Basic Neuro-urology
Workshop 13
Monday 23 August 2010, 09:00 – 12:00

Time	Time	Topic	Speaker
09:00	09:20	Neurogenic lower urinary tract (LUT) dysfunction - from Neurophysiology via Pathophysiology to Clinics	John Heesakkers
09:20	09:30	Discussion	
09:30	09:50	Diagnostic workup How informative are basic diagnostics, are urodynamics essential?	Jean Jacques Wyndaele
09:50	10:00	Discussion	
10:00	10:10	How to maintain normal renal function, how to achieve continence/to manage incontinence Therapeutic strategies in 2010 – introduction	Helmut Madersbacher
10:10	10:30	Management of the overactive detrusor, combined with overactive sphincter, underactive sphincter and normal sphincter	Piotr Radziszewski
10:30	11:00	Break	
11:00	11:10	Discussion	
11:10	11:30	Management of the underactive (acontractile) detrusor, combined with overactive sphincter, underactve sphincter and normal sphincter	Helmut Madersbacher
11:30	12:00	General discussion	
12:00		End of workshop	

Aims of course/workshop

Target Audience

This educational course is for doctors, nurses and physiotherapists, who are interested in Neuro-Urology. We assume that the participants have only little experience with this subspeciality. The main focus will be on the every-day care of a patient with neurogenic bladder and on the therapy which is available in every centre.

In the first part of this workshop Prof. J. Heesakkers (The Netherlands) will talk on neurogenic lower urinary tract dysfunction, giving you firstly information on the neurophysiology of the lower urinary tract and secondly on the pathophysiology related to cerebral, spinal and peripheral lesions and how they are reflected in clinical symptoms and findings.

Prof. J. Wyndaele (Belgium) will inform you about the diagnostic workup:
Patients with known neurologic disease often need evaluation to objectivity neurologic bladder, not only if symptoms occur, but as a standard diagnostic approach if neurogenic bladder has a high prevalence in this disease. A possible neurologic cause of « idiopathic » LUTS should be considered. LUTS in neurologic patients do not necessarily relate to the neurologic pathology. Other diseases such as prostate pathology, pelvic organ prolapse, might have an influence. Extensive diagnostic workout seems useful and necessary only to tailor an individual treatment based on complete neuro-functional data. This may not

be needed in every patient e.g. patients with suprapontine lesions or in patients where treatment will consist merely of bladder drainage due to bad medical condition or limited life expectancy. Diagnostic methods of neurologic LUT dysfunction and neurologic urinary incontinence are not very different from what is done in non neurologic patients. Clinical neurological findings correlate well in some pathology but not in other pathology with the dysfunction of the LUT as diagnosed by urodynamic studies. Therefore, one should not rely solely on a clinical neurological examination to outline the urological management in such patients. Urine test, blood test, sensation related bladder diary, imaging can be important

Classic urodynamic techniques permit the acquisition of multiple functional parameters in patients with neurologic bladder. The literature gives enough evidence of the value of different techniques in neurologic urinary incontinence and retention

- Pressure-flow study can demonstrate an obstructive pattern (high pressure voiding) also in neurologic patients due to urethral relaxation failure or a more anatomical obstruction as from prostate
- Video urodynamics permit to evaluate bladder neck and urethral sphincter activity during filling and voiding, can help detect vesicoureteral reflux and diverticula.
- CMG filling rate seems to be very important especially in neurologic patients.
- The determination of CMG filling sensation is important for diagnosis and treatment.

Special tests, ice water test, bethanechol supersensitivity test, as well as electrodiagnostic tests can be applied in specific indications to help improve the diagnosis.

The management of neurogenic lower urinary tract dysfunction still aims to maintain normal renal function, to manage urinary incontinence or possibly to achieve continence.
Therapy depends firstly on the underlying dysfunctional pattern of the lower urinary tract, secondly also on the individual patient who often has limitating co-morbidities. Moreover, one and the same dysfunctional pattern can be caused by different neurological diseases with different prognosis and different course of the disease, which may also influence the choice of treatment.

In the therapeutic part we will give you an overview on the therapeutic strategies in 2010 in patients (1) with an overactive detrusor combined either with an overactive sphincter, an underactive sphincter or a normal sphincter. This will be pointed out by Prof. P. Radizewski (Poland); (2) Prof. H. Madersbacher (Austria) will give an overview on the management of the underactive (acontractile) detrusor again either combined with an underactive sphincter, an overactive sphincter or a normal sphincter.

Educational Objectives

Having participated in this course, which will also include case presentations discussed with the audience, you should have a basic knowledge on neurogenic lower urinary tract dysfunction, its pathophysiology, its diagnostic workup, moreover you should be aware what can be offered to the individual patient nowadays.

For more information see the handouts of this course, which delegates can download from the ICS-IUGA website and which will be also on your meeting-USB-stick.

ICS-IUGA 2010

Workshop 13

Basic Neurourology

Chair: Helmut Madersbacher

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Speakers:	Country:
1: John Heesakkers	The Netherlands
2: Jean Jacques Wyndaele	Belgium
3: Piotr Radizewsky	Poland
4: Helmut Madersbacher	Austria

Agenda & Itinerary

- **Neurogenic lower urinary tract (LUT) dysfunction**
  – from Neurophysiology via Pathophysiology to Clinics
  J. Heesakkers (The Netherlands) 20 min.

- **Diagnostic workup:**
  How informative are basic diagnostics, are urodynamics essential ?
  J.J. Wyndaele (Belgium) 20 min

Break

- **How to maintain normal renal function, how to achieve continence / to manage incontinence**
  Therapeutic strategies in 2007

- **With overactive detrusor**
  + overactive sphincter
  + underactive sphincter
  + normal sphincter
  Piotr Radizewski (Poland) 20 min

- **With underacitve (acontractile) detrusor**
  + underactive sphincter
  + overactive sphincter
  + normal sphincter
  H. Madersbacher (Austria) 20 min

Aims of course/workshop

This Educational course is for doctors, nurses and physiotherapists, who are interested in Neuro-Urology. We assume, that the participants have no or only little experience with this subspeciality.

Key learning points

The main focus will be on the every-day care of a patient with neurogenic bladder and on the therapy which is available in every centre.

Concluding key points

Having participated in this course, which will also include case presentations, you should have a basic knowledge on neurogenic lower urinary tract dysfunction, its pathophysiology and its diagnostic workup, moreover you should be aware what can be offered to the individual patient nowadays.

Neurogenic Lower Urinary Tract Dysfunction
– *from Neurophysiology via Pathophysiology to Clinics*

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INTRODUCTION

The lower urinary tract (LUT), the urinary bladder and urethra, serves two reciprocal functions: storage of urine without leakage and periodic evacuation of urine. These two functions depend on central as well as peripheral autonomic and somatic neural pathways,[1, 2] but also on voluntary control which requires the participation of higher centers in the brain. Because of the complex neural regulations, the central and peripheral nervous control of the LUT is prone to a variety of neurological disorders. In this lecture the principals of neuronal control of the LUT function will be summarized as well as the pathophysiology of neurogenic LUT dysfunction in specific lesions.

NEUROPHYSIOLOGY OF THE LOWER URINARY TRACT

Normal LUT function

The LUT function can be divided in storage and voiding functions. Normal storage function includes 1) sensation bladder fullness, 2) postpone urination, 3) maintaining continence and 4) low bladder pressure. Normal voiding function means to void voluntarily and smoothly without straining or post-void residual.

