

# Guidelines on Neuro-Urology

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# 1. INTRODUCTION

## 1.1 Aim

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 thus 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 on the lower urinary tract (LUT) as published by the International Continence Society (ICS) [1-4]. Readers are advised to consult the other EAU Guidelines which may address different aspects of the topics discussed in this document.

## 1.2 Publication history

The EAU published the first Neuro-Urology Guidelines in 2003 with updates in 2008, 2014 and 2015. In 2009, a review paper was published in European Urology [5].

Standard procedure for EAU Guidelines includes an annual assessment of newly published literature in the field to guide future updates. A shorter reference document, the Pocket Guidelines, is also available, both in print and as a mobile application, presenting the main findings of the Neuro-Urology Guidelines. These versions are abridged and therefore may require consultation with the full text version. All are available through the EAU website: <http://www.uroweb.org/guidelines/>.

For this 2015 print updates were made to:

- Chapter 3A: A new table summarising epidemiology of neuro-urological disorders has been added (Table 1) and text in this chapter has consequently been replaced.
- Chapter 3D: The sections on botulinum toxin sphincter injection (3D.2.5.4) and surgical treatment (3D.2.6) have been revised and updated.
- Chapter 3F: Sexual (dys)function and fertility has been revised and updated.

Additionally, the text has been significantly reduced so that only key information is included and re-formatted according to the EAU template for non-oncology Guidelines so that all Guidelines follow a similar format.

This document was peer-reviewed prior to publication.

## 1.3 Panel composition

The EAU Neuro-Urology Guidelines panel consists of an international multidisciplinary group of experts, including urologists specialised in the care of spinal cord injured (SCI) patients and a specialist in the field of urodynamic technologies.

## 1.4 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. Any disturbance of the nervous system involved, including the peripheral nerves in the pelvis, can result in neuro-urological symptoms. Depending on the extent and location of the disturbance, a variety of different LUT changes might occur, which can be symptomatic or asymptomatic. Moreover, neuro-urological symptoms can cause a variety of long-term complications; the most dangerous being deterioration in renal function. Since symptoms and long-term complications do not correlate [6], it is important to identify patients with neuro-urological symptoms, and establish if they have a low or high-risk of subsequent complications.

According to current knowledge, elevated storage pressure in the bladder, either alone or combined with vesicoureteric reflux (VUR), is the most important risk factor for renal damage [7]. Sustained elevated storage pressure in the bladder is mainly due to a combination of increased detrusor activity during the storage phase (detrusor overactivity [DO] or low compliance), combined with detrusor-sphincter dyssynergia (DSD). The combination of these findings is usually caused by suprasacral infrapontine spinal lesions. Furthermore, elevated detrusor leak point pressure has been demonstrated to be a risk factor for renal deterioration in patients with meningomyelocele [8]. Therefore, renal failure has been the leading cause of death in patients with SCI for a long time [9]. Even today, 26% of patients with meningomyelocele who do not undergo urological treatment develop renal damage. Detrusor leak point pressure > 40 cm H<sub>2</sub>O and low bladder compliance are the main risk factors for renal damage [10].

In recent years, adequate diagnosis and treatment of neuro-urological symptoms in patients with spinal cord lesions have improved the situation of these patients. Nowadays, respiratory diseases are the most frequent (21%) cause of death in patients with SCI [11].

In all other patients with neuro-urological symptoms, the risk of renal damage is significantly lower. However, in multiple sclerosis (MS), urodynamics and clinical symptoms may not correlate, which means that asymptomatic patients can present with abnormal urodynamic findings [12]. LUT symptoms do not always lead to urological evaluation in MS patients, even if the symptoms are troublesome [13]. Therefore, urological assessment is important [14]; although respiratory diseases are currently the leading cause of death in MS patients [15].

In Parkinson's disease (PD), neuro-urological disorders have not been reported as a significant cause of death. Moreover, patients with PD commonly suffer from overactive bladder without DSD [16], which does not seem to be as threatening to the upper urinary tract (UUT) as DO with DSD. In PD, urodynamic diagnosis of DO correlates well with diagnosis made by questionnaires [17]. Therefore, regular urodynamic follow-up might be less important in patients with PD compared with MS or SCI. The same is true for diabetes mellitus, which frequently leads to neuro-urological symptoms [18], but cardiovascular diseases are the main cause of death in these patients [19].

In summary, treatment and intensity of follow-up examinations are based on the type of neuro-urological disorder and the underlying cause.

## **2. METHODS**

There is a need for ongoing re-evaluation of the information presented in the current Guidelines by an expert Panel. 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.

Literature searches were carried out for all sections of the Neuro-Urology Guidelines. Focus of all searches was identification of all level 1 scientific papers (systematic reviews and meta-analyses of randomised controlled trials) in accordance with EAU methodology. If sufficient data was identified to answer the clinical question, the search was not expanded to include lower level literature. Searches were carried out in Medline and Embase on the Ovid platform. The searches used the controlled terminology of the respective databases.

References used in this text are graded according to their level of evidence (LE) and Guidelines are given a grade of recommendation (GR), according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence [20]. The aim of grading recommendations is to provide transparency between the underlying evidence and the recommendation given. In this 2015 EAU Guidelines compilation, all standard information on LE and GR has been taken out of the individual Guidelines topics for the sake of brevity. The methodology section (see the introduction chapter of the complete book) outlines the LE and GR criteria which are used throughout the Guidelines.

## **3. THE GUIDELINE**

### **3A EPIDEMIOLOGY, AETIOLOGY AND PATHOPHYSIOLOGY**

#### **3A.1 Introduction**

Neuro-urological symptoms may be caused by various diseases and events affecting the nervous systems controlling the LUT. The resulting neuro-urological symptoms depend grossly 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 those 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 figures. This reflects the variability in the cohort (e.g. early or late stage disease) and the frequently smaller sample sizes, resulting in low level of evidence in most published data (summarised in Table 1).

**Table 1: Epidemiology of Neuro-Urological Disorders**

<b>Suprapontine and pontine lesions and diseases</b>		
<b>Neurological Disease</b>	<b>Frequency in General Population</b>	<b>Type and Frequency of Neuro-Urological Symptoms</b>
Cerebrovascular accident (Strokes)	450 cases/100,000/yr (Europe) [21] (10% of cardiovascular mortality)	Nocturia - OAB - UUI - DO (other patterns less frequent) [22]. 57-83% of neuro-urological symptoms at 1 month post stroke, 80% of spontaneous recovery at 6 months [23]. Persistence of UI correlates with poor prognosis [24].
Dementias: Alzheimer's disease (80%), Vascular (10%), Other (10%)	6.4% of adults > 65 yrs [25, 26]	OAB - UUI - DO 25% of incontinence in Alzheimer's disease, ≥ 25% in other dementias: Lewy body, NPH, Binswanger, Nasu-Hakola, Pick Disease [27]. Incontinence 3 times more frequent in geriatric patients with dementia than without (42.3/1000 women and 33.5/1000 men vs 19.6/1000 women, 18.6/1000 men) [28].
Parkinsonian syndrome Idiopathic Parkinson's disease (IPD): 75-80% of Parkinsonian syndromes  Non-IPD: Parkinson's-plus (18%): Multi system atrophy (MSA), - Progressive supranuclear palsy, - Corticobasal degeneration, - Dementia with Lewy bodies.  Secondary Parkinson's (2%)	1.5% in > 65 yrs [29] 2nd neurodegenerative disease after Alzheimer's disease Prevalence: 150/100,000/yr Incidence: 20/100,000/yr  MSA is the most frequent non-IPD.	LUTS frequency 30% at onset, 70% after 5 yrs. Storage phase symptoms: Nocturia (60%) OAB - UUI - DO [30].  OAB and DO at the initial phase, intrinsic sphincter deficiency and impaired contractility appear as the disease progress. Complications of neuro-urological symptoms (infections) account for a major cause of mortality in MSA [31].
Brain tumors	26.8/100,000/yr in adult (> 19 yrs) (17.9 benign, 8.9 malignant) [32].	Neuro-urological symptoms vary according to tumour location. Incontinence occurs mainly in frontal location (part of frontal syndrome or isolated in frontal location) [33]. Voiding dysfunction may occur in other location.
Mental retardation and cerebral palsy  <i>Intellectual disability in children is a very heterogenous group: including perinatal injury, materno-foetal infections, metabolic disease, genetic disorders and cerebral palsy</i>	Mental retardation other than cerebral palsy  Cerebral Palsy: 3.1-3.6/1,000 in children aged 8 yrs [34].	Incontinence: In 65% of severe and profoundly retarded adult patients [35, 36]. DO and impaired contractility also reported.  89% incontinence, 70% uninhibited detrusor contraction at urodynamic examination. Recurrent urinary tract infection and radiologic abnormalities in > 10% of cases.

