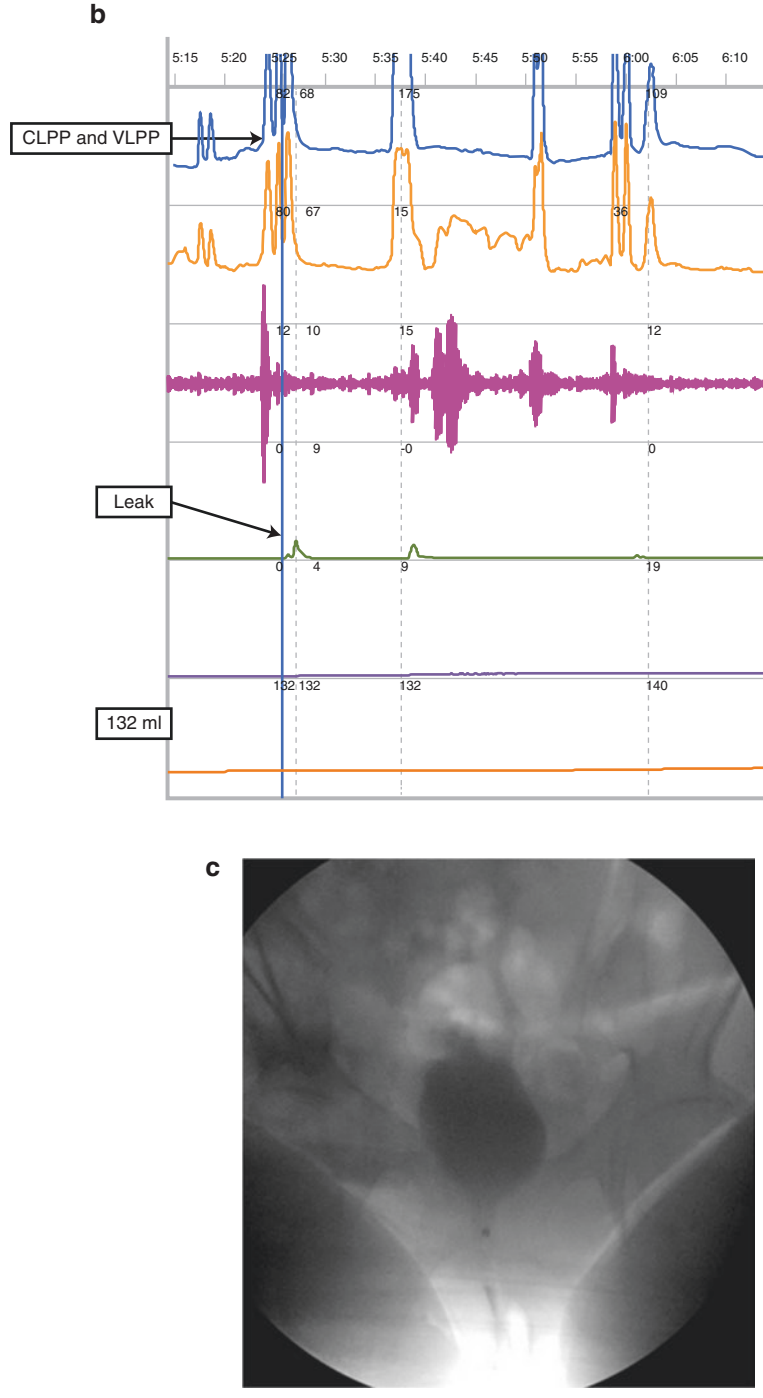

Fig. 9.3 (continued)

Treatment

Conservative Treatment

Pelvic Floor Muscle Therapy Pelvic floor rehabilitation is the conservative therapy of SUI. Although well-conducted studies of neurologically impaired patients are few and far between, such treatment should be considered, as it is cheap, widely available, and rarely complicated. This might sometimes require support from caregivers and health-care professionals to be successful. It is also beneficial to introduce this treatment in conjunction with education about lower urinary tract function for the patient and/or their family members and carers [50]. Thus, some aspects of these techniques are described in Chap. 17, "Patient Education."

Pelvic floor muscle therapy aims to strengthen and to improve the functional activity of the pelvic floor muscles, which ameliorates the symptoms of SUI [51]. A recently published study on standardized pelvic floor exercises (12-week course) for improvement of SUI in women with intrinsic sphincter deficiency has shown that this specific group of patients benefits subjectively and objectively from this modality [52]. However, authors of this paper did not reveal the underlying causes of intrinsic sphincter deficiency. A study by McClurg et al. demonstrated concurrent results in patients with multiple sclerosis suffering from SUI [53]. It is clear that physiotherapy cannot be universally applied but may be taken into account in willing patients with an ability to contract the pelvic floor muscles since it has no deleterious side effects. Individual therapy in pelvic floor rehabilitation is a necessity and should be tailored to the patient's capabilities.

Surgery

The surgical approach for NSD aims to increase the bladder outlet resistance but may also cause high intravesical pressure. Therefore, surgery is recommended when the detrusor activity can be controlled and when no significant vesicoureteral reflux is present [16]. Regardless of the type of procedure, simultaneous or delayed bladder augmentation and intermittent catheterization may sometimes be necessary. A recent meta-analysis, evaluating all surgical treatment options for neurogenic SUI, demonstrated that in neurogenic individuals complication rates and reoperation rates are higher and success rates are lower compared to non-neurogenic patients [54]. Artificial urinary sphincter (AUS) had the highest percentage of success, followed by urethral sling procedures, compared to the urethral bulking agents, which reported the highest rate of failure.

Artificial Urinary Sphincter Whereas post-prostatectomy incontinence is the main indication for implantation of AUS, SUI due to NSD can also be treated with this modality. AUS is advocated by many authors as primary or secondary treatment of neurogenic patients who have failed other forms of bladder outlet surgery [55, 56]. The device comprises a compressive urethral cuff, an intra-abdominal pressure-regulating balloon, and a pump (intra scrotal or labial) to enable patients to deflate the cuff when they wish to void (Figs. 9.4 and 9.5) [57, 58]. The pump temporarily transfers the fluid from the cuff to the reservoir in order to open the urethra and void. AUS helps patient to void spontaneously, in contrast to a sling or reconstruction of the bladder neck, which both create a fixed outlet resistance with a higher risk of retention [3]. Available data report that almost 50% of patients after AUS placement are able to void adequately without retention-related complications or need for additional treatment such as intermittent catheterization [59]. Nonetheless, treatment of neurogenic individuals is not strongly supported by current literature. The majority of studies investigated children and adolescents with myelomeningocele and showed promising results with an overall success rate of up to 80% [59–63]. A study of Fulford et al. analyzed 68 patients (34 with NSD, median age 26 years, range 8–76) who underwent AUS implantation and showed that up to three-quarters of them achieved satisfactory continence [64]. Another study of 90 individuals with NSD (mean age 26 years, range 13–62) achieved continence in 92% of patients [65]. A retrospective analysis

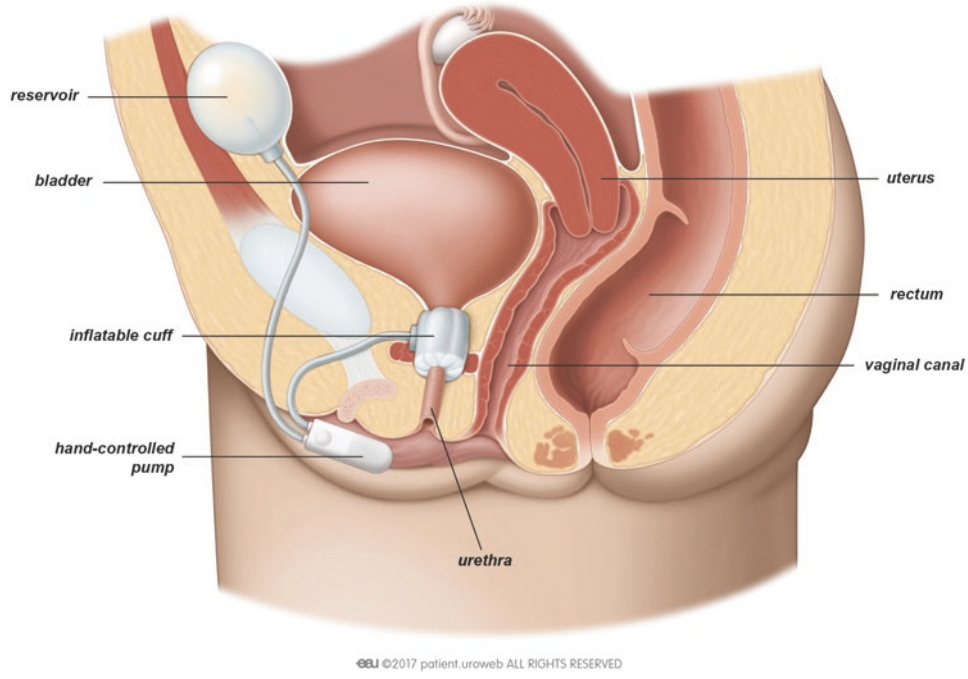

Fig. 9.4 AUS implantation in the female lower urinary tract (Courtesy of the European Association of Eurology [57], with permission)

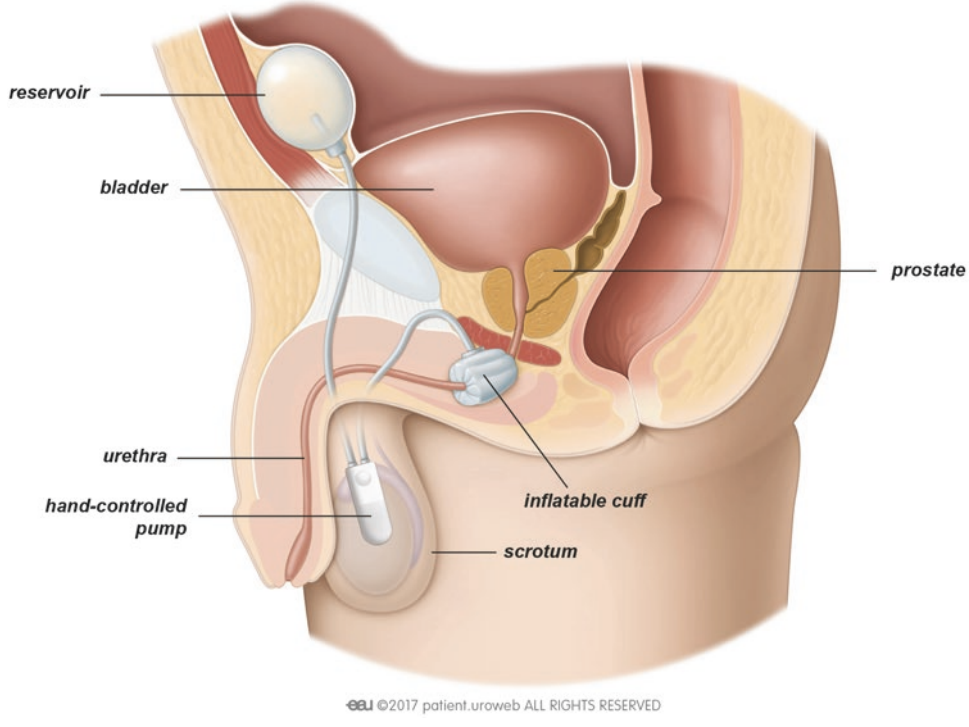

Fig. 9.5 AUS implantation in the male lower urinary tract. Of note, in neurogenic patients, it is recommended to place the cuff around the prostate, close to the bladder neck (Courtesy of the European Association of Eurology [58], with permission)

of 51 adult neurogenic male patients demonstrated that 74% of them had perfect or moderate continence [66]. Currently, AUS is considered as the gold standard for the treatment of SUI, demonstrating a high efficacy of 23–100% (mean 70%) in restoring urinary continence in neurogenic patients [67]. However, randomized clinical trials are actually lacking and the majority of available data for adults refers to male patients [2, 8].

AUS should be considered in particular for NSD patients with good bladder capacity, proper bladder compliance, no indications for augmentation cystoplasty, spontaneous voiding without the assistance of a catheter, adequate manual efficiency and dexterity, as well as intellectual ability and adequate cognitive function to operate the device [3, 68]. Pre-operative endoscopic evaluation is highly recommended, as unrecognized urethral pathology can complicate surgical implantation and possibly affect expectations of long-term outcomes.

Nowadays, the most frequently implanted AUS worldwide is the AMS800 device (Boston Scientific, Marlborough MA, USA) (Fig. 9.6) [69]. A recently conducted consensus conference on AUS developed the recommendations regarding indications, management/implantation, and follow-up/revision of AMS800™ [70]. Report of this conference with well-developed guidelines undoubtedly constitute a reference document and can substantially help urologists in their day-to-day clinical practice.

Fig. 9.6 AMS 800 urinary control system (Courtesy of Boston Scientific [69], Marlborough MA, USA, with permission)

Authors of this comprehensive document reported that pre-operative prophylactic antibiotics should be administered within 60 min of the incision. Moreover, all efforts should be made to ensure low bacterial counts at the time of AUS placement. All infection sites, including the urinary tract, should be treated before the procedure, to protect the operative field from potential bacterial contamination [71]. Skin bacterial counts should also be lowered with immediate pre-operative skin preparation. Surgery for AUS implantation may be performed either in lithotomy or supine position. Surgeons should be permitted their choice of razors or clippers for pre-operative preparation of the male genitalia. Then, skin preparation with chlorhexidine-alcohol (superior to povidone-iodine) needs to be performed. Furthermore, 5-min pre-operative, topical antimicrobial scrub is recommended. The perineal incision is preferred for AUS cuff placement but in some patients with spine or limb deformities or neuro-motor conditions, the transscrotal incision may be a useful alternative to perineal cuff placement. Urethral dissection should be performed sharply with direct visualization, confirming the integrity of the urethra. There are two implantation approaches, periurethral and trans-corporal. Whereas the first is considered as the standard approach, the second may be considered under certain circumstances, such as patients presenting with a history of previous urethral surgery or in those with urethral abnormalities. After dissection, the surgeon determines the proper cuff size to be used by measuring the circumference of the tissue around the urethra or bladder neck. If the measurement is between sizes, the larger size should be chosen. In neurological patients, the majority of available studies prefer placement at the bladder neck (in male around the prostate) rather than bulbar urethra [3]. Bladder neck placement can reduce the risk of AUS damage when rigid cystoscopy has to be performed due to complications of neurogenic bladder. As neurological patients frequently need

additional intermittent catheterization, AUS location at the bladder neck has been reported to limit the risk of urethral erosion in the context of long-term intermittent catheterization [72]. Moreover, in wheelchair-bound individuals, extended sitting may produce elevated pressure on the bulbar urethra, increasing the risk of erosion due to decubitus ulcers when the cuff is placed in this area. A study of 51 males with NSD who underwent AUS implantation with cuff placement at the bladder neck reported satisfying results in the majority of patients [66]. After implantation, prosthesis may be filled with either sterile saline or contrast filling solution. A pressure-regulating balloon of 61–70 cm H_2O is most often used but in patients with bladder neck cuff, the 71–80 cm H_2O pressure-regulating balloon may be preferred, depending on surgeon preference. The pressure-regulating balloon should be filled with 22–27 cc fluid while the cuff is empty. After filling, the pressure-regulating balloon must be placed under the abdominal wall fascia and may be inserted into the retro-pubic space or into a space created between the abdominal musculature and the transversalis fascia. The next step involves pump placement in the dependent portion of the scrotum, anterior to the testicle, to ensure that patients can access it postoperatively. When all components have been implanted, the required connections need to be made. Use of the AMS Quick Connect (Boston Scientific, Marlborough MA, USA) in all AUS placement is recommended. The final stage of AUS implantation involves inspection of the urethra for potential injury and intra-operative assessment of efficacy. The device should be cycled several times under direct visualization to ensure adequate function of the hydraulic mechanism. Postoperative care includes short-term catheterization (less than 14 Fr, removed after a brief period, usually overnight), oral analgesia, and/or stool softener, as well as proper education of physical activity and lifting (limited physical activity during the 6-week postoperative period). Standard administration of postoperative antibiotics is not currently recommended. AUS should be activated at 4–6 weeks post-implantation. Physical long-term follow-up should be ensured between 3 and 6 months postoperatively and periodically thereafter, at least yearly. Mandatory evaluation should include assessment of symptoms consistent with device malfunction, infection, and/or erosion.

For neurologically impaired patients, modified implantation techniques have been proposed. One proposal, investigated in patients after spinal cord injury, suggested that pump replacement with a subcutaneous port enables adjustment of the cuff pressure also postoperatively and omits the necessity to repetitively activate the pump. During 8-year follow-up, this modification proved to be successful, reliable, safe, and cost-effective [73]. Nevertheless, this technique remains a single center experience on 51 patients. The second proposal, with the AUS cuff placement at the bladder neck without implantation of both the reservoir and the pump, achieved only 31% continence rate [74]. Recent studies also report the feasibility of implanting the AUS using the da Vinci robot [72]. Although these modifications may help to achieve better results, they cannot be recommended for daily clinical practice.

It has been shown that individuals with neurogenic lower urinary tract dysfunction have higher numerical complication rate vs. post-prostatectomy patients [75]. Possible complications include erosion (cuff erosion into the urethra and pump erosion into the scrotum/labia), urethral atrophy, infection, and mechanical/device-related failure leading to reoperation with revision, replacement, or removal in 7–100% of implanted cases [67]. Specific complications of AUS placement in a group of neurogenic patients, mainly because of retro-pubic and bladder neck dissections, may also include bladder neck, urethral, and rectal perforations [60, 65]. The mean reoperation rate for the AUS has been estimated as 51%, which is a relatively high percentage in comparison to the reoperation rate of 27% in non-neurogenic patients [54]. AUS erosion is the major cause of AUS removal in a contemporary neurogenic bladder series, with a reported rate from 6 to 31% [61, 76]. AUS removal resulting from sphincter infection has been found to be more frequent (up to 8%) in neurogenic than in non-neurogenic persons [73]. If AUS infection is suspected, cystourethroscopy should be undertaken to evaluate the urethra for cuff erosion. In gross or persistent infections, the entire device

should be explanted as soon as it is clinically safe [70]. Note that the AUS infection rate does not appear to increase in patients who catheterize compared to those who void spontaneously or who empty their bladders with the Credé maneuver [77]. However, intermittent catheterization frequently leads to high-level erosion due to repeated urethral traumas [60, 78]. This emphasizes the importance of proper patient education with the catheterization technique preceded by the AUS deactivation procedure. In some patients, simultaneous augmentation cystoplasty should be considered and can be done safely at the time of AUS implantation [3].

It is currently recommended that neurogenic patients who receive AUS must undergo long-term urological follow-up with UDS monitoring and upper tract imaging to detect upper urinary tract deterioration [70]. A potential risk of AUS placement in patients with NSD is the new onset of detrusor overactivity. This complication occurs frequently, in about 30% of patients after AUS insertion, and the onset may be delayed by several years [79]. Studies reported that 4–42% of AUS recipients with neurogenic lower urinary tract dysfunction may eventually require augmentation cystoplasty [60, 76, 80]. This stresses the need for lifelong surveillance with urodynamic control after AUS placement in patients with NSD [80].

A median AUS lifespan is about 5–7 years [81–83]. Since people with neurogenic lower urinary tract dysfunction are often comparatively young, AUS should be considered with caution in young individuals, as it is highly probable that AUS replacement will be needed [49]. Because each revision requires replacement of the AUS cuff to a different location along the urethra, lifetime management with the AUS may not be possible if implemented in relatively young patients [3].

Slings The flash point of the sling procedure is to increase the bladder outlet resistance by compressing the urethra. As AUS implantation in neurogenic patients has a high complication rate and cannot be considered lifelong management, sling implantation has the potential of long-term durability. A recent meta-analysis revealed that AUS has higher reoperation rates when compared to urethral sling placements [54]. On the other hand, the patient cannot expect to spontaneously void, and intermittent catheterization is almost universally needed [3].

In a population of neurogenic patients, sling implantations have been mainly reported in children with spina bifida. Multiple studies on autologous fascial slings showed its effectiveness in the treatment of urinary incontinence due to NSD [84–88]. Although the evidence for sling procedure is limited in the adult neurogenic population compared to children, there are several studies reporting positive outcomes [3]. It has been shown that up to 90% of adult females suffering from incontinence due to NSD reported satisfaction after treatment with pubovaginal autologous fascial slings [89, 90]. However, those completely dry usually had to start intermittent catheterization. The data are sparse in male neurogenic patients treated with puboprostatic sling repair (the sling is passed around the bladder neck in a plane between the seminal vesicles and the bladder neck) [3]. The results of a study of 13 men treated with bladder neck slings reported total dryness with intermittent catheterization in 9 (69.2%) patients, improved continence in 2 (15.4%), and complete failure in 2 [91]. Those completely dry and with improved continence had a rectus fascial sling. The two failed patients underwent placement of synthetic slings and both experienced urethral erosion necessitating eventual transurethral excision. A subsequent study with rectus fascial slings in 12 adult men reported an overall success rate of 83% with 8 patients completely dry between catheterizations and 2 with significant improvement and only a minimal leakage [92]. Although the initial use of autologous slings showed continence improvement, the operative morbidity and complications of harvest site pain and infection are strong limitations of this treatment [93].

Currently the majority of procedures with autologous slings have been replaced by retropubic (tension-free vaginal tape, TVT) or transobturator (TOT) mid-urethral synthetic slings (Figs. 9.7 and 9.8) [57]. The placement of synthetic slings at the mid-urethral level is based on anatomical and pathophysiological studies [94].

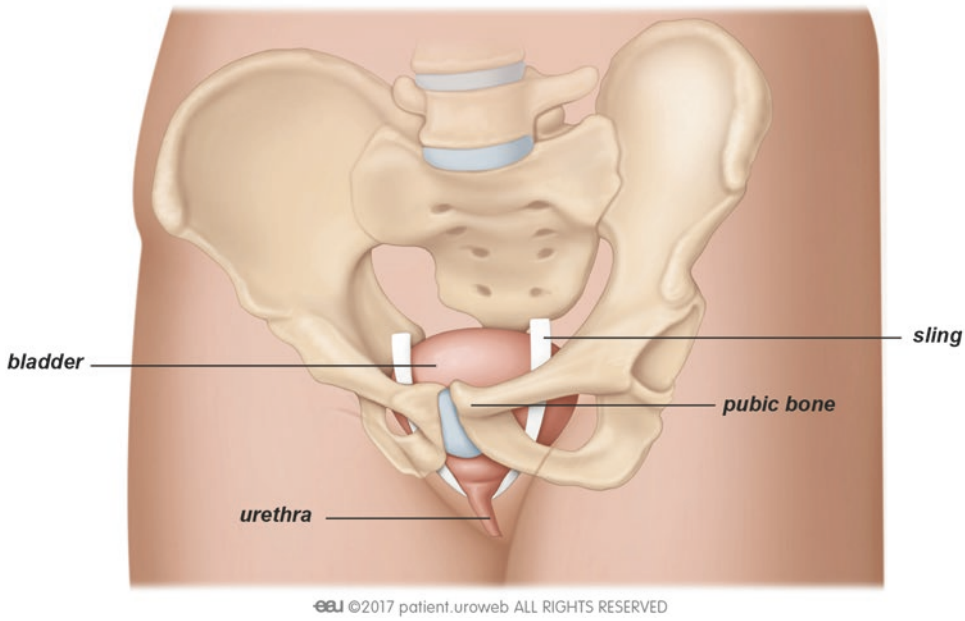

Fig. 9.7 A retropubic (tension-free vaginal tape, or TVT) female sling. The ends of sling are attached just above the pubic bone (Courtesy of the European Association of Eurology [57], with permission)

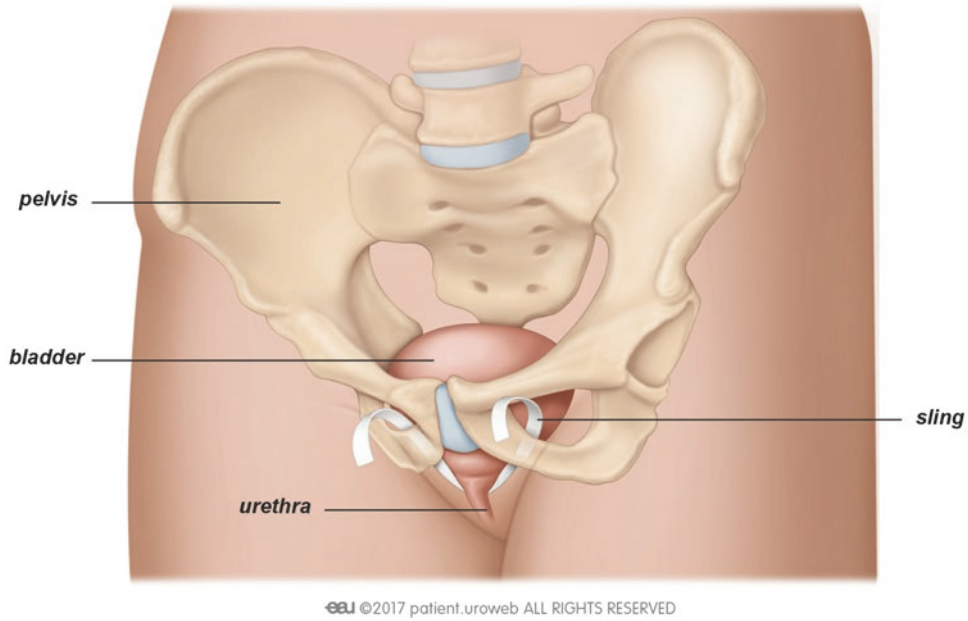

Fig. 9.8 A transobturator (TOT) female sling. The ends of sling are attached to tissue around the groin (Courtesy of the European Association of Eurology [57], with permission)

Synthetic slings are considered to be the standard treatment for SUI in non-neurogenic patients [30]. In males, mid-urethral synthetic slings have been used to treat mild to moderate post-prostatectomy incontinence (Figs. 9.9 and 9.10) [58, 95, 96]. However, reports on neurological

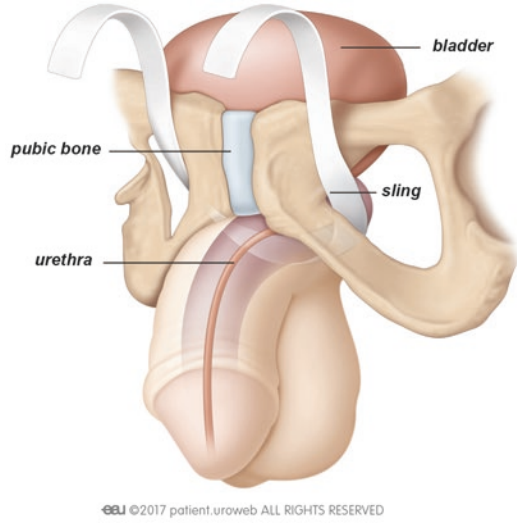

Fig. 9.9 A common type of retropubic two-armed sling. In two-armed slings, the ends of the sling are put in position on both sides of the urethra, shaping the sling like a hammock. Then, the ends of the sling are attached to tissue either just above the pubic bone, or around the groin (Courtesy of the European Association of Eurology [58], with permission)

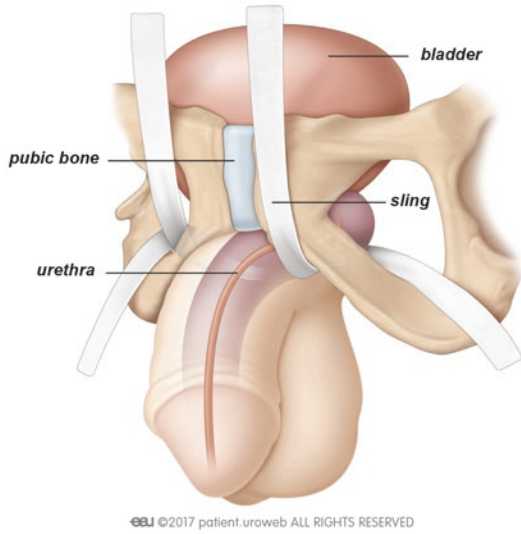

Fig. 9.10 A common type of four-armed sling. In four-armed slings, two ends of the sling are attached to the groin, while two others are attached to tissue around the pubic bone (Courtesy of the European Association of Eurology [58], with permission)

patients with NSD treated with syntetic slings are few and far between. A study on long-term outcomes of treatment with a TVT for female NSD has shown encouraging results [97]. Twelve women (mean age 53.3 years, range 41–80) were treated with a TVT and monitored for 10 years. At 10 years follow-up, three patients were lost from observation, seven were completely dry, and the remaining two were improved and satisfied with using one or two pads/day. Two patients showed neurogenic detrusor overactivity confirmed on video-urodynamics, with no evidence of SUI. All patients were using bladder-emptying techniques (suprapubic compression or intermittent catheterization). Importantly, all patients also before surgery had performed bladder drainage techniques. These results also compare favorably to previously reported success rates with a TVT during short-term follow-up [98]. A recently published analysis compared efficacy and safety of TVT to pubovaginal sling in treating SUI in women with lower motor neuron lesions [99]. The study evaluated 40 women: 20 TVT and 20 pubovaginal sling. Authors demonstrated comparable treatment outcomes in both groups with cure rates of 80% for TVT and 85% for pubovaginal slings. Interestingly, while all patients operated on for pubovaginal slings had PVR >150 mL after surgery and required intermittent catheterization, eight patients (53%) in the TVT group had PVR <150 mL and did not require intermittent catheterization after surgery. Of the remaining 12 patients in the TVT group, five were using intermittent catheterization before surgery and seven had de novo increased PVR (PVR >150), thus requiring intermittent catheterization after surgery. Authors concluded that de novo postoperative intermittent catheterization after TVT can be avoided in 50% of patients.

One study reported long-term outcomes of treatment with TOT for female NSD and showed concurrent results [100]. Twenty-seven patients (mean age 56 years, range 30–82) were observed for mean follow-up of 5.2 years. Twenty-two patients (81.5%) reported complete dryness after surgery. One patient reported incontinence only when her bladder was very full, but was satisfied. Those patients (85.2%) were happy with treatment outcomes. Four patients (14.8%) remained wet. Twenty-five patients (92.6%) had no change in bladder management after the procedure. Two out of five patients (40%) who voided by

straining prior to surgery required clean intermittent self-catheterization postoperatively. Two patients developed de novo detrusor overactivity. Interestingly, the results are comparable to those achieved in the general population undergoing TOT surgery [101–104].

In view of the above reported findings, TVT/TOT may be considered safe and effective with good medium/long-term outcomes in neurogenic females suffering from incontinence due to NSD. This treatment modality might be of benefit to NSD women who have good voiding function with PVR <150 mL and do not require intermittent catheterization at baseline. Patients should be carefully informed about the possible risk of intermittent catheterization, particularly those who void by straining pre-operatively [100].

There is a paucity of data on synthetic sling procedures in neuropathic male patients with NSD. One study evaluated feasibility, efficacy, and safety of the AdVance male sling (Boston Scientific, Marlborough MA, USA) in 20 consecutive neuropathic males. Positive effects were reported in 13 patients at 1-year follow-up (8 patients were cured, 5 improved) and 7 failed. Authors concluded that an acceptable outcome and high patient satisfaction for this minimally invasive treatment option are feasible [105]. A recently published retrospective analysis evaluated 13 males after spinal cord injury who received a TOT and 3 who underwent implantation of a retropubic adjustable system (Fig. 9.11) [58, 106]. In the TOT group, 9 patients became continent, 1 patient was improved, and 3 patients remained unchanged. In the group treated with the adjustable system, no patient improved, and 2 out of 3 had to undergo device extraction due to severe infection. Another study evaluated the use of four different types of slings in 20 neuropathic men [107]. The overall success rate was only 29%, and 7 patients presented with either new onset of low-compliance bladder ($n = 5$) or detrusor overactivity ($n = 2$). In addition, 30% of patients underwent sling removal due to either infection or wound breakdown.

Based on these findings, synthetic sling implantation may be an effective minimally invasive treatment option in carefully selected males suffering from incontinence due to NSD.

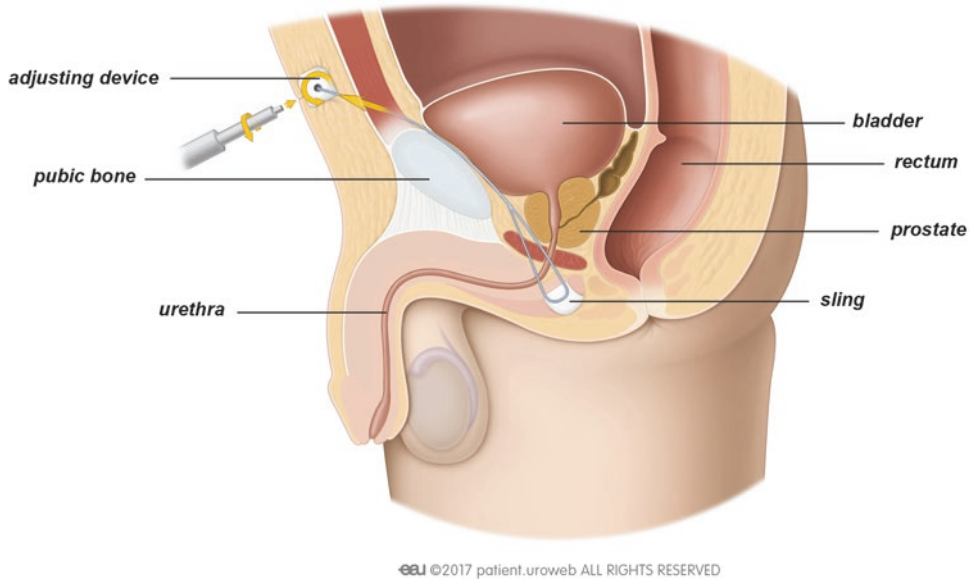

Fig. 9.11 A common type of adjustable sling. Several adjustable systems exist and each type of sling has specific characteristics, results, and possible complications (Courtesy of the European Association of Eurology [58], with permission)

TOT seems to be a promising, minimally invasive surgical modality with acceptable success rates and tolerable complication rates. However, the selection criteria for the appropriate patients have to be defined, and long-term results are currently unavailable. Prospective long-term studies are required to reliably support clinicians in their daily clinical practice. Male patients who void spontaneously pre-operatively (similarly to females) may need to perform intermittent catheterization postoperatively and should be carefully counselled that there is an increased likelihood of dependence on intermittent catheterization after sling insertion.

Possible exacerbation of bladder dysfunction after sling placement needs to be further acknowledged. Neurogenic detrusor overactivity may be worsened or sling implantation might result in de novo detrusor overactivity, possibly due to the activation of the voiding reflex by stimulation of the afferent receptors in the proximal urethra [100, 108]. Rates of de novo detrusor overactivity in the general population after mid-urethral sling surgery are reported to be as high as 15% [109]. Available data for neurologically impaired patients are sparse. Interestingly, preliminary results show that the incidence of overactive detrusor after sling treatment in neurogenic patients is within acceptable limits [100]. The lifelong surveillance with urodynamic monitoring still needs to be implemented after surgical treatment of NSD (even with a minimally invasive approach), since the long-term effect of this bladder outlet procedure has not been extensively investigated in neurogenic patients. Some experts suggest that individuals with obvious detrusor overactivity or low compliance should undergo pressure-decreasing surgery prior to sling implantation [105].

Potential intra-operative complications of sling implantation include bleeding and urethral/bladder injury [110]. The overall risk of complications related to surgery for non-neurogenic SUI is considerably lower with the transobturator approach than with the retropubic variant [111]. Early postoperative complications include storage and voiding dysfunction, retention, infection, extrusion, and pain. Clinicians should also remember that excessive tape tensioning may prohibit the continued successful performance of intermittent catheterization postoperatively, requiring tape incision to relieve bladder outlet resistance. It is particularly important to tension the tape judiciously in order to minimize a disturbance in postoperative voiding function. Late postoperative complications include extrusion (vaginal exposure), erosion (mesh inside lower urinary or gastrointestinal tract), storage/voiding dysfunction, retention, and recurrent urinary tract infections.

Bulking Agents Endoscopic treatment of SUI in patients with NSD involves the injection of implantable bulking materials at the bladder neck or posterior urethra in order to increase bladder outlet resistance [3]. The bulking agent is injected as a liquid and hardens into a spongy material (Fig. 9.12) [58]. Bulking agents can be made of synthetic materials (e.g., bovine collagen, dextranomer/hyaluronic acid, polydimethylsiloxane, carbon) or human tissue.

Peri-urethral injections with bulking agents for NSD-related incontinence have been used with mixed results, often showing short-term improvement, but long-term results tend to be poor [3, 112]. The majority of studies have been performed within the pediatric population [113–119]. Studies of injectable agents in adults with incontinence due to NSD are limited. A study of six adult females suffering from NSD-related incontinence showed positive results [120]. At limited follow-up, all women achieved complete urinary control with use of intermittent catheterization. Another study of 11 patients demonstrated concurrent results [121]. Seven patients were cured or significantly improved and 4 reported only minor improvement or no effect after injection. Use of bulking agents as a supplemental (adjuvant) procedure has also been investigated but demonstrated disappointing results [3].

Even though injection of bulking agents has been shown to be of limited value in treating NSD, this approach may be considered in carefully selected patients due to its low complication rate (mainly adverse reactions to the injected substance or infections). This includes patients

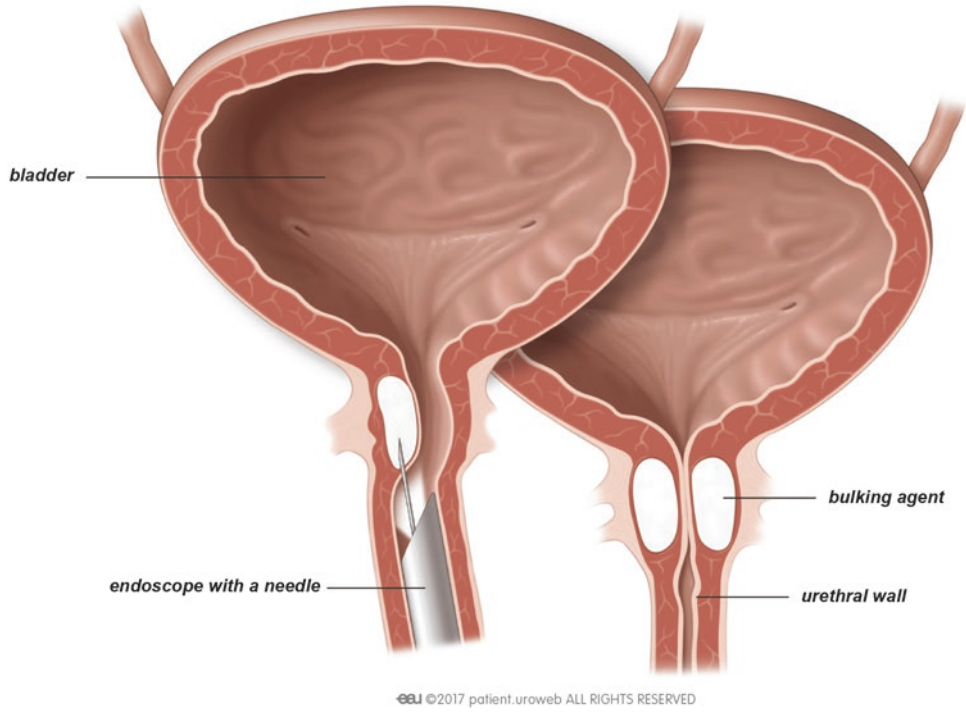

Fig. 9.12 Bulking agents are injected into the urethral wall (Courtesy of the European Association of Eurology [58], with permission)

who have failed other treatment options, have been disqualified from more invasive procedures, and have a strong desire to improve continence.

Artificial Compression Devices (Balloon Insertion) Artificial compression devices compress the urethra below the bladder neck. The device consists of two balloons inserted on either side of the urethra, small titanium ports, and tubes that connect the ports to the balloons (Figs. 9.13 and 9.14) [57, 58]. The ports allows the physician to regulate the amount of fluid in the balloons.

The overall success rate of the adjustable continence device in the non-neurogenic population ranges between 52 and 80% (proportion of completely continent patients) [122–126]. A retrospective study of 13 male and 24 female neurogenic patients with urinary incontinence due to NSD has shown that implantation of the adjustable continence device is minimally invasive and safe [127]. During 4-year follow-up, the mean number of urinary incontinence episodes and the mean number of pads used per 24 h decreased twice, with 54.5% of patients indicating more than 50% improvement of SUI symptoms, of whom 38.9% indicated complete continence. Nonetheless, 39.4% of patients required permanent explantation of the device after 4 years of follow-up. On the other hand, such explantation and complication rates were well within the ranges described in non-neurogenic patients. Authors concluded that artificial compression devices can significantly improve neurogenic SUI in the long term. Thus, it might be a reasonable option for patients who are unwilling, unsuitable, or not yet ready for more invasive surgery such as AUS or sling placement. Authors stressed that concomitant neurogenic detrusor overactivity that is not treated or insufficiently treated can adversely influence the complication rate and final outcome. In these patients, balloon insertion should be avoided. Currently, there is a lack of other studies investigating this method.

Placement of an artificial compression device is considered as a short and minimally invasive procedure that allows for fast healing and short

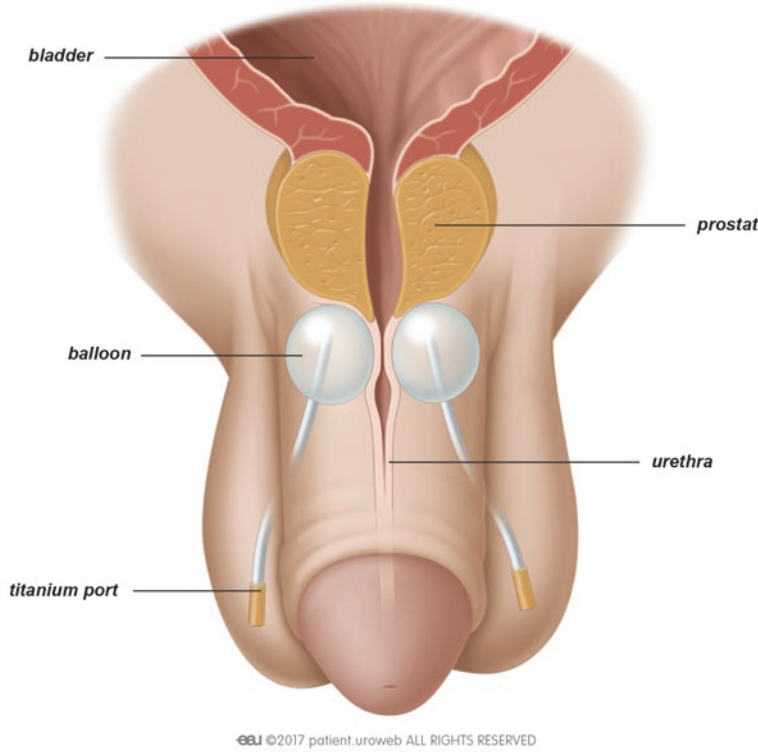

Fig. 9.13 An artificial compression device (balloons) compressing the male urethra (Courtesy of the European Association of Eurology [58], with permission)

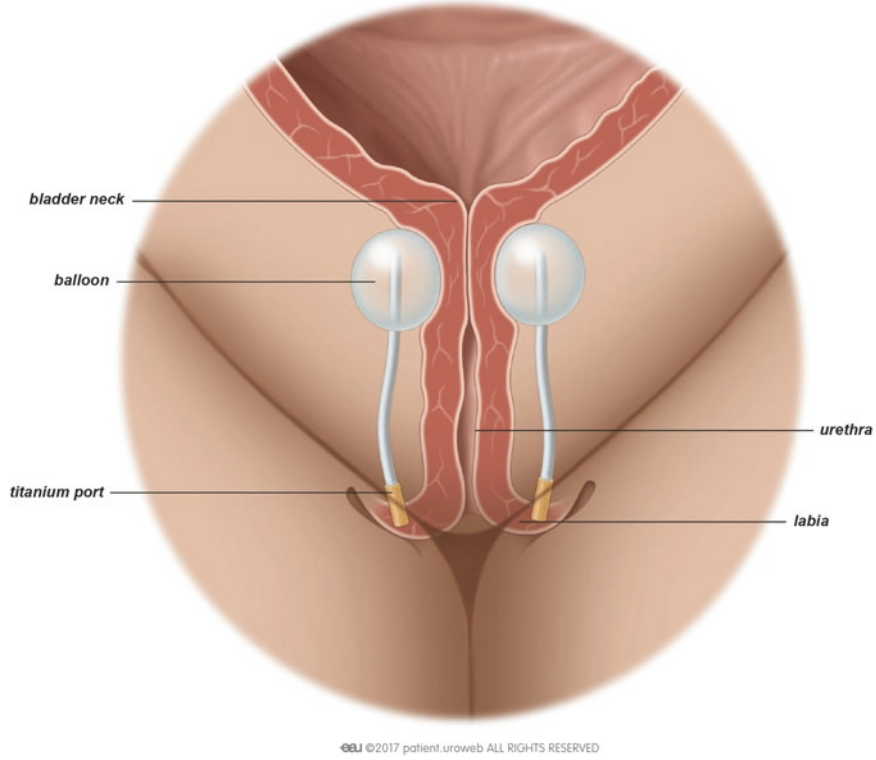

Fig. 9.14 An artificial compression device (balloons) compressing the female urethra (Courtesy of the European Association of Eurology [57], with permission)

hospital stay. Patients usually receives spinal or general anesthesia. Then, the surgeon makes an incision in the labia/perineum and, using X-ray for guidance, places the balloons on both sides of the urethra. After that, the titanium ports are placed in the labia/scrotum and connected to the balloons. Postoperative adjustment is usually necessary to optimize the effect on urinary continence. Best outcomes were reported after four or five refillings [123].