Reflex pathways controlling urine storage and voiding

Coordinated activities of the peripheral nervous system innervating the LUT during urine storage and voiding depend on multiple reflex pathways organized in the brain and spinal cord. The central pathways regulating LUT function are organized as on-off switching circuits that maintain a reciprocal relationship between bladder and its outlet.[1-3]

The storage phase

The accommodation of the bladder to increasing volumes of urine is primarily a passive phenomenon dependent on the intrinsic properties of the detrusor.[1-4] In addition to this passive accommodation mechanism, the afferent activity induced by bladder distention can trigger reflex activation of the sympathetic outflow to the LUT. It contributes to the storage mechanism that inhibits the parasympathetic efferent outflow to the bladder and promotes closure of the urethra through activation of α_{1A}-adrenoceptors. Furthermore it facilitates relaxation of the detrusor via activation of β_{3}-adrenoceptors[4] (**Figure 1A**). This reflex is organized in the lumbosacral spinal cord. During bladder filling, the bladder afferent input also activates the pudendal motoneurons innervating the external urethral sphincter (EUS) [3, 5] and increases EUS activity. The EUS motor neurons are also activated by urethral/perineal afferents in the pudendal nerve[6]. These excitatory sphincter reflexes are organized in the spinal cord. Moreover, a supraspinal urine storage center located in the dorsolateral pons sends descending excitatory inputs to the EUS motoneurons to increase urethral resistance[7,8] (**Figure 1A**).

The voiding phase

The storage phase can be switched to the voiding phase either involuntarily or voluntarily. When bladder volume reaches the micturition threshold, bladder afferents in the pelvic nerves trigger the micturition by acting on neurons in the sacral spinal cord, which then send their axons rostrally to the periaqueductal gray (PAG), which in turn communicates with the pontine micturition center (PMC)[9, 10]. Activation of the PMC reverses the pattern of efferent outflow to the LUT, inhibiting sympathetic and somatic pathways and activating parasympathetic pathways. The voiding phase consists of an initial relaxation of the urethral sphincter followed by a contraction of the bladder. Thus voiding reflexes depend on a spinobulbospinal pathway (**Figure 1B**). Secondary reflexes elicited by urine flow into the urethra also facilitate bladder emptying.[1, 3] Inhibition of EUS activity during voiding depends, at least in part, on supraspinal mechanisms.

Peripheral and spinal pathways

The peripheral nervous mechanisms for bladder emptying and urine storage involve efferent and afferent signaling in pelvic (parasympathetic), hypogastric (sympathetic) and pudendal (somatic) nerves.[1, 2] (**Figure 2**).

Efferent pathways of the LUT

1. Parasympathetic pathways

Pelvic parasympathetic nerves, which arise at the sacral spinal cord (S_2-S_4), provide an excitatory input to the bladder and an inhibitory input to the bladder neck and urethral smooth muscle to eliminate urine [1, 2, 11] (**Figure 2**). Parasympathetic preganglionic neurons send axons to peripheral ganglia. Parasympathetic postganglionic neurons in humans are located in the bladder wall.[3] Parasympathetic postganglionic nerve terminals release Acetylcholine (ACh), which can excite muscarinic receptors in the detrusor smooth muscle cells, leading to bladder contractions.[12,13] The postganglionic parasympathetic input to the urethra elicits inhibitory effects mediated at least in part through the release of nitric oxide (NO), which directly relaxes the urethral smooth muscle.[3, 14, 15] Therefore, the excitation of sacral parasympathetic efferent pathways induces a bladder contraction and urethral relaxation to promote bladder emptying during micturition.

2. Sympathetic pathways

Hypogastric sympathetic nerves, which arise at the thoraco-lumbar level of the spinal cord (Th_{11}-L_2), provide a noradrenergic inhibitory input to the bladder and excitatory input to the urethra to facilitate urine storage[3] (**Figure 2**). The sympathetic activation causes inhibition of the parasympathetic pathways at spinal and ganglionic levels, and releases noradrenaline (NA) from its postganglionic terminals, which elicit relaxation the bladder body and contractions of the bladder neck and urethral smooth muscle[3].

3. Somatic pathways

Somatic efferent motoneurons which activate the external striated urethral sphincter muscle and the pelvic floor muscle are located along the lateral border of the ventral horn in the sacral spinal cord (S_2-S_4), commonly referred to as the Onuf's nucleus [16] (**Figure 2**). The somatic motoneurons send axons into the pudendal nerves. Combined activation of sympathetic and somatic pathways increases bladder outlet resistance and realises urinary continence.

Afferent pathways of the LUT

The pelvic, hypogastric, and pudendal nerves also contain afferent axons that transmit information from the LUT to the spinal cord (**Figure 2**). [1, 2, 17, 18] The pelvic afferent nerves, which monitor the volume of the bladder and intravesical pressure, consist of small myelinated A◎ and unmyelinated C fibers. Normal micturition reflex is mediated by myelinated A◎ fibers, which respond to bladder distention and active contraction[3, 18, 19] (**Figure 3**). The activation threshold for A◎ fibers is 5-15 cmH_2O[1]. C-fiber afferents have a high mechanical threshold and are usually unresponsive to mechanical stimuli such as bladder distention[19] and therefore have been termed as "silent C fibers". However, these fibers respond primarily to chemical, noxious, or cold stimuli. During inflammation or neuropathic conditions, there is recruitment of C-fiber bladder afferents, which form a new afferent pathway that can cause detrusor overactivity and bladder pain[20] (**Figure 3**).

Brainstem (Pons)

The dorsal pontine tegmentum has been established as an essential control center for micturition and called as the "pontine micturition center (PMC)" or the "M region" due to its median location.[10, 21, 22] Brain imaging studies have revealed increase in blood flow in this region of the pons during micturition.[23] Neurons in the PMC provide direct synaptic inputs to sacral PGN, as well as to GABA-nergic neurons in the sacral dorsal commissure (DCM).[21] The former neurons carry the excitatory outflow to the bladder, whereas the latter neurons are thought to be important in mediating an inhibitory outflow on EUS motoneurons during micturition[24]. As a result of these reciprocal connections, the PMC can promote coordination between the bladder and urethral sphincter. In the cat, another area, located in the ventrolateral pontine tegmentum and is called the "L-region", which controls the motoneurons of the pelvic floor, including the external urethral sphincter.[25] This region might be considered as the pontine storage center **(Figure 1A)**. In humans the laterally located L-region is especially active in volunteers who tried but did not succeed to micturate.[25, 26]

Suprapontine pathways

Studies in humans indicate that voluntary control of urine storage and voiding depends on connections between the frontal cortex and the septal/preoptic region of the hypothalamus as well as connections the paracentral lobule and the brainstem.[1, 3] Lesions to these areas of cortex exhibit detrusor overactivity (DO) because of lack of

cortical inhibitory control. Brain imaging studies in right-handed both male and female volunteers have demonstrated decreased blood flow in the right anterior cingulate gyrus during urine withholding prior micturition and increased blood flow in the right dorsomedial pontine tegmentum, in the PAG, in the hypothalamus and in the right inferior frontal gyrus during voiding.[23, 26, 27] It has been implicated that the midbrain PAG receives bladder filling information, and the hypothalamus has a role in the beginning of micturition.[28] Furthermore, the human cingulate and prefrontal cortices are activated during both micturition and continence, indicating that these areas are important for the onset of micturition, but not for the reflex itself.

