EAU Guidelines on
Neuro-Urology

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1. INTRODUCTION

1.1 Aim and objectives

The European Association of Urology (EAU) Neuro-Urology Guidelines aim to provide information for clinical practitioners on the incidence, definitions, diagnosis, therapy, and follow-up of neuro-urological disorders. These Guidelines reflect the current opinion of experts in this specific pathology and represent a state-of-the art reference for all clinicians, as of the publication date.

The terminology used and the diagnostic procedures advised throughout these Guidelines follow the recommendations for investigations of the lower urinary tract (LUT) as published by the International Continence Society (ICS) [1-3]. Readers are advised to consult other EAU Guidelines that may address different aspects of the topics discussed in this document.

It must be emphasised that clinical guidelines present the best evidence available to the experts but following guideline recommendations will not necessarily result in the best outcome. Guidelines can never replace clinical expertise when making treatment decisions for individual patients, but rather help to focus decisions - also taking personal values and preferences/individual circumstances of patients into account. Guidelines are not mandates and do not purport to be a legal standard of care.

1.2 Panel composition

The EAU Neuro-Urology Guidelines Panel consists of an international multidisciplinary group of neuro-urological experts. All experts involved in the production of this document have submitted potential conflict of interest statements which can be viewed on the EAU website: http://www.uroweb.org/guideline/neuro-urology/.

1.3 Available publications

A quick reference document, the Pocket Guidelines, is available in print and as an app for iOS and Android devices. These are abridged versions which may require consultation with the full text version. A guideline summary has also been published in European Urology [4]. All are available through the EAU website: http://www.uroweb.org/guideline/neurourology/.

1.4 Publication history

The EAU published the first Neuro-Urology Guidelines in 2003 with updates in 2008, 2014, and 2017. This 2020 document represents a limited update of the 2019 publication. The literature was assessed for all chapters.

1.5 Background

The function of the LUT is mainly storage and voiding of urine, which is regulated by the nervous system that coordinates the activity of the urinary bladder and bladder outlet. The part of the nervous system that regulates LUT function is disseminated from the peripheral nerves in the pelvis to highly specialised cortical areas. Any disturbance of the nervous system involved, can result in neuro-urological symptoms. The extent and location of the disturbance will determine the type of LUT dysfunction, which can be symptomatic or asymptomatic. Neuro-urological symptoms can cause a variety of long-term complications; the most significant being deterioration of renal function. Since symptoms and long-term complications do not correlate [5], it is important to identify patients with neuro-urological symptoms, and establish if they have a low or high risk of subsequent complications. The risk of developing upper urinary tract (UUT) damage and renal failure is much lower in patients with slowly progressive non-traumatic neurological disorders than in those with spinal cord injury or spina bifida [6]. In summary, treatment and intensity of follow-up examinations are based on the type of neuro-urological disorder and the underlying cause.

2. METHODS

2.1 Introduction

For the 2020 Neuro-Urology Guidelines, new and relevant evidence has been identified, collated and appraised through a structured assessment of the literature. A broad and comprehensive literature search, covering all sections of the Neuro-Urology Guidelines was performed. Databases searched included Medline, EMBASE, and the Cochrane Libraries, covering a time frame between May 31st 2018 and 1st April 2019. A total of 754 unique records were identified, retrieved and screened for relevance. A detailed search strategy is available online: http://uroweb.org/guideline/neuro-urology/?type=appendices-publications.

For each recommendation within the guidelines there is an accompanying online strength rating form, the bases of which is a modified GRADE methodology [7, 8]. Each strength rating form addresses a number of key elements namely:

1. the overall quality of the evidence which exists for the recommendation, references used in this text are graded according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence [9];
2. the magnitude of the effect (individual or combined effects);
3. the certainty of the results (precision, consistency, heterogeneity and other statistical or study related factors);
4. the balance between desirable and undesirable outcomes;
5. the impact of patient values and preferences on the intervention;
6. the certainty of those patient values and preferences.

These key elements are the basis which panels use to define the strength rating of each recommendation. The strength of each recommendation is represented by the words 'strong' or 'weak' [10]. The strength of each recommendation is determined by the balance between desirable and undesirable consequences of alternative management strategies, the quality of the evidence (including certainty of estimates), and nature and variability of patient values and preferences.

Additional information can be found in the general Methodology section of this print, and online at the EAU website; http://www.uroweb.org/guideline/. A list of associations endorsing the EAU Guidelines can also be viewed online at the above address.

2.2 Review

Publications ensuing from panel-led systematic reviews have all been peer-reviewed. The 2015 Neuro-Urology Guidelines were subject to peer review prior to publication.

3. THE GUIDELINE

3.1 Epidemiology, aetiology and pathophysiology

3.1.1 ***Introduction***

Neuro-urological symptoms may be caused by a variety of diseases and events affecting the nervous system controlling the LUT. The resulting neuro-urological symptoms depend predominantly on the location and the extent of the neurological lesion. There are no exact figures on the overall prevalence of neuro-urological disorders in the general population, but data are available on the prevalence of the underlying conditions and the relative risk of these for the development of neuro-urological symptoms. It is important to note that the majority of the data shows a very wide range of prevalence/incidence. This reflects the variability in the cohort (e.g. early or late stage disease) and the frequently small sample sizes, resulting in a low level of evidence in most published data (summarised in Table 1).

Table 1: Epidemiology of Neuro-Urological Disorders

Supraportine and pontine lesions and diseases		
Neurological Disease	**Frequency in General Population**	**Type and Frequency of Neuro-Urological Symptoms**
Cerebrovascular accident (Strokes)	450 cases/100,000/yr (Europe) [11], 10% of cardiovascular mortality.	Nocturia - overactive bladder (OAB) - urgency urinary incontinence (UUI) - detrusor overactivity (DO), other patterns less frequent [12]. 57-83% of neuro-urological symptoms at 1 month post-stroke, 71-80% spontaneous recovery at 6 months [13]. Persistence of urinary incontinence (UI) correlates with poor prognosis [14].
Dementias: Alzheimer's disease (80%), Vascular (10%), Other (10%).	6.4% of adults > 65 yrs [15].	OAB - UUI – DO 25% of incontinence in Alzheimer's disease, > 25% in other dementias: Lewy body, NPH, Binswanger, Nasu-Hakola, Pick Disease [16]. Incontinence 3 times more frequent in geriatric patients with dementia than without [17].
Parkinsonian syndrome (PS) Idiopathic Parkinson's disease (IPD): 75-80% of PS.	Second most prevalent neurodegenerative disease after Alzheimer's disease. Rising prevalence of IPD with age [18].	Urinary symptoms affect 50% at onset, with urgency and nocturia being the most common. Patients with urinary symptoms at presentation have worse disease progression in Parkinson's disease [19].
Non-IPD: Parkinson's-plus (18%): - Multiple system atrophy (MSA), - Progressive supranuclear palsy, - Corticobasal degeneration, - Dementia with Lewy bodies. Secondary Parkinson's (2%)	MSA is the most frequent non-IPD PS.	Infections account for a major cause of mortality in MSA [20]. Impaired detrusor contractility with post-void residual (PVR) > 150 mL seems to be the urodynamic finding distinguishing MSA from IPD [21-23].
Brain tumours	26.8/100,000/yr in adults (> 19 yrs), (17.9 benign, 8.9 malignant) [24].	Incontinence occurs mainly in frontal location (part of frontal syndrome or isolated in frontal location) [25].
Cerebral palsy	Cerebral palsy: 3.1-3.6/1,000 in children aged 8 yrs [26].	46% of patients with cerebral palsy suffer from UI, with 85% of patients having abnormal urodynamic studies (NDO most common 59%). Upper tract deterioration is rare (2.5%) [27].
Traumatic brain injury	235/100,000/yr [28].	44% storage dysfunction, 38% voiding dysfunction, 60% urodynamic abnormalities [29].
Normal pressure hydrocephalus	0.5% of the population > 60, up to 2.9% of those > 65 [30].	Classic triad of gait and cognitive disturbance along with UI. Incontinence affects 98-100% of patients [30].

Lesions and diseases between caudal brainstem and sacral spinal cord		
Spinal cord injury (SCI)	Prevalence of traumatic SCI in developed countries ranges from 280 to 906/million [31].	Neurogenic detrusor overactivity (NDO) and detrusor sphincter dyssynergia (DSD) (up to 95%) and detrusor underactivity (up to 83%) depending on the level of the lesion [32].
Spina bifida (SB)	Spina bifida 3-4/10,000 Lumbar and lumbosacral form are the most common (60%) [33].	Bladder function is impaired in up to 96% of SB patients [34]. Over 50% of patients are incontinent [35]. Patients with open and closed defects can have equally as severe neurogenic lower urinary tract dysfunction [36].
Lesions and diseases of the peripheral nervous system		
Lumbar spine Degenerative disease Disk prolapse Lumbar canal stenosis	Male (5%) and female (3%) > 35 yr have had a lumbosciatic episode related to disc prolapse. Incidence: approx. 5/100,000/yr More common in females > 45 yr.	26% difficulty to void and acontractile detrusor [37]. Detrusor underactivity (up to 83%) [32]. Tarlov cysts: early sensation of filling (70%), NDO (33%), urethral instability (33%) and stress urinary incontinence (SUI) (33%) [38].
Iatrogenic pelvic nerve lesions	Rectal cancer. Cervical cancer (multimodal therapy, radiotherapy and surgery). Endometriosis surgery.	After abdomino-perineal resection: 50% urinary retention. After total mesorectal excision: 10-30% voiding dysfunction [39].
Peripheral neuropathy Diabetes Other causes of peripheral neuropathy causing neuro-urological symptoms: alcohol abuse; lumbosacral zona and genital herpes; Guillain Barré syndrome.	Worldwide, prevalence of pharmacologically treated diabetes 8.3% [40].	Urgency/frequency +/- incontinence [41]. Hyposensitive and detrusor underactivity at later phase [41].
Disseminated central diseases		
Multiple sclerosis (MS)	Prevalence: 83/100,000 in Europe [42].	10% of MS patients present with voiding dysfunction at disease onset, 75% of patients will develop it after 10 yrs of MS [43]. DO: 86% [43]. DSD: 35% [43]. Detrusor underactivity: 25% [43].

3.2 Classification systems

3.2.1 ***Introduction***

Relevant definitions can be found in the general ICS standardisation reports [2, 3, 44]. Supplementary online Tables S1 and S2 list the definitions from these references, partly adapted, and other definitions considered useful for clinical practice: https://uroweb.org/guideline/neuro-urology/?type=appendices-publications.