Possible adverse events include erosion/migration, device infection or failure, implantation site pain, bladder stone formation, and difficult intermittent self-catheterization. The reported explantation rate in non-neurogenic patients is between 8 and 58% [122–126]. Interestingly, balloons can be explanted as ambulatory surgery using local anesthesia in case of adverse events with the option of reimplantation at 3 months [127].

Invasive Surgery Alternative surgical options to AUS and sling implantation are bladder neck reconstructive procedures. There are various techniques that have been used to increase bladder outlet resistance and to achieve a continent proximal urethra. The most commonly reported are the Young-Dees-Leadbetter, the modified Leadbetter-Mitchell repair, the Kropp repair, and the Pippi Salle [3]. They have shown reasonable success rates in the hands of specially trained surgeons [128] but published evidence is mainly limited to pediatric patients. Moreover, subsequent procedures, including cystoscopy and intermittent catheterization, are rendered difficult [49]. Functional sphincter augmentation with a transposition of the gracilis muscle to the bladder neck or proximal urethra is currently only rarely performed [129–131].

In patients who have failed all treatment options or are likely to fail all, supraurethral diversion might become necessary [132, 133]. This technique creates an abdominal stoma that can be continent or incontinent (see Chap. 13, "Renal Failure"). Simultaneous closure of the bladder neck or urethra may be required, particularly in women. Bladder neck/urethra closure is often seen as a last-resort treatment, reserved for a urethra that is unsalvageable, secondary to long-term indwelling catheter or pressure ulcer destroying the perineal urethra [134]. Supraurethral diversion with bladder neck/urethra closure should be reserved for severe patients with intractable persistent incontinence.

Figure 9.15 presents the treatment algorithm for NSD.

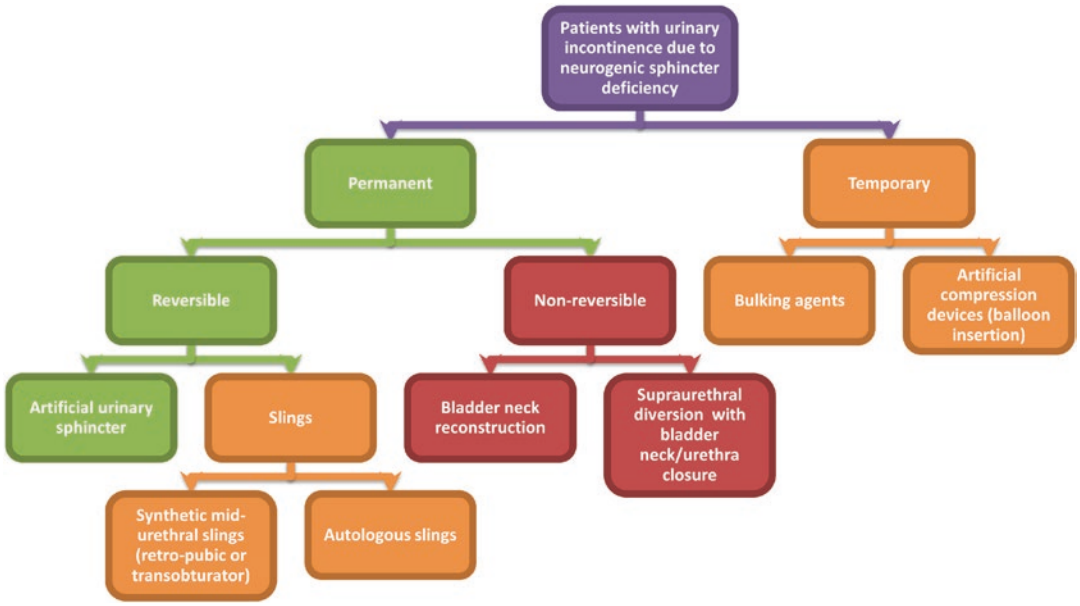

Fig. 9.15 Treatment of urinary incontinence due to neurogenic sphincter deficiency

Conclusion (Table 9.1)

Table 9.1 Conclusion

Summary	Level of evidence
Data on prevalence of urinary incontinence due to neurogenic sphincter deficiency (NSD) is sparse. NSD is observed when neurological lesions or injuries appear below the sacral spinal cord and lead to de-innervation of the intrinsic sphincter. These are typically individuals with myelodysplasia, sacral agenesis, sacral/infra sacral spinal cord injury, laminectomy complications, vertebral disk disease, severe pelvic fractures, and nerve injury from resection of low colorectal cancers	3/4
Evaluation of incontinent patients includes a comprehensive medical history with a bladder diary and questionnaires, physical examination, urinalysis/urine culture, blood chemistry, pad-weighing test, urinary tract ultrasound, assessment of post-voiding residual volume, free flowmetry, cystoscopy, computed tomography, magnetic resonance imaging, nuclear renogram, voiding cystourethrography, and urodynamics	4 (Expert opinion)
Low maximal urethral closure pressure (MUCP) (<20 cm H_2O) and low abdominal leak point pressure (ALPP) (<60 cm H_2O) are commonly used as indicators of intrinsic sphincter deficiency	4 (Expert opinion)
Conservative treatment with pelvic floor rehabilitation has not been well studied in neurogenic patients suffering from NSD-related incontinence	3/4
Surgical options for NSD include artificial urinary sphincters, slings (autologous and synthetic), periurethral bulking agents, adjustable continence devices, bladder neck reconstruction techniques, and supraurethral diversion with bladder neck/urethra closure	4 (Expert opinion)
Procedures that aim to increase bladder outlet resistance might result in de novo overactive detrusor or lead to exacerbation of pre-existing neurogenic detrusor overactivity	2/3
The artificial urinary sphincter has been proved to be effective. Nevertheless, its limited mechanical life and high costs bring disadvantages. Long-term follow-up demonstrated significant complication rates, requiring surgical revision in a substantial percentage of patients	2
Treatment with autologous slings has shown good continence improvement but the operative morbidity and complications of harvest site pain and infection limit this modality	2
Synthetic mid-urethral slings seem to be a promising, minimally invasive surgical modality with acceptable success rates and tolerable complication rates. However, the selection criteria for the appropriate patients have to be defined and long-term results are currently not available	3
Bulking agents have been found to have poor long-term success	2
Adjustable continence devices have shown efficacy in preliminary studies but available data for neurogenic patients is strongly limited and this therapy is not well established	3
The most commonly reported bladder neck reconstruction techniques are the Young-Dees-Leadbetter, the modified Leadbetter-Mitchell repair, the Kropp repair and the Pippi Salle. Surgical treatment of NSD with supraurethral diversion and bladder neck/urethral closure has also been reported	3

Recommendation	Grade of recommendation
An extensive medical history with carefully conducted physical examination followed by urinalysis/urine culture, blood chemistry, pad-weighing test, upper tract imaging, and urodynamic study are recommended in every incontinent patient suspected of NSD	Expert opinion
Other necessary investigations should be performed if indicated by the clinical scenario (based on underlying neurological pathology, patient history as well as relevant symptoms and signs)	Expert opinion
There remains a lack of knowledge regarding the optimal treatment modalities for NSD-related incontinence	Expert opinion
Conservative treatment may be considered in a willing patient with an ability to contract the pelvic floor muscles. Pelvic floor rehabilitation therapy should be tailored to individual patient's capabilities. Patients, their family members, and/or carers should be educated about lower urinary tract function and treatment goals	Expert opinion

(continued)

Table 9.1 (continued)

Recommendation	Grade of recommendation
Before performing any form of subvesical obstruction in order to treat NSD-related incontinence, it is mandatory to adequately treat detrusor overactivity or reduced bladder compliance as otherwise increased storage pressures can jeopardize renal function	Expert opinion
Implantation of the artificial urinary sphincter can successfully manage urinary incontinence due to NSD. The device should be placed with caution as neurogenic individuals have higher numerical complication rate versus non-neurogenic patients	B
AUS candidates should be carefully informed about expected rates of mechanical failure, erosion, and infection	Expert opinion
Autologous or synthetic mid-urethral slings (TVT, TOT) may be considered as an alternative minimally invasive surgical treatment option for carefully selected patients	C
Sling candidates should be informed about risk of urinary retention managed with intermittent or indwelling catheterization	Expert opinion
Bulking agents can be used to treat NSD-related incontinence when there is a demand for a minimally invasive treatment. The patient should be aware that the technique has a low success rate and poor long-term results	C
Adjustable continence devices may be considered in patients who are not willing, not suitable or not yet ready for more invasive surgery, such as implantation of artificial urinary incontinence or sling placement	C
Surgery with bladder neck reconstruction may be indicated when previous options have failed or patients present with contraindications for less invasive alternatives	C
Supraurethral diversion with bladder neck/urethra closure should be offered as an ultimate treatment option for severe patients with intractable persistent incontinence	C
An intensive follow-up for patients who underwent bladder outlet procedure is mandatory, since the long-term effects are not well known. Ongoing urodynamic and upper tract monitoring is recommended to maintain safe intravesical pressures and reduce the risk of long-term renal damage	Expert opinion

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Part IV

Consultations for Complications of Neurogenic Bladder

Urinary Tract Infection

10

Introduction

Urinary tract infection (UTI) is the most common complication observed among patients suffering from neurogenic lower urinary tract dysfunction. The risk of UTI depends mainly on underlying urodynamic pathology and the bladder-emptying technique used. UTI risk increases with indwelling catheterization, incorrectly performed intermittent catheterization, and with application of external appliances [1]. Other risk factors include high bladder pressures, low bladder compliance, impaired voiding with poor bladder emptying, urine stasis, bladder overdistension, bladder outflow obstruction, altered intrinsic defense mechanisms, urinary tract stones, bladder diverticula, vesicoureteral reflux, instrumentation of the urinary tract, catheter composition, medications, immunosuppression secondary to medical therapy, decreased fluid intake, poor hygiene, perineal colonization, decubiti/other evidence of local tissue trauma, and reduced host defense associated with chronic illness [2–5]. Because of the heterogeneity of underlying disorders causing neurogenic bladder dysfunction, each patient must be approached individually, as risk factors vary significantly among patients.

Definitions

UTI is the onset of signs and/or symptoms accompanied by laboratory findings (bacteriuria, leukocyturia, positive urine culture) [6]. The specific cut-off values for the quantification of laboratory findings vary and remain a matter of dispute.

Currently available guidelines propose that a significant bacteriuria can be diagnosed with $>10^2$ colony-forming units per milliliter of urine (CFU/mL) in persons performing intermittent catheterization, $>10^4$ CFU/mL from clean-void specimens, and any detectable concentration from suprapubic aspirates [7, 8]. Insufficient data exist to recommend a standardized level of significant bacteriuria in individuals managed with chronic indwelling catheterization [9]. It has been generally proposed that in catheterized patients (intermittent, indwelling urethral, indwelling suprapubic, condom) concentration of $>10^3$ CFU/mL of ≥ 1 bacterial species in a single catheter urine specimen can be classified as a significant bacteriuria [9]. Of note, bacteriuria does not necessarily signify a UTI. Clinicians should remember that only symptomatic bacteriuria allows diagnosing UTI. The standard of care among clinicians is not to treat asymptomatic

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_10

bacteriuria—traditionally defined as 10^5 CFU/mL of 1 or more organisms in an appropriately collected specimen in an asymptomatic person—with antibiotics [9].

Leukocyturia (pyuria) refers to the presence of leukocytes in the urine. There is disagreement regarding a threshold for significant leukocyturia. It has been proposed that ten or more leukocytes in centrifuged urine samples per microscopic field (400×) can be considered as significant [7]. Similarly to bacteriuria, pyuria alone is not diagnostic of infection, as it may result from irritative effects from a urinary catheter, particularly at a low level of less than or equal to 30 white blood cells per high-power field (WBC/HPF) [5]. More than 50 WBC/HPF is an indicator of high-level pyuria and has been associated with increased morbidity [5].

Bacterial colonization is differentiated from UTI by the absence of an inflammatory response and the associated symptoms and signs that result from bacterial invasion. Bacterial colonization of the bladder in neurogenic patients suffering from neurogenic lower urinary tract dysfunction is the norm, regardless of bladder-emptying technique, including indwelling or intermittent catheterization [10]. Because of the risk of developing more invasive and resistant organisms, bladder colonization with asymptomatic bacteriuria should not be routinely treated [10].

Epidemiology

The incidence of UTI in the population of neurogenic bladder patients is high and may vary in cause of underlying pathology. It has been estimated that the overall rate of UTI in these patients is 2.5 episodes per patient per year [11]. The incidence of febrile UTI has been gauged as 1.8 per patient per year [3]. The rate of bacteriuria following the introduction of a catheter is 5–8% for each day of catheterization, with a 100% incidence of bacteriuria with long-term indwelling catheters within 4 weeks [12–15]. Prevalence of bacteriuria in those performing clean intermittent catheterization varies from 23–89% [16]. A retrospective study of 46,271 patients with neurogenic lower urinary tract dysfunction showed that more than one-third (29.2–36.4%) of patients were diagnosed with a UTI within the first year of diagnosis of bladder dysfunction [17]. Importantly, 20% of these patients required hospitalization. The study noted that spinal cord injury (SCI) patients required more hospitalizations due to UTI than patients with multiple sclerosis. Prospective cohort studies of SCI individuals have shown concurrent results and revealed that hospitalized patients required an average length of hospital stay of 15.5 days [18]. The outcomes of a recently published large cohort study of SCI patients are of the utmost importance for daily clinical practice. Authors demonstrated that 51.2% of the emergency department visits in the aftermath of UTI could potentially be prevented [19]. UTI is the most common type of all infections and the most common cause of fever in the SCI patient [20, 21]. As neurologically impaired individuals are more susceptible to developing UTI, virtually all kinds of procedures within the urinary tract have higher risk of infection. For instance, the incidence of post-urodynamic UTI has been estimated as 16%, significantly higher compared to the non-neurogenic population [22–24]. Some experts proposed that sterilization of urine before urodynamics can reduce the risk of UTI by half [22]. In male patients who empty their bladders by increasing intravesical pressure, either by Valsalva or Crede maneuvers, reflux of urine into the prostate and seminal vesicles occurs in more than 50% of patients and can lead to other complications such as epididymoorchitis [12]. Seminal vesiculitis, prostatitis, epididymitis, and orchitis may all be seen in patients with long-term urethral catheterization with blockage of the ejaculatory and prostatic ducts [12].

UTI may also aggravate underlying neurological pathology, in particular, multiple sclerosis. Available data suggest that bacterial infection within the urinary tract may be a significant trigger factor of disease exacerbation [25]. Up to 30% of patients with multiple sclerosis may experience disease exacerbation as a consequence of UTI [26]. Furthermore, patients with documented bacterial infection have shown little

response to steroid therapy until appropriate antibiotics are co-administered [26]. Recurrent UTI may result in overall disease progression, and individuals suffering from multiple sclerosis have a more pressing need for rapid diagnosis and prompt treatment [2]. Thus, it has been proposed that in these patients diagnosis can be made with urine dipstick followed by treatment based on dipstick results [27]. When urine culture results are available, treatment may be discontinued or modified (if required), with emphasis on avoiding treatment delay for the primary illness of multiple sclerosis [2, 27, 28].

The Enterobacteriaceae family represents the most commonly isolated organisms in the neurogenic population [29–32]. *Escherichia coli* and *Klebsiella* species dominate with *E. coli* comprising 50% of all isolated strains. However, patients with neurogenic bladder tend to have an increased rate of infection with other organisms such as *Pseudomonas* (8.7–15%), *Acinetobacter* (6–15%), *Enterococcus* (6–12%), and multiorganismic infections (26%) [31, 33]. The incidence of polymicrobial infections represents the greatest difference between infections in the neurogenic bladder as opposed to a healthy bladder [2]. Individuals with neurogenic lower urinary tract dysfunction are also prone to develop fungal infections. Possible risk factors of fungal infection include recent antibiotic use and indwelling catheterization. A prospective study of SCI patients has found that candiduria may be present in up to 17% of these patients. Those managed with indwelling catheterization (both urethral and suprapubic) are ten-fold more likely to develop candiduria compared to individuals who performed clean intermittent catheterization [34]. To make matters worse, multiple antibiotic treatment for recurrent UTIs contributes to rising multi-drug resistance. It has been shown that up to 50% of SCI patients may complain of UTI caused by multi-drug resistant strains [30]. More than 50% of these strains are resistant to ampicillin, levofloxacin, cefazolin, and clavulin [31]. This issue affects both inpatient and outpatient individuals.

With the increased frequency and severity of UTI, there is higher risk of morbidity and mortality secondary to urosepsis and end-stage renal disease compared to the general population [35]. Although advances in diagnostic procedures and medical care have significantly improved during past decades and have reduced the morbidity and mortality of UTI in patients with neurogenic bladders, currently up to 10–15% of these patients may die from sepsis of urinary origin [36]. Importantly, UTI in neurogenic patients may also indicate change or evolution of bladder dysfunction, thus requiring new urodynamic assessment in some cases.

Diagnosis

Symptoms and Signs

Because of impaired bladder sensations, traditional symptoms and signs of UTI (urgency, frequency, dysuria) in patients with neurogenic lower urinary tract dysfunction may be replaced by distinguishing symptomatology. The most common signs and symptoms suspicious of an infection within the urinary tract in those patients are [7, 37, 38]:

- Fever, rigors, chills
- Discomfort or pain in back or abdomen (pain may be elicited by palpation or percussion)
- New onset or increase in incontinence, including leakage around an indwelling catheter or between intermittent catheterizations
- Increased need to perform catheterization
- Cloudy urine with increased urine odor (complaint that the urine is not clear, with a distinct change in urine odor, and strong foul smell that persists on change of catheter equipment)
- Increased urinary sediment
- Increased spasticity (compared with the patient's usual self-assessed baseline or on examination with increased resistance to stretch)
- Malaise, lethargy, or sense of unease (feeling tired or unwell, different from the person's usual state of health)
- Nausea and vomiting
- Sweating
- New onset or worsening of autonomic dysreflexia

Because of these specific symptoms, patients with SCI are able to predict the presence of a UTI with an accuracy of only 61–66% [39, 40]. It has been shown that SCI patients were better able to predict the absence, rather than the presence, of UTI [39]. The highest accuracy and sensitivity in predicting the presence of UTI have been reported for cloudy urine and pyuria [9, 39]. The absence of pyuria was noted as a strong indicator for no infection [8, 36, 41]. Fever had very high specificity but very low sensitivity. In contrast, malodorous urine is not equivocal proof of infection [9, 42]. Concurrent results were demonstrated for autonomic dysreflexia, as it may be triggered by multiple causes. It has been estimated that one-third of patients with neurogenic bladder dysfunction who present with UTI experience an isolated sign, one-third experience two signs and one third experienced three signs [43]. Despite the uncertainty of symptoms, patient self-evaluation and awareness remain an important component of early detection and possible intervention [2]. Length of time of onset or increase in subjective symptom/symptoms should be carefully documented [37]. The individual would be expected to have an onset or increase of symptoms within 2 weeks.

Cystitis is the most common form of infection within the lower urinary tract in neurogenic patients [5]. In individuals with indwelling urethral catheters, urethritis may occur. It is frequently caused by *Neisseria gonorrhoeae*, *Escherichia coli,* and *Chlamydia trachomatis* [44]. Additional blockage of the periurethral gland by the catheter may lead to the formation of a periurethral abscess. The abscess can drain spontaneously to the penile skin, inside the urethral lumen (creating a diverticulum), or simultaneously at both sides (forming a urethrocutaneous fistula) [5]. Surgical excision needs to be performed for either diverticulum or fistula. Epididymitis is another form of catheter-related infection. Initial infection of the bladder or urethra can reach the epididymis via the vas deferens in a retrograde manner. Further involvement of testicles may also be seen and present as epididymoorchitis [12]. Acute epididymitis is a clinical syndrome consisting of pain, swelling, and inflammation of the epididymis of less than 6 weeks [5]. However, in neurologically impaired patients, pain may be absent because of impaired sensation. Therefore, the only clinical sign is often swelling and/or flare. Fever may sometimes be detected in the acute stage. Infected urine refluxing into prostatic ducts can lead to prostatitis. In neurogenic patients, high pressure voiding (due to neurogenic detrusor overactivity) or presence of a urethral catheter (due to neurogenic detrusor underactivity or detrusor sphincter dyssynergia) can significantly contribute to this condition. The most common cause of prostatitis in patients with neurogenic bladder is *Escherichia coli* (65–80%) [5]. *Pseudomonas aeruginosa*, *Serratia* species, *Klebsiella* species, and *Enterobacter aerogenes* are identified in a further 10–15%. In the acute phase of infection patients complain of fever, pain in the genital area and lower back, burning or painful urination, as well as urinary urgency and frequency. The prostate gland is very tender to palpation through the rectum. Chronic infection is usually asymptomatic and may affect 25–43% of patients with a history of recurrent UTIs [5, 45].

Upper urinary tract infection (pyelonephritis) may also affect patients with neurogenic bladder. The main risk factors for this complication include impaired antireflux mechanism (leading to vesicoureteral reflux) and detrusor-sphincter dyssynergia (leading to urine stasis and high intravesical pressure during voiding with retrograde urine flow into the kidneys) [5]. The main clinical symptom of acute pyelonephritis is high fever, up to 40 °C. Patients may also report abdominal pain that radiates along the flank towards the back, vomiting, malaise, decreased appetite, and the whole spectrum of lower urinary tract symptoms (LUTS). Chronic pyelonephritis implies recurrent kidney infections and can result in scarring of the renal parenchyma, resulting in impaired renal function (see Chap. 13, “Renal Failure”).

Laboratory Testing

Neurourology Guidelines of the European Association of Urology indicate urine culture and urinalysis as the gold standard for UTI diagnosis [7]. The dipstick test alone seems to be useful in excluding the presence of infection if the results for both nitrites and leukocyte esterase are negative [46]. The usefulness of the dipstick test alone to rule in infection is uncertain [46, 47]. Urine culture remains the definitive proof of infection. Microbiologic testing in persons with neurourological disorders is mandatory, as bacterial strains and resistance patterns may differ from those of able-bodied patients [7, 48]. In addition, an antibiogram providing a sensitivity pattern of relevant antimicrobials is highly recommended [37]. Multiresistance has been defined as the resistance to three or more different antimicrobial agents to which the microorganism would normally be susceptible [49, 50]. Colonization with multiresistant organisms may be especially suspected in individuals with neurogenic bladder dysfunction who have been managed with indwelling catheterization, multiple antibiotics, mechanical ventilation, and for pressure ulcers [37, 49, 51–53]. The antibiogram can also be used in revealing reinfection (infection by different type/strain of organism), relapse (infection by the same organism), or chronic/biofilm infection [54]. Discovery of a chronic/biofilm infection can justify prolonged antibiotic treatment and may initiate additional examination [41]. In patients with epididymitis and prostatitis, urinalysis or even urine culture may not reveal any abnormalities.

The interpretation of the results obtained should include analysis of bladder-emptying technique and account for the presence of an indwelling catheter [1]. The results should also be interpreted in the context of previous urological history and treatment, as well as presence of confounding diseases and/or comorbidities. Appropriate urine samples include clean-catch midstream samples, samples taken from a freshly inserted intermittent sterile catheter, and samples taken from a catheter port [55]. In patients already treated with indwelling catheter (urethral or suprapubic), the urine specimen should be obtained from a new freshly inserted catheter [5]. The external urethral meatus must be exposed and cleaned with antiseptic solution. The first 50 mL urine is passed without collection. Afterward, approximately 50 mL midstream urine is collected in a sterile container. In patients who wear a condom catheter, a fresh condom catheter should be applied with subsequent urine collection [9]. The urine should be analyzed/cultured as soon as possible or kept refrigerated and cultured within 24 h [56]. It is not acceptable to collect a urine culture from a pre-existing catheter, from a collection bag, or from a container [37].

In patients with generalized infection (pyelonephritis, urosepsis), blood tests may show a polymorphonuclear leukocytosis, increased erythrocyte sedimentation rate, elevated C-reactive protein concentration, as well as elevated creatinine levels if renal impairment developed [5].

Additional Testing

In patients with relapsing or persistent infections and recurrent catheter blockage, a search for the source of infection must be undertaken. This may include a cystoscopy (to rule out a stone); upper tract imaging (to rule out stasis, stone, renal abscess, or hydronephrosis); intravenous urogram (to rule out stasis, stone, hydronephrosis, or vesicoureteral reflux); and ensuring that the patient has changed all of his/her reusable catheters and is not reinfecting himself/herself [12]. Common findings in patients with recurrent UTIs are follicular cystitis and cystitis cystica et glandularis, which may be considered within the spectrum of normal bladder as an immunological response to infection (Figs. 10.1 and 10.2) [57]. Computed tomography imaging is commonly used in patients suspected of acute pyelonephritis or renal abscess (Figs. 10.3 and 10.4) [58]. Nevertheless, it may also be used in patients with

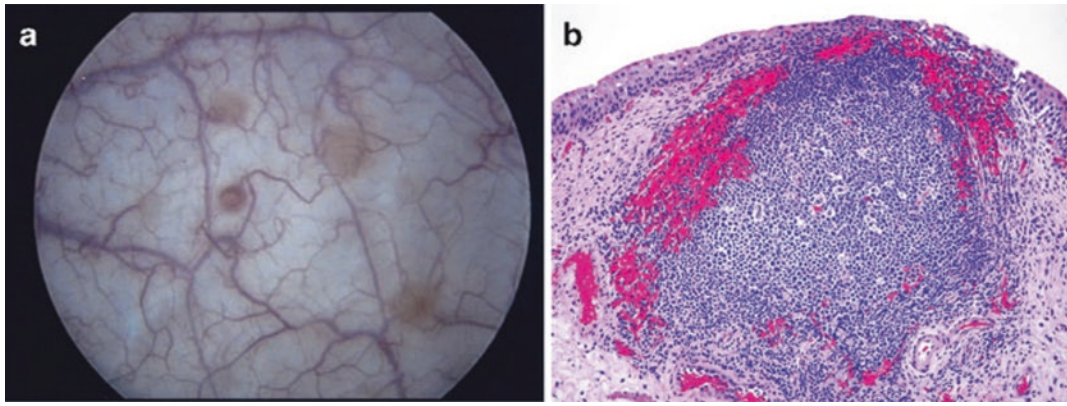

Fig. 10.1 Follicular cystitis. (**a**) Multiple discrete small mucosal irregularities are present. They do not significantly obscure the vasculature beneath them. (**b**) Lamina propria contains lymphoid follicles, often with a germinal center (From MacLennan et al. [57], with permission)

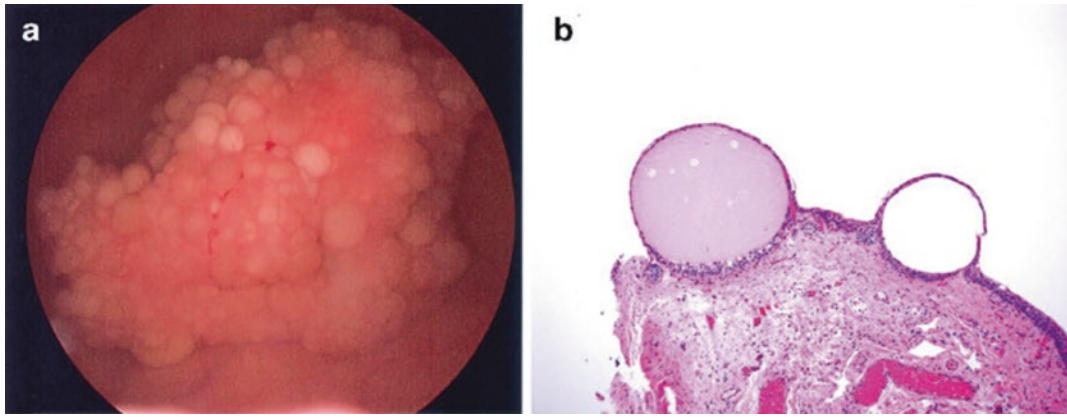

Fig. 10.2 Cystitis cystica. (**a**) The mucosal surface is studded with innumerable bleb-like lesions that appear to contain straw-colored fluid. The remainder of the mucosa looks normal. (**b**) Normal urothelial cells often have eosinophilic secretions. The lumens of some cells are lined by taller columnar-type cells, consistent with cystitis glandularis of the typical type. The cystic spaces lined by goblet cells comprise cystitis glandularis of the intestinal type, also sometimes designated intestinal metaplasia (From MacLennan et al. [57], with permission)

chronic pyelonephritis (Fig. 10.5) [59]. Those suspected of epididymis or epididymoorchitis are typically examined with ultrasound (Fig. 10.6 and see Fig. 10.7) [60].

A basic data set for UTI (International SCI UTI Basic Data Set) has been developed to standardize collection and reporting of the minimal amount of information required to define a possible UTI (Fig. 10.8) [37, 61]. Although the data set has been designed primarily for SCI individuals, it may also be used for other neurologically impaired patients.

Treatment

In individuals with neurogenic bladder, asymptomatic bacteriuria of varying degrees is the norm. Thus, asymptomatic bacteriuria should not be screened or treated unless there is suspicion of UTI [7, 9]. Treatment of asymptomatic bacteriuria may result in significantly more resistant bacterial strains without improving the outcome [62]. Exceptions include pregnant women and patients before urological procedures within the urinary tract. In those on immunosuppression

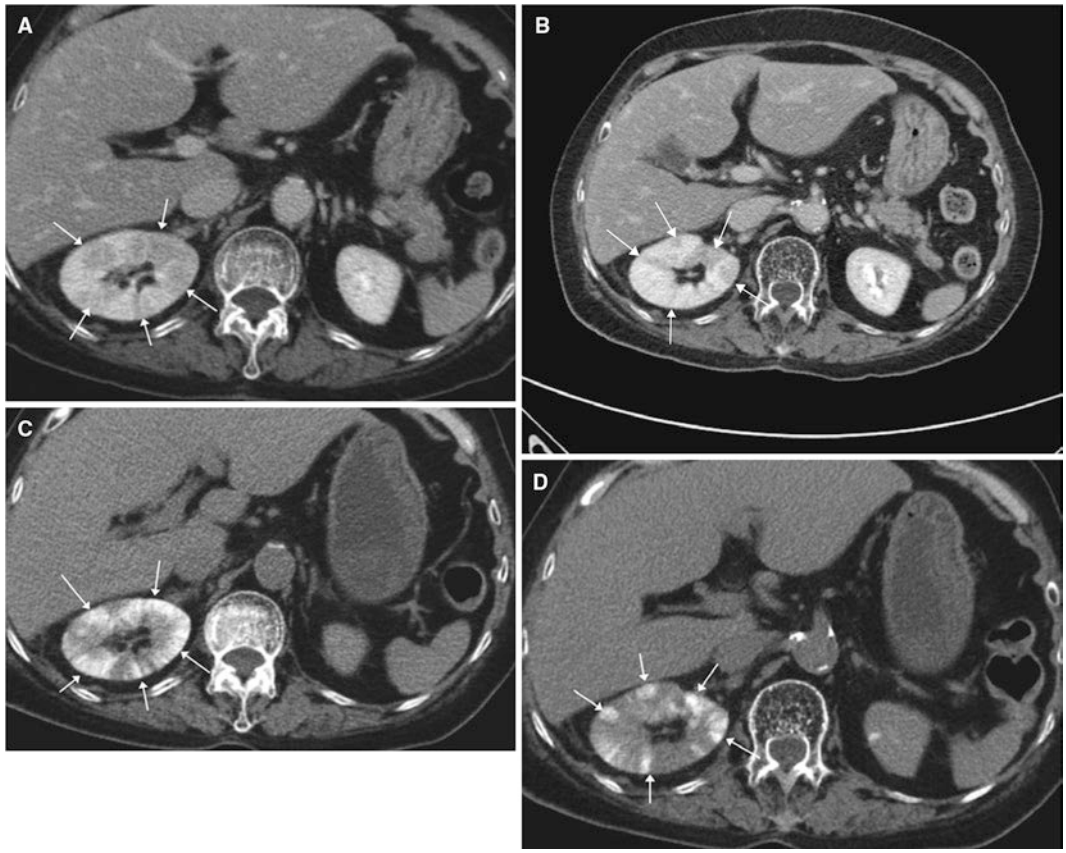

Fig. 10.3 Findings of acute pyelonephritis on delayed CT. (**a, b**) Contrast-enhanced CT scans show enlarged right kidney with multiple, wedge-shaped lesions of low attenuation (*arrows*). (**c**, **d**) Delayed CT scans taken 6 h later without further injection of contrast material show retained contrast material (*arrows*) in the area of poor enhancement at initial CT (From Cho [58], with permission)

(e.g., individuals with multiple sclerosis), treatment of asymptomatic bacteriuria may be considered [63, 64]. Antibiotic therapy can be given simultaneously with corticosteroid treatment [63].

UTI in patients with neurogenic lower urinary tract dysfunction is categorized as complicated [7]. Treatment duration has not been well established and depends on infection severity and location (cystitis, urethritis, prostatitis, epididymitis, pyelonephritis). It has been generally proposed that a 5- to 7-day course of antibiotic therapy should be employed [7, 62]. This time interval can be extended up to 14 days, according to the extent of the infection. In patients with indwelling catheters, initial treatment course of 7–10 days is recommended [9, 65]. Patients presenting with UTI and fever (infection within the upper urinary tract) should be treated for 14 days [62]. Antibiotic therapy should be chosen based on the results of urine culture and sensitivity. The urine specimen for testing should be obtained before the initiation of antimicrobial therapy. Once treatment is initiated, all catheters should be changed. In patients performing intermittent catheterization, frequent complete emptying is required. If immediate therapy is mandatory (e.g., patients with fever, sepsis, or risk of deterioration of other concomitant disorders), the choice of treatment should be based on local and individual resistance profiles [21]. Clinicians should be aware that bacterial isolates may vary in outpatient and inpatient settings and higher rates of resistance to commonly prescribed antibiotics are not rare, making broad-spectrum

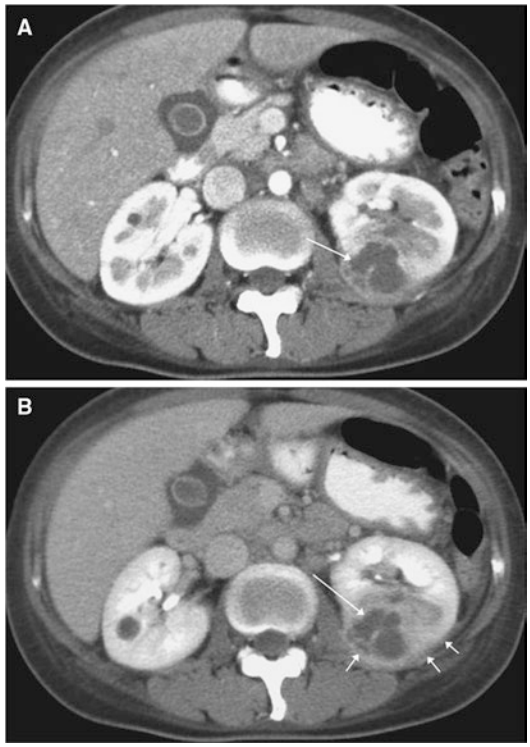

Fig. 10.4 Renal abscess. (**a**, **b**) Contrast-enhanced CT scans show a low-attenuated, nonenhancing lesion *(arrow)* in the left kidney. Note thickened renal fascia (*small arrows*) (From Cho [58], with permission)

antibiotics mandatory in severe cases [31, 64]. When immediate treatment is necessary, it usually involves fluoroquinolones, trimethoprim/sulfamethoxazole (if there is a suspicion of methicillin-resistant *Staphylococcus aureus* in outpatient settings) or vancomycin (if there is a suspicion of methicillin-resistant *S. aureus* in inpatient settings) [29]. In patients with upper urinary tract infection, double intravenous antibiotics (ampicillin–gentamicin) should be started until the results of cultures appear [5]. On the third day, appropriate oral antibiotic therapy may be introduced. If symptoms persist beyond 72 h, the possibility of perinephric or intrarenal abscesses or obstruction should be considered and radiologic investigation with ultrasound or computed tomography should be performed. Urine and blood cultures should be repeated at appropriate intervals and antimicrobial therapy should be adjusted, if necessary [5]. Figure 10.9 presents an algorithm of UTI diagnosis and management [62, 64] (Fig. 10.9).

Patients with recurrent UTIs should be carefully evaluated for underlying causes of recurrent infections. These include but are not limited to: inadequate diagnosis and/or management of neurogenic bladder dysfunction, evolution of bladder behavior, incorrectly performed intermittent catheterization, prolonged indwelling catheterization, lithiasis, and renal stasis. Moreover, recurrent courses of antibiotics result in higher rates of antibiotic-resistant isolates [66, 67]. Patients with neurogenic lower urinary tract dysfunction who present with recurrent UTIs should be first treated by attempting to optimize their bladder management [10].

Prevention

Many modalities have been proposed with the goal of reducing the incidence of UTI. Patient education may be one of the most valuable interventions, with instruction for more frequent and complete voiding, prevention of bladder distention, and hygienic methods for catheter use and care (see Chap. 17, "Patient Education") [2]. Subsequent strategies can be categorized as mechanical and medical. UTI prevention should be considered particularly if the improvement of bladder function and removal of foreign bodies/stones have not prevented recurrent UTIs [7]. Improvement of bladder function also includes injections of onabotulinumtoxinA into detrusor muscle or implantation of a neural sacral modulator in individuals with neurogenic detrusor overactivity, as these therapies have demonstrated efficacy in decreasing the incidence of UTIs [29, 68–71].

Mechanical Strategies for UTI Prevention

Intermittent Catheterization In patients performing intermittent catheterization, catheterization technique should be reassessed. Patients should be questioned about catheter cleaning

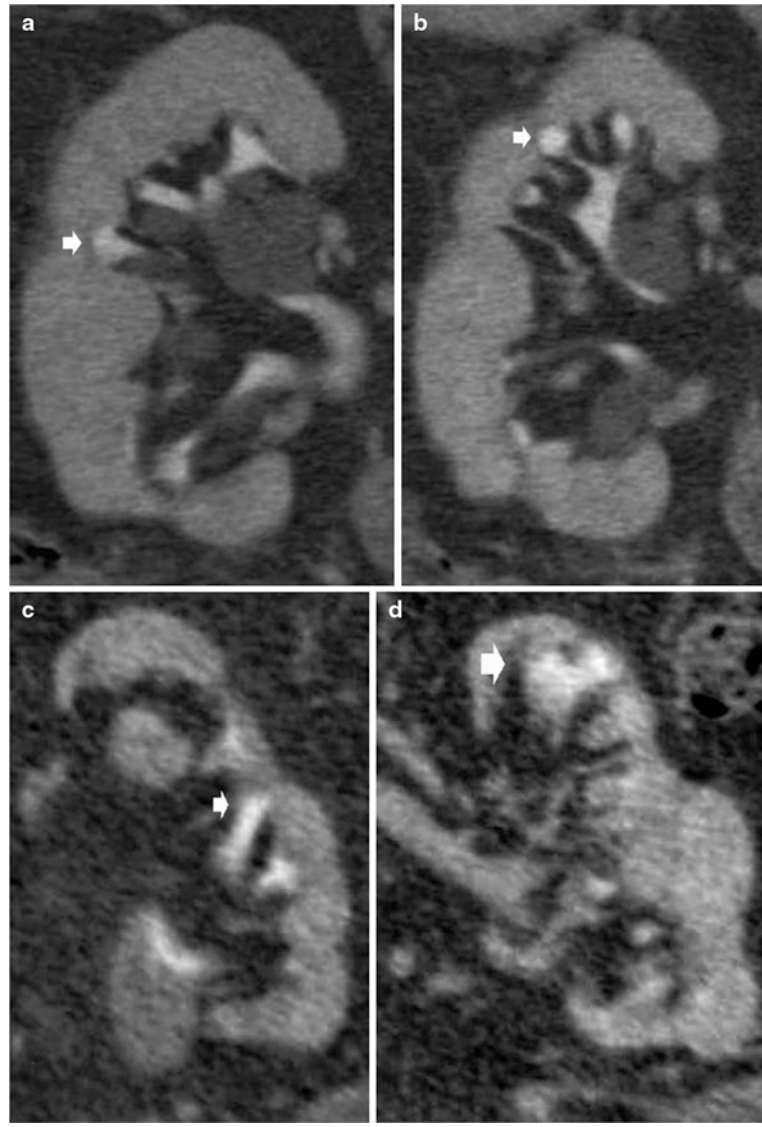

Fig. 10.5 Chronic pyelonephritis. Multidetector CT urography. Coronal reformations. (**a**, **b**) Right kidney. Calyceal distortion and clubbing (*arrows*) due to the underlying renal parenchymal damage with renal parenchymal scarring and focal reduction of renal parenchymal thickness. (**c**, **d**) Left kidney. Diffuse reduction of the renal parenchymal thickness with calyceal distortion (*arrows*) (From Quaia et al. [59], with permission)

method. Rinsing with water, air-drying, microwaving, or soaking catheters in various agents are all effective in reducing bacteria on catheters [10]. Nonetheless, there is a paucity of reliable data evaluating the effectiveness of these cleaning methods in preventing bacteriuria or UTI [9]. Replacing a clean reused catheter with sterile single-use catheters may be of benefit in patients performing clean intermittent catheterization [72]. Hydrophilic-coated catheters tend to decrease the incidence of UTI [73]. In some patients with recurrent UTIs, complete sterile technique of intermittent catheterization may be considered. Clinicians should keep in mind that sterile technique significantly increases cost compared with the clean method [73]. Furthermore, there is inadequate evidence to confirm that sterile variants are superior to clean technique with respect to UTI incidence [73].