<b>Lesions and diseases between caudal brainstem and sacral spinal cord</b>		
Spinal cord injury	Non-congenital SCI cases exceed 200,000 in the US with new cases 8/10,000/yr.	Suprasacral lesion leads to DO and DSD (95%). Lower lesions (sacral conus) lead to detrusor hypocontractility (83%) and to complete EUS denervation (60%) [37-39].
Myelomeningocele and nerve tube defects	Spina bifida and congenital nerve tube defects in G8 = 3-4/10,000 live birth/stillbirths with/without pregnancy termination [40]. Lumbar and lumbosacral form are the most common (60%).	Urethrovessical dysfunction in myelomeningocele is very high (90-97%). 50% of these children demonstrate DO. Low compliance is also frequent (alone/associated with can develop with time). Urethral behaviour varies from dyssynergia (50%), normal reflexes (25%) and denervation (25%) [41].
<b>Lesions and diseases of the peripheral nervous system</b>		
Lumbar spine Degenerative disease Disk prolapse	Male (5%) and female (3%) > 35 yrs have had a lumbosacral episode related to disc prolapse.	26% difficulty to void and acontractile detrusor at urodynamic testing. 14% frequent voiding while normal urodynamics testing [42]. Cauda equina lesions lead to detrusor hypocontractility (83%) and complete EUS denervation (60%) [37-39].
Lumbar canal stenosis	Incidence: approx. 5/100,000/yr More common: > 45 yrs, females.	27% significant LUTS (mainly difficulty to void) [42].
Iatrogenic pelvic nerve lesions	Rectum cancer  Cervical cancer (multimodal therapy, radiotherapy and surgery) Endometriosis surgery	After APR: 50% urinary retention. After TME: 10-30% voiding dysfunction. Voiding phase dysfunction described. Voiding phase dysfunction if no nerve sparing approach.
Peripheral neuropathy  Diabetes  Other causes of peripheral neuropathy can cause neuro-urological symptoms: alcohol abuse, lumbosacral zona and genital herpes, Guillain Barré syndrome, porphyria, sarcoidosis.	In Europe, prevalence of pharmacologically treated diabetes ranges from 2.8-3.8%.  50% of patients will develop neuropathy, with 75-100% of these developing neuro-urological symptoms.	"Diabetic Cystopathy"[18, 43].  OAB and DO initially.  Hyposensitive and hypocontractile detrusor at later phase.

<b>Disseminated central diseases</b>		
Multiple Sclerosis	Prevalence: 1/1,000 adult in developed country, geographic variation (north > south).  First neurological disorder in young adults [44].	80% of patients present neuro-urological symptoms after 10 yrs.  10% of MS patients present voiding dysfunction at disease onset.  DO due to suprapontine lesions most frequent dysfunction (> 60%).  DSD due to spinal cord lesions in 25%.  Hypocontractility in 20%.  Dysfunction may change during the course of the disease [45].

APR = abdominoperineal resection; DO = detrusor overactivity; DSD = detrusor sphincter dyssynergia; G8 = 8 most developed countries; IPD = idiopathic Parkinson's disease; LUTS = lower urinary tract symptoms; MSA = multi system atrophy; NPH = normal pressure hydrocephalus; OAB = overactive bladder; SCI = spinal cord injury; TME = total mesorectal excision; UUI = urinary urge incontinence.

## 3B CLASSIFICATION SYSTEMS

### 3B.1 Introduction

Several national and international guidelines have already been published for the care of patients with neuro-urological disorders [1, 46-48]. The ICS neuro-urological standardisation report [1] deals specifically with the standardisation of terminology and urodynamic investigation in neuro-urological patients. Other relevant definitions are found in the general ICS standardisation report [49].

Section 3B.2 lists the definitions from these references, partly adapted, and other definitions considered useful for clinical practice (Tables 2 and 3). For specific definitions relating to urodynamic investigation, the reader is referred to the appropriate ICS report [1].

### 3B.2 Definitions

**Table 2: Definitions useful in clinical practice**

Acontractility, detrusor	See below under voiding phase (Table 3)
Acontractility, urethral sphincter	See below under storage phase (Table 3)
Autonomic dysreflexia	Increase of sympathetic reflex due to noxious stimuli with symptoms or signs of headache, hypertension, flushing face, and perspiration
Capacity	See below under storage phase
Catheterisation, indwelling	Emptying of the bladder by a catheter that is introduced (semi-) permanently
Catheterisation, intermittent (IC)	Emptying of the bladder by a catheter that is removed after the procedure, mostly at regular intervals
• Aseptic IC	The catheters remain sterile, the genitals are disinfected or washed, and disinfecting lubricant might be used
• Clean IC	Disposable or cleansed re-usable catheters, genitals washed
• Sterile IC	Complete sterile setting, including sterile gloves, forceps, gown and mask
• Intermittent self-catheterisation	IC performed by the patient
Compliance, bladder	See below under storage phase
Condition	Evidence of relevant pathological processes
Diary, bladder	Record of times of micturitions and voided volumes, incontinence episodes, pad usage, and other relevant information



• Frequency volume chart (FVC)	Times of micturitions and voided volumes only
• Micturition time chart	Times of micturitions only
Filling rate, physiological	Below the predicted maximum: body weight (kg) /4 in mL/s [2, 50]
Hesitancy	Difficulty in initiating micturition; delay in the onset of micturition after the individual is ready to pass urine
Intermittency	Urine flow stops and starts on one or more occasions during voiding
Leak point pressure	See below under storage phase
Lower motor neuron lesion (LMNL)	Lesion at or below the S1-S2 spinal cord level
NLUTD	LUTD secondary to confirmed pathology of the nervous supply
Observation, specific	Observation made during specific diagnostic procedure
Overactivity, bladder	See below under symptom syndrome (Table 3)
Overactivity, detrusor	See below under storage phase
Rehabilitation, LUT	Non-surgical non-pharmacological treatment for LUTD
Sign	To verify symptoms and classify them
Sphincter, urethral, non-relaxing	See below under voiding phase
Symptom	Subjective indicator of a disease or change in condition, as perceived by the patient, carer, or partner that may lead the patient to seek help from healthcare professionals
Upper motor neuron lesion (UMNL)	Lesion above the S1-S2 spinal cord level
Voiding, balanced: In patients with neurourological disorders	Voiding with physiological detrusor pressure and low residual (< 80 mL or < 20% of bladder volume)
Voiding, triggered	Voiding initiated by manoeuvres to elicit reflex detrusor contraction by exteroceptive stimuli
Volume, overactivity	See below under storage phase

**Table 3: Further definitions useful in clinical practice**

<b>Storage phase</b>	
<b>Maximum anaesthetic bladder capacity</b>	<b>Maximum bladder filling volume under deep general or spinal anaesthesia</b>
Increased daytime frequency	Self-explanatory; the normal frequency can be estimated at about 8 times per day [51]
Nocturia	Waking at night one or more times to void
Urgency	The symptom of a sudden compelling desire to pass urine that is difficult to defer
Urinary incontinence	Any involuntary leakage of urine
• Stress urinary incontinence	On effort or exertion, or on sneezing or coughing
• Urgency urinary incontinence	Accompanied by or immediately preceded by urgency
• Mixed urinary incontinence	Associated with urgency but also exertion, effort, sneezing, or coughing
• Continuous urinary incontinence	
Bladder sensation	
<i>Normal</i>	
• Symptom and history	Awareness of bladder filling and increasing sensation up to a strong desire to void
• Urodynamics	First sensation of bladder filling, first desire to void, and strong desire to void at realistic bladder volumes
<i>Increased</i>	
• Symptom and history	An early and persistent desire to void
• Urodynamics	Any of the three urodynamic parameters mentioned under 'normal' persistently at low bladder volume
<i>Reduced</i>	
• Symptom and history	Awareness of bladder filling but no definite desire to void
• Urodynamics	Diminished sensation throughout bladder filling
Absent	
No sensation of bladder filling or desire to void	
Non-specific	Perception of bladder filling as abdominal fullness, vegetative symptoms, or spasticity