3.3 Diagnostic evaluation

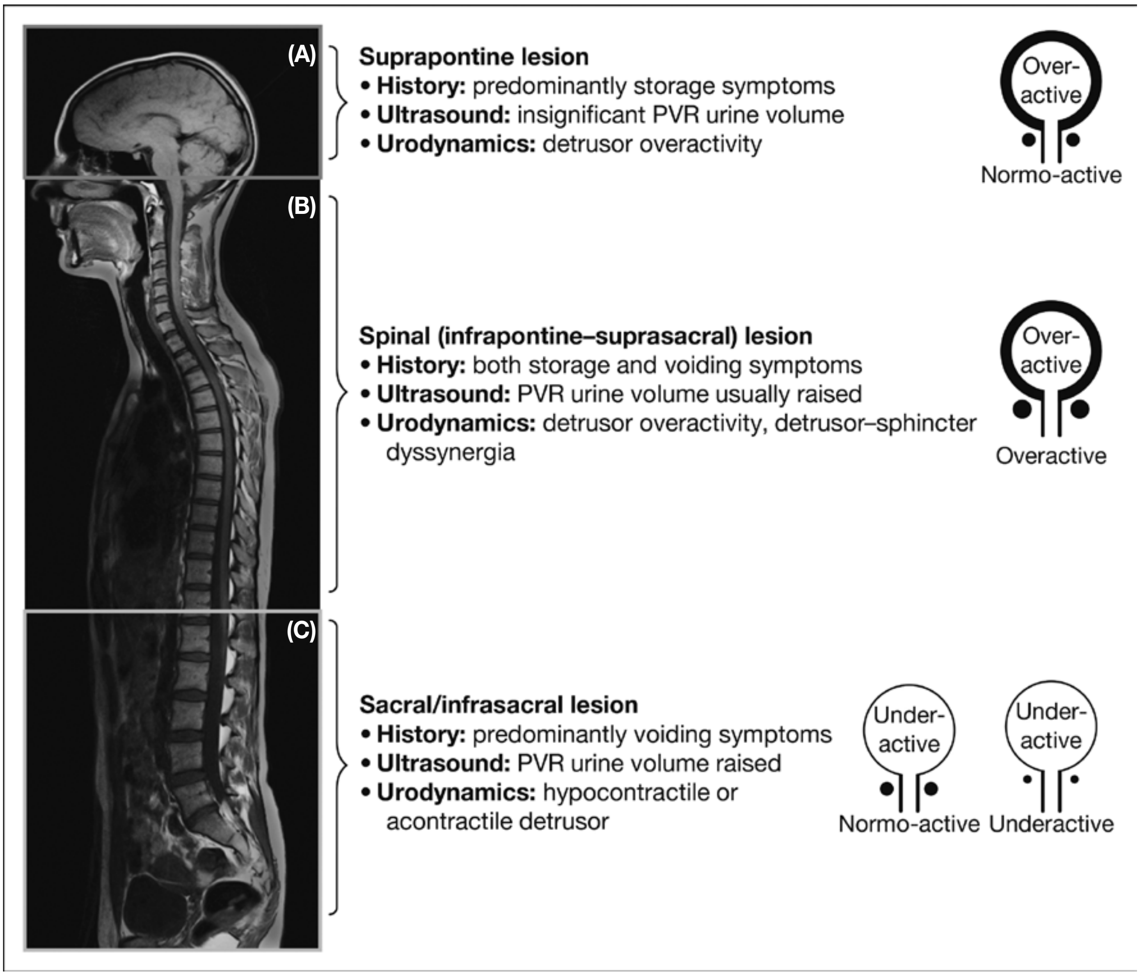
3.3.1 ***Introduction***

The normal physiological function of the LUT depends on an intricate interplay between the sensory and motor nervous systems. When diagnosing neuro-urological symptoms, the aim is to describe the type of dysfunction involved. A thorough medical history, physical examination and bladder diary are mandatory before any additional diagnostic investigations can be planned. Results of the initial evaluation are used to decide the patient's long-term treatment and follow-up.

3.3.2 ***Classification systems***

The pattern of LUT dysfunction following neurological disease is determined by the site and nature of the lesion. A very simple classification system for use in daily clinical practice to decide on the appropriate therapeutic approach is provided in Figure 1 [6].

Figure 1: Patterns of lower urinary tract dysfunction following neurological disease



The pattern of LUT dysfunction following neurological disease is determined by the site and nature of the lesion. Panel (A) denotes the region above the pons, panel (B) the region between the pons and the sacral cord and panel (C) the sacral cord and infrasacral region. Figures on the right show the expected dysfunctional states of the detrusor-sphincter system. Figure adapted from Panicker et al. [6] with permission from Elsevier.
PVR = post-void residual.

3.3.3 ***Timing of diagnosis and treatment***

Early diagnosis and treatment are essential in both congenital and acquired neuro-urological disorders [45]. This helps to prevent irreversible changes within the LUT, even in the presence of normal reflexes [46, 47]. Furthermore, urological symptoms can be the presenting feature of neurological pathology [48, 49]. Early intervention can prevent irreversible deterioration of the LUT and UUT [50]. Long term follow up (life-long) is mandatory to assess risk of UUT damage, renal failure and bladder cancer [51-53].

3.3.4 ***Patient history***

History taking should include past and present symptoms and disorders (Table 4). It is the cornerstone of evaluation, as the answers will aid selection of diagnostic investigations and treatment options.

- In non-traumatic neuro-urological patients with an insidious onset, a detailed history may find that the condition started in childhood or adolescence [54].
- Urinary history consists of symptoms associated with both urine storage and voiding.
- Bowel history is important because patients with neuro-urological symptoms may also have related neurogenic bowel dysfunction [55].

- Sexual function may be impaired because of the neuro-urological condition [56].
- Special attention should be paid to possible warning signs and symptoms (e.g. pain, infection, haematuria and fever) requiring further investigation.
- Patients with SCI usually find it difficult to report urinary tract infection (UTI)-related symptoms accurately [57, 58].
- The presence of urinary, bowel and sexual symptoms without neurological symptoms could be suggestive of an underlying neurological disease or condition.
- Ambulatory status after acute SCI does not predict presence or absence of unfavourable urodynamic parameters [59].

Table 4: History taking in patients with suspected neuro-urological disorder

Past history
Childhood through to adolescence and into adulthood
Hereditary or familial risk factors
Specific female: menarche (age); this may suggest a metabolic disorder
Obstetric history
History of diabetes
Diseases, e.g. multiple sclerosis, parkinsonism, encephalitis, syphilis
Accidents and operations, especially those involving the spine and central nervous system
Present history
Present medication
Lifestyle (smoking, alcohol and drugs); may influence urinary, sexual and bowel function
Quality of life
Specific urinary history
Onset of urological history
Relief after voiding; to detect the extent of a neurological lesion in the absence of obstructive uropathy
Bladder sensation
Initiation of micturition (normal, precipitate, reflex, strain, Credé)
Interruption of micturition (normal, paradoxical, passive)
Enuresis
Mode and type of voiding (catheterisation)
Frequency, voided volume, incontinence, urgency episodes
Sexual history
Genital or sexual dysfunction symptoms
Sensation in genital area
Specific male: erection, (lack of) orgasm, ejaculation
Specific female: dyspareunia, (lack of) orgasm
Bowel history
Frequency and faecal incontinence
Desire to defecate
Defecation pattern
Rectal sensation
Initiation of defecation (digitation)
Neurological history
Acquired or congenital neurological condition
Mental status and comprehension
Neurological symptoms (somatic and sensory), with onset, evolution and any treatment
Spasticity or autonomic dysreflexia (especially in lesions at or above level Th 6)
Mobility and hand function

3.3.4.1 Bladder diaries

Bladder diaries provide data on the number of voids, voided volume, pad weight and incontinence and urgency episodes [3, 60]. Although a 24-hour bladder diary (recording should be done for three consecutive days) is reliable in women with UI [61, 62], no research has been done on bladder diaries in neuro-urological patients. Nevertheless, bladder diaries are considered a valuable diagnostic tool.

3.3.5 *Patient quality of life questionnaires*

An assessment of the patient's present and expected future quality of life (QoL) is important to evaluate the effect of any therapy. Quality of life is an essential aspect of the overall management of neuro-urological patients, for example when evaluating treatment related changes on a patient's QoL [63]. The type of bladder management has been shown to affect health-related QoL (HRQoL) in patients with SCI [64, 65] and MS [66], as does the presence or absence of urinary and faecal incontinence [67]. Other research has also highlighted the importance of urological treatment and its impact on the urodynamic functionality of the neuro-urological patient in determining patient QoL [68].

In recent years a proliferation in the number of questionnaires to evaluate symptoms and QoL has been seen. Condition-specific questionnaires can be used to assess symptom severity and the impact of symptoms on QoL. A patient's overall QoL can be assessed using generic questionnaires. It is important that the questionnaire of choice has been validated in the neuro-urological population, and that it is available in the language that it is to be used in.

3.3.5.1 *Available Questionnaires*

Three condition-specific questionnaires for urinary or bowel dysfunction and QoL have been developed specifically for adult neuro-urological patients [69]. In MS and SCI patients the Qualiveen [70, 71] is validated and can be used for urinary symptoms. A short form of the Qualiveen is available [70, 71] and it has been translated into various languages [72-77]. Although several objective and subjective tools have been used to assess the influence of neurogenic bladder on QoL in SCI, the Quality life index-SCI and Qualiveen are the only validated condition-specific outcomes that have shown consistent sensitivity to neurogenic bladder [78]. The Neurogenic Bladder Symptom Score (NBSS) has been validated in neurological patients to measure urinary symptoms and their consequences [79, 80]. The QoL scoring tool related to Bowel Management (QoL-BM) [81] can be used to assess bowel dysfunction in MS and SCI patients.

In addition, sixteen validated questionnaires that evaluate QoL and asses urinary symptoms as a subscale or question in neuro-urological patients have been identified [82, 83] (Table 5). The condition-specific Incontinence-Quality of Life (I-QoL) questionnaire which was initially developed for the non-neurological population has now also been validated for neuro-urological patients [84].

A patient's overall QoL can be assessed by generic HRQoL questionnaires, the most commonly used being the I-QOL, King's Health Questionnaire (KHQ), or the Short Form 36-item and 12-item Health Survey Questionnaires (SF-36, SF-12) [69]. In addition, the quality-adjusted life year (QALY), quantifies outcomes, by weighing years of life spent in a specified health state, adjusted by a factor representing the value placed by society or patients on their specific health state [85].

No evidence was found for which validated questionnaires are the most appropriate for use, since no quality criteria for validated questionnaires have been assessed [69].

