Chapter 12
Pathophysiology, Clinical Presentation and Management of Neurogenic Bladder

Giuseppe Pelliccioni, Daniele Castellani, Camilla Rocchi, Valentina Cameriere, Deborah Sabbatini, and Pietro Pelliccioni

12.1 Introduction

The voluntary control of micturition requires complex connections between sympathetic and parasympathetic systems, somatic nerves and different brain areas. The coordination between the bladder, urethra and sphincters is mediated by a complex neural control system in the brain, spinal cord, peripheral ganglia and peripheral nerves. Therefore, lower urinary tract (LUT) dysfunction is present in different neurological diseases [1, 2]. A practical model of bladder dysfunction can be useful for neurological clinical practice and diagnostic workup.

G. Pelliccioni (✉) · V. Cameriere · D. Sabbatini
Neurology Department, IRCCS INRCA-National Institute of Health and Science on Aging, Ancona, Italy
e-mail: g.pelliccioni@inrca.it; v.cameriere@inrca.it; d.sabbatini@inrca.it

D. Castellani
Urology Department, Azienda Ospedaliero-Universitaria Ospedali Riuniti di Ancona, Università Politecnica delle Marche, Ancona, Italy
e-mail: daniele.castellani@ospedaliriuniti.marche.it

C. Rocchi
Neurology Unit, Department of Systems Medicine, Policlinico Tor Vergata, University of Rome "Tor Vergata", Rome, Italy
e-mail: camilla.rocchi@ptvonline.it

P. Pelliccioni
Neurology Clinic, Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy

G. Micieli et al. (eds.), *Autonomic Disorders in Clinical Practice*,
https://doi.org/10.1007/978-3-031-43036-7_12

12.2 Neural Control of Urinary Tract

The bladder and urethra have two primary functions: the storage and the periodic elimination of urine; these activities need neural coordination in the central, somatic and autonomic peripheral nervous systems. The voluntary control of micturition requires complex connections between sympathetic and parasympathetic autonomic nerves, pudendal somatic nerves and many areas in the brain. Parasympathetic preganglionic cholinergic outflow, giving excitatory input to the bladder, arises in the sacral parasympathetic nucleus (SPN), localised in the intermediolateral column from the S2–S4 spinal segments. The parasympathetic fibres then travel through pelvic nerves to intramural bladder ganglia and pelvic plexus, where the postganglionic fibres induce detrusor contraction and urinary flow. The parasympathetic activation of M_3 muscarinic and P2X purinergic receptors is involved in the voiding reflex while nitric oxide transmission mediates inhibition of urethral smooth muscle. The sympathetic system, which plays a primary role in the continence mechanism inhibiting the parasympathetic action, originates from the intermediolateral columns in the T11–L2 spinal cord segments. Preganglionic may synapse on postganglionic in the paravertebral sympathetic chain or pelvic plexus; the hypogastric nerve, conveying sympathetic afferents and efferents, releases noradrenaline (NA) on bladder and urethra. The sympathetic efferents therefore activate β_3-adrenergic inhibitory receptors in the detrusor muscle relaxing the bladder, and α_1-adrenergic excitatory receptors in the bladder neck and urethra allowing the continence and urine storage and preventing retrograde ejaculation. The somatic cholinergic pathway originating from S2-S4 motor neurons in Onuf's nucleus (ON) innervates through pudendal nerves the external urethral sphincter (EUS) and pelvic floor muscles, including external anal sphincter (EAS) (Fig. 12.1). The somatic afferents from the bladder neck and the urethra are conveyed from pudendal nerves to the dorsal horns of the spinal cord in the S2–S4 tract, while the sensation of bladder fullness travels through pelvic and hypogastric nerves to the spinal cord, by means of afferent Aδ-fibres, lightly myelinated, and unmyelinated C fibres, up to the cerebral cortex. While Aδ-fibres respond to active contraction and passive distension, C-fibres are activated only in pathological conditions, in particular in spinal injuries, and they are probably involved in the pathophysiological mechanism underlying detrusor hyperreflexia.

Both bladder and the other functional unit consisting of the bladder neck, urethra and EUS are activated and coordinated by various central neural circuits, involving midbrain periaqueductal grey (PAG), cell groups of the preoptic and caudal hypothalamus, the pontine micturition centre (PMC) and the medial frontal cortex. The PMC is activated during voiding (M-region) and bladder filling (L-region or pontine storage centre), and it appears to initiate and coordinate lower urinary tract function.

The cortical-diencephalic circuitry has three major functions: amplification of bladder contraction to allow complete micturition, control of micturition

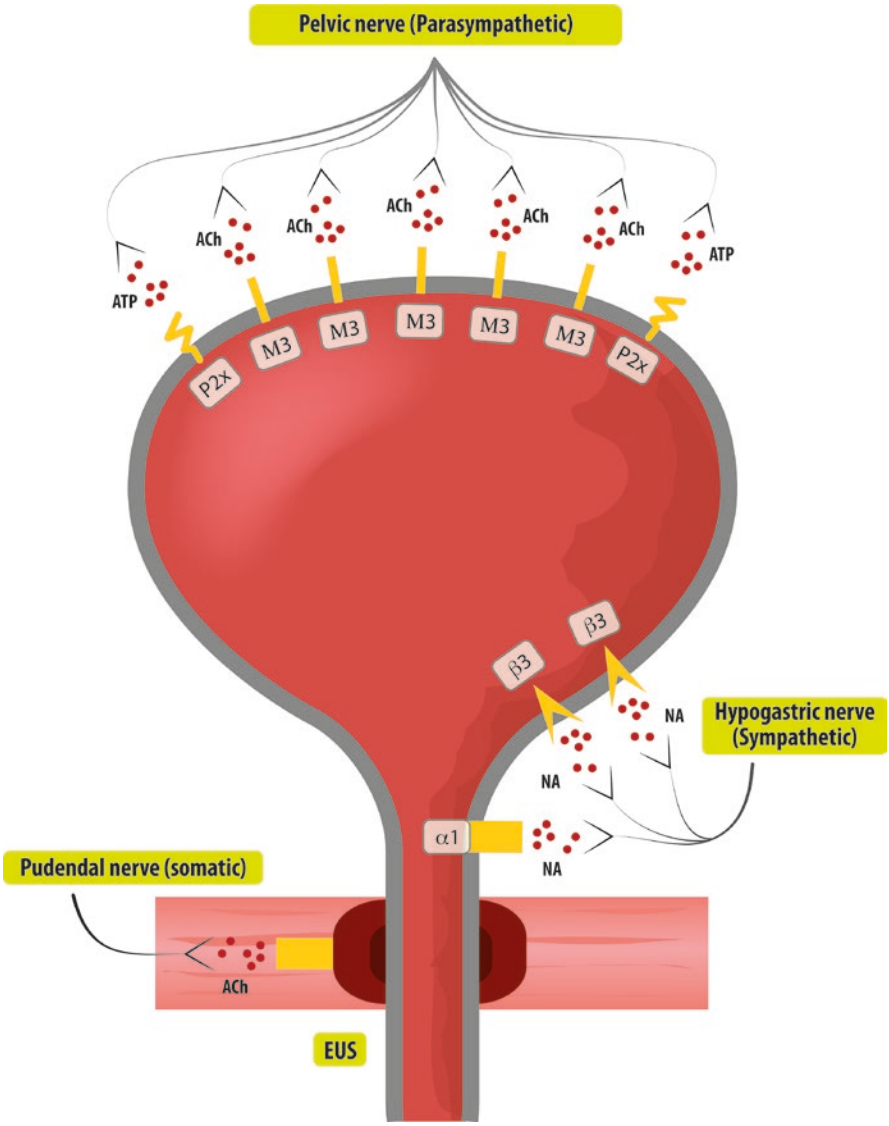

Fig. 12.1 Neurotransmitter mechanisms regulating urinary bladder and EUS function. Distribution of different autonomic and somatic axons. (From Micieli et al. "Disfunzioni Autonomiche" © 2022 Il Pensiero Scientifico Editore with permission)

frequency and coordination of the activity of lower urinary tract muscles. Overlapping between voluntary control and a reflex mechanism is allowed by sympathetic, parasympathetic and somatic peripheral innervation of the bladder and urethra. Higher centres in the CNS induce a modulatory effect over PMC,