<i>Definitions valid after urodynamic confirmation only</i>	
Cystometric capacity	Bladder volume at the end of the filling cystometry
• Maximum cystometric capacity	Bladder volume at strong desire to void
• High-capacity bladder	Bladder volume at cystometric capacity far over the mean voided volume, estimated from the bladder diary, with no significant increase in detrusor pressure under non-anaesthetised condition
Normal detrusor function	Little or no pressure increase during filling; no involuntary phasic contractions despite provocation
Detrusor overactivity	Involuntary detrusor contractions during filling; spontaneous or provoked
• Phasic DO	Characteristic phasic contraction
• Terminal DO	A single contraction at cystometric capacity
• High pressure DO	Maximal detrusor pressure > 40 cm H <sub>2</sub> O [1, 52]
• Overactivity volume	Bladder volume at first occurrence of DO
• Detrusor overactivity incontinence	Self-explanatory
Leak point pressure	
• Detrusor leak point pressure (DLPP)	Lowest value of detrusor pressure at which leakage is observed in the absence of abdominal strain or detrusor contraction
• Abdominal leak point pressure	Lowest value of intentionally increased intravesical pressure that provokes leakage in the absence of a detrusor contraction
Bladder compliance	Relationship between change in bladder volume ( $\Delta V$ ) and change in detrusor pressure ( $\Delta p_{det}$ ): $C = \Delta V / \Delta p_{det}$ (mL/cm H <sub>2</sub> O)
• Low bladder compliance	Compliance $C = \Delta V / \Delta p_{det} < 20$ mL/cm H <sub>2</sub> O [53]
Break volume	Bladder volume after which a sudden significant decrease in bladder compliance is observed
Urethral sphincter acontractility	No evidence of sphincter contraction during filling, particularly at higher bladder volumes, or during abdominal pressure increase
<b>Voiding phase</b>	
• Slow stream	Reduced urine flow rate
• Intermittent stream (intermittency)	Stopping and starting of urine flow during micturition
• Hesitancy	Difficulty in initiating micturition
• Straining	Muscular effort to initiate, maintain, or improve urinary stream
• Terminal dribble	Prolonged final part of micturition when the flow has slowed to a trickle/dribble
<i>Definitions valid after urodynamic confirmation only</i>	
Normal detrusor function	Voluntarily initiated detrusor contraction that causes complete bladder emptying within a normal time span
Detrusor underactivity	Contraction of reduced strength/duration
Acontractile detrusor	Absent contraction
Non-relaxing urethral sphincter	Self-explanatory
Detrusor sphincter dyssynergia (DSD)	Detrusor contraction concurrent with an involuntary contraction of the urethra and/or periurethral striated musculature
<b>Post-micturition phase</b>	
Feeling of incomplete emptying (symptom only).	
Post-micturition dribble: involuntary leakage of urine shortly after finishing the micturition.	
Pain, discomfort or pressure sensation in the LUT and genitalia that may be related to bladder filling or voiding, may be felt after micturition, or be continuous.	
Symptom syndrome: combination of symptoms	
Overactive bladder syndrome: urgency with or without urgency incontinence, usually with frequency and nocturia.	
Synonyms: urgency syndrome, urgency-frequency syndrome.	

## 3C DIAGNOSTIC EVALUATION

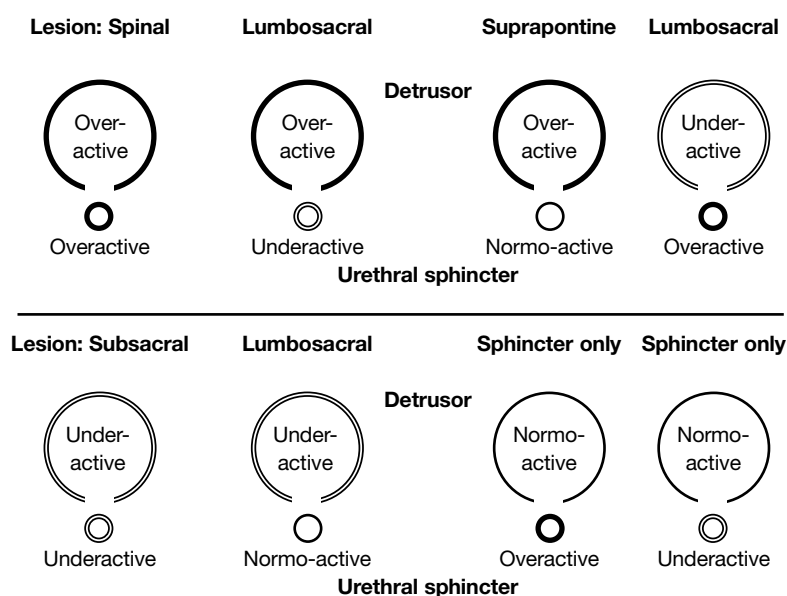
### 3C.1 Introduction

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.

### 3C.2 Classification systems

Several classification systems for neuro-urological symptoms have been proposed. The Madersbacher [54] (LE: 4) classification describes neuro-urological function in terms of the contraction state of the bladder and external urethral sphincter during filling and voiding phases, which can then be used to decide on the appropriate therapeutic approach [54] (Figure 1).

**Figure 1: Madersbacher classification system [54] showing typical neurogenic lesions\***



\*Adapted from Madersbacher et al.

### 3C.3 The timing of diagnosis and treatment

Early diagnosis and treatment are essential in both congenital and acquired neuro-urological disorders [55]. This helps to prevent irreversible changes within the LUT, even in the presence of normal reflexes [56, 57] (LE: 3). Furthermore, urological symptoms can be the presenting feature of neurological pathology [58, 59] (LE: 3). Early intervention can prevent irreversible deterioration of the LUT and UUT [60] (LE: 3).

### 3C.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 in diagnostic investigations and treatment options.

- In non-traumatic neuro-urological patients with a slow insidious onset, history may find that the condition started in childhood or adolescence [61] (LE: 4).
- Urinary history consists of symptoms associated with both urine storage and evacuation.
- Bowel history is important because patients with neuro-urological symptoms may also have a related neuropathic lower gastrointestinal tract [62] (LE: 4).
- Sexual function may be impaired because of the neurological condition.
- 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 UTI-related symptoms accurately [1, 63, 64] (LE: 3).

**Table 4: History taking in patients with suspected neuro-urological disorders\***

<b>Past history</b>
Childhood through to adolescence and in adulthood
Hereditary or familial risk factors
Menarche (age); this may suggest a metabolic disorder
Obstetric history
History of diabetes; in some cases, correction will resolve the neurological problem
Diseases, e.g. syphilis, parkinsonism, multiple sclerosis, encephalitis
Accidents and operations, especially those involving the spine and central nervous system
<b>Present history</b>
Present medication
Lifestyle (smoking, alcohol and drugs); may influence urinary, sexual and bowel function
Quality of life
<b>Specific urinary history</b>
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, volumes voided, incontinence, urge episodes
<b>Bowel history</b>
Frequency and faecal incontinence
Desire to defecate
Defecation pattern
Rectal sensation
Initiation of defecation (digitation)
<b>Sexual history</b>
Genital or sexual dysfunction symptoms
Sensation in genital area
Specific male: erection, (lack of) orgasm, ejaculation
Specific female: dyspareunia, (lack of) orgasm
<b>Neurological history</b>
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

\* Adapted from Bors and Turner [61] (LE: 4; GR: C) and Stöhrer et al. [1] (LE: 4; GR: C).

### 3C.4.1 Bladder diaries

Bladder diaries provide data on the number of voids, volume voided, pad weight, incontinence and urge episodes. Although a 24-hour bladder diary (recording should be done for three consecutive days) is reliable in women with UI [65, 66] (LE: 3) and helpful in IC [1] (LE: 4), no research has been done on bladder diaries in neuro-urological patients. Nevertheless, bladder diaries are considered a valuable diagnostic tool.

### 3C.5 Quality of life

An assessment of the patient's present and expected future quality of life (QoL) is important to evaluate the effect of any therapy (or refrained from using) on this parameter. Despite the limitations associated with neurological diseases, adequate treatment with social independence is possible in most patients.