PATHOPHYSIOLOGY OF THE LOWER URINARY TRACT DYSFUNCTION

When a neurological lesion is present, the type of LUT dysfunction roughly depends on the site and the extent of the lesion[29].
Neurological pathology can be divided in 1) suprapontine, 2) brainstem (pontine), 3) suprasacral spinal cord, and 4) sacral and subsacral (cauda equine and peripheral nerve) lesions (**Figure 4**). Madersbacher et al described the common patterns of neurogenic detrusor-sphincter dysfunction in a diagram associated with these lesions (**Figure 5**).[30]

Suprapontine lesions

Patients with lesions above the pons commonly demonstrate DO caused by lack of cortical inhibitory control, but they preserve coordinated synergic sphincter function (**Figure 5-A**). However, these patients sometimes may purposely increase sphincter activity during an overactive detrusor contraction to avoid urgency incontinence[31].
Typical suprapontine lesions include cerebro-vascular accident (CVA), dementia, brain tumors, and cerebral palsy.

Cerebro-vascular accident (CVA)

The most common LUT symptoms after stroke are nocturia (36%), urge incontinence (29%) and difficulty in voiding (25%) [32]. There is a positive correlation between the occurrence of LUT dysfunction and hemiparesis[32]. Urodynamic studies revealed DO in 68%, uninhibited sphincter relaxation in 36%[32]. In patients with brainstem strokes, voiding symptoms are more predominant[33].

Brainstem (pontine) lesions

As the pontine micturition center (PMC) and the lateral storage centre are located in the brain stem, lesions of this area demonstrate a variety of LUT dysfunction. Both storage and voiding dysfunctions often occur simultaneously. The common diseases of this region include Parkinson's disease, multiple system atrophy (MSA), and multiple sclerosis.

Parkinson's disease

LUT dysfunction occurs in 37-71% of patients[39, 40]. Storage symptoms were observed in 28%, voiding symptoms in 11%, and both symptoms in 21% [40]. The frequency of LUT symptoms correlated with the severity of the disease, but not with the duration of the illness or sex[40]. DO was observed in 81%, external sphincter relaxation failure in 33%, and underactive detrusor in 66% of women and 40% of men[41].

Multiple system atrophy (MSA)
MSA involves various syndromes resulted from degeneration of neurons and associated fibers of motor and extrapyramidal systems including the cerebellum and brain stem. LUT symptoms often precede orthostatic hypotension and other autonomic nervous system symptoms in MSA patients[42]. Almost 100% of MSA patients have some kind of LUT symptoms[43, 44]. The most common urodynamic abnormalities are abnormal sphincter EMG (in 82-91%)[42, 44, 45], DO (in 56%)[44], DSD (in 45-47%)[44, 46, 47], uninhibited external sphincter relaxation (in 33%)[44], and underactive detrusor (in 71% of women and 63% of men)[44]. Significant PVR is observed in about half of MSA patients[48].

Suprasacral spinal cord lesions
Spinal lesions mostly cause simultaneous dysfunction of the detrusor and the sphincter. In suprasacral spinal cord lesions a typical pattern of the LUT dysfunction is DO associated with DSD (**Figure 5-B**). If the lesion is complete, sensation of bladder filling disappears. Basically spontaneous reflex voiding is possible, however, it is uncontrolled, causing reflex incontinence, and unphysiological. DSD leads to unbalanced voiding with the possibility of a dangerous high pressure situation. While most traumatic spinal cord lesions give LUT dysfunction which can be predicted fairly well from the level and completeness of injury, the LUT dysfunction in many other neurological disorders such as myelomeningocele are more difficult to categorise[29] (**Figure 5-B, C , E &F**).

Spinal cord injury (SCI)
DO was demonstrated in 95%[49], and DSD in 68%[50] of the patients with suprasacral lesions. In patients with sacral lesion, an acontractile detrusor was found in 86%, and low compliance in 79%[49]. Upper urinary tract changes were observed in 30-42% of SCI patients[51, 52].

Multiple sclerosis (MS)
The LUT dysfunction is mainly due to spinal lesions, although brain lesions may contribute[30]. Impairment of neurological function results from demyelinating plaques of the white matter of the brain and spinal cord, especially the posterior and lateral columns of the cervical cord. The prevalence of LUT dysfunction in MS patients is 33-52%, and its incidence is related to the disability status[53]. Urodynamic studies revealed DO in 44-99%, DSD in 6-66%, and detrusor underactivity in 31-38% [54-56]. The upper urinary tract is rarely involved[57].

Sacral and subsacral (cauda equina and peripheral nerves) lesions

Lesions of conus causing dysfunction of the sacral parasympathetic neurons and the EUS motoneurons are categorized as the same group as subsacral (cauda equina and peripheral nerves) lesions. For complete sacral or subsacral lesions, classically named as lower motor neuron lesions, loss of bladder sensation and acontractile detrusor with incompetent urethra are characteristic (**Figure 5-E**). However, acontractile detrusor combined with normal or overactive urethra may occur in lesions, comprising the conus and nearby area above (**Figure 5-D & F)**. In lumbo-sacral lesions, espetially in myelomeningocele, overative detrusor combined with incompetent urethra sometimes occur (**Figure 5-C)**. Subsacral (cauda equina and peripheral nerves) lesions are often imcomplete and associated with a variety of combination patterns of the detrusor and urethral dysfunctions. For example, in case of pelvic nerve plexus injury after radical pelvic organ surgery, if the pudendal nerves remain intact, impaired bladder sensation and underactive/acontractile detrosor may be combined normally functioning urethra (**Figure 5-D)**. On the other hand, the pudendal nerves are selectively disrupted, for instance, in traumatic pelvic fracture, incompetent urethra may occur with normal detrusor function (**Figure 5-H)**

Myelodysplasia (Myelomeningocele MMC) and spina bifida

The incidence of LUT dysfunction is very high (>90%) in MMC patients[29]. Most have LUT dysfunction leading to incontinence and/or upper tract deterioration.

Diabetes Mellitus

Ther are no proper epidemiological studies on the incidence of diabetes-related LUT dysfunction. Neurogenic LUT dysfunction occurs in 43-87% of insulin-dependent DM patients with no sex or age differences[58]. LUT dysfunction is characterized as reduced bladder sensation and impaired empting function due to detrusor underactivity[59-61].

Peripheral neuropathy after pelvic surgery

No good epidemiological studies on the incidence of LUT dysfunction related with peripheral nerve injury in pelvic surgery were performed. Neurogenic LUT dysfunction occurs in 30-50% of patients after extensive pelvic surgery. LUT dysfunction is characterized as reduced bladder sensation, low compliant detrusor and impaired empting function due to detrusor underactivity[29].

