**Dysfunction of lower urinary tract in patients with spinal cord injury**

BRIGITTE SCHURCH ¹, CÉCILE TAWADROS ², AND STEFANO CARDA ¹

¹ Neuropsychology and Neurorehabilitation Service, Department of Clinical Neuroscience, Lausanne University Hospital, Lausanne, Switzerland
² Urology Service, Lausanne University Hospital, Lausanne, Switzerland

“One who has a dislocation in the vertebral column of the back of his neck and he is unaware of his legs and his arms and his urine dribbles: [this is] a medical condition that cannot be healed.” Dating from the 17th century BC, the Edwin Smith papyrus is a unique treatise containing the oldest known descriptions of signs and symptoms of injuries of the spinal column and spinal cord (Breasted, 1930). At this time, the chain of events often associated with spinal cord injury (SCI) was already well known; namely, urinary retention followed by overflow incontinence. Later on, in the 19th century and at the beginning of the 20th century, many efforts were made to manage the bladder of patients with SCI in order to preserve the upper urinary tract.

To treat these disturbances, different methods were tried (intermittent catheterization, suprapubic catheter or tidal drainage) (Curling, 1833; Munro and Hahn, 1935; Bumpus et al., 1947; Pearman and England, 1976). However, most were not able to avoid pyelonephritis and urosepsis. In 1947, Sir Ludwig Guttmann sought to reduce the incidence of infection by resorting to intermittent catheterization using a non-touch technique (Guttmann, 1949), and the overall infection rate dropped markedly. Only 62% of patients discharged left the rehabilitation unit with sterile urine. However, it should not be forgotten that Munro, on the other side of the ocean, went to the same concept and obtained the same results (Munro and Hahn, 1935) and Jack Lapides, who is considered to be one of the fathers of clean intermittent self-catheterization (CISC) (Lapides et al., 1972). Over the last 60 years, many techniques have evolved, such as the use of anticholinergic drugs to control detrusor overactivity, the development of neuro-modulation, and the introduction of botulinum toxin treatment for detrusor and sphincter overactivity.

**INCIDENCE, MORTALITY, AND MORBIDITY**

Disturbances of micturition are, in fact, very common after SCI. Reports from the Model Spinal Cord Injury Systems of Care show that approximately 81% of SCI patients have some degree of impaired bladder function 1 year after injury (Breasted, 1930; Stover et al., 1995). During the acute phase, impaired voiding is present in all patients with complete and motor complete lesion (American Spinal Injury Association (ASIA) Impairment Scale (AIS) A and B). Moreover, Patki et al. (2006b) reported that, in a group of mobile patients with incomplete spinal lesion, a voiding dysfunction was present in 100%, 82%, and 41% of patients with motor incomplete lesions AIS C, D, and E, respectively.

The amazing development in neurogenic bladder management has allowed a dramatic change in morbidity and mortality of patients with SCI patients. Until 1969 up to 75% of deaths after SCI were due to renal failure and/or urosepsis (Tribe and Silver, 1969; Whiteneck et al., 1992; Soden et al., 2000), while at present, mortality from the same cause is around 2.3% (Devivo et al., 1989, 1993). In spite of this enormous improvement, it should be pointed out that the standardized mortality ratio due to urinary system diseases is still 22.8 in SCI patients and even more (172.3) due to sepsis, mainly secondary to urinary tract-related infections (Soden...
et al., 2000). According to these data, it seems evident that good knowledge of lower urinary tract dysfunction (LUTD) in SCI is mandatory for clinicians confronted with this disease. It should not be forgotten that neurologic bladder control is an important determinant in quality of life after SCI, and that better control of urinary symptoms, mainly incontinence, can improve it significantly (Ku, 2006).

**PATHOPHYSIOLOGY: SPINAL CORD INJURIES**

The range of bladder symptoms caused by neurologic lesions is wide and determined by whether the lesion primarily affects the supraspinal control, the pontine–sacral neural circuit, or the sacral nerves, and whether these lesions are predominantly motor or sensory, or both. Deep comprehension of bladder neurophysiology is mandatory to understand LUTD in SCI (see Chapter 5).

Although several classifications of neurogenic LUTD have been proposed in the literature, the most commonly utilized are those developed by Madersbacher (1990b). According to this classification, four types of neurologic bladder are recognized (Fig. 14.1):

1. detrusor hyperreflexia in combination with a hyperreflexive (spastic) sphincter
2. detrusor hyporeflexia in combination with a hyperreflexive (spastic) sphincter
3. detrusor hyporeflexia (areflexia) in combination with a hyporeflexive (flaccid) sphincter
4. detrusor hyperreflexia in combination with sphincter hypo-normoreflexia.

Type 1 dysfunction is the most frequently seen in supracausal SCI; type 2 can be observed in conal lesions, and type 3 in cauda equina lesions. Type 4 is typically seen in suprapontine lesions.

In the next section, the underlying physiopathology of these subtypes of neurologic LUTD will be assessed in detail.

**The bladder in “spinal shock”**

After an acute SCI above the sacral micturition center and usually during the first 2 weeks to 3 months after injury, the central synapses between the afferent and efferent arms of the micturition reflex will be rendered inactive. This phase is called “spinal shock.” The exact neurophysiologic mechanism of spinal shock remains unclear and its correct definition is also controversial (Ditunno et al., 2004). Most likely, intramedullary facilitation or total depression of interneuronal activity and release of inhibitory neurotransmitters are the main determinants of this phenomenon: the detrusor muscle is paralyzed (an acontractile, areflexic detrusor), and there is no conscious awareness of bladder fullness (Rossier et al., 1979, 1980). In this phase, the bladder neck has been found to be closed or barely open. There is a marked activity of the external urethral sphincter, whereas the bladder is hypotonic and inactive (Rossier, 1974; Rossier and Fam, 1979; Rossier et al., 1979). After a variable period of time (from a few days to 12 weeks), reflex activity under the neurologic lesional level reappears, usually with a caudocranial pattern. It is important to underline that the only reflex activity that is preserved or returns almost immediately after the spinal shock is the anal and the bulbocavernous reflex. Urinary retention and overflow incontinence occur and urinary tract infections (UTIs) resulting from large residual urine may lead to pyelonephritis and urosepsis.

**Upper motor neuron lesions**

**SUPRASACRAL NEUROGENIC DETRUSOR OVERACTIVITY**

Reflex bladder function generally occurs in humans after suprasacral cord injury within weeks or months after injury. Bladder sensation may be somewhat preserved (in incomplete lesions) but voluntary inhibition of the micturition reflex arc is lost. The initial retention of urine will be followed by neurogenic detrusor overactivity, resulting in a small, hyperreflexic bladder. Dyssynergic contraction of the external sphincter, increased guarding reflex, and impaired detrusor contraction result in inefficient voiding. Overall, reorganization of the central nervous system leads to a high voiding pressure, residual urine in the bladder, and incontinence. These subsequently might induce recurrent UTI, stone formation, hydronephrosis, and finally renal failure.
(McGuire and Savastano, 1983). In incomplete suprasacral lesion, synergistic relaxation of the external sphincter may be preserved. Balanced voiding may occur but urgency and urge incontinence usually persist.