Indwelling Catheterization Regular catheter changes (urethral and suprapubic) are mandatory. Frequency of catheter change depends on catheter material and size of the lumen. It has been proposed to change siliconized latex catheters every 1–2 weeks and silicone or hydrogel-coated

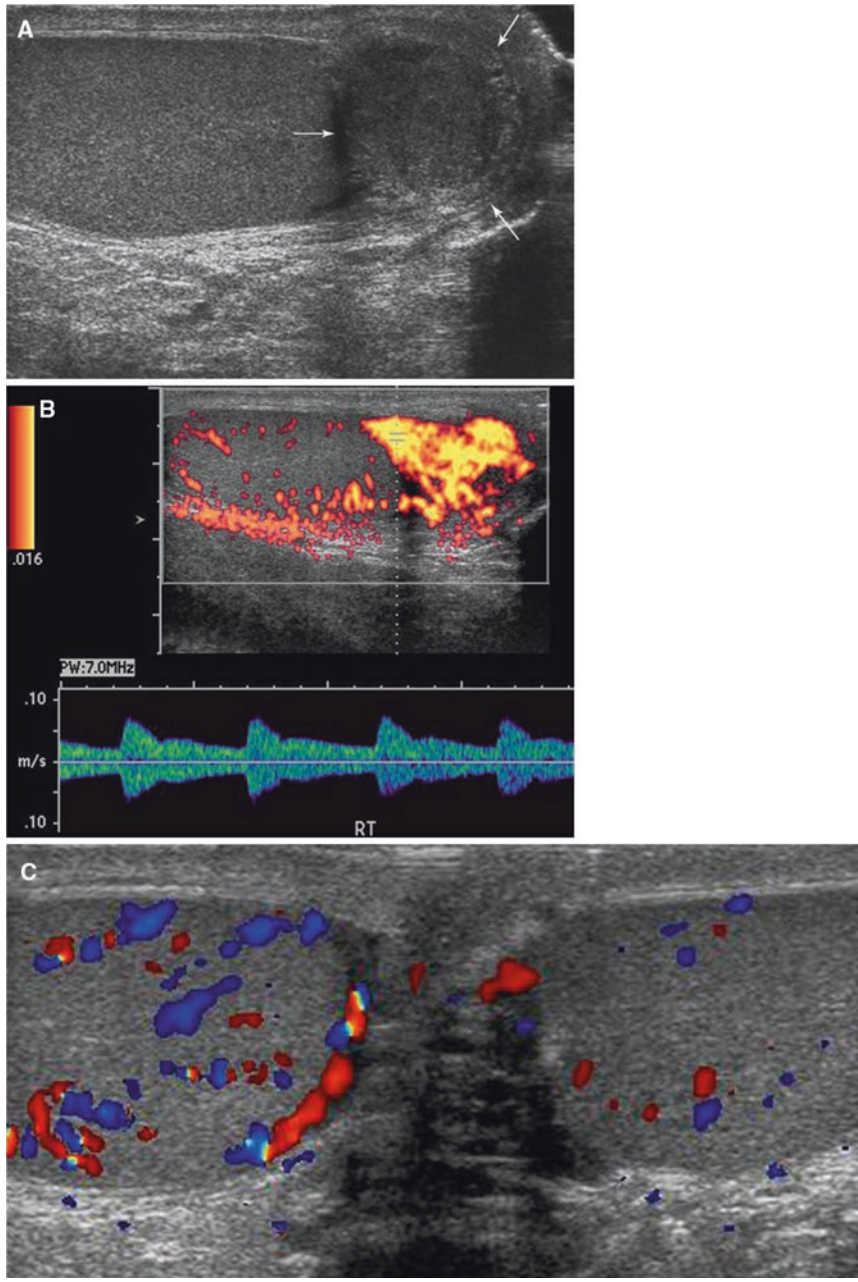

Fig. 10.6 Acute epididymoorchitis. (**a**) Longitudinal ultrasound (US) of the right scrotum shows heterogeneous hypoechogenicity (*arrows*) of right epididymal tail and reactive thickening of the adjacent scrotal wall. (**b**) Spectral Doppler US along the left epididymis shows hypervascularity and high-resistance waveforms. (**c**) Transverse color Doppler US of the scrotum shows markedly increased vascularity in the right testis, suggesting associated orchitis (From Lee and Kim [60], with permission)

catheters every 2–4 weeks or longer [74]. In those with a history of catheter encrustation or bladder stones, catheter change every 1–2 weeks should be considered [75]. Closed catheter drainage systems remain one of the most important preventive measures against infection and should be employed in patients managed with indwelling catheters [9]. Frequent violation of the closed

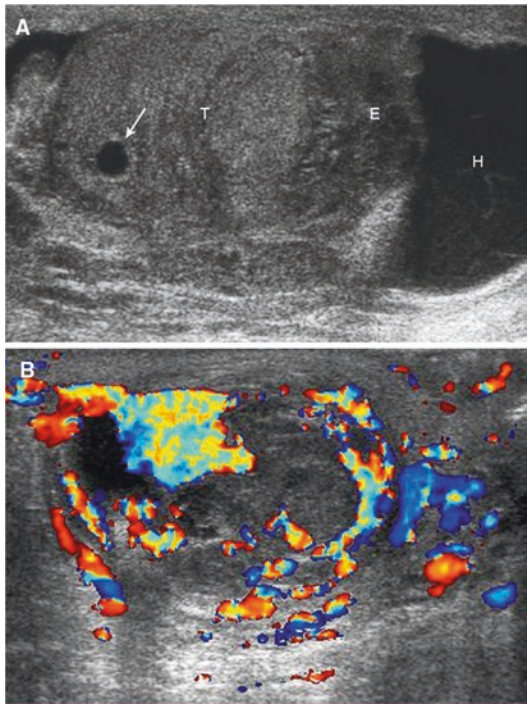

Fig. 10.7 Acute epididymoorchitis. (**a**) Longitudinal ultrasound (US) of the right scrotum shows enlarged heterogeneous right testis (T) and epididymis (E) with reactive hydrocele (H). Note intratesticular cyst (*arrow*). (**b**) Transverse color Doppler US of right scrotum shows markedly increased vascularity in the enlarged epididymis at the tail portion with diffuse thickening of the scrotal wall (From Lee and Kim [60], with permission)

drainage junction should be avoided, as it has been shown to significantly increase the risk of UTI [9, 76, 77]. The drainage bag and tubing should be situated below the level of the bladder. In patients with chronic urethral indwelling catheters, suprapubic catheterization may help to reduce the risk of recurrent UTIs [33] but it also increases the risk of stone formation [78, 79]. Silver-coated and antibiotic-coated catheters did not demonstrate significant reductions in UTIs, even in randomized clinical trials [80, 81]. Some benefits have been noted only in the very short term [82, 83]. Data on long-term use are lacking. Bladder irrigation has not been proven effective [84]. Some experts suggest that this practice may itself increase the risk of UTI [10]. Concurrent results have been shown in terms of bacteriuria. No difference in effectiveness has been found between saline and other products, including antibiotic solutions [81]. The use of antimicrobials or antiseptics in the urinary drainage bag is not recommended and should be avoided [85–89]. In patients with recurrent UTIs, external (condom) catheters do not seem a proper solution. Inadequate bladder drainage with condom catheters may result in increased residual urine volume, chronic urinary retention, and elevated bladder pressures, thus promoting UTIs. The use of external catheters does not prevent chronic bacterial colonization and pyuria [10]. The incidence of UTI with condom catheters appears to be comparable to that of clean intermittent catheterization [9, 11, 33]. Penile skin breakdown and scarring can also occur with long-term condom catheter use.

Medical Strategies for UTI Prevention

Antibiotic Prophylaxis Oral antibiotic prophylaxis has been highly debated and a long-term benefit remains unclear [2]. Use of antibiotic prophylaxis, often successful in individuals without neurogenic bladder dysfunction, is less effective in neurogenic patients [10]. A meta-analysis of 15 randomized clinical trials did not support the use of antibiotic prophylaxis for prevention of UTI in patients with neurogenic lower urinary tract dysfunction [66]. Positive outcomes with decreased incidence of asymptomatic bacteriuria (but with no change in the rate of symptomatic infections) were demonstrated only in patients in the acute phase of SCI. Moreover, one patient would need to be treated 3.7 weeks in order to prevent one episode of asymptomatic bacteriuria. Additionally, a two-fold increase in resistance was noted. Rapid recolonization and development of bacterial resistance are indicated as possible limitations of antibiotic prophylaxis. A Cochrane review assessing antibiotic prophylaxis in patients with long-term catheterization was unable to provide recommendations for daily clinical practice in terms of antibiotic prophylaxis in catheterized patients due to low quality of data [90]. Therefore, antibiotic prophylaxis is not currently recommended for the prevention of asymp-

INTERNATIONAL SPINAL CORD INJURY DATA SETS
URINARY TRACT INFECTION BASIC DATA SET (Version 1.0) - FORM

Date of data collection: YYYYMMDD

Length of time of sign(s)/symptom(s) (tick one only):
☐ Less than 1 day ☐ 1 to 3 days ☐ 4 days-1 week ☐ >1week-2 weeks
☐ >2weeks-1 month ☐ >1month-3 months ☐ > 3 months

Signs/symptoms (tick all that apply):
☐ Fever
☐ Incontinence, onset or increase in episodes, including leaking around catheter
☐ Spasticity, increased
☐ Malaise, lethargy or sense of unease
☐ Cloudy urine (with or without mucus or sediment) with increased odor
☐ Pyuria
☐ Discomfort or pain over the kidney or bladder or during micturition
☐ Autonomic dysreflexia
☐ Other _____

Urine dipstick test for nitrite (tick one only):
☐ Negative ☐ Positive ☐ Unknown

Urine dipstick test for leukocyte esterase (tick one only):
☐ Negative ☐ Positive ☐ Unknown

Urine culture (tick one only):
☐ Negative ☐ Positive ☐ Unknown
If positive, give species and amount of colony forming units (CFU)/mL (10^1-10^5CFU/mL), and the resistance pattern:

1) _____ species, _____CFU/mL
Resistance pattern (tick one only): ☐ Normal ☐ Multi-drug resistant (agents from 3 or more different drug classes)
2) _____ species, _____CFU/mL
Resistance pattern (tick one only): ☐ Normal ☐ Multi-drug resistant (agents from 3 or more different drug classes)
3) _____ species, _____CFU/mL
Resistance pattern (tick one only): ☐ Normal ☐ Multi-drug resistant (agents from 3 or more different drug classes)
4) _____ species, _____CFU/mL
Resistance pattern (tick one only): ☐ Normal ☐ Multi-drug resistant (agents from 3 or more different drug classes)
5) _____ species, _____CFU/mL
Resistance pattern (tick one only): ☐ Normal ☐ Multi-drug resistant (agents from 3 or more different drug classes)

Fig. 10.8 Urinary Tract Infection Basic Data Set (Version 1.0) (Courtesy of the International Spinal Cord Society (ISCoS) [61], with permission)

tomatic bacteriuria and UTI in patients with neurogenic bladder [7, 9]. Some experts proposed that antibiotic prophylaxis might be cautiously considered in patients with severe and frequent infections [64]. Alternating antibiotic schedules are used in practice, with the hypothesis that it may reduce the risk of resistance by continually changing the bacterial flora with antimicrobials that target different mechanisms. Preliminary study on antibiotic prophylaxis with two different antibiotics administered individually on a weekly basis showed reduced rate of UTIs from 9.4 per year to 1.8 per year [91]. Nevertheless, such an approach should not be routinely implemented and be considered only in highly selected patients.

Non-antibiotic Prophylaxis: Cranberry Prophylaxis with cranberries is a potential prevention strategy. Health benefits are associated with the high concentrations of polyphenols such as proanthocyanidins found in these berries. The

Fig. 10.9 Algorithm of diagnosis and management of urinary tract infection in patients with neurogenic bladder

proposed mechanisms explaining the protective effect of cranberries include inhibition of the adhesion of bacteria to the uroepithelial cells and reduction of the urinary pH to prevent bacterial growth [92]. A recently published systematic review with meta-analysis has shown the potential use of cranberries in a clinical condition of UTI [93]. The weighted risk ratio observed indicates that the use of cranberry products significantly reduced the incidence of UTIs. The results of subgroup analysis demonstrated that the patients at some risk of developing UTIs (particularly women with recurrent UTIs) were more susceptible to the effects of the ingestion of cranberries. The effectiveness of cranberry products is likely to depend on their concentration of proanthocyanidins. The daily recommended amount of proanthocyanidins in order to decrease the number of UTIs is at least 36 mg [93]. However, there is no evidence to support the efficacy of cranberries products for chronic use. The large number of dropouts/withdrawals indicates that cranberry juice may not be acceptable as a long-term treatment option [10, 94]. There is lack of consistency among the administered dosages of proanthocyanidins in currently available studies. Importantly, studies of SCI patients do not support prophylaxis with cranberries. The effectiveness of cranberries for prevention of UTIs in SCI patients was investigated in four studies [95–98]. No benefit of cranberries supplementation was reported in three of these trials [95, 96, 98]. One study with positive outcomes has been criticized for its small sample size and for the fact that 74% of patients were managed with a condom catheter [97]. A recent randomized double-blind study of patients with neurogenic bladder of different etiology found that concentrated cranberry supplementation did not reduce colony counts or prolong the time it takes UTI symptoms to appear

[99]. Therefore, cranberry supplementation is not effective at preventing UTIs in individuals with neurogenic bladder dysfunction [92].

Other Non-antibiotic Measures Methenamine hippurate is not an effective prophylactic measure in individuals with neurogenic lower urinary tract dysfunction [100]. A meta-analysis of available trials has shown that oral intake of methenamine hippurate does not have sufficient evidence for UTI prevention to merit recommendation [66]. The effectiveness of ascorbic acid at preventing UTIs and reducing urinary pH in neurogenic patients was assessed in two studies, and ascorbic acid was determined to be insufficient in the prevention of UTI in neurogenic patients [101, 102]. Furthermore, both studies presented serious methodological limitations, including unknown randomization, convenience sampling, high number of dropouts, and no intention-to-treat analysis [92]. To make things worse, vitamin C supplementation may represent a risk factor for calcium oxalate stones. Products containing D-mannose, green tea extracts, and probiotics have not been studied for UTI prevention in neurogenic patients [10]. Bacterial interference is characterized by intentional bladder colonization with a bacterial strain of low virulence in order to deter uropathogenic bacterial binding, internalization, and subsequent infection [29]. The inoculation of apathogenic *Escherichia coli* strains into the bladder has demonstrated positive results only in the initial studies [103–105]. Therefore, this method cannot be recommended for daily clinical practice [7].

Conclusion (Table 10.1)

Table 10.1 Conclusion

Summary	Level of evidence
Urinary tract infection (UTI) is the onset of signs and/or symptoms accompanied by laboratory findings of a UTI (bacteriuria, leukocyturia, positive urine culture)	4 (Expert opinion)
Significant bacteriuria can be diagnosed with $>10^2$ colony-forming units per milliliter of urine (cfu/mL) in persons performing intermittent catheterization, $>10^4$ cfu/mL from clean-void specimens, and any detectable concentration from suprapubic aspirates	4 (Expert opinion)
Significant leukocyturia can be diagnosed with ten or more leukocytes in centrifuged urine samples per microscopic field (400×)	4 (Expert opinion)
The overall rate of UTI in neurogenic patients is 2.5 episodes per patient per year, and more than one third of patients are diagnosed with a UTI within the first year of diagnosis of bladder dysfunction	3
Asymptomatic bacteriuria is a common finding in neurogenic individuals, affecting almost all patients managed with long-term intermittent and indwelling catheterization	2/3
The Enterobacteriaceae family represents the most commonly isolated organisms in the neurogenic population. Nevertheless, patients with neurogenic bladders tend to have an increased rate of infection with other organisms, including multi-drug resistant species	2/3
In the neurogenic population, traditional symptoms and signs of UTI may be replaced by different symptomatology	4 (Expert opinion)
Laboratory testing includes urinalysis and urine culture	4 (Expert opinion)
Treatment duration has not been well established and depends on infection severity and location (cystitis, urethritis, prostatitis, epididymitis, pyelonephritis)	4 (Expert opinion)
Many modalities have been proposed with the goal of reducing the incidence of UTI. These include patient education as well as mechanical and medical strategies for UTI prevention	4 (Expert opinion)

(continued)

Table 10.1 (continued)

Recommendation	Grade of recommendation
Presence of UTI should raise attention to incorrect bladder management or evolution of bladder dysfunction	Expert opinion
Urinalysis with a dipstick test is more useful to exclude than to prove UTI in neurogenic patients	C
Urine culture with antibiogram remains the definitive proof of infection	Expert opinion
In individuals with neurogenic bladder dysfunction, asymptomatic bacteriuria should not be screened or treated unless there is suspicion of UTI. Exceptions include pregnant women, patients before urological procedures within the urinary tract, and those on immunosuppression	C
Antibiotic therapy should be chosen based on the results of urine culture and sensitivity. Once treatment is initiated, all catheters should be changed	Expert opinion
An acute episode of UTI should be treated with antibiotics for 5–14 days, depending on infection severity and location	Expert opinion
If immediate therapy is mandatory, the choice of treatment should be based on local and patient-based resistance patterns	Expert opinion
Patients with recurrent UTIs should be carefully evaluated for underlying causes of recurrent infections, and their bladder management should be optimized	B
Mechanical strategies for UTI prevention should be considered in all catheterized patients	Expert opinion
Medical strategies, including antibiotic prophylaxis, have been determined to be insufficient in the prevention of UTI in neurogenic patients and should not be routinely used	C
UTI prevention should be individualized based on demonstrated risk factors and clinical scenario. There is currently no preventive measure that can be recommended without limitations	Expert opinion

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Urolithiasis

11

Introduction

Urolithiasis is a well-documented complication of neurogenic bladder with significant morbidity and even mortality. Underlying neurological disorder can often make the clinical diagnosis and treatment of this condition more challenging than in non-neurogenic patients. Therefore, evaluation and medical management of stone disease in neurogenic patients should be personalized. Identifying the risk factors for the development of urolithiasis and introduction of the precautionary measures may help to minimize recurrence and improve these patients' prognosis and future quality of life.

Epidemiology

The incidence and prevalence of urolithiasis among patients with neurogenic lower urinary tract dysfunction vary, depending on the underlying neurological disorder and developed risk factors. The risk of urinary tract stone disease in patients with neurogenic bladder is significantly higher than in the general population. The lifetime risk for urolithiasis in the general population is estimated at 12% for men and 6% for women with age standardized annual incidence rates from 0.36 to 1.22/1000 person-years [1]. The prevalence of urolithiasis in patients with spinal cord injury (SCI) has been reported to be as high as 38% and the risk of stone formation appears to increase over time [2–4]. The annual risk for forming bladder stones in SCI patients has been calculated as 4% [5]. It has been estimated that up to 20% of SCI individuals will develop struvite stones within 10 years of injury and up to 7% of them will complain of renal stones [6, 7]. Interestingly, the incidence of renal calculi appears to peak during the period immediately after SCI (3–6 months) [2, 4, 6]. This early risk of stone formation is hypothesized to be a result of a significantly increased calcium excretion because of immobilization and loss of calcium from the lower extremity skeleton [8]. In myelomeningocele patients, the incidence of renal calculi may be greater [9]. The annual risk of forming bladder stones in individuals who have already formed one stone is 16% [5]. Once a kidney stone develops, there is a 34% chance of a second renal stone developing within the next 5 years [4]. The frequency of recurrences may be even higher, with reported episodes up to 64 and 72% [10, 11]. Patients with SCI also have a high incidence of bilateral stones (23–74%) [12–14].

Risk Factors

The main risk factors for stone development in neurogenic patients are [8, 11, 15–20]:

- Recurrent urinary tract infections (UTIs), in particular with urea-splitting organisms

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_11

(*Proteus, Pseudomonas, Klebsiella, Staphylococcus, Mycoplasma*)
- Bacteriuria
- Indwelling catheterization (both suprapubic and urethral)
- Urine stasis (may be seen either in patients with an indwelling catheter that does not drain well or in those who catheterize infrequently or who fail to empty fully)
- Vesicoureteral reflux
- Hydronephrosis
- Renal scarring
- Lower urinary tract reconstruction (in particular with surgical interposition of bowel segments)
- Bladder diverticula (may predispose to incomplete emptying and thus stone formation in the diverticulum)
- Foreign bodies (e.g., hair introduced during clean intermittent catheterization)
- Previous history of urolithiasis and persistent stone fragments and residual fragments left after previous treatment
- High spinal cord lesions
- Complete spinal cord lesions
- Paraplegic and quadriplegic dysfunctions
- Chronic immobilization
- Metabolic abnormalities
  - hypercalciuria (resulting from immobilization and demineralization of bone)
  - hypocitraturia (resulting from a reduced filtered load of citrate)
  - dehydration (resulting from hyperhidrosis, reduced fluid intake in order to reduce the number of catheterizations or postural oliguria from autonomic disturbances)
  - Increased urinary pH (resulting from bacterial infection)
- Young and old age
- Specific geographic variations and environmental risk factors (may exert a greater magnitude of risk than they do in the general population)

Among them, the most important causes of urolithiasis in the neurogenic population are urinary stasis and infection [16]. Even though calculi can occur at any level of the urinary tract, they are usually found in the bladder, particularly if bladder augmentation has been performed [21, 22].

Stone Composition

The majority of urolithiasis in the SCI population is either apatite (calcium phosphate) or struvite (magnesium ammonium phosphate) in composition [17]. Whereas the first type occurs as a result of the alkaline pH of infected urine, the latter is the direct result of urinary infection with urease-producing bacteria (*Proteus, Klebsiella, Pseudomonas*) [14]. In the past decades, >90% of stones in patients after SCI were reported to be struvite [23, 24]. However, contemporary studies have suggested that the proportion of struvite stones has decreased and that stones of a metabolic origin now predominate in patients with SCI [8]. A study of individuals with musculoskeletal anomalies found struvite stones in only 18% of patients [14]. The most common stone type was calcium apatite (50%), which is an uncommon stone in the general population. It has been proposed that the shift from an infectious to a metabolic etiology may represent reduced risk of UTIs among patients with SCI because of dedicated SCI units, commonness of clean intermittent catheterization, better bladder augmentation techniques, and more precise urodynamic assessment [8, 25]. Therefore, when a metabolically derived stone is identified, the patient should be offered metabolic evaluation with medical and dietary therapy [26].

Diagnosis and Treatment

Comprehensive guidelines for diagnosis and treatment of urolithiasis have been developed and they can be applied in the management of patients with neurogenic bladder. This includes Guidelines of the European Association of Urology (EAU) [27], the American Urological Association (AUA) [28], and the Canadian Urological Association (CUA) [29]. Importantly, the proposed guidelines also highlight and support management of metabolically derived stones. Nevertheless, some differences in diagnosis and treatment of urolithiasis in neurogenic individuals have to be stressed.

Diagnosis

Ureteral stones can cause acute unilateral flank pain radiating to the groin, often accompanied by nausea, vomiting, and urinary symptoms [30]. The diagnosis of urolithiasis in neurologically impaired patients may be more difficult because of atypical presentation and non-specific symptoms, including feeling unwell, abdominal discomfort, sweating, increased spasms, and autonomic dysreflexia [15]. Depending on the level of neurologic dysfunction, many patients do not experience flank pain [8]. Urolithiasis may also be demonstrated by storage symptoms (urgency, frequency, incontinence), hematuria, difficulties in self-catheterization, recurrent catheter blockages, and recurrent UTIs or even sepsis. Relapsing infection within the urinary tract is considered the most common presentation in individuals with neurogenic lower urinary tract dysfunction that leads to a stone diagnosis [10].

With the exception of pregnant women, the imaging modality of choice for diagnosis in the general population is computed tomography of the kidneys, ureters, and bladder, characterized by a sensitivity of 95–96% and specificity of 98% (Fig. 11.1) [31, 32]. While ultrasound is free of radiation, it has a relatively low sensitivity and specificity of 45 and 94%, respectively (Fig. 11.2) [33–35]. A plain frontal supine radiograph of the abdomen can support the diagnosis of stone disease (Fig. 11.3) [36]. However, in neurogenic patients, the final diagnosis of urinary stones is often made using endoscopy [37, 38]. The National Institute for Health and Care Excellence recommends referring neurogenic patients with symptoms that suggest the presence of bladder stones for cystoscopy (Figs. 11.4 and 11.5) [39–41].

Treatment

Shockwave lithotripsy (SWL), ureteroscopy (URS), and percutaneous nephrolithotomy (PCNL) are commonly used treatment modalities of stone disease. Whereas open surgery is currently rarely used in the general population, it still remains a valuable treatment option in neurogenic patients [42].

Preoperative Considerations in Neurogenic Patients Suffering from Urolithiasis

Bacterial Colonization Colonization of urine occurs in the majority of patients with neurogenic lower urinary tract dysfunction (see Chap. 10, "Urinary Tract Infections"). Bacterial strains resistant to multiple antibiotics are not uncommon and contribute to polymicrobial colonization of the urinary tract. This increases the risk of sepsis as a result of treatment of the stone [43]. Preoperative treatment with appropriate antibiotics is necessary, as untreated bacteriuria can lead to serious complications [44]. Postoperative urosepsis has been reported in the literature in up to 14% of operated patients [12, 45]. Furthermore, it has been shown that the retreatment and complication rates are higher in neurogenic patients, primarily because of bacterial colonization and recurrent UTIs with infected stones [12, 17]. Preoperative treatment should always be based on a recent urine culture at least 7 days prior to stone treatment [17]. In individuals colonized by multi-resistant strains of bacteria, intravenous antibiotics may be necessary. Once treatment is initiated, all catheters should be changed. In patients performing intermittent catheterization, more frequent and complete emptying is required. Appropriate prophylactic antibiotic therapy during the procedure is recommended in order to minimize the chances of urosepsis during urinary tract manipulation and stone fragmentation [17]. Further proposals include re-culturing the urine and obtaining sensitivities immediately following the procedure, as bacteria released from fragmented stones may differ from the pre-operative urinary tract flora [17]. Additional perioperative urine cultures should always be obtained when indicated by the clinical scenario.

Orthopedic Factors Scoliosis, limb contractures, skeletal deformities, and spinal hardware may hamper positioning of patients and obtaining retrograde access for URS or good visualization of the upper urinary tract with fluoroscopy for PCNL [44–46]. Poor visualization and complicated anatomy may contribute to an increase in complications. Careful assessment of extremity and trunk mobility and range of movement

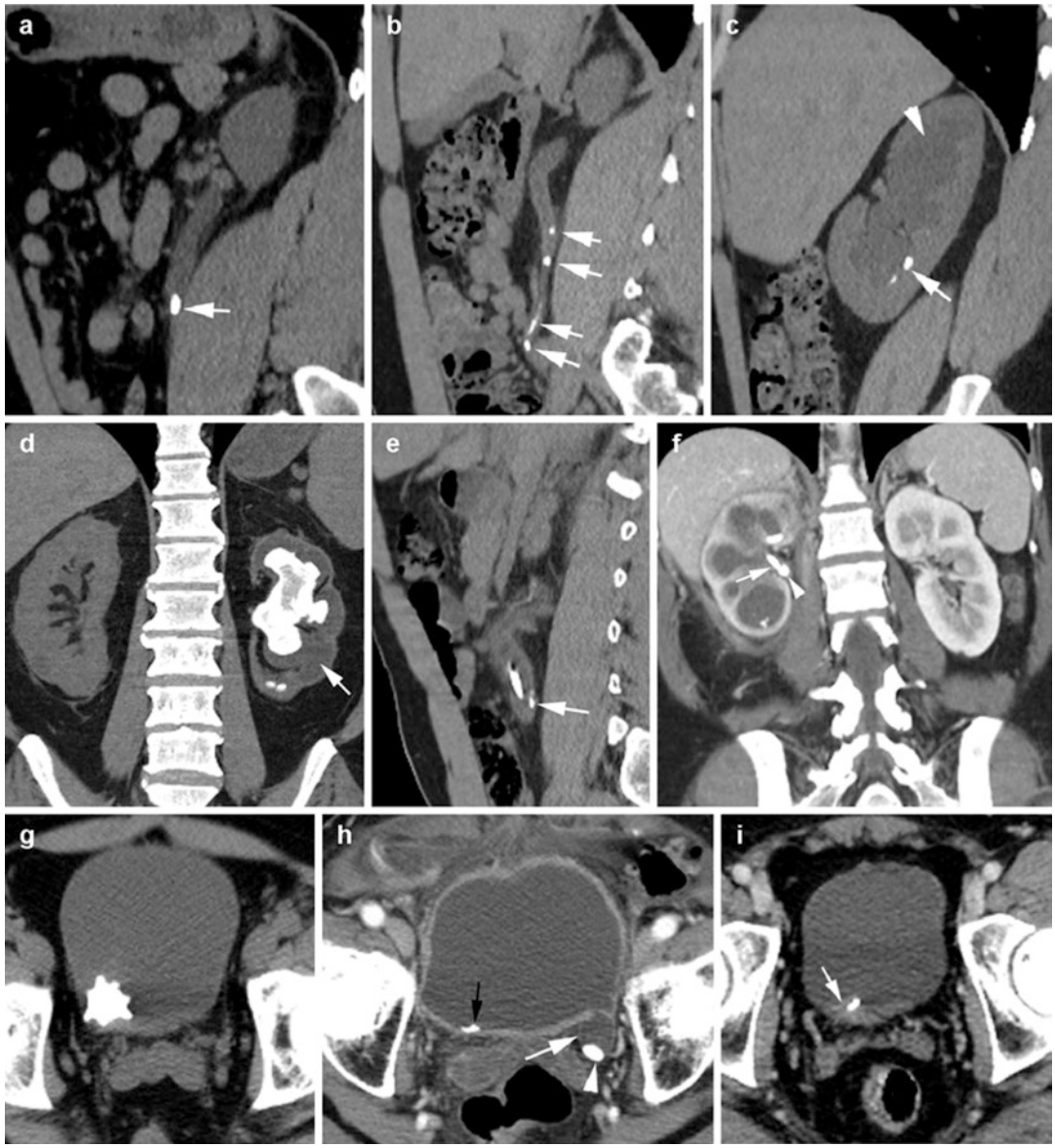

Fig. 11.1 Urinary stones in different patients. Noncontrast sagittal reformatted CT (**a**) shows a single stone (*arrow*) in the ureter, which is dilated proximal to the stone. (**b**, **c**) Multiple stones in the right ureter (*arrows*) with hydronephrosis (*arrowhead*) and stones in lower pole calyces (*arrow*). (**d**) Coronal reformatted image shows large staghorn stone in the left kidney with hydronephrosis. The calyces distal to the stone are dilated and fluid filled (*arrow*). (**e**) Sagittal reformatted image shows stone (*arrow*) along with stent and hydroureter. (**f**) Postcontrast coronal reformatted image shows a stone (*arrowhead*) with stent *(white arrow*) at ureteropelvic junction causing hydronephrosis. Axial CT (**g**) shows a jackstone urinary bladder. Axial CT shows (**h**) a stone (*arrowhead*) in Hutch diverticulum (*white arrow*) and a small stone within the bladder (*black arrow*). (**i**) Stone at ureterovesical junction with surrounding soft tissue (*arrow*) of the bladder wall (with permission from Agarwala [32])

should be performed before any procedure to ensure that the patient can be positioned properly during the operation. To overcome orthopedic issues, different positions such as modified flank or flank and biplanar fluoroscopy with more dynamic visualization can be used to achieve treatment success [44]. In those patients in whom retrograde access cannot be achieved, a

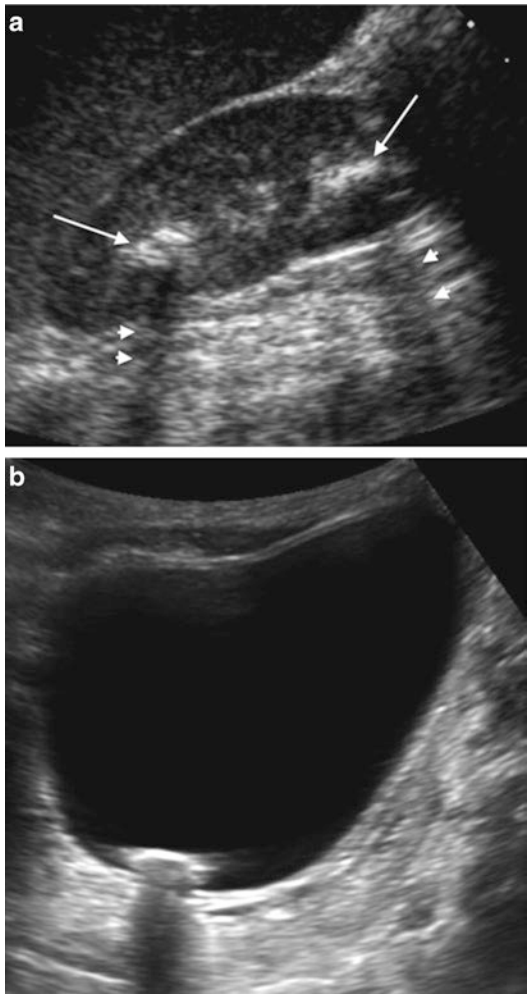

Fig. 11.2 (**a**) Renal stones in the upper and lower poles. Both stones are echogenic (*long arrows*) with posterior acoustic shadowing (*arrow heads*). (**b**) Bladder stone. Similar to the renal stones, the bladder stone is echogenic and demonstrates clear posterior acoustic shadowing (with permission from Ching et al. [35])

percutaneous approach may be useful to perform antegrade flexible ureteroscopy and lithotripsy [8]. Regardless of the chosen treatment, patients should be protected from pressure ulcers during the procedure by appropriate padding of all pressure points.

Patients After Reconstructive Surgery within the Urinary Tract Although it has been demonstrated that retrograde endourologic techniques are feasible and safe (with success rates of 75%) in patients with urinary diversion [47], altered anatomic relations of the urinary tract after reconstructive surgery can make retrograde access to the ureter challenging and lead to additional complications and lower clearance rates. Preoperative surgical history should carefully document any prior procedures within the urinary tract. The patient's medical documentation may be of value in choosing a proper treatment.

Hydronephrosis or Suspicion of Upper Tract Obstruction In cases of preoperative hydronephrosis, some experts recommend appropriate drainage with a stent or a nephrostomy tube prior to any procedure [44]. Hydronephrosis in neurogenic patients may indicate pyonephrosis, even with negative urine cultures. Thus, if hydronephrosis is not appropriately drained and diagnosed preoperatively, postoperative urosepsis may lead to serious life-threatening complications.

Autonomic Dysreflexia In patients with high-level SCI, surgery may trigger autonomic dysreflexia (see Chap. 14, "Autonomic Dysreflexia"). Bladder overdistension is the most common trigger of this disorder, characterized by high blood pressure, bradycardia, headache, flushing, and sweating. Treatment consists of draining the bladder and placing the patient in the upright position if he or she is awake. If this fails, a fast-acting antihypertensive should be administered [48]. Standard anesthesia monitoring (including blood pressure control) is therefore required for all patients during any procedure of stone treatment.

Treatment Options

Management of urolithiasis in individuals with neurogenic bladder is similar to that in non-neurogenic patients and is described in reliable guidelines but some important issues need to be acknowledged:

- General anesthesia may sometimes be necessary because of the impossibility of using spinal anesthesia due to spinal deformities or injuries.
- The length of hospital stay in a population of neurogenic patients may be longer than that for the general population [49]. Prolonged hospitalization may result from surgical

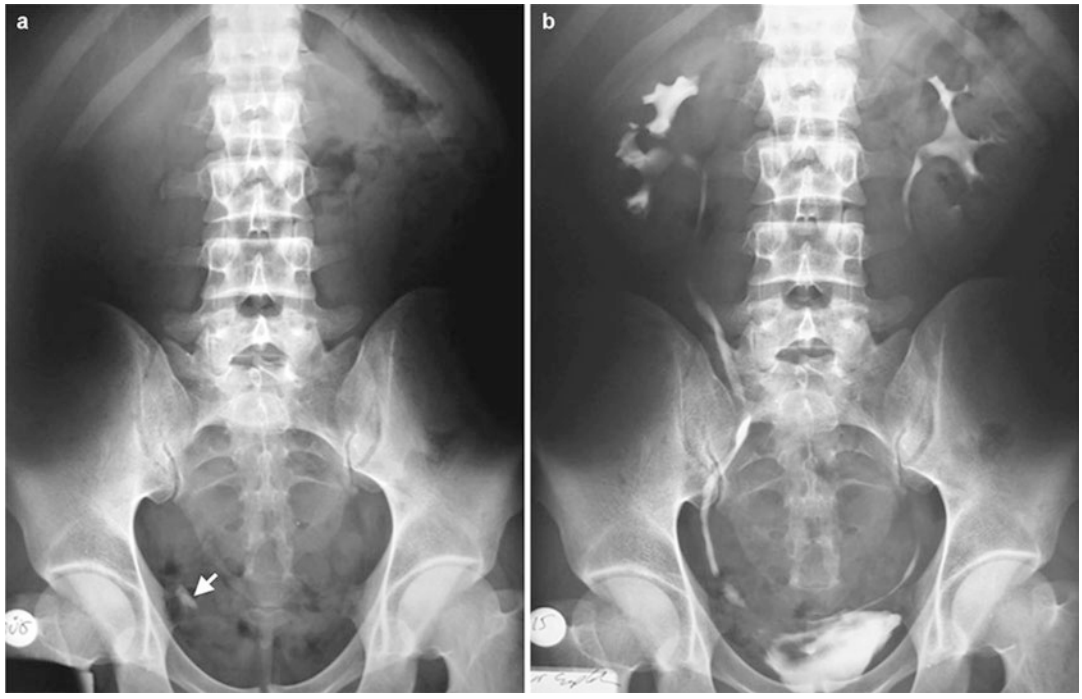

Fig. 11.3 Partially obstructing right distal ureter stone (*arrow*) on plain film (**a**) and as a filling defect on intravenous pyelogram (**b**) (with permission from Ünsal and Karaman [36])

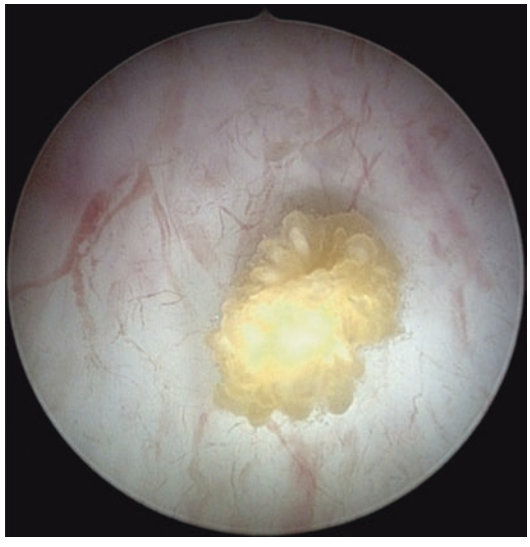

Fig. 11.4 Cystoscopy with a bladder stone (with permission from Maffi and Lima [40])

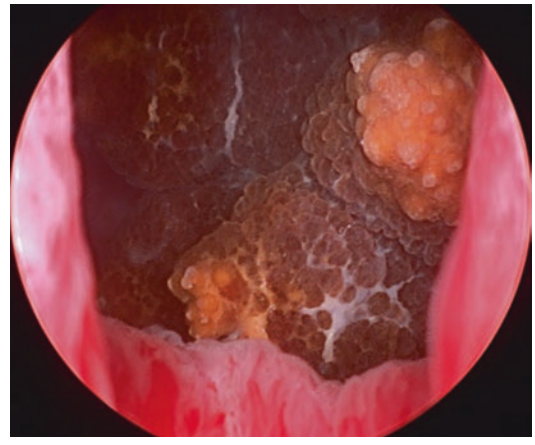

Fig. 11.5 Large bladder stone between lobes of the prostate (with permission from Schulsinger [41])

complications as well as issues with management of other medical comorbidities.

- Chosen treatment should aim to completely remove all stone particles, regardless of size. SWL may be effective at breaking a stone, but neurogenic patients may be unable to clear the pieces due to impaired voiding, reduced mobility, and often large stone burden [8]. Small residual fragments may contribute to rapid stone recurrence and relapsing infections [50, 51]. In SCI patients, success rates and stone-free rates of SWL vary from 50 to over 70% [52]. Therefore, URS or PCNL may represent a better treatment modality to ensure complete stone-free status postoperatively [53]. On the other hand, SWL is feasible without additional anesthesia in most patients, and the rates of intra-operative complications, including autonomic dysreflexia, are low [52]. SWL may be a good option for treating patients who are anesthetic risks or prone to autonomic dysreflexia. Quadriplegics with high-level cord injuries requiring cardiac pacemakers and those with baclofen pumps have safely undergone SWL without complications [54, 55]. To sum up, SWL in patients with neurogenic lower urinary tract dysfunction may be considered as part of a multimodality strategy in stone management, rather than a standalone treatment.
- Flexible URS may be of value in achieving stone-free status postoperatively, particularly in patients after reconstructive surgery within the urinary tract or those with orthopedic issues hindering proper patient positioning. Moreover, fibrosis and thickening of the bladder wall, often seen in neurogenic bladders, alter the ureteral orifice anatomy and make ureteral access challenging [56]. When retrograde URS fails to clear the stones, alternative approaches (SWL or antegrade flexible URS following percutaneous renal access and tract dilation) should be considered [17, 44]. However, there is a paucity of data to support clinicians with reliable recommendations on treating neurogenic patients with URS.
- Although high stone-free rates of PCNL in neurogenic patients have been reported, particularly in those after SCI, PCNL in this specific population still remains a more complex approach, often requiring multiple procedures to achieve stone clearance [12, 13, 57–59]. Complication rates are fairly high, in comparison to non-neurogenic patients, with significantly increased rates of urosepsis, systemic inflammatory response syndrome, perirenal abscess, and post-PCNL pyrexia [12, 58–60]. In the neurogenic population, PCNL is associated with a major complication rate as high as 20% and even perioperative death has been reported [58]. This stresses the need for culture-specific antibiotic therapy prior to the procedure. The majority of PCNL procedures are performed with the patient in the prone position (Fig. 11.6) [61] but in neurologically impaired individuals, especially in those with

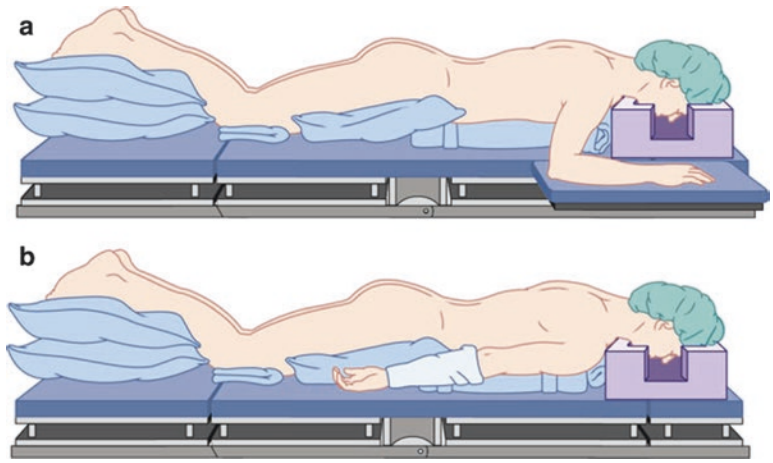

Fig. 11.6 (**a**) Prone position with arms in the "Superman" position and (**b**) with arms tucked at the patient's sides. The neck is in neutral position, the thorax and abdomen are placed on bolsters, and all pressure points are padded (with permission from Gal et al. [61])

SCI, the supine or lateral technique can be more useful when prone positioning is not possible because of musculoskeletal deformity (Figs. 11.7 and 11.8) [8, 61]. Image guided puncture with ultrasonography or computed tomography may be used as an alternative to ureteral access with retrograde injection of contrast media for a fluoroscopy-guided puncture. If pyonephrosis is found when obtaining access, the procedure is

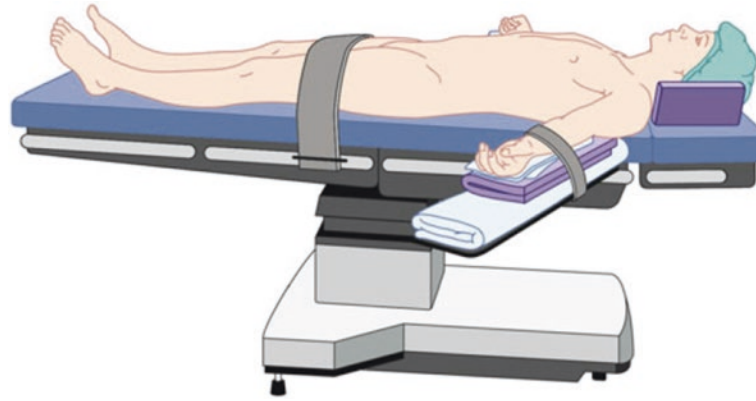

Fig. 11.7 Supine position. The neck is placed in neutral position. The arms are abducted <90°, supinated, and padded underneath. All other pressure points are padded with a cushioned mattress (with permission from Gal et al. [61])

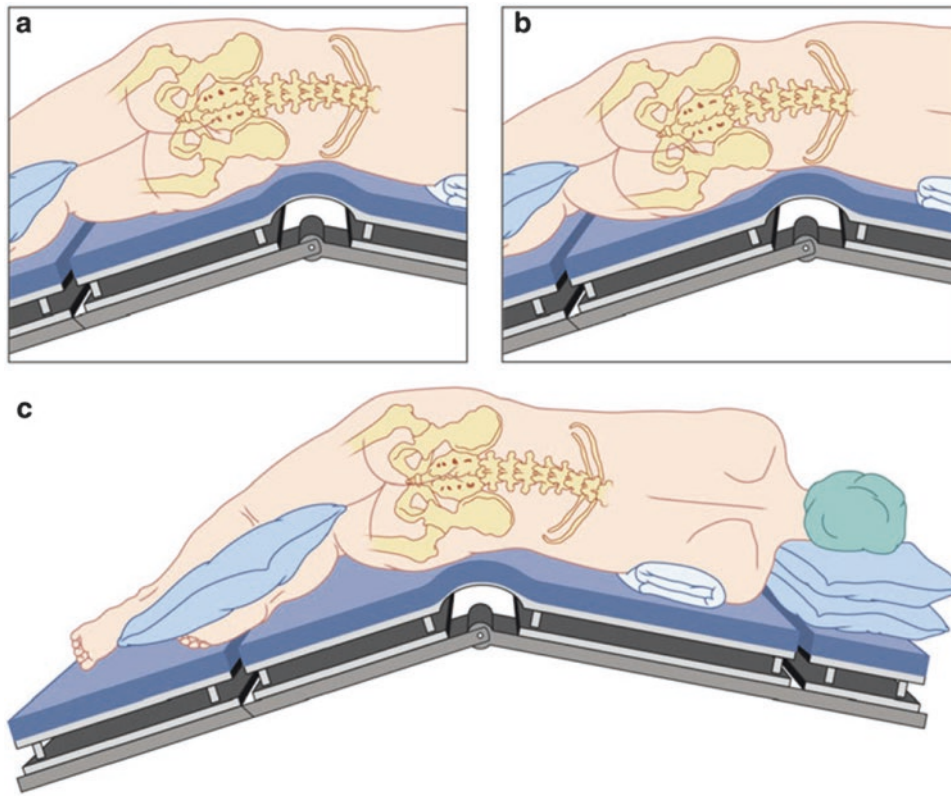

Fig. 11.8 Jackknife lateral decubitus position. Improper placement of kidney rest at (**a**) below the flank and (**b**) dependent costal margin. (**c**) Correct positioning below dependent iliac crest (with permission from Gal et al. [61])

Fig. 11.9 The Ellik-evacuator with locking adapter (with permission from courtesy of Trokamed GmbH)

immediately terminated and a nephrostomy tube is left for drainage [44].