QoL is a very important aspect of the overall management of neuro-urological patients, e.g. to evaluate treatment related changes on a patient's QoL [67] (LE: 2a). The type of bladder management has been shown to affect health-related QoL (HRQoL) in patients with SCI [68]. 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 [69].

QoL is related to an individual's ability to cope with a new life situation [70]. QoL can be influenced by several factors, including family support, coping ability, productivity, self-esteem, financial stability, education, and the physical and social environment [71] (LE: 3). Age, sex, ethnicity and the patient's acceptance of the condition also need to be considered when assessing QoL [72] (LE: 3).

Although several questionnaires have been developed to assess QoL, there are no specific QoL questionnaires for the neuro-urological patient. However, a validated specific tool for QoL in SCI and MS patients (Qualiveen®) appears to be a discriminative evaluation instrument [69, 73, 74]. A short-form is available [75] and various validated translations [76-79].

A patient's QoL can be assessed secondarily by generic HRQoL questionnaires, including the Incontinence Quality of Life Instrument (I-QOL), King's Health Questionnaire (KHQ), Short Form 36 Health Survey Questionnaire (SF-36), Euro Quality of Life-5 Domains (EQ-5D), Short Form 6D Health Survey Questionnaire (SF-6D), or the Health Utilities Index (HUI). In addition, the quality-adjusted life year (QALY) quantifies outcomes by weighing years of life spent in a specified health state by a factor representing the value placed by society or patients on the specific health state [80] (LE: 3).

### 3C.5.1 Recommendations

Recommendations	GR
Quality of life should be assessed when evaluating and treating the neuro-urological patient.	B
The available validated tools are Qualiveen®, a specific long-form and short-form tool for spinal cord lesion and multiple sclerosis patients. In addition, generic (SF-36) or specific tools for incontinence (I-QOL) questionnaires can be used.	B

*I-QOL = incontinence quality of life instrument.*

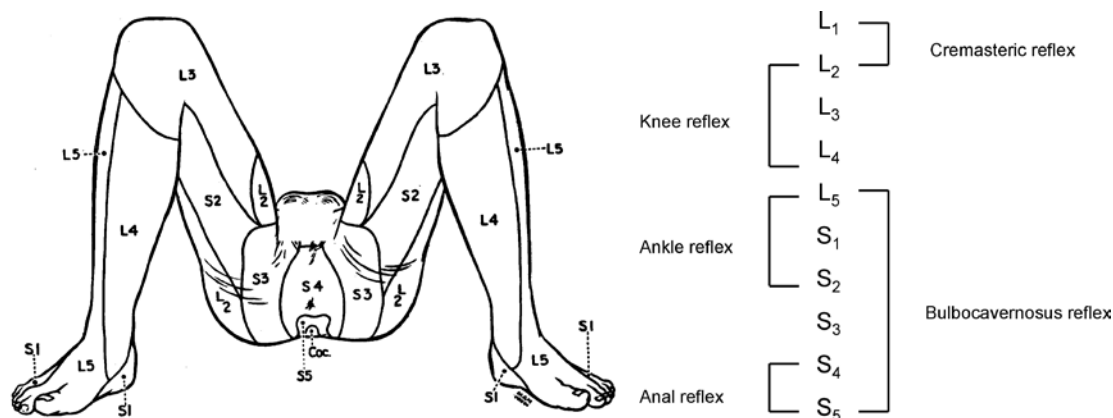
### 3C.6 Physical examination

In addition to a detailed patient history, attention should be paid to possible physical and mental handicaps with respect to the planned investigation. Neurological status should be described as completely as possible (Figure 1). Patients with very high 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. Furthermore, detailed testing of the anal sphincter and pelvic floor functions must be performed (Figure 2). It is essential to have this clinical information to reliably interpret later diagnostic investigations.

#### 3C.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 can present in any type of suprasacral lesion but generally manifests above level Th 5-Th 6. The stimulus can be distended bladder or bowel. It can also be secondary to a noxious stimulus, e.g. infected toe nail or pressure sore. Hypertension is a relatively common manifestation of AD and can have life-threatening results if not properly managed [81-83] (LE: 3; GR: C).

**Figure 2: The neurological status of a patient with neuro-urological symptoms must be described as completely as possible: (a) dermatomes of spinal cord levels L2-S4; (b) urogenital and other reflexes in the lower spinal cord.**



**Table 5: Neurological items to be specified\***

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

\*Adapted from Stöhrer et al. [1] (LE: 4; GR: C).

### 3C.6.2 Recommendations for history taking and physical examination\*

History taking	GR
An extensive general history is mandatory, concentrating on past and present symptoms including urinary, sexual, bowel, and neurological functions.	A
Special attention should be paid to the possible existence of alarm signs, e.g. pain, infection, haematuria, fever, that warrant further specific diagnosis.	A
A specific history should be taken for each of the four mentioned functions.	A
<b>Physical examination</b>	
Individual patient handicaps should be acknowledged in planning further investigations.	A
The neurological status should be described as completely as possible. Sensations and reflexes in the urogenital area must all be tested.	A
The anal sphincter and pelvic floor functions must be tested.	A
Urinalysis, blood chemistry, bladder diary, residual and free flowmetry, incontinence quantification and urinary tract imaging should be performed.	A

\* All grade A recommendations are based on panel consensus.

## 3C.7 Urodynamics

### 3C.7.1 Introduction

Urodynamic investigation is the only method that can objectively assess the (dys-) function of the LUT. In these patients, the invasive urodynamic investigation is even more provocative than in general patients. Any technical source of artifacts must be critically considered. It is essential to maintain the quality of the urodynamic

recording and its interpretation [2]. Same session repeat urodynamic investigations can be helpful in clinical decision making, since repeat measurements may yield completely different results [84].

In patients at risk for AD, it is advisable to measure blood pressure during the urodynamic study. 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 ICS technical recommendations and standards [1, 2, 85].

### 3C.7.2 **Urodynamic tests**

*Free uroflowmetry and assessment of residual urine:* This provides a first impression of the voiding function and is compulsory prior to planning any invasive urodynamics. For reliable information, it should be repeated at least 2-3 times [1, 2]. 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 is the only method for quantifying the filling function (undertaken at a very slow rate ~20 mL/min). 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 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, as fast filling and room-temperature saline are provocative. Possible pathological findings include DO, low bladder compliance, abnormal bladder sensations, incontinence, and an incompetent or relaxing urethra.

*Detrusor leak point pressure (DLPP) [52]:* This appears to have no use as a diagnostic tool. Some positive findings have been reported [86, 87], but sensitivity is too low to estimate the risk to the UUT or for secondary bladder damage [88].

*Pressure flow study:* This reflects the co-ordination between detrusor and urethra or pelvic floor during the voiding phase. It is even more powerful if combined with filling cystometry and with video-urodynamics. LUT function must be recorded during the voiding phase. Possible pathological findings include detrusor hypocontractility, DSD, a high urethral resistance, and residual urine.

Most types of obstruction caused by neuro-urological disorders are due to DSD [89, 90], non-relaxing urethra, or non-relaxing bladder neck [1, 91, 92]. Pressure-flow analysis mostly 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):* This 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, hyper-reflexive contractions, onset of voiding, coughing, Valsalva manoeuvre) suggesting a diagnosis of DSD.

*Urethral pressure measurement:* This has a very limited role in neuro-urological disorders. There is no consensus on parameters indicating pathological findings [93].

*Video-urodynamics:* This is the combination of filling cystometry and pressure flow study with imaging. It is the gold standard for urodynamic investigation in neuro-urological disorders [1]. Possible pathological findings include all those described in the cystometry and the pressure flow study sections, and any morphological pathology of the LUT and UUT.

*Ambulatory urodynamics:* This is the functional investigation of the urinary tract, which uses the predominantly natural filling of the urinary tract to reproduce the patient's normal activity [94]. Although this type of study might be considered when conventional urodynamics do not reproduce the patient's symptoms, the role in the neuro-urological patient needs to be determined.

*Provocative tests during urodynamics:* LUT 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 (UMNL/LMNL) [95, 96]. Patients with UMNL develop a detrusor contraction if the detrusor muscle is intact, while patients with LMNL do not. However, the test gives false-positive results in young children [97] and does not seem to fully discriminative in other types of patient [98].