Table 5: Patient questionnaires

Questionnaire	Underlying neurological disorder	Bladder	Bowel	Sexual function
FAMS [86]	MS	X		X
FILMS [87]	MS	X	X	
HAQUAMS [88]	MS	X	X	X
I-QOL [84]	MS, SCI	X		X
MDS [89]	MS	X	X	
MSISQ-15 / MSISQ-19 [90, 91]	MS	X	X	X
MSQLI [92]	MS	X	X	X
MSQoL-54 [93]	MS	X	X	X
MSWDQ [94]	MS	X	X	
NBSS [95]	MS, SCI, Congenital neurogenic bladder	X		
QoL-BM [81]	SCI		X	
Qualiveen/SF-Qualiveen [71, 96]	MS, SCI	X		X
RAYS [97]	MS	X		X
RHSCIR [98]	SCI	X	X	X
Fransceschini [97]	SCI	X	X	X

3.3.6 ***Physical examination***

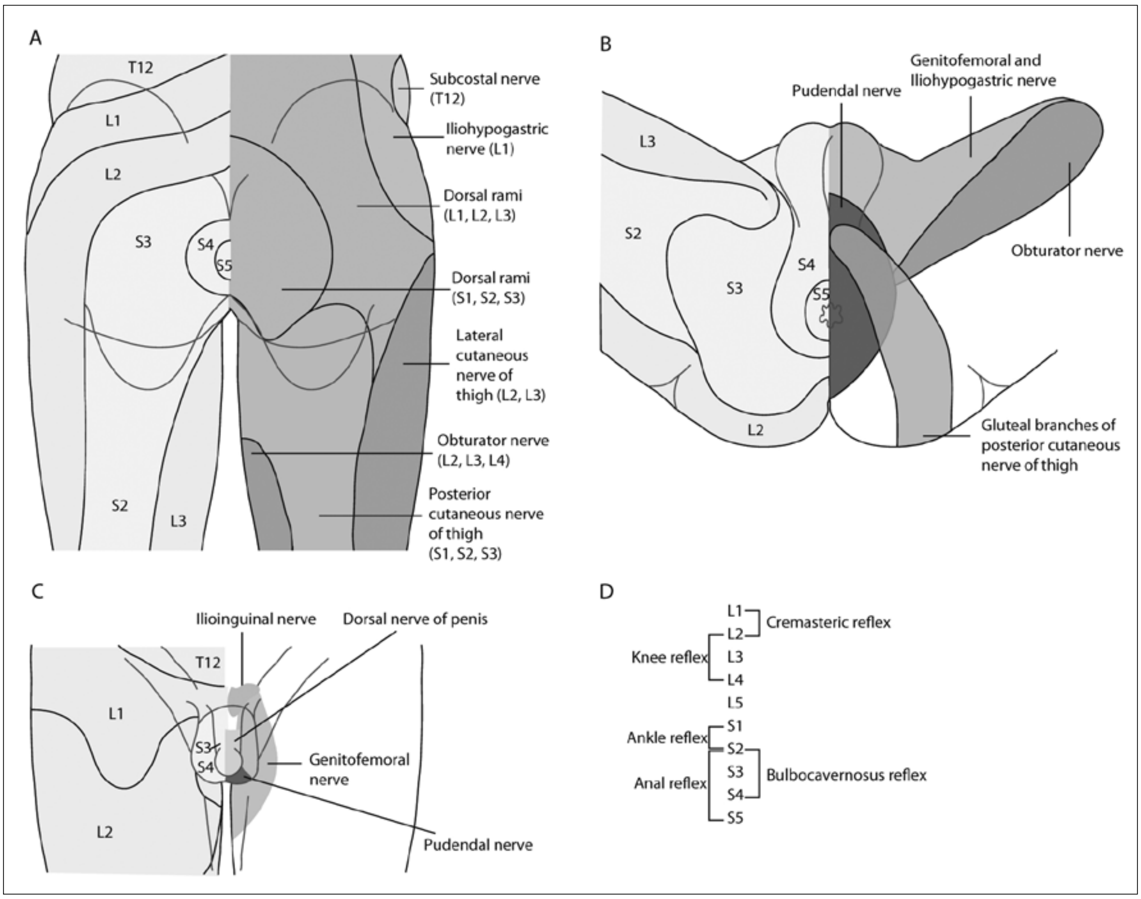
In addition to a detailed patient history, attention should be paid to possible physical and intellectual disabilities with respect to the planned investigations [99, 100]. Neuro-urological status should be described as completely as possible (Figure 2) [6]. Patients with a high spinal cord lesion or supraspinal neurological lesions may suffer from a significant drop in blood pressure when moved into a sitting or standing position. All sensations and reflexes in the urogenital area must be tested [6]. Furthermore, detailed testing of the anal sphincter and pelvic floor functions must be performed (Figure 2) [6, 101]. It is essential to have this clinical information to reliably interpret later diagnostic investigations.

Additionally, urinalysis, blood chemistry, ultrasonography, residual and free flowmetry and incontinence quantification should be performed as part of the routine assessment of neuro-urological patients [6, 102].

3.3.6.1 Autonomic dysreflexia

Autonomic dysreflexia (AD) is a sudden and exaggerated autonomic response to various stimuli in patients with SCI or spinal dysfunction. It generally manifests at or above level Th 6. The stimulus can be distended bladder or bowel. For example, iatrogenic stimuli during cystoscopy or urodynamics can trigger AD [103]. It can also be secondary to sexual stimulation or a noxious stimulus, e.g. infected toe nail or pressure sore. Autonomic dysreflexia is defined by an increase in systolic blood pressure > 20 mmHg from baseline [104] and can have life-threatening consequences if not properly managed.

Figure 2: Lumbosacral dermatomes, cutaneous nerves, and reflexes



The physical examination includes testing sensations and reflexes mediated through the lower spinal cord. Abnormal findings would suggest a lesion affecting the lumbosacral segments; mapping out distinct areas of sensory impairment helps to further localise the site of the lesion. Distribution of dermatomes (areas of skin mainly supplied by a single spinal nerve) and cutaneous nerves over the perianal region and back of the upper thigh (A), the perineum [105] (B), male external genitalia [106] (C) and root values of lower spinal cord reflexes (D). Figure adapted from Panicker et al. [6] with parts A-C adapted from Standring [107], both with permission from Elsevier.

Table 6: Neurological items to be specified

Sensation S2-S5 (both sides)
Presence (increased/normal/reduced/absent)
Type (light touch/pin prick)
Affected dermatomes
Reflexes (increased/normal/reduced/absent)
Bulbocavernous reflex
Perianal/anal reflex
Knee and ankle reflexes
Plantar responses (Babinski)
Anal sphincter tone
Presence (increased/normal/reduced/absent)
Voluntary contractions of anal sphincter and pelvic muscles (increased/normal/reduced/absent)
Prostate palpation
Descensus (prolapse) of pelvic organs

3.3.6.2 Summary of evidence and recommendations for history taking and physical examination

Summary of evidence	**LE**
Early diagnosis and treatment are essential in both congenital and acquired neuro-urological disorders to prevent irreversible changes within the LUT.	4
An extensive general history is the basis of evaluation focusing on past and present symptoms including urinary, sexual, bowel and neurological functions.	4
Assessment of present and expected future QoL is an essential aspect of the overall management of neuro-urological patients and is important to evaluate the effect of any therapy.	2a
Quality of life assessment should be completed with validated QoL questionnaires for neuro-urological patients.	1a
Bladder diaries provide data on the number of voids, voided volume, pad weight and incontinence and urgency episodes.	3

Recommendations	**Strength rating**
History taking	
Take an extensive general history, concentrating on past and present symptoms.	Strong
Take a specific history for each of the four mentioned functions - urinary, bowel, sexual and neurological.	Strong
Pay special attention to the possible existence of alarm signs (e.g. pain, infection, haematuria, fever) that warrant further specific diagnosis.	Strong
Assess quality of life when evaluating and treating the neuro-urological patient.	Strong
Use available validated tools including the Qualiveen and I-QoL for urinary symptoms and the QoL-BM for bowel dysfunction in multiple sclerosis and spinal cord injury patients. In addition, generic (SF-36 or KHQ) questionnaires can be used.	Strong
Use MSISQ-15 and MSISQ-19 to evaluate sexual function in multiple sclerosis patients.	Strong
Physical examination	
Acknowledge individual patient disabilities when planning further investigations.	Strong
Describe the neurological status as completely as possible, sensations and reflexes in the urogenital area must all be tested.	Strong
Test the anal sphincter and pelvic floor functions.	Strong
Perform urinalysis, blood chemistry, bladder diary, residual and free flowmetry, incontinence quantification and urinary tract imaging.	Strong

I-QoL = Incontinence Quality of Life Instrument; QoL-BM = Quality of Life Bowel Management scoring tool; KHQ = King's Health Questionnaire; SF-36 = Short Form 36-item Health Survey Questionnaires; MSISQ 15/19 = Multiple Sclerosis Intimacy and Sexuality Questionnaire 15/19 question version.

3.3.7 ***Urodynamics***

3.3.7.1 Introduction

Urodynamic investigation is the only method that can objectively assess the function and dysfunction of the LUT. In neuro-urological patients, invasive urodynamic investigation is even more challenging than in general patients. Any technical source of artefacts must be critically considered. It is essential to maintain the quality of the urodynamic recording and its interpretation [1]. Same session repeat urodynamic investigations are crucial in clinical decision making, since repeat measurements may yield completely different results [108].

In patients at risk of AD, it is advisable to measure blood pressure during the urodynamic study [109, 110]. The rectal ampulla should be empty of stool before the start of the investigation. All urodynamic findings must be reported in detail and performed, according to the ICS technical recommendations and standards [1, 111].

3.3.7.2 Urodynamic tests

Free uroflowmetry and assessment of residual urine: Provides a first impression of the voiding function and is compulsory prior to planning any invasive urodynamics in patients able to void. For reliable information, it should be repeated at least two to three times [1]. Possible pathological findings include a low flow rate, low voided volume, intermittent flow, hesitancy and residual urine. Care must be taken when assessing the results in patients unable to void in a normal position, as both flow pattern and rate may be modified by inappropriate positions.

Filling cystometry: This test is the only method for quantifying the patient's filling function. The status of LUT function must be documented during the filling phase. However, this technique has limited use as a solitary procedure. It is much more effective combined with bladder pressure measurement during micturition and is even more effective in video-urodynamics.

The bladder should be empty at the start of filling. A physiological filling rate should be used with body-warm saline. Possible pathological findings include DO, low bladder compliance, abnormal bladder sensations, incontinence, and an incompetent or relaxing urethra. There is some evidence that a bladder capacity < 200 mL and detrusor pressures over 75 cm H_2O are independent risk factors for UUT damage in patients with SCI [51].

Detrusor leak point pressure [112]: Appears to have no use as a diagnostic tool. Some positive findings have been reported [113-115], but sensitivity is too low to estimate the risk to the UUT or for secondary bladder damage [116, 117].

Pressure flow study: Reflects the coordination between detrusor and urethra or pelvic floor during the voiding phase. It is even more effective if combined with filling cystometry and video-urodynamics. Lower urinary tract function must be recorded during the voiding phase. Possible pathological findings include detrusor underactivity, bladder outlet obstruction (BOO), DSD, a high urethral resistance, and residual urine.

Most types of obstruction caused by neuro-urological disorders are due to DSD [118, 119], non-relaxing urethra, or non-relaxing bladder neck [120, 121]. Pressure-flow analysis mainly assesses the amount of mechanical obstruction caused by the urethra's inherent mechanical and anatomical properties and has limited value in patients with neuro-urological disorders.