- Techniques to treat bladder stones in the neurogenic population do not differ much from the procedures used to treat bladder stones in the general population because of straightforward access to the bladder (either transurethrally or percutaneously). The stone can be fragmented endoscopically by mechanical forceps; holmium laser; or by ultrasonic, pneumatic, or electrohydraulic lithotripsy [15]. Small fragments can then be washed out from the bladder by the Ellik evacuator (Fig. 11.9).
- Invasive surgery is indicated for large stones that cannot be removed with minimally invasive techniques. A combination of laparoscopic and percutaneous techniques, which allows for the use of large instruments and minimizes the risk of leaving residual stone fragments, have been reported [62]. Large bladder stones (>6 cm) or heavy stone burdens can be treated percutaneously with an ultrasonic lithotripter (through an Amplatz dilated 30F cytostomy tract) or by a traditional open cystolithotomy [17]. Open bladder surgery is also indicated when bladder capacity is small.
- Overall, the postoperative stone-free (clearance) rates in the neurogenic population tend to be lower compared to neurologically unaffected controls, thus often requiring multiple and repeated interventions. Patients with neurogenic bladder are also at increased risk for complications after treatment of stone disease.

Prevention

Recurrence rates of stone disease in patients suffering from neurogenic lower urinary tract dysfunction are high. In patients who do not receive prophylaxis following the first attack, recurrence rates are reported as 10% in the first year, 35% in the next 5 years, and 50% in 10 years [63]. Minimizing the risk factors contributing to urolithiasis will minimize morbidity in these specific patients. Successful and efficient long-term stone prevention includes [27, 64]:

- Adequate hydration
- Treatment and prevention of UTIs, especially with eradication of urea-splitting organisms
- Careful and timely catheterization
- Avoiding the use of indwelling catheters (if an indwelling Foley catheter must be used, weekly catheter changes should be performed)
- Correction of metabolic disorders
- Optimization of bladder management, particularly with restoration of normal voiding function (if possible)
- Regular positioning
- Early mobilization

The issue of whether or not neurogenic patients should be imaged on a regular interval remains controversial. Annual ultrasound screening has been recommended to detect asymptomatic stone disease by multiple authors [2, 12, 13, 17, 65, 66]. Nonetheless, there is a paucity of data regarding the incidence of asymptomatic stones detected on annual follow-up or regarding the role of computed tomography surveillance of the upper tracts in this group of patients [52]. Despite variations in urological practices and the lack of clear-cut guidelines for follow-up (see Table 6.2 in Chap. 6, “Bladder Management and Follow-Up Plan”), the increased incidence of urolithiasis among neurogenic patients argues for routine genitourinary imaging surveillance in order to identify and treat those individuals who are at the highest risk.

Conclusion (Table 11.1)

Table 11.1 Conclusion

Summary	Level of evidence
Individuals with neurogenic bladder dysfunction have a high prevalence of urolithiasis compared to the general population. These patients are also at increased risk for stone recurrence and bilateral stone disease. Currently available data are mainly limited to patients after spinal cord injury	2/3
The increased risk is due to multiple factors, including urinary stasis, infection, chronic catheterization, immobilization, and specific metabolic changes	3
Recent literature has suggested an increase in calculi of a metabolic etiology in this population, secondary to more aggressive medical management	3
The clinical presentation of stone disease in patients with neurogenic lower urinary tract dysfunction tends to involve atypical symptoms, including frequent infections of the urinary tract and urosepsis	4 (Expert opinion)
The treatment of upper and lower urolithiasis in neurogenic patients is more challenging and less successful. The increased stone burden in this specific group of patients contributes to longer operative time and lower clearance rates. The overall complication rate is also higher than in the general population, and infection-related complications predominate	2/3
Neurologically impaired patients may require prolonged hospitalization and multiple procedures or modalities to be rendered stone free	3
Treatment methods include shockwave lithotripsy (SWL), ureteroscopy (URS), percutaneous nephrolithotomy (PCNL), transurethral bladder lithotripsy, and invasive surgery	4 (Expert opinion)
Success rates and stone-free rates of SWL vary from 50 to over 70%	3
There is a paucity of data on URS treatment in neurogenic patients	4 (Expert opinion)
High stone-free rates (approximately 90%) of PCNL in neurogenic patients have been reported	3
Recommendation	Grade of recommendation
As urolithiasis is a common problem among patients with neurogenic bladder dysfunction, it should be addressed during routine urological care in order to minimize the increased risk of renal insufficiency and to improve long-term prognosis	Expert opinion
Diagnosis and treatment should be conducted based on reliable and well-developed guidelines	Expert opinion
A careful preoperative assessment of bacterial colonization, orthopedic factors, and history of reconstructive surgery within the urinary tract is recommended	Expert opinion
A higher baseline rate of bacterial colonization coupled with active stone disease predisposes to urosepsis and other complications. Thus, preoperative cultures and sensitivity-tailored antibiotics are recommended to minimize morbidity in neurogenic patients	C
The goal of treatment should be to remove all residual fragments, regardless of size	Expert opinion
It is important to render the patient stone free, even if multiple treatments are needed, because residual fragments can lead to a rapid stone recurrence and are a potential source for future infection	C
If a stone is obstructing the kidney in the setting of infection, emergency renal drainage is mandatory	Expert opinion
Multiple strategies for stone prevention should be considered in all patients	Expert opinion

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Hydronephrosis

12

Introduction

Hydronephrosis, a dilation of the renal collecting system (renal pelvis and/or calyces), may be diagnosed in patients suffering from neurogenic lower urinary tract dysfunction. One or both kidneys may be affected. If hydronephrosis coexists with a distension of the ureter, the presenting disorder can be termed *hydroureteronephrosis.* It is important to emphasize that hydronephrosis is an anatomic finding, not a functional diagnosis [1]. If not appropriately treated, this condition can lead to progressive kidney atrophy and functional failure. Parenchyma loss in patients with hydronephrosis is a long, gradual, pathologic process.

Pathophysiology

In patients with neurogenic bladders, significant hydronephrosis can result from either underlying urodynamic dysfunction or already developed complications. Therefore, a dilation of the renal collecting system can be caused by:

- Urinary retention (detrusor underactivity or detrusor-sphincter dyssynergia) or primarily generated high bladder pressures (neurogenic detrusor overactivity, detrusor-sphincter dyssynergia, and/or decreased bladder compliance) when the antireflux mechanism of the ureterovesical junction becomes overwhelmed and the elevated pressures are eventually transmitted to the upper tracts (vesicoureteral reflux)
- Obstruction of one or both ureters from stones, tumors, infection, urethral stricture, or detrusor thickening from fibrosis (with gradual remodeling of the ureteral orifices and progressive destruction of the bladder wall)
- Other abnormalities also seen in the non-neurogenic population (e.g., congenital defects, injury, surgery, radiation therapy, prostatic hypertrophy, retroperitoneal fibrosis)

Diagnosis

Medical History and Physical Examination

Clinical presentation and reported symptoms vary, depending on whether the obstruction is acute or chronic, partial or complete, unilateral or bilateral, or even present or absent. Severity of hydronephrosis is related to the chronicity and degree of obstruction. Importantly, in patients without obstruction to urine flow, hydronephrosis may remain asymptomatic for a long time and the condition is detected on imaging for other reasons or during follow-up monitoring [2].

Rapidly developing obstruction of the renal collecting system often causes severe pain along the flank with radiation toward the ipsilateral

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_12

groin or lower abdominal quadrant [2]. Nausea and vomiting may also occur. With underlying infectious pathology, patients may present with fever and blood or pus in the urine. When obstruction is subacute to chronic, symptoms may be absent or less intense and non-specific (e.g., dull discomfort).

Carefully conducted medical history should also rule out any possible causes of hydronephrosis not related to neurogenic bladder dysfunction.

Physical examination may not reveal hydronephrosis-related abnormalities but should be performed. Abdominal, pelvic, and genitourinary examinations should be conducted.

Laboratory Testing

If not already obtained by the referring physician, laboratory tests should be performed as soon as reasonably possible. These include:

- blood chemistry—creatinine (with calculation of glomerular filtration rate, GFR), blood urea nitrogen, electrolytes (potassium, sodium, chloride, bicarbonate, phosphate, magnesium, calcium)
- urinalysis/urine culture with sediment examination

Imaging

Ultrasound

Renal ultrasonography remains a first-line imaging modality in the evaluation of patients suspected of hydronephrosis because of its availability, low cost, safety, and lack of ionizing radiation [1]. Renal ultrasound has been found to be a highly sensitive and specific test for hydronephrosis in both the adult and pediatric population with reported sensitivity and specificity of this modality for hydronephrosis as >90% (Fig. 12.1) [2]. Nevertheless, no consensus exists regarding the standardized definition of hydronephrosis. In daily clinical practice, when a patient presents with hydronephrosis, it is usually classified as mild, moderate, or severe (Fig. 12.2) [3]. The proposed system of assessment includes four grades [4]:

- Grade I (mild)—dilation of the renal pelvis without dilation of the calyces
- Grade II (mild)—dilation of the renal pelvis with a few but not all calices
- Grade III (moderate)—dilation of the renal pelvis with all calices
- Grade IV (severe)—dilation of the renal pelvis with all calices and parenchymal atrophy

As intra-observer variations in ultrasound assessment are well known, the results can vary significantly among clinicians. However, severe hydronephrosis can easily be diagnosed with characteristic ultrasound image consisting of collecting system dilation extended into renal parenchyma with cortical loss in long-standing cases. Ultrasound may also help in identifying potential causes of hydronephrosis, but its functionality is limited. Review of the literature revealed that ultrasound has a pooled sensitivity and specificity of 45% and 94%, respectively, for the detection of ureteric calculi, and 45% and 88%, respectively, for renal calculi [5]. It has also been demonstrated that ultrasound overestimates renal stone size compared to computed tomography, particularly for stones 5 mm or less.

Utilization of Doppler function with measurement of blood flow and resistance in the intrarenal arterial waveforms can also be used to assess the impact of hydronephrosis on renal function [6]. Doppler ultrasonography can help in differentiating between acute and chronic hydronephrosis [7, 8]. Ultrasonography with color Doppler function can also reliably identify ureteric jet dynamics in the bladder and help to distinguish between obstructive and non-obstructive hydronephrosis (Figs. 12.3 and 12.4) [9, 10]. Decreased frequency, duration, and peak velocity of ureteral jets indicate obstructive pathology [11]. Of note, this technique requires good hydration of the patient and is limited by the requirement of a normal contralateral collecting system for comparison [1]. Color flow Doppler ultrasound may also support and eventually

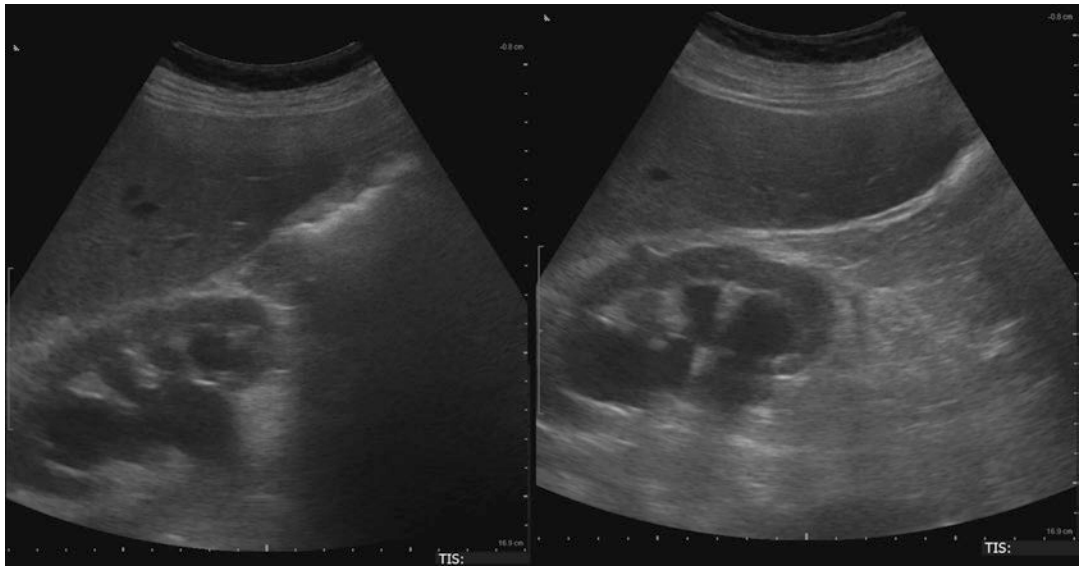

Fig. 12.1 Hydronephrosis of the right kidney. The renal collecting system is symmetrically dilated, including dilation of the renal calyces and central collecting system

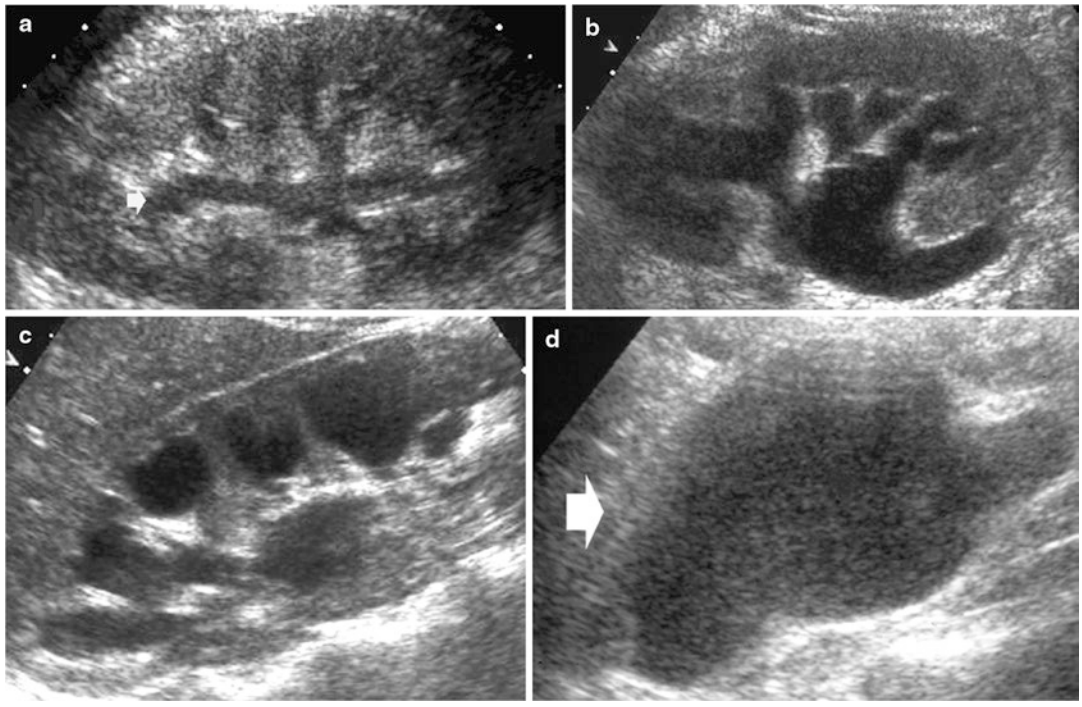

Fig. 12.2 Hydronephrosis grading. Progressive dilation of the intrarenal collecting system and pyelocaliectasis with a progressive reduction of the renal cortical thickness (**a**). First grade with mild dilation of the intrarenal urinary tract (*arrow*) (**b**). Second grade with pyelocaliectasis and normal morphology of the renal calyx (**c**). Third grade with pyelocaliectasis and renal calyces with a balloon shape (**d**). Fourth grade with a progressive thinning of the renal parenchyma (*arrow*) (with permission from Quaia et al. [3])

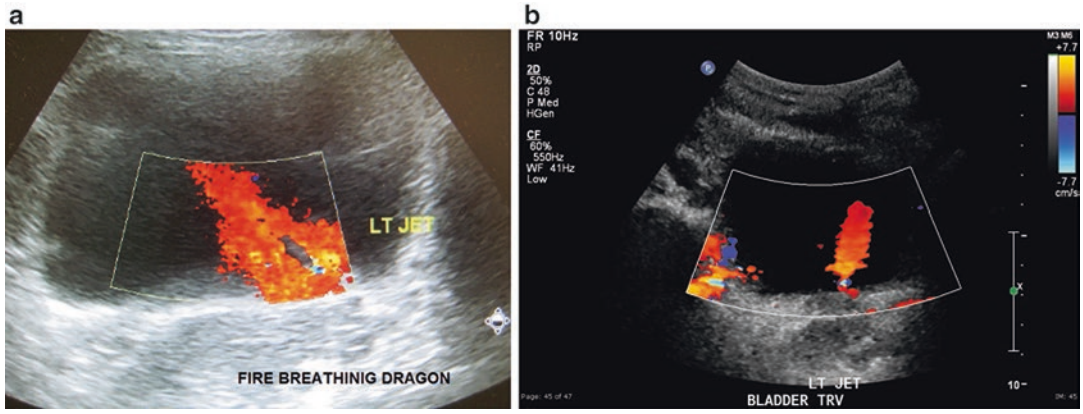

Fig. 12.3 (**a**) A strong left ureteral jet: pulsatile egress of urine into bladder gives the appearance of a fire-breathing dragon. (**b**) A strong left ureteral jet (*arrows*) in a patient with a left double pigtail ureteral stent. Note that the direction of the jet is slightly toward left of bladder and vertical, secondary to changes in the orientation of the orifice with the stent in place (with permission from Eshghi [10])

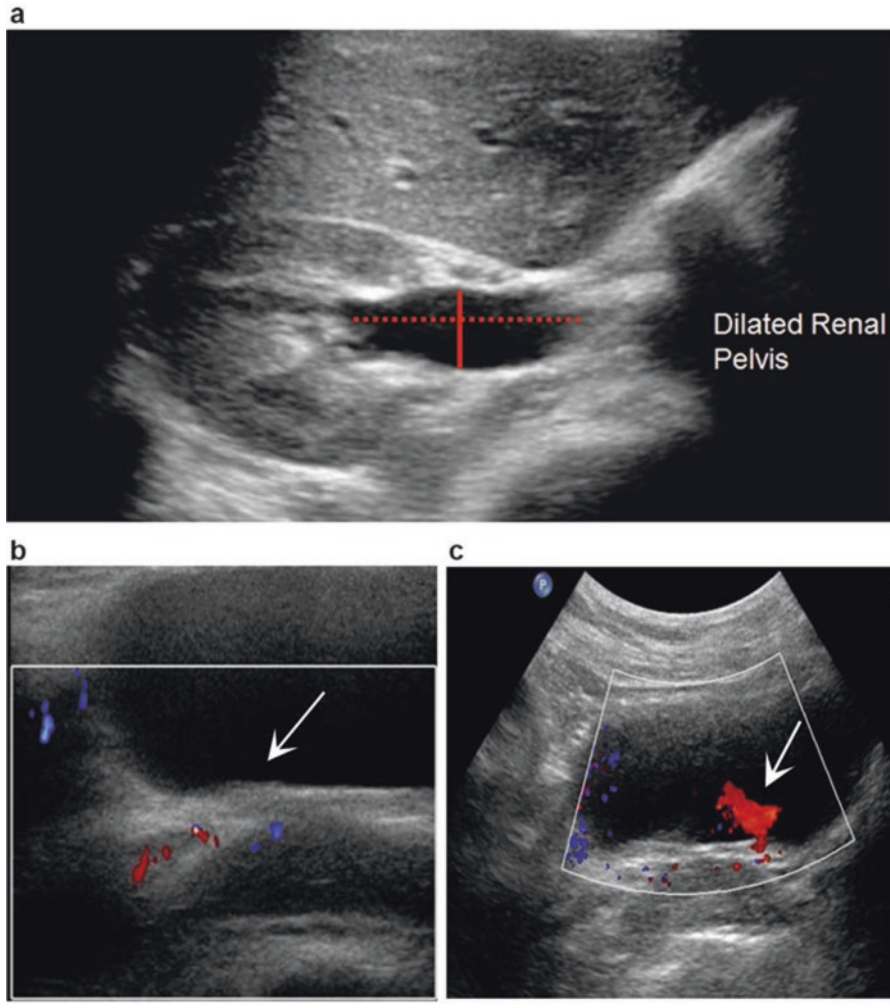

Fig. 12.4. (**a**) Hydronephrosis on the right side with dilation of the renal pelvis due to acute ureteral obstruction. (**b**) Absence of right ureteral jet (*arrow*). (**c**) Presence of a strong left ureteral jet (*arrow*). (with permission from Eshghi [10])

replace voiding cystourethrogram in the detection of vesicoureteral reflux. When reflux is found in patients with neurogenic disorder, it further contributes to the development of hydronephrosis. The severity of vesicoureteral reflux has been most commonly reported using the classification of the International Reflux Study (Fig. 12.5) [12–14]:

- Grade I: reflux into a non-dilated ureter
- Grade II: reflux into the renal pelvis and calyces without dilation
- Grade III: mild-to-moderate dilation of the ureter, renal pelvis, and calyces with minimal blunting of the fornixes
- Grade IV: moderate ureteral tortuosity and dilation of the pelvis and calyces
- Grade V: gross dilation of the ureter, pelvis, and calyces; loss of papillary impressions; and ureteral tortuosity

It has been shown that color Doppler ultrasonography can diagnose all grade IV and V refluxes, almost 90% of grade III, more than 80% of grade II, and almost 60% of grade I [15].

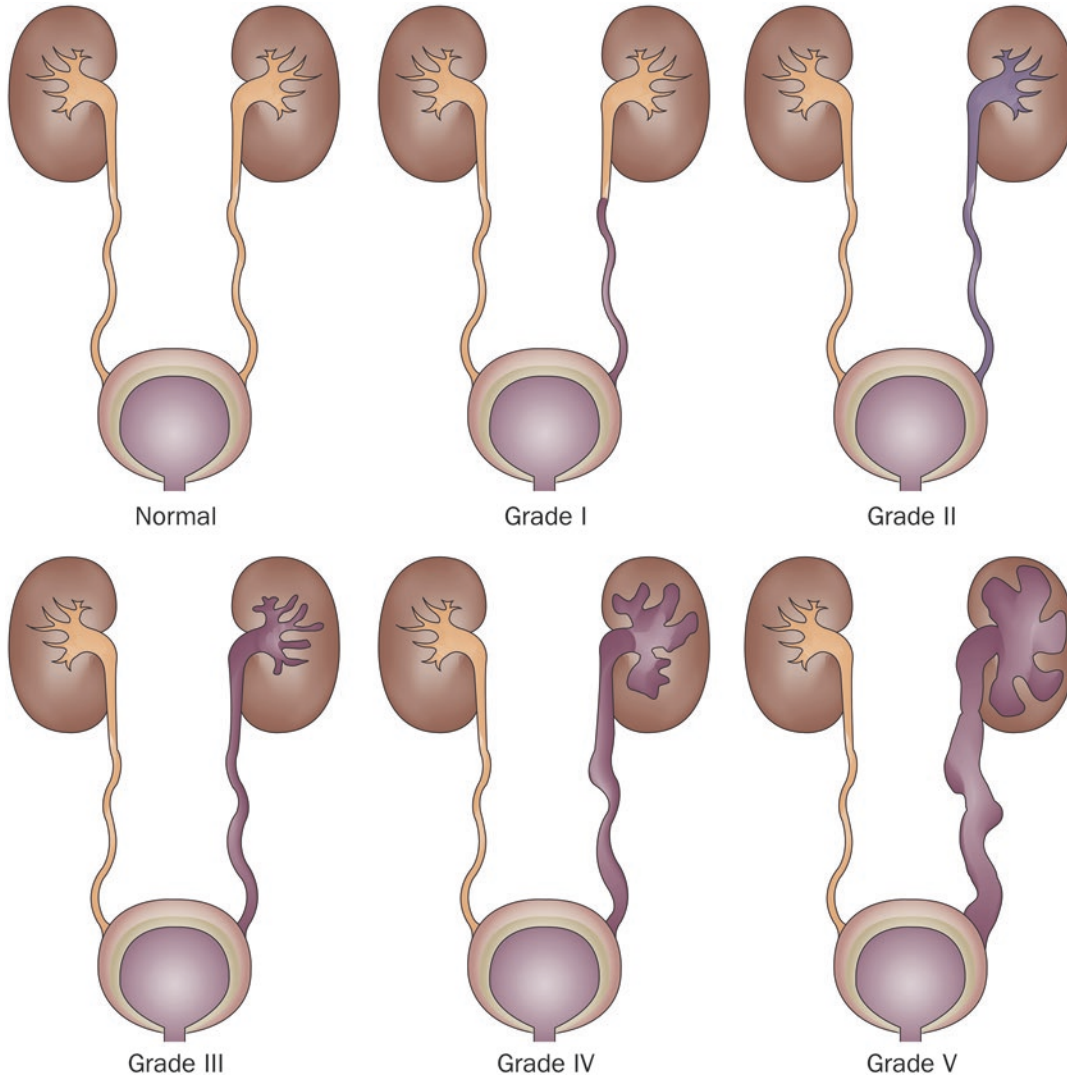

Fig. 12.5 International Reflux Grading System (reprinted with permission from Cooper [14]. Macmillan Publishers Ltd: Nat Rev Urol. 2009)

Computed Tomography

Computed tomography (CT) of the abdomen helps to localize potential causes of hydronephrosis. CT scans without intravenous contrast medium provide a precise location of a ureteral calculus and has become the imaging modality of choice for patients suspected of having ureteral obstruction [1]. CT has a reported sensitivity of 96% for stone detection with a specificity and positive predictive value of 100% [16]. If renal function is normal, CT urography (without and then with contrast and delayed images of the urinary tract) should be considered in order to generate greater anatomic definition. Multidetector CT urography is now considered the imaging modality of choice for a comprehensive evaluation of the urinary tract (Figs. 12.6 and 12.7) [1, 17, 18]. In patients with contraindications for CT scan or when results from previous imaging methods are inconclusive, magnetic resonance imaging (MRI) should be considered. The reported sensitivity of MRI in diagnosing upper urinary tract obstruction is up to 100% [19] but clinicians should remember that MRI cannot directly detect a stone, which is a frequent cause of hydronephrosis in neurogenic patients (Fig. 12.8) [20]. The sensitivity of

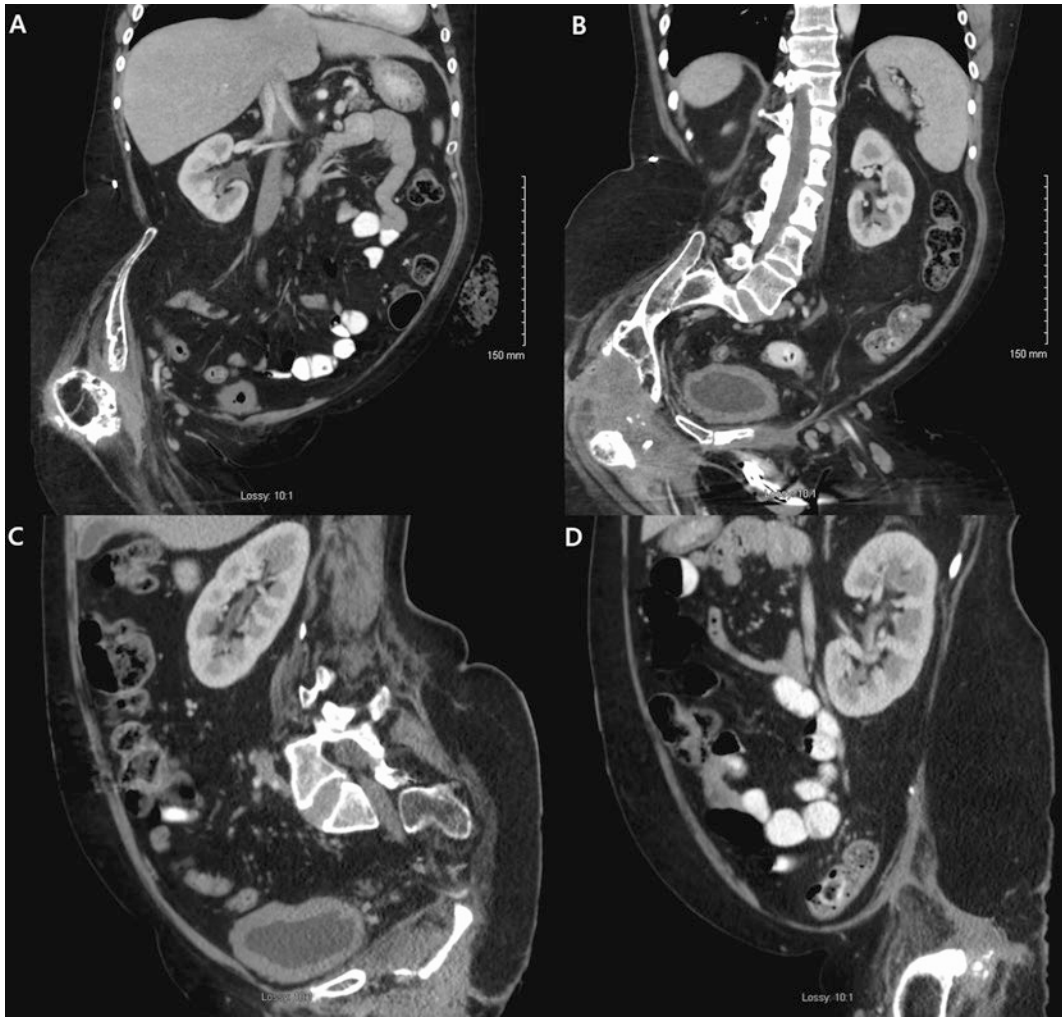

Fig. 12.6 Bilateral moderate hydronephrosis of patient after spinal cord injury (difficult patient positioning). There is also marked diffuse thickening of the bladder wall: (**a**, **b**) coronal view, (**c**, **d**) sagittal view

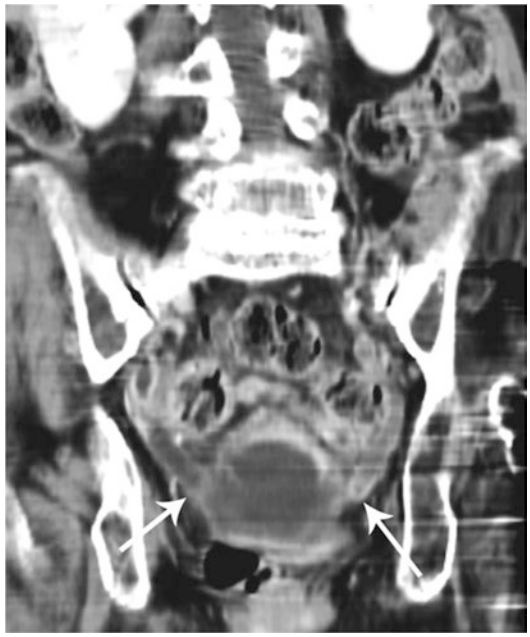

Fig. 12.7 Neurogenic bladder with bilateral vesicoureteral reflux. Coronally reconstructed CT image shows the bilaterally dilated ureters (*arrows*) due to vesicoureteral reflux and diffuse wall thickening of the bladder (with permission from Sung and Sung [18])

MRI for detecting stones has been reported to be 68.9–81% [21, 22]. Sensitivity can be improved up to 90–100% with gadolinium-enhanced excretory MRI [23].

Other Techniques

Intravenous urogram (excretory urography) is useful for assessing the anatomical location of the obstruction (Fig. 12.9). In past decades considered the imaging modality of choice for evaluating urinary tract obstruction, including urolithiasis, it has now been widely replaced by CT scans. The utility of intravenous urograms is also limited in patients with renal insufficiency. However, it may still be considered in individuals with contraindications for increased radiation exposure. Cystogram/voiding cystogram constitutes the present-day gold standard approach to reflux detection (Fig. 12.10) [12]. Voiding cystourethrogram is also obtained to exclude anatomical abnormalities such as posterior urethral valves and bladder neck obstruction. Vesicoureteral reflux may also be revealed by videourodynamics (Fig. 12.11). Antegrade (the injection of contrast

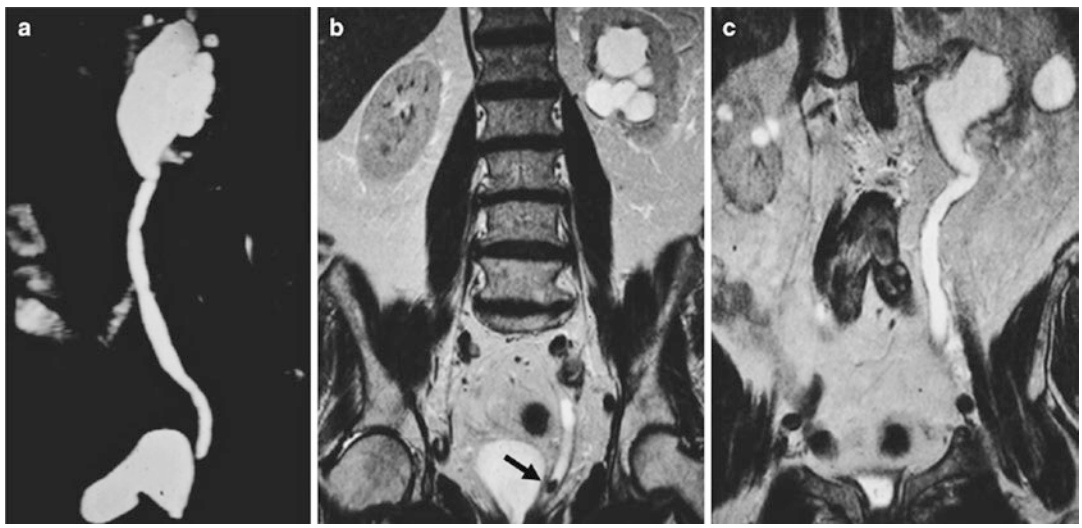

Fig. 12.8 Excessive signal intensity of urine. (**a**) Static-fluid MR urography (single-shot thick slab fast spin-echo sequence) shows the hydroureteronephrosis. The dilated ureter terminates just before the ureterovesical junction. However, no filling defects are seen within the ureter. (**b**, **c**) Thin section T2-weighted fast spin-echo images document the dilated pelvis and ureter and a small stone with low signal intensity in the distal ureter (*arrow* in **b**) (with permission from Pozzi Mucelli [20])

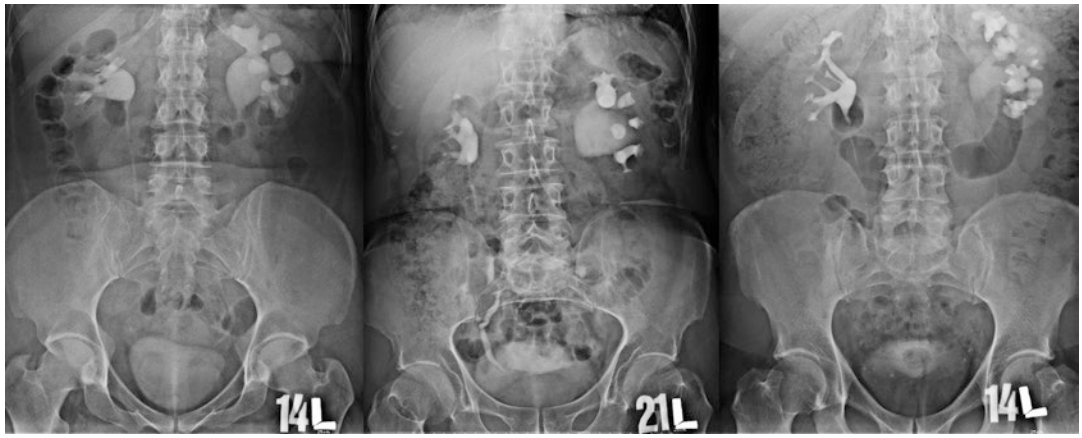

Fig. 12.9 Intravenous urography. Images showing different views of hydronephrosis of the left kidneys

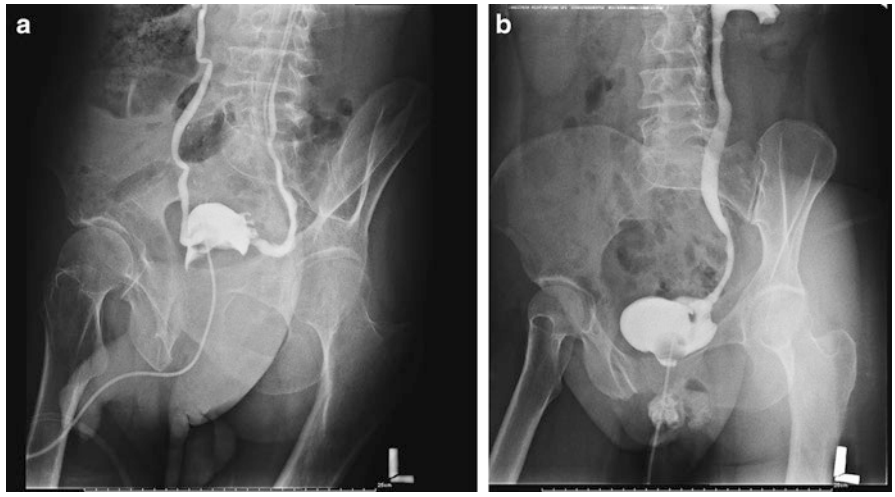

Fig. 12.10 Cystogram (contrast bladder filling phase) with vesicoureteral reflux: (**a**) bilateral, (**b**) unilateral

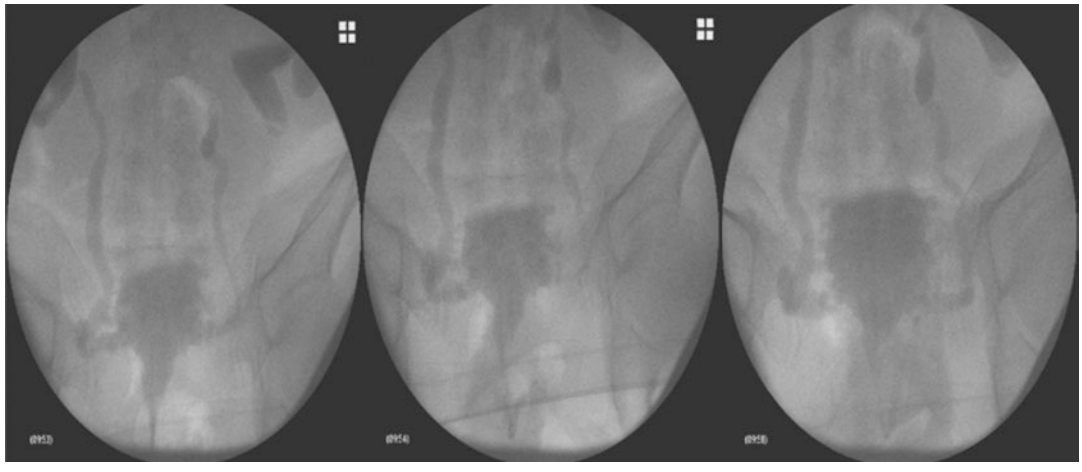

Fig. 12.11 Videourodynamics with vesicoureteral reflux

into the upper collecting system through a percutaneous approach) or retrograde (the injection of contrast into the upper collecting system through a cystoscopic approach) ureterograms may be considered during further work-up.

Treatment

The primary approach to treatment of hydronephrosis in patients suffering from neurogenic bladder is proper management of the underlying urodynamic pathology [24]. Appropriate therapeutic measures should transform a high-pressure system to a low-pressure reservoir, thus subsequently treating diagnosed hydronephrosis. Studies have shown that intra detrusor injections of botulinum toxin A have a positive influence on vesicoureteral reflux and renal pelvis dilation in patients with neurogenic detrusor overactivity [25–28]. New onset or worsening of pre-existing vesicoureteral reflux after botulinum toxin injections have not been currently reported [24]. Treatment of obstructed hydronephrosis focuses on the removal of the obstruction, and specific treatment depends on the cause of the obstruction and where the obstruction lies. The renal parenchyma thickness is a predictor of the ability to recover renal function despite the introduced treatment [29]. However, renal drainage might become necessary. Indications for kidney drainage include: rising creatinine, pyelonephritis (febrile infection), and intractable pain [30, 31]. Immediate (emergency) kidney drainage should specifically be considered if obstruction involves a solitary functioning kidney or both kidneys simultaneously, when hydronephrosis is accompanied by fever and/or complicated by undrained infection, as well as in patients presenting with symptoms of acute renal failure (oliguria/anuria, nausea, vomiting, pedal edema, and altered sensorium) and/or electrolyte imbalance and acidosis. [1, 32].

Drainage

Kidney drainage is necessary to relieve pain and prevent renal deterioration. It may serve as a temporary measure (before a definitive procedure for underlying cause of hydronephrosis) or permanent solution. In cases of obstructive pathology, hydronephrosis may persist after relief of the obstructing cause.

Treatment involves percutaneous nephrostomy tubes and ureteral double J stents. Both methods have been demonstrated to be equally effective in relieving an obstructed collecting system with similar complication rates [33]. The choice of drainage depends on the indication for the procedure, the patient's medical condition, the patient's individual anatomy, and preferences of both patient and physician [34].

Percutaneous Nephrostomy

Percutaneous nephrostomy may be used to drain the upper urinary tract collecting system when obstruction occurs at an intrarenal location, at the ureteropelvic junction, or anywhere in the ureter [34]. The general scheme of this technique is to place a needle (trocar) and nephrostomy tube through the skin into the collecting system of the upper urinary tract (Fig. 12.12) [35]. Advantages of percutaneous nephrostomy include:

- Implantation with local anesthesia and ultrasound guidance (fluoroscopic guidance can also be used, but it is less convenient and less expedient for simple drainage of the kidney)
- Greater initial success rate compared to ureteral stent placement
- Post-implantation superior drainage (especially if purulent fluid is present)
- Possible irrigation to prevent clogging
- Measurement of kidney urine output
- Avoidance of excessive ureteral manipulation

In neurologically impaired patients with hydronephrosis resulting from bladder dysfunction, bilateral nephrostomy tubes are often necessary. Percutaneous nephrostomy should be considered particularly in patients with obstruction complicated by infection and in those who need rapid intervention [36].