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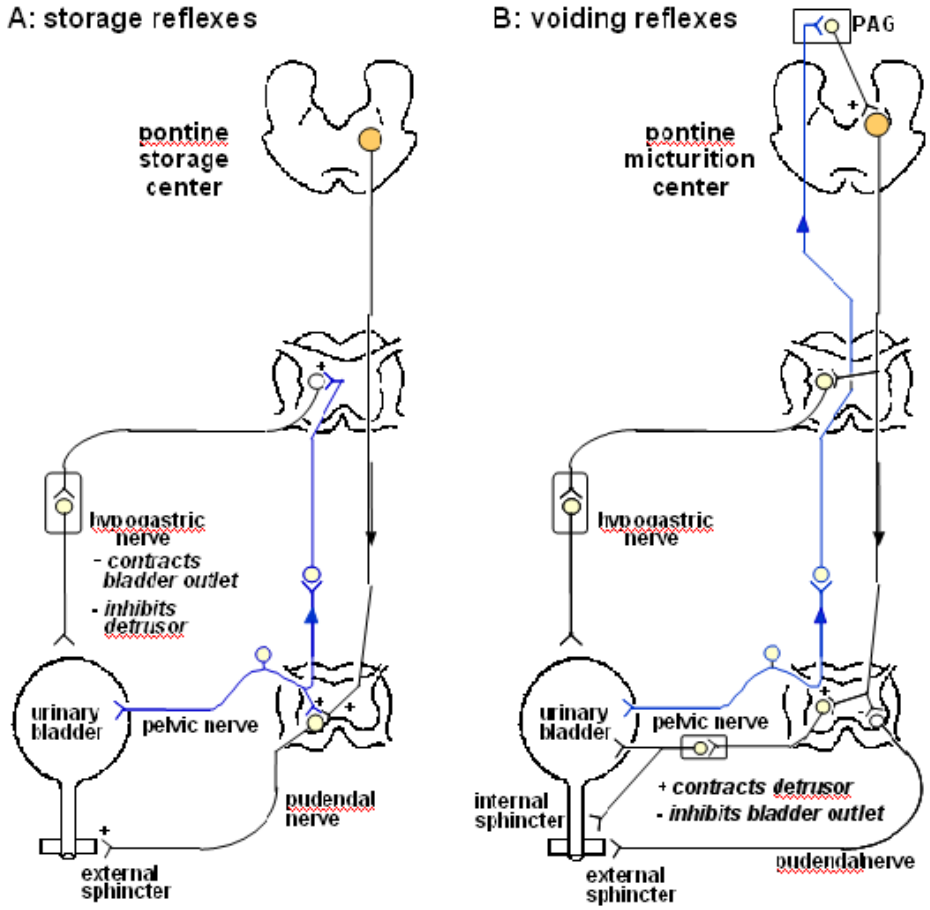

Figure 1. Neural circuits controlling continence and micturition. A: Storage reflexes, B: Voiding reflexes (Modified from Yoshimura & de Groat[2])

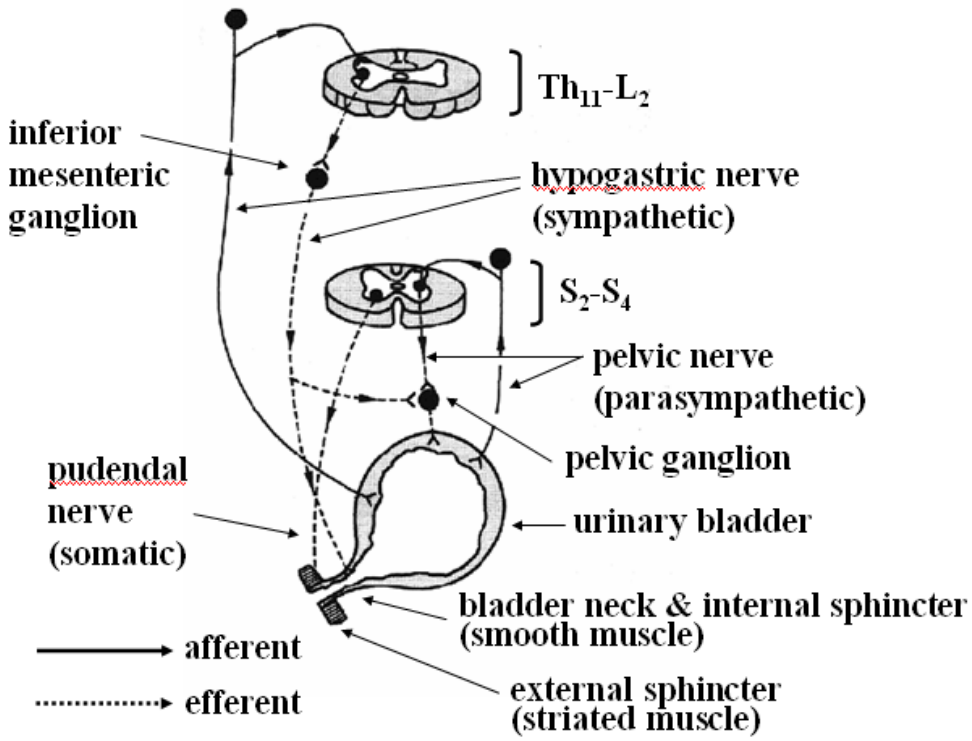

Figure 2. Sympathetic, parasympathetic, and somatic innervation of the lower urinary tract. (Reproduced from Yoshimura & de Groat[2])

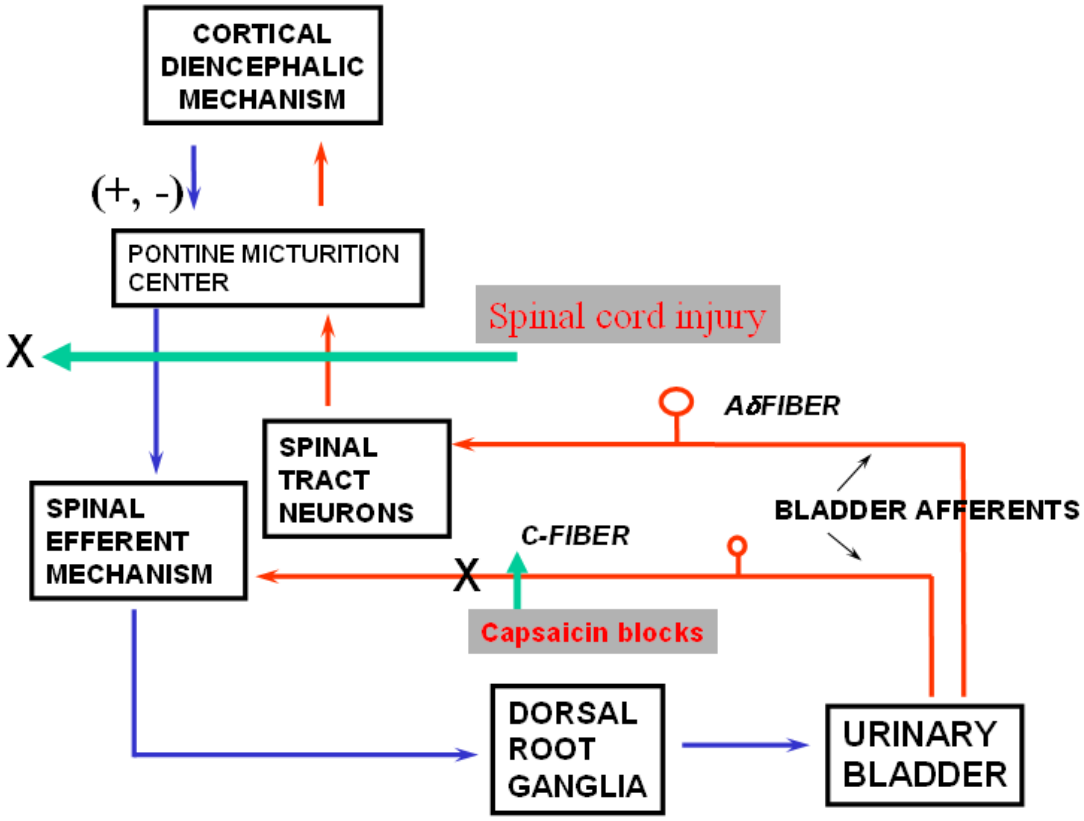

Figure 3. The central reflex pathways that regulate micturition in normal and spinal-cord-injured cats (Modefied from Yoshimura et al[3])