DETRUSOR SPHINCTER DYSSYNERGIA

Detrusor sphincter dyssynergia (DSD) frequently correlates with completeness of the SCI (Siroky and Krane, 1982; Schurch et al., 2004) and is responsible for the bladder outlet obstruction. The diagnosis of DSD is made by urodynamic testing, and is characterized by the presence of an elevated electromyographic activity on the urethral/anal sphincter during detrusor contraction, in the absence of Valsalva and Crede maneuvers (De et al., 2005; Spettel et al., 2011), see Table 14.3. DSD was classified in the 1980s by Blaivas et al. into three types: (1) type I: concomitant increase in both detrusor pressure and sphincter electromyogram activity; (2) type II: sporadic contractions of the external urethral sphincter throughout the detrusor contraction; and (3) type III: crescendo–decrescendo pattern of sphincter contraction which results in urethral obstruction throughout the entire detrusor contraction (Blaivas et al., 1981). More recently, this classification has been simplified by Weld et al. (2000) into two types: continuous or intermittent DSD. Patients with continuous sphincter activity during the voiding phase are at higher risk for upper urinary tract lesions, since the obstruction is persistent during the urine outflow (Schurch et al., 1994; Mahfouz and Corcos, 2011). Concomitant uncoordinated bladder and bladder neck contractions result in bladder neck functional obstruction (i.e., bladder neck dyssynergia) and reinforce bladder outlet obstruction (Schurch et al., 1994).

Lower motor neuron lesion

As opposed to lesions above the the sacral micturition center at S1–4, SCI to the sacral micturition center determines a loss of parasympathetic control of the bladder detrusor and a somatic denervation of the external urethral sphincter, with associated loss of some afferent pathways. In a complete lesion, consciousness awareness of bladder fullness will be lost and the micturition reflex is absent. Some pain sensation may be preserved due to the hypogastric (sympathetic) nerve remaining intact. Urinary retention and stress incontinence are the milestones of the lower motor neuron bladder (see Table 14.3).

BLADDER

Lower motor neuron lesions induce detrusor acontractility, resulting in non-voiding or incomplete voiding. Dramatic changes also appear in the detrusor muscle fibers so that bladder compliance may be altered. This is a very common finding in patients with myelodysplasia (McGuire et al., 1981), whereas in adult patients with SCI bladder compliance usually remains preserved, if patients are correctly managed with intermittent catheterization (Gajewski et al., 1992).

URETHRA AND EXTERNAL URINARY SPHINCTER

The most common finding after lower motor neuron lesion is an incompetence of the urinary sphincter with a significant reduction of the maximal urethral pressure that induces stress or overflow incontinence (Gajewski et al., 1992). However, in some patients, some muscle tone can be present and it is not rare to observe a paradoxical obstruction of the external urethral sphincter that may be due to a secondary fibrotic degeneration of the muscle (Bauer et al., 1977) or to bladder neck dyssynergia (Awad and Downie, 1977).

BLADDER NECK AND PROXIMAL URETHRA

In contrast to healthy subjects, in patients with lower motor neuron bladder, the bladder neck typically remains open even during the filling phase, although the origin of this modification is unclear and has been attributed to either rheologic modifications of detrusor muscle or autonomous contractions (McGuire and Wagner, 1977; Gajewski et al., 1992). This modification increases overflow and stress incontinence.

Correlation between neurologic findings and urodynamic patterns

Correlation between clinical neurologic findings and urodynamic pattern is strong in SCI patients, even if not direct. Weld and Dmochowski (2000a) found that, in a population of 243 patients with SCI, suprasacral lesions were associated with detrusor hyperreflexia and/or DSD in 94.9%, and sacral lesions with detrusor areflexia in 85.7% of cases. These results have been replicated by other authors (Schurch et al., 2004; Agrawal and Joshi, 2013). Even if this roughly corresponds to the classic differentiation in upper and lower motor neuron bladder, it should be kept in mind that the completeness or incompleteness of the lesion and the possible association of multiple injury levels can complicate the picture, so much so that a urodynamic evaluation is mandatory in order to correctly assess and classify LUTD in SCI patients (Stöhrer et al., 2009).

CLINICAL EXAMINATION

In patients with SCI, the neurologic assessment is based on the International Standard for the Neurologic Classification of Spinal Cord Injury, formerly the ASIA standards (American Spinal Injury Association, 2011; Kirshblum et al., 2011).
Milestones of this examination are the determination of the neurologic level for light touch, pinprick sensation, strength of key muscles, and the neurologic rectal examination.

Sensory level is defined as the most caudal normally innervated dermatome for both modalities. The normal dermatome level is located immediately above the first dermatome level with impaired or absent light touch or pinprick sensation.

Motor level is defined as the most caudal normally innervated myotome. It is the most caudal key muscle with a grade of at least 3, when the key muscle above is graded 5. For levels C1–3, T2–12, and S2–5, the motor level is the same as the sensory level.

If at S4-S5 level there is no pinprick or light touch sensation, the sensitivity to deep anal pressure should be assessed and noted.

With these elements, a spinal lesion can be graded as motor and sensory complete, or motor only complete, or sensory and motor incomplete (AIS grade A, B, C, and D). If both motor and sensory functions are normal, the lesion is graded E (Table 14.1).

It is very important also to test sacral reflexes, such as the anal wink reflex (left and right), the bulbocavernous reflex, and, in men, the cremasteric reflex.

**NEUROUROLOGIC INVESTIGATIONS**

The neurourologic investigations will aim to identify the bladder at risk for the upper urinary tract. After recovery from spinal shock and then annually, a complete assessment is usually proposed, including videourodynamicstics, ultrasound scan, and renal function measurement. A closer reassessment is mandatory if any neurologic or urologic change happens, as well as during pregnancy. Usually the patient fills in a 3-day bladder diary and symptom questionnaire before the investigative tests (Stöhrer et al., 2002). It is recommended to assess bowel and sexual function as well at that time (Table 14.2).

**Flowmetry**

Free flowmetry is obtained by urinating into a funnel device that measures the urinary flow rate. Pathologic findings are low flow rate, low volume, and intermittent flow. Along with a postvoid residual urine measurement, this non-invasive screening test provides information on a possible obstruction or pathologic detrusor contraction. Its use in SCI patients is limited to patients with an incomplete lesion who can void.

**Videourodynamics**

Urodynamics study explores vesicourethral function during the bladder filling and voiding phase, using filling cystometry and pressure–flow study, respectively. Urodynamics study is mandatory in understanding bladder dysfunction, as symptoms alone are not reliable in SCI patients (Wyndaele, 1997). The investigation consists

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**Table 14.1**

American Spinal Injury Association (ASIA) Impairment Scale (AIS)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Status</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Complete</td>
<td>No sensory or motor function is preserved in the sacral segment S4–5</td>
</tr>
<tr>
<td>B</td>
<td>Sensory incomplete</td>
<td>Sensory, but not motor, function is preserved below the neurologic level and includes the sacral segments S4–5 (light touch or pinprick at S4–5 or deep anal pressure) and no motor function is preserved more than three levels below the motor level on either side of the body</td>
</tr>
<tr>
<td>C</td>
<td>Motor incomplete</td>
<td>Motor function is preserved below the neurologic level,* and more than half of key muscle functions below the neurologic level of injury (NLI) have a muscle grade &lt;3 (grades 0–2)</td>
</tr>
<tr>
<td>D</td>
<td>Motor incomplete</td>
<td>Motor function is preserved below the neurologic level,* and at least half (half or more) of key muscle functions below the NLI have a muscle grade &gt;3</td>
</tr>
<tr>
<td>E</td>
<td>Normal</td>
<td>If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial spinal cord injury does not receive an AIS grade</td>
</tr>
</tbody>
</table>


*For an individual to receive a grade of C or D, i.e., motor incomplete status, he or she must have either voluntary anal sphincter contraction or sacral sensory sparing with sparing of motor function more than three levels below the motor level for that side of the body. The International Standards at this time allow even non-key muscle function more than three levels below the motor level to be used to determine motor incomplete status (AIS B versus C).