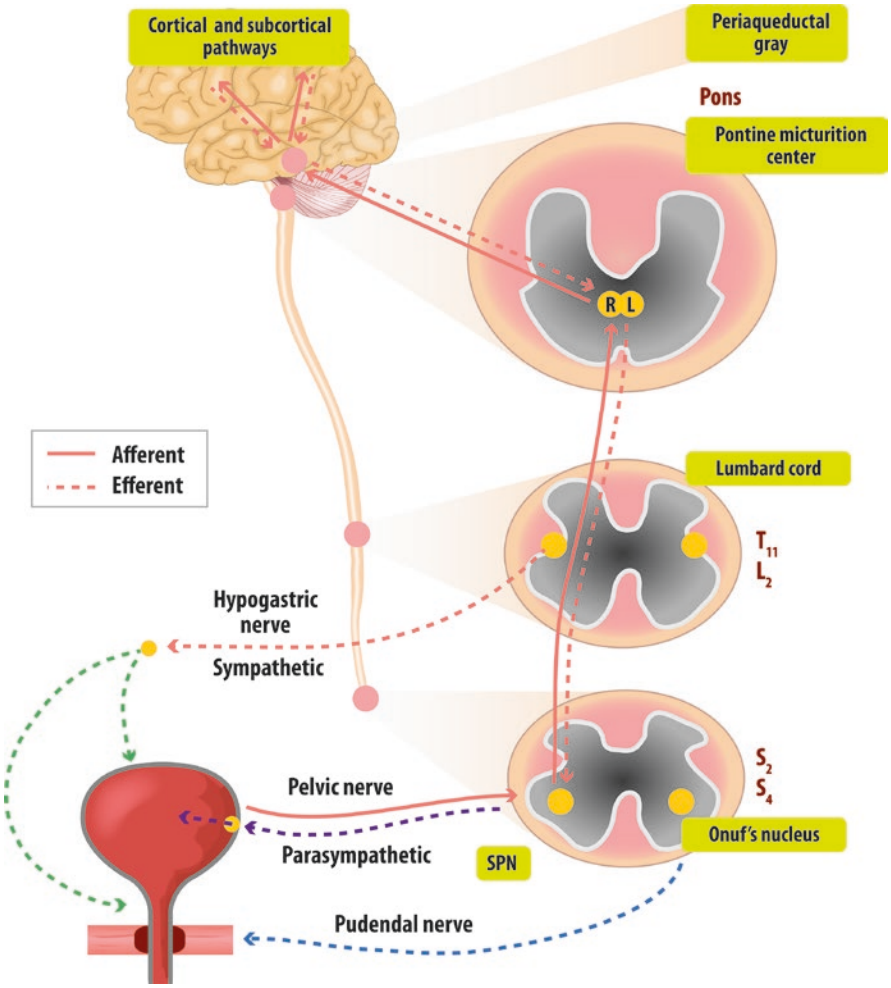

Fig. 12.2 Central and peripheral pathways involved in functional neural control of the urinary tract. (From Micieli et al. "Disfunzioni Autonomiche" © 2022 Il Pensiero Scientifico Editore with permission)

primarily mediated by an inhibitory input. The PMC appears to initiate and coordinate lower urinary tract function, pairing detrusor contraction with inhibition of urethral outlet and sphincter release, while the sacral micturition centre triggers an involuntary reflex detrusor contraction in response to rapid bladder filling. In fact, two distinct voiding reflex pathways exist: a suprasacral reflex that is physiologically active in normal subjects and a sacral reflex which allows voiding in pathological conditions (Fig. 12.2).

12.3 Neurogenic Lower Urinary Tract Disorders

The results of neurological lesions on urinary function can be represented by different voiding dysfunctions on three different levels: the supraspinal (suprapontine) level, the spinal (intrapontine-suprasacral) level, and the sacral and peripheral level [3]. Moreover, there are cases of bladder dysfunction without organic lesions of the urinary tract and with normal patterns in the nervous system's regulation and control [1, 2, 4]. The different clinical, ultrasound and urodynamic features can be explained on the basis of knowledge of the voiding centres (Figs. 12.3 and 12.4).

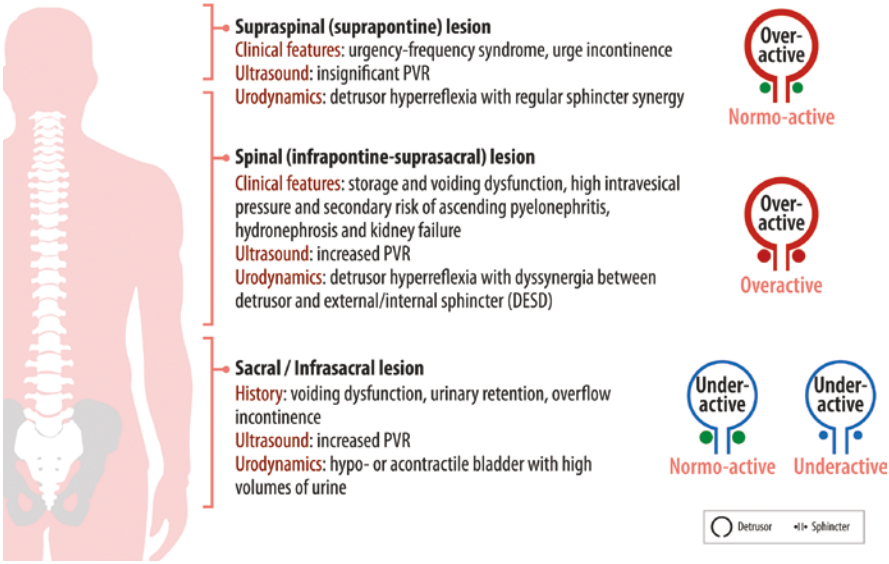

Fig. 12.3 Patterns of LUT dysfunction based on level of neurological disease. (From Micieli et al. "Disfunzioni Autonomiche" © 2022 Il Pensiero Scientifico Editore with permission)

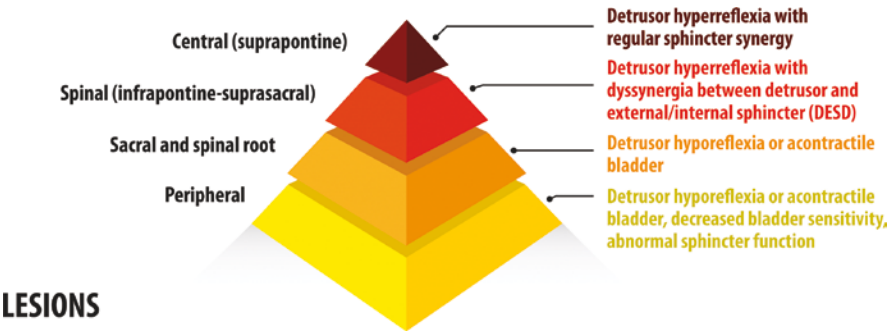

Fig. 12.4 Urodynamic features based on level of neurological disease. (From Micieli et al. "Disfunzioni Autonomiche" © 2022 Il Pensiero Scientifico Editore with permission)

12.3.1 Central Supraspinal Injuries

Patients with supraspinal lesions mainly complain of urinary symptoms characterised by urgency-frequency syndrome and urge incontinence. Cerebrovascular diseases, infantile cerebral palsy, normal pressure hydrocephalus, dementia, intracranial tumours, cranioencephalic trauma, multiple system atrophy (MSA), Parkinson's disease and parkinsonisms [5], multiple sclerosis and other demyelinating disorders, as well as other supraspinal injuries more frequently induce *detrusor hyperreflexia with regular sphincter synergy*, i.e. with a coordinated activity of the external sphincter and bladder neck (Figs. 12.3 and 12.5). In these cases, the cortical inhibition is reduced and it induces uninhibited bladder contractions in response to lower bladder filling volumes, generally much lower (trigger point) than normal bladder capacity, which is about 400 mL.

Uninhibited bladder contractions, especially in the elderly, may also be poorly sustained over time, resulting not only in urgency-frequency syndrome or incontinence but also in incomplete bladder voiding despite the release of external urethral sphincter. This clinical and urodynamic condition, which is common in MSA patients and is the second most common cause of bladder voiding dysfunction in the elderly, is named *detrusor hyperactivity with impaired contractility* (DHIC).

In the presence of relative integrity of the pontine centre, a physiological release of the external urethral sphincter is ensured during bladder contraction. Therefore if a sustained uninhibited contraction is present, the bladder empties efficiently without a significant post-voiding residual volume (PVR). The presence of an elevated PVR suggests DHIC or a preexisting condition of outflow obstruction. It is important to consider that voiding dysfunctions signs and symptoms may differ in relation to the presence of incomplete spinal cord lesions, of associated central and/or peripheral lesions, of drugs use or of urinary outflow obstructions, such as prostate hypertrophy or tumours.

12.3.2 Spinal Injuries (Intrapontine-Suprasacral)

Anatomically, traumatic and non-traumatic spinal cord injuries are defined by level and are classified as cervical, thoracic and lumbosacral. However, when analysing the effects of spinal injuries on voiding disorders, it is preferable to classify these same injuries into suprasacral and sacral.