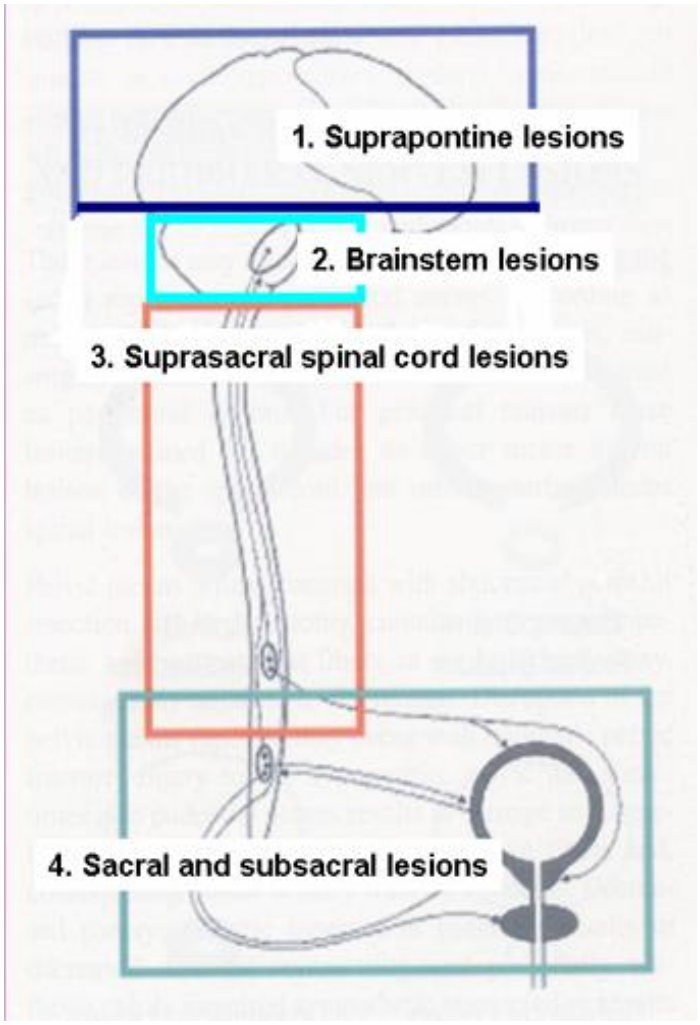

Figure 4. Classification of neurological lesions
(Modified from Madersbacher et al[30])

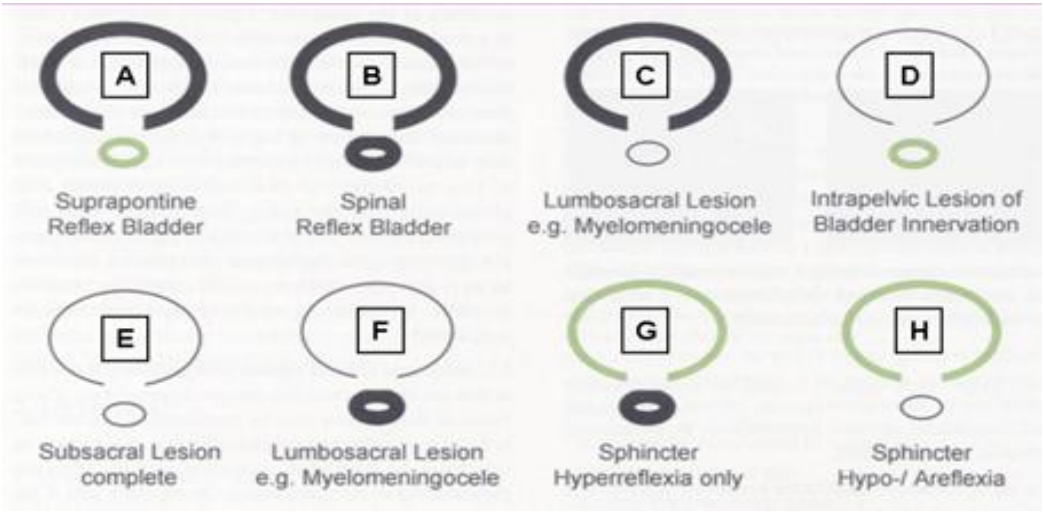

Figure 5. Madersbacher classification system with typical neurogenic lesions (Modified from Madersbacher et al[30])
Heavy lines symbolize overactivity, thin lines underactive or acontractile and green lines normal function of the relevant structure

Diagnostic workup:
How informative are basic diagnostics, are urodynamics essential ?

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Diagnostic methods of neurologic LUT dysfunction and neurologic urinary incontinence are not very different from what is done in non neurologic patients. It consists of clinical assessment including voiding history and voiding diary, urodynamic studies including cystometry (+ EMG), video-urodynamics, uroflowmetry, pressure-flow study, diagnostic imaging with voiding cystourethrography and ultrasonography of the kidneys and LUT. Some tests developed for the diagnosis of neurologic dysfunction have been evaluated more specifically: dynamic bulbocavernosus reflex, bethanechol supersensitivity test , ice water test ,neurophysiologic studies including electrosensation determination.

Clinical examination

Wyndaele and De Sy[1] , Marshall and Boston[2] found that clinical neurological findings in children with lumbosacral myelodysplasia did not correlate well with the existing dysfunction of the LUT as diagnosed by urodynamic studies. Therefore, one should not rely on a clinical neurological examination to outline the urological management in such patients.
In 92 patients with spinal cord lesion, out of spinal shock, Wyndaele [3] found a significant correlation between different levels of spinal cord lesion, the function of bladder neck and sphincter and the anal/ bulbocavernosus reflexes. Higher lesions corresponded more with a reflex LUT and somatic motor activity, lower lesions more with areflexic. In patients with lesions between thoracic 10 and lumbar 2 as many reflex as areflex LUT dysfunctions were found. The presence or absence of perineal sensation of light touch corresponded significantly with the presence or absence of sensation in the LUT. Detrusor and striated sphincter reflexia/areflexia corresponded significantly with the presence/absence of bulbocavernosus and anal reflexes.
Shenot et al [4] determined if intact perianal pin sensation (PPS) and bulbocavernosus reflex (BCR) shortly after SCI are predictive of bladder function recovery in patients ,Frankel Classification A-D, spinal injury level C4-T12, admitted within 72 hours of injury. The presence of intact PPS and BCR were correlated with the patient's voiding function and urodynamic evaluation results 1 year postinjury. Although PPS and BCR proved moderately sensitive in predicting the return of spontaneous voiding, they could not predict detrusor hyperreflexia and sphincter dyssynergia.
Therefore, urodynamic study remains an essential component of initial urologic

evaluation after SCI. Also, Schurch et al [5] determined whether early sensory examination, voluntary anal sphincter contraction, or bulbocavernosus reflex (BCR) might predict bladder function in patients with a spinal fracture at the thoracolumbar level. They found that in these patients neurologic voiding dysfunction cannot be predicted by the early sensory evaluation. Pinprick sensation in the perineal area is of negative predictive value: absence of pinprick sensation predicts poor bladder recovery. Most patients with a spinal fracture at T12-L1 did not improve in voiding function.
In men, who were at risk for obstructive uropathy, Nitti et al [6] evaluated whether, after a cerebrovascular accident, the cause of voiding dysfunction could be predicted by the type (obstructive or irritative) or time of onset of symptoms. Presenting symptoms did not predict the urodynamic findings of bladder outlet obstruction or DOA. The significant incidence of onset of symptoms after stroke suggests that the cerebrovascular accident induced voiding dysfunction in the face of preexisting bladder outlet obstruction may exacerbate the symptoms of the latter condition or vice versa.