Note: When assessing the extent of motor sparing below the level for distinguishing between AIS B and C, the motor level on each side is used, whereas to differentiate between AIS C and D (based on proportion of key muscle functions with strength grade 3 or greater) the neurologic level of injury is used.

of inserting pressure catheters into the bladder and the rectum to measure respectively the abdominal pressure and therefore the subtracted detrusor pressure, the true bladder pressure (Figs 14.2 and 14.3).

**Cystometry**

The bladder is filled slowly with contrast media, and fluoroscopic images (video) of the urinary tract are taken.

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**Table 14.2**

Recommendations for urodynamics in patients with neurogenic bladder

<table>
<thead>
<tr>
<th>Before urodynamics</th>
<th>Bladder diary 2–3 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Uroflowmetry when void</td>
</tr>
<tr>
<td></td>
<td>Postvoid residual</td>
</tr>
<tr>
<td>During urodynamics</td>
<td>Simultaneous intravesical and abdominal pressure measurement</td>
</tr>
<tr>
<td></td>
<td>Use of video</td>
</tr>
<tr>
<td></td>
<td>Slow filling rate</td>
</tr>
<tr>
<td></td>
<td>Filling cystometry followed by pressure–flow study</td>
</tr>
<tr>
<td></td>
<td>Provocative tests and uroneurophysiologic tests are elective procedures</td>
</tr>
</tbody>
</table>

Modified from Abrams et al. (2010) and Stöhrer et al. (2009).

**Table 14.3**

Main urodynamic findings in patients with spinal cord injury

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Usual clinical finding</th>
<th>Usual urodynamic finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supraconal lesion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>Reflex incontinence</td>
<td>Detrusor overactivity</td>
</tr>
<tr>
<td></td>
<td>Reflex voiding</td>
<td>Detrusor-sphincter</td>
</tr>
<tr>
<td></td>
<td></td>
<td>dyssynergia</td>
</tr>
<tr>
<td>Incomplete</td>
<td>Urge incontinence</td>
<td>Detrusor overactivity</td>
</tr>
<tr>
<td></td>
<td>Reflex voiding</td>
<td>Detrusor-sphincter</td>
</tr>
<tr>
<td></td>
<td></td>
<td>dyssynergia</td>
</tr>
<tr>
<td>Conal lesion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>No voiding</td>
<td>Detrusor acontractility</td>
</tr>
<tr>
<td></td>
<td>Overflow incontinence</td>
<td>Incompetent urethral</td>
</tr>
<tr>
<td></td>
<td>Stress incontinence</td>
<td>closure</td>
</tr>
<tr>
<td>Incomplete</td>
<td>Stress incontinence</td>
<td>Detrusor</td>
</tr>
<tr>
<td></td>
<td>Voluntary voiding using</td>
<td>hypocontractility</td>
</tr>
<tr>
<td></td>
<td>straining</td>
<td>Incompetent urethral</td>
</tr>
<tr>
<td></td>
<td></td>
<td>closure</td>
</tr>
<tr>
<td>Mixed lesion</td>
<td>All possible symptoms</td>
<td>All possible findings</td>
</tr>
<tr>
<td></td>
<td>(combining 1+2)</td>
<td></td>
</tr>
</tbody>
</table>

The patient is asked to describe any sense of bladder filling or need to void. Urine leakage is investigated, sometimes with provocative tests such as coughing or tapping on the suprapubic area. This phase allows recording of bladder sensitivity, capacity, and compliance as well as urethral and detrusor activity during filling.

**Pressure–flow study**

During voiding or attempt to void, fluoroscopic images are taken to investigate the bladder neck and urethra, looking for signs of DSD. The presence and amplitude of detrusor contractions are recorded.

Vesicoureteric reflux, kidney and bladder stones can be identified during the videourodynamics. In patients with autonomic dysreflexia blood pressure measurement during urodynamics is emphasized. A complete report of urodynamic findings is provided by the International Continence Society (Abrams et al., 2003). Possible urodynamic findings in SCI patients are listed in Table 14.2.

**Additional urodynamic tests**

Some provocative tests aim to discriminate between different neurogenic bladder patterns (Chancellor et al., 1998; Riedl et al., 2000; Al-Hayek and Abrams, 2010). During the iced-water test cooled water is rapidly infused into the bladder and detrusor activity is recorded by cystometry. Uninhibited detrusor contraction will appear in patients with upper motor neuron lesion (Fig. 14.4). During the betahanechol test, detrusor activity is recorded by cystometry after administrating betahanechol 5 mg subcutaneously. Detrusor contraction of more
than 25 cm H₂O indicates a detrusor denervation hypersensitivity and muscular integrity of an acontractile detrusor.

At the present time, no specific reports exist about the optimal frequency and techniques of follow-up urodynamics in patients with neurogenic LUTD. A possible recommendation is to perform the first examination as soon as possible after the end of the spinal shock phase. It is then advisable to perform another urodynamic study at 6 months and 12 months after the injury (Abrams et al., 2008). An annual examination is preferable in SCI patients with cervical and thoracic injury for the first 5 years, deferring it to one every 2 years after attaining a low-pressure reservoir with continence and complete emptying. In case of lumbar injury, urodynamics are done annually for the first 2 years and once every 2 years thereafter (Patki et al., 2006b), since bladder dysfunction can change over time without clinical signs of deterioration. Maximal attention should be paid to patients with incomplete suppression of detrusor overactivity and to those who empty their bladder by reflex voiding (Nosseir et al., 2007).

Fig. 14.3. Samples of urodynamic findings.

(A) Normal micturition pattern. B3 (severe urge) at 423 ml. Vertical thin lines: voluntary cough. Vertical white filled arrow: end of filling phase and start of micturition, with a debimetry showing a normal, «bell-shaped», pattern (horizontal dashed line). Please note that the EMG was not recorded.

(B) Areflexic, acontractile lower motor neuron bladder. No filling sensation at the end of filling phase, 520 ml (vertical white filled arrow). From several unsuccessful micturition attempts are realized (vertical dotted arrows, showing the increase in abdominal pressure). Solid black arrow shows that no urinary flow is detected.

(C) Detrusor sphincter dyssynergia. While the ladder fills, a neurogenic detrusor overactivity is detected (solid black arrow). At this time the detrusor contracts (white solid arrow) with a marked concomitant activation of the sphincter (horizontal dotted line), consistent with detrusor sphincter dyssynergia. No micturition is shown at uroflowmetry.
The prophylactic use of antibiotics in patients with SCI having urodynamics is not recommended as routine and potential benefits have to be weighed against risks (Foon et al., 2012).

**Specific uroneurophysiologic tests**

Different neurophysiologic tests may be of use as part of the neurologic clinical assessment of the SCI patient. In the management of neurogenic bladder there are only two tests commonly used: electromyographic activity of pelvic floor, urethral, anal sphincter, and pudendal nerve conduction studies. The former is used commonly with surface electrode during urodynamics and to help diagnose DSD (Blaivas et al., 1981); the latter assess conus medullaris integrity and have a prognostic value (Curt et al., 1997). Recording the sympathetic skin responses from the perineal skin has proven to be useful for assessing sympathetic dysfunction. This impairment is associated with bladder neck incompetence in patients with autonomic disorders due to lesions of the thoraco-lumbar spinal cord. Whereas urodynamic testing remains mandatory for evaluating the functional aspect of voiding disorders in spinal cord-injured patients, the sympathetic skin response partially assesses the neurogenic origin of such disorders. (Borodic et al., 1992; Rodic et al., 2000).

**Ultrasound scan**

Urinary tract ultrasound scan should be performed routinely to identify urinary tract complications such as hydronephrosis and stones (Cameron et al., 2012). Postvoid residual measurement is used to follow bladder emptying in patients who can void. Further imaging, such as computed tomography (CT) scan or isotopic renography, may be necessary for patients with recurrent UTIs or impaired renal function. For the diagnosis of stone, CT scan has a better specificity and sensibility than ultrasound (Tins et al., 2005). Its use is mandatory before any surgical approach of the lower or upper urinary tract in SCI patients (Fig. 14.5).