Electromyography (EMG): Reflects the activity of the external urethral sphincter, the peri-urethral striated musculature, the anal sphincter and the striated pelvic floor muscles. Correct interpretation may be difficult due to artefacts introduced by other equipment. In the urodynamic setting, an EMG is useful as a gross indication of the patient's ability to control the pelvic floor. Possible pathological findings include inadequate recruitment upon specific stimuli (e.g. bladder filling, involuntary detrusor contractions, onset of voiding, coughing, Valsalva manoeuvre) suggesting a diagnosis of DSD [122].

Urethral pressure measurement: Has a very limited role in neuro-urological disorders. There is no consensus on parameters indicating pathological findings [123].

Video-urodynamics: Is the combination of filling cystometry and pressure flow studies with imaging. It is the optimum procedure for urodynamic investigation in neuro-urological disorders [5]. Possible pathological findings include all those described in the cystometry and the pressure flow study sections, and any morphological pathology of the LUT and reflux to the UUT [124].

Ambulatory urodynamics: This is the functional investigation of the urinary tract, which predominantly uses the natural filling of the urinary tract to reproduce the patient's normal activity. Although this type of study might be considered when conventional urodynamics does not reproduce the patient's symptoms, its role in the neuro-urological patient still needs to be determined [125, 126].

Triggered tests during urodynamics: Lower urinary tract function can be provoked by coughing, triggered voiding, or anal stretch. Fast-filling cystometry with cooled saline (the 'ice water test') will discriminate between upper and lower motor neuron lesions [127, 128]. Patients with upper motor neuron lesions develop a detrusor contraction if the detrusor is intact, while patients with lower motor neuron lesions do not. However, the test does not seem to be fully discriminative in other types of patients [129].

Previously, a positive bethanechol test [130] (detrusor contraction > 25 cm H_2O) was thought to indicate detrusor denervation hypersensitivity and the muscular integrity of an acontractile detrusor. However, in practice, the test has given equivocal results. A variation of this method was reported using intravesical electromotive administration of the bethanechol [131], but there was no published follow-up. Currently, there is no indication for this test.

3.3.7.3 Specialist uro-neurophysiological tests

The following tests are advised as part of the neurological work-up [132]:

- electromyography (in a neurophysiological setting) of pelvic floor muscles, urethral sphincter and/or anal sphincter;
- nerve conduction studies of pudendal nerve;
- reflex latency measurements of bulbocavernosus and anal reflex arcs;
- evoked responses from clitoris or glans penis;
- sensory testing on bladder and urethra.

Other elective tests, for specific conditions, may become obvious during the work-up and urodynamic investigations.

3.3.7.4 Summary of evidence and recommendations for urodynamics and uro-neurophysiology

Summary of evidence	LE
Urodynamic investigation is the only method that can objectively assess the (dys-)function of the LUT.	2a
Video-urodynamics is the optimum procedure for urodynamic investigation in neuro-urological disorders.	4
Specific uro-neurophysiological tests are elective procedures and should only be carried out in specialised settings.	4

Recommendations	Strength rating
Perform a urodynamic investigation to detect and specify lower urinary tract (dys-)function, use same session repeat measurement as it is crucial in clinical decision making.	Strong
Non-invasive testing is mandatory before invasive urodynamics is planned.	Strong
Use video-urodynamics for invasive urodynamics in neuro-urological patients. If this is not available, then perform a filling cystometry continuing into a pressure flow study.	Strong
Use a physiological filling rate and body-warm saline.	Strong

3.3.8 ***Renal function***

In many patients with neuro-urological disorders, the UUT is at risk, particularly in patients who develop high detrusor pressure during the filling phase. Although effective treatment can reduce this risk, there is still a relatively high incidence of renal morbidity [133, 134]. Patients with SCI or SB have a higher risk of developing renal failure compared with patients with slowly progressive non-traumatic neurological disorders, such as MS and Parkinson's disease (PD) [135].

Caregivers must be informed of this risk and instructed to watch carefully for any signs or symptoms of a possible deterioration in the patient's renal function. In patients with poor muscle mass cystatin C based glomerular filtration rate (GFR) is more accurate in detecting chronic kidney disease than serum creatinine estimated GFR [136, 137]. There are no high level evidence publications available which show the optimal management to preserve renal function in these patients [138].

3.4 Disease management

3.4.1 Introduction

The primary aims for treatment of neuro-urological symptoms, and their priorities, are [139, 140]:

- protection of the UUT;
- achievement (or maintenance) of urinary continence;
- restoration of LUT function;
- improvement of the patient's QoL.

Further considerations are the patient's disability, cost-effectiveness, technical complexity and possible complications [140].

Renal failure is the main mortality factor in SCI patients who survive the trauma [141, 142]. Keeping the detrusor pressure during both the filling and voiding phases within safe limits significantly reduces the mortality from urological causes in these patients [143-145] and has consequently become the top priority in the treatment of patients with neuro-urological symptoms [139, 140].

In patients with high detrusor pressure during the filling phase (DO, low bladder compliance), treatment is aimed primarily at conversion of an overactive, high-pressure bladder into a low-pressure reservoir despite the resulting residual urine [139]. Reduction of the detrusor pressure contributes to urinary continence, and consequently to social rehabilitation and QoL. It is also pivotal in preventing UTIs [146, 147]. However, complete continence cannot always be obtained.

3.4.2 Non-invasive conservative treatment

3.4.2.1 Assisted bladder emptying - Credé manoeuvre, Valsalva manoeuvre, triggered reflex voiding

Incomplete bladder emptying is a serious risk factor for UTI, high intravesical pressure and incontinence. Methods to improve the voiding process should therefore be practiced.

Bladder expression: The downwards movement of the lower abdomen by suprapubic compression (Credé) or by abdominal straining (Valsalva) leads to an increase in intravesical pressure, and generally also causes a reflex sphincter contraction [148, 149]. The latter may increase bladder outlet resistance and lead to inefficient emptying. The high pressures created during these procedures are hazardous for the urinary tract [150, 151]. Therefore, their use should be discouraged unless urodynamics show that the intravesical pressure remains within safe limits [140].

Long-term complications are unavoidable for both methods of bladder emptying [149]. The already weak pelvic floor function may be further impaired, thus introducing or exacerbating already existing stress urinary incontinence [151].

Triggered reflex voiding: Stimulation of the sacral or lumbar dermatomes in patients with a upper motor neuron lesion can elicit a reflex detrusor contraction [151]. The risk of high pressure voiding is present and interventions to decrease outlet resistance may be necessary [152]. Triggering can induce AD, especially in patients with high level SCI (at or above Th 6) [153]. All assisted bladder emptying techniques require low outlet resistance. Even then, high detrusor pressures may still be present. Hence, patients need dedicated education and close urodynamic and urological surveillance [151, 154, 155].

Note: In the literature, including some of the references cited here, the concept "reflex voiding" is sometimes used to cover all three assisted voiding techniques described in this section.

External appliances: Social continence may be achieved by collecting urine during incontinence, for instance using pads. Condom catheters with urine collection devices are a practical method for men [140]. The penile clamp is absolutely contraindicated in case of NDO or low bladder compliance because of the risk of developing high intravesical pressure and pressure sores/necrosis in cases of altered/absent sensations.

3.4.2.2 Neuro-urological rehabilitation

3.4.2.2.1 Bladder rehabilitation including electrical stimulation

The term bladder rehabilitation summarises treatment options that aim to re-establish bladder function in patients with neuro-urological symptoms. Strong contraction of the urethral sphincter and/or pelvic floor, as well as anal dilatation, manipulation of the genital region, and physical activity inhibit micturition in a reflex manner [140, 156]. The first mechanism is affected by activation of efferent nerve fibres, and the latter ones are produced by activation of afferent fibres [116]. Electrical stimulation of the pudendal nerve afferents strongly inhibits the micturition reflex and detrusor contraction [157]. This stimulation might then support the restoration of the balance between excitatory and inhibitory inputs at the spinal or supraspinal level [140, 158]. Evidence for bladder rehabilitation using electrical stimulation in neurological patients is mainly based on small non-comparative studies with high risk of bias.

Peripheral temporary electrostimulation: Tibial nerve stimulation and transcutaneous electrical nerve stimulation (TENS) might be effective and safe for treating neurogenic LUT dysfunction, but more reliable evidence from well-designed randomised controlled trials (RCTs) is required to reach definitive conclusions [158-160]. In post-stroke patients TENS has been shown to effectively improve urodynamic findings and QoL [161-163].

Peripheral temporary electrostimulation combined with pelvic floor muscle training and biofeedback: In MS patients, combining active neuromuscular electrical stimulation with pelvic floor muscle training and EMG biofeedback can achieve a substantial reduction of neuro-urological symptoms [164, 165]. This treatment combination seems to be more effective than either therapy alone [166, 167]. However, the combination of intravaginal electrostimulation and pelvic floor muscle training was not superior to pelvic floor muscle training alone in reducing urinary incontinence in women with incomplete spinal cord injury [168].

Intravesical electrostimulation: Intravesical electrostimulation can increase bladder capacity and improve bladder filling sensation in patients with incomplete SCI or myelomeningocele (MMC) [169]. In patients with neurogenic detrusor underactivity, intravesical electrostimulation may also improve voiding and reduce residual volume [170, 171].

Repetitive transcranial magnetic stimulation: Although improvement of neuro-urological symptoms has been described in PD and MS patients, this technique is still under investigation [172, 173].

Summary: To date, bladder rehabilitation techniques are mainly based on electrical or magnetic stimulation; however, there is a lack of well-designed studies.

3.4.2.3 Drug treatment

A single, optimal, medical therapy for neuro-urological symptoms is not always available. Commonly, a combination of different therapies (e.g. intermittent catheterisation and antimuscarinic drugs) is advised to prevent urinary tract damage and improve long-term outcomes, particularly in patients with a suprasacral SCI or MS [151, 174-176].

3.4.2.3.1 Drugs for storage symptoms

Antimuscarinic drugs: Are the first-line choice for treating NDO, increasing bladder capacity and reducing episodes of UI secondary to NDO by the inhibition of parasympathetic pathways [140, 177-183]. Antimuscarinic drugs have been used for many years to treat patients with NDO [181, 182, 184], and the responses of individual patients to antimuscarinic treatment are variable. Despite a meta-analysis confirming the clinical and urodynamic efficacy of antimuscarinic therapy compared to placebo in adult NDO, a more recent integrative review has indicated that the information provided is still too limited for clinicians to be able to match trial data to the needs of individual patients with SCI, mainly due to the lack of use of standardised clinical evaluation tools such as the American Spinal Injury Association bladder diary and validated symptoms score [182, 185].