Periprocedural antimicrobial coverage for simple percutaneous drainage of the upper urinary tract collecting system is uncertain [34].

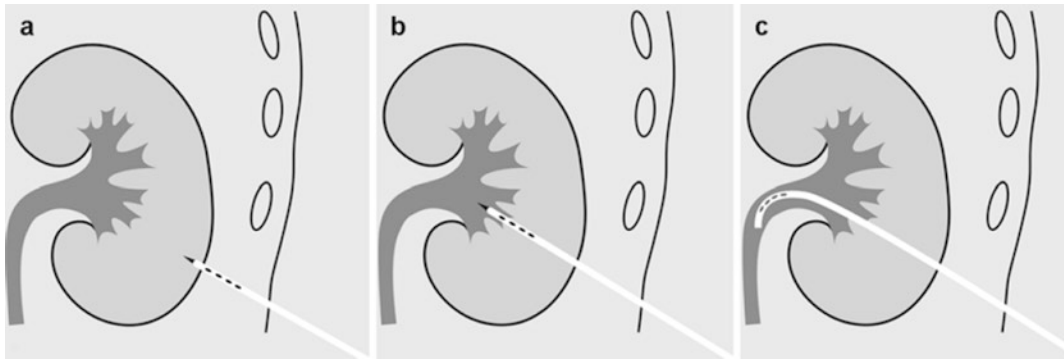

Fig. 12.12 Trocar technique for percutaneous nephrostomy. With a drainage catheter already mounted on a trocar stylet, the calyx is targeted (**a**). When the needle has entered the collecting system (**b**) and urine can be aspirated, the drainage catheter is advanced while the stylet is kept in place (**c**) (with permission from Fischbach and Hohl [35])

Nonetheless, it has been proposed that positive preoperative urine cultures should be treated, and even if bacteriologic cure is not possible (a common problem in neurourological patients), bacterial counts should be suppressed as much as possible to reduce the risk of infectious complications [34]. On the other hand, negative results of urine cultures do not assure protection from sepsis because the voided urine culture may not reflect the intrarenal urine [37–39]. Oral anticoagulant or antiplatelet activity medications should be discontinued before the procedure [40]. As the preoperative cessation periods vary, it has been proposed that aspirin and herbal medicines should be withdrawn 1 week before the procedure, warfarin/clopidogrel 5 days before, and nonsteroidal anti-inflammatory agents 3–7 days before [34]. Pre-procedural INR should be <1.3, APTT < 1.5 times normal, and platelet count >50–100 × 10^9 [32]. For patients on clopidogrel or aspirin for secondary stroke prevention (especially after a recent stroke)—often seen in neurourological practice—cessation of the agent may be contraindicated and should be carefully counselled with a neurologist to evaluate competing risks and to determine the necessity for bridging therapy [40]. Any metabolic abnormalities, including hyperkalemia and/or metabolic acidosis, should be corrected. The prone position for percutaneous access to the upper urinary tract collecting system has been widely used and remains the standard [41]. It has the advantage of presenting a large surface area with multiple choices of stable access sites but in some neurogenic individuals, it may be unfeasible (especially in those after spinal cord injury) or lead to decrease in cardiac index and pulmonary capacity [42, 43]. Furthermore, the prone position can be associated with neuro-musculoskeletal complications such as stretch injury or nerve compression. Thus, the prone-oblique or supine positions can be used for placing a nephrostomy tube. Multiple variants of the supine position (completely supine, supine with the ipsilateral side elevated, supine combined with varying degrees of ipsilateral flank elevation) may be considered to achieve success [44–48]. In patients in whom both supine and prone positioning are difficult, the flank (lateral decubitus) position may offer some potential benefits [49]. Regardless of the chosen position, careful placement of padding is important in every patient. The remaining steps of percutaneous renal collecting system drainage in neurogenic individuals are similar to non-neurogenic patients, with the general rules that the subcostal access is the safest route to the kidney (as pleural injuries are rare with entry below the 12th rib), and the percutaneous access should never be directly into an infundibulum or the renal pelvis (which greatly increases the risk of vascular injury) [34, 50].

Possible minor complications include: pain and discomfort, microscopic and macroscopic hematuria (clears within 12–48 h), catheter malfunction

(dislodgment, blockage), urine extravasation, and respiratory insufficiency due to prone position. Major complications include: septic shock (fever, chills, hypotension with the incidence 1–3%; in setting of pyonephrosis 7–9%): hemorrhage requiring transfusion (1–4%); vascular injury requiring nephrectomy or embolization (0.1–1%); bowel transgression sometimes accompanied by peritonitis (0.2%); pleural transgression with pneumothorax, empyema, hydrothorax, or hemothorax (0.1–0.2%); and renal pelvis injury [51]. CT seems to be the most reliable and sensitive tool for determining postoperative complications [52, 53].

Ureteral Stents

This approach includes placement of a 5-, 6-, or 7-Fr straight ureteral catheter up into the renal pelvis, using fluoroscopy and visually guided by cystoscopy (Fig. 12.13) [34, 54]. The advantages of internal stents are [55]:

- increased patient comfort and better compliance with long-term treatment
- lower potential risk of bleeding complications
- greater success rates of placement compared to percutaneous nephrostomy in obese patients and those with a hypermobile or abnormally situated kidney
- procedure can be performed with ongoing anticoagulant or antiplatelet therapy

Of note, neurogenic patients with ureteral stents usually require additional indwelling catheterization to drain the kidneys efficiently. Internal ureteral stenting may be unfeasible in some neurogenic individuals when the retrograde approach is not possible or fails. Regional or general anesthesia is usually required but stent placement with local anesthesia using lidocaine jelly is also feasible and may be considered in compliant patients in whom difficult stent placement is not expected [56, 57].

Antibiotic prophylaxis before endoscopic stent placement with oral fluoroquinolones is recommended [58]. Ureteral stenting can be performed either in a supine position (see Fig. 11.7 in Chap. 11, usually with flexible cystoscopy) or in a lithotomy position (Figs. 12.14 and 12.15, usually with rigid cystoscopy) [59]. Fluoroscopic guidance during the placement is advised in order to confirm the correct position of the guidewire and subsequently placed stent [60].

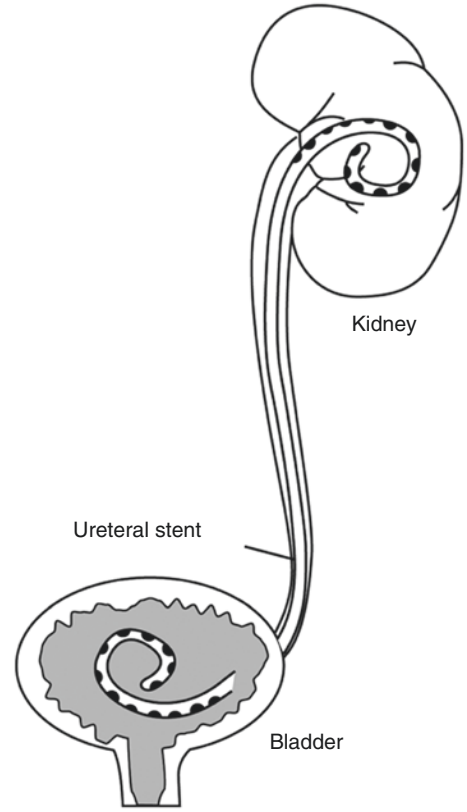

Fig. 12.13 Left side of the urinary tract containing a ureteric stent (with permission from Graham and Choong [54])

Possible complications include: iatrogenic perforation of the renal collecting system or ureter; encrustation resulting in stent malfunction and fracture; loss of stent patency from obstructing blood clots or transient severe mucosal edema; malpositioning or migration of the stent; bladder irritative symptoms (urgency, frequency, dysuria, and both bladder and flank pain); ascending urinary tract infection; mild hematuria (common, caused by irritation of the urothelium and clears spontaneously); persistent hematuria (may be seen in patients with ureteral tumors eroded by the stent); erosion of the stent through the renal pelvis (causing urinoma, vascular injury, or retroperitoneal abscess formation); and erosion

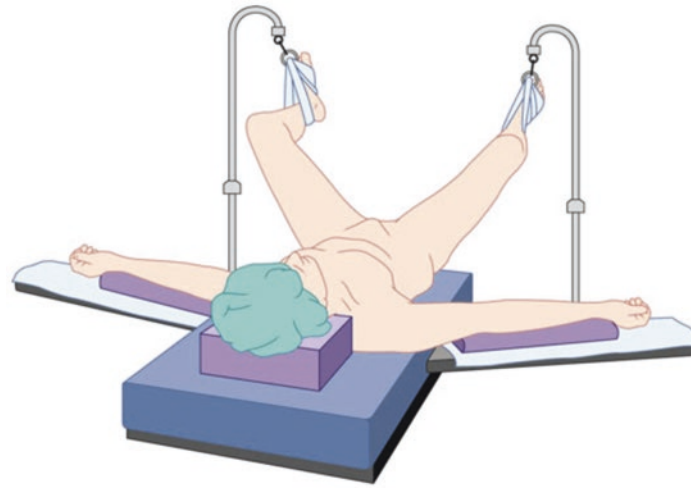

Fig. 12.14 Lithotomy position. Lower extremities are suspended in candy cane stirrups and externally rotated, avoiding compression by stirrups on lateral aspect of legs (with permission from Gal et al. [59])

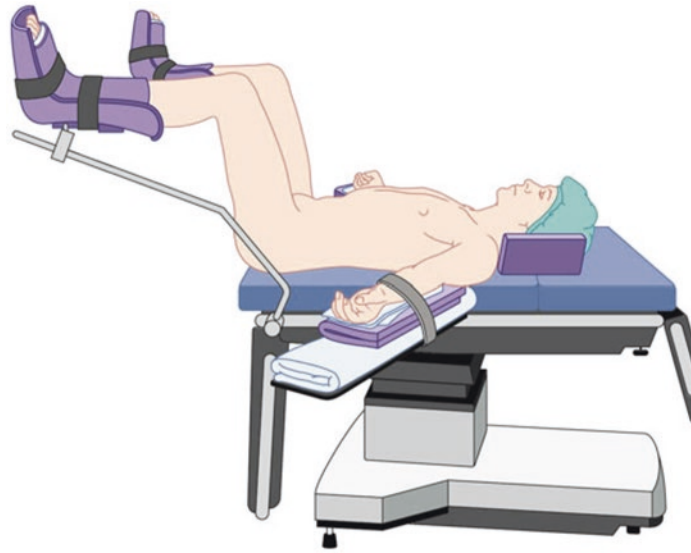

Fig. 12.15 Lithotomy position. Hips are flexed <100°; knees are flexed with legs parallel to patient's torso. Arms are abducted <90° and positioned away from table hinge point (with permission from Gal et al. [59])

of the stent into the iliac artery (causing intermittent or massive hematuria) [61].

Generally, removal or exchange of the stent is recommended within 4 months of placement. In patients with additional risk factors for encrustation such as neurogenic lower urinary tract dysfunction, a 6- to 8-week interval is recommended [62].

Other

In patients with chronic and ineffectively treated hydronephrosis, invasive and permanent treatment with reconstruction of the lower urinary tract (e.g., ileal conduit or urinary reservoir with ureteral reimplantation) may be considered [63]. Clinicians should keep in mind that a continent reservoir may worsen kidney function due to substantial reabsorption of urinary constituents that will overload already deteriorated kidneys [64]. The patient's prognosis and renal function should be carefully evaluated before more invasive surgery.

Vesicoureteral Reflux

Treatment of vesicoureteral reflux in patients with neurogenic lower urinary tract dysfunction differs from the treatment of primary reflux in

the pediatric population. Urodynamic disorders are typically the basic cause of reflux in this population. As vesicoureteral reflux results from either urine retention or primarily generated high bladder pressures, resulting in overload of intact antireflux mechanism of the ureterovesical junction, standard treatment consisting of ureteral reimplantation or endoscopically administered bulking agents in the ureteral orifice will not show long-term efficacy due to poorly treated dysfunctional bladder [63]. With vesicoureteral reflux, the low-pressure upper tracts are exposed to higher pressures and result in loss of renal function. Studies have demonstrated that the presence or new onset of vesicoureteral reflux is particularly associated with chronic kidney disease [65]. Therefore, treatment of vesicoureteral reflux in patients suffering from neurogenic bladder primarily aims to improve bladder function and decrease bladder pressures. Reflux may occur with all forms of bladder management and it is most commonly seen in patients with an indwelling catheter [66]. If reflux is diagnosed, intermittent catheterization is the best method of bladder drainage and can be supported with anticholinergic therapy to lower bladder pressures [67–69]. If bladder pressure is lowered and subsequently maintained, vesicoureteral reflux usually withdraws. When the treatment employed does not improve bladder and renal function nor resolve progression of reflux, invasive surgery with reconstruction of the urinary tract (usually bladder augmentation, with or without ureteral reimplantation) should be considered. Surgeons should remember that the antireflux procedure in a very thickened neurogenic bladder may not be easy to perform, and that well-designed, prospective controlled trials of this approach are lacking [70].

Conclusion (Table 12.1)

Table 12.1 Conclusion

Summary	Level of evidence
Hydronephrosis (dilation of the renal collecting system—renal pelvis and/or calyces) is an anatomic finding, not a functional diagnosis. If not appropriately treated, it may lead to progressive kidney atrophy and functional failure. Hydronephrosis and renal parenchymal thickness have an inverse relationship	4 (Expert opinion)
In patients with neurogenic lower urinary tract dysfunction, significant hydronephrosis may result from either underlying urodynamic dysfunction or already developed complications	4 (Expert opinion)
Renal ultrasonography remains a first-line imaging modality in the evaluation of the patient suspected of hydronephrosis because of its availability, low cost, safety, and lack of ionizing radiation	4 (Expert opinion)
Computed tomography of the abdomen and pelvis helps to localize potential obstructive causes of hydronephrosis	4 (Expert opinion)
Treatment of hydronephrosis in patients suffering from neurogenic bladders includes proper management of underlying urodynamic dysfunction, appropriate treatment of obstructive pathology, and/or kidney drainage	4 (Expert opinion)
Intradetrusor injections of botulinum toxin A have been shown to have a positive influence on urinary collecting system dilation and vesicoureteral reflux	3

(continued)

Table 12.1 (continued)

Recommendation	Grade of recommendation
As hydronephrosis is not a primary disorder and functional diagnosis, underlying etiology must be investigated and renal function should be assessed	Expert opinion
Diagnosis of hydronephrosis and/or vesicoureteral reflux in neurogenic patients should be primarily looked on as a failure to control bladder pressure	Expert opinion
Optimization of management of underlying urodynamic dysfunction should be considered in all neurogenic patients presenting with hydronephrosis in order to achieve/maintain low pressure bladder system	Expert opinion
If obstructive pathology is present, it should be treated. Timely and appropriate management of kidney obstruction prevents long-term kidney damage	Expert opinion
Renal drainage should be considered in patients with rising creatinine, pyelonephritis (febrile infection), intractable pain, solitary functioning kidney, bilateral hydronephrosis, acute renal failure, and electrolyte imbalance/acidosis	Expert opinion
The choice of drainage depends on the indication for the procedure, the patient's medical condition, individual anatomy, and the preferences of both the patient and the physician	Expert opinion
Acute upper urinary tract obstruction is usually treated by the insertion of a nephrostomy tube. Chronic obstruction of the upper urinary tract can also be managed by the insertion of a ureteric stent (mainly to improve the patient's compliance with long-term therapy)	Expert opinion
The best treatment for reflux is to normalize the detrusor pressure	C
As hydronephrosis can lead to chronic renal failure, protection of the upper urinary tract function should be incorporated into the routine follow-up of neurogenic patients	Expert opinion

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Renal Failure

13

Introduction

The ultimate consequence of all upper urinary tract complications in neurogenic patients is the impairment of renal function. Despite the improvement of bladder management strategies in recent years, renal failure remains a significant cause of morbidity in this specific population. Renal failure represents a significant late consequence of neurogenic bladder dysfunction. Acute/chronic abnormalities contributing to renal insufficiency in neurologically impaired patients include [1–5]:

- General/urological abnormalities:
  - pyelonephritis and other infections (in particular recurrent and chronic)
  - renal stone formation
  - hydronephrosis (with or without upper urinary tract obstruction)
  - vesicoureteral reflux
  - complete neurogenic lesions
  - quadriplegic dysfunctions
  - high spinal lesions
  - indwelling catheterization
  - aggressive treatment methods aiming to increase urethral resistance without management of bladder pressure
  - bladder-emptying techniques with increase of bladder/abdominal pressures (e.g., Valsalva or Crede maneuvers)
- Urodynamic abnormalities:
  - high storage pressure (>40 cm H_2O)
  - high voiding pressure (>90 cm H_2O)
  - sustained high-pressure detrusor contractions
  - duration of detrusor overactivity (longer than one-third of the duration of cystometry)
  - decreased bladder compliance (<10 cm H_2O)
  - reduced bladder capacity
  - detrusor-sphincter dyssynergia
  - high post-void residual (>30% of bladder capacity)

Epidemiology

Individuals with neurogenic lower urinary tract dysfunction are at higher risk of renal deterioration compared to the general population. However, current epidemiological data are strongly limited. The majority of studies insufficiently analyzed the severity and duration of the underlying neurological disease or did not perform specific subgroup analyses. It is agreed that the risk of renal dysfunction increases with the time and progression of the underlying disease. The greater the impairment with underlying neurological disorder, the greater the risk of upper tract deterioration. It has been estimated that the rate ratio of renal failure com-

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_13

pared with the general population for neurogenic patients ranges between 0.4 and 11.5 [6]. Those after spinal cord injury (in particular with suprasacral lesions) and neural tube defects were found to have a substantially increased risk of renal insufficiency. One-third of these individuals will develop some degree of renal deterioration over time [7–10]. On the other hand, the occurrence of renal insufficiency secondary to neurogenic bladder dysfunction in patients with multiple sclerosis is not particularly common and close to that in the general population [6, 11]. Epidemiological data of end-stage renal disease in other neurological conditions are sparse. It is worth pointing out that during past decades renal failure was the leading cause of death in neurogenic patients, particularly in those after spinal cord injury [12, 13]. Improvements in follow-up monitoring, bladder management strategies, and treatment of complications have virtually eliminated neurogenic bladder-related mortality in developed countries and have significantly contributed to increase the lifespan of these patients [14]. The leading causes of death in neurogenic patients are now reported to be pneumonia/influenza, septicemia, cancer, ischemic heart disease, and suicide [15].

Diagnosis

Renal deterioration is typically diagnosed during routine follow-up of asymptomatic neurogenic individuals (chronic kidney disease). This condition is a consequence of poorly managed neurogenic bladder and/or chronically developing complications. Renal failure might also be diagnosed as a result of acute clinical conditions requiring further investigation (acute kidney injury). The diagnosis in both cases is primarily laboratory-based.

Chronic Kidney Disease (Chronic Renal Failure)

Definitions and Staging

The Kidney Disease Outcomes Quality Initiative of the National Kidney Foundation and the Kidney Disease Improving Global Outcomes (international guideline group) have developed definitions, classifications and guidelines of chronic kidney disease (CKD) [16]. The guidelines define CKD as abnormalities of kidney function or structure, present for >3 months, with implications for health. Criteria for CKD include:

- Decreased glomerular filtration rate (GFR) (for >3 months)
  - GFR <60 mL/min per 1.73 m^2
- Markers of kidney damage (≥1 for >3 months)
  - albuminuria (albumin excretion rate ≥30 mg/24 h or albumin-creatinine ratio ≥30 mg/g)
  - urine sediment abnormalities
  - electrolyte and other abnormalities due to tubular disorders
  - histological abnormalities
  - structural abnormalities detected by imaging
  - history of kidney transplantation

It was also emphasized that in patients with or suspected of CKD, chronic renal failure or renal function should be classified with GFR and albuminuria categories as they most reliably express the level of severity:

- GFR category
  - stage 1—kidney damage with normal or increased GFR (>90 mL/min/1.73 m^2)
  - stage 2—mild reduction in GFR (60–89 mL/min/1.73 m^2)
  - stage 3a—moderate reduction in GFR (45–59 mL/min/1.73 m^2)
  - stage 3b—moderate reduction in GFR (30–44 mL/min/1.73 m^2)
  - stage 4—severe reduction in GFR (15–29 mL/min/1.73 m^2)
  - stage 5—kidney failure (GFR <15 mL/min/1.73 m^2 or dialysis)
- Albuminuria category
  - stage 1—normal to mildly increased (albumin excretion rate <30 mg/24 h or albumin-creatinine ratio <30 mg/g)
  - stage 2—moderately increased (albumin excretion rate 30–300 mg/24 h or albumin-creatinine ratio 30–300 mg/g)

– stage 3—severely increased (albumin excretion rate >300 mg/24 h or albumin-creatinine ratio >300 mg/g)

It should be noted that in the absence of evidence of kidney damage, neither G1 nor G2 GFR categories alone fulfill the criteria for CKD. It has been proposed that GFR and albuminuria levels should be used together, rather than separately, to improve prognostic accuracy in the assessment of CKD. This combined evaluation should be performed particularly in risk assessment for overall mortality, cardiovascular disease, end-stage kidney failure, acute kidney injury, and the progression of CKD. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation has been recommended for reporting estimated GFR, because of having less bias than the MDRD equation [17].

Signs and Symptoms

CKD may remain asymptomatic and clinically silent for a long time. Clinical manifestations typically appear in stages 4–5 of GFR (<30 mL/min/1.73 m^2) when metabolic/endocrine disturbances with fluid/electrolyte imbalances become apparent. The majority of symptoms are nonspecific, wide ranging, and gradual in onset. Possible signs and symptoms include but are not limited to [18]:

- Malnutrition
- Anorexia
- Body mass loss
- Reduced exercise capacity
- Weakness
- Fatigue
- Sleep disturbances
- Impaired cognitive and immune function
- Peripheral edema
- Pulmonary edema
- Hypertension
- Heart failure
- Anemia

Evaluation of patients with renal deterioration should also include assessment of current medications, both prescribed and over-the-counter, as these may precipitate or worsen kidney dysfunction. These agents include, but are not limited to: blockers of the renin-angiotensin-aldosterone system (including angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, aldosterone inhibitors, direct renin inhibitors); diuretics; nonsteroidal anti-inflammatory drugs; metformin; lithium; calcineurin inhibitors; digoxin; and herbal remedies [19].

Laboratory Data

Laboratory testing should include: complete blood count; basic metabolic panel (creatinine, blood urea nitrogen (BUN), bicarbonate, electrolytes, serum pH); urinalysis (urine pH, gravity, osmolarity, albumin concentration); serum albumin levels; and lipid profile. However, data for neurogenic patients, in particular for those after spinal cord injury, suggest that the creatinine clearance based on serum creatinine levels has little value as a screening measure for renal disease in this population because of its variability in serial testing [20–22]. Muscle denervation, muscle disuse, decreased muscle mass (muscle atrophy), body habitus, as well as type and chronicity of dysfunction/injury substantially contribute to lower creatinine production, with resultant lower serum creatinine measurements [23]. Therefore, it is highly possible that neurogenic patients with a serum creatinine and creatinine-based GFR in the normative range may have severely impaired renal function. Renal function evaluation by serum creatinine-based equations is biased, and renal function of neurogenic patients is thus potentially systematically overestimated. Concurrent findings have been demonstrated for the estimation of creatinine clearance with the 24-h urine collection [20, 24]. Urine collection may be additionally impaired by incomplete collection of all urine produced during 24 h (especially in incontinent patients), inaccurate measurement of urine volume, and variability of the laboratory test for urinary creatinine concentration. Moreover, a complete 24-h urine collection often requires a well-informed patient and adequate staff support, thereby limiting the utility of the test. Inaccurate assessment of renal function may delay medical and urological

management aiming to protect the upper urinary tract. In view of these findings, it has been proposed to not rely on serum creatinine and estimated GFR in isolation for monitoring renal function in people with neurogenic lower urinary tract dysfunction [25].

When an accurate measurement of GFR is required (e.g., in patients with acute decrease in renal function or if imaging of the kidneys suggests that renal function might be compromised), isotopic GFR with radionuclide scans should be considered [21, 25]. Nonetheless, because this test is time-consuming, labor-intensive, and expensive, it may be impractical for routine use. Therefore, another method of renal assessment that should be considered in the neurogenic population and in patients with muscle-wasting conditions involves the measurement of serum cystatin C [26, 27]. If cystatin C is measured, it has been recommended to use a GFR estimating equation to derive GFR from serum cystatin C rather than relying on the serum cystatin C concentration alone [19]. The CKD-EPI cystatin C equation has been shown to be the most precise in estimating cystatin C-based renal function in patients with neurogenic bladder [24]. Studies have demonstrated that in neurogenic patients the cystatin C-estimated GFR is a better screening test for early renal insufficiency that is not detected by creatinine-based calculations [28–30]. It should be considered particularly in individuals with creatinine-estimated GFR between 45 and 59 mL/min/1.73 m^2 who do not have markers of kidney damage and may suffer from silent clinical deterioration of kidney function [19]. Of note, physicians should bear in mind that cystatin C and creatinine-based GFR are insensitive in detecting unilateral renal damage [26]. Unilateral kidney damage still requires nuclear medicine scans.

Imaging Studies

Imaging studies that can be used in the diagnosis of CKD include renal ultrasound, computed tomography, magnetic resonance imaging, renal radionuclide scanning (renal scintigraphy), intravenous urography, and retrograde pyelography. The use of a specific imaging technique depends on the clinical scenario and any developed complications of neurogenic bladder. Small contracted kidneys are typical imaging findings in those with end-stage renal disease (Fig. 13.1) [31].

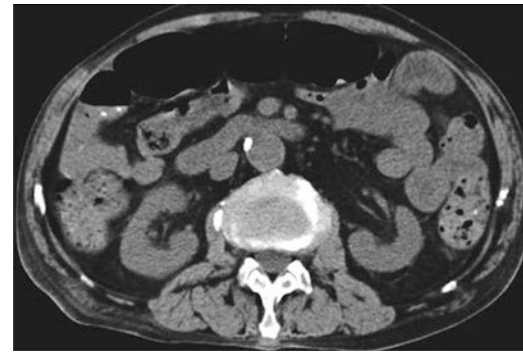

Fig. 13.1 End-stage renal disease. Nonenhanced CT shows small contracted both kidneys and prominent fatty tissues in the renal sinus and perirenal space (with permission from Kim and Kim [31])

Acute Kidney Injury

Definitions and Staging

Acute kidney injury (AKI), previously termed *acute renal failure,* is an abrupt or rapid decline in renal filtration function [32]. AKI has been defined as any of the following [19]:

- Increase in serum creatinine by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 h
- Increase in serum creatinine of 50% or greater (1.5-fold from baseline), which is known or presumed to have occurred within the prior 7 days
- Urine volume <0.5 mL/kg/h for 6 h

AKI is classified as prerenal, intrinsic, and postrenal. In daily clinical practice of neurourological patients, clinicians may encounter those with intrinsic and postrenal causes. The first group includes inflammatory insults to the kidney (pyelonephritis) and the second group encompasses obstruction to the passage of urine (stone disease). Furthermore, AKI may develop as a breakdown of CKD, and some recommend

Table 13.1 Staging of the severity of acute kidney injury

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline or ≥0.3 mg/dL (≥26.5 μmol/L) increase	<0.5 mL/kg/h for 6–12 h
2	2.0–2.9 times baseline	<0.5 mL/kg/h for ≥12 h
3	3.0 times baseline or increase in serum creatinine to ≥4.0 mg/dL (≥353.6 μmol/L) or initiation of renal replacement therapy or in patients ≤18 years, decrease in GFR to <35 mL/min per 1.73 m^2	<0.3 mL/kg/h for ≥24 h or anuria for ≥12 h

that all persons with CKD are considered to be at increased risk of AKI [19]. AKI is staged for severity according to the certain criteria detailed in Table 13.1 [29].

For day-to-day clinical practice, AKI can also be classified as oliguric or non-oliguric on the basis of daily urine excretion. Oliguria is defined as a daily urine volume of less than 400 mL and oliguric AKI has a worse prognosis compared to non-oliguric failures. Anuria is defined as a urine output of less than 100 mL/day and, if abrupt in onset, suggests bilateral obstruction or severe injury to both kidneys. Other staging systems (e.g., the RIFLE classification) may be considered [33].

Signs and Symptoms

The main complaints depend on the clinical scenario and underlying cause of AKI. Relevant signs and symptoms of pyelonephritis and urolithiasis have been discussed in Chaps. 10 and 11, respectively. Despite cause-related signs and symptoms, patients may present with abnormalities specific to AKI. These include cardiovascular decompensation with irregular rhythms and blood pressure, pulmonary decompensation with difficult breathing and impaired physical activity, metabolic disturbances with abnormal levels of electrolytes (in particular acidosis and hyperkalemia), and neurological impairment with decreased cognitive function. Nevertheless, due to neurological impairment, the early stages of AKI are usually asymptomatic and the diagnosis is typically based on elevated creatinine levels. It may take 24 h or more for initially normal creatinine levels to show a definitive increase. Similarly to CKD, the patient's medication list should be carefully reviewed, as many of prescribed and over-the-counter drugs may worsen renal function.

Laboratory Data

Laboratory testing in patients with AKI should include: complete blood count; basic metabolic panel (creatinine, BUN, bicarbonate, electrolytes, serum pH); urinalysis (urine pH, gravity, osmolarity, albuminuria); liver function tests; coagulation tests; and glucose level.

Imaging Studies

As the most common causes of AKI in neurogenic patients are pyelonephritis and stone disease, computed tomography should be a first-line imaging modality for this population. The remaining methods of imaging should be considered when indicated by the clinical scenario.

Treatment

Treatment of Chronic Kidney Disease

The urological care of patients with CKD should focus on delaying or halting the progression of CKD by treatment of the underlying bladder dysfunction. This primarily includes reassessment of bladder management. Preservation or improvement of already deteriorated renal function is achieved through treatment aimed at minimizing the generation of elevated pressure in the lower urinary tract. New urodynamic evolution might sometimes be necessary. Other conditions that contribute to renal dysfunction (e.g., hydronephrosis, stone disease, recurrent urinary tract infections) should be properly treated. Previous chapters covered the treatment of specific bladder

dysfunctions and related complications. If low-pressure bladder system cannot be achieved, invasive non-reversible surgery with urinary diversion should be considered. However, in some patients the only treatment options for renal failure are dialysis or renal transplantation.

Urinary Diversion

Urinary diversion, although frequently performed in the past for the treatment of neurogenic lower urinary tract dysfunction, is now required only in special circumstances. This invasive treatment option may be considered for the protection of the upper urinary tract and for the improvement of quality of life in patients with [34, 35]:

- Multiple failures of non-invasive and less invasive management methods
- Worsening hydronephrosis accompanied by progressive renal deterioration or intractable vesicoureteral reflux due to thick-walled bladder
- Recurrent episodes of urosepsis
- Persistent storage and emptying failure
- Unacceptable incontinence
- Inability to perform intermittent catheterization
- Complications of indwelling catheterization, including urethral destruction and urethrocutaneous fistulas
- Perineal pressure ulcer
- Bladder malignancy requiring cystectomy

The selection of urinary diversion procedure is largely based on the surgeon's experience and opinion, as well as patient's medical condition. The main considerations are presented in Fig. 13.2 [34].

The first choice for urinary diversion recommended by the European Association of Urology

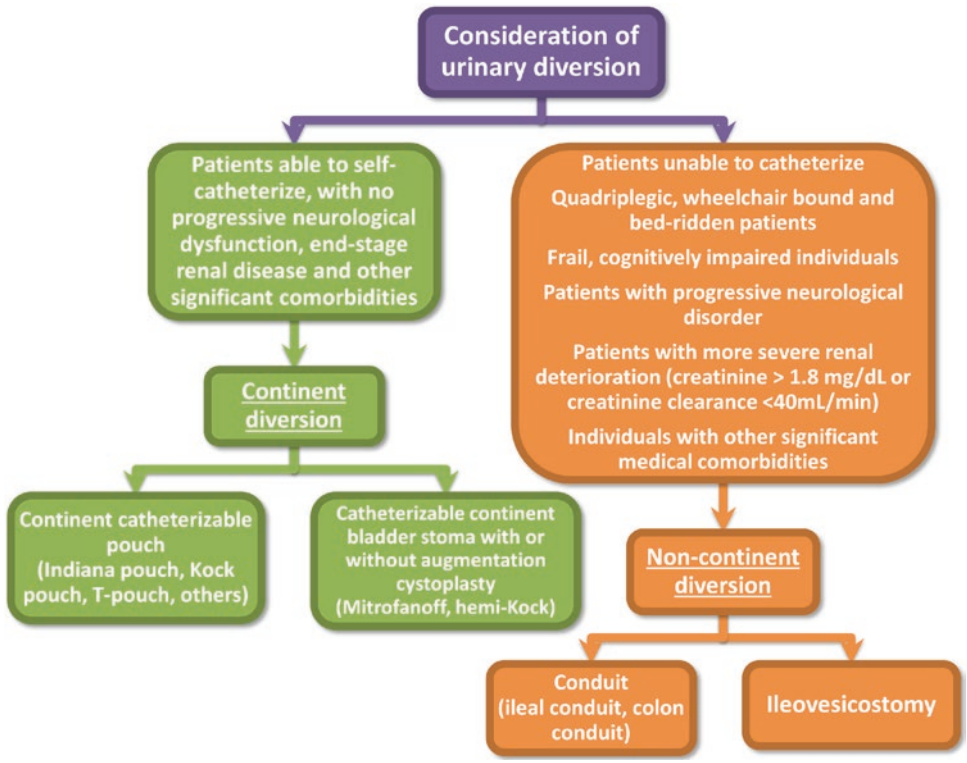

Fig. 13.2 Selection algorithm for urinary diversion

is continent diversion [36]. It includes any reservoir subserved by a catheterizable efferent mechanism other than the native urethra and bladder neck [37]. Continent urinary diversion is generally available for patients who are unable to perform clean intermittent catheterization through the urethra owing to upper-limb disability, difficulties in reaching the urethra, or urethral destruction [38]. It is a viable alternative to an indwelling catheter. A recently published systematic review has confirmed that continent urinary diversion appears to be an effective treatment option in neurourological patients unable to perform clean intermittent catheterization through the urethra [38]. Nevertheless, the complication rate is relevant and there is insufficient evidence to demonstrate the superiority of one technique over others. Uncertainty remains about which technique is the most effective. Long-term revision rates for continent diversions are up to 39%, substantially higher compared to revision rates for incontinent diversions [39]. Incontinent diversion is the most appropriate choice in elderly, debilitated patients and in those who lack the hand–eye coordination or manual dexterity for self-catheterization or the motivation to care for a continent pouch [34]. Multiple surgical techniques have been described for either continent or non-continent diversion (see Fig. 13.2). An appropriate technique should be chosen and individually tailored for each patient by a specially trained neurourologist. Short- and long-term outcomes of urinary diversion procedures are positive with good protection of renal function (and continence rates of 80% and higher in patients with continent diversions) [36, 39–55].

Urinary diversion should be used with caution in individuals who are too debilitated to undergo a major surgical procedure or who have one of the following conditions [35]:

- Inflammatory bowel disease
- Pelvic irradiation
- Prior extensive bowel resection
- Severe abdominal adhesions from previous surgery
- Intraperitoneal malignancy
- Compromised renal function

Complications of urinary diversion can be categorized as general and metabolic. The first group includes [34, 56–60]:

- Early postoperative complications (e.g., wound infection, bleeding, bowel necrosis)
- Ureteroileal leakage (3–9% within the first 7–10 days of surgery with descending prevalence over time)
- Ureteroileal stenosis or obstruction (1–14%)
- Failure of the reservoir with poor conduit emptying
- Pouch/conduit infection (typically manifested by pain in the region of the pouch/conduit accompanied by increased pouch contractility)
- Pouch/conduit and renal calculi
- Pouch/bladder stoma perforation resulting from catheterization, endoscopic examination, fall, or spontaneously (1–2%)
- Stomal stenosis sometimes along with urinary retention (10–24% stenosis resulting in difficult catheterization is the main specific complication of continent diversions)
- Intestinal stenosis (obstruction)
- Intestinal fistulas
- Pyelonephritis
- Deterioration of the upper urinary tract

Metabolic complications depend upon multiple factors such as the segment of bowel that was used, the surface area of this segment, the time that the urine is exposed to the bowel, the concentration of the solutes in and pH of the urine, and the renal function. Metabolic abnormalities seem to be worse in patients with continent diversions due to increased intestinal absorption compared to non-continent reservoirs. Possible metabolic complications are [61–64]:

- Acidosis with hypo/hyperkalemia, hypo/hypernatremia, hypo/hyperchloremia and subsequent dehydration, weakness, lethargy, nausea, vomiting, weight loss, and anorexia
- Osteomalacia (as a result of persistent acidosis, vitamin D resistance, and renal calcium loss)

Thus, in patients with significant renal deterioration, incontinent diversions might be superior due to the metabolic acidosis and exacerbated azotemia associated with continent diversions and augmentations. Most of the complications related to urinary diversions occur within the first 5 years after the initial surgery [39, 45, 65]. Nonetheless, they can still occur more than 15 years after surgery.

Even though a urinary diversion should create a low-pressure system and improve renal function, kidney failure can still be present either because the diversion was performed too late after significant renal damage had occurred or because of the development of complications, chronic infection, or chronic vesicoureteral reflux [1]. Clinicians should also remember that renal deterioration may be caused by other factors, non-related to neurogenic bladder dysfunction.

Renal Replacement Therapy

Renal replacement therapy includes dialysis and renal transplantation. In daily clinical practice, kidney replacement therapy should be primarily introduced on the basis of clinical factors rather than numerical criteria such as the estimated GFR alone [19, 66, 67]. Indications include:

- Symptoms or signs attributable to kidney failure (in particular severe metabolic acidosis, hyperkalemia, pericarditis, peripheral neuropathy, intractable gastrointestinal symptoms)
- Inability to control volume status or blood pressure
- Progressive deterioration in nutritional status refractory to dietary intervention,
- Worsening cognitive impairment (encephalopathy)
- GFR <10 mL/min/1.73 m^2, irrespective of the signs and symptoms, cause of the CKD or presence or absence of other comorbidities

Note that living donor pre-emptive renal transplantation in adults should be considered earlier, when the GFR is <20 mL/min/1.73 m^2 [19]. A retrospective study on 21 males with spinal cord injury and renal failure secondary to neurogenic bladder who underwent renal transplants has shown acceptable long-term outcomes of allograft kidney transplantation with reduction of incidence of urolithiasis and upper urinary tract infection [68]. Interestingly, asymptomatic bacteriuria or pyuria (common problems in neurourological patients) did not show to affect renal transplant in this population, even though one would expect that subsequent immunosuppression after the transplant could provoke more frequent and intensified urinary tract infections. Rates of other complications of transplantation might be higher than in the general population of transplant receivers due to related comorbidity.

It is highly recommended to refer persons with CKD to specialist kidney care services in the following circumstances [19]:

- AKI or abrupt sustained fall in GFR
- GFR <30 mL/min/1.73 m^2 (stages 4 and 5 of GFR)
- A consistent finding of significant albuminuria (ACR ≥300 mg/g [≥30 mg/mmol] or albumin excretion rate ≥300 mg/24 h, approximately equivalent to protein-to-creatinine ratio ≥500 mg/g [≥50 mg/mmol] or protein excretion rate ≥500 mg/24 h)
- Progression of CKD
- Urinary red cell casts, RBC >20 per high power field sustained and not readily explained
- CKD and hypertension refractory to treatment with 4 or more antihypertensive agents
- Persistent abnormalities of serum potassium
- Recurrent or extensive nephrolithiasis
- Hereditary kidney disease

Patients with detailed conditions should be comprehensively managed, as they may suffer

from complications of CKD. Therefore, they may require additional management of arterial hypertension, anemia, neuropathy, vitamin D deficiency, osteopenia, malnutrition, proteinuria, excessive protein/salt intake, abnormal glycemic/lipid profile, and other metabolic abnormalities. This specific population should be provided with dietary counselling, and education about different modalities of renal replacement therapy including transplant options, as well as psychological and social care. In day-to-day neurourological practice, urologists often refer neurogenic patients to nephrologists when CKD stage 2 (GFR less than 90 mL/min/1.73 m^2) is identified [30].

Individuals with CKD should be assessed at least annually. As neurogenic patients are typically at higher risk of CKD progression compared to the general population, follow-up monitoring can be more frequent. As small fluctuations in GFR are common, a minimal change of 25% (or greater) in GFR should be considered as a progression of CKD and should suggest closer follow-up. Rapid progression has been defined as a sustained decline in GFR of more than 5 mL/min/1.73 m^2/year [19].

Treatment of Acute Kidney Injury

Treatment of AKI is typically multidimensional and conducted in the emergency setting with general principles (Fig. 13.3) [19]. The role of a urologist in the management of individuals suffering from AKI includes specific therapy tailored to the cause of AKI (upper urinary tract infection see Chap. 11, and urolithiasis see Chap. 12). Renal drainage (with preference of unilateral/bilateral nephrostomy tubes) is usually required. Relief of obstruction is often followed by a post-obstructive diuresis. Clinicians should bear in mind fluid replacement therapy following this condition, which should be based on frequent measurements of urine volume and urinary electrolytes.

