Summary of European Association of Urology (EAU) Guidelines on Neuro-Urology

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Abstract

Context: Most patients with neuro-urological disorders require life-long medical care. The European Association of Urology (EAU) regularly updates guidelines for the diagnosis and treatment of these patients.

Objective: To provide a summary of the 2015 updated EAU Guidelines on Neuro-Urology.

Evidence acquisition: Structured literature searches in several databases were carried out to update the 2014 guidelines. Levels of evidence and grades of recommendation were assigned where possible.

Evidence synthesis: Neurological disorders often cause urinary tract, sexual, and bowel dysfunction. Most neuro-urological patients need life-long care for optimal life expectancy and quality of life. Timely diagnosis and treatment are essential to prevent upper and lower urinary tract deterioration. Clinical assessment should be comprehensive and usually includes a urodynamic investigation. The neuro-urological management must be tailored to the needs of the individual patient and may require a multidisciplinary approach. Sexuality and fertility issues should not be ignored. Numerous conservative and noninvasive possibilities of management are available and should be considered before a surgical approach is chosen. Neuro-urological patients require life-long follow-up and particular attention has to be paid to this aspect of management.

Conclusions: The current EAU Guidelines on Neuro-Urology provide an up-to-date overview of the available evidence for adequate diagnosis, treatment, and follow-up of neuro-urological patients.

Patient summary: Patients with a neurological disorder often suffer from urinary tract, sexual, and bowel dysfunction and life-long care is usually necessary. The update of the EAU Guidelines on Neuro-Urology, summarized in this paper, enables caregivers to provide optimal support to neuro-urological patients. Conservative, noninvasive, or minimally invasive approaches are often possible.

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1. Introduction

Any disturbance of the nervous systems that control the lower urinary tract (LUT) can result in urological symptoms. The neuro-urological condition depends on the extent and location of the disturbance and can be symptomatic or asymptomatic. This can lead to a variety of long-term sequelae of which the most significant are renal damage and urosepsis. Elevated storage pressure in the bladder, with or without vesico-uretero-renal reflux, is the most important risk factor [1]. Urinary incontinence and bladder evacuation disorders with associated urinary tract infections can be other troublesome consequences of a disturbed neurological function. Finally, problems concerning bowel and sexual function as well as fertility often exist.

This paper is a summary of the 2015 updated European Association of Urology Guidelines on Neuro-Urology. An earlier guidelines summary appeared in 2009 and reflected the 2008 guidelines [2]. The purpose of the guidelines is to provide information for clinical practitioners on the discernible aspects of neuro-urological disorders in adult patients.

2. Evidence acquisition

Structured literature searches in Medline, Embase, and the Cochrane Library were carried out. The search results were assessed by the panel members, discussed internally and finally used to provide levels of evidence (LEs) and grades of recommendation (GRs) as defined in the full text version (http://www.uroweb.org/guidelines/). The link between the LEs and the GRs is not directly linear. As an example, a GR A may be assigned, even in the absence of a high LE, if there is overwhelming clinical experience and consensus. Future well-designed studies could reveal a too high GR in such a case.

3. Evidence synthesis

3.1. Epidemiology

All central and peripheral neurological disorders carry a high risk of causing functional disturbances of the urinary tract. For example, 95% of the patients with a suprasacral spinal cord injury (SCI) have detrusor overactivity (DO) and detrusor-sphincter dyssynergia [3]. Multiple sclerosis (MS) leads to neuro-urological symptoms in almost all patients with a disease duration of more than 10 yr [4].

3.2. Terminology

The terminology used and the diagnostic procedures outlined in these guidelines follow the recommendations published by the International Continence Society [5].

3.3. Diagnostic evaluation

3.3.1. Introduction

The type of LUT dysfunction in patients with neurological pathology may not be obvious from the neurological lesion and the patient’s symptoms. Clinical assessment of these patients includes a detailed history, a systematic physical examination, a bladder diary, and urodynamic tests (Table 1).

3.3.2. Classification systems

A useful classification system for neuro-urological dysfunctions was developed by Madersbacher [6]. It is based on the contraction state of the bladder and external urethral sphincter during the storage and voiding phase (Fig. 1).