**Renal function**

Creatinine clearance is preferred to creatinine measurement due to muscular atrophy in SCI patient but creatinine alone is a good test for individual follow-up (MacDiarmid et al., 2000). Other techniques may be proposed, such as isotopic renography and cystatine C measurement (Erlandsen et al., 2012).

**COMPLICATIONS**

**Renal failure**

The incidence of renal failure in SCI patients has dramatically decreased since intermittent self-catheterization has been generally adopted in clinical practice (Strauss et al., 2006). While renal failure was affecting 50% of SCI patients in their 50s, this risk is now estimated to
be low, with only a 3.5-time risk of dialysis compared to the general population (Lawrenson et al., 2001). Neurogenic bladders with presence of high-amplitude detrusor overactivity, DSD, low bladder compliance, and straining to void are considered to be at higher risk, and will require thorough follow-up and management. Among bladder management indwelling urethral and suprapubic catheters are associated with a higher incidence of renal failure (Weld and Dmochowski, 2000b) as well as Credé maneuver (Chang et al., 2000). Other risk factors include amyloidosis, lithiasis, and pyelonephritis.

Vesicoureteric reflux

Vesicoureteric reflux is a consequence of high bladder pressure in SCI patients. It is a risk factor for upper UTIs, stones, and renal function alteration.

Urinary infections

Asymptomatic bacteriuria is common in SCI patients, especially in those who use CISC, and should not be checked systematically or treated. If treated, bacteriuria would recur, with the risk of bacterial stains showing increased antimicrobial resistance (Waites et al., 1993). Symptomatic urinary infections should be treated with antibiotic therapy following an antibiogram (Grabe et al., 2013). Even if a single randomized controlled study shows that 14 days of antibiotic therapy offers a higher microbiologic cure rate than a 3-day course in patients with SCI (Dow et al., 2004), at the present time, the optimal duration of treatment is uncertain (Pannek, 2011). Bladder management, including the CISC technique, should be reassessed in case of recurrent infections. The presence of stones should be excluded by CT scan or by cystoscopy.

Stones

Upper and lower urinary tract stones are more frequent in SCI patients (Bartel et al., 2014), especially during the first year after injury, probably due to immobilization hypercalciuria (Chen et al., 2000). In SCI survivors there is a higher incidence of “infection” stones (struvite and carboxyapatite) than in the general population (DeVivo et al., 1984), but this tends to change with the increase of “metabolic” stones, due to better general management and survival of SCI patients (Matlaga et al., 2006). Long-term risk factors are mainly indwelling urethral and suprapubic catheter as well as bladder augmentation and non-continent diversion (Chartier-Kastler et al., 2002; Ord et al., 2003). The lifetime risk for urinary bladder stones in the general population is 12% for men and 6% for women, with an age-standardised annual incidence of 0.36–1.22/1000 person-years (Chen et al., 2000; Curhan, 2007), whereas in SCI survivors the incidence is 8/1000 person-years (Chen et al., 2000). The cumulative proportion of patients with SCI who had renal stones was 38% in a study with 45 years’ follow-up (which is the longest at this time) (Hansen et al., 2007). Risk factors are hypercalcemia, UTIs, vesicoureteric reflux, indwelling catheter, urinary diversion, and enterocystoplasty (Ku et al., 2006). Screening of urinary tract stones, especially in patients with a high level of injury who may not feel renal colic, is important to prevent further complications, such as infection and renal failure (Gupta et al., 1994; Vaidyanathan et al., 2000).

Bladder cancer

Bladder cancer, in particular squamous cell carcinoma, is more frequent in SCI patients (Hess et al., 2003). Even if bladder cancer incidence significantly varies among authors (from 0.11% to 10% of the SCI population) (Welk et al., 2013), recent data show that the incidence is probably 0.1–2.4% (or an age-standardized incidence rate of 19–77/100 000 persons-year) (Groah et al., 2002a). This is higher than in the general population, where the incidence is 0.02% and age-standardized incidence is 16/100 000 (Canadian Cancer Society’s Steering Committee on Cancer Statistics, 2012). Moreover, patients with SCI develop bladder cancer earlier than the general population. The mean age at time of diagnosis was 48–61 years for people with SCI (Subramonian et al., 2004) compared to 60–70 years in the general population (Silverman et al., 1992), and cancers are more aggressive, with a specific mortality that is 71-fold higher than that in the general population (Groah et al., 2002a). This may be due to chronic inflammation, especially in those with indwelling catheter (West et al., 1999; Groah et al., 2002b). Follow-up by cystoscopy and biopsy is recommended (Groah et al., 2002b; Stöhrer et al., 2009).

THERAPY

Conservative treatment of neurogenic bladder in SCI patients

In SCI patients the goals of treatment of LUTD are:

- to achieve full continence, which is essential to improve social participation and quality of life
- to regularly and fully empty the bladder to reduce the risk of developing lower UTIs and stones
- to maintain or enhance bladder volume, while maintaining low bladder pressure
- to reduce the risk of damaging the high urinary tract, thus preventing chronic renal failure.

To achieve these goals, there are different treatment strategies that can be utilized alone or in combination:
1. Conservative methods, which include:
   (a) triggered reflex voiding
   (b) Crede and Valsalva maneuvers
   (c) drainage systems (CISC, permanent catheterization, external drainage systems)
   (d) drugs (systemic, intradetrusorial, intravesical)
   (e) physical modalities (electric stimulation)
2. Surgical methods.

**Conservative methods**

**Triggered reflex voiding**

This method of voiding consists of triggering uninhibited reflex detrusor muscle contractions to start bladder voiding, usually by suprapubic tapping or by scratching the skin of the inner thigh. In order to achieve this, the sacral micturition reflex must be intact, e.g., an upper motor neuron lesion. However, as DSD is a very common finding in these patients, triggered reflex voiding carries the risk of developing high bladder pressures and vesicorenal reflux. Therefore, it is mandatory to check bladder pressure voiding (which must be below 40 cm H₂O) by urodynamic testing (McGuire and Savastano, 1983). Moreover, in patients with SCI lesions above T6, triggered reflex voiding may carry the risk of autonomic dysreflexia. As reflex bladder contractions are involuntary, nearly all patients who use triggered reflex voiding will require an external collecting device. Even if this method is no longer considered as a first-line treatment in SCI patients, it can be considered in male patients who have neurogenic bladder resistant to anticholinergics, or in tetraplegic male patients unable to perform CISC, mainly after sphincterotomy, as long as the patient can be equipped with a condom catheter. However, these recommendations are based on experts’ consensus and not on scientific evidence (Consortium for Spinal Cord Medicine, 2006).

**Crede and Valsalva maneuvers**

Other methods of voiding are the Crede and Valsalva maneuvers, by which intra-abdominal pressure is raised, thus facilitating urine outflow. It is contraindicated in patients who have a bladder outlet obstruction, and therefore can be considered only for patients with an underactive detrusor muscle associated with an incompetent sphincter (e.g., lower motor neuron lesion or after bladder neck incision).

However, complications are common with these voiding techniques, such as epididymoorchitis, prolapse, and hemorrhoids. Silent upper urinary tract reflex is also not uncommon and careful monitoring is strongly recommended if the patient opts for this emptying method (Giannantoni et al., 1998; Chang et al., 2000). As a consequence, both techniques are currently usually discouraged (Consortium for Spinal Cord Medicine, 2006).