Higher doses or a combination of antimuscarinic agents may be an option to maximise outcomes in neurological patients [178, 179, 186-189]. However, these drugs have a high incidence of adverse events, which may lead to early discontinuation of therapy. Despite this, NDO patients have generally shown better treatment adherence compared to idiopathic DO patients [190].

Choice of antimuscarinic agent: Oxybutynin [140, 178, 179, 181, 182, 191], trospium [182, 188, 192], tolterodine [193] and propiverine [182, 194] are established, effective and well tolerated treatments even in long-term use [181, 182, 195, 196]. Darifenacin [197, 198] and solifenacin [199] have been evaluated in NDO secondary to SCI and MS [182, 197-199] with results similar to other antimuscarinic drugs. A pilot study using solifenacin in NDO due to PD showed an improvement in UI [200]. Fesoterodine, an active metabolite of tolterodine, has also been introduced; to date there has been no published clinical evidence for its use in the treatment of neuro-urological disorders. Favourable results with the new drug imidafenacin have been reported in suprapontine as well as SCI patients [201, 202].

Side effects: Controlled-release antimuscarinics have some minor side effects, e.g. dry mouth [203]. It has been suggested that different ways of administration may help to reduce side effects [204]. Imidafenacine has been safely used in neurological patients with no worsening of cognitive function [201].

Beta-3-adrenergic receptor agonists
The role of mirabegron in neuro-urological patients is still unclear. In MS and SCI patients, with very short follow up, mirabegron has not demonstrated any significant effect on detrusor pressure or cystometric capacity despite the reported improvement in LUTS [205, 206]. A significant subjective improvement in OAB symptoms has also been reported using lower dosages of mirabegron in patients affected by CNS lesions without any negative effects on voiding function [207]. A standard dosage of 50 mg has been found effective with no worsening of cognitive function in patients with PD [208]. Combination therapy with mirabegron and desmopressin in MS patients has shown promising results; however, clinical experience is still very limited in neuro-urological populations [209].

Other drugs
In preliminary studies, improvements in daily incontinence rates, nocturia, daytime and 24 hour voids, as well as the low risk of adverse events, suggest that cannabinoids may be effective and safe in MS patients [210]. A concomitant improvement in OAB symptoms has been reported in male MS patients using daily tadalafil to treat neurogenic erectile dysfunction (ED) [211]. A systematic review found that desmopressin may be effective for treating nocturia in MS patients; however, adverse events were common, with the included studies being heterogeneous and of low quality [212].

3.4.2.3.2 Drugs for voiding symptoms
Detrusor underactivity: Cholinergic drugs, such as bethanechol and distigmine, have been considered to enhance detrusor contractility and promote bladder emptying, but are not frequently used in clinical practice [213]. Only preclinical studies have documented the potential benefits of cannabinoid agonists for improving detrusor contractility when administered intravesically [214, 215].

Decreasing bladder outlet resistance: α-blockers (e.g. tamsulosin, naftopidil and silodosin) seem to be effective for decreasing bladder outlet resistance, PVR and AD [216-218].

Increasing bladder outlet resistance: Several drugs have shown efficacy in selected cases of mild SUI, but there are no high-level evidence studies in neurological patients [140].

3.4.2.4 Summary of evidence and recommendations for drug treatments

Summary of evidence	**LE**
Long-term efficacy and safety of antimuscarinic therapy for NDO is well documented.	1a
Mirabegron does not improve urodynamic outcomes in NDO patients.	1b
Maximise outcomes for neurogenic detrusor overactivity by considering a combination therapy.	3

Recommendations	**Strength rating**
Use antimuscarinic therapy as the first-line medical treatment for neurogenic detrusor overactivity.	Strong
Prescribe α-blockers to decrease bladder outlet resistance.	Strong
Do not prescribe parasympathomimetics for underactive detrusor.	Strong

3.4.2.5 Minimally invasive treatment
3.4.2.5.1 Catheterisation
Intermittent self- or third-party catheterisation [219, 220] is the preferred management for neuro-urological patients who cannot effectively empty their bladders [140]. Sterile IC, as originally proposed by Guttmann and Frankel [219], significantly reduces the risk of UTI and bacteriuria [140, 221, 222], compared with clean IC introduced by Lapides *et al.* [220]. However, it has not yet been established whether or not the incidence of UTI, other complications and user satisfaction are affected by either sterile or clean IC, coated or uncoated catheters or by any other strategy [223].

Sterile IC cannot be considered a routine procedure [140, 222]. Aseptic IC is an alternative to sterile IC [224]. The use of hydrophilic catheters was associated with a lower rate of UTI [225].

Contributing factors to contamination are insufficient patient education and the inherently greater risk of UTI in neuro-urological patients [140, 226-230]. The average frequency of catheterisations per day is four to six times [231] and the catheter size most often used is between 12-16 Fr. In aseptic IC, an optimum frequency of five times showed a reduction of UTI [231]. Ideally, bladder volume at catheterisation should, as a rule, not exceed 400-500 mL.

Indwelling transurethral catheterisation and, to a lesser extent, suprapubic cystostomy are associated with a range of complications as well as an enhanced risk for UTI [140, 232-239]; therefore, both procedures should be avoided, when possible. Silicone catheters are preferred as they are less susceptible to encrustation and because of the high incidence of latex allergy in the neuro-urological patient population [240].

3.4.2.5.2 Summary of evidence and recommendations for catheterisation

Summary of evidence	LE
Intermittent catheterisation is the standard treatment for patients who are unable to empty their bladder.	3
Indwelling transurethral catheterisation and suprapubic cystostomy are associated with a range of complications as well as an enhanced risk for UTI.	3

Recommendations	Strength rating
Use intermittent catheterisation, whenever possible aseptic technique, as a standard treatment for patients who are unable to empty their bladder.	Strong
Thoroughly instruct patients in the technique and risks of intermittent catheterisation.	Strong
Avoid indwelling transurethral and suprapubic catheterisation whenever possible.	Strong

3.4.2.5.3 Intravesical drug treatment

To reduce DO, antimuscarinics can also be administered intravesically [204, 241-244]. The efficacy, safety and tolerability of intravesical administration of 0.1% oxybutynin hydrochloride compared to its oral administration for treatment of NDO has been demonstrated in a recent randomised controlled study [204]. This approach may reduce adverse effects due to the fact that the antimuscarinic drug is metabolised differently [241] and a greater amount is sequestered in the bladder, even more than with electromotive administration [242].

The vanilloids, capsaicin and resiniferatoxin, desensitise the C-fibres for a period of a few months [245, 246]. Clinical studies have shown that resiniferatoxin has limited clinical efficacy compared to botulinum toxin A injections in the detrusor [245].

Although preliminary data suggest that intravesical vanilloids might be effective for treating neurogenic LUT dysfunction, their safety profile appears to be unfavourable [247]. Currently, there is no indication for the use of these substances, which are not licensed for intravesical treatment.

3.4.2.5.4 Summary of evidence and recommendations for intravesical drug treatment

Summary of evidence	LE
A significant reduction in adverse events was observed for intravesical administration of oxybutynine compared to oral administration.	1a

Recommendation	Strength rating
Offer intravesical oxybutynin to neurogenic detrusor overactivity patients with poor tolerance to the oral route.	Strong

3.4.2.5.5 Botulinum toxin injections in the bladder

Botulinum toxin A causes a long-lasting but reversible chemical denervation that lasts for about nine months [248, 249]. The toxin injections are mapped over the detrusor in a dosage that depends on the preparation used. Botulinum toxin A has been proven effective in patients with neuro-urological disorders due to MS, SCI and PD in multiple RCTs and meta-analyses [250-252]. Urodynamic studies might be necessary after treatment in patients with maximal filling pressure of > 40 cm H_2O cm in order to monitor the effect of the injections on bladder pressure [253]. Repeated injections seem to be possible without loss of efficacy, even after initial low response rates, based on years of follow up [248, 254-257]. The clinical efficacy of botulinum toxin A injection in patients with low morbidity after failure of augmentation enterocystoplasty has been demonstrated [258]. A switch between different toxin variations may improve responsiveness [259]. The most frequent side effects are UTIs, urinary retention and haematuria [260]. Intermittent catheterisation may become necessary, this is especially relevant in MS patients as they do not often perform IC prior to intravesical botulinum toxin injections. However, a lower dose of botulinum toxin A (100 U) may reduce the rate of clean IC in MS patients [261]. Rare complications include generalised muscle weakness and AD [260]. Current research focuses on different delivery approaches to injection such as liposome encapsulated botulinum toxin to decrease side effects [262]. Neuro-urological patients with an indwelling catheter and concomitant bladder pain and/or catheter bypass leakage could benefit from intravesical botulinum injections [263].

3.4.2.5.6 Bladder neck and urethral procedures

Reduction of the bladder outlet resistance may be necessary to protect the UUT. This can be achieved by chemical denervation of the sphincter or by surgical interventions (bladder neck or sphincter incision or urethral stent – Section 3.4.3.1). Incontinence may result and can be managed by external devices (Section 3.4.2.1).

Botulinum toxin A: This can be used to treat DSD effectively by injecting the sphincter at a dose that depends on the preparation used. The dyssynergia is abolished only for a few months, necessitating repeat injections. The efficacy of this treatment has been reported to be high with few adverse effects [264-266]. However, a recent Cochrane report concluded that, because of limited evidence, future RCTs assessing the effectiveness of botulinum toxin A injections also need to address the uncertainty about the optimal dose and mode of injection [267]. In addition, this therapy is not licensed.

Balloon dilatation: Favourable immediate results were reported [268], but there have been no further reports since 1994; therefore, this method is no longer recommended.

Increasing bladder outlet resistance: This can improve the continence condition. Despite early positive results with urethral bulking agents, a relative early loss of continence is reported in patients with neuro-urological disorders [140, 269, 270].

Urethral inserts: Urethral plugs or valves for the management of (female) stress incontinence have not been applied in neuro-urological patients. The experience with active pumping urethral prosthesis for treatment of the underactive or acontractile detrusor were disappointing [271].

3.4.2.5.7 Summary of evidence and recommendations for botulinum toxin A injections and bladder neck procedures

Summary of evidence	**LE**
Botulinum toxin A has been proven effective in patients with neuro-urological disorders due to MS or SCI in multiple RCTs and meta-analyses.	1a
Bladder neck incision is indicated only for secondary changes (fibrosis) at the bladder neck.	4

Recommendations	**Strength rating**
Use botulinum toxin injection in the detrusor to reduce neurogenic detrusor overactivity in multiple sclerosis or spinal cord injury patients if antimuscarinic therapy is ineffective.	Strong
Bladder neck incision is effective in a fibrotic bladder neck.	Strong

3.4.3 Surgical treatment

There is considerable heterogeneity in outcome parameters and definitions of cure used to report on outcome of surgical interventions for SUI in neuro-urological patients [272]. The heterogeneity of outcome reporting makes it difficult to interpret and compare different studies and therapies. A consistent comparison of the outcomes of therapy can only be made after standardisation of outcome parameters and definitions of cure or success; therefore, it would seem prudent to develop a core outcome set (COS) for use in UI research in neuro-urological patients [272]. Until such a COS is developed it would seem feasible to use both a subjective and objective outcome parameter and the combination of both to define cure [272]. Due to the importance of QoL for neuro-urological patients a disease-specific QoL questionnaire or a bother questionnaire validated for neuro-urological patients should be used as the subjective outcome parameter [272].