Urodynamic tests
Classic urodynamic techniques permit the acquisition of multiple functional parameters in patients with neurologic bladder. The literature gives enough evidence of the value of different techniques in neurologic urinary incontinence: urodynamic investigations in patients with a traumatic SCI permitted not only a urodynamic diagnosis but also an objective follow up of treatment as of reeducation techniques, after sphincterotomy and after urethral overdilatation by indwelling catheters [7].

- CMG + EMG has been studied by several authors:

Sundin and Petersen [8] found reliable information as to whether a DSD exists. Mayo and Kiviat [9] found that bladder pressure and sphincter EMG measurement during voiding, combined with fluoroscopy, are ideal methods to identify the factors responsible for incomplete emptying in problem cases. Blaivas et al [10] described on the basis of CMG -EMG 3 types of dyssynergia: type 1 had a crescendo increase in electromyographic activity that reached a maximum at the peak of the detrusor contraction, type 2 had clonic sphincter contractions interspersed throughout the detrusor contraction and type 3 was characterized by a sustained sphincter contraction that coincided with the detrusor contraction. There was no correlation between the clinical neurologic level and the type of dyssynergia.
Simultaneous recording of intravesical pressure, sphincter electromyography and uroflowmetry (CMG.UFM.EMG study) was compared by Aoki et al [11] with cystometry + EMG. They found some influence of the catheter in the urethra. Micturition pressure and opening pressure were larger with CMG+ EMG, incidence of detrusor-sphincter dyssynergia was greater. The authors also found that the Credé maneuver exaggerated the DSD. Urodynamics with EMG permitted Kirby [12] to differentiate between patients with pelvic nerve injury, distal autonomic neuropathy, progressive autonomic failure - multiple system atrophy, and idiopathic Parkinson's

disease. This influenced the selection of patients for transurethral surgery. Pavlakis et al [13] studied CMG concomitant with perineal floor and rectus abdominis EMG and concluded that the addition of rectus EMG can improve the recognition of intravesical pressure elevation owing to voluntary contraction of the abdominal musculature.

- Pressure-flow study can demonstrate an obstructive pattern (high pressure voiding) also

in neurologic patients due to urethral relaxation failure

- Video urodynamics permit a clear image of bladder neck and urethral sphincter activity during filling and voiding.

Zerin et al[14] concluded that, although not as precise as urodynamic testing, significant descent of the bladder neck is a reliable urographic finding of complete LMN denervation of the external urethral sphincter in infants and children with myelodysplasia.

- CMG filling rate seems to be very important especially in neurologic patients:

De Gennaro et al [15].Zermann et al [16] investigated the diagnostic value of natural fill cystometry (NFC) in children with neurologic bladder in comparison to conventional videocystometry (CVC). In 45%, NFC detected new findings compared with CVC diagnoses. CVC findings were confirmed in another 45%.

Ko et al [17] found significant differences between CMG and FCMG in hyperreflexic neurologic bladders with respect to a decrease in MPdet and increase in compliance with FCMG. However, there were no significant differences in MPdet and compliance in hyporeflexic or areflexic neurologic bladders between the two techniques.

- The determination of CMG filling sensation is important. In 52 SCI

patients, 26 % of those with a supposed complete lesion had sensation of bladder filling during cystometry [3]. Also in 41 patients with myelodysplasia the perception of bladder filling proved, rather unexpectedly, to be present in a majority of patients [18]. In a large cohort study it was clearly shown that impaired perception of bladder filling during CMG is a sign of neuropathy [19]. Ersoz and Akyuz [20] investigated bladder-filling sensation in SCI patients with complete lesions above T11 and below T10 and with incomplete lesions Bladder-filling sensation was present to some degree in all incomplete SCI patients, in 82.4% of the patients with complete lesions below T10, and in 38.9% of the patients with complete lesions above T11. Bladder-filling sensation investigations were reproducible in terms of bladder filling sensation category in 36 SCI patients who had second cystometric examination. The authors concluded that presence of bladder-filling sensation in many SCI patients reveal the potential for sensation-dependent bladder emptying, especially in the ones with complete lesions below T10 and the ones with incomplete lesions.

Special tests

Ice water test

The literature results from IWT show some value in the diagnosis of neurologic bladder and in the differentiation between reflex and areflex neurologic bladders. However studies are contradictory and further studies will have to be done to position this test more clearly in the diagnosis of neurologic urinary incontinence.

Bethanechol supersensitivity test

The literature on the value of the bethanechol test for the diagnosis of neurologic pathology is contradictory. Several authors state that a positive bethanechol supersensitivity test (BST) usually indicates neurologic detrusor areflexia. Others are more cautious and position the test as one of many in the global evaluation of neurologic LUT dysfunction.

Electrodiagnostic tests

EMG of Sphincter

- EMG can be valuable in the diagnosis of patients with neurologic bladder dysfunction.
- EMG of the anal sphincter seems unreliable.

Dynamic Bulbocavernosus reflex (BCR)
still has to be considered as experimental.

Nerve conduction study

There are some arguments that the technique can be usefull in the further differentiation of the nerve deficits in cases of neurologic pathology of the bladder.

Somatosensory evoked potentials (SSEP)
can be of use in the further diagnosis of nervous deficits related to LUT dysfunction

Electrosensitivity in the LUT

To determine the electrosensation in the LUT is valuable to evaluate the afferent innervation in cases of neurologic bladder. Absent electrosensitivity is valuable to decide on further neurologic tests in patients with LUT dysfunction[21-22].

Sympathetic skin response
are of value to evaluate the integrity of the LUT related sympathetic function and especially for bladder neck competence, incompetence and dyssynergia[23].

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HOW TO MAINTAIN NORMAL RENAL FUNCTION, HOW TO ACHIEVE CONTINENCE, HOW TO MANAGE INCONTINENCE

THERAPEUTIC STRATEGIES in lYhuY

The two aims in the management of patients with neurogenic lower urinary tract dysfunction (LUT-dysfunction) are (1) to protect the upper urinary tract to guarantee adequate (normal) life expectancy, and (2) achieve continence or to manage incontinence for improving their quality of life.
The most important objective is to achieve a safe situation urodynamically, which requires a bladder of sufficient capacity, filling at low pressure and emptying fully without hyperpressure or obstruction of the outlet. The indication for a therapeutic option must be based on the underlying pathophysiology, on risk-factors involved, however, also disease specific considerations as well as the abilities and the needs of the individual patient must be taken into account.

Depending on the localisation and the extent of the neurological lesion, the detrusor and sphincter may react either with overactivity or underactivity (acontractility), mostly both, detrusor and sphincter, are affected.

THE MANAGEMENT OF THE OVERACTIVE ("HYPERREFLEXIC") DETRUSOR

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How to maintain normal renal function, how to achieve continence / to manage incontinence
Therapeutic strategies in 2008

With overactive detrusor

+ overactive sphincter
+ underactive sphincter
+ normal sphincter

Neurogenic detrusor overactivity (NDO) could cause incontinence and or renal functions impairment. The key factor is the sphincteric function. Therefore management of patients with NDO should always focus on both bladder and outflow region.