**Drainage systems**

Even if this may be considered a simple but possibly quite invasive solution, drainage aids are the mainstay of LUTD management in SCI and include:

1. intermittent catheterization
2. permanent catheterization (indwelling or suprapubic drainage)
3. external drainage system (condoms).

**Intermittent catheterization.** For more than 60 years, intermittent catheterization has been the method of choice to empty the bladder, achieve continence, and maintain a normal bladder volume and detrusor compliance in SCI patients. This method greatly reduces the incidence of renal failure, urinary reflux, stone formation, urothelial cancer, and probably UTIs compared to other indwelling catheterization (Weld and Dmochowski, 2000b; Groah et al., 2002b; Ord et al., 2003). Ruz et al. (2000) found, in patients with SCI, that the number of UTIs/100 person-days was 2.72 for indwelling catheterization in males and only 0.41 for intermittent catheterization. As early as 1947, intermittent catheterization during spinal shock was strongly advocated by Sir Ludwig Guttmann, who first published in 1949. He was an energetic supporter of a no-touch, sterile technique to reduce the risk of UTIs (Guttmann and Frankel, 1966). Some years later, Lapides et al. (1972) published a paper, which is still considered a milestone in neurourology, defending the use of CISC. The conceptual basis of his work was that a healthy urothelium is more resistant to infections than a sick one. Accordingly, bladder distension with increased intravesical pressure may create an ischemic environment, which fosters infections. Lapides’ concept was that frequency was more important than sterility. CISC is nowadays the method of choice to empty the bladder in all types of neurogenic bladder and, independently from spinal shock, as soon as detrusor overactivity is under control.

There is nowadays enough evidence to say that sterile intermittent catheterization is not superior to the clean technique in reducing UTI risk, both in the rehabilitation setting (Moore et al., 2006) and at home (Moore et al., 2007). Pathogenesis and strategies needed to reduce the risk of UTI are still not completely understood and clearly need more research, as pointed out in a comprehensive review on CISC and UTIs (Wyndaele et al., 2012). It should be considered that, even if CISC is the modality of choice for many SCI patients and it carries...
the lowest risk of long-term renal complications, it has
some risk of urethral complications (mainly lesions,
abrasions, and hemorrhage, with an incidence of 19%)
with further development of infections (urethritis or epidi-
dymoorchitis, with an incidence of 28.5%) (Groah et al.,
2002a). Moreover, in male patients, these complica-
tions can also hamper fertility (Ku, 2006). If CISC is
chosen as bladder management, urodynamic evaluations
are warranted to ensure that filling is achieved at low
pressure and that no vesicorenal refluxes are present,
and an early adequate management of high pressure
detrusor overactivity is mandatory.

To summarize, at present CISC is considered as the
technique of choice in the management of bladder void-
ing after SCI. It can be utilized early, during the phase of
spinal shock and throughout the patient’s life, for every
patient who is willing to learn the technique, has enough
motor control of the hand (or has a caregiver willing
to perform clean intermittent catheterization for the
patient) (Giannantoni et al., 1998; Consortium for
Spinal Cord Medicine, 2006).

Permanent catheterization. Permanent catheteriza-
tion, mainly with a urethral indwelling catheter, is usu-
ally used for acute bladder management immediately
after SCI. Even if it is possible with this method to both
continuously monitor urine output and avoid bladder
overfilling and dissention, permanent catheterization
should be discontinued as soon as possible. Indeed, the
utilization of an indwelling catheter is burdened by fre-
cquent complications (urethritis, urethral erosions,
stones, infections, bladder cancer) (Weld and
Dmochowski, 2000b; Welk et al., 2013). Katsumi et al.
(2010) published a retrospective study in which patients
with SCI and indwelling catheter were followed for sev-
eral years (indwelling urethral catheter group: 133
patients for 23.4 years; suprapubic catheter group:
46 patients for 14.3 years). The rate of complications
was not statistically different between the two groups
(UTI 93% and 98%; urosepsis 15% and 11%; bladder
stone 38% and 41% in the indwelling urethral and supra-
pubic catheter group, respectively). The number of ure-
thral strictures and fistulas, scrotal abscess, and
epididymitis was higher in patients with urethral cathe-
ters but the difference between the two groups was
not statistically significant (Katsumi et al., 2010). The
use of silver alloy-coated catheters or nitrofurazone-
impregnated catheters has not significantly reduced
the risk of UTI (at least in the short term), even if the cost
of these devices is higher than standard catheters (Lam
et al., 2014). Suprapubic catheterization requires a
minimal surgical act, with the risk of bleeding and of
lesions to adjacent organs. The main advantage usually
claimed is a reduction in complication rates, such as
urethral lesions, erosions, and infections (Weld and
Dmochowski, 2000b). However, evidence supporting
these advantages is very limited, and some clinicians
have encountered frequent complications even with
these devices with long-term use (Katsumi et al., 2010;
Hunter et al., 2013). Although Nwadiaro et al. (2007)
published that suprapubic catheterization carries a lower
risk of infections and subsequent mortality in SCI
patients as compared to indwelling catheterization
(65% vs 14%), a recent review found that suprapubic
catheterization is associated with a similar risk of upper
urinary tract damage and stone formation (Hunter et al.,
2013).

Permanent catheterization (both indwelling and
suprapubic) carries the risk of rapidly diminishing blad-
ner compliance, with subsequent development of a
small, hypocompliant bladder, followed by vesicoenal
reflux. Also the risk of bladder stone formation by
permanent catheterization as compared to CISC is
increased. Some authors (Weld and Dmochowski,
2000b; Ord et al., 2003) found that the risk ratio is
10.5 for suprapubic catheters and 12.8 for indwelling ure-
thal catheters (Ord et al., 2003). Therefore, indwelling
catheterization as long-term management of LUTD in
SCI patients should be considered only in older and more
compromised subjects, in those who are not compliant
with intermittent catheterization or in those who refuse
surgery.

External drainage systems. External drainage sys-
tems (condom catheters) may be proposed in male
patients with neurogenic bladder. Drawbacks with the
long-term use of these appliances are bacteriuria, cuta-
neous erosions, UTIs, and penile retraction. Bladder
pressure should be maintained low to avoid high urinary
tract damage, and cutaneous hygiene should be as strin-
gent as possible.

Drugs
Pharmacologic treatments are aimed to act on the detru-
sor muscle or on the bladder neck/sphincter.

Since the detrusor muscle is activated by the action
of acetylcholine on M3 muscarinic receptors and
detrusor overactivity is the most frequent finding in
supraconal lesions, the main pharmacologic tools are
antimuscarinic drugs.

There are several effective antimuscarinic drugs,
including oxybutinin, tolterodine, and trospium chloride.

Despite their extensive clinical use, there are rela-
tively few good randomized, double-blind, placebo-
controlled trials looking at the efficacy of antimuscarinic
drugs in detrusor overactivity in SCI patients (Stöhrer
et al., 1991, 1999; O’Leary et al., 2003; Ethans et al.,
2004; Hortsmann et al., 2006). The majority of studies
published with these medications included patients with neurogenic detrusor overactivity from a different origin, even if the majority of patients had SCI. It should be noted that, in these studies, urodynamic parameters (such as maximum cystometric bladder capacity, maximal detrusor contraction, and bladder capacity) have been taken into account, whereas clinical outcomes (such as incontinence episodes, number of voids per day, or quality of life) are only rarely reported.

Propiverine (Stöhrer et al., 1999), oxybutinin (O’Leary et al., 2003), and trospium chloride (Stöhrer et al., 1991) have been shown to be effective in improving maximum cystometric bladder capacity and in reducing the number of voids per day.