Suprasacral lesions most frequently include spinal injuries, myelitis, multiple sclerosis, and primary or metastatic bone marrow tumours. As in supraspinal injuries, suprasacral injuries may present urodynamic detrusor hyperreflexia with uninhibited contractions as the bladder reaches its trigger point. More commonly, detrusor hyperreflexia is characterised by a *dyssynergia between detrusor and external sphincter* (DESD), since the pontine centre is no longer able to coordinate the relaxation of the external sphincter during bladder contraction. In the absence of an

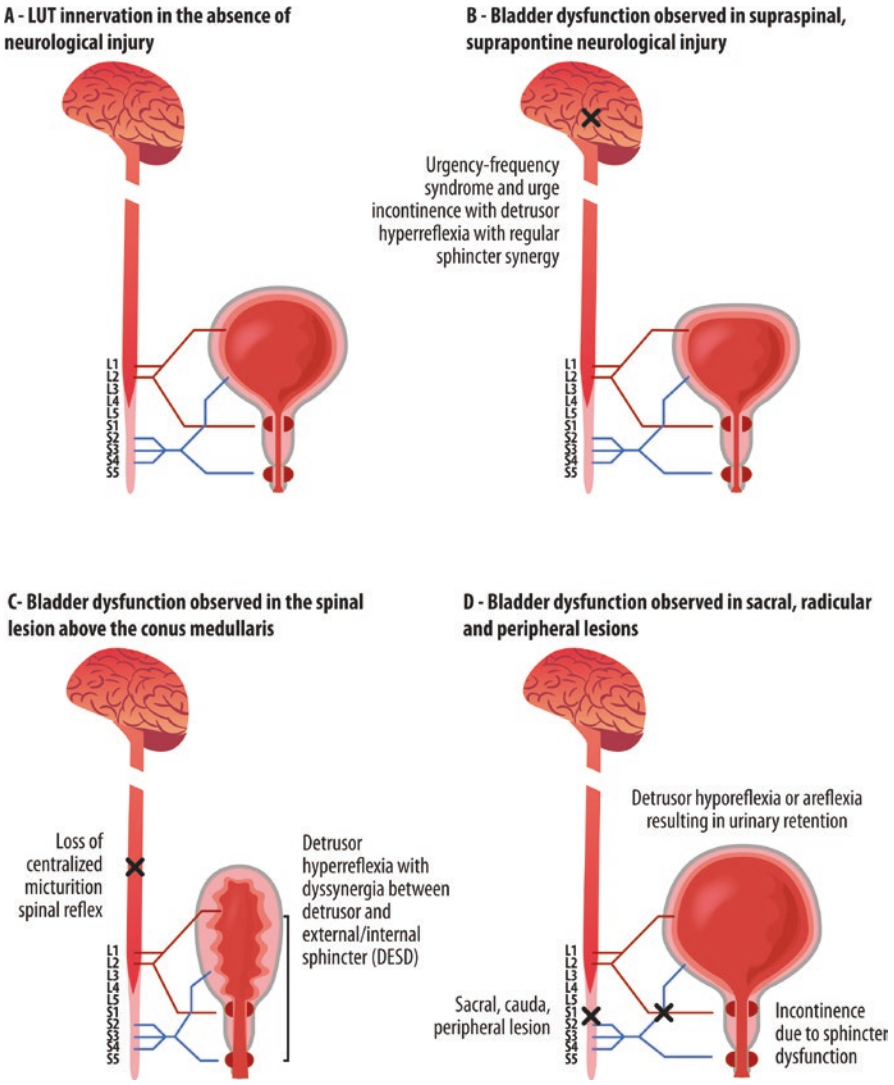

Fig. 12.5 Types of bladder dysfunction typically observed after neurological injury. (From Micieli et al. "Disfunzioni Autonomiche" © 2022 Il Pensiero Scientifico Editore with permission)

input from the pontine centre, uninhibited bladder contractions stimulate a sphincter contraction reflex. DESD should therefore be considered as an exaggerated continence reflex (Figs. 12.3 and 12.5).

In healthy subjects, the continence reflex produces an increase in sphincter activity in order to prevent incontinence in case of excessive bladder filling or increased intra-abdominal pressure. There is not a definite relationship between dyssynergia and lesion level or duration, but the presence of a DESD is certainly more frequent

in higher spinal cord lesions than in lower ones. Moreover, it is important to remember that DESD can be associated with a dyssynergia of the internal sphincter or bladder neck during bladder contraction.

In suprasacral lesions, as in supraspinal injuries, different clinical and urodynamic patterns can occur due to variations in the function of the bladder and sphincter related to partial damage or hidden lesions, not detectable by normal imaging techniques but which can sometimes be confirmed by appropriate electrophysiological investigations.

Patients suffering from detrusor hyperreflexia and DESD frequently show increased connective tissue in the bladder wall, especially those suffering from outflow obstruction due to sphincter dyssynergia. Consequences of this phenomenon are high intravesical pressure and the secondary risk of ascending pyelonephritis, hydronephrosis and kidney failure.

Patients with suprasacral lesions and regular bladder sensations usually show urgency-frequency syndrome but may also be incontinent without any awareness.

It must be emphasised that incomplete bladder voiding can exacerbate detrusor hyperreflexia and that an overactive bladder, stimulated by a relevant post-voiding residual volume (PVR), induces additional urgency-frequency symptoms.

12.3.3 Sacral and Spinal Root Injuries

Different types of lesions can involve sacral cord or nerve roots such as trauma, herniated discs, tumours, myelodysplasias, arteriovenous malformations, congenital and acquired lumbar stenosis, and inflammatory processes (arachnoiditis). Trauma is the most frequent cause of conus or cauda equina lesions, followed by L4–L5 and L5–S1 herniated discs that are the cause of cauda equina syndrome in 1–15% of patients.

The damage to the sacral cord or roots is usually responsible for an acontractile bladder with high volumes of urine. However, particularly in patients with incomplete spinal lesions, areflexia may be accompanied by a reduction in bladder compliance resulting in a progressive increase in intravesical pressure during filling. The mechanism by which the disconnected sacral parasympathetic centre induces a decrease in bladder compliance is unclear. In patients with sacral lesions, the external sphincter is often less involved than the detrusor, due to the different positions of the nuclei that provide innervation; the combination of detrusor areflexia with a functionally intact sphincter contributes to bladder overdistention and decompensation (Figs. 12.3 and 12.5). Such patients frequently complain of a sensation of suprapubic fullness, incontinence, and inability to empty the bladder. This clinical picture is caused by urinary retention with overflow incontinence and high post-voiding residual volumes. Furthermore, if bladder sensitivity is relatively normal, a syndrome of increased frequency with the elimination of low amounts of urine, subsequent rapid bladder filling, and new voiding urgency may occur.

12.3.4 Peripheral Nerve Injuries

Peripheral lesions show variable urodynamic and clinical findings based on the type of parasympathetic, sympathetic, and/or somatic peripheral injury. Moreover, bladder dysfunction is also frequent in diffuse polyneuropathies involving small calibre fibres, because of bladder widespread autonomic innervation. Dysimmune neuropathies, distal autonomic neuropathies, amyloidosis and diabetes may involve bladder-inducing alterations of detrusor contractility, urinary flow reduction and PVR increase.

Detrusor areflexia is the result of parasympathetic lesions, while sympathetic injury can cause incontinence due to impaired internal urethral sphincter closure. On the other hand, the involvement of motor and/or sensory nerves usually induces chronic bladder overdistension with an increase in post-voiding residual volumes. Patients with exclusive sensory involvement may initially have bladder contractions and normal bladder capacity; however, decreased bladder sensitivity usually leads to chronic overdistention of the bladder itself, with subsequent decompensation and consequent detrusor areflexia (Figs. 12.3 and 12.5).

12.4 Clinical Evaluation

A thorough history and a neurological and urological examination should always be performed in order to diagnose neurogenic pelvic dysfunction and to plan further electrophysiological tests [6, 7]. The examination includes anal sphincter tone, S1–S2 innervated muscle strength (gastrocnemius, gluteal muscles), sensation extending from the soles of the feet to the perianal area, and the presence of anal and bulbocavernosus reflexes.