3.4.3.1 Bladder neck and urethral procedures

Increasing the bladder outlet resistance has the inherent risk of causing high intravesical pressure. Procedures to treat sphincteric incontinence are therefore suitable only when the detrusor activity can be controlled and when no significant reflux is present. A simultaneous bladder augmentation and IC may be necessary [140].

Urethral sling: Various materials have been used for this procedure with enduring positive results. The procedure is established in women with the ability to self-catheterise [140, 273-276]. There is growing evidence that synthetic slings can be used effectively with acceptable medium to long-term results and minimal morbidity in neurological patients [277, 278]. Besides the pubovaginal sling, which has been considered the procedure of choice in this subgroup of patients, recent reports suggest that both the transobturator and the retropubic approaches may also be considered, with similar failure rates and a reduction in the need for IC. However, for both approaches a higher incidence of *de novo* urgency was reported [278, 279]. In men, both autologous and synthetic slings may also be an alternative [280-284].

Artificial urinary sphincter (AUS): This device was introduced by Light and Scott for patients with neuro-urological disorders [285]. It has stood the test of time and acceptable long-term outcomes can be obtained [286]. However, the complication rates and re-operation rates are higher than in non-neurogenic patient groups (up to 60%), so it is advisable that patients are conscientiously informed about the success rates as well as the complications that may occur after the procedure [287, 288]. In a case series with 25 years follow up only 7.1% of patients were revision free at 20 years [289]. Re-interventions are commonly due to infection, urethral atrophy or erosion and mechanical failure.

There is growing interest in the use of this device in women with development of laparoscopic and robot-assisted approaches which appear to reduce infection and erosion rates [290-293]. Long-term surgical and patient-reported outcomes are needed to determine the role of AUS placement in female patients with neurogenic SUI [294].

Adjustable continence device - ProACT/ACT®: The efficacy of this device has been reported mainly in post-prostatectomy incontinence. A marginally lower cure rate has been reported in neurological patients when compared to non-neurological patients [295]. A retrospective study in neuro-urological patients reported a low rate of efficacy and high complication rate for this device [296].

Functional sphincter augmentation: Transposing the gracilis muscle to the bladder neck [297] or proximal urethra [298], can enable the possible creation of a functional autologous sphincter by electrical stimulation [297-299]; therefore, raising the prospect of restoring control over the urethral closure.

Bladder neck and urethra reconstruction: The classical Young-Dees-Leadbetter procedure [300] for bladder neck reconstruction in children with bladder exstrophy, and Kropp urethra lengthening [301] improved by Salle [302], are established methods to restore continence provided that IC is practiced and/or bladder augmentation is performed [140, 303].

Endoscopic techniques for treating anatomic bladder outlet obstruction [304]:

- Transurethral resection of the prostate is indicated in male patients with refractory LUT symptoms due to benign prostatic obstruction. Special consideration should be given to pre-operative abnormal sphincter function which can lead to *de novo* or persistent UI [305, 306].
- Bladder neck resection is indicated in patients with high PVR and when a prominent obstruction of the sclerotic ring in the bladder neck is identified during cystoscopy. The resection can be performed between the three or nine o'clock position or full circle [307].
- Urethrotomy is indicated in patients with urethral strictures. Cold knife or neodymium:YAG contact laser urethrotomy at the twelve o'clock position can be performed [308, 309]. In recurrent strictures, open surgery should be considered.
- Sphincterotomy has been shown to be an efficient technique for the resolution of AD, hydronephrosis and recurrent UTI, and for decreasing detrusor pressures, PVR and vesicoureteral reflux. It is irreversible and should be limited to men who are able to wear a condom catheter. By staged incision, bladder outlet resistance can be reduced without completely losing the closure function of the urethra [139, 140, 310]. The incision with less complications is the twelve o'clock sphincterotomy with cold knife [311] or neodymium:YAG laser [312]. Sphincterotomy needs to be repeated at regular intervals in many patients [313], but it is efficient and does not cause severe adverse effects [139, 268]. Secondary narrowing of the bladder neck may occur, for which combined bladder neck incision might be considered [314].

Bladder neck incision: This is indicated only for secondary changes at the bladder neck (fibrosis) [139, 315]. This procedure is not recommended in patients with detrusor hypertrophy, which causes thickening of the bladder neck [139].

Stents: Implantation of urethral stents results in continence being dependent on adequate closure of the bladder neck [140]. The results are comparable with sphincterotomy and the stenting procedure has a shorter duration of surgery and hospital stay [316, 317]. However, the costs [139], possible complications and re-interventions [318, 319] are limiting factors in their use [320-323].

3.4.3.2 Denervation, deafferentation, sacral neuromodulation

Sacral anterior root stimulation (SARS) is aimed at producing detrusor contraction. The technique was developed by Brindley [324] and is only applicable to complete lesions above the implant location, as its stimulation amplitude is over the pain threshold. The urethral sphincter efferents are also stimulated, but because the striated muscle relaxes faster than the smooth muscle of the detrusor, so-called "post-stimulus voiding" occurs. This approach has been successful in highly selected patients [325-327]. Although it has been shown that detrusor pressure during SARS decreases over time, the changes do not seem to be clinically relevant during the first decade after surgery [328]. By changing the stimulation parameters, this method can also induce defecation or erection. A recent study reported that Charcot spinal arthropathy should be considered as a potential long-term complication of SARS, leading to spinal instability and to SARS dysfunction [329].

Sacral rhizotomy, also known as sacral deafferentation, has achieved some success in reducing DO [330-332], but nowadays, it is used mostly as an adjuvant to SARS [325, 333-336]. Alternatives to rhizotomy are sought in this treatment combination [337-339].

Sacral neuromodulation [340] might be effective and safe for treating neuro-urological symptoms, but there is a lack of RCTs and it is unclear which neurological patients are most suitable [341-344].

3.4.3.3 Bladder covering by striated muscle

When the bladder is covered by striated muscle, that can be stimulated electrically, or ideally that can be contracted voluntarily, voiding function can be restored to an acontractile bladder. The rectus abdominis [345] and latissimus dorsi [346] have been used successfully in patients with neuro-urological symptoms [347, 348].

3.4.3.4 Bladder augmentation

The aim of auto-augmentation (detrusor myectomy) is to reduce DO or improve low bladder compliance. The advantages are: low surgical burden, low rate of long-term adverse effects, positive effect on patient QoL, and it does not preclude further interventions [139, 140, 349-352].

Replacing or expanding the bladder by intestine or other passive expandable coverage will improve bladder compliance and at least reduce the pressure effect of DO [353, 354]. Improved QoL and stable renal function has been reported during long-term follow-up [355]. Patients performing IC with augmentation cystoplasty had better urinary function and satisfaction with their urinary symptoms compared to patients performing IC with or without botulinum toxin treatment [356]. Long-term complications included bladder perforation (1.9%), mucus production (12.5%), metabolic abnormalities (3.35%), bowel dysfunction (15%), and stone formation (10%) [355].

The procedure should be used with caution in patients with neuro-urological symptoms, but may become necessary if all less-invasive treatment methods have failed. Special attention should be paid to patients with pre-operative renal scars since metabolic acidosis can develop [357]. Bladder substitution with bowel after performing a supratrigonal cystectomy [354], to create a low-pressure reservoir, is indicated in patients with a severely thick and fibrotic bladder wall [140]. Intermittent catheterisation may become necessary after this procedure. The long-term scientific evidence shows that bladder augmentation is a highly successful procedure that stabilises renal function and prevents anatomical deterioration; however, lifelong follow-up is essential in this patient group given the significant morbidity associated with this procedure [355, 358].

3.4.3.5 Urinary diversion

When no other therapy is successful, urinary diversion must be considered for the protection of the UUT and for the patient's QoL [140].

Continent diversion: This should be the first choice for urinary diversion. Patients with limited dexterity may prefer a stoma instead of using the urethra for catheterisation. For cosmetic reasons, the umbilicus is often used for the stoma site [359-364]. A systematic review of the literature concluded that continent catheterisable tubes/stomas are an effective treatment option in neuro-urological patients unable to perform intermittent self-catheterisation through the urethra [365]. However, the complication rates were significant with 85/213 post-operative events requiring re-operation [365]. Tube stenosis occurred in 4-32% of the cases. Complications related to concomitant procedures (augmentation cystoplasty, pouch) included neovesicocutaneous fistulae (3.4%), bladder stones (20-25%), and bladder perforations (40%). In addition, data comparing HRQoL before and after surgery were not reported [365].

Incontinent diversion: If catheterisation is impossible, incontinent diversion with a urine-collecting device is indicated. Ultimately, it could be considered in patients who are wheelchair bound or bed-ridden with intractable and untreatable incontinence, in patients with LUT destruction, when the UUT is severely compromised, and in patients who refuse other therapy [140]. An ileal segment is used for the deviation in most cases [140, 366-369]. Patients gain better functional status and QoL after surgery [370].

Undiversion: Long-standing diversions may be successfully undiverted or an incontinent diversion changed to a continent one with the emergence of new and better techniques for control of detrusor pressure and incontinence [140]. The patient must be carefully counselled and must comply meticulously with the instructions [140]. Successful undiversion can then be performed [371].

3.4.3.6 Summary of evidence and recommendations for surgical treatment

Summary of evidence	LE
Bladder augmentation is an effective option to decrease detrusor pressure and increase bladder capacity, when all less-invasive treatment methods have failed.	3
Urethral sling placement is an established procedure, with acceptable medium- to long-term results, in women with the ability to self-catheterise.	3
Artificial urinary sphincter insertion is a viable option, with acceptable long-term outcomes, in males. The complication and re-operation rates are higher in neuro-urological patients; therefore, patients must be adequately informed regarding the success rates as well as the complications that may occur following the procedure.	3

Recommendations	Strength rating
Perform bladder augmentation in order to treat refractory neurogenic detrusor overactivity.	Strong
Place an autologous urethral sling in female patients with neurogenic stress urinary incontinence who are able to self-catheterise.	Strong
Insert an artificial urinary sphincter in male patients with neurogenic stress urinary incontinence.	Strong

3.5 Urinary tract infection in neuro-urological patients

3.5.1 Epidemiology, aetiology and pathophysiology

Urinary tract infection is the onset of signs and/or symptoms accompanied by laboratory findings of a UTI (bacteriuria, leukocyturia and positive urine culture) [360]. There are no evidence-based cut-off values for the quantification of these findings. The published consensus is that a significant bacteriuria in persons performing IC is present with > 10^2 cfu/mL, > 10^4 cfu/mL in clean-void specimens and any detectable concentration in suprapubic aspirates. Regarding leukocyturia, ten or more leukocytes in centrifuged urine samples per microscopic field (400x) are regarded as significant [360].