Propiverine, at a dose of 15 mg three times a day, has been shown to be more effective than placebo in a randomized controlled trial on a population of 124 patients with SCI, in increasing bladder capacity (by 72 mL vs 35 mL under placebo) and maximal cystometric capacity (by 104 mL, in comparison with a decrease with placebo), in reducing maximal detrusor contractions (by 27±32 cm H2O), and in improving clinical symptoms (63.3% of the patients reported “improved” symptoms in comparison with 22.6% under placebo) (Stöhrer et al., 1999).

In a randomized controlled trial on 61 patients with SCI, trospium chloride, at a dose of 20 mg twice a day, has been shown to be more effective than placebo in improving maximal cystometric capacity and in reducing maximal detrusor pressure, with a low rate of side-effects that did not differ between placebo and active treatment group (Stöhrer et al., 1991). This study did not report data regarding incontinence or other urinary symptoms.

In a randomized controlled trial conducted on a small population of SCI survivors (10 patients), an extended-release form of oxybutinin, at a dose of 10 mg/day (progressively increased to 30 mg/day), has been shown to improve maximal cystometric capacity and to reduce the mean number of voids per day by concomitant reduction of the number of incontinence episodes per week (O’Leary et al., 2003).

Stöhrer and colleagues (2007) compared the efficacy and side-effects of propiverine (15 mg three times per day) with oxybutinin (5 mg three times a day) in a randomized controlled trial conducted on a population of 131 patients with SCI. They showed that both drugs were effective, with no significant difference between them in improving maximal cystometric capacity, in decreasing maximal detrusor pressure, and in improving bladder compliance. The propiverine group reported fewer side-effects than those treated with oxybutinin. They also found a decrease of 1.3 incontinence episodes following oxybutinin compared with a decrease of 1.6 episodes following propiverine.

However, in clinical practice, it is common for patients to need a combination of antimuscarinic drugs or a regimen of progressively increased doses, beyond the recommended upper limits. To evaluate the efficacy of this strategy of treatment and its safety, Amend and colleagues (2008) conducted a study on 27 patients with SCI, who were formerly and unsuccessfully treated with a single anticholinergic drug. Patients were divided into three groups: one received 8 mg tolterodine and 15–30 mg oxybutinin; another group received 90 mg trospium chloride and 4–8 mg tolterodine; the third group received 30 mg oxybutinin and trospium chloride (45–90 mg). Data showed that there was no significant difference between groups (either in efficacy or in side-effects) in decreasing the number of incontinence episodes and improving bladder capacity, as well as detrusor compliance. Treatment was considered successful in 85% of patients independently of which group they were assigned to.

In summary, in all these trials antimuscarinic drugs were shown to be effective at reducing urine leakage between catheterizations and in improving urodynamic parameters (such as reflex volume, amplitudes of detrusor contractions, and bladder capacity) as compared to placebo (Stöhrer et al., 1991, 2007, 2013; Ethans et al., 2004). Therefore, all antimuscarinic agents are the primary treatment for urinary incontinence and the prevention of high voiding pressure in SCI patients. However, even if effective, the side-effects of these medications (dry mouth, constipation, and blurred vision, among others) frequently limit their use in the clinical setting (Stöhrer et al., 2007; Amend et al., 2008). Active controlled studies reported a higher frequency of side-effects for oxybutynin 5 mg three times per day compared to trospium chloride 20 mg twice per day (23% of patients reporting dry mouth vs 4%), with a lower discontinuation rate for trospium chloride (6% vs 16%) (Madersbacher et al., 1995).

Trospium chloride is a quaternary ammonium compound that does not pass the blood–brain barrier; therefore, it is less prone to develop cognitive side-effects. It is recommended in older patients or in those with cognitive impairment, but other side-effects, like dry mouth, remain. Increasing the dose or combination therapy can be offered to maximize efficacy but patient compliance with long-term utilization of multiple drugs can be a serious issue and caution is recommended in SCI patients with cardiac arrhythmias, especially with the combination of these medications.

Transdermal administration of oxybutinin could have been an alternative to oral medication, with the same positive effect and less dry mouth (Kennelly et al., 2009), but one-third of patients in this study had to stop this medication due to cutaneous eruption.
Other drugs that have been utilized to reduce detrusor overactivity in SCI patients are vanilloids, capsaicin, and resiniferatoxin (Chancellor and de Groat, 1999). The rationale for their use is that the vanilloid receptor TRPV1 plays a role in detrusor contraction, and is essential for purinergic signaling (Birder et al., 2002). In SCI patients with detrusor overactivity, TRPV1 is overexpressed, and the use of one of its agonists, such as capsaicin, can inactivate C-fiber conduction and reduce bladder overactivity (see Chapter 5). Resiniferatoxin, which is 1000 times stronger than capsaicin, can also be used. Intravesical instillations of resiniferatoxin and capsaicin have been utilized to reduce detrusor overactivity in SCI patients, with significant urodynamic improvements (de Sèze et al., 2004; Shin et al., 2006). The main advantage of resiniferatoxin is that it seems to have fewer side-effects (e.g., pain, hematuria), than capsaicin, which is now abandoned, even if the side-effects observed may have been provoked by the alcoholic solvent concentration rather than the drug itself (de Sèze et al., 2004). However, the relatively short duration of the effects of resiniferatoxin and the instability of the solution have also led to its limited clinical use.

Anticholinergic drugs such as atropine and nociceptin/orphanin FQ have also been utilized intravesically to treat neurogenic detrusor overactivity (Lazzieri et al., 2006; Fader et al., 2007), but currently their use is limited to clinical trials, with the exception of oxybutinin.

Drugs that have been utilized to improve bladder obstruction due to overactivity of the bladder neck and the external sphincter are alpha-adrenergic antagonists, such as moxisylyte, terazosin, or tamsulosin (Costa et al., 1993; Linsenmeyer et al., 2002; Abrams et al., 2003). As example, in the study of Abrams and colleagues, long-term tamsulosin treatment (0.4 and 0.8 mg once daily) was shown to be effective and well tolerated in patients with neurogenic LUTD in improving bladder storage and emptying, and decreasing symptoms of autonomic dysreflexia. However, is important to note that all these studies showed a reduced arterial pressure in SCI patients, which is a dose-dependent effect. Therefore, these drugs should be utilized cautiously in SCI patients with orthostatic hypotension or in tetraplegic patients with acquired hypotension.

Finally, there is also some experience with the utilization of alpha-adrenergic agonists and beta-adrenergic agonists to increase resistance in patients with an incompetent sphincter, with some beneficial effect, even if the evidence is weak in patients with neurogenic bladder and side-effects have usually limited the clinical use of these drugs (Alhasso et al., 2005).

Botulinum toxin. The first use of botulinum toxin type A (BoNT-A) to treat neurogenic detrusor overactivity in SCI patients was published in 2000 by Schurch et al. (2000a, b). After this non-placebo-controlled trial, the same authors published a rigorous, randomized, placebo-controlled trial that confirmed the significant effect of botulinum toxin on continence and urodynamic parameters (e.g., maximum cystometric capacity, bladder compliance, and maximum detrusor pressure). Improvements were maintained for up to 6 months (Schurch et al., 2005). The authors found, in the groups treated with BoNT-A 200 and 300 IU, a reduction in incontinence episodes of nearly 50% and a mean improvement in maximum cystometric capacity of 186.1 and 215.8 mL, and a reduction in maximum detrusor pressure of 66.3 and 52.9 cm H2O (in the 300 and 200 IU groups respectively). These three parameters did not change significantly in the placebo group.