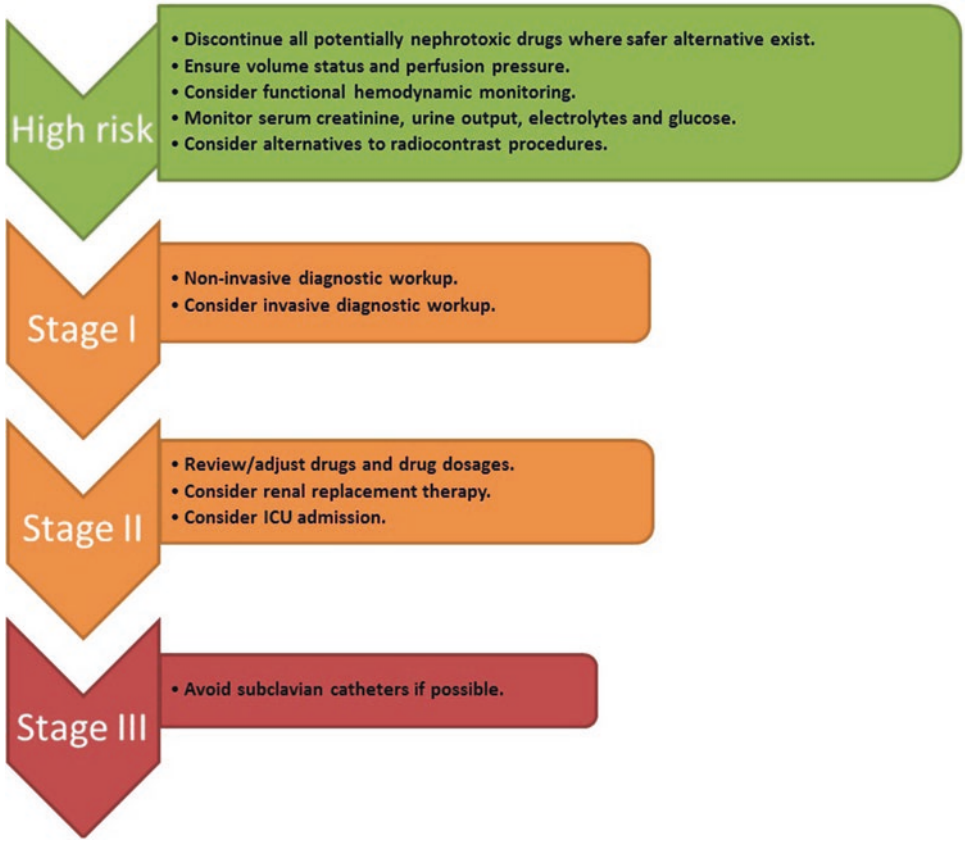

Fig. 13.3 General principles of treatment for acute kidney injury

Conclusion (Table 13.2)

Table 13.2 Conclusion

Summary	Level of evidence
Patients with neurogenic bladder dysfunction have a significantly higher risk of developing renal failure than the general population. Those with spinal cord injury (in particular with suprasacral lesions) and neural tube defects are at the highest risk of upper tract damage and morbidity	3
Neurogenic patients may develop either chronic or acute renal failure	4 (Expert opinion)
Chronic kidney disease may remain asymptomatic and clinically silent for a long time. Clinical manifestations typically appear with GFR <30 mL/min/1.73 m^2 when metabolic/endocrine disturbances with fluid/electrolyte imbalances become apparent. The majority of symptoms are non-specific, wide ranging, and gradual in onset	4 (Expert opinion)
Neurourological patients may present with intrinsic (pyelonephritis) and postrenal (stone disease) causes of acute kidney injury. Acute kidney injury may also develop as a breakdown of chronic kidney disease	4 (Expert opinion)
Laboratory testing of kidney dysfunction includes: complete blood count; basic metabolic panel (creatinine, cystatin C, blood urea nitrogen, bicarbonate, electrolytes, serum pH); urinalysis (urine pH, gravity, osmolarity, albumin concentration); serum albumin levels; lipid profile; liver function tests; and coagulation tests and glucose level	4 (Expert opinion)
There is no consensus on how to best monitor for decreased renal function in patients suffering from neurogenic lower urinary tract dysfunction	4 (Expert opinion)
Serum creatinine level and creatinine estimated glomerular filtration rate (GFR) are not sensitive in detecting early deterioration of renal function in neurogenic patients, particularly in those after spinal cord injury. The results obtained generally significantly overestimate the true creatinine clearance	2
Studies comparing the reliability of cystatin C and creatinine to determine the GFR in the general and neurogenic populations show that cystatin C is superior	2
Urinary diversion, although frequently performed in the past for the treatment of neurogenic lower urinary tract dysfunction, is now required only in special circumstances	3
Studies have shown positive short- and long-term outcomes of urinary diversion in neurogenic patients with good protection of renal function (and continence rates of ≥80% in patients with continent diversions)	2
Renal transplant appears to be a reasonably promising therapeutic option for spinal cord injury patients with renal failure from neurogenic bladder	3

Recommendation	Grade of recommendation
Chronic kidney disease should be diagnosed based on decreased GFR (<60 mL/min per 1.73 m^2 for >3 months) and/or presence of markers of kidney damage (≥1 for >3 months)	Expert opinion
Acute kidney injury should be diagnosed based on increase in serum creatinine by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 h; increase in serum creatinine of 50% or greater (1.5-fold from baseline), which is known or presumed to have occurred within the prior 7 days and/or urine volume <0.5 mL/kg/h for 6 h	Expert opinion
The use of cystatin C rather than creatinine is recommended in patients with mild renal insufficiency, significant muscle wasting conditions, spina bifida, or spinal cord injury if deterioration of renal function is suspected	C
Appropriate management of underlying neurogenic bladder dysfunction has been reported to reduce the risk of renal failure. Thus, preservation of renal function should be primarily achieved through treatment aimed at minimizing the generation of elevated pressure in the lower urinary tract	C

(continued)

Table 13.2 (continued)

Recommendation	Grade of recommendation
Optimizing management of underlying urodynamic dysfunction should be considered in all neurogenic patients presenting with renal insufficiency in order to achieve/maintain low pressure bladder system	Expert opinion
Urinary diversion remains an important surgical treatment for those with refractory symptoms who have failed treatment with botulinum toxin A and neuromodulation or who are not candidates for those treatments	B
Continent diversion should be considered first in patients who require urinary diversion	Expert opinion
Patients with significant renal impairment should undergo incontinent diversions, as metabolic acidosis and exacerbated azotemia are typically associated with continent diversions	Expert opinion
Close surveillance of renal function is important in detecting the early onset of renal insufficiency. Although the annual measurement of serum creatinine level appears to be the most commonly used surveillance protocol, the sensitivity of this method in detecting clinically important changes in renal function has not been well analyzed	Expert opinion

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Autonomic Dysreflexia

14

Introduction

Autonomic dysreflexia (AD) is a potentially life-threatening condition that is considered to be a clinical emergency and is characterized by a constellation of signs and/or symptoms in response to a noxious or non-noxious stimuli originating below the level of the neurological lesion in individuals with spinal cord injury (SCI) at or above T6 [1–4]. AD may present rapidly and dramatically, and can have catastrophic consequences. This syndrome is also known as *autonomic hyper-reflexia, spinal poikilopiesis, paroxysmal neurogenic hypertension, autonomic reflex, sympathetic hyper-reflexia, mass reflex,* and *neurovegetative syndrome* [5]. Studies to date have shown that AD is relatively often unrecognized by individuals with SCI, their caregivers, or even health care professionals [6].

Pathophysiology

In healthy individuals, an afferent stimulus enters the spinal cord and then ascends to the brain. Some interneurons are reflexively connected with preganglionic sympathetic neurons and excite them, thus resulting in vasoconstriction below the neurologic lesion and causing a rise in blood pressure. In non-neurologically impaired persons, higher centers inhibit these sympathetic effects by a compensatory vasodilatation of the splanchnic circulatory bed and result in normalization of the blood pressure.

In patients after SCI, these higher inhibitory pathways are not intact and cannot reach the splanchnic bed, resulting in high blood pressure (hypertension with persistent sympathetic activity *below* the lesion). As a parasympathetic reflex from baroreceptors of the carotid sinus and aortic arch is activated, the heart beat is simultaneously reduced via the vagus nerve, which is intact (bradycardia with withdrawal of sympathetic activity *above* the lesion) [7–9].

Epidemiology

It has been estimated that up to 85% of individuals with a cervical or high-thoracic SCI may develop AD [9–15]. AD in paraplegic patients with lesions below T6 is a rare finding. The severity of AD episodes appears to increase with the level, extent, and completeness of injury. Therefore, studies have shown that the syndrome occurs in approximately 60% of SCI patients with cervical lesions and 20% of those with thoracic injury [16, 17]. AD has been reported in both complete and incomplete SCI, but the symptoms are milder and less frequent in patients with incomplete injury [18, 19]. The

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_14

symptoms and signs of AD develop over time after SCI and typically start after the phase of spinal shock (which usually lasts 6–12 weeks). Approximately 90% of quadriplegic individuals will experience an episode of AD within 6 months of their injury [11]. AD may also worsen with time after SCI [20]. However, AD can also be seen during the acute and subacute phase after injury (in up to 5% of patients within the first days and weeks) and should be considered in the differential diagnosis [11, 21, 22]. Clinicians should also bear in mind that while AD is most commonly associated with SCI, it may also result from non-traumatic causes such as spinal cord tumors or after neurosurgery above the level of T6 [23, 24]. AD in patients with multiple sclerosis and transverse myelitis has also been reported [25–27].

Etiology

AD may be triggered by activation of pain receptors or from distension of hollow organs (distension of viscera) below the level of the SCI [5]. Possible triggers include [8, 9, 28, 29]:

- Genitourinary causes (responsible for 81–87% of cases overall)
  - bladder distention (the most common precipitant, accounting for 75–85% of all episodes; bladder distention may result from insufficient frequency of bladder catheterization, blocked indwelling catheter, malposition of the catheter tip, defective catheter tubing/drainage bags, overfilling of the drainage bag, or from de novo urine retention)
  - detrusor-sphincter dyssynergia
  - decreased bladder compliance
  - urinary tract infection (including epididymitis, orchitis)
  - urethral catheterization, movements of an indwelling catheter
  - sexual intercourse, erection, ejaculation, vaginal manipulation
  - upper and lower tract calculi
  - testicular torsion
- Gastrointestinal causes
  - bowel and rectal distention (impaction, constipation, enema administration)
  - anal strictures
  - hemorrhoids
  - gastric ulcer or gastritis
  - cholelithiasis or cholecystitis
  - appendicitis
  - gastroesophageal reflux
- Dermatological causes
  - pressure ulcers
  - tight dressings to skin infections
  - constrictive clothing
  - burns or sunburns
  - ingrown or infected toenails
  - insect bite
  - contact with hard or sharp objects
- Musculoskeletal causes
  - position changes
  - spasticity
  - long-bone fracture, trauma, or dislocation
  - tight clothing
  - heterotopic ossification
  - exercise
- Surgical and invasive diagnostic procedures
  - cystoscopy (lower risk with flexible cystoscopy)
  - cystography
  - urodynamics
  - electroejaculation, vibroejaculation
  - shock wave lithotripsy
  - percutaneous nephrolithotomy
  - anesthesia
  - general surgery
  - postoperative pain/discomfort
- Others
  - medications (pseudoephedrine, sympathomimetics)
  - cold temperatures
  - alcohol abuse
  - excessive caffeine and other diuretic intake
  - menstruation
  - pregnancy, labor and delivery
  - deep vein thrombosis
  - pulmonary embolus or infarction
  - hyperthyroidism
  - intramuscular injection

Diagnosis

Symptoms and Signs

AD classically presents as sudden, severe, uncontrolled hypertension and accompanying bradycardia. The amount of the rise in blood pressure that is required to diagnose AD remains a matter of dispute [8]. It has been proposed that a minimum increase of systolic blood pressure of 20mmHg from baseline is diagnostic for AD [3, 4]. Another proposal suggests a rise in blood pressure by 20% with at least one accompanying symptom [8, 22]. Of note, clinicians should be aware that the basal systolic and diastolic blood pressure in SCI individuals is approximately 15 mmHg lower than in neurologically intact persons, as a result of reduced sympathetic activity [30]. Although reflex bradycardia typically forms the episode of AD, it is seen in only 10% of cases [16, 18, 31]. The majority of patients with AD present with tachycardia, arrhythmias (atrial fibrillation, premature ventricular contraction, atrioventricular conduction abnormalities), or even with no significant change in heart rate.

In daily clinical practice, patients also present with various and non-specific symptoms and signs. To make matters worse, patients may experience one or more of them in diverse combinations and with varied intensity from uncomfortable symptoms to life-threatening crises. The other clinical features of AD are [5, 8, 9]:

- Symptoms:
  - Severe pounding headache (usually occipital, bitemporal, and bifrontal in >50% of patients; sometimes misdiagnosed as cluster headaches and migraines)
  - Excessive sweating and flushing of the face, neck, and shoulders (with cold limbs)
  - Blurred vision with or without the appearance of spots in the visual field
  - Congestion of the nasal passages
  - Nausea/vomiting
  - Tightness in chest, dyspnea
  - Bladder and bowel spasms and cramps
  - Piloerection/paresthesia with gooseflesh and shivering (above or below the lesion)
  - Feeling of anxiety, agitation, apprehension, and altered mental status
- Signs
  - Above the lesion (secondary to parasympathetic/vagal effects and vasodilatation)
  - Flushing and sweating of head and neck
  - Splotches of the face and neck
  - Mucous membrane congestion
  - Conjunctivitis, lid retraction, mydriasis, Horner's syndrome, oculosympathetic spasm
  - Respiratory distress or bronchospasms
  - Transient aphasia
  - Change in the level of consciousness,
  - Below the lesion (secondary to sympathetic effects and vasoconstriction)
  - Pallor with cold extremities
  - Increased spasticity
  - Intense contraction of bladder and bowel
  - Piloerection
  - Penile erection and seminal fluid emission

Some SCI patients may be entirely asymptomatic (silent AD). It has been estimated that 35–50% of those after injury at T6 or above may have significantly elevated blood pressure without any other symptoms or signs of AD [10, 17, 31, 32]. In these cases, the diagnosis of AD may be established by inducing the condition in a controlled setting, such as by the bladder filling during urodynamic study with appropriate blood pressure and pulse monitoring [10, 20, 32]. One-minute intervals of monitoring have been proposed [20]. Furthermore, this approach might be particularly useful for educating the patient regarding the recognition of early warning symptoms and signs that will enable immediate preventive measures to be taken [9, 33]. This also emphasizes the need for appropriate blood pressure and pulse monitoring of these patients during any instrumentation (e.g., cystoscopy) at regular intervals, as a significant number of them may be asymptomatic [8]. Episodic recurrence of AD may in itself be an important clinical sign of underlying disease or developed complications of neurogenic bladder (e.g., urinary tract infection, uriolithiasis) and should raise special attention. The differential diagnosis of recurrent

AD should also include pheochromocytoma, migraine and cluster headaches, posterior fossa neoplasms, toxemia of pregnancy, and uncontrolled hypertension [9, 14].

Consequences

AD may have dramatic and extremely serious consequences if not appropriately treated in timely manner or left uncontrolled. Reported consequences include subarachnoid hemorrhage (as systolic blood pressure may rise up to 300 mmHg and diastolic up to 220 mmHg) [11, 12, 18, 34], intracerebral bleeds [35], hypertensive encephalopathy [36], retinal hemorrhage [9], cardiac arrhythmias/myocardial failure [37, 38], seizures/convulsions [39], neurogenic pulmonary edema [40], renal failure (prolonged vasoconstriction in the renal vascular bed) [41], coma [42], and death [34]. Death occurs most commonly when associated with complications of the central nervous system [43]. Nevertheless, proper management significantly decreases the likelihood of these complications.

Treatment

Acute Management

Early recognition of AD is important. Immediate management aims to identify and treat the triggering factor/factors as well as manage the hypertension and/or other potential complications. The patient should be seated with head raised and the blood pressure should be continuously measured (every 2–5 min), as significant and rapid fluctuations in these parameters may appear [34, 44]. The triggering factor/factors should be immediately identified and adequately stopped/removed. Removal of the precipitating stimulus may reverse the onset of acute episode of AD without the need for additional treatment (including pharmacological agents). Any constrictive devices and tight clothing, including belts, dressings, plaster casts, and catheter leg bags, should be loosened. As the commonest cause of AD is bladder overdistension, bladder catheterization should be employed. If the patient has already been catheterized, free drainage of urine down the catheter tubing into the drainage bag is of utmost importance. Therefore, any catheter, tubing, and bag should be checked for obstruction and, if required, irrigated (with 10–15 mL of warm saline) or replaced (if previous attempt to relieve the obstructed catheter has failed to decompress the bladder). Both large volumes and cold irrigation solutions should be avoided because they can also exacerbate AD. If there is no catheter, the patient should be catheterized as soon as possible. As catheterization itself can exacerbate AD, intraurethral lidocaine jelly 2% should be generously applied at least 2 min before insertion or change of a urethral catheter in order to decrease sensory input and relax the urinary sphincter [44]. A coudé tip catheter may be considered if catheterization is difficult or associated with bladder neck obstruction. Neither the Valsalva nor the Crede maneuver should be attempted to empty the patient's bladder because these could increase the severity of the syndrome [45]. When the clinical scenario indicates urinary tract infection as a potential cause of AD, a urine sample should be examined by dipstick analysis and sent for microscopy and culture for infection. Moreover, high-dose intravenous antibiotics should be considered. Rectal examination for fecal impaction with gentle manual evacuation should be considered if there is no urological cause found for the presenting condition and blood pressure remains elevated after bladder catheterization [44]. As additional stimulation may further exacerbate AD, it is recommended to perform gentle disimpaction after introducing intrarectal lidocaine jelly 2% for at least 2 min before the maneuver. However, a prospective randomized study has failed to show any significant difference between the use of 2% topical lidocaine jelly and controls prior to anorectal procedures [46]. If AD worsens during rectal

manipulation, the manual evacuation should be stopped and rechecked after 20 min. Skin examination should be performed to identify superficial infection and bed sores. The external genitalia should be examined to look for epididymitis/orchitis or testicular torsion, and the perianal areas should be checked for other conditions such as thrombosed hemorrhoids, thrombophlebitis, and perianal abscesses [9]. If the triggering factor has not been identified, acute abdominal conditions (e.g., appendicitis, intestinal obstruction, peritonitis, pyelonephritis) must be urgently excluded [5]. It is noteworthy that this more in-depth investigation of the triggering cause should not preclude the course of emergency treatment. Thus, if the blood pressure remains high (≥150 mmHg) despite bladder catheterization or rectal evacuation, or the triggering factor remains unclear or not found within the first few minutes, antihypertensive drugs should be introduced [1, 44, 47]. These include:

- Captopril (25 mg) sublingually [47, 48], or
- Nitroglycerin 0.4 mg/spray (1 spray every 5 min up to 3 times as needed) [47], or
- 2% nitroglycerine ointment/paste (1 inch of nitropaste on hairless skin of upper chest, additional inch may be administered as needed) [49, 50], or
- Nifedipine (10 mg) bite-and-swallow [5, 47] (sublingual administration and subsequent absorption of nifedipine has been shown less effective [51]), or
- Chlorpromazine (1 mg) intravenously (the intensive care unit setting) [52], or
- Phentolamine (5 mg) intravenously (the intensive care unit setting) [52]

Of note, when nitrates are considered, it should be made certain that the patient has not taken phosphodiesterase 5 inhibitors (e.g., sildenafil, tadalafil, vardenafil) in the past 24–48 h (risk of precipitous hypotension) [47]. This check is especially important, as a large proportion of male patients after SCI have coexisting erectile dysfunction, for which they are likely to take these drugs. When nifedipine is considered, clinicians should keep in mind the possible serious adverse events, including cerebrovascular accident, myocardial infarction, or even death, reported in hypertensive emergencies of non-SCI individuals [53]. Caution with nifedipine use might therefore be necessary and cardiovascular monitoring may be helpful even though a review of the literature has not shown any reported adverse effects of nifedipine when used to treat AD [44]. Furthermore, oral nifedipine has been shown clearly effective in treating severe hypertension in the acute setting and has a role in preventing the significant morbidity and potential mortality associated with AD [9].

Patients should be monitored for at least 2 h (up to 48 h) following resolution of AD, depending on the acuity of the episode (patient should be monitored for both recurrent AD and hypotension) [47]. They should be educated in how to monitor their symptoms to identify a possible recurrence. Patients might also experience hypotension after resolution of the trigger, especially if the patient has been given antihypertensive medication. If hypotension occurs, the patient should be placed supine with legs elevated. Administration of intravenous fluids and adrenergic agonist may be considered if the hypotension is symptomatic or refractory [42].

All episodes of AD should be carefully documented in medical records and should include information regarding signs and symptoms at presentation, the trigger responsible for the acute episode, the treatment instituted, and treatment outcomes. If blood pressure and heart rate came back to normal, the noxious stimulus has been removed and symptoms resolved, the patient can be routinely followed up. In cases of persistent AD or when the noxious stimulus has not been identified, the patient should be admitted or sent to the emergency department [47]. Spinal anesthesia has been recommended in an acute episode of AD refractory to medical management, as it successfully blocks the sympathetic response [54].

Chronic Management (Prevention)

Patients, their families/caretakers, and health care providers should be properly educated regarding this syndrome and how to identify causes/noxious stimuli able to trigger AD as well as symptoms and signs of this condition. Bladder distension should be avoided by proper schedule of intermittent catheterization and regular change of an indwelling catheter. Urethral or suprapubic catheters should be changed with great care and attention (with an aseptic technique and local anesthetic jelly) to prevent initiating an episode of AD. Appropriate treatment of urinary tract infections and stone disease is of utmost importance in this population. A proper bowel regime and intestine re-education program are also crucial. A skin care plan should be developed and patients, their family members, and caregivers should be taught how to care for skin and skin injury and how to avoid pressure sores. Patients who experience or are susceptible to AD should be instructed in management strategies and should be equipped with sufficient supplies at home (properly sized cuff for blood pressure measurement, catheter supplies, nitroglycerin spray, sublingual captopril) [47]. Incidence of AD during iatrogenic urological procedures in patients with injuries above T6 varies, ranging from 42 to 78% for urodynamics and up to 70 and 23% for cystoscopy and shock wave lithotripsy, respectively [28]. It has been reported that cystoscopy in SCI individuals induces greater changes in systolic blood pressure than urodynamics [55]. Thus, diagnostic and surgical procedures should be performed with accurate blood pressure and heart rate monitoring [56]. Although the evidence is weak, anesthetic jelly should always be used to reduce stimulation for any manipulation, including before vaginal examinations, urinary catheterizations, or rectal manipulation. One proposal includes administration of nifedipine (10 mg) sublingually 30–60 min before any urological (e.g., endoscopy, botulinum toxin injections, urodynamics) and non-urological procedure that may trigger the condition in vulnerable patients [52, 54]. On a long-term basis (patients with recurrent acute episodes of AD), chronic α-adrenergic blockade (prazosin 1 mg daily [52] or 3 mg BID [57]) might be helpful. AD prevention with terazosin (varying doses of 1–10 mg daily) may also be considered to achieve success [15, 58, 59]. Clinicians shoule bear in mind that successful pharmacological prevention does not eliminate the need for appropriate care to genitourinary, gastrointestinal, and other systems to eliminate avoidable triggers, nor does it eliminate the need for careful monitoring during any surgical and more invasive diagnostic procedures [15, 44, 60].

Underlying neurogenic bladder dysfunction should be appropriately treated. However, reliable data are few regarding how to prevent AD with proper bladder management. It has been demonstrated that botulinum toxin injections into the detrusor muscle may be a safe and effective AD prevention therapy for patients with SCI who perform clean intermittent self-catheterization and have incontinence that is resistant to anticholinergic medication [1, 6]. Intravesical drug treatment may be effective in reducing the frequency of AD, and resiniferatoxin has been shown more effective than capsaicin. Bladder augmentation may result in a decrease in intravesical and urethral pressure, thus it may diminish or resolve episodes of AD. Moreover, enterocystoplasty may result in better long-term viability relative to sphincterotomy. Interestingly, anticholinergics are not associated with a reduced incidence of episodes of AD, and conflicting results have been reported regarding the effectiveness of sacral deafferentation in the prevention of AD. Other studies demonstrated that AD occurrence does not seem to be influenced by the severity of reported lower urinary tract symptoms or the treatment used, including bladder-emptying techniques [20].

When referring to other specialists (e.g., radiologists, andrologists, anesthesiologists, gynecologists), clinicians should remember to alert their colleagues to this disorder. Patients should be advised carry a card containing critical information regarding AD on their person. This document should include a brief description of AD with possible causes, clinical presentation, and emergency management (Fig. 14.1) [61]. Patients may also be encouraged to get MedicAlert bracelets (MedicAlert Foundation, Salida CA, USA).

Fig. 14.1 Emergency card for autonomic dysreflexia (with permission from courtesy of the Christopher & Dana Reeve Foundation [61])

Conclusion (Table 14.1, Fig. 14.2)

Table 14.1 Conclusion

Summary	Level of evidence
Autonomic dysreflexia (AD) is a potentially life-threatening clinical emergency that occurs in patients after spinal cord injury (SCI) at or above the mid-thoracic spinal cord level (typically T6)	4 (Expert opinion)
AD afflicts a significant proportion of individuals with tetraplegia or high paraplegia. The syndrome is less common and less severe in those with incomplete lesions	3
AD often presents as a rapid and dramatic condition (with high blood pressure as the leading symptom), although occasionally the symptoms and signs of AD may remain minimal or even absent despite significant hypertension	2
The most common source of triggering stimulation is the genitourinary tract (the most common trigger being bladder distension), followed by gastrointestinal tract, skin, and a wide variety of other trigger factors. The condition usually resolves as soon as the precipitating stimuli are eliminated	4 (Expert opinion)
Emergency treatment involves immediate reversal of precipitating factors followed by pharmacotherapy to normalize the accompanying severe hypertension	3
Medical treatment involves the use of drugs leading to immediate reduction of blood pressure, including captopril, nitroglycerin, nifedipine, chlorpromazine, and phentolamine	3/4
Potential complications include intracranial and retinal hemorrhage, hypertensive encephalopathy, arrhythmias, convulsions, neurogenic pulmonary edema, coma, and death	4
Urodynamic examination has been determined to be an effective and standardized diagnostic procedure for provoking signs of AD and an appropriate screening tool	2
Preventive measures include proper education of patients, their families/carers, and health care providers; and taking care to avoid excessive bladder distension, urinary tract infections, constipation, pressure sores, and any other painful condition that may provoke autonomic stimulation	4
There is a severe lack of controlled trials in the management and prevention of AD. Available data are predominantly supported by evidence from non-controlled studies, case reports, and consensus statements	4 (Expert opinion)
Recommendation	Grade of recommendation
AD is a life-threatening condition that requires urgent and appropriate medical attention	Expert opinion
Currently available guidelines recommend the use of nonpharmacological maneuvers as the first line treatment of AD	Expert opinion
Once the diagnosis of AD is established, it is of utmost importance to promptly identify and aggressively reverse or correct any triggering factors	B
Blood pressure and heart rate checks every 2–5 min have been recommended	Expert opinion
As the most common cause of AD is bladder overdistension, all patients should be catheterized during an acute episode of AD. In the presence of an indwelling catheter, free drainage of urine should be confirmed. If the hypertension is not reversed, fecal impaction should be ruled out. If the cause of the AD is not found, a systematic search for other possible trigger factors should be instituted	Expert opinion
Drug treatment should be introduced when the hypertension is not reversed by non-pharmacological measures (≥150 mmHg) or if a trigger factor is not identified within a reasonable period of time	Expert opinion
Antihypertensive medication should preferably have a rapid onset and short duration of action	Expert opinion
Urodynamic study accompanied by continuous blood pressure and heart rate monitoring during the examination can be considered as a screening tool for individuals with SCI prone to AD, in particular for those with silent (asymptomatic) AD	B

(continued)

Table 14.1 (continued)

Summary	Level of evidence
Blood pressure and heart rate monitoring at 1-min intervals during urodynamic investigations is recommended	Expert opinion
Clinicians should be aware of the iatrogenic factors that might trigger AD; therefore, blood pressure and heart rate monitoring should be performed during surgical and invasive diagnostic procedures in individuals with SCI	A
With recurrent episodes of AD, prevention should be considered	C
SCI patients, their families/carers, and health care professionals should be educated about the existence of this condition, its signs and symptoms, potential causes and complications, prompt recognition, and effective treatment	Expert opinion
A well-defined bladder, bowel, and skin care management program should be implemented into the rehabilitation of individuals with SCI at or above the mid-thoracic spinal cord segment	Expert opinion
SCI patients who are at risk of AD should carry a medical emergency card with brief description of the etiology, presentation, and emergency management	Expert opinion

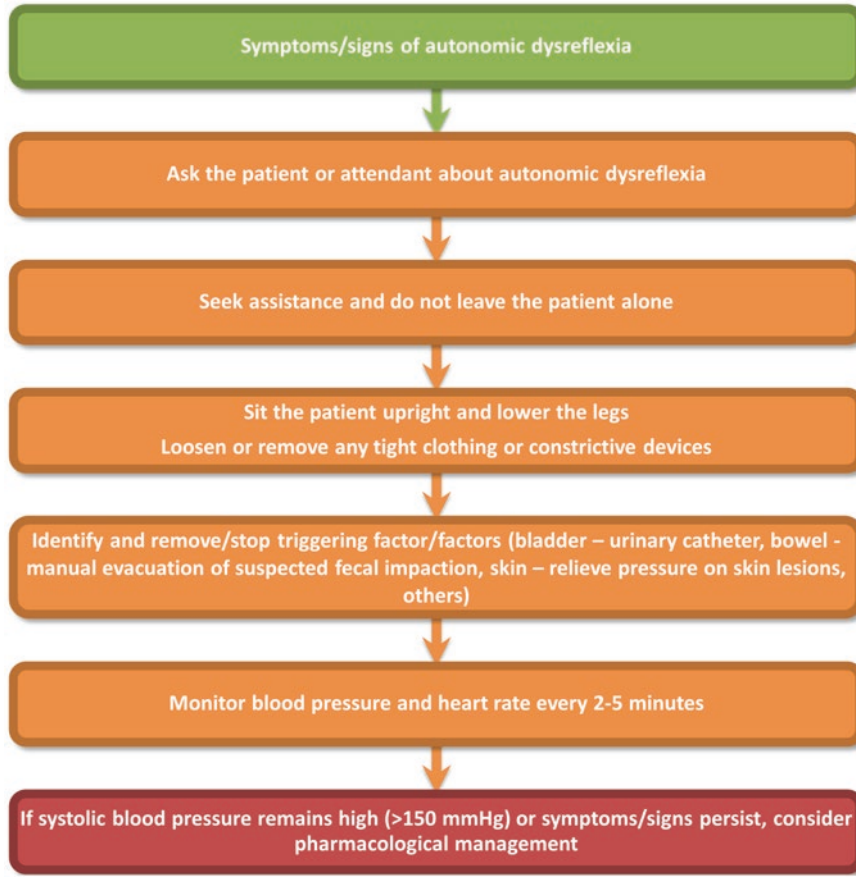

Fig. 14.2 Emergency management of autonomic dysreflexia [1, 42, 47]

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Other (Bladder Cancer, Sexual Dysfunction)

15

Bladder Cancer

Epidemiology

It has been estimated that patients suffering from neurogenic lower urinary tract dysfunction have 16- to 28-fold increased risk of bladder cancer compared to the general population, with incidence rates ranging from 0.1 to 10% (the pooled incidence of 0.6%) [1–6]. Studies of those after spinal cord injury (SCI) demonstrated that bladder cancer tends to present at an earlier age (with an average of 18–24 years after initial injury) and in more advanced stages, thus resulting in poor long-term survival [7]. Concurrent findings were shown for patients with spina bifida [8]. Those with multiple sclerosis (but not with Parkinson disease) were also found to have an increased risk of bladder cancer [9, 10]. In the SCI population, 58–100% of new bladder cancers are muscle invasive at presentation compared to 25% in the general population [7, 11]. The mean patient age at bladder cancer diagnosis in a neurogenic population has been calculated as 50 years (in the general population, 73 years with the highest percentage between ages 75 and 84 years) [1]. Furthermore, studies have shown that the standardized mortality ratio due to bladder cancer among SCI individuals is 7- to 70-fold higher than that of the general population [3, 12]. The 1-year overall survival rates after treatment of bladder cancer in neurogenic patients range between 61 and 70% [13, 14]. A recently published systematic review with meta-analysis revealed that transitional cell carcinoma is the most common histological type (46.3%, in the general population 90%) followed by squamous cell carcinoma (36.8%, in the general population 2–7%) and other pathological types (17.1%) [1].

Risk Factors

Potential risk factors for bladder cancer among neurogenic individuals include [7, 15]:

- Indwelling catheter usage (time-dependent risk factor)
- Chronic urinary tract infections
- Bladder stone disease
- Increased urine contact time
- Altered immunological function
- Other factors commonly found in a non-neurogenic population (e.g., smoking, workplace exposure, pelvic radiation, cyclophosphamide exposure)

It has been demonstrated that bladder management with chronic indwelling catheterization (both transurethral and suprapubic) leads to certain histological changes, including papillary or polypoid cystitis, widespread cystitis glandularis, moderate to severe acute and chronic inflammatory changes in bladder mucosa, follicular cystitis, squamous metaplasia, and urothelial dysplasia [16–18]. However, clinicians should be

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_15

aware that up to 50% of neurogenic patients diagnosed with bladder cancer have not been managed with an indwelling catheter [6]. This supports the idea that perhaps the neurogenic bladder itself is the primary risk factor for cancer neogenesis. The role of augmentation cystoplasty in the development of bladder cancer is still controversial, as the long-term results are not available [19]. Nevertheless, it seems possible that ileal/colonic bladder augmentation (with the exception of gastrocystoplasty) does not appear to increase the risk of bladder malignancy [20]. Note that these findings refer to the adult population, as bladder cancer is a known complication of bladder augmentation in the pediatric population [19, 21]. The urodynamic type of neurogenic bladder dysfunction seems not to influence the development of bladder neoplasm [22].

Screening

Because the exact mechanism of increased risk of bladder cancer in neurogenic patients, particularly in those after SCI, has not been well analyzed, strong recommendations cannot be provided. The bladder cancer screening strategy of this specific population remains a matter of dispute and seems to depend on presenting risk factors.

The majority of neurogenic patients who have developed bladder cancer present with traditional symptoms, such as gross hematuria, suprapubic mass, or hydronephrosis/renal failure [7]. Any episode of gross hematuria should be investigated in the same manner as in the general population. It is important to stress that neurogenic patients may also present with less specific symptoms or signs, including frequent urinary tract infections, bladder calculi, penile discharge, or scrotal infection. These symptoms, although commonly associated with benign causes, should lead to a differential diagnosis of bladder cancer.

Some experts emphasize that routine cystoscopic surveillance is mandatory, as it detects malignant lesions at an early stage [23]. Importantly, studies have shown that endoscopic findings may not significantly differ between symptomatic and asymptomatic groups [24]. Others emphasize that cystoscopy screening does not fulfill the necessary criteria for the screening of bladder cancer in a neurogenic population and cannot be recommended [25–27]. Therefore, different follow-up strategies have been developed. It has been proposed that regular cystoscopic monitoring (with 1-year interval) should be considered in patients who have one or more of the following risk factors: smoking and age >50 years, enterocystoplasty or any augmentation cystoplasty over 10 years, any neurogenic bladder over 15 years [28]. Evaluation should be performed with urethrocystoscopy and biopsy/bladder-washing cytology if suspected lesions have been detected (Figs. 15.1, 15.2, and 15.3) [29]. Other proposals recommend performing

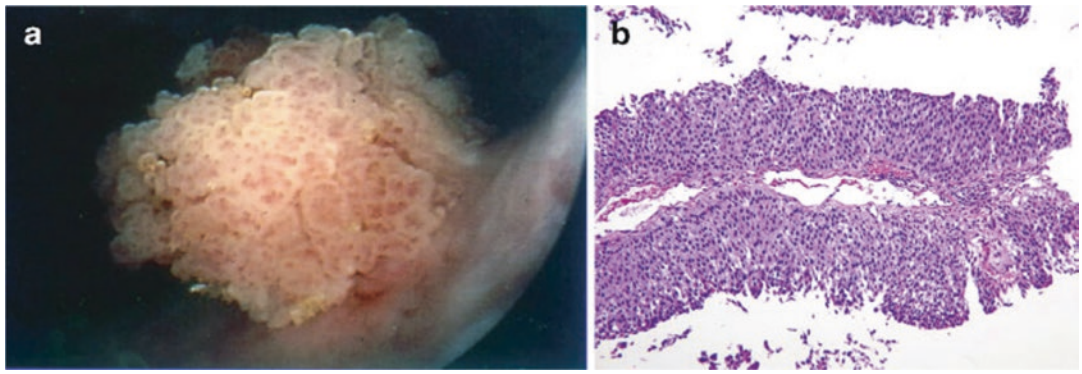

Fig. 15.1 (**a**) Papillary urothelial neoplasm of low malignant potential. (**b**) Tumor cells have a low nuclear/cytoplasmic ratio and their nuclei are of uniform size and shape. Mitotic figures are absent or rare (with permission from MacLennan et al. [29])

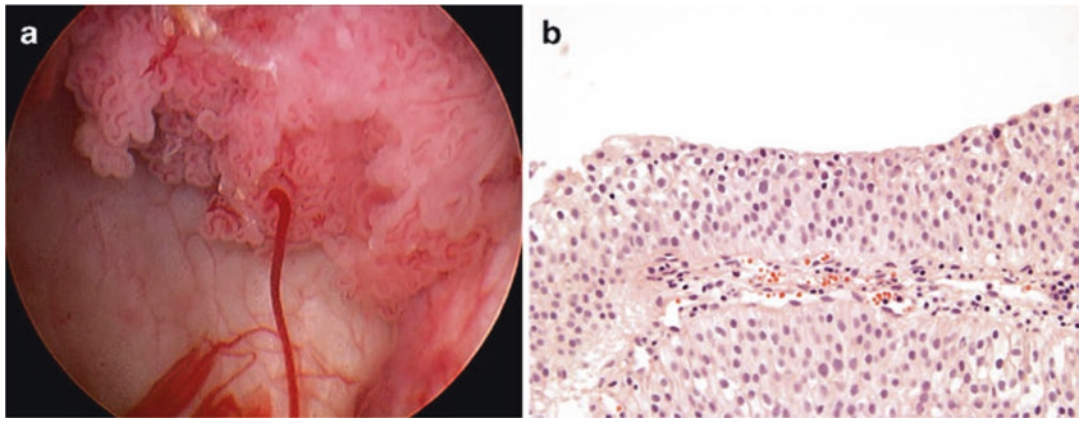

Fig. 15.2 Low-grade papillary urothelial carcinoma. (**a**) These lesions are universally papillary and exophytic. (**b**) Cell nuclei are moderately variable in size and shape with some nuclei being hyperchromatic and some having one or more distinct nucleoli. Mitotic figures are readily found (with permission from MacLennan et al. [29])

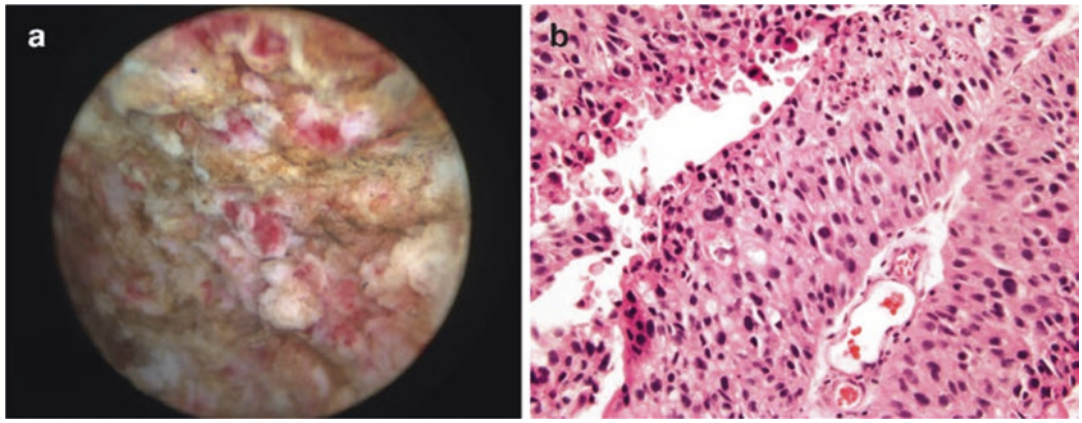

Fig. 15.3 High-grade urothelial carcinoma. (**a**) The lesion is erythematous, nodular, and highly irregular. (**b**) Histological examination reveals marked cellular atypia, with complete loss of cellular orientation. Nuclei are large and hyperchromatic, and many have prominent nucleoli. Tumor cells have high nuclear/cytoplasmic ratios, and vary considerably in shape and size. Abundant mitotic figures are present (with permission from MacLennan et al. [29])

surveillance urethrocystoscopy and bladder washing cytology on patients suffering from neurogenic bladder for at least 5 years on a regular short-term basis, that is, every 1–2 years [24, 30]. However, yearly monitoring with cystoscopy and biopsy in patients after SCI (without multiple risk factors for cancer neogenesis) from 5 years after catheter insertion has been found to be a poor screening test, with chronic cystitis and squamous metaplasia being the most common findings [26]. In view of these findings, a careful assessment of patient risk factors may be of utmost importance in choosing a screening strategy for bladder cancer in the neurogenic population. In a recent meta-analysis of neurogenic patients, cystoscopy demonstrated a sensitivity of 64% (95% CI, 49.3–76.5% I^2 = 37.7%) for detecting bladder cancer [1]. To sum up, cystoscopy alone is not sufficient and biopsy is required to make the final diagnosis because long-standing inflammatory changes or squamous metaplasia may be difficult to distinguish from cancerous lesions. A recently published prospective analysis of 129 neurogenic patients concluded that sur-

veillance urethrocystoscopy might be warranted, although the ideal starting point and frequency remain to be determined in further studies [30].

Urine cytology is another possible method of bladder cancer screening. A retrospective study of 208 SCI patients monitored for more than 5 years demonstrated that positive cytology has a sensitivity of 71% and a specificity of 97% [31]. Authors recommended a minimum of annual cytology in all patients with chronic indwelling catheters or other risk factors, followed by biopsy when the cytology was positive or if any suspicious findings have been detected. Another proposal includes annual urine cytology in neurogenic patients after 10 years of injury or diagnosis of underlying neurological disorder [16]. If the cytology is positive or doubtful (because of the difficulty in interpreting the results due to chronic bacteriuria and hematuria from catheter use), cystoscopy and cold cup biopsy should be performed randomly if no suspicious lesion is found. Although urine cytology may be of benefit in monitoring patients with additional risk factors for bladder cancer, one must remember that cytology is generally normal in patients with low grade transitional cell carcinoma and in those with non-transitional types of bladder cancer [32]. Moreover, several authors have found cytology to have a very low diagnostic yield [33–36]. This has been supported by results of a recent meta-analysis that estimated the sensitivity of cytology as 36.3% (95% CI, 21.5–54.3%, I^2 = 40.2%) [1]. As intra-observer variations exist, the usefulness of cytology also likely depends on the ability of the cytopathologist to interpret samples with background inflammation [31]. To conclude, cytology alone may be a poor screening test in neurogenic patients.

A screening strategy with abdominal imaging in the form of ultrasound has been found inferior to cystoscopy and should not be considered a substitute for urethrocystoscopy and bladder washing cytology (Fig. 15.4) [37]. Contrast computed tomography as a screening method has not been well studied (Figs. 15.5 and 15.6).

As presented above, the gold standard screening test has not been established and available methods do not fill the criteria of proper screening test for effective cancer surveillance. These criteria are [38]:

- A safe, inexpensive, reliable screening test with high sensitivity and specificity
- Improved morbidity and mortality for early treatment relative to the primary disease process
- Significant morbidity and mortality for untreated tumor
- A high prevalence rate at a low stage
- An identifiable patient population at risk of developing a malignancy in which the cancer incidence is frequent enough to fiscally merit screening

It is noteworthy that bladder cancer can occur rapidly, making annual screening less likely to detect the disease at an earlier stage [7]. The cost, use of resources, and the possibility of morbidity associated with different screening procedures along with the lack of evidence for benefit make proposed screening strategies for bladder cancer in neurogenic patients less appealing [8].

Diagnosis and Treatment

Comprehensive guidelines for the diagnosis and treatment of bladder cancer have been developed and they can be directly applied to management of patients with neurogenic lower urinary tract dysfunction [39]. These include Guidelines of the European Association of Urology (EAU) [40, 41], the American Urological Association (AUA) [42, 43], and the Canadian Urological Association (CUA) [44].