3.3.3. The timing of diagnosis and treatment

Early diagnosis and treatment are essential in both congenital and acquired neuro-urological disorders to prevent irreversible deterioration of the lower and upper urinary tract (UUT), even in the presence of normal neurological reflexes [7–9]. Additionally, LUT symptoms can be the presenting feature of neurological pathology [10].

3.3.4. Patient history

History taking should include past and present symptoms and disorders of the urinary tract and bowel, as well as sexual and neurological function. Special attention should be paid to possible warning signs and symptoms (eg, pain, infection, haematuria, and fever) requiring further investigation. Present medication, lifestyle, mobility, hand function, and possible autonomic dysreflexia (especially in lesions at or above level T6) are items that should not be overlooked.

3.3.4.1. Bladder diaries. A bladder diary should be recorded over at least 2–3 d. Possible pathological findings include a high bladder evacuation frequency, very low or very high stored volumes, nocturnal voidings, urgency, and incontinence.

3.3.5. Quality of life

Quality of life (QoL) is an important aspect of the overall management of neuro-urological patients, for example, to evaluate treatment related changes of a patient’s QoL [11]. The type of bladder management and its impact on the urodynamic functionality have been shown to affect health-related QoL in patients with SCI [12]. An assessment of the

| Table 1 – Recommendations for urodynamics and uro-neurophysiology |
|-------------------------|-----------------|
| Recommendations | GR |
| The recording of a bladder diary is advisable. | A |
| Noninvasive testing is mandatory before invasive urodynamics is planned. | A |
| Urodynamic investigation is necessary to detect and specify LUT dysfunction. | 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. | A |
| A physiological filling rate and body-warm saline should be used. | A |
| Specific uro-neurophysiological tests are elective procedures. | C |

GR = grade of recommendation; LUT = lower urinary tract.
patient’s present and expected future QoL is therefore essential.

There are no specific QoL questionnaires for neuro-urological patients in general. Qualiveen is a validated questionnaire specifically for SCI and MS patients and a short form is available [12,13].

Several generic health-related QoL questionnaires can be used to assess a patient’s QoL secondarily. In addition, treatment outcomes can be quantified using quality-adjusted life years [14].

3.3.6. Physical examination
Neurological status should be described as completely as possible. All sensations and reflexes in the urogenital area as well as anal sphincter and pelvic floor function must be tested. This clinical information is essential to reliably interpret later diagnostic investigations.

3.3.7. Urodynamics
3.3.7.1. Introduction. Urodynamic investigation is the only method that can objectively assess the function of the LUT. It can however cause potentially life-threatening autonomic dysreflexia in patients with a spinal cord lesion, especially at or above T6, requiring stopping the examination and immediate emptying of the bladder. In some refractory cases an antihypertensive treatment (for instance nifedipine) might become necessary.

3.3.7.2. Noninvasive urodynamic tests. Free uroflowmetry and ultrasound assessment of post void residual (PVR) should be repeated at least two/three times [5]. Possible pathological findings include a low maximum flow rate, low voided volumes, intermittent flow, and PVR.

3.3.7.3. Invasive urodynamic tests. Filling cystometry is the only method for quantifying the bladder storage function. The filling rate (in ml/min) should ideally not exceed body weight (in kg)/4 [15]. Possible pathological findings include DO, low bladder compliance, abnormal sensations, incontinence, and an incompetent or relaxing urethra. Detrusor leak point pressure measurement has limited diagnostic value [16].

Pressure-flow study reflects the coordination between detrusor and urethra or pelvic floor during the voiding phase. Possible pathological findings include detrusor underactivity or acontractility, detrusor sphincter dyssynergia, a high urethral resistance, and PVR.

Electromyography is useful as a gross indication of the patient’s ability to control the pelvic floor.

Urethral pressure measurement has a very limited role in neuro-urological disorders. There is no consensus on parameters indicating pathological findings [17].

Video-urodynamics is the combination of filling cystometry and pressure-flow study with radiological imaging. It can detect morphological abnormalities of the urinary tract including vesico-uretero-renal reflux.

The role of ambulatory urodynamics in the neuro-urological patient needs to be determined.

3.3.7.4. Specialist uro-neurophysiological tests. Several tests are available to determine the motor or sensory function of the pelvic floor muscles, urethral and anal sphincter, pudendal nerves, bladder, and urethra.