After these pivotal studies, other well-conducted randomized controlled studies were published (Ehren et al., 2007; Schurch et al., 2007; Cruz et al., 2011; Ginsberg et al., 2012; Sussman et al., 2013), which all came to the conclusion that, at present, BoNT-A is a cornerstone in the treatment of neurogenic detrusor overactivity in patients with SCI (Mehta et al., 2013). After intramuscular injection in the detrusor muscle (done under cystoscopy) BoNT-A mainly acts by inhibiting the release of acetylcholine at the presynaptic junction. Along with this primary action, some authors have proposed that BoNT-A may inhibit the release of various neurotransmitters, like adenosine triphosphate, substance P, and calcitonin gene-related peptide (Apostolidis et al., 2006). Even if detrusor overactivity is the most frequent indication for BoNT-A treatment in SCI patients, it may also be utilized to treat DSD, using a transperineal or a cystoscopic approach (Schurch et al., 1996; de Sèze et al., 2002; Kuo, 2003). In the treatment of DSD, the mean dose of onabotulinumtoxinA usually varies between 50 and 100 IU (Schurch et al., 1996; de Sèze et al., 2002; Gallien et al., 2005).

To treat neurogenic detrusor overactivity, doses commonly administered are between 200 and 300 IU of onabotulinumtoxinA (Botox) (Schurch et al., 2005; Cruz et al., 2011; Ginsberg et al., 2012) or 500–1000 IU of abobotulinumtoxinA (Dysport) (Del Popolo et al., 2008; Grise et al., 2010). Reimbursement is accepted in almost all countries for dosage up to 200 units of onabotulinumtoxinA (Botox). The effect of one injection session lasts on average 9 months (Schurch et al., 2005; Cruz et al., 2011; Herschorn et al., 2011). Repeated injections up to five times show similar results as after the first injection (Reitz et al., 2007), without ultrastructural detrusor changes before and after BoNT-A treatment (Haferkamp et al., 2004).

Beside its therapeutic effect, it seems that BoNT-A treatment can reduce costs and resource use for patients
DYSFUNCTION OF LOWER URINARY TRACT IN PATIENTS WITH SPINAL CORD INJURY

Physical modalities (electric stimulation)

Electrical stimulation has been utilized for years in the treatment of LUTD. Several techniques have been utilized, such as anogenital electric stimulation, transcutaneous electric stimulation, and percutaneous posterior tibial nerve stimulation. However, in this section we will focus on techniques that have been utilized in patients with SCI:

1. Intravesical stimulation (IVES)
2. Neuromodulation
3. Sacral root stimulation (SRS) combined with sacral root deafferentation (SRD)

Intravesical stimulation. Even if it has been in use since the 19th century (the first report was produced by Saxtorph, a Danish surgeon in 1878) (Madersbacher, 1990a), IVES treatment is still controversial, with little evidence concerning its efficacy. Its main mechanism is to elicit detrusor muscle contraction by electric stimulation, making this treatment a possible option for patients with partial lower motor neuron bladder. IVES has also been utilized to improve bladder sensation in incomplete SCI patients. However, at present, only a few, uncontrolled studies focusing on this topic have been published (Madersbacher et al., 1982; Lombardi et al., 2013).

Neuromodulation. Vodusek et al. showed, in 1986, that an overactive detrusor muscle could be inhibited by stimulation of the pudendal nerve. Similar results have been obtained later in patients with SCI by other authors, who pointed out that some carry-over effect can also be achieved (Wheeler et al., 1992; Previnaire et al., 1996). Magnetic (Sheriff et al., 1996) or electric stimulation (Chartier-Kastler et al., 2001) of the sacral roots S2–4 probably has the same effect as stimulation of the pudendal nerve. However, the main problem with this treatment is that, even if it is effective in the short term, its application as long-term use is more difficult.

In 2010 Sievert et al. published a small controlled study on the early application of bilateral sacral neuromodulation in patients with complete SCI above T12. Up to 39 months after implantation, none of the patients treated with neuromodulation developed an overactive bladder. Further studies are required to confirm these data.

Sacral root stimulation combined with sacral root deafferentation. The electric stimulation of the sacral roots to improve bladder control in patients with SCI was developed by Brindley in 1969; he published his first results in 1982. By this method, bladder emptying is achievable by electrical stimulation of the anterior sacral roots (SRS). However, to obtain a low filling bladder pressure, electrode stimulation has to be preceded by posterior root rhizotomy (SRD) of S2–4. After SRD, the bladder becomes areflexic, allowing a greater capacity and low bladder filling pressures. The most utilized electrostimulation system (known as the Finetech–Brindley system) consists of an implanted stimulator with a receiver that can be controlled by an external transmitter device. By varying patterns of stimulation it is possible for the patient to control bladder and bowel function. Despite its drawbacks of altered male sexual function due to SRD, global satisfaction with SRS combined with SRD is generally high (Creasey et al., 2001; Martens et al., 2011). Kirkham et al. (2002) proposed the application of SRS without dorsal rhizotomy, using an electrosystem able to stimulate both anterior and posterior roots. Increased bladder capacity could be observed in 60% of patients; however, incomplete voiding remained due to persisting DSD. In the same vein and more recently, Possover (2009) introduced a new technique in patients with SCI, utilizing a laparoscopic placement of neural electrodes on both dorsal and ventral sacral nerves as well as the pudendal nerves (laparoscopic implantation of neuroprosthesis: LION procedure) aiming to improve voiding and bladder filling. The procedure was reported as minimally invasive, with a small complication rate. In his small case series (eight patients), bladder emptying was complete up to
27-month follow-up. However, long-term follow-up has not yet been published and the results have not yet been replicated by other groups. As a consequence, further investigations are needed.

**Summary**

CISC of the bladder is so far the gold standard to void a neurogenic overactive bladder in SCI. In selected patients reflex triggered voiding can be utilized, but the upper urinary tract must be kept safe with low bladder pressure. In many patients with supraconal spinal lesions, detrusor muscle overactivity limits maximum bladder volume and therefore continence, even with a careful intermittent catheterization plan. In this case, antimuscarinic drugs are the first choice to reduce detrusor overactivity, and in turn to protect the kidneys and achieve continence. When antimuscarinic drugs are not effective or not tolerated, BoNT-A is a good alternative to control neurogenic detrusor overactivity.

In refractory patients, SRS may be utilized to control detrusor overactivity. However, to obtain satisfying control of bladder overactivity, SRD is usually necessary, with secondary loss of reflex erections and ejaculation in males. Newer techniques (anterior and posterior stimulation, LION procedure) may reduce these problems but further studies are needed.

In patients with lower motor neuron bladder, intermittent catheterization is usually the better choice, even if, in some patients with low outflow resistance, voiding by Credé and Valsalva maneuvers can be also be used.

When conservative treatment fails or the risk of deterioration of the urinary tract is high, surgery is taken into consideration.

**Surgical Management**

Surgical therapy is indicated when adequate bladder management is not achieved with other measures and in cases when renal failure develops. The aim of any surgical management is to preserve the upper urinary tract and improve quality of life. It should cater to the patient’s desire to be treated, as well as the patient’s cognitive and mobility abilities. Patients with supraconal lesion and reflex bladder may require surgery due to refractory detrusor overactivity and loss of bladder capacity and patients with conal lesion and areflexic bladder may require surgery due to stress incontinence. In some other conditions, surgical intervention should definitely be considered, including tetraplegia, decreased ability to catheterize, e.g., due to aging or obesity, difficulties with undressing (spasticity, limitations at the upper limbs), and in the case of bladder cancer.

**Enterocystoplasty**

Bladder augmentation enterocystoplasty is a standard treatment option for patients with neurogenic bladder, low bladder compliance, and preserved renal function (Chartier-Kastler et al., 2000). Usually an ileal segment is detubulated and applied to the opened bladder, or after supratrigonal excision of the bladder (Karsenty et al., 2008; Gobeaux et al., 2012). However, other segments (colon or stomach) can be utilized. The rationale for this technique is that, by increasing the radius of the bladder, pressure is lowered with unchanging wall tension (following Laplace’s law). The patient will have to catheterize either through the urethra or through an abdominal stoma to empty the bladder because the intestinal segment used to augment the bladder has only passive elastic properties.