The pathogenesis of UTI in neuro-urological patients is multifactorial. Male gender seems to be a risk factor for febrile UTI [372]. Several etiological factors have been described: altered intrinsic defence mechanisms, impaired washout and catheterisation [373]. Poor glycemic control has been established as a risk factor for UTI in women with type 1 diabetes [374]. However, the exact working mechanisms remain unknown. The presence of asymptomatic bacteriuria in SCI patients is higher than in the general population, and varies depending on bladder management. Prevalence of bacteriuria in those performing clean IC varies from 23-89% [375]. Sphincterotomy and condom catheter drainage has a 57% prevalence [376]. Asymptomatic bacteria should not be routinely screened for in this population [377].

Individuals with neuro-urological symptoms, especially those with SCI, may have other signs and symptoms in addition to or instead of traditional signs and symptoms of a UTI in able-bodied individuals. Other problems, such as AD, may develop or worsen due to a UTI [225]. The most common signs and symptoms suspicious of a UTI in those with neuro-urological disorders are fever, new onset or increase in incontinence, including leaking around an indwelling catheter, increased spasticity, malaise, lethargy or sense of unease, cloudy urine with increased urine odour, discomfort or pain over the kidney or bladder, dysuria, or AD [225, 378]. New incontinence is the most specific symptom, whereas cloudy and foul smelling urine has the highest positive predictive value for UTI diagnosis [379].

3.5.2 ***Diagnostic evaluation***
Urine culture and urinalysis are the optimum tests for the diagnosis of UTI in neuro-urological patients. A dipstick test may be more useful to exclude than to prove UTI [380, 381]. As bacterial strains and resistance patterns in persons with neuro-urological disorders may differ from those of able-bodied patients, microbiologic testing is mandatory [382].

3.5.3 ***Disease management***
Bacteriuria in patients with neuro-urological disorders should not be treated. Treatment of asymptomatic bacteriuria results in significantly more resistant bacterial strains without improving the outcome [383]. Urinary tract infections in persons with neuro-urological disorders are by definition a complicated UTI; therefore, single-dose treatment is not advised. There is no consensus in the literature about the duration of treatment as it depends on the severity of the UTI and the involvement of kidneys and the prostate. Generally, a five to seven day course of antibiotic treatment is advised, which can be extended up to fourteen days according to the extent of the infection [383]. The choice of antibiotic therapy should be based on the results of the microbiologic testing. If immediate treatment is mandatory (e.g. fever, septicaemia, intolerable clinical symptoms, extensive AD), the choice of treatment should be based on local and individual resistance profiles [384]. In patients with afebrile UTI, an initial non-antibiotic treatment may be justified [385, 386].

3.5.3.1 Recurrent UTI
Recurrent UTI in patients with neuro-urological disorders may indicate suboptimal management of the underlying functional problem, e.g. high bladder pressure during storage and voiding, incomplete voiding or bladder stones. The improvement of bladder function, by treating DO by botulinum toxin A injection in the detrusor [387], and the removal of bladder stones or other direct supporting factors, especially indwelling catheters, as early as possible, are mandatory [382].

3.5.3.2 Prevention
If the improvement of bladder function and removal of foreign bodies/stones is not successful, additional UTI prevention strategies should be utilised. In a meta-analysis the use of hydrophilic catheters was associated with a lower rate of UTI [225]. Bladder irrigation has not been proven effective [388].

Various medical approaches have been tested for UTI prophylaxis in patients with neuro-urological disorders. The benefit of cranberry juice or probiotics for the prevention of UTI could not be demonstrated in RCTs [389, 390]. Methenamine hippurate is not effective in individuals with neuro-urological symptoms [391]. There is no sufficient evidence to support the use of L-methionine for urine acidification to prevent recurrent UTI [392]. There is only weak evidence that oral immunotherapy reduces bacteriuria in patients with SCI [393] and that recurrent UTIs are reduced [394]. Low-dose, long-term, antibiotic prophylaxis can reduce UTI frequency, but increases bacterial resistance and is therefore not recommended [383].

Weekly cycling of antibiotic prophylaxis provided long-term positive results, but the results of this trial need to be confirmed in further studies [395]. Another possible future option, the inoculation of apathogenic *Escherichia coli* strains into the bladder, has provided positive results in initial studies, but because of the paucity of data [396], cannot be recommended as a treatment option. There is initial evidence that homeopathic treatment can decrease UTI frequency [397]. In addition, intravesical gentamycin instillations can reduce UTI frequency without increasing the number of multi-resistant bacteria [398].

In summary, based on the criteria of evidence-based medicine, there is currently no preventive measure for recurrent UTI in patients with neuro-urological disorders that can be recommended without limitations. Therefore, individualised concepts should be taken into consideration, including immunostimulation, phytotherapy and complementary medicine [399]. Prophylaxis in patients with neuro-urological disorders is important to pursue, but since there are no data favouring one approach over another, prophylaxis is essentially a trial and error approach.

3.5.4 *Summary of evidence and recommendations for the treatment of UTI*

Summary of evidence	LE
Treatment of asymptomatic bacteriuria results in significantly more resistant bacterial strains without improving patient outcome.	1a
Low-dose, long-term, antibiotic prophylaxis does not reduce UTI frequency, but increases bacterial resistance.	2a
Recurrent UTI in patients with neuro-urological disorders may indicate suboptimal management of the underlying functional problem. Improvement of bladder function as early as possible is mandatory.	3
There is currently no preventive measure for recurrent UTI in patients with neuro-urological disorders that can be recommended without limitations.	3

Recommendations	Strength rating
Do not screen for or treat asymptomatic bacteriuria in patients with neuro-urological disorders.	Strong
Avoid the use of long-term antibiotics for recurrent urinary tract infections (UTIs).	Strong
In patients with recurrent UTI, optimise treatment of neuro-urological symptoms and remove foreign bodies (e.g. stones, indwelling catheters) from the urinary tract.	Strong
Individualise UTI prophylaxis in patients with neuro-urological disorders as there is no optimal prophylactic measure available.	Strong

3.6 Sexual function and fertility

These Guidelines specifically focus on sexual dysfunction and infertility in patients with a neurological disease [400, 401]. Non-neurogenic, male sexual dysfunction and infertility are covered in separate EAU Guidelines [402, 403]. In neuro-urological patients sexual problems can be identified at three levels: primary (direct neurological damage), secondary (general physical disabilities) and tertiary (psychosocial and emotional issues) sexual dysfunction [404]. Adopting a systematic approach, such as the PLISSIT model (Permission, Limited Information, Specific Suggestions and Intensive Therapy) [405], provides a framework for counselling and treatment involving a stepwise approach to the management of neurogenic sexual dysfunction. Sexual dysfunction is associated with neurogenic LUT dysfunction in patients with MS [406] and SB [407]. Although various patient reported outcome measures (PROMs) are available to evaluate sexual function, the evidence for good PROMs is limited and studies with high methodological quality are needed [408].

3.6.1 *Erectile dysfunction*

3.6.1.1 *Phosphodiesterase type 5 inhibitors (PDE5Is)*

Phosphodiesterase type 5 inhibitors (PDE5Is) are recommended as first-line treatment in neurogenic ED [400, 401]. In SCI patients, tadalafil, vardenafil and sildenafil have all improved retrograde ejaculation and improved erectile function and satisfaction on IIEF-15. Tadalafil 10 mg was shown to be more effective than sildenafil 50 mg. All currently available PDE5Is appear to be effective and safe, although there are no high level evidence studies in neuro-urological patients investigating the efficacy and side effects across different PDE5Is, dosages and formulations [409].

For MS patients two studies reported significant improvement in ED when using sildenafil and tadalafil. One study; however, showed no improvement in ED with sildenafil.

In PD normal erectile function was described in over half of the patients using sildenafil 100 mg and a significant improvement in IIEF-15 score was found compared to placebo. While most neuro-urological patients require long-term therapy for ED some have a low compliance rate or stop therapy because of side effects [410, 411], most commonly headache and flushing [401]. In addition, PDE5Is may induce relevant hypotension in patients with tetraplegia/high-level paraplegia and multiple system atrophy [410, 411]. As a prerequisite for successful PDE5I-therapy, some residual nerve function is required to induce erection. Since many patients with SCI use on-demand nitrates for the treatment of AD, they must be counselled that PDE5Is are contraindicated when using nitrate medication.

3.6.1.2 *Drug therapy other than PDE5Is*

Fampridine to treat neurogenic spasticity has been shown to be beneficial in improving ED in two domains of the IIEF-15 in SCI and MS patients, however, with a significant discontinuation rate due to severe adverse events [412]. Sublingual apomorfine was shown to have poor results on ED in SCI patients and side-effects in half of the patients [413]. In PD pergolide mesylate showed a significant improvement in IIEF-15 scores up to twelve months follow-up [414].

3.6.1.3 Mechanical devices

Mechanical devices (vacuum tumescence devices and penile rings) may be effective but are less popular [415-419].

3.6.1.4 Intracavernous injections and intraurethral application

Patients not responding to oral drugs may be offered intracavernous injections (alprostadil, papaverine and phentolamine) that have been shown to be effective in a number of neurological conditions, including SCI, MS, and diabetes mellitus [420-426], but their use requires careful dose titration and some precautions. Complications of intracavernous drugs include pain, priapism and corpora cavernosa fibrosis.

Intracavernous vasoactive drug injection is the first-line therapeutic option in patients taking nitrate medications, as well as those with concerns about drug interactions with PDE5Is, or in whom PDE5Is are ineffective. The impact of intracavernous injections on ejaculation and orgasmic function, their early use for increasing the recovery rate of a spontaneous erection, and their effectiveness and tolerability in the long-term are unclear [410]. Intra-urethral alprostadil application is an alternative, but a less effective, route of administration [422, 427].

3.6.1.5 Sacral neuromodulation

Sacral neuromodulation for LUT dysfunction may improve sexual function; however, high level evidence studies are lacking.

3.6.1.6 Penile prostheses

Penile prostheses may be considered for treatment of neurogenic ED when all conservative treatments have failed. At a mean follow-up of seven years 83.7% of patients with SCI were able to have sexual intercourse [401]. Serious complications, including infection and prosthesis perforation, may occur in about 10% of patients, depending on implant type [428-430].