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**Fig. 1 – Madersbacher classification system [6] showing typical neurological lesions.**
Table 2 – Recommendations for treatment

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>For neurogenic detrusor overactivity, antimuscarinic therapy is the recommended first-line medical treatment.</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>Alternative routes of administration (ie, transdermal or intravesical) of antimuscarinic agents may be used.</td>
<td>2</td>
<td>A</td>
</tr>
<tr>
<td>Outcomes for neurogenic detrusor overactivity may be maximized by considering a combination of antimuscarinic agents.</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>To decrease bladder outlet resistance, α-blockers could be prescribed.</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>For underactive detrusor, no parasympathomimetic should be prescribed.</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>In neurogenic stress urinary incontinence, drug treatment should not be prescribed.</td>
<td>4</td>
<td>A</td>
</tr>
<tr>
<td>Botulinum toxin injection in the detrusor is the most effective minimally invasive treatment to reduce neurogenic detrusor overactivity.</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>Sphincterotomy is a treatment option for detrusor sphincter dyssynergia.</td>
<td>3</td>
<td>A</td>
</tr>
<tr>
<td>Bladder neck incision is effective in a fibrotic bladder neck.</td>
<td>4</td>
<td>B</td>
</tr>
<tr>
<td>In order to treat refractory neurogenic detrusor overactivity, bladder augmentation is recommended.</td>
<td>3</td>
<td>A</td>
</tr>
<tr>
<td>In female patients with neurogenic stress urinary incontinence who are able to self-catheterize, placement of an autologous urethral sling should be used.</td>
<td>4</td>
<td>B</td>
</tr>
<tr>
<td>In male patients with neurogenic stress urinary incontinence, artificial urethral sphincter should be used.</td>
<td>3</td>
<td>A</td>
</tr>
</tbody>
</table>

GR = grades of recommendation; LE = levels of evidence.

3.4. Disease management

The primary aims for treatment of neuro-urological symptoms are: (1) protection of the UUT; (2) achieving or maintaining urinary continence; (3) restoration of the LUT function; and (4) improvement of QoL. Further considerations are the patient’s disability, cost-effectiveness, technical complexity, and possible complications [18] (Table 2).

In patients with high detrusor pressure during the storage phase, treatment is aimed primarily at "conversion of an overactive, high-pressure bladder into a low-pressure reservoir" despite the resulting PVR [2]. This contributes to urinary continence, social rehabilitation, QoL, and preventing UTI [19].

3.4.1. Noninvasive conservative treatment

3.4.1.1. Bladder emptying technique – Credé maneuver, Valsalva maneuver, triggered reflex voiding. Voiding by bladder compression (Credé maneuver) or abdominal straining (Valsalva maneuver) leads to an increase in intravesical pressure and may also lead to an increased bladder outlet resistance due to a reflex sphincter contraction. Damage to the urinary tract and inefficient bladder emptying may result [20]. Eliciting reflex detrusor contractions in patients with upper motor neuron lesions by stimulation of sacral or lumbar dermatomes bears the risk of high pressure voiding and autonomic dysreflexia [20]. These techniques must therefore be used with caution. Intermittent catheterization (see below) is a better alternative in the majority of patients.

3.4.1.2. External appliances. Condom catheters and incontinence pads can be used to achieve social continence. Both methods bear the risk of infection [21]. The penile clamp is absolutely contraindicated in case of neurogenic DO or low bladder compliance because of the risk of developing high intravesical pressure.

3.4.1.3. Lower urinary tract rehabilitation. Evidence for LUT rehabilitation in neurological patients using electrical stimulation of the tibial, pudendal, and dorsal genital nerve is mainly based on pilot studies with small patient numbers. Repetitive transcranial magnetic stimulation has also been applied. Combining these techniques with pelvic floor muscle training and electromyography biofeedback can improve results [22].

3.4.1.4. Drug treatment

3.4.1.4.1. Drugs for treatment of detrusor overactivity. Antimuscarinics are the first-line choice for treating neurogenic DO [23]. A change of antimuscarinic may be beneficial in case of an insufficient therapeutic effect or experienced adverse effects due to differences in efficacy and side effect profiles [24]. Neurological patients may need a higher-than-recommended dose or a combination of antimuscarinics [25]. Antimuscarinics can also be administered transdermally or intravesically. Long-term use of antimuscarinics is expected to be beneficial for renal function, but good-quality studies on this topic are lacking [23].