Previously, a positive bethanechol test [99] (detrusor contraction > 25 cm H<sub>2</sub>O) 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 [100], but there was no published follow-up.

### 3C.7.3 **Specialist uro-neurophysiological tests**

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

- 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.

### 3C.7.4 **Recommendations for urodynamics and uro-neurophysiology**

Recommendations	GR
The recording of a bladder diary is advisable.	A
Non-invasive testing is mandatory before invasive urodynamics is planned.	A
Urodynamic investigation is necessary to detect and specify lower urinary tract (dys-) function and help with formulating a management plan.	A
Same session repeat measurement can be helpful in clinical decision making.	C
Video-urodynamics is the gold standard for invasive urodynamics in neuro-urological patients. If this is not available, then a filling cystometry continuing into a pressure flow study should be performed.	A
A physiological filling rate and body-warm saline should be used.	A
Specific uro-neurophysiological tests are elective procedures.	C

### 3C.7.5 **Typical manifestations of neuro-urological disorders**

Table 6 lists typical signs indicating further neurological evaluation, as neuro-urological symptoms may be the presenting symptom [59].

**Table 6: Typical findings in neuro-urological disorders**

<b>Filling phase</b>
Hyposensitivity or hypersensitivity
Vegetative sensations
Low compliance
High-capacity bladder
Detrusor overactivity, spontaneous or provoked
Sphincter underactivity
<b>Voiding phase</b>
Detrusor underactivity or acontractility
Detrusor sphincter dyssynergia
Non-relaxing urethra
Non-relaxing bladder neck

## 3C.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 [56].

Caregivers must be informed of this condition and instructed to watch carefully for any signs or symptoms of a possible deterioration in the patient's renal function. If necessary, the renal function should be checked regularly.



## 3D DISEASE MANAGEMENT

### 3D.1 Introduction

The primary aims for treatment of neuro-urological symptoms and their priorities are [101, 102]:

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

Further considerations are the patient's disability, cost-effectiveness, technical complexity, and possible complications [102].

Renal failure is the main mortality factor in SCI patients who survive the trauma [9, 103, 104].

Keeping the detrusor pressure during both the filling and voiding phases within safe limits significantly reduces the mortality from urological causes in these patients [105, 106] and has consequently become the golden rule in the treatment of patients with neuro-urological symptoms [101, 102].

In patients with high detrusor pressure during the filling phase (DO, low bladder compliance), treatment is aimed primarily at "conversion of an active, aggressive high-pressure bladder into a passive low-pressure reservoir" despite the resulting residual urine [101]. Reduction of the detrusor pressure contributes to urinary continence, and consequently to social rehabilitation and QoL. It is also pivotal in preventing UTI [9, 104]. Complete continence can however not always be obtained.

### 3D.2 Non-invasive conservative treatment

#### 3D.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 during the filling phase, and incontinence. Methods to improve the voiding process are therefore practiced.

*Bladder expression (Credé manoeuvre) and voiding by abdominal straining (Valsalva manoeuvre):* 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 [107, 108]. 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 [109, 110]. Their use should therefore be discouraged unless urodynamics show that the intravesical pressure remains within safe limits [107, 110-113].

Long-term complications are unavoidable for both methods of bladder emptying [108]. The already weak pelvic floor function may be further impaired, thus introducing or exacerbating already existing stress urinary incontinence (SUI) [110].

*Triggered reflex voiding:* Stimulation of the sacral or lumbar dermatomes in patients with UMNL can elicit a reflex detrusor contraction [110]. The risk of high pressure voiding is present and interventions to decrease outlet resistance may be necessary [114]. Triggering can induce AD in patients with high level SCI (above Th 6) [115]. All assisted bladder emptying techniques require low outlet resistance. Even then, high detrusor pressures may still be present. Patients hence need dedicated education and close urodynamic and urological surveillance [110, 111, 113, 116].

*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 [101, 117]. Condom catheters with urine collection devices are a practical method for men [117]. The infection risk must be closely observed [117]. The penile clamp is absolutely contraindicated in case of DO or low bladder compliance because of the risk of developing high intravesical pressure, and in case of significant reflux.

#### 3D.2.2 *Lower urinary tract rehabilitation*

##### 3D.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 [117, 118]. The first mechanism is affected by activation of efferent nerve fibres, and the latter ones are produced by activation of afferent fibres [88]. Electrical stimulation of the pudendal nerve afferents strongly inhibits the micturition reflex and detrusor contraction [119]. This stimulation might then support the restoration

of the balance between excitatory and inhibitory inputs at the spinal or supraspinal level [117, 120, 121]. Evidence for bladder rehabilitation using electrical stimulation in neurological patients is mainly based on pilot studies with small patient numbers.

*Peripheral temporary electrostimulation:* Percutaneous tibial nerve stimulation and external (e.g. penile/clitoral or intracavitary) temporary electrical stimulation suppress neurogenic DO during acute stimulation [122, 123]. Both techniques have also demonstrated sustained effects in patients with MS [124-126]. LUT function remained improved 2 years after transcutaneous electrical stimulation of the bladder in patients with SCI [127]. Electrostimulation also improved continence in children with MMC [128].

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 [129]. Furthermore, this treatment combination is significantly superior to electrostimulation alone. Biofeedback can be used for supporting the alleviation of neuro-urological symptoms [130].

*Intravesical electrostimulation:* Intravesical electrostimulation can increase bladder capacity and improve bladder compliance and bladder filling sensation in patients with incomplete SCI or MMC [131]. In patients with neurogenic detrusor underactivity, intravesical electrostimulation may also improve voiding and reduce residual volume [132, 133].

*Chronic peripheral pudendal stimulation:* A pilot study in patients with incomplete SCI showed that chronic peripheral pudendal stimulation (defined as 15 min, twice daily, during two weeks) may produce neuromodulatory effects in the brain. These effects are correlated with clinical improvement [134]. Semiconditional electrical stimulation of the dorsal penile nerve during 14-28 days improved bladder storage function in patients with SCI [135].

*Repetitive transcranial magnetic stimulation:* Although improvement of neuro-urological symptoms has been described in PD and MS patients, this technique is still under investigation [136, 137].

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

### 3D.2.3 **Drug treatment**

A single, optimal, medical therapy for neuro-urological symptoms is not yet 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 SCI with a suprasacral lesion or MS [110, 138-142].

#### 3D.2.3.1 *Drugs for treatment of storage neuro-urological symptoms*

*Antimuscarinic drugs:* They are the first-line choice for treating neurogenic detrusor overactivity (NDO), increasing bladder capacity, reducing episodes of urinary incontinence secondary to NDO by the inhibition of parasympathetic pathways [5, 143-149].

Although antimuscarinic drugs have been used for many years to treat patients with NDO, the evidence is still limited [145, 146, 150], and the responses of individual patients to antimuscarinic treatment are variable. Only a recent meta-analysis has confirmed the clinical and urodynamic efficacy of antimuscarinic therapy compared to placebo in adult NDO [146]. In children, only oxybutynin is approved, despite prospective trials supporting the efficacy and tolerability of tolterodine, propiverine and solifenacin [151-153]. A prospective randomised study using fesoterodine in children with NDO is ongoing [154].

Higher doses or a combination of antimuscarinic agents may be an option to maximise outcomes in neurological patients [138, 140, 155-158] (LE: 3). However, these drugs have a high incidence of adverse events, which may lead to early discontinuation of therapy [146, 155, 157]. Dry mouth is the most frequent side effect.

*Choice of antimuscarinic agent:* Oxybutynin [5, 138, 140, 144-146, 149, 155, 156, 159-161], trospium [146, 157, 162], tolterodine [151, 163, 164] and propiverine [5, 146, 160, 165-168] are established, effective and well tolerated treatments even in long-term use (LE: 1a).

Darifenacin and solifenacin have been evaluated recently in NDO secondary to SCI and MS [146, 169-172] with results similar to other antimuscarinic drugs. A study using solifenacin in NDO due to Parkinson's disease is currently suspended [173]. The relatively new fesoterodine, an active metabolite of tolterodine, has also been introduced, even though to date there has been no published clinical evidence of its use in the treatment of neuro-urological disorders.