Medical history:

- Current and past symptoms.
- Family history and neurological and urological risk factors (diabetes mellitus, multiple sclerosis, parkinsonism, encephalitis, cerebrovascular encephalopathy, etc.).
- Previous surgical interventions.
- Pharmacological therapy.
- Cognitive status and evolution of somatic and/or sensory symptoms.
- Bowel: the desire to defecate, rectal tenesmus, pattern and modality of defecation (use of abdominal press, faecal and/or gas incontinence, soiling, etc.).
- Evaluation of lower urinary tract symptoms (investigate both the filling and voiding phases): onset, urinary urgency and frequency, presence and type of incontinence, bladder sensation, the beginning of micturition (use of the abdominal press, strain, Credé manoeuvre, sitting urination), the possible presence of haematuria. Special attention has to be paid to hematuria that requires further investigation to rule out stones and urinary tract cancers. A urinalysis is recommended

in all patients, especially to detect haematuria; treatment of asymptomatic bacteriuria or pyuria is not recommended.

- Completion of the voiding diary at baseline and controls (bladder diaries): number of micturitions, voided volume (information on functional cystometric capacity), episodes of urgency and urinary incontinence. The voiding diary, when compiled for a few days, is a simple and objective method to measure the type of symptoms and their severity. Although not fully validated in neurological patients, three consecutive 24-h bladder diaries are usually reliable tools in daily practice. The number of micturitions, nocturia and episodes of incontinence are thus rapidly evaluated and can be compared with the number and severity of events after the administration of therapy.
- Specific questionnaires for the assessment of urinary symptoms:
  - International Prostate Symptoms Score (IPSS): 8 questions with scores from 0 to 35 (higher score = more symptoms). Validated also in women.
  - Neurogenic Bladder Symptoms Score (NBSS): 25 questions to assess urinary symptoms in neurological patients.
- Evaluation of bowel history: taking a bowel history is also an important step in patient assessment because neurogenic bowel dysfunction may be associated with neuro-urological symptoms. Physicians should ask patients about their defecation habitus, exploring the desire to defecate and rectal sensation, and defecation pattern (e.g. straining or digitation to start defecation and faecal incontinence).
- Evaluation of the sexual sphere: orgasm, dyspareunia, erectile dysfunction, ejaculation, symptoms and sensitivity of the pelvic area. Validated questionnaires: Male Sexual Health Questionnaire, International Index of Erectile Function, Female Sexual Function Index.

12.5 Neurological and Urological Physical Examination

- Comprehensive assessment of lower spinal cord-mediated reflexes and sensitivities (normal/increased/decreased/absent) in accordance with the distribution of dermatomes and cutaneous nerves of the genital, perianal, perineal, and thigh areas. Cremasteric (L1–L2), Patellar (L2–L4), Achilles (S1–S2), Anal (S2–S4), Bulbocavernosus (S2–S4) reflexes.
- Bulbocavernosus reflex: it is a somatic reflex that provides information on the state of the segments of the sacral spinal cord. It can be induced (contractions of the bulbocavernosus muscles and/or external anal sphincter) by painless stimulation (squeezing) of the glans or clitoris. If present, it indicates that the spinal reflex arc (spinal segments S2–S4) with afferent and efferent nerves through the pudendal nerve is intact.
- Assessment of anal sphincter tone (preserved, increased, reduced, absent).

- Rectal exploration: evaluation of prostate volume. Digital rectal examination is the easiest way to assess prostate volume, but the correlation to prostate volume is poor; however, it is sufficient to discriminate between prostate volume above or below 50 mL.
- Palpation of the suprapubic area: the presence of a bladder globe is generally associated with a reduction in the sensation of bladder filling.
- Evaluation of urogenital prolapse.
- Cough test (evaluation of stress incontinence in women), as standardised by the International Continence Society: in supine/lithotomy position with a bladder filling of 200–400 mL. At least four strong coughs with simultaneous visualisation of the external urethral meatus for the presence of leakage. Leakage of fluid/urine from the urethral meatus coincident with or simultaneous to the cough is considered a positive test.

12.5.1 Investigating Lower Urinary Tract Function: Urodynamics

The term *urodynamics* encompasses several investigations, invasive and not, widely used in urological clinical practice as a helpful adjunct to diagnosis. Urodynamic investigations are very useful tests in assessing objectively the function and dysfunction of the LUT. In neurological patients, urodynamics is the cornerstone to provide or confirm diagnosis, to simplify counselling, and to predict and evaluate treatment outcomes. Urodynamics include the following investigations: uroflowmetry, ultrasound measuring of PVR, filling cystometry, pressure-flow study, leak point pressure, electromyography, and triggered tests. There are also advanced tests that are video-urodynamics and ambulatory urodynamics. It must be emphasised that urodynamics has been standardised by the International Continence Society and should be performed according to technical recommendations. Besides, standardised terminology should be used to ensure correct knowledge among practitioners involved in patient care.

12.5.2 Non-invasive Tests: Free Uroflowmetry and Ultrasound Measuring of PVR

Usually, both tests are performed in the same session to provide the first judgement regarding the voiding phase and to screen for bladder outlet obstruction. They are the first steps before planning invasive studies in patients able to void. In free uroflowmetry, patients are asked to come to the outpatient clinic with a “normal” desire to void. Since it is usually difficult to get an adequate and reliable flow in the outpatient clinic, the bladder should be comfortably full and a voided volume of at least

150–200 mL should be obtained. Then, micturition should be performed in privacy, patients should be relaxed and allowed to void in their usual position (standing or sitting) and the test should be repeated at least three times to ensure reproducibility. Soon after voiding, PVR should be assessed. Urine flow is described in terms of flow rate and pattern. The following data are reported:

1. *Flow rate*: volume expelled per unit of time (mL/s)
2. *Maximum flow rate*: maximum measure value of the flow
3. *Voided volume*: total volume expelled (mL)
4. *Average flow rate*: voided volume divided by flow time
5. *Time to the maximum flow*: elapsed time from the onset to the maximum flow

Several nomograms have been developed to relate the maximum flow rate to the voided volume taking sex and age into account. Plotting data in nomograms is helpful to assess bladder outlet obstruction.

– *"Normal" flow pattern* (unobstructed voiding): the curve has a bell shape and the maximum flow is reached within 5 s from the micturition start. The final phase trace usually ends with a rapid decrease from the maximum flow rate. The flow rate differs according to the different voided volumes, but the first and final appearance of the shape is similar. PVR is usually absent or not significant (less than 100–150 mL or <30% of the filled bladder). The bladder should not be overfilled (>400 mL) because the efficiency of the detrusor begins to decrease and the corresponding maximum flow rate becomes lower. The correct bladder filling should be between 200 and 400 mL.
– *Detrusor overactivity flow pattern:* usually, very high maximum flow rates are seen with a very rapid increase in the flow (1–3 s) due to high detrusor contraction velocity.
– *Bladder outlet obstruction flow pattern*: the curve is characterised by a low maximum flow rate and a reduced average flow. The maximum flow rate is reached slower (3–10 s) and the flow decreases slowly giving a flattened bell-shaped (benign prostatic hyperplasia, BPH) or plateau-flattened curve (urethral stricture). The curve may also be intermittent in BPH obstruction due to abdominal straining.
– *Detrusor underactivity flow pattern:* detrusor underactivity is difficult to diagnose with a simple free uroflowmetry because there is a substantial overlap with the obstructed voiding pattern. However, it can be suspected. A low maximum flow rate is present and the time to get the peak flow is usually reached in the second part of the trace. High PVR (>250 mL) is often seen.

Patients suffering from autonomic LUT disorders present in different stages of the disease with a broad spectrum of urodynamics findings that range from an initial phase of detrusor overactivity to a final stage of detrusor underactivity and chronic urinary retention. Therefore, voiding patterns can modify with time from a detrusor overactivity flow pattern at the very beginning to poor flow due to concomitant bladder outlet obstruction and detrusor underactivity in a late stage. Thus, free uroflowmetry and PVR measurement are not enough to understand the disease stage and

usually, invasive urodynamics is required to understand the underlying condition and to break the chain of LUT failure and likely subsequent upper tract deterioration (bilateral hydronephrosis and renal failure due to chronic urinary retention).

12.5.3 Invasive Tests: Filling Cystometry and Pressure-Flow Study

Non-invasive urodynamic tests are not reliable in assessing the micturition correctly. Free uroflowmetry gives little information about the filling phase and urine flow is a consequence of the interaction between the detrusor contraction (pressure) force and urethral resistance. Unobstructed micturition in males is characterised by high flow and low pressure. Obstructed micturition is characterised by low flow and high pressure, but low flow (with low pressure) is also possible in detrusor underactivity. At the same time, a high flow (with high pressure) is also possible in case of obstructed micturition. Then, measurement of detrusor pressure is required to better understand micturition, particularly in males. A bladder and rectal catheter are required to measure detrusor pressure that is the difference between bladder pressure (bladder catheter) and abdominal pressure (rectal catheter).