Phosphodiesterase inhibitors may become an alternative or adjunct to antimuscarinic treatment [26]. β3-Adrenergic receptor agonists have recently been introduced as a treatment of overactive bladder symptoms, but clinical experience in neurological patients is lacking. Combined therapy with antimuscarinics may become an option.

Additional treatment with desmopressin might improve the clinical efficacy of treatment in patients with nocturia or nocturnal enuresis [27]. Hyponatremia may however occur.

3.4.1.4.2. Drugs for treatment of detrusor underactivity. Available studies do not support the use of parasympathomimetic agents. Studies on intravesical administration of cannabinoind agonists to improve detrusor contractility as well as to decrease the bladder outlet resistance are in the preclinical phase only [28].

3.4.1.4.3. Drugs for decreasing bladder outlet resistance. Alpha-blockers seem to be effective for decreasing bladder outlet resistance, PVR, and autonomic dysreflexia [29].
3.4.1.4.4. Drugs for increasing bladder outlet resistance. There are no high-level evidence studies showing efficacy in the medical treatment of stress urinary incontinence in neurological patients [30].

3.4.2. Minimally invasive treatment

3.4.2.1. Catheterization. Intermittent self-catheterization is the preferred management of patients who cannot effectively empty their bladders. Third-party catheterization is an option if intermittent self-catheterization is not possible. Sterile intermittent catheterization (IC) significantly reduces the risk of urinary tract infection (UTI) and bacteriuria compared with clean IC, but cannot be considered a routine procedure [20]. Aseptic IC is an alternative that significantly reduces external contamination of the catheter. Contributing factors to contamination are insufficient patient education and the inherently greater risk of UTI in neuro-urological patients [30].

The catheter size most often used is 12–16 Fr. Keeping a bladder diary may be helpful in determining the optimal frequency of catheterization. This is usually four/six times per d. As a rule, bladder volume at catheterization should not exceed 400–500 ml. Indwelling transurethral catheterization and, to a lesser extent, suprapubic cystostomy are associated with a range of complications as well as an enhanced risk factor for UTI and 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.

3.4.2.2. Intravesical drug treatment. Intravesical application of antimuscarinics to reduce DO may reduce adverse effects. The vanilloids capsaicin and resiniferatoxin desensitize the C-fibers and thereby decrease DO for a few mo. They have limited clinical efficacy compared to botulinum toxin-A injections in the detrusor and do not constitute a registered therapy [31].

3.4.2.3. Botulinum toxin injections in the bladder. OnabotulinumtoxinA has been proven effective in patients with neuro-urological disorders in phase III randomized placebo-controlled trials [32,33]. The injections are mapped over the detrusor in a dosage that depends on the preparation used. Botulinum toxin causes a reversible chemical denervation that lasts for about 9 mo. Repeated injections seem to be possible without loss of efficacy. The most occurring side effects are UTIs and elevated PVR [32,33]. IC may become necessary. Rare but severe adverse events include autonomic dysreflexia and respiratory problems.

3.4.2.4. Intravesical electrostimulation. Intravesical electrostimulation enhances the sensation for bladder filling and urgency to void and may restore the volitional control of the detrusor [34]. Daily stimulation sessions of 90 min are used for at least 1 wk. The results in literature are not unequivocal: both positive and negative results have been reported.

3.4.2.5. Bladder neck and urethral procedures for functional obstruction, urinary incontinence, and detrusor underactivity. Reduction of the bladder outlet resistance may be necessary to protect the UUT. This can be achieved with surgical interventions (bladder neck incision, sphincterotomy, or urethral stent) or with chemical denervation of the sphincter. Incontinence may result and can be managed by external devices (see Section 3D.1.2).

Botulinum toxin-A sphincter injection can be used to treat detrusor sphincter dyssynergia. The therapy is not registered and repeat injections are necessary after a few mo [35]. Balloon dilatation is no longer recommended as immediate results have been published only [35]. With sphincterotomy by staged incision, bladder outlet resistance can be reduced without completely losing the closure function of the urethra. The laser technique appears to be advantageous [36]. Sphincterotomy needs to be repeated at regular intervals in a subset of patients [37]. Secondary narrowing of the bladder neck may occur.