Sexual Dysfunction

Sexual dysfunction (SD) has been traditionally categorized as primary (direct neurological damage); secondary (general physical disabilities, e.g., urinary incontinence, bowel dysfunction, fatigue, discoordination, impaired mobility, muscle weakness, spasticity, cognitive dysfunction); and tertiary (psychosocial and emotional issues,

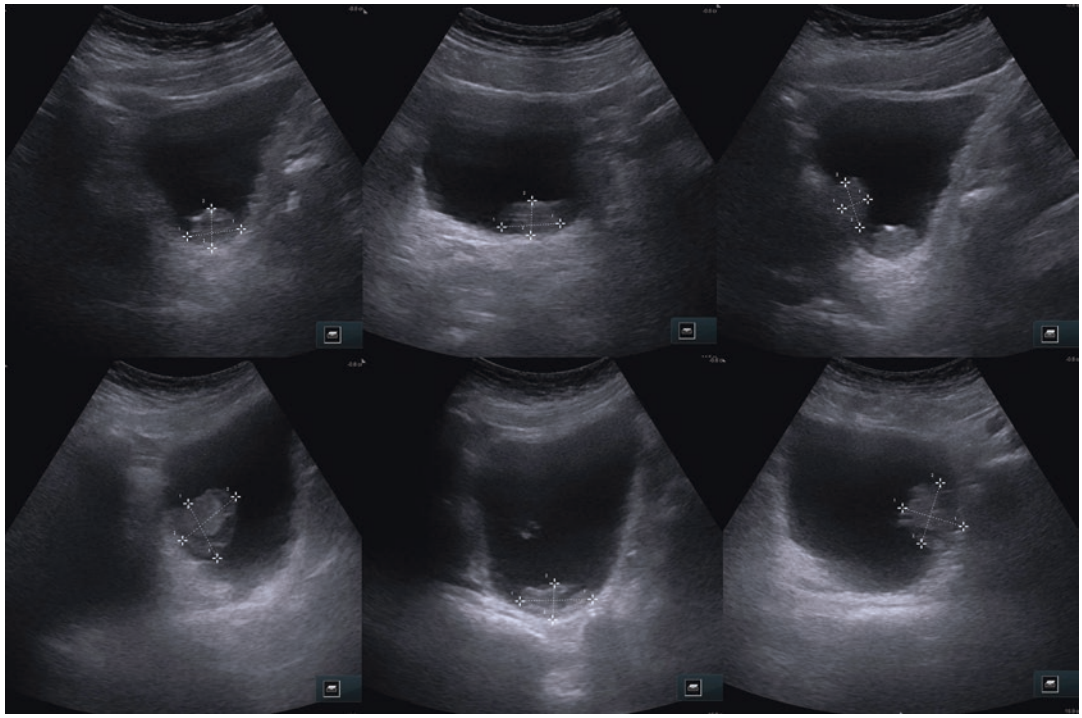

Fig. 15.4 Ultrasounds of bladder tumors

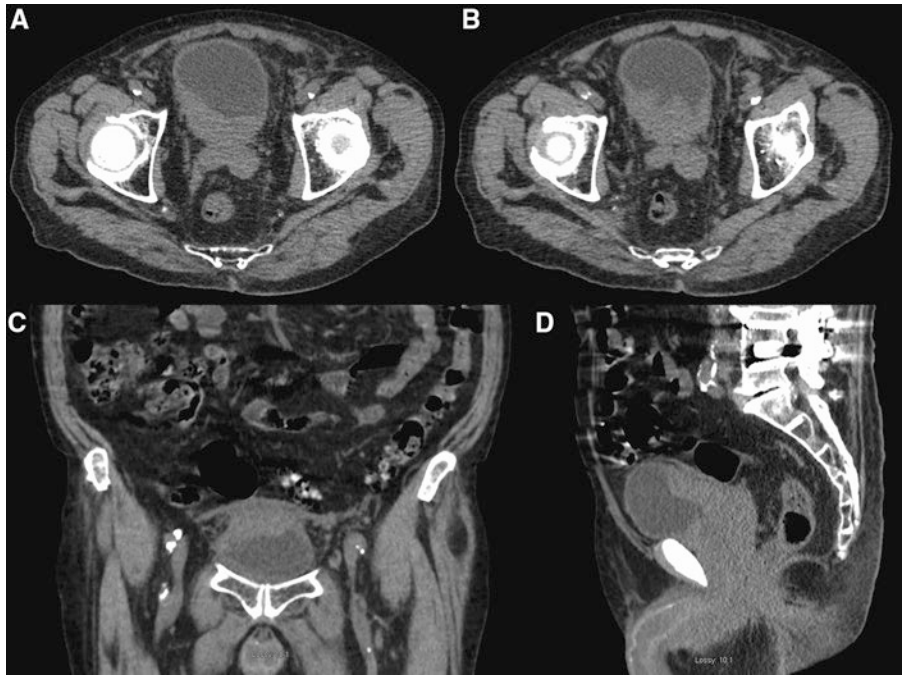

Fig. 15.5 CT scan demonstrating a large mass in the posterior part of the bladder. (**a**, **b**) Axial view. (**c**) Coronal view. (**d**) Sagittal view

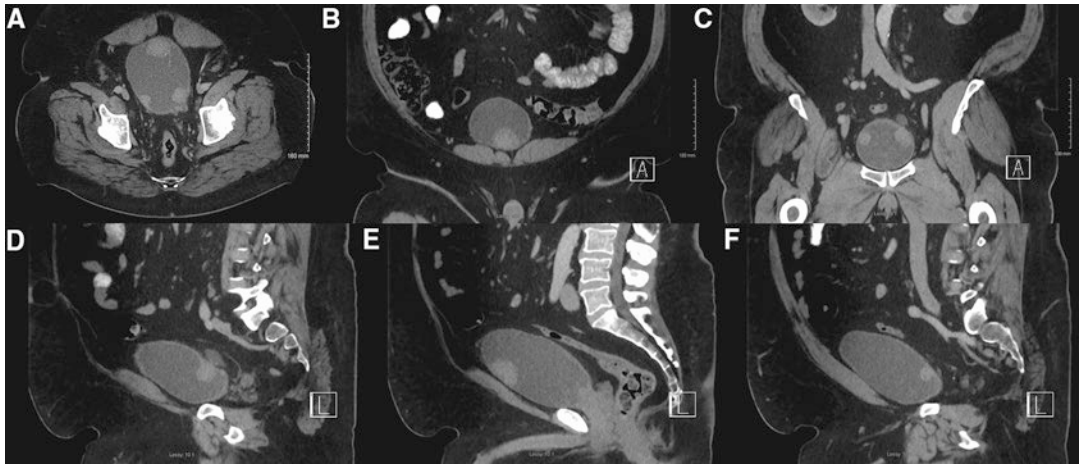

Fig. 15.6 CT scan demonstrating three bladder tumors, largest anteriorly measuring 3.2 × 3 cm. The lesion extends to the wall without extravesicle extension. There are no abnormal pelvic lymph nodes. (**a**) Axial view. (**b**, **c**) Coronal view. (**d**–**f**) Sagittal view

e.g., sexual and social isolation, low self-esteem and self-confidence, body-image changes, mood dysregulation, anxiety, depression) [45]. Initial categorization helps to identify and clarify certain symptoms and may be useful for the purpose of counselling the patient. Nonetheless, clinicians should be aware that in the daily clinical practice of neurourology, it is often hard to classify the patient into one category. Underlying neurological disorder often produces generalized condition-specific symptoms (typically leading to problems with positioning and mobility during sexual activity) or requires condition-specific drugs (often with a wide range of side effects), additionally influencing already impaired sexual function (secondary SD). Initially organic SD substantially contributes to psychogenic SD with decreased self-confidence (tertiary SD).

Epidemiology

SD among patients suffering from neurogenic lower urinary tract dysfunction is a serious concern. Although variations in definition, methodology, and study populations exist, it has been demonstrated that the prevalence of SD is high in the neurogenic population. Up to 40% of male patients after SCI report dissatisfaction with their sexual life [46, 47] and 25% of SCI females report decreased sexual satisfaction [48–50]. Estimated rates of successful intercourse in men with SCI range from 5 to 75% [51]. Only 12% of complete and 33% of incomplete SCI males can ejaculate during intercourse or masturbation without the aid of medication or devices [52]. Orgasm can be achieved by up to 50% of SCI patients [46]. Different degrees of SD may occur, depending on the level of SCI, extent of lesion, and timing from injury. Interestingly, lower lesions (particularly affecting sacral segments) are associated with more frequent and more severe SD compared to higher injuries, as they lead to impairment of reflex activity and maintain only psychogenic potential, which, however, lacks the muscular component to maximize sexual function [53]. The overall prevalence of SD among females suffering from multiple sclerosis has been estimated as 82.5%, and 45% reported worsening of their sexual functioning after the onset of the disease [54]. In male patients, SD related to multiple sclerosis is generally understudied in spite of its apparent high prevalence [45]. One of the few studies demonstrated that in males with multiple sclerosis erectile dysfunction, ejaculatory dysfunction, and decreased libido can be observed in approximately 63%, 50%, and 40%, respectively [55].

Once the diagnosis of multiple sclerosis has been established, up to 60% of men and 25% of women complain of SD. Stroke-related SD is also fairly frequent and affects up to 75% of stroke patients [56]. SD prevalence of 50–70% is documented in sufferers of Parkinson disease [57–61]. Similar findings have been shown for those affected by multiple system atrophy [62, 63]. It is estimated that 50–75% of adult patients with myelomeningocele are unable to have sexual intercourse [64–67]. As shown, SD is very common in neurogenic patients but still often overlooked and underestimated by medical staff, not only by urologists [54, 68].

Clinicians should keep in mind that SD with concomitant neurogenic lower urinary tract dysfunction, especially in young-onset neurological diseases (in particular multiple sclerosis), usually leads to a serious impact on the quality of life. In young-age neurogenic patients sexual relationships are still quite young and their family planning is not always completed [45]. On the other hand, older age might promote eventual comorbidities, for instance, cardiovascular disease, diabetes, impaired mobility, depression, and cognitive dysfunction, thus additionally deteriorating already-impaired sexual activity.

Diagnosis

There is universal agreement that identification and recognition of the problem should be the first step in the assessment of SD [45]. As patients are often reluctant to initiate the discussion themselves, the clinician should start the conversation. The presence of the partner in the discussion is recommended, as it helps to assess the impact of SD on the relationship. Privacy and confidentiality of reported SD should be stressed before taking the sexual history. Patients should be questioned about the onset and duration of symptoms, their severity (mild, moderate, severe), and timing (once, always, situational) to help confirm the dysfunction and identify the diagnosis. A complete review of medications is necessary to exclude iatrogenic causes of SD, as a wide variety of antispastics (e.g., baclofen, tizanidine, dantrolene), anticonvulsants (e.g., carbamazepine, phenytoine), antidepressants (e.g., SSRIs, venlafaxine), and anti-fatigue drugs (e.g., amantadine) are recognized causes of SD [69]. In males, physicians should investigate other common causes of erectile dysfunction (e.g., cardiovascular disease, hypertension, hypercholesterolemia, diabetes) or reversible risk factors (e.g., smoking, obesity, alcohol, lack of regular exercises) [70–72]. It is important to establish the presence of erectile dysfunction, often confused with other sexual dysfunctions, including premature ejaculation and inability to reach orgasm. Clinical examination should rule out penile deformities, hypogonadism, or prostatic disease (>50 years). A rectal exam is important to assess rectal tone and reflexes (bulbocavernosal and anal). In female patients, physicians should question about decreased libido, impaired arousal, orgasmic dysfunction, pain from attempted or completed intercourse, difficulty with vaginal entry (due to muscle spasticity), and the awareness of vaginal lubrication. Physical examination should assess sensory function as well as reflexes and muscle tone of the pelvic area. In both sexes, tertiary causes of SD should be carefully evaluated. Additional tests depend on the clinical scenario. These may include hormonal testing (especially in perimenopausal women or those in whom hormonal replacement therapy is considered to treat libido and arousal disorders [73, 74]), metabolic profile, vascular studies, electrophysiological tests, psychodiagnostic testing, and other specialized tests. The majority of such tests are not routinely used and should be reserved for special circumstances [75].

Using validated questionnaires can support evaluation of SD in neurogenic patients, especially when the interviewer is not familiar with the condition and when a measurable clinical response is needed (to assess treatment response and efficacy or disease progression). For those suffering from multiple sclerosis, clinicians can use specific questionnaires including the Functional Assessment of Multiple Sclerosis Quality of Life, or FAMS [76], the Hamburg Quality of Life Questionnaire in Multiple Sclerosis, or HAQUAMS [77], the Multiple Sclerosis Intimacy and Sexuality Questionnaires,

or MSISQ-15/MSISQ-19 [78, 79], Multiple Sclerosis Quality of Life Inventory, or MSQLI [80], Multiple Sclerosis Quality of Life-54 Instrument, or MSQoL-54 [81] and RAYS [82]. Patients after SCI can be questioned with SCI specific questionnaires, including the Rick Hansen Spinal Cord Injury Registry, or RHSCIR [83] and Fransceschini [82]. Other questionnaires that have been validated in a neurogenic population and can be widely used among patients with either multiple sclerosis/SCI and other neurological disorders include the Incontinence Quality of Life Questionnaire, or IQOL [84] or Qualiveen/SF-Qualiveen [85, 86]. Patients with SD can also be assessed by other generic questionnaires for either females (the Female Sexual Function Index, or FSFI, the most frequently used female questionnaire; the Derogatis Sexual Functioning Inventory, or DSFI; the Female Sexual Distress Scale, or FSDS; the Sexual Function Questionnaire, or SFQ) and males (the International Index of Erectile Function, or IIEF, the most frequently used male questionnaire; the Sexual Health Inventory for Men, or SHIM) [87–89]. It is important that the questionnaire of choice be validated in the language in use. Each questionnaire can be used alone or in combination with other questionnaires to improve assessment or monitoring of treatment outcomes.

If the clinician experiences negative emotions and/or difficulties with patient cooperation, it can be beneficial to refer patients and their partners to professional counselors, psychiatrists, psychologists, or sex therapists.

Treatment

Management of Sexual (Erectile) Dysfunction in the Male

Oral Pharmacological Therapy (Phosphodiesterase Type 5 Inhibitors)

Phosphodiesterase type 5 inhibitors (PDE5Is) represent the first-line treatment in patients with neurogenic erectile dysfunction [90–92]. Sildenafil, vardenafil, and tadalafil have been demonstrated as safe and effective, but there is still lack of well-designed studies in neurourological patients [93, 94]. There are limited data on the efficacy and safety of the newer PDE5Is, avanafil and mirodenafil, in neurologically impaired individuals [95]. Up until now, positive results of PDE5Is have been shown in patients with SCI, multiple sclerosis, Parkinson disease, multiple system atrophy, and spina bifida, and treatment efficacy has been most widely investigated in those after SCI [94, 96, 97]. PDE5Is have also been found as the best treatment of SD in terms of cost-effectiveness [98, 99]. However, it is currently impossible to indicate the superiority of one drug over another, and head-to-head trials evaluating specific PDE5Is within the neurogenic population are required [97]. The medication should be taken 30 min before anticipated intercourse. The period of responsiveness ranges between 6 and 8 h for sildenafil/vardenafil and up to 24–36 h for tadalafil [100, 101]. Tadalafil, due to the long half-life, offers efficacy without planning and allows spontaneous sexual activities, thus reducing dependency on a pill but may be contraindicated in elderly and cardiac patients [45]. Sildenafil should not be taken during meals, as this may delay the time of onset of efficacy [100, 102]. There is minimal or no interaction between vardenafil/tadalafil and food intake [100].

The side effects of the PDE5Is are mild and transient and include headache, flushing, dyspepsia, visual disturbance, nasal congestion, epistaxis, and dizziness [103]. PDE5Is are contraindicated for those taking nitrates or nitric oxide donors and for individuals for whom sexual intercourse is not recommended for cardiac reasons (unstable angina, recent myocardial infarction). Those after suprasacral SCI with episodes of autonomic dysreflexia must be counselled that PDE5Is are contraindicated when using nitrate medication [90].

Drugs other than PDE5Is, including fampridine, apomorphine, and pergolide mesylate, are not routinely recommended [90, 104–106]. Studies indicate that 30–35% of men with SCI do not respond to PDE5Is therapy [92]. In particular, the highest rate of failure is documented in those with complete damage of the sacral segment (S2–S4) [107, 108]. In these patients, other treatment modalities should be implemented.

Mechanical (Vacuum Constriction) Devices

The vacuum constriction device (also known as vacuum erection device) is a long-standing treatment for erectile dysfunction, attractive to patients because it is a drug-free and surgery-free option. The vacuum constriction device has three components: a plastic cylinder into which the penis is placed, a pump that removes air from the cylinder, and an elastic constriction band. There are both automated (battery-operated) and manual pump mechanisms, which differ mainly in cost and ease of use (Fig. 15.7) [109]. The vacuum constriction devices have been found effective in up to 90% of patients after SCI and remain a non-invasive means to achieve erection [97, 110–113]. Although the devices are not commonly used or well-accepted (mainly due to pain, difficulty using the device, or cold penis) and long-term evidence is lacking, they have demonstrated to have a significant impact on sexual activity and sexual satisfaction. Vacuum therapy need not be used in isolation and might be combined with pharmacotherapy, including oral, intracavernosal, intraurethral, and topical agents [114–118].

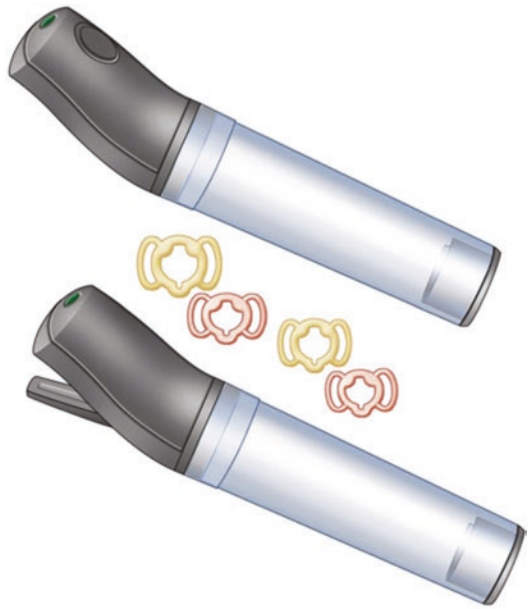

Fig. 15.7 Model of a vacuum constriction device. Both battery-operated (*top*) and manual (*bottom*) pump mechanisms are depicted. Elastic constriction rings of varying sizes are available (with permission from Hecht and Hedges [109])

Erection is obtained by inserting the penis into the cylinder with negative pressure to draw blood into the penis (Fig. 15.8) [109]. Then a constriction band is placed on the base of the penis to hold the blood in place. The maximum rigidity should be reached gradually (in order to adapt tissues to the stress of the vacuum), and using the pump twice a week for the first month is recommended [119]. The vacuum constriction device should be considered in patients with contraindications for pharmacotherapy [45]. Precautions for use include [119]:

- Impaired penile sensation
- Anticoagulant medications use
- High risk for priapism (sickle cell disease, multiple myeloma)
- Bleeding diathesis
- Severe Peyronie disease or other penile deformities

Common reasons for rejection include perceived cumbersome operation, lack of spontaneity, and partner rejection [120, 121]. Possible complications include discomfort (20–40%, tends to improve with familiarization with the device), numbness, penile cyanosis/coldness; petechiae (stopping use for 5–7 days is recommended if such appear); bruising; and skin trauma and pain (due to an excessively tight constriction ring) [113, 119]. Clinicians should be aware that neurogenic patients tend to be at higher risk for complications due to decreased sensation and subsequent excessive suction or constriction [122]. Impaired manual dexterity (often seen in neurogenic individuals) may also complicate device use, thus an understanding partner can certainly assist. Other limitations include lack of spontaneity, artificiality of erection, and cost due to non-insurance coverage [97].

Intracavernosal Injection Therapy

Intracavernous injections should be considered in patients who have not responded to oral pharmacotherapy with PDE5Is, with intolerable side effects, or who may not benefit from PDE5Is [45,

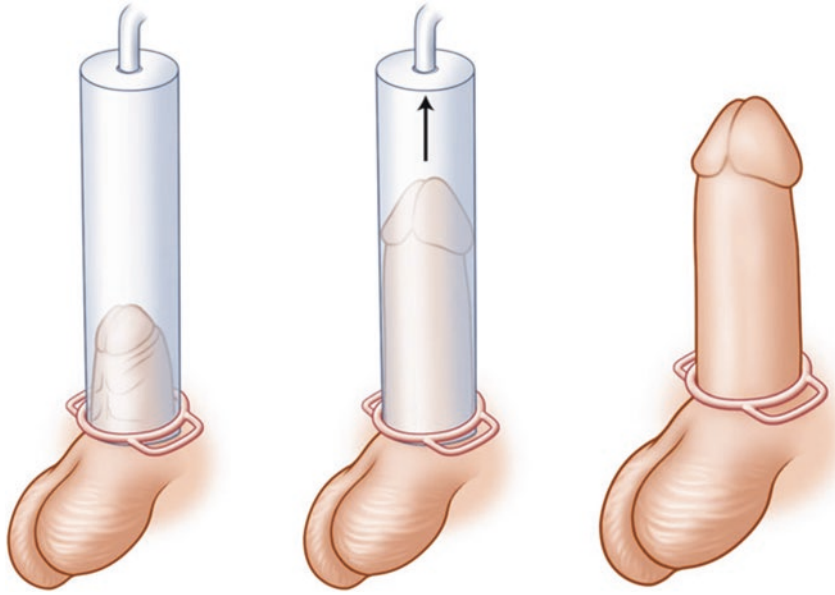

Fig. 15.8 Achieving erection with a vacuum constriction device. The *first panel* shows initial placement of the vacuum constriction device over the flaccid penis, taking care not to involve the scrotum. The constriction ring should be placed on the base of the pump, using lubrication to help apply the band. Plenty of water-soluble lubricant should be placed on the tip and base of the penis as well as inside the base of the device to assist in creating a good seal. The *second panel* shows engorgement of the penis as air is slowly pumped out of the cylinder, creating a vacuum (pumping too fast may cause discomfort within the penis). It may take several cycles of pumping to reach a fully rigid erection. Once a full erection is achieved, the erection is maintained by placing the constriction ring around the base of the penis. The *final panel* shows an erect penis with the constriction band in place. The constriction ring around the base of the penis should be removed after sexual activity or should not remain in place longer than 30 min. To remove the constriction ring, the lubricant should be reapplied (with permission from Hecht and Hedges [109])

90]. This modality is recommended as the first-line treatment in those taking nitrate medications and in individuals with concerns about drug interactions with PDE5Is [90]. Intracavernous injections should also be considered when a penile vacuum device is considered too burdensome by the patient and/or his partner/spouse [123]. Several drugs have been investigated (including alprostadil, papaverine, and phentolamine) and have been found effective in patients with SCI and multiple sclerosis [124–130]. The bimixtures and trimixtures agents combining prostaglandins (endogenous molecule), papaverine (vasodilation effect), and possibly phentolamine (smooth-muscle relaxant) are also available to maximize the effect of each drug while minimizing their side effects [53]. Nevertheless, the long-term evidence is lacking and overall data quality for neurogenic patients is low, therefore no specific dose recommendations can be made [92, 97]. The majority of studies did not report the residual erection of neurogenic patients at baseline nor statistically assess whether the type and degree of their residual erection were possible predictable factors for treatment success.

The compound is injected 5–10 min before sexual intercourse (Fig. 15.9) [123]. Intracavernosal injection therapy is contraindicated if the individual [123, 131]:

- Is on a monoamine oxidase (MAO) inhibitor
- Has a predisposition to priapism due to underlying hematologic disorders (e.g., sickle cell anemia, multiple myeloma, leukemia)
- Has uncontrolled hypertension
- Has a penile prosthesis or penile abnormalities (Peyronie disease, cavernosal fibrosis)
- When sexual activity is inadvisable

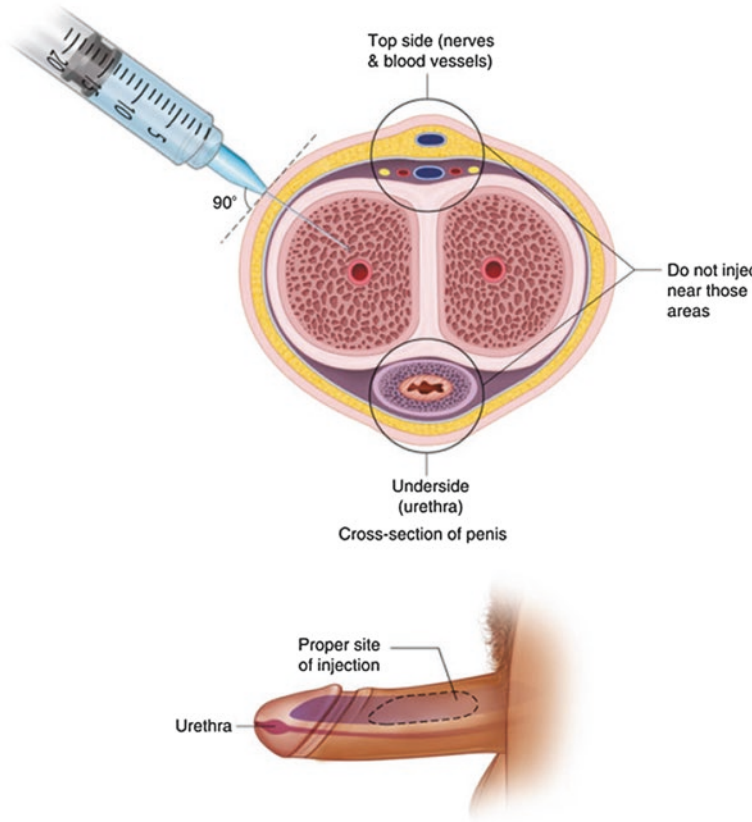

Fig. 15.9 Intracavernosal injection. The medication has to be injected into the lateral area of the one of two corpora cavernosa. Injections can be performed alternatively into the right or the left corpus cavernosum to avoid local fibrosis (with permission from Narus [123])

If the therapy is not contraindicated, certain precautions exist and include [123]:

- Obese abdomen resulting in the inability to self-visualize the penis
- History of vasovagal episode secondary to needle anxiety
- Dexterity problems (arthritis, tremors, Dupuytren contractures)
- Anticoagulation (not a formal contraindication [132])

Clinicians should also bear in mind that intracavernous injections as well as other methods of treatment requiring varying degrees of manual dexterity might not be useful to patients with high-level lesions and injuries. It has been proposed that patients who are candidates for intracavernous injections should be assessed with a Duplex color sonogram with an intracavernosal injection of a standard 3 μg dose of PGE1 [45]. This test has both a diagnostic (vascular evaluation) and a therapeutic value (clinical responsiveness to the drug). If the test is positive, the patient is enrolled into an injection training program with increasing dosages of PGE1 injected in the clinic (once a week). It is of utmost importance to adequately educate patients, as it has been shown that a fear or anxiety with penile injections is present in up to 43% of patients [133]. A specialized nurse usually injects the first two doses, then the patient performs the next injection under supervision. Once the patient or partner is able to perform an injection, the final titration is performed at home. One or two injections per week are recommended. To minimize the risk of prolonged erection, patients should start with lower doses than normally required in non-neurogenic patients. If a prolonged erection occurs (in up to 2% of patients), the patient should be advised to contact a urologist [134–136]. Although this complication is rare, the patient should be admitted

and a simple puncture of the corpora cavernosa (to aspirate a small volume of blood to decompress the corpora) should be performed. The corpora cavernosa may be irrigated using normal saline and diluted solution of phenylephrine or other similar α-adrenergic agents under careful cardiovascular monitoring, particularly in patients with a previous history of cardiovascular disease [129, 137]. Other possible complications include penile discomfort or pain, bleeding or ecchymosis at injection site, cavernosal fibrosis (mainly with papaverine, often disappears upon temporary cessation of treatment), hematuria from an intraurethral injection, and trauma to subcutaneous and erectile tissue if injection site is not rotated to alternate injection sites on penile shaft [123].

Patient should be informed to *not* [123]:

- Perform injection of a second dose on the same day if there is a poor or no response to the first injection
- Take oral erectile agents (sildenafil, vardenafil, avanafil) within 18 h of an injection or inject within 18 h of one of these agents
- Perform more than three injections per week

Intraurethral application of alprostadil is an alternative option but less effective (Fig. 15.10) [138, 139]. Moreover, the intraurethral route has not been extensively studied in a neurogenic population. A new cream product with a prostaglandin gel (Vitaros) has been recently introduced, but has not yet been evaluated in a neurogenic population.

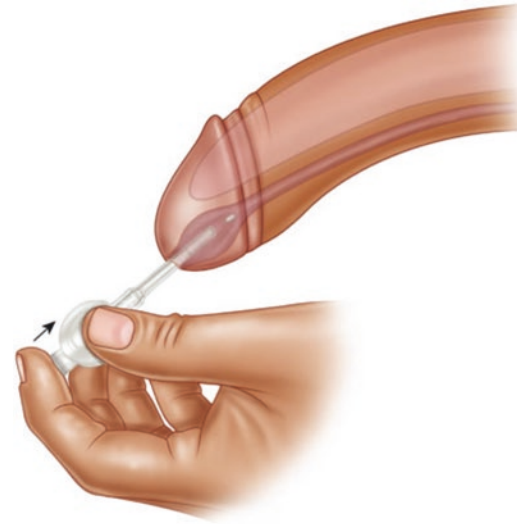

Fig. 15.10 Illustration of hand and applicator location during insertion (with permission from Mulhall and Jenkins [139])

Penile Prostheses

Penile prostheses may be considered when all other treatment options have failed or patients refuse intracavernosal injections or a vacuum device. Penile prostheses should be considered as a last alternative because they destroy the internal penile tissues. Implantation of a penile prosthesis has the highest satisfaction and efficacy rates (ranging between 69 and 98%) in patients with severe erectile dysfunction [140–150]. Types of penile prostheses include semi-rigid (Fig. 15.11) and inflatable (two-piece/three-piece) devices. A three-piece device consists of cylinders, a pump, and a reservoir (not present in a two-piece device) (Fig. 15.12) [151]. The paired cylinders are implanted in the corpora cavernosa. The pump is implanted into the scrotum between the internal and external spermatic fascia. The reservoir can be implanted either into the space of Retzius or ectopically between the transversalis fascia and the remainder of the abdominal wall [152]. Compression of the pump transfers fluid from the reservoir into the cylinders, resulting in an erection. Compression of the release valve transfers fluid from the cylinders into the reservoir. A lockout valve prevents auto inflation.

Inflatable devices are currently preferred and most widely used but semi-rigid devices may still be considered in patients with undue risk of surgical manipulation, including reservoir placement (e.g., history of renal transplant or neobladder). Semi-rigid implants may also be indicated in patients suffering from incontinence to facilitate the application and maintenance of a urine-collecting device (condom catheter) as well as to provide stability for intermittent catheterization [153, 154]. On the other hand, semi-rigid prostheses should be used with caution in some neurogenic patients with lack of sensation

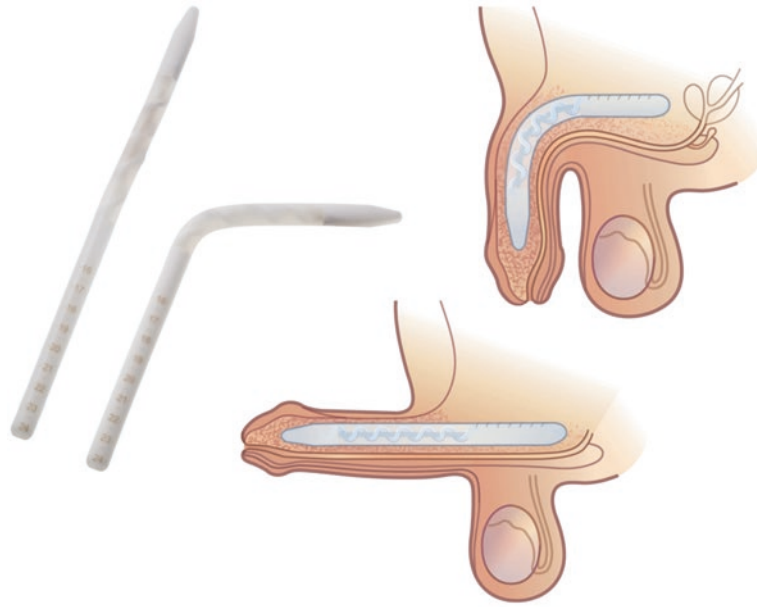

Fig. 15.11 A semi-rigid penile prosthesis (with permission from courtesy of Coloplast et al. [151])

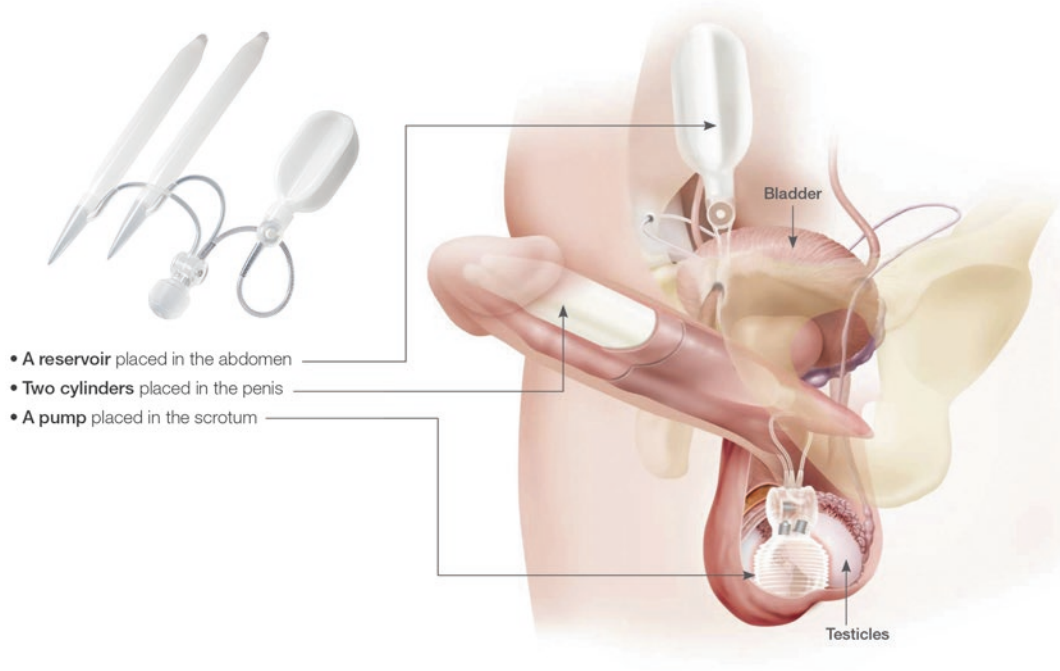

Fig. 15.12 A three-piece penile prosthesis (with permission from courtesy of Coloplast et al. [151])

(unperceived infections), when in the sitting position (friction), and with occasional spasms (traumas) that can cause irritations and infections or even perforation [53, 153, 155, 156]. Patients with concomitant neurogenic sphincter deficiency should be counselled regarding the possibility of dual procedure with the simultaneous placement of an artificial urinary sphincter or

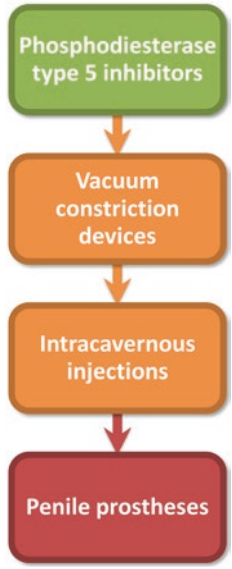

Fig. 15.13 Management algorithm of male patients with neurogenic erectile dysfunction

sling [157]. Untreated neurogenic voiding dysfunction is a contraindication to surgical implantation of a penile prosthesis [152]. Penile prostheses provide an on-demand erection as well as preserve penile sensation and ejaculatory function.

Complications are not uncommon during and after penile prosthesis surgery. Potential complications include perioperative problems (scrotal swelling, pain, infection, urinary retention, bleeding, hematoma with wound leakage, corporal and urethral perforation, corporal crossover, bladder/bowel perforation); new or exacerbation of angulation/curvature; difficulty with ejaculation (usually transient); impaired sensation or sensory loss; infection (particularly in patients with diabetes and immunosuppression); erosion (especially with semi-rigid implants); phimosis; mechanical failure (device malfunction, cylinder aneurysm, cylinder malposition, tubing fracture, connector disruption); over/under-inflation; inguinal hernia; and genital change (e.g., perceived loss of length). Complications in penile prosthetic surgery are sometimes inseparable, but if managed adequately they have minimal impact on device success and patient quality of life [158]. Nowadays, one of the most serious complications, erosion/infection, has been dramatically reduced with the introduction of special coatings and improved surgical techniques. These factors have contributed to the reduction of infection rate in revision cases from 8–10% to 2–3% [159–165]. Similarly, device survival has significantly increased. Multiple series have shown device functioning at 5 years ranging from 83.9 to 93.7% [144, 145, 166–168]. Concurrent results have been shown for neurogenic patients, with 83.7% of those after SCI able to have sexual intercourse at a mean follow-up of 7 years [92]. Freedom from mechanical failure at 10 and 15 years are also not rare with rates of 79.4 and 71.2%, respectively [169]. Despite these positive findings, it should be noted that data for neurogenic patients are limited to single studies [92, 153, 170]. Nonetheless, it can be stated that implantation of modern penile prosthesis is a relatively safe procedure associated with high patient and partner satisfaction rates. Patients can be discharged home the same day of surgery or the following day with a proper follow-up plan [152].

Other Treatment Options

These include perineal electrostimulation and neuromodulation. Both of them have shown promising results but there is lack of strong evidence to recommend these modalities for daily clinical practice [95, 171, 172]. Figure 15.13 presents a treatment algorithm of neurogenic erectile dysfunction.

Management of Sexual Dysfunction in the Female

Treatment of SD in neurologically impaired women is rather limited and poorly studied. There are no evidence-based therapeutic options to treat neurological women with sexual dysfunction [95]. The EAU Guidelines recommends not offering medical therapy for the treatment of neurogenic sexual dysfunction in women [90]. Studies on PDE5Is in women provide contradictory results [53]. Psychological interventions and a more holistic approach, including peer support and sexuality-related rehabilitation services, have been proposed to manage these patients [90]. However, there is lack of high level evidence, and women are more reluctant than men to receive

sexual counselling and help [173–175]. Secondary causes of SD, in particular urinary incontinence (considered as the greatest physical barrier to sexual activity), should be appropriately treated [47, 48, 176–178]. It is well known that patients managed with intermittent catheterization have a better sex life compared to those with indwelling urethral catheters. When an indwelling catheterization is required, a suprapubic tube might be an option to improve sexual life.

Conclusion (Table 15.1)

Table 15.1 Conclusion

Summary	Level of evidence
The risk of bladder cancer in patients with neurogenic lower urinary tract dysfunction is significantly higher than in the general population. The majority of studies on bladder cancer in neurogenic patients have focused on those with spinal cord injury (SCI)	2/3
The increased mortality from bladder cancer among neurogenic patients may be partly explained by the increased clinical stage at presentation and the comorbidities associated with this population	4 (Expert opinion)
Several risk factors have been identified, including indwelling catheterization, recurrent urinary tract infections, and bladder calculi	2/3
Screening strategies for bladder cancer in neurogenic patients are mainly based on expert proposals and consensus statements. Recommendations for the screening protocol and timing vary	4 (Expert opinion)
Multiple studies have advocated the use of cystoscopy as an annual screening tool in specific groups of neurogenic patients; others have suggested yearly cytology	2/3
Phosphodiesterase type 5 inhibitors have been found effective and safe in the male neurogenic population, especially in patients after SCI	1/2
Vacuum constriction devices have been shown positive results in male neurogenic patients	3
Although satisfactory results have been documented for intracavernosal injection therapy in patients suffering from neurogenic erectile dysfunction, good quality data is lacking	3
More than 80% of individuals are able to have successful intercourse in the medium and long-term follow-up after implantation of penile prosthesis. However, the available data for neurogenic population are limited to single studies	3
There are no evidence-based therapeutic options to treat neurological women with sexual dysfunction	4 (Expert opinion)

Recommendation	Grade of recommendation
Clinicians need to have a high index of suspicion for bladder cancer among neurogenic patients, in particular among those after SCI and/or managed with long-term indwelling catheters	C
The use of routine screening urine cytology, cystoscopy, and random bladder biopsy has not been shown to significantly decrease mortality and should not be routinely performed	C
Surveillance with regular cystoscopy/cytology for those with multiple risk factors for bladder cancer may be considered	Expert opinion
Early recognition is important to improve these patients' prognosis with surgical resection and their future quality of life	Expert opinion
Oral phosphodiesterase type 5 inhibitors should be considered as the first-line medical treatment in patients with neurogenic erectile dysfunction	B
The vacuum constriction device can be used for the treatment of erectile dysfunction as an alternative or support to oral pharmacotherapy	C

(continued)

Table 15.1 (continued)

Recommendation	Grade of recommendation
Intracavernosal injection therapy should be considered as a second line treatment option for neurogenic patients suffering from erectile dysfunction in whom oral therapy is contraindicated, not tolerated, or ineffective	C
Intracavernous injections should not be prescribed without proper patient education and initial dose titration in the clinic. Signed consent should be obtained before starting injections. The patient should be counselled with regard to side effects such as hematoma and priapism	Expert opinion
Penile prostheses may be proposed when all other treatments have failed or have been refused	C
Candidates for penile prosthesis should be adequately and carefully counselled regarding all potential benefits and risks (about infection, in particular)	Expert opinion
Sexual counselling with multidisciplinary/holistic approach should be considered in all neurogenic patients, regardless of sex, and tailored to the individual's remaining sexual potential	Expert opinion

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Benign Prostatic Hyperplasia and Neurogenic Bladder

16

Introduction

Proper diagnosis and treatment of benign prostatic hyperplasia (BPH) in neurogenic individuals remains a challenge for urologists. On the one hand, the assumption that reported lower urinary tract symptoms are fixedly due to the underlying neurological pathology may result in inadequate treatment of BPH [1]. Furthermore, bladder outflow obstruction secondary to BPH, considered as a progressive disease, may further increase the risk of complications to the lower and upper urinary tract with severe renal damage. On the other hand, disregarding the underlying neurological disorder may exacerbate symptoms and dramatically worsen quality of life. Therefore, clinicians should carefully balance all circumstances in choosing proper management, as surgical treatment for BPH in some patients may result in urinary incontinence instead of retention.

Epidemiology

BPH is the most common male urological disease. It has been shown that 10% of men of 40 years of age and 90% of those 80 years of age can be diagnosed with BPH [2–4]. A small study of 28 men (mean age 66.4 years) revealed that BPH patients, particularly those >65 years of age, commonly have neurogenic bladder dysfunction [5]. Multiple cerebral infarction (upper neuron disorder) and lumbar spondylosis (lower neuron disorder) might contribute to neurogenic detrusor overactivity and neurogenic detrusor underactivity, respectively. Epidemiological data of BPH among neurogenic patients with confirmed and specific neurological diagnosis are sparse. As some neurological disorders commonly appear in middle-aged and elderly men (e.g., Parkinson and Alzheimer disease), it can be assumed that a significant percentage of these patients suffer from BPH.

Diagnosis

Comprehensive guidelines for the diagnosis and treatment of BPH have been developed and they can be applied to patients with neurogenic lower urinary tract dysfunction. These include Guidelines of the European Association of Urology (EAU) [6], the American Urological Association (AUA) [7], and the Canadian Urological Association (CUA) [8]. However, in those with bothersome symptoms of bladder outflow obstruction and concomitant neurological disorder, further evaluation is necessary. BPH in men with neurogenic bladder dysfunction may be indicated by increasing difficulty or pain during intermittent catheterizations, growing residual urine volumes in those who void by Valsalva or Crede maneuvers, and higher rates of urinary tract infections. Difficulty with catheterization

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_16

has been reported as the most suspicious symptom of BPH in the neurogenic population [9–11]. Patients typically report that they feel increasing difficulty in passing a catheter into the bladder while using catheters that previously passed smoothly. A carefully conducted medical history will elicit that this has developed over time. Patients may also complain of hematuria (either spontaneous or in combination with catheterization) due to the increased size of the prostate and neovascularity of the enlarged gland [12–14]. Those who void by Valsalva or Crede maneuver may report an increase in the feeling of incomplete emptying, a weaker stream than usual, or a complete inability to void [10]. Further evaluation should include cystourethroscopy to assess the contour of the prostate and, in cases of hematuria, to rule out bladder malignancy [15].

Urodynamic study in neurogenic patients suspected of BPH is recommended. Whereas BPH represents an organic obstruction, urodynamic testing can substantially support the differential diagnosis of functional bladder obstruction presented as detrusor-sphincter dyssynergia (see Chap. 8). In some patients, these two conditions may coexist. Video urodynamics with electromyography seems to be the optimal diagnostic modality to diagnose this discoordination. Urodynamic study is also the gold standard to differentiate retention resulting from bladder outlet obstruction and retention due to underactive detrusor [16]. Calculation of the bladder outlet obstruction index (BOOI) helps clinicians reach the proper diagnosis. The BOOI (BOOI = $P_{det}Q_{max} - 2Q_{max}$) is derived from the Abrams–Griffiths nomogram [17] and divides patients into three different groups according to their degree of obstruction:

- BOOI > 40: obstructed
- BOOI = 20–40: equivocal
- BOOI < 20: unobstructed

The true cause (neurogenic vs. non-neurogenic) of detrusor overactivity in neurogenic patients with concomitant BPH is often difficult to establish. Nevertheless, coexistence of detrusor-sphincter dyssynergia and detrusor overactivity typically indicates a neurological cause of overactive detrusor [1]. Of note, treatment of BPH in these patients should be especially considered because the increased outlet resistance in combination with an overactive detrusor can lead to extremely high bladder pressures with elevated residual urine volumes and urinary retention, significantly increasing the risk of renal failure [10].

Treatment

Pharmacological Treatment

Experts indicate a conservative approach as the first-line treatment option of BPH in patients suffering from neurogenic lower urinary tract dysfunction [18]. The use of α-blockers (α-adrenoreceptor antagonists) in mild/moderate obstruction has shown significant voiding improvement [19, 20] but clinicians should expect poor results in those with more severe neurological impairments [21, 22]. Combining this with a 5-α reductase inhibitor in order to reduce the size of the prostate, decrease symptoms, and allow for continued catheterization (if performed), may be taken into account [10, 23–25].

It is important to emphasize that it is sometimes impossible to discriminate between lower urinary tract symptoms resulting from BPH and those secondary to neurological disease. Symptoms secondary to BPH such as poor urine flow, frequency, urgency, and nocturia may also be induced by neurogenic bladder dysfunction. Urodynamic study may also present ambiguous findings. In these settings, conservative treatment is preferable to irreversible surgical intervention [1].