3.6.1.7 Summary of evidence and recommendations for erectile dysfunction

Summary of evidence	**LE**
The long-term efficacy and safety of oral PDE5Is for the treatment of ED is well documented.	1b
Intracavernous vasoactive drug injections have been shown to be effective in a number of neurological conditions, including SCI and MS; however, their use requires careful dose titration and precautions.	3
Mechanical devices (vacuum tumescence devices and penile rings) may be effective but are less popular.	3
Reserve penile prostheses for selected patients, those in which all conservative treatments have failed, with neurogenic ED.	4

Recommendations	**Strength rating**
Prescribe oral phosphodiesterase type 5 inhibitors as first-line medical treatment in neurogenic erectile dysfunction (ED).	Strong
Give intracavernous injections of vasoactive drugs (alone or in combination) as second-line medical treatment in neurogenic ED.	Strong
Offer mechanical devices such as vacuum devices and rings to patients with neurogenic ED.	Strong

*3.6.2 **Male fertility***

Male fertility can be compromised in the neurological patient by ED, ejaculation disorder, impaired sperm quality or various combinations of these three disorders. Among the major conditions contributing to neurogenic infertility are pelvic and retroperitoneal surgery, diabetes mellitus, SB, MS and SCI [431]. Erectile dysfunction is managed as described previously. Retrograde ejaculation may be reversed by sympathomimetic agents contracting the bladder neck, including imipramine, ephedrine, pseudoephedrine, and phenylpropanolamine [431]. The use of a balloon catheter to obstruct the bladder neck may be effective in obtaining antegrade ejaculation [432]. If antegrade ejaculation is not achieved, the harvest of semen from the urine may be considered [433].

Prostatic massage is safe and easy to use for obtaining semen in men with lesions above Th 10 [434]. In several patients, vibrostimulation or transrectal electroejaculation are needed for sperm retrieval [431, 435, 436]. Semen retrieval is more likely with vibrostimulation in men with lesions above Th 10 [437-439]. In men with SCI, especially at or above Th 6, AD might occur during sexual activity and ejaculation [440, 441]; patients at risk and fertility clinics must be informed and aware of this potentially life-threatening condition. In SCI patients the use of oral midodrine can improve sperm retrieval at vibrostimulation [442].

In men with MS, use of disease modifying drugs during the conception phase, has not been associated with altered pregnancy outcomes [443]. Surgical procedures, such as, microsurgical epididymal sperm aspiration (MESA) or testicular sperm extraction (TESE), may be used if vibrostimulation and electroejaculation are not successful [444, 445]. Pregnancy rates in patients with SCI are lower than in the general population, but since the introduction of intracytoplasmic sperm injection (ICSI), men with SCI now have a good chance of becoming biological fathers [446-448].

3.6.2.1 Sperm quality and motility

The following has been reported on sperm quality and motility:
- bladder management with clean IC may improve semen quality compared to indwelling catheterisation, reflex voiding or bladder expression [449];
- in SCI patients sperm quality decreases at the early post traumatic phase demonstrating lower spermatozoid vitality (necrospermia), reduced motility (asthenospermia) and leucospermia [444];
- long-term valproate treatment for epilepsy negatively influences sperm count and motility [450];
- vibrostimulation produces samples with better sperm motility than electrostimulation [451, 452];
- electroejaculation with interrupted current produces better sperm motility than continuous current [453];
- freezing of sperm is unlikely to improve fertility rates in men with SCI [454].

3.6.2.2 Summary of evidence and recommendations for male fertility

Summary of evidence	**LE**
Vibrostimulation and transrectal electroejaculation have been shown to be effective for sperm retrieval in neuro-urological patients.	1b
Surgical procedures, such as, microsurgical epididymal sperm aspiration or testicular sperm extraction, may be used if vibrostimulation and electroejaculation are not successful.	3
In men with SCI at or above Th 6, AD might occur during sexual activity and ejaculation.	3

Recommendations	**Strength rating**
Perform vibrostimulation and transrectal electroejaculation for sperm retrieval in men with spinal cord injury.	Strong
Perform microsurgical epididymal sperm aspiration, testicular sperm extraction and intracytoplasmic sperm injection after failed vibrostimulation and/or transrectal electroejaculation in men with spinal cord injury.	Strong
Counsel men with spinal cord injury at or above Th 6 and fertility clinics about the potentially life-threatening condition of autonomic dysreflexia.	Strong

*3.6.3 **Female sexuality***

The most relevant publications on neurogenic female sexual dysfunction are in women with SCI and MS. After SCI, about 65-80% of women continue to be sexually active, but to a much lesser extent than before the injury, and about 25% report a decreased satisfaction with their sexual life [455-458]. Although sexual dysfunction is very common in women with MS, it is still often overlooked by medical professionals [459, 460].

The greatest physical barrier to sexual activity is UI. A correlation has been found between the urodynamic outcomes of low bladder capacity, compliance and high maximum detrusor pressure and sexual dysfunction in MS patients. Problems with positioning and spasticity affect mainly tetraplegic patients. Peer support may help to optimise the sexual adjustment of women with SCI in achieving a more positive self-image, self-esteem and feelings of being attractive to themselves and others [455, 461-463].

The use of specific drugs for sexual dysfunction is indicated to treat inadequate lubrication. Data on sildenafil for treating female sexual dysfunction are poor and controversial [401]. Although good evidence exists that psychological interventions are effective in the treatment of female hypoactive sexual desire disorder and female orgasmic disorder [464], there is a lack of high-level evidence studies in the neurological population.

Neurophysiological studies have shown that women with the ability to perceive Th 11-L2 pin-prick sensations may have psychogenic genital vasocongestion. Reflex lubrication and orgasm is more prevalent in women with SCI who have preserved the sacral reflex arc (S2-S5), even when it has not been shown in an individual woman that a specific level and degree of lesion is the cause of a particular sexual dysfunction. In SCI women with a complete lesion of the sacral reflex, arousal and orgasm may be evoked through stimulation of other erogenous zones above the level of lesions [465-467].

Sacral neuromodulation for LUT dysfunction may improve sexual function but high-evidence studies are lacking [401].

Women with SCI reported dissatisfaction with the quality and quantity of sexuality-related rehabilitation services and were less likely to receive sexual information than men [465, 468, 469].

3.6.4 ***Female fertility***

There are few studies on female fertility in neurological patients. More than a third (38%) of women with epilepsy had infertility and the relevant predictors were exposure to multiple (three or more) antiepileptic drugs, older age and lower education [470].

Although it seems that the reproductive capacity of women with SCI is only temporarily affected by SCI with cessation of menstruation for approximately six months after SCI [471], there are no high-level evidence studies. About 70% of sexually active women use some form of contraception after injury, but fewer women use the birth control pill compared to before their injury [472].

Women with SCI are more likely to suffer complications during pregnancy, labour and delivery compared to able-bodied women. Complications of labour and delivery include bladder problems, spasticity, pressure sores, anaemia, and AD [473-477]. Obstetric outcomes include higher rates of Caesarean sections and an increased incidence of low birth-weight babies [472, 475-477].

Epidural anaesthesia is chosen and effective for most patients with AD during labour and delivery [478, 479].

There is very little published data on women's experience of the menopause following SCI [480]. Women with MS who plan a pregnancy should evaluate their current drug treatment with their treating physician [481-483]. Clinical management should be individualised to optimise both the mother's reproductive outcomes and MS course [482-484].

3.6.4.1 Summary of evidence and recommendation for female sexuality and fertility

Summary of evidence	LE
Data on specific drugs for treating female sexual dysfunction are poor and controversial.	4
There are limited numbers of studies on female fertility in neurological patients, clinical management should be individualised to optimise both the mother's reproductive outcomes and medical condition.	4

Recommendations	Strength rating
Do not offer medical therapy for the treatment of neurogenic sexual dysfunction in women.	Strong
Take a multidisciplinary approach, tailored to individual patient's needs and preferences, in the management of fertility, pregnancy and delivery in women with neurological diseases.	Strong

3.7 Follow-up

3.7.1 ***Introduction***

Neuro-urological disorders are often unstable and the symptoms may vary considerably, even within a relatively short period. Regular follow-up is therefore necessary to assess the UUT [138].

Depending on the type of the underlying neurological pathology and the current stability of the neuro-urological symptoms, the interval between initial investigations and control diagnostics may vary and in many cases should not exceed one to two years. In high-risk neuro-urological patients this interval should be much shorter. Urinalysis should be performed only when patients present with symptoms [485]. The UUT should be checked by ultrasonography at regular intervals in high-risk patients; about once every six months [6, 486]. In these patients, physical examination and urine laboratory should take place every year [6, 486]. In MS patients higher scores on the Expanded Disability Status Scale (EDSS) are associated with risk factors for UUT deterioration [53]. A urodynamic investigation should be performed as a diagnostic baseline, and repeated during follow-up, more frequently in high-risk patients [6, 486]. In addition, bladder wall thickness can be measured on ultrasonography as an additional risk assessment for upper tract damage [487], although a 'safe' cut-off threshold for this has not been agreed [488]. The utility of DMSA for follow-up of neuro-urological patients has not been fully evaluated [489]. Any significant clinical change warrants further, specialised, investigation [6, 486]. However, there is a lack of high level evidence studies on this topic and every recommendation must be viewed critically in each individual neuro-urological patient [138].

The increased prevalence of muscle invasive bladder cancer in neuro-urological patients also warrants long-term follow-up [490]. The exact frequency of cystoscopy with or without cytology remains unknown, but presence of risk factors similar to the general population should trigger further investigation [485].

Adolescent patients with neurological pathology are at risk of being lost to follow-up during the transition to adulthood. It is important that a standardised approach during this transition is adopted to improve follow-up and specific treatment during adult life [491].

3.7.2 Summary of evidence and recommendations for follow-up

Summary of evidence	LE
Neuro-urological disorders are often unstable and the symptoms may vary considerably, therefore, regular follow-up is necessary.	4

Recommendations	Strength rating
Assess the upper urinary tract at regular intervals in high-risk patients.	Strong
Perform a physical examination and urine laboratory every year in high-risk patients.	Strong
Any significant clinical changes should instigate further, specialised, investigation.	Strong
Perform urodynamic investigation as a mandatory baseline diagnostic intervention in high-risk patients at regular intervals.	Strong

3.8 Conclusions

Neuro-urological disorders have a multi-faceted pathology. They require an extensive and specific diagnosis before one can embark on an individualised therapy, which takes into account the medical and physical condition of the patient and the patient's expectations about their future. The urologist can select from a wealth of therapeutic options, each with its own pros and cons. Notwithstanding the success of any therapy embarked upon, close surveillance is necessary for the patient's entire life.

These Guidelines offer you expert advice on how to define the patient's neuro-urological symptoms as precisely as possible and how to select, together with the patient, the appropriate therapy. This last choice, as always, is governed by the golden rule: as effective as needed, as non-invasive as possible.

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5. CONFLICT OF INTEREST

All members of the Neuro-urology working group have provided disclosure statements of all relationships that they have that might be perceived as a potential source of a conflict of interest. This information is publically accessible through the European Association of Urology website: http://uroweb.org/guideline. This guidelines document was developed with the financial support of the European Association of Urology. No external sources of funding and support have been involved. The EAU is a non-profit organisation and funding is limited to administrative and travel and meeting expenses. No honoraria or other reimbursements have been provided.

6. CITATION INFORMATION

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