Bladder neck incision is indicated only for secondary changes (fibrosis) and makes no sense if the narrowing of the bladder neck is caused by a hypertrophied detrusor [36]. The results of implantation of urethral stents are comparable with sphincterotomy [35]. The costs and possible complications and reinterventions are limiting factors in its use.

Increasing the bladder outlet resistance can improve continence. Bulking agents often have a limited duration of efficacy in neuro-urological patients and bear the risk of causing high bladder pressures [18]. Results of urethral inserts for the treatment of stress urinary incontinence and detrusor underactivity in women are lacking or disappointing.

3.4.3. Surgical treatment

3.4.3.1. Bladder neck and urethral procedures for urinary incontinence. Procedures to treat sphincteric incontinence bear the risk of causing high intravesical pressure. They 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. The artificial urinary sphincter has stood the test of time and has an acceptable long-term outcome [18]. Various materials have successfully been used for a urethral sling procedure [18]. In women, autologous material seems to be preferential [38]. Several bladder neck and urethra reconstruction procedures have been described.

3.4.3.2. Denervation, deafferentation, sacral neuromodulation. Sacral anterior root stimulation is applicable in selected patients to produce a detrusor contraction. It is usually combined with sacral rhizotomy [18]. Sacral neuromodulation has successfully been applied in the neuro-urological patient but there is a lack of randomized controlled trials [39].

3.4.3.3. Bladder covering by striated muscle. For example, the rectus abdominis or latissimus dorsi, may be able to restore bladder voiding function [40].
3.4.3.4. Bladder augmentation. This is indicated for an overactive or low compliance bladder when more conservative approaches have failed [18]. Autoaugmentation (detrusor myectomy) and replacement or expansion of the bladder by passive expandable coverage are alternatives [18].

3.4.3.5. Urinary diversion. This must be considered when no other therapy is successful [18]. A continent diversion should be the first choice. An incontinent diversion is indicated if catheterization is impossible or if the patient refuses other therapy [18].

3.5. UTI

3.5.1. Introduction
UTI is the new onset of signs or symptoms accompanied by laboratory findings of bacteriuria, leukocyturia, and positive urine culture [41]. There are no evidence-based cutoff values for the quantification of these findings. Consensus values depend on the bladder emptying method. Neurological patients, especially those with SCI, may have other signs and symptoms than able-bodied individuals. The most common ones are fever, increased incontinence, increased spasticity, malaise, lethargy or sense of unease, cloudy urine with increased urine odor, discomfort or pain over the kidneys or bladder, dysuria, and autonomic dysreflexia [42,43].

3.5.2. Diagnostic evaluation
The advised method for the diagnosis is urine culture and urinalysis. Microbiologic testing is mandatory as bacterial strains and resistance patterns may differ from those of able-bodied patients [44]. A dipstick test may be more useful to exclude than to prove UTI [45].

3.5.3. Disease management
Treatment of asymptomatic bacteriuria results in significantly more resistant bacterial strains without improving the outcome and is therefore dissuaded [46]. A UTI in neuro-urolological patients is by definition complicated and single-dose treatment is therefore not advised. The duration of treatment depends on the severity of the UTI and the involvement of the kidneys and the prostate. Generally, a 5–7 d course is advised, that can be extended up to 14 d [46]. The choice of the antibiotic therapy should be based on the results of the microbiologic testing. If immediate treatment is mandatory (eg, fever, septicemia, intolerable clinical symptoms, extensive autonomic dysreflexia), the choice of treatment should be based on local and individual resistance profiles [47].

3.5.4. Recurrent UTI
Recurrent UTI in neuro-urolological patients may indicate a suboptimal management of the underlying functional problem, for example, high bladder pressures, incomplete voiding, or bladder stones. The improvement of bladder function and the removal of exacerbating factors, especially indwelling catheters, are recommended [44,48].