Invasive urodynamic investigation (Fig. 12.6) should usually be taken into consideration in neurological patients complaining of LUT symptoms. Indeed, filling cystometry and pressure-flow study are the best tests to reproduce the patient's symptoms and to understand the physiopathology underlying LUT disorders.

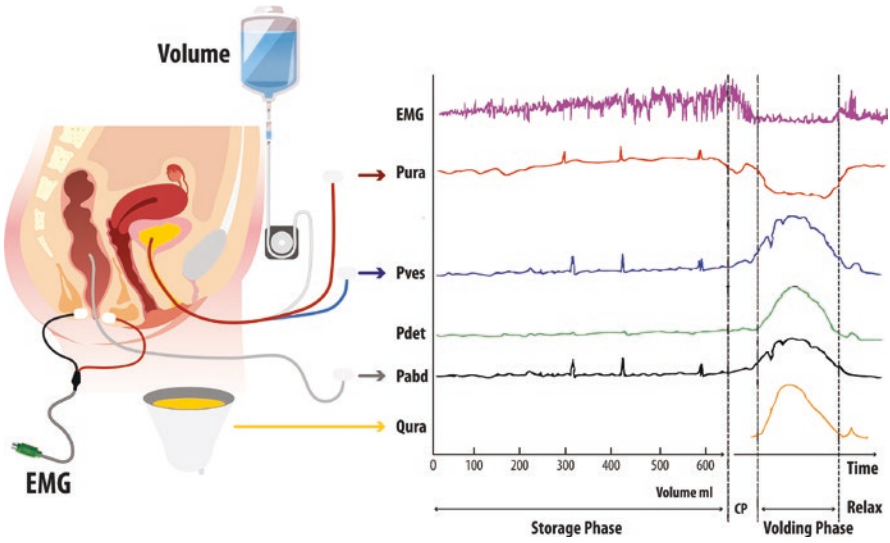

Fig. 12.6 Urodynamic examination. (From Micieli et al. "Disfunzioni Autonomiche" © 2022 Il Pensiero Scientifico Editore with permission)

Invasive urodynamics also enables effective treatment to be given. Filling cystometry assesses the storage phase of micturition, whereas pressure flow studies the voiding phase. It is useful to think about micturition by defining the behaviour of bladder and urethral function as distinct during the storage and voiding phase. The bladder is relaxed with low pressure during filling inside and contracts during voiding. Conversely, the urethra is contracted during filling and relaxed during voiding. This represents the physiological micturition cycle. Then, abnormal function of the bladder and the urethra translates into the failure of their physiological behaviour. However, the bladder cannot be underactive during filling and overactive during voiding, and the urethra cannot be overactive during filling and underactive during voiding. Thus four simple questions help us to understand if bladder and urethral function are "normal" during micturition: (1) Is the bladder relaxed during storage? (2) Is the urethra contracted during storage? (3) Does the bladder contract adequately during voiding? (4) Does the urethra open properly during voiding?

12.5.3.1 Filling Cystometry

Cystometry aims to assess detrusor and urethral function during filling. Bladder filling is usually performed with a sterile 0.9% saline solution at room temperature. The filling velocity is set at 50 mL/min. However, such fast filling in the neurogenic bladder produces artifactual low compliance. Therefore in neurogenic patients filling should commonly start at 10 mL/min. If there is no rise in the detrusor pressure this can be increased to 20–30 mL/min, but if the pressure begins to rise then filling should be stopped for 5–10 min, and then restarted at 10 mL/min. Bladder pressure (*Pves*) and rectal pressure (*Pabd*) are measured by catheters. Bladder contraction is measured as the detrusor pressure (*Pdet*) and by detracting abdominal pressure from intravesical pressure ($Pdet = Pves - Pabd$). A detrusor contraction is present when a pressure change is seen on *Pves* and *Pdet* but not in *Pabd*. A detrusor contraction and an increased abdominal pressure are present in the case of a concomitant increase in *Pves*, *Pabd*, and *Pdet*. Finally, if a rise in pressure is seen only in *Pabd* and *Pves* with no increase in *Pdet* then the rise is only due to increased abdominal pressure. Thus, detrusor function is evaluated by watching the pressure changes, while urethral function is by any fluid leakage. During the filling phase, each desire to void (from first to strong desire; pain sensation) together with urgency and incontinence episodes should be registered and described to assess bladder sensitivity and compliance, and incontinence. This leads to two possible diagnoses: *normal detrusor function with an incompetent urethra* (leaks of filling fluid, urodynamic stress incontinence); *detrusor overactivity with normal* (urgency) *or incompetent urethra* (urodynamic urge-incontinence). However, patients frequently complain of *urgency without any rise in detrusor pressure* (sensory urgency). It is of utmost importance that the urodynamic diagnosis is related to symptoms complaining and the urodynamic findings should be assessed according to the clinical problem. Another

important function to evaluate during the filling phase is bladder compliance, which defines the relationship between bladder volume and bladder pressure and is expressed as an increase in bladder volume per centimetre of water increase in pressure (mL/cmH_2O). In a physiologically working lower urinary tract, intravesical pressure should change a little from empty to full. For example, in a bladder with a capacity of 400 mL, the change in pressure from empty to full should be less than 10 cmH_2O, giving normal compliance of greater than 40 mL/cmH_2O. In case of significant bladder fibrosis, compliance may be reduced.

12.5.3.2 Pressure-Flow Study

The pressure-flow study aims to assess the voiding phase. Once the bladder has filled during cystometry and a strong desire to void has been reached, the patient is asked to void in privacy. Care must be ensured to inform to avoid touching the catheters during voiding, as this might cause artefacts. Both detrusor and urethral functions can be defined separately whilst remembering that they work as a single unit. Detrusor activity can be divided as follows:

- Normal: detrusor contracts to empty the bladder with a high flow rate.
- Underactive: detrusor contraction is powerless to empty the bladder and the flow rate is weak, fluctuating, and interrupted.
- Acontractile: no detrusor contraction can be seen during voiding (no change/increase in *Pdet*) and usually patients are not able to void or they void little with an abdominal strain.

During voiding, the urethral outlet is relaxed, allowing the bladder to empty. Even if the urethral sphincter is relaxed there might be a mechanical obstruction such as in the case of benign prostatic enlargement that limits the opening of the prostatic urethra. However, urethral mechanical obstruction may occur at any level from the bladder neck to the external urethral meatus, leading to an increased voiding (i.e. *Pdet*) pressure with, usually, a reduced flow rate (i.e. low *Qmax*). Urethral resistance may be elevated intermittently in case of *urethral overactivity*, which is characterised by intermittent urethral contraction during voiding instead of complete relaxation. In this circumstance, urethral function can be divided into:

- Detrusor-sphincter dyssynergia (DESD): characterised by intermittent contraction of the intrinsic urethral striated muscle during detrusor contraction that produces very high detrusor pressure and an interrupted flow. This condition is typical of neurological patients with high-level (cervical) spinal cord injury.
- Dysfunctional voiding has the same patterns of detrusor-sphincter dyssynergia but is present in patients with intermittent voiding caused by contraction of the pelvic floor muscles.
- Nonrelaxing urethral sphincter obstruction where there is a lack of urethral relaxation during the whole voiding phase, as seen in meningomyelocele patients.

12.5.3.3 Video Urodynamics

Video urodynamics is the integration of pressure/flow study with contemporary cystourethrography with the intent of better understanding LUT function. Video urodynamics should be reserved only for more complex patients who may have concomitant anatomical abnormality (e.g. vesicoureteric reflux) and LUT disorders. This approach is justified not only for the invasiveness of pressure/flow study but also for the radiation exposure. Cystourethrography is usually performed at rest and during filling, couching/straining, and voiding. The following information can be acquired:

- Full bladder, at rest: bladder capacity shape, and outline (e.g. diverticulum and trabeculation), vesicoureteric reflux.
- Strain/cough. Assessment of degree of bladder base descent and bladder neck competence.
- Voiding: speed and extent of the bladder neck opening, calibre, and shape of the urethra, site of any urethral narrowing/dilatation/diverticula, and vesicoureteric reflux.
- Post-voiding: urine residual.

12.5.4 Neurophysiological Evaluation

Extensive neurophysiological investigations should be performed in any patient with LUT and anorectal disorders of suspected central or peripheral neurogenic aetiology [8, 9]. These tests include concentric needle EMG of different pelvic floor muscles, measurement of sacral reflex latency (pudendo-anal or bulbocavernosus reflex), pudendal and anal somatosensory-evoked potentials (SEPs), and motor-evoked potentials (MEPs) from the pelvic floor and EAS muscles by transcranial and lumbosacral magnetic stimulation. Pudendal nerve terminal motor latency (PNTML) has been used in different clinical conditions, but its clinical value has been questioned because the reproducibility, sensitivity, and specificity are uncertain. The recording of a sympathetic skin response (SSR) from the saddle region is useful for testing the lumbosacral autonomic sympathetic system.