The most frequent complication of enterocystoplasty is the accumulation of mucus production from the intestinal mucosa, requiring bladder washing. The most severe complication is perforation, which may have fatal consequences. Chartier-Kastler et al. (2000) reported, in a group of 17 patients with SCI followed up to 10.5 years, complete continence under CISC in 88.5% and, as a long-term complication, a patient who had recurrent pyelonephritis. In females, since no effective external collecting device exists, additional stress incontinence surgery may be offered at the same time, such as an artificial urinary sphincter (Khoury et al., 1992) or a urethral sling and colposuspension (see later). Current evidence strongly suggests that enterocystoplasty improves bladder capacity and compliance (Singh and Thomas, 1995; Chartier-Kastler et al., 2000), with an improvement in quality of life (Khastgir et al., 2003).

**Urinary diversion**

Urinary diversion is a surgical procedure in which urine is no longer drained into the bladder but into a reservoir that is made for urine storage. This allow the replacement of a non-functional bladder, for example in patients with spina bifida or bladder malformation, after a radical cystectomy for bladder cancer, or in some SCI patients with a refractory overactive bladder.

Urinary diversions have been made by surgeons for more than 150 years, with the first procedure described being ureteroproctostomy by Simon in 1851, although it was in 1950 that Eugene M. Bricker made the first neo-bladder with an ileal loop. In this procedure the ureters are resected from the bladder and an anastomosis is created with a detached section of ileum. At present, there are different techniques (Koch pouch, Indiana pouch, orthotopic diversion, and others) that have evolved from Bricker’s intervention.
Currently, urinary diversion falls into two categories:

1. continent diversions
2. non-continent diversions.

**CONTINENT DIVERSIONS**

In continent diversions the neobladder, made from a detubularized ileal segment, is connected to the abdominal wall by a small abdominal stoma, which can be created using an ileal conduit (using the Mitrofanoff procedure (Sylora et al., 1997) or other procedure such as Yang–Monti modified technique (Casale, 1999)). Neobladder emptying is performed by regular CISC through a stoma, which can be hidden in the umbilicus. This technique is recommended in people with tetraplegia and difficulties in performing CISC and mainly in female patients (Chartier-Kastler et al., 2002; Karsenty et al., 2008), or in patients who have severe urethral erosions and incontinence (Colli and Lloyd, 2011). People with kidney failure or limited liver function are usually not considered good candidates for continent diversions, due to potential problems with reabsorption of urea through the ileal wall. At present, data on patient satisfaction, continence, and neobladder functioning are encouraging (Sylora et al., 1997; Chartier-Kastler et al., 2002; Karsenty et al., 2008). However, the procedure can be complicated by infections (pyocystitis and pyonephritis) and both reservoir and new-onset upper tract stones (32% and 22.5% of patients respectively) (Chen and Kuo, 2009). Moreover, the long-term safety (especially with respect to malignancies) is still unknown.

**NON-CONTINENT DIVERSIONS**

This is the most widely known procedure. The neobladder is connected to the abdominal wall through a small stoma, permitting urine output, that is collected into a bag and regularly emptied by the patient or caregiver. The main indications for non-continent bladder diversion are: (1) a neurologic bladder associated with complications that prevent restoration of an adequate bladder; (2) SCI patients without sufficient upper-limb skills to provide clean self-catheterization; (3) patients showing lower urinary complications secondary to indwelling catheters (urethral destruction, mainly in females, and urethrocystourethral fistulas); and (4) hydronephrosis secondary to vesicoureteral reflux or a thickened bladder wall.

According to the literature, continence rate and patient satisfaction are high (Chartier-Kastler et al., 2002; Kato et al., 2002), even if the procedure is accompanied by some complications (36% of patients in the study by Chartier-Kastler et al. had one or more postoperative complication, mainly infectious, but also intestinal obstruction due to adhesions and strictures and stone disease).

Bladder diversion techniques are often carried out with cystectomy due to the risk of recurrent infection, pyocystitis, or bladder cancer.

**Artificial urethral sphincter**

In 1946, Frederic Foley proposed the implantation of an artificial sphincter, which was an inflatable cuff put around the urethra. After the development of different models, in 1983, the first completely implantable system with a deactivation button was introduced (AMS 800). This technique has been developed to treat stress incontinence, but it has also been utilized in patients with SCI. The technique should be somewhat modified in male SCI patients, since voiding the bladder by CISC can induce urethral erosions. Moreover, in these cases, the cuff will usually be placed at the periprostatic urethra because of the prolonged sitting position in a wheelchair that creates the risk of overpressure on the cuff and subsequent decubitus.

The implantation of an artificial sphincter in patients with SCI has been proved to significantly improve continence in nearly all patients at short-term follow-up and in more than an half in the longer term (Patki et al., 2006a; Bersch et al., 2009; Chartier Kastler et al., 2011). Main risks are infection and malfunctioning of the device. In patients with myelomeningocele and poorly compliant bladder, the implantation of a sphincter prothesis is usually associated with enterocystoplasty. In patients with neurogenic stress urinary incontinence who are not willing to undergo or unsuitable for this invasive surgery, a periurethral balloon device placed in the perineal area might be an alternative (Mehnert et al., 2012).

**Transurethral sphincterotomy**

Transurethral sphincterotomy is a common surgical method to treat DSD. It is usually indicated in tetraplegic male patients with SCI and DSD, in association with condom catheters and in patients unwilling or unable to perform intermittent catheterization. This procedure reduces urinary outflow resistance with the objective of reducing intravesical pressure. Improvement in bladder emptying and stabilization of the upper urinary tract has been shown in 70–90% of treated SCI patients (Wein et al., 1976; Perkash, 2007).

Different techniques exist, but the most commonly utilized and described in the literature is the transurethral approach, inserting an endoscope in front of the verumontanum and descending it through the sphincter to the bulbar urethra. The sphincter may be cut by a diathermy electrode or laser. Laser sphincterotomy seems
to be burdened with fewer complications (Noll et al., 1995; Perkash, 1996) and is at present the recommended technique. Bladder leak point pressure greater than 40 cm H$_2$O seems to be a useful parameter in predicting sphincterotomy success or surgical outcome (Vapnek et al., 1994; Juma et al., 1995). Moreover, in the long term, the reoperation rate is around 30% (Juma et al., 1995).

Several studies have evaluated the efficacy of urethral stent placement instead of sphincterotomy (Abdill et al., 1994; Chancellor et al., 1995; Mehta and Tophill, 2006; Seoane-Rodriguez et al., 2007; Abdul-Rahman et al., 2010). The main finding of these studies (which are case series or retrospective studies) is that stent placement might be an effective short-term technique in reducing voiding pressure, postvoid residual volume, autonomic dysreflexia, and UTIs. However, the overall life duration of a stent is relatively short (usually 2 years), due to deformation, migration, and incrustation of the device (Mehta and Tophill, 2006).

To answer the question of whether a urethral stent placement is a valid alternative to endoscopic transurethral sphincterotomy, Chancellor et al. (1999) conducted a randomized study in 57 patients with SCI. The two techniques were equally effective at reducing maximal bladder pressure and postvoid volume as well as in improving quality of life and patient satisfaction. In the long term, the need to replace the stent was present in 19% of cases and for repeated transurethral sphincterotomy was 8% (Chancellor et al., 1999).

CONCLUSION

Better understanding and management of LUTD in SCI patients have led to a dramatic change in survival and quality of life for these patients.

Both evaluation and treatment should be carried out in specialized institutions with physicians who are trained in spinal cord medicine.

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