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### Table 3 – Recommendations for the treatment of UTI

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic bacteriuria in patients with neuro-urological disorders should not be treated.</td>
<td>4</td>
<td>A</td>
</tr>
<tr>
<td>The use of long-term antibiotics in recurrent UTIs should be avoided.</td>
<td>2a</td>
<td>A</td>
</tr>
<tr>
<td>In patients with recurrent UTI, treatment of neuro-urological symptoms should be optimized and foreign bodies (eg, stones, indwelling catheters) should be removed from the urinary tract.</td>
<td>3</td>
<td>A</td>
</tr>
<tr>
<td>Prophylaxis must be individualized since there is no optimal prophylactic measure available.</td>
<td>4</td>
<td>C</td>
</tr>
</tbody>
</table>

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3.5.5. Prevention
In men performing IC, the use of hydrophilic catheters is associated with a lower rate of UTI. Such an effect could not be demonstrated in women [49]. The administration of an alternate antibiotic once per wk demonstrated a significant decrease of UTI in SCI patients without increased colonization with multi-drug resistant bacteria [50]. There is a lack of evidence for many other approaches that have been tested as UTI prophylaxis, including the use of cranberry juice, methenamine hippurate, L-methionine, and oral immunotherapy. Low-dose, long-term antibiotic prophylaxis cannot reduce UTI frequency, but increases bacterial resistance and is therefore not recommended [46]. Prophylaxis is essentially a trial and error approach, in which individualized concepts should be taken into consideration [51] (Table 3).

3.6. Sexual (dys)function and fertility

3.6.1. Male erectile dysfunction

3.6.1.1. Phosphodiesterase type 5 inhibitors. Phosphodiesterase type 5 inhibitors (PDE5Is) are recommended as first-line treatment in men with erectile dysfunction and neurological disease [52]. The efficacy and safety of these drugs have been demonstrated. The patient must have some residual nerve function to induce an erection.

The most common side effects of PDE5Is are headache, flushing, dyspepsia, and nasal congestion. Hypotension may occur in patients with tetraplegia/high-level paraplegia and multiple system atrophy [53]. PDE5Is are contraindicated in patients using nitrate medication, for example, for autonomic dysreflexia.

3.6.1.2. Mechanical devices. Mechanical devices (vacuum tumescence devices and penile rings) may be effective but are less popular [54].

3.6.1.3. Intracavernous injections and intraurethral application. Intracavernous injectable medications (alprostadil, papaverine, and phentolamine) have been shown to be effective in a number of neurological conditions, including SCI, MS, and diabetes mellitus [55]. Careful dose titration and some precautions are required. Complications include pain, priapism, and corpora cavernosa fibrosis.
Intracavernous injection of vasoactive medication is the first therapeutic option to consider in patients in whom PDE5Is are contraindicated or ineffective. Alprostadil can also be applied intraurethrally, but it appeared less effective in SCI patients [56].

3.6.1.4. Penile prostheses. Penile prostheses may be considered when all conservative treatments have failed. Serious complications, including infection and prosthesis perforation, may occur in about 10% of patients [57].

3.6.2. Male fertility
Neurological damage may impair erectile function, ejaculation, and semen quality, thus causing infertility [58]. Erectile dysfunction is managed as described above. Retrograde ejaculation may be reversed by sympathomimetic agents contracting the bladder neck [58]. The use of a balloon catheter to obstruct the bladder neck may also be effective [59]. If these measures fail, the harvest of semen from the urine may be considered [58]. Other methods of sperm retrieval include vibrostimulation with or without midodrine, transrectal electroejaculation, and prostatic massage. Surgical procedures, such as microsurgical epididymal sperm aspiration and testicular sperm extraction, may be used if these methods are not successful [60]. Intracytoplasmic sperm injection is a valuable option for men with SCI [61].

Patients and fertility clinics must be informed about the possible occurrence of autonomic dysreflexia during sexual activity and ejaculation, especially in men with SCI at or above T6.

3.6.3. Female sexuality
The greatest physical barrier to sexual activity in female neurological patients is urinary incontinence. Problems with positioning and spasticity may also play a role. Specific drugs are indicated to treat inadequate lubrication. Sildenafil may improve subjective sexual arousal, while vasoactive drugs (alone or in combination) are the recommended second-line medical treatment. In neurogenic ED, mechanical devices such as vacuum devices and rings can be effective and may be offered to patients. In neurogenic ED, penile prostheses should be reserved for selected patients. There is no effective medical therapy for the treatment of neurogenic sexual dysfunction in women.