Unfortunately, a clinically useful test for evaluating the sacral parasympathetic system, which is crucial for LUT and anorectal functioning, has not been found yet. Tests are usually capable of demonstrating neuropathic lesions and helping to define the specific affected sensory, motor, or autonomic pathway. The severity of lesions can be also assessed, and the underlying mechanisms can be identified. Even when all other functional tests do not show altered findings, the electrophysiological tests can be positive, therefore leading to a surgical or conservative approach and assessing the functional prognosis.

12.5.4.1 Electromyography (EMG)

Needle EMG is the most important neurophysiological technique for evaluating patients with suspected neurogenic aetiology of pelvic floor dysfunction [3]. EMG assessment of pelvic floor, EAS [10] and external urethral sphincter (EUS) is primarily indicated to evaluate:

- the presence of pathological spontaneous activity at rest, fibrillation potentials and positive sharp waves of denervated muscle fibres;
- the presence of collateral reinnervation activity of muscle fibres;
- normal tonic contraction (3–5 Hz) in the EAS, puborectalis muscle and EUS and adequate contraction or relaxation during squeeze or straining;
- recruitment pattern and motor-unit potential (MUP) waveform.

EAS muscle needle EMG examination is the test that is most commonly used to assess the functional state of the pelvic floor and sacral myotomes. EAS is easy to access, its needle evaluation is not very painful and very useful information can be acquired.

When the needle advances in the EAS muscle, the continuous firing of low-threshold MUPs is normally appreciated, and during a brief period of relaxation, the presence of spontaneous activity, fibrillation, or jasper potentials can be recorded.

EMG recordings from the EAS are performed at rest and during squeezing, coughing, and straining that simulate rectal evacuation. In healthy subjects, squeeze and cough increase the MUP recruitment pattern, whereas strain decreases or inhibits MUP firing.

An abnormal EMG pattern may be recorded with surface or needle electrodes during bladder filling or emptying, coughing, or straining. The utility of this technique is to detect a possible dyssynergic functional behaviour, for example the paradoxical contraction of the external urethral sphincter concomitant to the contraction of the detrusor (during the urodynamic test) or a similar inadequate activation of the puborectalis muscle in the attempt to evacuate (constipation from paradoxical contraction of the puborectalis muscle).

12.5.4.2 Sacral Reflexes

Sacral reflexes are motor responses, derived from the pelvic striated floor and sphincter muscles, to electrical stimulation of the dorsal penile or clitoral nerve, perianal skin, bladder neck or proximal urethra. Sacral reflexes evaluate the functional status of the afferent neural fibres of the clitoris or penis, the S2–S4 spinal segments, and the efferent pathways to EAS and bulbocavernosus (BC) muscles. The central circuit at the spinal level is complex and probably involves many sacral interneurons. The motor response in EAS and BC muscles is recorded either with a concentric needle or wire electrodes and can be analysed separately for each side of both muscles. These sacral reflexes, named pudendo-anal and bulbocavernosus reflex, reveal two components with different thresholds at the electrical stimulation:

a first component with a shorter latency of 26–36 ms, probably oligosynaptic, and a second component with a longer latency at about 50–75 ms, typical for a polysynaptic response. The first component is morphologically constant, stable and does not habituate, while the second component or long latency response is not always demonstrable and rapidly habituates. The cutaneous-anal reflex, like the other two reflexes, consists of two or three motor contractions (early response at 5 ms, intermediate at 15 ms and late at about 50 ms) of EAS muscle in response to scratching or pricking the perianal skin. This reflex, which is abolished by transection of the posterior S4 roots, shows marked habituation, is quite variable (35–80 ms) and therefore cannot be used as a diagnostic tool. Vesico-urethral and vesico-anal reflexes are described following stimulation of the bladder neck and mucosa, but their usefulness as a diagnostic tool is considered to be limited.

Recently, a technique for transcutaneous electrical stimulation of the S3 motor root, recording from EAS muscle, has also been described.

A common scheme of sacral evoked responses consists of the anterior electrical stimulation (penile/clitoral) and recording by needle electrode from different pelvic muscles (BC, EAS, and levator ani). Sacral reflexes are useful in different pelvic floor disorders and have been recommended for the assessment of cauda equina and conus medullaris lesions. In the presence of unilateral/asymmetrical lesions of pudendal nerves, sacral roots or lumbosacral plexus, these reflexes may show a reduction of response amplitude and/or increased latencies or a total absence. Only the largest myelinated, fastest fibres convey the neurophysiological signals travelling in the afferent limb of these reflexes. Unfortunately, many disorders of bladder, bowel and sexual function are the result of unmyelinated fibre dysfunction; conduction in these fibres is not tested by these procedures and autonomic and small-fibre neuropathies may not be revealed by these tests.

12.5.4.3 Somatosensory Evoked Potential

Somatosensory evoked potential (SEP) of the pudendal nerve is a method for evaluating the afferent sensory pathway to the parietal cortex and it is used in investigating central and peripheral neurological diseases that affect pelvic floor functional integrity [11]. SEP findings may help in showing lesions in somatosensory pathways, localising them and defining a prognostic value. In a similar way to the other neurophysiological tests, pudendal SEPs may be normal in latency and amplitude also in case of an underlying organic disease. The peripheral electrical stimulation used to obtain a SEP activates predominantly, if not entirely, the large diameter fast-conducting group Ia muscle and group II cutaneous afferent fibres. Loss of dorsal column or lemniscal sensory pathways is invariably associated with abnormal SEPs, indicating that within the spinal cord, the SEPs are mediated predominantly via these tracts. Generally, SEPs are best recorded over the somatosensory cortex and several of their components are widely distributed over the scalp. The pudendal SEPs technique, first described by Haldeman in 1983, depends on the recording by a disk electrode affixed to the scalp of a typical “W-shaped” waveform, as a response

that appears with a given latency depending on site stimulation. Although several studies have shown that SEPs can effectively be recorded after dorsal penile and clitoral stimulation, only a few investigations have been published concerning anal somatosensory evoked responses. It is necessary to remind that pudendal SEPs after anal and dorsal penile/clitoral nerve stimulation cannot be considered to produce equivalent results due to separate branches of the pudendal nerve innervating the pelvic region. Therefore, obtaining separate reference values in both sexes for anal and penile/clitoral latencies when evaluating pelvic floor neurophysiology is considered to be relevant. The analogous morphology of pudendal and tibial SEPs might suggest a common neurophysiological mechanism to produce both responses.

The responses are bipolarly recorded using surface electrodes from the scalp, 2 cm behind Cz, referred to as Fz or Fpz (10–20 EEG International System), roughly overlying the sensorimotor cortex for the genital and anal area. Electrical stimulation is performed using a bipolar surface electrode positioned at the anal orifice, at the base of the penis or cranial to the clitoris. The typical recording consists of a series of waves that reflect the sequential activation of neural structures along the somatosensory pathways. A first positive peak can be recorded in normal subjects at about 42 ms using a stimulus intensity of two to four times the sensory threshold. Later negative and positive peaks show a large variability in amplitude between individuals. SEP amplitudes have, however, not been found to differentiate between normal and pathologic responses. SEPs can be used in perineology to confirm and localise sensory abnormalities affecting anal or genitourinary neural pathways. Some authors have already discussed the limitations of pudendal SEPs, showing that sometimes in pathological conditions penile/clitoral SEPs are normal. Pudendal SEPs are considered to be useful in diagnosing impotence associated with spinal cord injury and diabetic neuropathy while in the case of primary erectile dysfunction, their utility is debated.

12.5.4.4 Motor Evoked Potential (MEP)

Conventional electrophysiological methods that activate the descending cortico-motoneuronal pathways use the electrical and magnetic stimulation techniques. However, transcranial magnetic stimulation (TMS) has the advantages of being painless and capable of stimulating the more deeply situated nervous structures; electrical stimulation is therefore mainly reserved for intraoperative monitoring. TMS has been commonly used to assess the central and peripheral conduction time to skeletal muscles of the upper and lower limbs, to evaluate the integrity and function of the cortico-spinal pathways. TMS is also applied to study the cortico-spinal pathway to the pelvic floor muscles, including EAS, which is the most common target muscle from which MEPs are recorded, and EUS and PRM, whose recordings are poorly reproducible. The intensity of TMS necessary to obtain an EAS MEP is much higher than the intensity to elicit an MEP in the limbs. This fact can be explained by the cortical representation of the anogenital area that is localised deep within the motor strip in the interhemispheric fissure. This method investigates

the motor efferent pathway from the brain and lumbosacral roots to the EAS, allowing us to determine the total conduction time and the lumbosacral latency. Cortical magnetic stimulation is usually performed in two conditions: at rest, with EAS relaxed (MEPs mean latency of about 27 ms), and during facilitation (MEPs mean latency of about 23 ms) due to a voluntary mild contraction of the pelvic floor and EAS muscles. The magnetic stimulation applied over the lower lumbar spine is known to activate the lumbosacral ventral roots at their exit from the vertebral canal. MEPs from lumbosacral magnetic stimulation are obtained only during rest conditions at about 3–6 ms since facilitation does not modify latencies during peripheral nerve stimulation.