The following scenarios are possible:
1.NDO and sphincteric underactivity
2.NDO and normal sphincteric functions
3.NDO and sphincteric overactivity

These scenarios could be further combined with normal or underactive functions of the detrusor during voiding.
When managing patients with neurogenic lower urinary tract dysfunction, preservation of normal kidney functions is an ultimate goal, with continence and quality of life restoration afterwards. It is also important to state if the dysfunction is due to complete or incomplete lesion, since it will influence further treatment and follow-up options.

To achieve the primary goal we must focus on maintenance low intravesical pressure and low post-void residual. Therefore before elaboration of the treatment strategies for treatment of the patients with NDO we have to establish these parameters and evaluate the sphincteric functions, as well as establish the kidney functions.

The minimal assessment program should include:
-ultrasound examination
-dipstick and urine culture
-serum kreatinine levels
-voiding cystouretrography
-basic urodynamics (both filling and voiding phase)

In selected cases, when the original therapy fails or when a worsening of kidney functions is observed the following diagnostic tests could be performed additionally:
-video urodynamics
-enhanced lower urinary tract CT or intravenous urography
-dynamic tests of kidney functions
-detailed neurphysiological tests

1.Neurogenic detrusor overactivity and normal sphincteric function treatment.
When the sphincter acts in a coordinated way and no (or minimal - less than 25% of cystometric capacity) post void residual exists the treatment strategy is directed at lowering the intravesical pressure, achievement of continence and monitoring of adequate bladder emptying.

The treatment strategy should be staged from non (minimally) invasive to invasive one:
1.Behavioural modifications, bladder training in combination with anticholinergics
2.Botulinum toxin injections
3.Neuromodulation with implantable devices
4.Bladder surgery (for very selected cases)

It is important to inform the patient that the therapy is life-long and a check-up of renal and bladder functions should be performed regularly/at least every 1-2 years in stable conditions /

Follow up of a patient with NDO and normal sphincteric functions is very much dependant on the underlying neuropathology and ICI guidelines how to follow-up a patient with specific neurogenic disease should be observed. For patients with complete lesion it is advisable to proceed promptly for more radical and definitive treatment options (surgery, neuromodulations) .

Worsening of incontinence, recurrent urinary tract infections, increased post void residual, hydronephrosis should trigger the detailed examination of the lower urinary tract for worsening of existing pathology or appearance of the new one.

2.Neurogenic detrusor overactivity and underactive sphincteric functions.
In this case we have a combination of both stress and urge incontinence, occasionally accompanied by detrusor underactivity during voiding.
Kidney failure is very rare and the cornerstone of therapeutic strategy should be focused on incontinence and monitoring of adequate bladder emptying.

The therapy for NDO should be staged as usual (see above), however one must bear in mind the parallel therapy for stress incontinence.
The concomitant stress incontinence therapy should also be staged:
1.Behavioral therapy and physiotherapy
2.Minimally invasive surgery:

- injectables
- micro-balloons
- mid-urethral slings
- bladder neck slings
- artificial urinary sphincter

In almost every case, except injectables, it is important to discuss with the patient the possibility of self-catheterization after surgery, and no patient could be qualified for stress incontinence surgery without demonstrating the willingness and ability for self-catheterization.

Stress incontinence surgery could worsen detrusor overactivity and lead to more invasive treatment options (including surgery), and this scenario should also be discussed with a patient. Sometimes it is better to have patient with minimal stress incontinence, than to face the stress incontinence surgery complications.
Patients with complete lesion should be managed accordingly to their disability status and kidney functions. Generally more radical treatment options (e.g. artificial sphincter with botulinum toxin or bladder surgery) are advisable.

Follow up of a patient should again observe the ICI guidelines for specific neuropathy.
Additionally, patients after the surgery for stress incontinence should be checked at least yearly for post-void residual and should have performed urodynamics.
If overactivity is worsening (despite staging the overactivity treatment) one must consider urethrolysis, even if this would make the patient incontinent again.

3.Neurogenic detrusor overactivity and sphincteric overactivity.
This situation represent the worse case scenario, which most often leads to chronic kidney failure. Therefore the treatment goal is the preservation of kidney function , while the quality of life issues (and incontinence) are of secondary importance.
Again staged approach (see above) for therapy of NDO should be observed, however the second and third line therapy should be considered much earlier.

The following treatment options for sphincteric overactivity could be considered:
1.Pharmacotherapy (minimally effective)
2.Botulinum toxin injections (for both NDO and sphincteric overactivity)
3.Neuromodulations (for both NDO and sphincteric overactivity)
4.Intraurethral stents
5.Sphincterotomy

Self-catheterization /either sterile or aseptic/ still remain the "golden standard" for the sphincteric overactivity treatment and should always be considered for this type of patients.

Complete lesion patients should be managed by definitive treatment options (botulinum toxin therapy or bladder surgery combined with self catheterization) and neuromodulation with implants should always be considered.
Follow-up should be performed accordingly to the ICI guidelines and additionally PVR, kidney function and bladder functions (urodynamics or video urodynamics) should be performed yearly or when a deterioration of incontinence or kidney functions is observed.

THE MANAGEMENT OF THE UNDERACTIVE/ACONTRACTILE DETRUSOR

+ underactive sphincter
+ overactive sphincter
+ normal sphincter

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According to ICS terminology (2002) detrusor underactivity is defined as a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete emptying within a normal timespan. Acontractile detrusor is one that can not be demonstrated to contract during urodynamic studies. Although not defined by the ICS as a detrusor with a maximum detrusor pressure (pdetr. max.) below 30 cm H2O in men and 15 cm H2O in women can be considered to be underactive.

The reasons for an underactive detrusor are several. In the context of neuropathology detrusor acontractility or detrusor underactivity are usually observed with damage of (1) the lumbosacral spinal cord, (2) the bladder peripheral efferent pathways, (3) the bladder peripheral afferent pathways and (4) maybe due to a secondary myogenic failure.
There are various options for the management of the underactive /acontractile detrusor, depending also on the function/dysfunction of the sphincter and whether the lesion is complete or incomplete.

1. MANAGEMENT OF THE ACONTRACTILE/UNDERACTIVE DETRUSOR COMBINED WITH AN UNDERACTIVE (INCOMPETENT) SPHINCTER

In complete lesions, the bladder and the striated sphincter as well as the pelvic floor musculature are acontractile. As the bladder capacity is high and the intravesical pressure is low, the kidneys are not at risk as long as regular low pressure emptying is provided. However, neurogenic stress incontinence due to the incompetent sphincter is a problem.

How to empty the bladder

- **Bladder expression**

Bladder expression has been recommended since a long time for these patients. With bladder expression (Valsalva or Credé manoeuvre) often unphysiologic high intravesical pressures are created. The reasons for difficulties in expressing the urine from the bladder are the difficulties to open the bladder neck and a functional obstruction at the level of the pelvic floor despite complete flaccid paralysis, resulting in deformation and narrowing of the membranous urethra (Madersbacher, 1975).

Therefore, bladder expression is potentially hazardous for the urinary tract. Before recommending bladder expression it must be proved that the situation in the LUT is urodynamically safe. Contraindications, such as vesico-uretero-renal reflux, prostatic reflux, urethral pathology, hernias, have to be excluded. ***In general, bladder expression should be replaced by CIC in most patients.*** Alpha-blockers may facilitate voiding, however, urinary stress incontinence may be induced or increased. Therefore Valsalva and Credé only guarantee a good quality of life and are cost effective in long term when the indication is proper and when the situation remains stabile throughout the years, best controlled by (video-)urodynamics.