In men with SCI, vibrostimulation and transrectal electroejaculation are effective methods of sperm retrieval.

In men with SCI, MESA, TESE or ICSI may be used after failed vibrostimulation and/or transrectal electroejaculation.

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.

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.

3.6.4. Female fertility
It seems that the reproductive capacity of women with SCI is only temporarily affected for approximately 6 mo after SCI [63]. Women with SCI are more likely to suffer complications during pregnancy, labor, and delivery compared to able-bodied women including bladder problems, spasticity, pressure sores, anemia, and autonomic dysreflexia [63]. Obstetric outcomes include higher rates of caesarean sections and an increased incidence of low birth-weight babies [64]. Epidural anesthesia is effective for most patients with autonomic dysreflexia during labor and delivery [63] (Table 4).

3.7. Follow-up
Regular follow-up is necessary as neuro-urological disorders are often unstable [65]. The interval between investigations should usually not exceed 1–2 yr. In high-risk patients, the UUT should be checked by ultrasonography at least once every 6 mo, while physical examination and urine laboratory should take place every yr. Any significant clinical change warrants further investigation. Urodynamic investigation is a mandatory baseline diagnostic. In high-risk patients, it should be repeated at regular intervals.

3.8. Conclusions
Neurological disorders often cause urinary tract, sexual, and bowel dysfunction. Most neuro-urological patients need life-long care for optimal life expectancy and QoL. Timely diagnosis and treatment are essential to prevent UUT and LUT deterioration. Clinical assessment should be comprehensive and usually includes a urodynamic investigation. The neuro-urological management must be tailored to the needs of the individual patient and may require a multidisciplinary approach. Conservative and noninvasive therapies must be tested before surgical procedures are considered. Sexuality and fertility are topics that should not be ignored.

Table 4 – Recommendations for the treatment of sexual (dys)function and fertility

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>In neurogenic ED, oral PDE5Is are the recommended first-line medical treatment.</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>In neurogenic ED, intracavernous injections of vasoactive drugs (alone or in combination) are the recommended second-line medical treatment.</td>
<td>3</td>
<td>A</td>
</tr>
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<td>B</td>
</tr>
<tr>
<td>In neurogenic ED, penile prostheses should be reserved for selected patients.</td>
<td>4</td>
<td>B</td>
</tr>
<tr>
<td>There is no effective medical therapy for the treatment of neurogenic sexual dysfunction in women.</td>
<td>4</td>
<td>A</td>
</tr>
<tr>
<td>In men with SCI, vibrostimulation and transrectal electroejaculation are effective methods of sperm retrieval.</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>In men with SCI, MESA, TESE or ICSI may be used after failed vibrostimulation and/or transrectal electroejaculation.</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>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.</td>
<td>3</td>
<td>A</td>
</tr>
<tr>
<td>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.</td>
<td>4</td>
<td>A</td>
</tr>
</tbody>
</table>

ED = erectile dysfunction; GR = grades of recommendation; ICSI = Intracytoplasmic sperm injection; LE = levels of evidence; MESA = microsurgical epididymal sperm aspiration; PDE5I = phosphodiesterase type 5 inhibitor; SCI = spinal cord injury; TESE = testicular sperm extraction.

Author contributions: Jan Groen had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Groen, Pannek, Castro Diaz, Del Popolo, Gross, Hamid, Karsenty, Kessler, Schneider, ’t Hoen, Blok.
Acquisition of data: Groen, Pannek, Castro Diaz, Del Popolo, Gross, Hamid, Karsenty, Kessler, Schneider, ’t Hoen, Blok.

Analysis and interpretation of data: Groen, Pannek, Castro Diaz, Del Popolo, Gross, Hamid, Karsenty, Kessler, Schneider, ’t Hoen, Blok.

Drafting of the manuscript: Groen.

Critical revision of the manuscript for important intellectual content: Groen, Pannek, Castro Diaz, Del Popolo, Gross, Hamid, Karsenty, Kessler, Schneider, ’t Hoen, Blok.

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Castro-Diaz: Company consultant (Astellas, Allergan, AMS); Company speaker honorarium (Astellas, Allergan); Trial participation (Allergan).

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