*Side effects:* Controlled release antimuscarinics have some minor side effects, e.g. dry mouth. It has been suggested that different ways of administration may help to reduce side effects. In a selected group of patients, transdermal oxybutynin was found to be well tolerated and effective [174-176]. Instead, although there are several studies reporting the efficacy and safety of intravesical oxybutynin, there are no standard protocols yet for its use [177-179]. Therefore, further research is needed into the use of alternative methods of administration, particularly long-term results (LE: 1b).

#### *Other agents*

*Phosphodiesterase inhibitors (PDE5Is):* In vivo and pilot studies seem to support that PDE5Is may become an alternative or adjunct to antimuscarinic treatment for NDO [180-182].

*Beta<sub>3</sub>-adrenergic receptor agonist:* They have recently been introduced and evaluated in OAB, but clinical experience in neuro-urological patients is limited. Studies on safety and effectiveness in NDO are ongoing. In the future, combined therapy with antimuscarinics may be an attractive option [183-185].

#### **3D.2.3.2 Drugs for voiding neuro-urological symptoms**

*Detrusor underactivity:* Cholinergic drugs, such as bethanechol and distigmine, have been considered to enhance detrusor contractility and promote bladder emptying, but are not routinely used in clinical practice [186]. Only preclinical studies have documented the potential benefits of cannabinoid agonists on improving detrusor contractility administered intravesically [187, 188]. Conversely, a randomised controlled study on the use of oromucosal nabixinols (an endocannabinoid modulator), did not report any significant reduction of incontinence episodes in MS patients, although a statistically significant improvement in frequency, urgency and nocturia was documented [189].

*Decreasing bladder outlet resistance:*  $\alpha$ -blockers (e.g. tamsulosin and naftopidil) seem to be effective for decreasing bladder outlet resistance, postvoid residual and autonomic dysreflexia [49]. Combination therapy with a cholinergic drug and an  $\alpha$ -blocker appears to be more useful than monotherapy with either agent [190, 191].

*Increasing bladder outlet resistance:* Several drugs have shown efficacy in selected cases of mild stress urinary incontinence, but there are no high level evidence studies in neurological patients [149].

#### **3D.2.4 Recommendations for drug treatments**

<b>Recommendations</b>	<b>LE</b>	<b>GR</b>
For NDO, antimuscarinic therapy is the recommended first-line medical treatment.	1a	A
Alternative routes of administration (i.e., transdermal or intravesical) of antimuscarinic agents may be used.	2	A
Outcomes for NDO may be maximised by considering a combination of antimuscarinic agents.	3	B
To decrease bladder outlet resistance, alpha-blockers could be prescribed.	1b	A
For underactive detrusor, no parasympathomimetics should be prescribed.	1a	A
In neurogenic stress urinary incontinence, drug treatment should not be prescribed.	4	A

*NDO = neurogenic detrusor overactivity.*

#### **3D.2.5 Minimal invasive treatment**

##### **3D.2.5.1 Catheterisation**

Intermittent self- or third-party catheterisation [192, 193] is the preferred management for neuro-urological patients who cannot effectively empty their bladders [101, 117].

Sterile IC, as originally proposed by Guttmann and Frankel [192], significantly reduces the risk of UTI and/or bacteriuria [117, 159, 194, 195] compared with clean IC introduced by Lapidès et al. [193]. However, it cannot be considered a routine procedure [117, 195].

Aseptic IC is an alternative [101, 196] that provides a significant benefit by reducing external contamination of the catheter [197-199]. Contributing factors to contamination are insufficient patient education and the inherently greater risk of UTI in neuro-urological patients [117, 198, 200-202]. The average frequency of catheterisations per day is 4-6 times [203] and the catheter size most often used are between 12-16 Fr. In aseptic IC, an optimum frequency of 5 times showed a reduction of UTI [203]. 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 [112, 117, 204-211]. Both

procedures should therefore be avoided when possible.

Silicone catheters are preferred because they are less susceptible to encrustation and because of the high incidence of latex allergy in the neuro-urological patient population [212].

### Recommendations for catheterisation

Recommendations	LE	GR
Intermittent catheterisation - whenever possible aseptic technique - should be used as a standard treatment for patients who are unable to empty their bladder.	3	A
Patients must be well instructed in the technique and risks of IC.	3	A
The catheter size should be 12-16 Fr.	4	B
Whenever possible, indwelling transurethral and suprapubic catheterisation should be avoided.	3	A

IC = intermittent catheterisation.

#### 3D.2.5.2 Intravesical drug treatment

To reduce DO, anticholinergics can also be applied intravesically [213-216]. This approach may reduce adverse effects because the anticholinergic drug is metabolised differently [214] and a greater amount is sequestered in the bladder, even more than with electromotive administration [213].

The vanilloids, capsaicin and resiniferatoxin, desensitise the C-fibres and thereby decrease DO for a period of a few months until the sensation of these fibres has been restored [217-219]. The dosage is 1-2 mMol capsaicin in 100 mL 30% alcohol, or 10-100 nMol resiniferatoxin in 100 mL 10% alcohol for 30 minutes. Resiniferatoxin has about a 1,000-fold potency compared to capsaicin, with less pain during the instillation, and is effective in patients refractory to capsaicin. Clinical studies have shown that resiniferatoxin has limited clinical efficacy compared to botulinum toxin A (BTX-A) injections in the detrusor [218].

#### 3D.2.5.3 Intravesical electrostimulation

Intravesical electrostimulation [220] enhances the sensation for bladder filling and urge to void and may restore the volitional control of the detrusor [221, 222]. Daily stimulation sessions of 90 minutes with 10 mA pulses of 2 ms duration at a frequency of 20 Hz [132, 222] are used for at least 1 week [132]. It appears that patients with peripheral lesions are the best candidates, that the muscle must be intact, and that at least some afferent connection between the detrusor and the brain must still be present [132, 222]. Also, the positioning of the stimulating electrodes and bladder filling are important parameters [223]. With these precautions, the results in the literature are still not unequivocal: both positive [131, 132, 221, 224] and negative [225, 226] (LE: 3) results have been reported.

#### 3D.2.5.4 Botulinum toxin injections in the bladder

BTX-A causes a long-lasting but reversible chemical denervation that lasts for about 9 months [12, 227]. The toxin injections are mapped over the detrusor in a dosage that depends on the preparation used. BTX-A has been proven effective in patients with neuro-urological disorders in phase III RCTs [228-230]. Repeated injections seem to be possible without loss of efficacy [12, 230, 231]. Generalised muscular weakness is an occasional adverse effect [12, 229, 231]. Histological studies have not found ultrastructural changes after injection [232].

#### 3D.2.5.5 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). Incontinence may result and can be managed by external devices (see Section 3D.2.1).

**BTX-A:** This can be used to treat detrusor sphincter dyssynergia effectively by injection at a dose that depends on the preparation used. The dyssynergia is abolished for a few months, necessitating repeat injections. The efficacy of this treatment has been reported to be high and with few adverse effects [233-235]. However, a recent Cochrane report concluded that because of limited evidence future RCTs assessing the effectiveness of BTX injections also need to address the uncertainty about the optimal dose and mode of injection [236]. In addition, this therapy is not registered.

**Balloon dilatation:** Favourable immediate results were reported [237], but there are no further reports since 1994 so this method is no longer recommended.

**Sphincterotomy:** By staged incision, bladder outlet resistance can be reduced without completely losing the

closure function of the urethra [101, 117, 228]. Different techniques are used, and laser treatment appears to be advantageous [238, 239]. Sphincterotomy needs to be repeated at regular intervals in many patients [240], but it is efficient and does not cause severe adverse effects [101, 237]. Secondary narrowing of the bladder neck may occur, for which combined bladder neck incision might be considered [241].

*Bladder neck incision:* This is indicated only for secondary changes at the bladder neck (fibrosis) [101, 238]. This procedure is not recommended in patients with detrusor hypertrophy, which causes thickening of the bladder neck [101].

*Stents:* Implantation of urethral stents results in continence being dependent on adequate closure of the bladder neck [102]. The results are comparable with sphincterotomy and the stenting procedure has a shorter duration of surgery and hospital stay [242, 243]. However, the costs [101], possible complications and re-interventions [244, 245] are limiting factors in its use [246-249].

*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 [102, 250, 251].

*Urethral inserts:* Urethral plugs or valves for 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 was disappointing [252].