- **Pharmacotherapy**

So far there is no randomized controlled study which proves the efficacy of cholinergics. They are not able to induce/increase detrusor contractions, however they seem to increase the muscle tone of the detrusor. The patient may feel the bladder at a lower filling volume. Lowering of outflow resistance is another option to facilitate bladder expression. However, there is no controlled trial, which really proves the efficacy of alpha-blockers. Dosages of spasmolytics needed for the relaxation of striated sphincter are often not tolerated because of side effects, especially general muscle weakness.

- **Intermittent catheterisation**

In complete lesions with detrusor acontractility therefore for many patients the method of choice to empty the bladder is intermittent catheterisation, either using the sterile or the hygienic technique.

- In **incomplete lesions** with preserved afferent fibres, **intravesical electrostimulation (IVES)** is useful to induce or to improve sensitivity and contractility of the detrusor (s. below).

How to manage neurogenic stress incontinence

The other problem with this type of neurogenic LUT dysfunction is the underactive, incompetent sphincter causing neurogenic urinary stress incontinence.

- **Behavioural therapy**

Neurogenic urinary stress incontinence can be improved to a certain degree by regular bladder emptying, controlled fluid intake and the avoidance of urinary tract infections.

- **Pharmacotherapy**

There is no controlled trial which really proves the efficacy of α-adrenergics in neurogenic urinary stress incontinence. Whether the 5-HT and NA-Reuptake inhibitor Duloxetin is able to improve neurogenic stress incontinence in incomplete lesions, still needs to be proved through studies.

- **Surgery**

Especially in "walkers" continence can only be restored through operative treatment. Although the design of the artificial sphincter has improved considerably over the years, there is still a complication rate of about 30 % in these patients on the long term. In women the risk of arosion at the bladder neck is high, overall long-term continence is satisfactory with about 90 % (Venn et al., 2000).
Prerequisites for the implantation of an artificial urinary sphincter is neurogenic stress incontinence, an acontractile detrusor (can be achieved by pharmacotherapy or other procedures), a motivated patient and adequate manual dexterity. Moreover, the system has to be replaced between 10 and 15 years after implantation. For women sling procedures (fascial slings) are also recommended.

- **Condom catheters and external appliances**

Despite all efforts, some patients with neurogenic bladder and urinary incontinence need some kind of assistance to gain social continence. In males, a condom catheter (CC) has been one of the choices. Until now, a wide variety of condom catheters has been available, such as a simple thin latex, plastic or silicon condom catheters or a condom catheter with a double rows of convulsions near the catheter tip to prevent kinking, with an inner flap to prevent the backflow of the urine to the shaft of the penis and an inner wall coated with a self-adhesive. Even a special condom with a passage for catheterization without removal of the condom has been developed.

Condom catheters still play a role in the control of urinary incontinence in male patients. Long-term use may cause bacteriuria, but does not increase the risk of UTI compared to other methods of bladder management. Complications may occur less often if the condom catheter is applied properly, and if all hygienic measures necessary are taken, i.e. frequent (daily) change of the condom catheter and maintenance of a low bladder pressure. To prevent a latex allergy, which is becoming more and more common, a silicone condom catheter should be used. To prevent compressive effects the proper size of the condom catheter with self-adhesive is recommended. Moreover, in order to prevent bladder and upper urinary tract damages regular bladder emptying with low bladder pressure and low PVU should be pursued also when a condom catheter is used.

In incomplete lesions pelvic floor reeducation may help in the individual patient.

2. MANAGEMENT OF THE ACONTRACTILE/UNDERACTIVE DETRUSOR COMBINED WITH AN OVERACTIVE ("SPASTIC", "HYPERREFLEXIC") SPHINCTER

This pattern can be seen with lesions at the conal and epiconal level of the spinal cord, e.g. in myelodysplastic children. The main problem is bladder emptying, the overactive sphincter secures continence, provided that the bladder is emptied regularly.

- **Intermittent (Self-)catheterisation**

This dysfunctional pattern is a clear indication for intermittent (self-) catheterisation which provides regular bladder emptying with low pressure and the spastic sphincter secures continence in between.

In **incomplete lesions** the underactive and hyposensitive detrusor is a good indication for intravesical electrostimulation (see below) to achieve bladder sensitivity, however, balanced voiding is mostly not achieved due to sphincter spasticity. Lowering of outflow resistance caused by the spastic striated sphincter is difficult to achieve (see above).

3. MANAGEMENT OF THE ACONTRACTILE/UNDERACTIVE DETRUSOR COMBINED WITH A NORMALLY FUNCTIONING SPHINCTER

This pattern is seen with peripheral lesions of bladder innervation especially after pelvic surgery. As the pelvic plexus contains both parasympathetic and sympathetic fibres, decreased parasympathetic innervation may result in decreased detrusor contractility or acontractility, while impaired sympathetic transmission results in incomplete bladder neck closure with weakness of the smooth muscle sphincter. After pelvic surgery urinary retention may occur and **intermittent catheterisation** is the method of choice , however reeducation of the bladder should be aimed as the **lesions are mostly incomplete**. Again **intravesical electrostimulation** is the method of choice to achieve or to speed up bladder rehabilitation. Also cholinergics in combination with alphablockers and with regular bladder emptying may be successful to achieve balanced voiding.

4. MANAGEMENT OF DETRUSORACONTRACTILITY IN THE SPINAL CORD INJURED PATIENT DURING THE SPINAL SHOCK PHASE

The acute phase of the spinal cord lesion is characterized by the "spinal shock phase" with absent spinal reflexes below the lesion. The bladder is able to store urine, but the patient unable to void; unless appropriate measures are taken, overflow incontinence with bladder-overdistention , urinary tract infections and damage to the upper urinary tract will occur. Prevention of early complications, such as bladder overdistention, urinary tract infections, stone formations and urethral injury is a prerequisite for successful rehabilitation of lower urinary tract dysfunction.

Securing of bladder emptying is of paramount importance. This can be done by intermittent catheterisation (IC), by a suprapubic catheter (SC) or by a transurethral indwelling catheter (ID), rarely adequate spontaneous voiding is possible in incomplete lesions.
Intermittent catheterisation has proved to have the lowest complication rate. The alternative of first choice is a **suprapubic catheter,** connected to a urine drainage bag. Only if a suprapubic catheter is contraindicated (injuries in the small pelvis, acute abdomen, pregnancy) **transurethral indwelling catheterisation** is indicated.

However, despite daily catheter care, changing of the catheter each week, continuous drainage into a closed urine collecting device and fixation of the penis at the abdomen near the groin to avoid a decubital ulcer in the urethra at the peno-scrotal angle, the rate of complications is high. Any catheter should be removed as soon as possible based on a daily decision.

5. LONG TERM-INDWELLING TRANSURETHRAL AND SUPRAPUBIC CATHETERS

The long-term use of indwelling catheters for the management of neuropathic bladder is not favorable due to unavoidable complications. In chronic patients, acceptable indications include impossibility to perform IC, uncontrollable urinary incontinence with problems in wearing continence devices (condom catheters) and in patients with an acute situation in the upper urinary tract including urosepsis. For long-term use, in general, a suprapubic catheter is preferable.