Magnetic shocks are delivered by a magnetic simulator; different shapes of coils exist, each of which produces different magnetic field patterns. The coil produces, normally, a peak magnetic field strength of 1.5 T, being placed flat on the scalp, centred on Cz (10–20 I.E.) to stimulate the motor cortex and on the lumbosacral region (L3–L4 interspace) to stimulate the lumbosacral roots. EMG recordings are taken from EAS using a needle electrode placed approximately 1 cm lateral to the anal orifice. The ground electrode is located around the upper portion of the leg. The different types of MEP abnormalities, i.e. responses with decreased amplitude or delayed latency, may imply axonal or demyelinating impairment underlying the different clinical pathological conditions. Corticospinal abnormalities detected by this method in patients with neurogenic bladder and bowel disorders have been reported.

12.5.4.5 Sympathetic Skin Response (SSR)

SSR is a technique that records changes in skin conductance after activation of sweat glands in skin areas rich in eccrine glands (commonly palmar, plantar, and saddle sites) under the neural control of sympathetic cholinergic (sudomotor) fibres. SSR is the only neurophysiological technique directly testing sympathetic fibres. Potentials generated by SSR can be recorded in response to various stimuli; these include electrical peripheral nerve stimulation, acoustic stimuli, and magnetic stimulation of nerves or the brain, although magnetic stimulation lacks specificity in terms of sensory pathways involved. SSR is dependent on the integrity of peripheral sympathetic cholinergic pathways, as it is preserved in selective sympathetic adrenergic failure, and it is absent in pure autonomic failure (PAF) (with sympathetic adrenergic and cholinergic failure) and in pure cholinergic dysautonomia. Different areas in the cerebral cortex and in the brainstem have been proposed as generator sites for the sensory signals of the SSR.

SSRs are recorded from palmar, plantar, and saddle surfaces, both left and right, using surface electrodes. Electrodes are placed on the volar site and on the corresponding area of the dorsal aspect of the hand or foot. For perineum recordings, the active electrode is attached to the perineum (below the scrotum) and the reference electrode to the iliac crest with the ground on the leg. This kind of recording from the perineal region increases the diagnostic sensitivity when evaluating sympathetic

function within the thoracolumbar spinal cord. Only a few studies exist regarding the relationship between bladder dysfunction and SSR abnormalities. In particular lack of SSR in bladder neck dyssynergia and in foot following spinal cord injury has been shown.

12.5.4.6 Pudendal Nerve Terminal Motor Latency (PNTML)

Pudendal nerve inferior rectal branches can be evaluated by measuring PNTML, which is the technique most commonly used for assessment in patients with idiopathic neurogenic faecal incontinence. The PNTML technique, first described in 1984 by Kiff and Swash, is determined by recording anal sphincter motor potential evoked by stimulation of the pudendal nerve into the rectum with a special bipolar surface electrode known as St. Mark's electrode. The stimulating electrode is fixed on the tip of a gloved index finger while the two recording electrodes, that pick up the contraction response of EAS, are placed at the base of the finger. On insertion of the finger into the rectum, an electrical stimulation is given near the ischial spine. The pudendal nerve is therefore stimulated as it leaves the pelvis, before branching into the perineal nerve and inferior rectal nerve, which innervate periurethral striated muscle and anal sphincter respectively.

The test owes its popularity to different studies showing abnormal latencies in various clinical situations. In fact, pudendal neuropathy is seen in up to 70% of patients with faecal incontinence, and in more than 50% of patients with sphincter injury. However, PNTML clinical value has been questioned, and two consensus statements, uro-neurological and gastroenterological, did not propose this test for evaluating patients with bladder and bowel dysfunction.

12.6 Management of Neurogenic Lower Urinary Tract Dysfunctions

The goals in neurogenic lower urinary tract dysfunctions are: to promote a regular bladder voiding, to obtain a low-pressure bladder, to achieve and maintain continence, to minimise symptoms and to improve quality of life, to prevent urinary tract infections and to preserve renal function, protecting the upper urinary tract; these are objectives that often require a multidisciplinary approach.

In addition, elderly patients may have concomitant diseases, such as bladder outlet obstruction due to BPH, stress incontinence, and urinary tract infections, which ought to be considered in management.

Management should consider both storage and voiding dysfunctions and determine the severity of symptoms and the risk of upper urinary tract damage [2, 6, 12]. The latter is of utmost importance as renal function impairment can impact survival.

12.6.1 Management and Treatment of Storage Dysfunction

Treatment of lower urinary tract dysfunctions in the neurogenic bladder:

1. Depends on the impact on quality of life
2. Must consider concomitant diseases (BPH obstruction, urinary infections, stress incontinence)
3. Must maintain continence
4. Must protect the upper urinary tract (avoiding chronic retention with bilateral hydroureteronephrosis and kidney failure)

Therefore, when detrusor overactivity is present, treatment should be aimed to convert a high-pressure overactive bladder into a low-pressure bladder, in order to maintain continence, prevent urinary infections and improve quality of life.

Lifestyle changes and bladder voiding strategies:

– Fluid intake reduction, particularly in the evening
– Treatment of constipation
– Timed micturition (every 2–4 h during the day)

Lifestyle interventions and voiding strategies are the first-line non-invasive treatments. Patients should be counselled to reduce fluid intake, particularly in the evening, and to treat constipation. Moreover, a timely voiding every 2–4 h during the day and the use of a double voiding technique may improve bladder emptying, reduce urgency and urge-incontinence episodes, minimising the risk of urinary infection. Older patients may need support from caregivers to carry on these strategies.

The second line of treatment for overactive bladder is pharmacological therapy which is based on the use of antimuscarinic drugs (oxybutynin, trospium, tolterodine, propiverine, darifenacin, solifenacin), that inhibit parasympathetic system, induce a reduction in urgency, micturition frequency and episodes of urge incontinence and increase cystometric capacity. All these drugs are established, effective, and well-tolerated treatments even in long-term use. Treatment must always start at low doses and with a gradual increase only in cases of poor efficacy and without side effects. However, higher doses and a combination of different agents are generally required in neurological patients. These drugs decrease maximum detrusor pressure by 30–40% and increase bladder capacity by 30%.

Antimuscarinics are the most studied drugs for the treatment of urge urinary incontinence and for the urge-frequency syndrome [12]. They are different from each other in pharmacokinetic and pharmacodynamic features, but they are superior to placebo in the treatment of incontinence episodes. Some of the most frequent side effects are xerostomia and constipation; despite the fact that urinary retention is quite rare, PVR should be frequently assessed. Slow-release formulations appear to have a lower incidence of side effects than rapid-release formulations and their pharmacokinetics (poor or absent penetration of the blood-brain barrier) make them more suitable than others for use in elderly patients, avoiding central effects such as

confusion. Treatment compliance to antimuscarinics is often low due to possible limited efficacy and to the presence of particularly significant side effects and costs. The antimuscarinic drugs fesoterodine, oxybutynin, propiverine, solifenacin, tolterodine, darifenacin and trospium are recommended with a high grade of recommendation by the European Association of Urology (EAU) guidelines on urinary incontinence [6].

Mirabegron is the first-in-class β3-agonist drug that activates β3 adrenergic receptors located in the bladder wall; these receptors induce relaxation of bladder detrusor smooth muscles. Although being recently approved for overactive bladder therapy, mirabegron seems to lead to greater compliance than antimuscarinics.

Estrogens used topically (vaginally) in postmenopausal women may reduce episodes of urge incontinence, but do not seem to impact stress incontinence.