Surgical Treatment

Surgical treatment of BPH in patients suffering from retention with concomitant neurological disorder remains a matter of dispute. The main concern includes post-surgical appearance or exacerbation of urinary incontinence instead of

retention. Unfortunately, there is a paucity of long-term and randomized studies performed on large cohorts. Existing data are limited to single studies or case reports and do not allow one to make reliable conclusions and recommendations.

It has been proposed that patients who do not suffer from sacral/infrasacral lesions and peripheral denervation involving the pudendal nerve responsible for the activity of the external sphincter (these lesions typically leads to neurogenic detrusor underactivity and/or neurogenic sphincter deficiency—see Chap. 3) should have no negative consequences (especially stress urinary incontinence) from prostatic surgery and might benefit from removal of bladder outflow obstruction [18].

Some data are available for patients suffering from Parkinson disease. Because Parkinson disease and BPH are common in late middle-aged males, their concurrence is probable and often seen. A retrospective study of 23 men suffering from Parkinson disease who underwent transurethral resection of the prostate (TURP) due to bladder outlet obstruction secondary to BPH and were followed for 3 years after surgery demonstrated interesting findings [26]. According to the preoperative Abrams–Griffiths nomograms 52% of patients were obstructed, 22% equivocal, and 26% unclassified, as they could not void but did demonstrate increase in detrusor pressure. Of the 14 patients with a preoperative indwelling urinary catheter, TURP restored voiding in 9 (64%), and only 5 (36%) required catheterization postoperatively. Of the 10 patients with preoperative urge urinary incontinence, continence was restored in 5 and improved in 3 following TURP. There were no cases of de novo urinary incontinence after transurethral prostate resection. To summarize, at a median postoperative follow-up of 3 years TURP was successful in 16 of the 23 patients (70%). Authors concluded that TURP for BPH in patients with Parkinson disease may substantially improve lower urinary tract function and the risk of de novo urinary incontinence is minimal. They added that Parkinson disease should no longer be considered a contraindication for TURP, provided that preoperative investigations including urodynamic assessment indicate prostatic bladder outflow obstruction. In view of these findings, multiple experts propose that patients with Parkinson disease and BPH can be considered for appropriate surgery and that preoperative investigations, including urodynamic assessment, should be used to confirm the diagnosis of BPH in such patients [18, 27, 28]. On the other hand, a retrospective study on post-TURP continence in 50 parkinsonian patients revealed a high incidence of incontinence following the procedure [29]. However, authors emphasized the fact that some of these patients were likely to have had multiple system atrophy, a disease with frequent denervation of the external urinary sphincter resulting in neurogenic sphincter deficiency [30]. Therefore, accurate differentiation between Parkinson disease and multiple system atrophy (more severe, rapidly progressive, multisystemic and fatal disease classified as a form of atypical parkinsonism—see Chap. 3) is critical before surgical intervention for BPH [1]. In patients with a diagnosis of Parkinson disease but who have clinical symptoms that are more aggressive and extensive, including pyramidal or cerebellar signs, erectile dysfunction, severe postural hypotension, and marked urinary incontinence, a diagnosis of multiple system atrophy should be suspected and investigated before proceeding to surgery [31].

A series of 39 patients with a history of one or more cerebrovascular accidents and who underwent TURP for BPH showed less encouraging results [32]. Only 50% had a satisfactory result from the operation and 11.7% died within 3 months of surgery. Better results were achieved in those under the age of 70 and who had their operation more than 1 year after the stroke. Authors also indicated that the degree of neurological deficit at the time of operation has a significant influence on final outcomes.

Another study on 89 patients after spinal cord injury suffering from detrusor-sphincter dyssynergia and bladder outflow obstruction secondary to BPH showed promising results [33]. Koyanagi et al. presented 90% of success characterized by a statistically significant reduction in the degree of detrusor-sphincter dyssynergia, an increase in

bladder compliance, and a reduction in detrusor overactivity. There was a 14% recurrence rate of detrusor-sphincter dyssynergia with time. The authors concluded that the results indicate that the adrenergic system has an effect on the distal sphincteric area in the genesis of detrusor-sphincter dyssynergia. Furthermore, the study suggested that TURP exerts this effect via a surgical sympathectomy, while continence is preserved by the activity of the untouched external urethral sphincter.

Recently, prostatic arterial embolization has been proposed as a potential minimally invasive procedure for patients with moderate to severe lower urinary tract symptoms due to BPH [34]. This modality may help to reduce the risk of intra- and postoperative complications of TURP such as bleeding, irritative voiding symptoms, abnormal ejaculation, and bladder neck contracture [35]. Although there is growing evidence of the efficacy and safety of prostatic arterial embolization for BPH, to date it has not been assessed in neurogenic patients [36]. Moreover, recent meta-analysis has indicated that prostatic arterial embolization should still be considered an experimental treatment modality even in non-neurogenic males [36].

Other Treatment Options

In patients for whom medical therapy and surgery are contraindicated or fails, other options include an indwelling catheter, either transurethral and suprapubic, with the preference for the latter for long-term use [37]. Urinary diversion should be considered as a treatment option of last resort.

Conclusion (Table 16.1)

Table 16.1 Conclusion

Summary	Level of evidence
Epidemiological data of benign prostatic hyperplasia (BPH) in neurogenic patients are sparse	4 (Expert opinion)
BPH in men with neurogenic bladder dysfunction may be indicated by pain or increasing difficulty with intermittent catheterizations, growing residual urine volumes in those who void by Valsalva or Crede maneuvers, and higher rates of urinary tract infections	4 (Expert opinion)
The use of α-blockers (α-adrenoreceptor antagonists) in mild/moderate obstruction offers limited but positive voiding improvement in neurogenic patients with concomitant BPH	3
Surgical treatment for BPH has shown positive results in those suffering from Parkinson disease and spinal cord injury	3
Recommendation	**Grade of recommendation**
Initial management of BPH in patients with neurogenic bladder dysfunction should include medical therapy consisting of an α-blocker alone or in combination with a 5-α reductase inhibitor	Expert opinion
When medical treatment of BPH has failed or is contraindicated, BPH surgery may be carefully considered in highly selected patients	Expert opinion
Patients who do not suffer from sacral/infrasacral lesions and peripheral denervation should have no negative consequences (especially stress urinary incontinence) from prostatic surgery and might benefit from removal of bladder outflow obstruction	Expert opinion
Careful medical history, symptom assessment, physical examination, and urodynamics/videourodynamics with sphincter electromyography should be included in preoperative evaluation in order to identify those with a high risk of postoperative urinary incontinence	Expert opinion

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Part V

Patient Education

Patient Education

17

Introduction

Patient education is an important principle during consultation with individuals suffering from neurogenic lower urinary tract dysfunction. It empowers patients to engage and participate in their own treatment. Active participation on the part of a willing patient is of utmost importance for individual motivation and long-term adherence. As a general rule, patient education should be tailored to the patient's level of understanding, and a caregiver or family member willing to assist in the interventions should be involved in the teaching process.

Intermittent Catheterization

Intermittent catheterization (IC) is considered the method of choice for bladder emptying when neurological disorder makes normal voiding impossible or incomplete [1]. The short- and long-term positive outcomes have been demonstrated. However, there is no one best technique, as the chosen method depends greatly on patient's individual anatomic, social, and economic possibilities. Regrettably, the literature to date does not clarify the definition of each specific technique. As a result, practice differs, even though the same name may be used. The European Association of Urology Nurses (EAUN) proposed standardizing the terminology as follows [2]:

- Sterile technique—all the material is sterile and catheterization is performed in sterile settings; complete sterile technique is only used in operating rooms and in diagnostic situations
- Aseptic technique—involves sterile catheter, disinfection of the genitals, sterile gloves (with sterile tweezers, if required) and sterile lubricant (if the catheter is not pre-lubricated)
- No-touch technique—an aseptic technique with a ready-to-use catheter (these catheters lubricate themselves as they are introduced into the urethra by a prelubricated outlet on the bag); a pull-in aid or special packages are used to touch the catheter; this technique should be considered particularly when toilet facilities are not readily available (e.g., during sports activities or travel)
- Clean technique (clean intermittent catheterization) used by patients or caretakers in the home setting with sterile (single-use) or reusable catheter and septic or no antiseptic solution for cleaning the hands and perineum. In clean self-IC, the catheter can be touched without gloves

A well-trained and experienced clinician, usually a specialized nurse, has an important role in training the patient for successful self-catheterization and long-term adherence with management, as there are multiple barriers to clean IC (Table 17.1) [3–5]. The pencil and paper test can be used to predict the ability of

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_17

Table 17.1 Possible barriers of clean intermittent catheterization and possible solutions to improve adherence

Possible barriers	Possible solutions
Patient-related factors (internal)	
Physical disabilities • Positioning • Mobility • Dexterity • Coordination • Balance • Visual impairment • Perception • Cognition Psychological concerns • Fear and anxiety • Social stigma • Depression • Decreased self-confidence and self-esteem • Embarrassment	• Individualized and tailored instructions with a clinician trained in teaching IC (some patients may require a few sessions to feel confident with the technique) • Documentation materials about IC (e.g., booklet, pamphlet, instruction movie) • Providing an overview of anatomy of the urinary tract and reported bladder dysfunction • Choosing the appropriate catheter (patient may need to try several catheters before finding the preferred type) • Use of catheter appliances to help locate the urethra – Catheter clips – Penis holders – Thigh abductors – Leg/knee spreaders – Mirrors – Labia spreaders
Environmental factors (external)	
• Limited access to public toilets and their inadequate facilities (e.g., for placing catheter products and accessories or transferring from a wheelchair onto the toilet; inadequate cleanliness and washing) • Limited access to well-trained healthcare providers • Low teaching quality and inappropriate training locations • Limited access to the right type of catheter and lack of knowledge of the products available on the market • Financial constraints • Inadequate follow-up monitoring	• Access to locked disabled toilets and measures that help locate toilet facilities (e.g., maps, smartphone apps) • Proper education and standardized training of healthcare providers (including district nurses) • Adequate training locations and time for teaching of patients • Involving caregivers/partners into training sessions • Regular follow-up monitoring • Financial support to patients suffering from neurogenic lower urinary tract dysfunction • Efficient catheter delivery system in the community including home delivery systems • Proper communication between primary and secondary/tertiary care

neurological patients to practice clean self-IC [6]. This test mimics the ability to open the packaging and handle a catheter, as well as cognitive strategies required to accomplish all clean self-IC maneuvers; it typically requires less than few minutes to complete. Sheets of paper and a pencil 20 cm long with a horizontal diameter of about 0.5 cm are the tools needed to perform the test. Each item of the test is quantified and simply graded as 0—impossible, 1—incomplete, 3—full but difficult, and 5—possible and easy. The maximal score is 15. A test score of less than 10/15 suggests that clean self-IC should not be proposed in a patient with neurological disease. In contrast, a test score of more than 10/15 suggests a high probability of success in learning and practicing clean self-IC. Table 17.2 lists the required gestures that mimic the usual maneuvers used during self-IC, along with the developed scoring system [6].

Clinicians and patients sometimes fail to consider self-IC as an option in the elderly because of a perception that it will be unmanageable or poorly tolerated. Nonetheless, recent data indicate that a high proportion of older patients can successfully be taught self-IC, thus it can be offered irrespective of age [7].

Even though the clinician's time and resources in daily clinical practice are limited, patients should be carefully educated on how to perform self-IC, and this learning process should be the standard of care. Patient education needs to have a structured procedure in order to evaluate the ability to understand, accept, and perform self-IC [8]. Studies have shown that clean self-IC can be taught to most patients in a short time, even

Table 17.2 Requested gestures of the pencil and paper test with scoring system

Sex	Gestures	Points			
		Impossible	Incomplete	Full but difficult	Full and easy
Males	Pencil clasped with index + thumb, then positioned in ear canal (dominant hand)	0	1	3	5
	Pencil clasped with palm + fingers, then kept vertical (non-dominant hand)	0	1	3	5
	Paper folded, torn + given	0	1	3	5
Females	Pencil clasped with index + thumb, then positioned in ear canal (dominant hand)	0	1	3	5
	Pencil positioned horizontally between thighs	0	0.5	1	2
	Pencil laid on thumb + index finger moved apart	0	0	0.5	1
	Pencil laid + kept up on chair between thighs	0	0.5	1	2
	Paper folded, torn + given	0	1	3	5

Table 17.3 Patients may be advised to adjust the frequency of their self-catheterization based on the drained urine volume

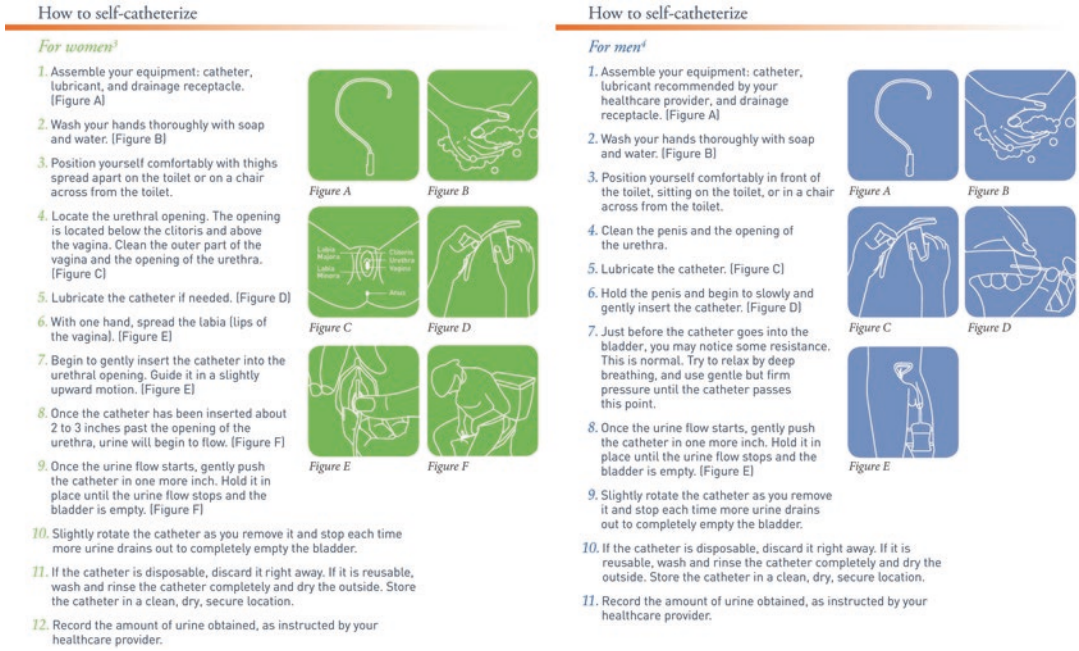
Urine volume (mL)	Catheterization frequency
>400	4–6 times a day
400–300	3 times a day
300–200	Twice a day
200–100	Daily

As a general rule, bladder volume should not exceed 400–500 mL

within a few minutes [9]. Clinicians should also be aware that their expectations are often too high when it comes to training patients in IC (e.g., see flexibility in frequency of catheterization, Table 17.3) [10, 11]. The no-touch technique may be preferred over the clean technique but available data are insufficient to make reliable recommendations (see Chap. 8). The clean technique is also an optimal choice in the home setting because individuals are there exposed to bacterial organisms that do not routinely cause infections.

At the beginning, the patient should be prepared verbally for the procedure [2]. It is beneficial to support initial teaching with documentation about intermittent catheterization (e.g., booklet, pamphlet, instruction movie) (Fig. 17.1). A brief explanation of the pathophysiology of bladder dysfunction is also encouraged. Providing an overview of anatomy with pictures or the use of an anatomic model of the genitals/perineum can be very helpful. Caregivers should be involved in the learning process. The clinician should also evaluate the patient's capability of performing self-IC, motivation to continue long-term catheterization, and awareness of the difficulties and possible complications associated with catheterization. If the referring physician has already recommended the optimal catheter type/material as well as catheterization technique and frequency (4 and 6 catheterizations per day are advocated in order to limit bladder distension and the total volume should not exceed 400–500 mL), the patient should be counselled on these issues again [12, 13].

The patient should then be informed about necessary supplies (catheter; lubrication, if catheter is not hydrophilic; toilet or other draining container; cleansing wipes or cleaning agent; and washcloth and gloves, if applicable) and possible locations where (and positions in which) IC can be performed (home, work, school, bed, bathroom, toilet, wheelchair) (Figs. 17.2 and 17.3). After that, the patient should be carefully instructed about hand washing (hands should be washed or aseptic towels should be used both before and after catheterization), glove wearing (if applicable), cleansing of the genitals, and insertion procedure. If the clean technique has



How to self-catheterize

For women[3]

1. Assemble your equipment: catheter, lubricant, and drainage receptacle. (Figure A)
2. Wash your hands thoroughly with soap and water. (Figure B)
3. Position yourself comfortably with thighs spread apart on the toilet or on a chair across from the toilet.
4. Locate the urethral opening. The opening is located below the clitoris and above the vagina. Clean the outer part of the vagina and the opening of the urethra. (Figure C)
5. Lubricate the catheter if needed. (Figure D)
6. With one hand, spread the labia (lips of the vaginal). (Figure E)
7. Begin to gently insert the catheter into the urethral opening. Guide it in a slightly upward motion. (Figure E)
8. Once the catheter has been inserted about 2 to 3 inches past the opening of the urethra, urine will begin to flow. (Figure F)
9. Once the urine flow starts, gently push the catheter in one more inch. Hold it in place until the urine flow stops and the bladder is empty. (Figure F)
10. Slightly rotate the catheter as you remove it and stop each time more urine drains out to completely empty the bladder.
11. If the catheter is disposable, discard it right away. If it is reusable, wash and rinse the catheter completely and dry the outside. Store the catheter in a clean, dry, secure location.
12. Record the amount of urine obtained, as instructed by your healthcare provider.

Figure A Figure B Figure C Figure D Figure E Figure F

How to self-catheterize

For men[4]

1. Assemble your equipment: catheter, lubricant recommended by your healthcare provider, and drainage receptacle. (Figure A)
2. Wash your hands thoroughly with soap and water. (Figure B)
3. Position yourself comfortably in front of the toilet, sitting on the toilet, or in a chair across from the toilet.
4. Clean the penis and the opening of the urethra.
5. Lubricate the catheter. (Figure C)
6. Hold the penis and begin to slowly and gently insert the catheter. (Figure D)
7. Just before the catheter goes into the bladder, you may notice some resistance. This is normal. Try to relax by deep breathing, and use gentle but firm pressure until the catheter passes this point.
8. Once the urine flow starts, gently push the catheter in one more inch. Hold it in place until the urine flow stops and the bladder is empty. (Figure E)
9. Slightly rotate the catheter as you remove it and stop each time more urine drains out to completely empty the bladder.
10. If the catheter is disposable, discard it right away. If it is reusable, wash and rinse the catheter completely and dry the outside. Store the catheter in a clean, dry, secure location.
11. Record the amount of urine obtained, as instructed by your healthcare provider.

Figure A Figure B Figure C Figure D Figure E

Fig. 17.1 Example of a patient pamphlet provided for the initial instruction (with permission from courtesy of Allergan, Parsippany NJ, USA)

been chosen, the patient should be carefully informed to wash hands right before the catheter insertion and not to touch the end of the catheter. It has to be stressed that the catheter must be introduced in a minimally infecting and atraumatic way (with no force). The first attempt can be done either by the healthcare professional or by the patient him/herself, and the patient should be informed not to remove the catheter until the bladder is completely empty. Females may be advised to use a mirror when performing self-IC, and should be instructed on where to place the catheter by showing how to separate the labia and identify the urethral opening. It is recommended that the patient repeat the insertion him or herself if the clinician has performed the first attempt. A minimum interval of 4 h is recommended between two catheterizations [8]. After performing the insertion, the clinician should assess whether the patient feels comfortable with the procedure and, if not, a change of catheter type, material, or technique should be considered. The clinician should also try to improve the patient's self-confidence. Figure 17.4 presents the general steps of teaching the patient when the clinician performs the initial catheterization [14–16].

Individuals who choose intermittent catheterization with reusable catheters need proper education with regard to catheter care. Washing the catheter after every use is recommended [17]. Rinsing and allowing catheters to air-dry between each use has been demonstrated as an effective technique to keep the bacteria on catheters at a low count [18]. Catheters should be cleaned with mild soap and water or antiseptic solution (peroxide and povidone-iodine), air-dried, and placed in a paper bag until ready to reuse [17, 19]. To minimize encrustations, patients should be encouraged to forcefully rinse the catheter lumen with tap water, making sure to remove all lubricant, if used [20]. If recurrent urinary tract infections occur, catheter sterilization by boiling it or heating it in a microwave oven, as well as use of single-use catheters, may be considered [21]. Nevertheless, clinicians should bear in mind that these techniques of sterilization may be insufficient to eradicate all microorganisms, including *Pseudomonas aeruginosa* or *Staphylococcus*

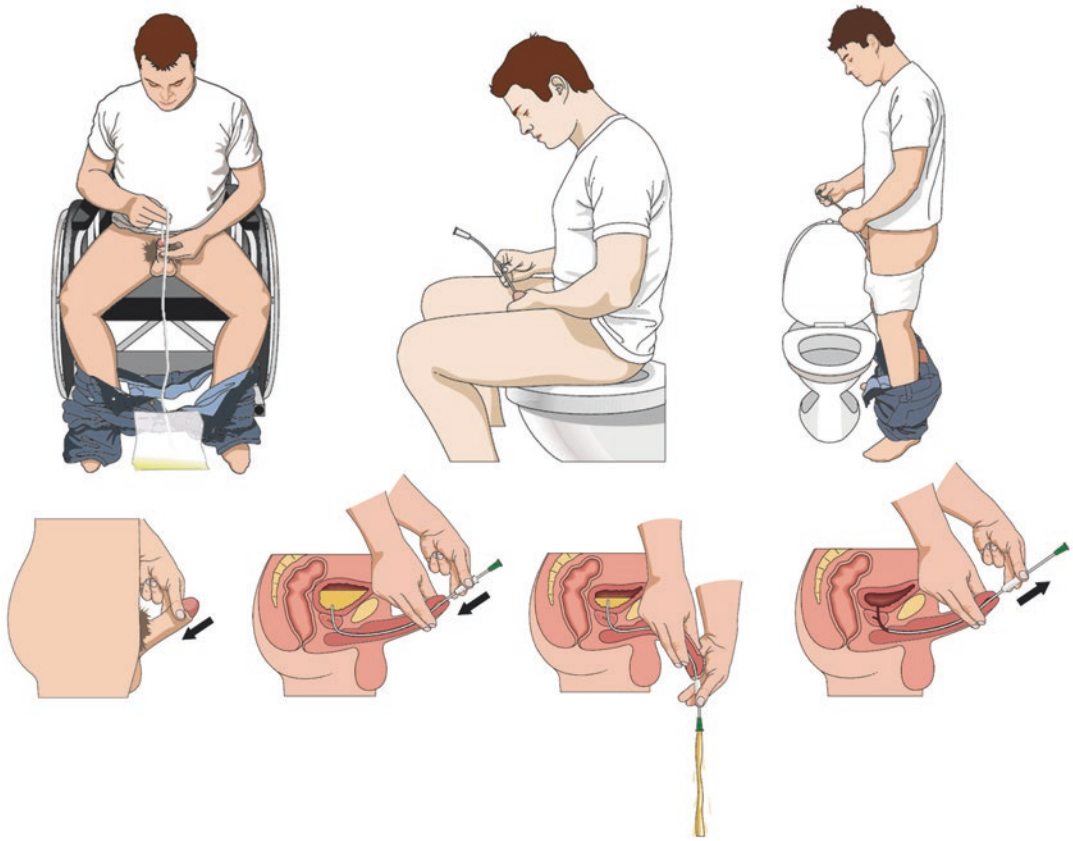


Fig. 17.2 Patient positioning during self-intermittent catheterization (male) (with permission from courtesy of Wellspect HealthCare and LoFric Academy, Mölndal, Sweden)

aureus [22]. Patients should be warned not to reuse the catheter if it looks worn, brittle, or cracked.

A wide variety of educational materials are available to patients in this regard and patients should be informed of reliable sources. These include but are not limited to:

- patients.uroweb.org—educational center developed by the European Association of Urology (EAU)
- urologyhealth.org—educational center developed by the Urology Care Foundation supported by the American Urological Association (AUA)
- cua.org/en/patient—patient information center developed by the Canadian Urological Association (CUA)
- continenceproductadvisor.org—educational website created by the International Consultation on Incontinence (ICI) and the International Continence Society (ICS)
- clinicalcenter.nih.gov—patient education resource site created by the Clinical Center of the National Institutes of Health, United States
- medlineplus.gov—patient medical encyclopedia created by the National Library of Medicine and National Institutes of Health, United States
- aboutkidshealth.ca—educational website developed by the Hospital for Sick Children in Toronto, Canada
- experiencejournal.com/journals/self-cathing—an online resource for patients and families who are recommended to initiate IC developed by the Boston Children's Hospital in Boston, United States

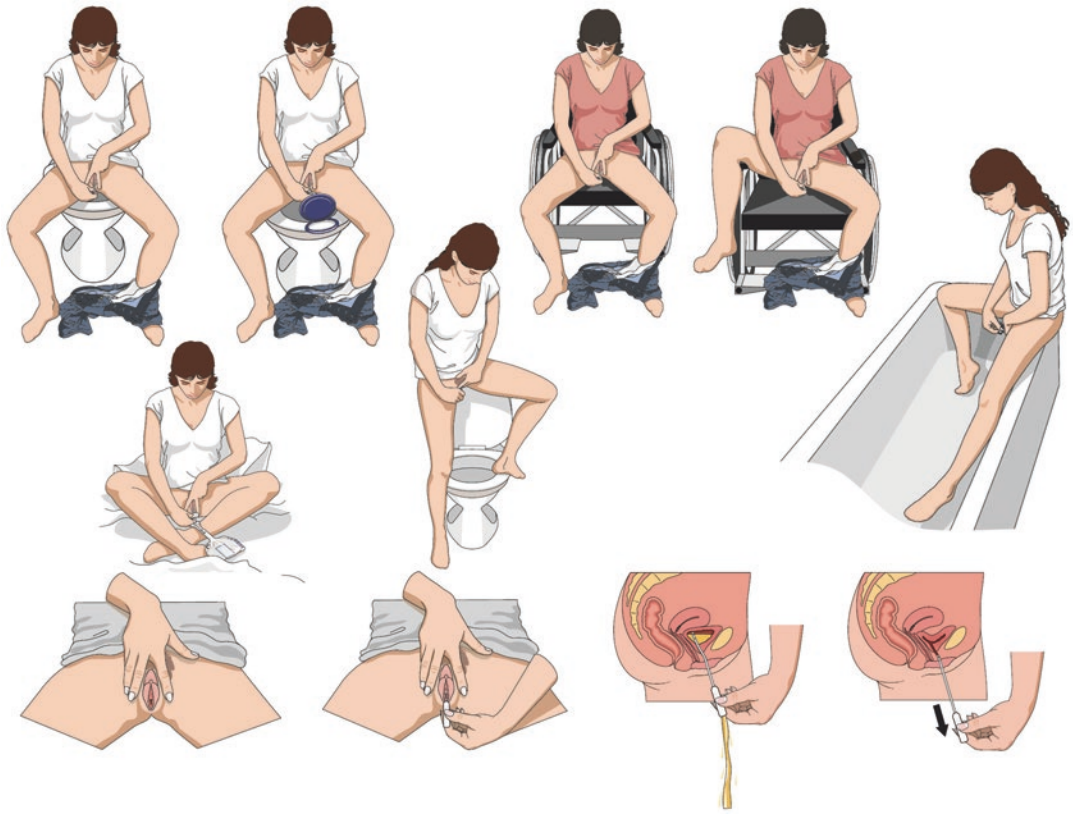


Fig. 17.3 Patient positioning during self-intermittent catheterization (female) (with permission from courtesy of Wellspect HealthCare and LoFric Academy, Mölndal, Sweden)

- catheter manufacturers and distributors (e.g., LoFric, Coloplast, Bard, Cook, Hollister, Convatec)

A recently published study has evaluated the educational content of YouTube videos relating to neurogenic bladder and intermittent catheterization [23]. Analysis indicated a poor, misleading, or irrelevant overall quality of the information, with some videos giving advice that is contradictory to well-developed guidelines for IC. The YouTube search algorithm did not prominently rank videos that the authors deemed of good quality, which suggests that users would be less likely to access those. The quality of information in videos with healthcare narrators was not consistently higher than in those featuring patient or merchant narrators. About half of the videos featuring catheter use also contained some kind of advertisement. Therefore, YouTube materials should be recommended only with caution, and clinicians should be aware of the dubious quality and veracity of the YouTube information. While Web-based interventions and social media are becoming common, clinicians should inform patients about concerns regarding the quality of such information.

Some samples can be given to patients for the initial days of management, and additional materials can be ordered as well. The skills acquired by the patient, as well as the self-catheterization experience, need to be regularly evaluated. An appointment is made 3–5 weeks after the therapeutic education, and then renewed according to the objectives and skills acquired [8]. The patient may need to try several catheters before finding the preferred type, and not all catheters are suitable to an individual's needs and circumstances

Fig. 17.4 General steps of patient teaching when the initial catheterization is performed by the clinician

[20]. This issue is of utmost importance for long-term compliance with treatment. Furthermore, some individuals may require one type of catheter for home use and another for catheterizing outside the home (e.g., work, travel, leisure). Centralized systems for patient education have been shown superior, compared to individual departments where primary services are not related to voiding care [24].

Behavioral Techniques

Behavioral techniques include two main treatments, scheduled voiding regimens (toileting assistance) and pelvic floor muscle therapy (PFMT).

Toileting Assistance

Toileting assistance refers to the behavioral process aiming to re-establish control of urinary continence [25]. Although the evidence of this management for neurogenic patients is sparse, these methods can still be recommended, considering that they have no negative impact on patient and have been successfully used in those with idiopathic overactive bladder (OAB) [26]. Behavioral techniques are a suitable component of the rehabilitation program for neurogenic individuals, but should be tailored to the patient's capabilities [25]. Toileting assistance for neurogenic individuals includes bladder training, timed voiding, habit retraining, and prompted voiding.

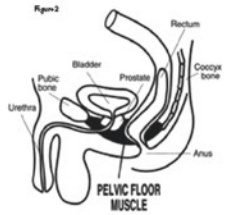
Bladder training involves a scheduled voiding regimen with gradually progressive intervals between voids until a normal pattern is established [27]. Techniques for urgency control and suppression (e.g., performing general relaxation, such as slow/deep breathing or 6–10 quick pelvic floor muscle contractions, which prevent the sphincter from relaxing when the urge is present) must be used in conjunction [26]. The voiding intervals are determined on an individual basis, depending on baseline pattern. In non-neurogenic patients, it has been proposed to increase time intervals by 15–30 min each week, depending on patient compliance and tolerance, until a voiding interval of 3–4 h is achieved [28, 29]. Although bladder training has not been well studied in neurogenic patients, it has been found effective in those suffering from OAB with urgency urinary incontinence [26, 30, 31]. Thus, bladder training may be considered as an additional therapy in patients with incontinence due to neurogenic detrusor overactivity in order to improve control over urgency, reduce incontinent episodes, and restore patient confidence in controlling bladder function (see Chap. 7).

Timed voiding (passive toileting assistance program) is characterized by a fixed interval between toileting to establish an appropriate voiding frequency. Instead of waiting for the patient to voice an urge to void, the patient is asked to toilet at regular intervals or based on a schedule. Until now, no precise intervals have been established; they should be derived from the voiding diary and other related factors (fluid intake, post-void residual urine volume, bladder volume, urodynamic parameters). Timed voiding should be considered particularly when incontinence is associated with cognitive and/or motor deficits resulting in independent toileting. Therefore, this method is more to avoid incontinence than to restore a normal bladder function. One study proposed that timed voiding can be recommended for patients with excessive bladder volumes, for instance for those with diabetes when impaired bladder filling sensation leads to retention [25].

Habit retraining aims to avoid incontinence by decreasing voiding intervals and finding a time interval that is shorter than the person's normal voiding pattern. This precedes the time period when incontinent episodes are expected [27]. It requires specific analysis of voiding patterns based on voiding diary in order to tailor a proper individual schedule of voiding. Prompted voiding is a technique used to teach patients to initiate their own toileting through requests for help and positive reinforcement from caregivers. Experts propose that habit retaining and prompted voiding can be useful for individuals with cognitive and/or motor deficits; they are more suitable for patients with diseases of brain than spinal cord [25].

Pelvic Floor Muscle Therapy

PFMT strengthens and improves the function of the pelvic floor and urethral stability. Although primarily used for treatment of stress incontinence and OAB [32–34], PFMT has been shown effective in patients with multiple sclerosis and spinal cord injury [35–42]. One proposal has been investigated in spinal cord injury patients, which includes a 6-week program of regular PFMT (Fig. 17.5) [42]. The program consists of up to 40 contractions of the pelvic floor divided into 4 sets (3 sets of prolonged contractions and 1 set of short contractions). Patients are asked to follow the program three times daily in different positions: lying down, sitting, and standing, if possible. Patients should also be encouraged to perform contractions of the pelvic floor at other times, as soon as they feel a bladder urge, and to integrate the exercises into activities of daily living. Another proposal investigated in patients suffering from multiple sclerosis consists of 30 slow pelvic floor muscle contractions and 3 min of fast contractions in the supine position with assistance of a perineometer in outpatient settings, with recommendation to repeat the same 30 slow contractions and 3 min of fast contractions, learned during the intervention, three times daily at home without assistance of any device, in different positions like sitting and standing. These patients are also advised to integrate the exercises into activities of daily life [37].



The PFM have important tasks in:

- Bladder and bowel continence
- Support to your pelvic organs
- Assist sexual performance

You should practice the following exercises every day of the week, 3 times per day.

Practice your exercises in the morning while you are lying down and the ones in the evening when you are in sitting and/or standing.

When you are ready Squeeze around the pelvic openings imagining an inward lift of your pelvic floor as if you were stopping a bowel movement or passing wind.

Tighten your PFM:

1. Before you cough, sneeze, lift, bend and/or do your transfers
2. As soon as you get the urge up until you get to the toilet
3. Immediately after passing urine
4. During sexual activity and slightly during walking

Do not: strain, hold your breath or tighten your buttocks and legs. No one should notice that you are doing your PFM exercises.

Follow the next program and remember to do each squeeze as strong as you can, hold it for as long as you can and after each squeeze, relax as much as you can.

WEEKS 1-2	Every day 3 sets of 5 squeezes Hold each squeeze for 5 sec Rest after each squeeze for 5 sec Rest after each set for 2 min Do 1 set of 10 fast squeezes
WEEKS 3-4	Every day 3 sets of 8 squeezes Hold each squeeze for 8 sec Rest after each squeeze for 8 sec Rest after each set for 2 min Do 1 set of 12 fast squeezes
WEEKS 5-6	Every day 3 sets of 10 squeezes Hold each squeeze for 10 sec Rest after each squeeze for 10 sec Rest after each set for 2 min Do 1 set of 14 fast squeezes

Fig. 17.5 Programme proposal of pelvic floor muscle therapy for patients after spinal cord injury. (Reprinted with permission from Vasquez et al. [42]. Macmillan Publishers Ltd: Spinal Cord. 2015)

Regardless of the program chosen, clinicians should promote compliance and adherence by actively motivating their patients and providing them with educational materials. It should be also noted that PFMT is effective only if the patient tightens the pelvic floor muscle correctly. Training should be conducted without tensing the leg, buttock, or abdominal muscles. To facilitate teaching, the patient can be asked to imagine the passing of gas without tensing any of the previously mentioned muscles.

Even though such programs have been primarily developed for patients after spinal cord injury and with multiple sclerosis, they can be implemented into the management of patients with other neurological disorders. The proposals can be extended and improved by adding biofeedback and electrical stimulation [43]. It has been shown that PFMT combined with neuromuscular electrical stimulation gives better results in patients with multiple sclerosis [44]. A randomized clinical trial of individuals with multiple sclerosis and bladder dysfunctions demonstrated that a multifaceted individualized bladder rehabilitation program reduced disability and improved quality of life compared to no intervention after 12 months of follow-up [45]. In selected patients, a referral to a rehabilitation specialist may be considered.

Lifestyle Intervention

Although there is a paucity of data for neurogenic individuals, some principles may be applied from studies conducted on patients with OAB. This would seem a logical recommendation because the treatment modalities listed below are relatively non-invasive and would benefit patients' overall health.

Dietary modifications include reduction or elimination of caffeinated and alcoholic beverages, as well as those containing aspartame, as they may worse urgency [28, 46]. The best approach is tailored to the individual, with patients reducing these items from their diet and continuously assessing their symptoms [26].

Fluid intake management should be based on the patient's 24-hour intake and subsequent 24-hour urinary output [28]. Comorbidities possibly affecting fluid management, including renal or cardiac disease, should be taken into consideration. Restricting fluid intake 2–4 h before bedtime or after 6 pm decreases nocturia and nighttime incontinence [46, 47].

Constipation is a common complaint in men and women with underlying neurological disease [48]. Thus, patients should be provided with strategies to avoid constipation. Clinical expertise suggests that diet modification with increased fiber intake, oral laxatives, rectal stimulants, digital stimulation, manual evacuation of feces, and abdominal massage are options that may be tried [49]. Nevertheless, clinicians should keep in mind that the available evidence for neurogenic patients is almost uniformly of low methodological quality [50].

Multiple studies have found obesity to be a significant risk factor for urinary incontinence [51, 52]. Patients should be provided with weight loss strategies or specialized nutrition counselling with a dietitian. The regime should also include regular, moderate, and tailored physical activity.

Nicotine has been shown to irritate the bladder detrusor, causing increased activity [46]. An increased intra-abdominal pressure from recurrent coughing in smokers may exacerbate urinary incontinence [53]. Even though a Cochrane review has shown that the effect of nicotine on OAB is uncertain, its elimination should be proposed to all patients as a general public health intervention [54].

Care of Urinary Diversion

Urinary diversions, both continent and incontinent, require daily care and manual skills. Self-stomal management may potentially decrease feelings of being controlled and increase feelings of being in control [55]. The first step in the education of patient and family/caregiver should identify the individual who is likely to take responsibility for diversion care. Next steps should include more practical than theoretical guidelines and should involve bag replacement training (removing the stoma appliance, measuring the stoma diameter, adjusting the size of the diameter in a new stoma appliance, fitting a new stoma appliance); hygiene and peristomal skin care (urine is cleansed from the skin by washing with mild soap and water and intact skin represents the first line of defense against infection); as well as tips regarding daily living with a diversion (e.g., deodorant tablets and adequate fluid intake to prevent urine odor) [56]. Patients should be encouraged to demonstrate their ability to perform ostomy care prior to discharge. Patients should also be counselled about changes in stoma color and elasticity of skin turgor (the stoma should appear red and moist) [57]. Signs of darkness or duskiness may indicate a loss of vascular supply. Beginning patient education before surgery is recommended, as is restarting it as soon as possible after the procedure [57]. Those with a continent urinary reservoir are taught how to self-catheterize and empty the pouch. It is done on a progressive schedule to permit the reservoir to expand capacity slowly without compromising the suture line and the continence mechanism. Studies have shown that there are clear advantages of stomal self-care, including independence, minimal burden on family members and other care providers, better quality of life, and psychological adjustment [55].

Conclusion (Table 17.4)

Table 17.4 Conclusions

Summary	Level of evidence (LE)
Studies have shown that long-term compliance with clean intermittent self-catheterization can be improved by proper education of patients	2
Toileting assistance includes bladder training, timed voiding, habit retraining, and prompted voiding	4 (Expert opinion)
Pelvic floor muscle therapy has been shown effective in patients with multiple sclerosis (LE 2) and those after spinal cord injury (LE 3)	2, 3
There is a paucity of data for lifestyle interventions (dietary/fluid intake modifications, weight control, bowel regularity, smoking cessation) in neurogenic individuals	4 (Expert opinion)

Recommendation	Grade of recommendation
Patients should be carefully educated on how to perform intermittent self-catheterization. Main components of any teaching program should include how to handle the catheter, maintain hygiene, identify the urinary meatus, and care for the catheter	Expert opinion
The physician or nurse should observe how the patient performs self-catheterization, explain particular steps individually, and identify inadequately performed maneuvers	Expert opinion
Toileting assistance to improve continence may be considered in conjunction with other therapies (pharmacotherapy, self-catheterization)	Expert opinion
Pelvic floor muscle therapy may be considered in patients with the physical ability to use this management	C
Lifestyle changes should be considered, as they are relatively non-invasive and can benefit the patient's overall health	Expert opinion
Acquiring the skill of stomal self-care is highly desired, as it is associated with improved quality of life and better psychological adaptation	C
Systematic patient education and counselling should be tailored to the patient's mental status and physical possibilities	Expert opinion
Patients should be informed regarding reliable Web-based resources and provided with educational materials	Expert opinion

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Part VI

Reports and Guidelines

Reports and Guidelines on Neurogenic Bladder

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Numerous reports and guidelines have been developed to support clinicians in their day-to-day clinical practice of neurourology. These documents have been constantly changing and should be followed to properly manage neurogenic individuals.

General Neurourological Guidelines

1. The European Association of Urology (EAU), Neuro-Urology Guidelines (published 2017, updated every year)
   http://uroweb.org/guideline/neuro-urology/
2. The International Consultations on Incontinence (ICI), Clinical Management Recommendations of the Neurologic Incontinence Committee of the Fifth ICI 2013 (published 2016)
   http://onlinelibrary.wiley.com/wol1/doi/10.1002/nau.23027/full
3. The National Institute for Health and Clinical Excellence (NICE), Urinary incontinence in neurological disease: management of lower urinary tract dysfunction in neurological disease (published 2012)
   https://www.nice.org.uk/guidance/cg148/evidence/full-guideline-188123437
4. The International Continence Society, The Standardization of Terminology in Neurogenic Lower Urinary Tract Dysfunction (published 1999)
   https://www.ics.org/Documents/DocumentsDownload.aspx?DocumentID=18

Patients After Spinal Cord Injury

5. The Agency for Clinical Innovation (ACI) of Australia, ACI Guidelines on Management of the Neurogenic Bladder for Adults with Spinal Cord Injuries (published 2014)
   https://www.aci.health.nsw.gov.au/__data/assets/pdf_file/0010/155179/Management-Neurogenic-Bladder.pdf
6. US Department of Veterans Affairs, VHA Publications, Spinal Cord Injury and Disorders (SCI/D) System of Care, Handbook (published 2011)
   https://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2365
7. Spinal Cord Injury Think Tank Group, A proposed guideline for the urological management of patients with spinal cord injury (published 2008)
   http://onlinelibrary.wiley.com/doi/10.1111/j.1464-410X.2008.07457.x/full
8. Consortium for Spinal Cord Medicine, Bladder Management for Adults with Spinal Cord Injury: A Clinical Practice Guideline for Health-Care Providers (published 2006)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1949036/

J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9_18

Pediatric Patients

9. The International Children's Continence Society (ICCS), ICCS recommendations for therapeutic intervention in congenital neuropathic bladder in children (published 2012)
   http://onlinelibrary.wiley.com/wol1/doi/10.1002/nau.22248/full

Urodynamics

10. The International Continence Society, Good Urodynamic Practices and Terms 2016: Urodynamics, uroflowmetry, cystometry, and pressure-flow study (published 2016)
    https://www.ics.org/Documents/DocumentsDownload.aspx?DocumentID=4677
11. The American Urological Association and Society for Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (published 2012)
https://www.auanet.org/documents/education/clinical-guidance/Adult-Urodynamics.pdf

Regional Guidelines

12. The Taiwan Urological Association (TUA), Clinical guidelines for the diagnosis and management of neurogenic lower urinary tract dysfunction (published 2014)
    http://www.tzuchi.com.tw/medjnl/files/2014/vol-26-3/2014-26-3-103-113.pdf
13. The Chinese Urologic Association (CUA), Guidelines on Neurogenic Bladder (published 2014)

    Liao LM. Guidelines on neurogenic bladder. In: Na YQ, Ye ZQ, Sun YH, Sun G, editors. Chinese guidelines on urologic diseases. 2nd ed. People's Medical Publishing House; Beijing, China; 2014. p. 267–329. (In Chinese)

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J. Corcos, M. Przydacz, *Consultation in Neurourology*, https://doi.org/10.1007/978-3-319-63910-9