#### 3D.2.5.6 Recommendations for minimal invasive treatment\*

Recommendations	GR
Botulinum toxin injection in the detrusor is the most effective minimally invasive treatment to reduce neurogenic detrusor overactivity.	A
Bladder neck incision is effective in a fibrotic bladder neck.	B

\*Recommendations for catheterisation are listed separately under Section 3D.2.5.1

### 3D.2.6 Surgical treatment

#### 3D.2.6.1 Urethral and bladder neck procedures

Increasing the bladder outlet resistance has the inherent risk of causing high intravesical pressure during filling, which may become even higher during the voiding phase. Procedures to treat sphincteric incontinence are suitable only when the detrusor activity is, or can be, controlled, when no significant reflux is present. Moreover, these procedures require the urethra and bladder neck to be in good condition and mostly result in IC being performed after the procedure [102].

*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 [102, 253-258]. In men there are a growing number of reports suggesting that both autologous and synthetic slings may also be an alternative [259-261].

*Artificial urinary sphincter:* This device has stood the test of time in patients with neuro-urological disorders [102]. It was introduced by Light and Scott [262] for this patient group, and the need for revisions [263] has decreased significantly with new generations of devices allowing one to obtain an acceptable long-term outcome [264-270].

*Functional sphincter augmentation:* By transposing the gracilis muscle to the bladder neck [271] or proximal urethra [272], there is a possibility of creating a functional autologous sphincter by electrical stimulation [271-273]. This opens the possibility of restoring control over the urethral closure.

*Bladder neck and urethra reconstruction:* The classical Young-Dees-Leadbetter [274] procedure for bladder neck reconstruction in children with bladder exstrophy, and Kropp urethra lengthening [275] improved by Salle [276], are established methods to restore continence provided that IC is practiced and/or bladder augmentation is performed [277].

*Urethral inserts:* See section 3D.2.5.5.

#### 3D.2.6.2 Denervation, deafferentation, sacral neuromodulation

Sacral rhizotomy, also known as sacral deafferentation, has achieved some success in reducing detrusor overactivity [278-280], but nowadays, it is used mostly as an adjuvant to sacral anterior root stimulation (SARS) [281-285]. Alternatives to rhizotomy are sought in this treatment combination [286-288].

SARS is aimed at producing detrusor contraction. The technique was developed by Brindley [289] and is only applicable to complete lesions above the implant location, because 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 [282, 290, 291]. By changing the stimulation parameters, this method can also induce defecation or erection.

Sacral neuromodulation (SNM) [292] might be effective and safe for treating neuro-urological symptoms but there is a lack of RCTs and it is unclear which neurological patient is most suitable [293].

#### 3D.2.6.3 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 [294] and latissimus dorsi [295] have been used successfully in patients with neuro-urological symptoms [296, 297].

#### 3D.2.6.4 Bladder augmentation

The aim of auto-augmentation (detrusor myectomy) is to reduce detrusor overactivity 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 [101, 102, 298-304].

Replacing or expanding the bladder by intestine or other passive expandable coverage will reduce bladder compliance and at least reduce the pressure effect of detrusor overactivity [305]. Inherent complications associated with these procedures are: recurrent infection, stone formation, perforation or diverticula, possible malignant changes, and for intestine metabolic abnormality, mucus production and impaired bowel function [102, 306-308]. 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.

Bladder augmentation is a valid option to decrease detrusor pressure and increase bladder capacity, whenever more conservative approaches have failed. Several different techniques have been published, with comparable and satisfactory results [300, 309-317]. Bladder substitution to create a low-pressure reservoir is indicated in patients with a severely thick and fibrotic bladder wall [318, 319].

#### 3D.2.6.5 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 [102, 320].

*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 [102]. A continent stoma is created using various techniques. However, all of them have frequent complications, including leakage or stenosis [102, 321]. The short-term continence rates are > 80% and good protection of the UUT is achieved [102, 322-330]. For cosmetic reasons, the umbilicus is often used for the stoma site [326, 329-336].

*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 [102]. An ileal segment is used for the deviation in most cases [102, 337-341].

*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 [102]. The patient must be carefully counselled and must comply meticulously with the instructions [102]. Successful undiversion can then be performed [342].

### 3D.2.6.6 Recommendations for surgical treatment

Recommendations	LE	GR
In order to treat refractory detrusor overactivity, bladder augmentation is recommended. Detrusor myectomy is an acceptable alternative in highly selected cases.	3	A
In female patients with neurogenic stress urinary incontinence who are able to self-catheterise, placement of an autologous urethral sling should be used.	4	B
In male patients with neurogenic stress urinary incontinence, artificial urinary sphincter should be used.	3	A

## 3E URINARY TRACT INFECTION IN NEURO-UROLOGICAL PATIENTS

### 3E.1 Epidemiology, aetiology and pathophysiology

Urinary tract infection (UTI) is the onset of signs and/or symptoms accompanied by laboratory findings of a UTI (bacteriuria, leukocyturia and positive urine culture) [343]. There are no evidence-based cutoff values for the quantification of these findings. The published consensus is that a significant bacteriuria in persons performing IC is present with  $> 10^2$  colony-forming units (cfu)/mL,  $> 10^4$  cfu/mL in clean-void specimens and any detectable concentration in suprapubic aspirates. Regarding leukocyturia, 10 or more leukocytes in centrifuged urine samples per microscopic field (400x) are regarded as significant [343].

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 autonomic dysreflexia, may develop or worsen due to a UTI [344]. 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 autonomic dysreflexia [344, 345].

### 3E.2 Diagnostic evaluation

The gold standard for diagnosis is urine culture and urinalysis. A dipstick test may be more useful to exclude than to prove UTI [346, 347]. As bacterial strains and resistance patterns in persons with neuro-urological disorders may differ from those of able-bodied patients, microbiologic testing is mandatory [348].

### 3E.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 [349]. UTI in persons with neuro-urological disorders are by definition complicated UTI. Therefore, single-dose treatment is not advised. There is no consensus in the literature about the duration of treatment. It depends on the severity of the UTI and the involvement of kidneys and the prostate. Generally, a 5-7 day course of antibiotic treatment is advised, that can be extended up to 14 days according to the extent of the infection [349]. The choice of the 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 autonomic dysreflexia), the choice of treatment should be based on local and individual resistance profiles [350].

#### 3E.3.1 Recurrent UTI

Recurrent UTI in patients with neuro-urological disorders may indicate a 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, e.g. by treating detrusor overactivity by BTX-A injection in the detrusor [351], and the removal of bladder stones or other direct supporting factors, especially indwelling catheters, as early as possible, are mandatory [348].

#### 3E.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 men performing IC, the use of hydrophilic catheters is associated with a lower rate of UTI; in women this effect is not demonstrated [352]. Bladder irrigation has not been proven effective [353].

Various medical approaches have been tested as UTI prophylaxis in patients with neuro-urological disorders. The benefit of cranberry juice for the prevention of UTI could not be demonstrated in RCTs [354]. Methenamine hippurate is not effective in individuals with neuro-urological symptoms [355]. There is not sufficient evidence to support the use of L-methionine for urine acidification to prevent recurrent UTI [356]. There is only weak evidence that oral immunotherapy reduces bacteriuria in patients with SCI, and no evidence that recurrent UTI are reduced [357]. Low-dose, long-term, antibiotic prophylaxis cannot reduce UTI frequency, but increases bacterial resistance and is therefore not recommended [349].

A newly proposed application scheme of antibiotic substances for antibiotic prophylaxis provided positive results, but the results of this trial need to be confirmed in further studies [358]. Another possible future option, the inoculation of apathogenic *E. coli* strains into the bladder, has provided positive results in initial studies, but because of the paucity of data [359], cannot be recommended as a treatment option.

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 [360]. 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.

### 3E.4 Recommendations for the treatment of UTI

Recommendations	LE	GR
Asymptomatic bacteriuria in patients with neuro-urological disorders should not be treated.	4	A
The use of long-term antibiotics in recurrent UTIs should be avoided.	2a	A
In patients with recurrent UTI, treatment of neuro-urological symptoms should be optimised and foreign bodies (e.g. stones, indwelling catheters) should be removed from the urinary tract.	3	A
In patients with neuro-urological disorders, UTI prophylaxis must be individualised since there is no optimal prophylactic measure available.	4	C

UTI = urinary tract infection.