The third line of treatment uses botulinum toxin type A, which is injected into the detrusor. It is indicated in patients who have had no benefit from antimuscarinic therapy. The 2022 guidelines of the EAU [6] advise, with a high degree of evidence, to propose intravesical botulinum toxin to patients with urge incontinence refractory to conservative therapy. On the other hand, it is important to inform patients treated with this technique about the short duration of response and the risk of inducing detrusor areflexia that needs intermittent catheterization. In fact, botulinum toxin causes a long-lasting chemical bladder denervation (on average 3–6 months) which translates into an increase in bladder capacity, a reduction in bladder pressure and a consequent reduction in episodes of urgency, frequency and urge incontinence. Frequent side effects are represented by urinary infections, hematuria, and urinary retention with possible need for intermittent catheterization.

The therapeutic technique of sacral neuromodulation can also be offered to patients who are refractory to conservative, pharmacological and intradetrusor treatments [13]. Neuromodulation is a technique that consists of the implant of a device that allows a therapeutic modification of the activity of the central, peripheral or autonomic nervous system by means of electrical or pharmacological stimulus. This method is safe, non-destructive and reversible, it does not preclude other therapies, and it shows positive long-term results on quality of life, with the possibility of testing its therapeutic efficacy before performing a permanent implant.

Sacral neuromodulation consists of the implant of a quadripolar electrode connected to a sacral stimulator that is implanted at the level of S3 foramen under local anaesthesia. The 2022 guidelines of the EAU [6] advise, with a high degree of evidence, to propose the sacral neuromodulation technique to patients with overactive bladder and urgency-frequency syndrome or urge incontinence refractory to antimuscarinic therapy.

Surgery to increase bladder capacity can be proposed only when all other conservative therapies have failed. The increase in bladder capacity can be achieved with bladder augmentation surgery using an ileal segment anastomosed with the bladder. At the same time, there is also a reduction in intravesical pressure. This treatment should only be offered as the last treatment in highly motivated patients who accept a possible intermittent self-catheterization in case of post-surgical urinary retention.

In fact, clean intermittent catheterization may become necessary to empty the bladder.

Urinary diversion may be offered as the last treatment when no other therapy was successful, in cases refractory to non-invasive therapies, with the creation of a catheterizable continent stoma, that is unfortunately characterised by high rates of complications. Urinary diversion aims to protect upper urinary tract deterioration (i.e. bilateral hydronephrosis) and renal failure. Continent diversion with a stoma at the umbilicus is the first choice for urinary diversion. This type of diversion is an effective treatment option in neuro-urological patients unable to perform intermittent self-catheterization through the urethra, despite having a high complication rate.

If catheterization is not possible, an incontinent stoma can be constructed using the intestine. In fact, if manual dexterity impairs stoma catheterization, incontinent diversion with a urine-collecting device is indicated. Incontinent diversion is also indicated in patients who are wheelchair-bound or bedridden with untreatable incontinence or in patients with severely compromised upper urinary tract.

12.6.2 Management and Treatment of Voiding Dysfunction

Incomplete bladder voiding can exacerbate detrusor overactivity and make treatments with antimuscarinic drugs and botulinum toxin less effective. The use of intermittent catheterization (IC) significantly improves continence management [14]. Catheterization 4–6 times/day is also recommended to manage complete urinary retention, with a goal of voiding 400–500 mL of urine with each catheterization. The following manoeuvres can be used to facilitate bladder emptying when it is incomplete (bladder expression):

1. Urination with simultaneous Valsalva manoeuvre
2. Urination with simultaneous manual compression of the lower abdomen (Credè manoeuvre)

These manoeuvres can be performed only if there is no increased intravesical pressure and vesicoureteric reflux during storage, due to the risk of upper urinary tract deterioration.

The frequency of catheterization depends on many factors such as bladder volume, fluid intake and post-voiding residual (PVR), and urodynamic factors such as compliance and detrusor pressure. IC, which is used in children with spina bifida and in the elderly with impaired bladder emptying, is also very effective in most patients with multiple sclerosis and, in combination with an oral anticholinergic drug, it is the treatment of choice in spinal cord diseases, where incomplete bladder emptying and detrusor hyperreflexia coexist. The incidence of symptomatic lower urinary tract infections is, fortunately, low despite the fact that bacteriuria is present in 50% of patients performing sterile IC. Patient motivation is essential for the correct use of this technique because they have to develop adequate manual skills. An indwelling catheter to be replaced cyclically or a suprapubic catheter is

recommended in patients for whom IC cannot be used; in these cases, there is a greater risk of infections, bladder stones and urethral and bladder neck lesions.

A1-blockers are the first line of pharmacological treatment of voiding dysfunction in men. They are indicated in subjects with moderate/severe symptoms (IPSS >8) and with no response to conservative treatment (reduction of fluid intake, particularly tea, alcohol and coffee, treatment of constipation, use of relaxed and double-voiding techniques, scheduled voiding). They inhibit the effects of endogenous norepinephrine on the smooth muscle cells of the prostate and bladder neck (relaxing effect), with a reduction of bladder neck resistance. The clinical efficacy of the available drugs (alfuzosin, doxazosin, silodosin, tamsulosin, terazosin, naftopidil) is similar and a few weeks are needed before clinical benefit. Clinical effects are represented by a variable reduction in IPSS of 30–40% and an increase in maximum peak flow of 20–25%. Asthenia, anejaculation, orthostatic hypotension, and intraoperative floppy iris syndrome during cataract surgery are the most frequent side effects.

5α-Reductase inhibitors are the second group of drugs used in men with a prostate volume larger than 40 mL. They induce the apoptosis of the prostate gland epithelial cells by inhibiting the conversion of dihydrotestosterone from testosterone and causing a decrease in prostate volume (18–28%) and a concomitant improvement of IPSS and maximum flow rate. Moreover, long-term use of these drugs reduces the risk of acute urinary retention and the need for surgery.

Surgical therapy of benign prostatic hyperplasia remains indicated in the following cases:

1. severe symptoms (IPSS >20),
2. symptoms refractory to medical therapy,
3. absolute indication in the presence of:
   - urinary retention (acute or chronic)
   - bladder diverticula
   - bladder stones
   - recurrent urinary tract infections
   - bilateral hydroureteronephrosis
   - haematuria due to prostatic cause

References

1. Panicker JN, Fowler CJ, Kessler TM. Lower urinary tract dysfunction in the neurological patient: clinical assessment and management. Lancet Neurol. 2015;14(7):720–32.
2. Panicker JN, Sakakibara R. Lower urinary tract and bowel dysfunction in neurologic disease. Continuum (Minneap Minn). 2020;26(1):178–99.
3. Fowler CJ, Brady CM, Frohman EM, Sakakibara R, Stewart JD, editors. Neurologic bladder, bowel, and sexual dysfunction. Amsterdam: Elsevier; 2001.
4. Wyndaele JJ. The management of neurogenic lower urinary tract dysfunction after spinal cord injury. Nat Rev Urol. 2016;13(12):705–14.

5. Sakakibara R, Tateno F, Yamamoto T, Uchiyama T, Yamanishi T. Urological dysfunction in synucleinopathies: epidemiology, pathophysiology and management. Clin Auton Res. 2018;28(1):83–101.
6. EAU guidelines on neuro-urology. Edn presented at the EAU annual congress Amsterdam. 2022. ISBN: 978-94-92671-16-5.
7. Ginsberg DA, Boone TB, Cameron AP, et al. The AUA/SUFU guideline on adult neurogenic lower urinary tract dysfunction: diagnosis and evaluation. J Urol. 2021;206(5):1097–105.
8. Podnar S, Vodusek DB. Protocol for clinical neurophysiologic examination of the pelvic floor. Neurourol Urodyn. 2001;20(6):669–82.
9. Pelliccioni G, Pelliccioni P. Neurophysiology and neurophysiological evaluation of the pelvic floor. In: Martellucci J, editor. Electrical stimulation for pelvic floor disorders. Cham: Springer; 2015.
10. Podnar S, Vodusek DB, Stâlberg E. Standardization of anal sphincter electromyography: normative data. Clin Neurophysiol. 2000;111(12):2200–7.
11. Pelliccioni G, Piloni V, Sabbatini D, Fioravanti P, Scarpino O. Sex differences in pudendal somatosensory evoked potentials. Tech Coloproctol. 2014;18(6):565–9.
12. Ginsberg DA, Boone TB, Cameron AP, et al. The AUA/SUFU guideline on adult neurogenic lower urinary tract dysfunction: treatment and followup. J Urol. 2021;206(5):1106–13.
13. van Ophoven A, Engelberg S, Lilley H, Sievert KD. Systematic literature review and meta-analysis of sacral neuromodulation (SNM) in patients with neurogenic lower urinary tract dysfunction (nLUTD): over 20 years' experience and future directions. Adv Ther. 2021;38(4):1987–2006.
14. Clark C, Haslam C, Malde S, Panicker JN. Urinary catheter management: what neurologists need to know. Pract Neurol. 2021;21(6):504–14.