## 3F SEXUAL (DYS)FUNCTION AND FERTILITY

These Guidelines specifically focus on sexual dysfunction and infertility in patients with a neurological disease [361]. Non-neurogenic, male sexual dysfunction and infertility are covered in separate EAU Guidelines [362, 363]. Adopting a systematic approach, such as the PLISSIT model (Permission, Limited Information, Specific Suggestions and Intensive Therapy) [364], provides a framework for counselling and treatment involving a stepwise approach to the management of neurogenic sexual dysfunction.

### 3F.1 Erectile dysfunction

#### 3F.1.1 Phosphodiesterase type 5 inhibitors

Phosphodiesterase type 5 inhibitors (PDE5Is) are recommended as first-line treatment in neurogenic erectile dysfunction (ED) [361]. All currently available PDE5Is appear to be effective and safe, although there are no high-evidence level studies in neuro-urological patients investigating efficacy and side effects across different PDE5Is, dosages and formulations. A recent network meta-analysis on a mixed ED population has suggested that tadalafil is the most effective agent [365]. Most common side effects of PDE5Is are headache, flushing, dyspepsia and nasal congestion, while PDE5Is may induce relevant hypotension in patients with tetraplegia/high-level paraplegia and multiple system atrophy [366, 367].

Several studies, including RCTs, show the efficacy and safety of PDE5Is for treating ED in patients with SCI [366, 368-371], MS [372-374], PD [375-377], diabetes mellitus [377-380], spina bifida [379] and after radical prostatectomy [381].

Most neuro-urological patients require long-term therapy for ED but some have a low compliance rate or stop therapy because of side effects [366, 367]. 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 autonomic dysreflexia, they must be counselled that PDE5Is are contraindicated when using nitrate medication.



### 3F.1.2 **Mechanical devices**

Mechanical devices (vacuum tumescence devices and penile rings) may be effective but are less popular [382-386].

### 3F.1.3 **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 [387-392], 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 therapeutic option in patients taking nitrate medications, for whom there are concerns about drug interactions with PDE5Is, or in patients for 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 [366].

Intraurethral alprostadil application is an alternative but less effective route of administration [393].

### 3F.1.4 **Penile prostheses**

Penile prostheses may be considered for treatment of neurogenic ED when all conservative treatments have failed. Serious complications, including infection and prosthesis perforation, may occur in about 10% of patients, depending on implant type [394-396].

### 3F.1.5 **Recommendations for erectile dysfunction**

Recommendations	LE	GR
In neurogenic ED, oral PDE5Is are the recommended first-line medical treatment.	1b	A
In neurogenic ED, intracavernous injections of vasoactive drugs (alone or in combination) are the recommended second-line medical treatment.	3	A
In neurogenic ED, mechanical devices such as vacuum devices and rings can be effective and may be offered to patients.	3	B
In neurogenic ED, penile prostheses should be reserved for selected patients.	4	B

ED = erectile dysfunction; PDE5Is = phosphodiesterase type 5 inhibitors.

## 3F.2 **Male fertility**

Among the major conditions contributing to neurogenic infertility are pelvic and retroperitoneal surgery, diabetes mellitus, spina bifida, MS and SCI [397]. ED is managed as described previously. Retrograde ejaculation may be reversed by sympathomimetic agents contracting the bladder neck, including imipramine, ephedrine, pseudoephedrine, and phenylpropanolamine [397]. The use of a balloon catheter to obstruct the bladder neck may be effective in obtaining antegrade ejaculation [398]. If antegrade ejaculation is not achieved, the harvest of semen from the urine may be considered [397]. Prostatic massage is safe and easy to use for obtaining semen in men with lesions above T10 [399]. In several patients, vibrostimulation or transrectal electroejaculation are needed for sperm retrieval [397, 400-403]. Semen retrieval is more likely with vibrostimulation in men with lesions above T10 [404-406]. In men with SCI, especially at or above T6, AD might occur during sexual activity and ejaculation [407, 408]; patients at risk and fertility clinics must be informed and aware of this potentially life-threatening condition.

Surgical procedures, such as microsurgical epididymal sperm aspiration (MESA) or testicular sperm extraction (TESE), may be used if vibrostimulation and electroejaculation are not successful [409, 410]. 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 [411-413].

### 3F.2.1 **Sperm quality and motility**

The following has been reported on sperm quality and motility:

- Vibrostimulation produces samples with better sperm motility than electrostimulation [402, 414].
- Electroejaculation with interrupted current produces better sperm motility than continuous current [415].
- Bladder management with clean IC may improve semen quality compared to indwelling catheterisation, reflex voiding or bladder expression [416].
- Sperm quality in men with SCI is enhanced by processing in able-bodied seminal plasma [417].
- Freezing of sperm is unlikely to improve fertility rates in men with SCI [400].

### 3F.2.2 Recommendations for male fertility

Recommendations	LE	GR
In men with SCI, vibrostimulation and transrectal electroejaculation are effective methods of sperm retrieval.	3	B
In men with SCI; MESA, TESE or ICSI may be used after failed vibrostimulation and/or transrectal electroejaculation.	3	B
In men with SCI, especially at or above T6, it is essential to counsel patients at risk and fertility clinics about the potentially life-threatening condition of autonomic dysreflexia.	3	A

SCI = spinal cord injury.

### 3F.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 [418-420]. Although sexual dysfunction is very common in women with MS, it is still often overlooked by medical professionals [421, 422].

The greatest physical barrier to sexual activity is urinary incontinence. 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 [418, 423-425].

The use of specific drugs for sexual dysfunction is indicated to treat inadequate lubrication. Sildenafil may partially reverse subjective sexual arousal difficulties, while manual and vibratory clitoral stimulation may increase genital responsiveness [426, 427]. Although good evidence exists that psychological interventions are effective in the treatment of female hypoactive sexual desire disorder and female orgasmic disorder [428], there is a lack of high-evidence level studies in the neurological population.

Neurophysiological studies have shown that women with the ability to perceive T11-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 [429-431].

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 [429, 432, 433].

#### 3F.3.1 Recommendation for female sexuality

Recommendation	LE	GR
There is no effective medical therapy for the treatment of neurogenic sexual dysfunction in women.	4	A

### 3F.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 [434].

Although it seems that the reproductive capacity of women with SCI is only temporarily affected by SCI with cessation of menstruation for approximately 6 months after SCI [435], there are no high-evidence level 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 [436].

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 [437, 438]. Obstetric outcomes include higher rates of Caesarean sections and an increased incidence of low birth-weight babies [436].

Epidural anaesthesia is chosen and effective for most patients with AD during labour and delivery [439, 440].

There is very little published data on women's experience of the menopause following SCI [441].

### 3F.4.1 Recommendation for female fertility

Recommendation	LE	GR
In women with a neurological disease, the management of fertility, pregnancy and delivery requires a multidisciplinary approach tailored to individual patient's needs and preferences.	4	A

## 3G FOLLOW-UP

### 3G.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 [46, 101, 305, 311, 338, 442-453].

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 1-2 years. In high-risk neuro-urological patients this interval should be much shorter. Urinalysis should be performed regularly; the frequency to be guided by patient symptoms. The UUT should be checked by ultrasonography at regular intervals in high-risk patients; at least once every 6 months. In these patients, physical examination and urine laboratory should take place every year. Any significant clinical change warrants further, specialised, investigation.

### 3G.2 Recommendations for follow-up

Recommendations	LE	GR
In high-risk patients, the upper urinary tract should be assessed at least every six months.	4	A
In high-risk patients, physical examination, and urine laboratory should take place every year.	4	A
Any significant clinical changes should instigate further, specialised, investigation.	4	A
Urodynamic investigation is a mandatory baseline diagnostic and in high-risk patients, should be done at regular intervals.	3	A

## 3H 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 his/her future.

The urologist or paediatric urologist can select from a wealth of therapeutical options, each with its own pros and cons. Notwithstanding the success of any therapy embarked upon, a 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 less invasive as possible.

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## **5. CONFLICT OF INTEREST**

All members of the Neuro-Urology Guidelines Panel have provided disclosure statements on all relationships that they have that might be perceived to be a potential source of a conflict of interest. This information is publically accessible through the EAU website. This guidelines document was developed with the financial support of the EAU. No external sources of funding and support have been involved. The EAU is a non-profit organisation, and funding is limited to administrative assistance and travel and meeting expenses. No honoraria or other reimbursements have been provided.