Guidelines on Neurogenic Lower Urinary Tract Dysfunction

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1. AIM AND STATUS OF THESE GUIDELINES

1.1 Purpose

The purpose of these clinical guidelines is to provide information on the incidence, definitions, diagnosis, therapy, and follow up observation of the condition of neurogenic lower urinary tract dysfunction (NLUTD), that will be useful for clinical practitioners. These guidelines reflect the current opinion of the experts in this specific pathology and thus represent a state of the art reference for all clinicians as of the date of its presentation to the European Association of Urology.

1.2 Standardization

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) (1-3).

1.3 REFERENCES

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2. BACKGROUND

2.1 Risk factors and epidemiology

NLUTD may be caused by various diseases and events affecting the nervous systems controlling the LUT. The resulting lower urinary tract dysfunction (LUTD) depends grossly on the location and the extent of the neurologic lesion (cf. 2.3.).
Overall figures on the prevalence of NLUTD in the general population are lacking, but data are available on the prevalence of the underlying conditions and the relative risk of those for the development of NLUTD.

2.1.1 Peripheral neuropathy

Diabetes: This common metabolic disorder has a prevalence of about 2.5% in the American population, but the disease may be subclinical for many years. No specific criteria exist for secondary neuropathy in this condition, but it is generally accepted that 50% of the patients will develop somatic neuropathy and 75-100% of those will develop NLUTD (1-2).

Alcohol abuse: This will eventually cause peripheral neuropathy, but its reported prevalence varies widely: 5-15% (3) to 64% (4). The NLUTD is probably more present in patients with liver cirrhosis and the parasympathetic system is attacked more than the sympathetic system (5).

Less prevalent peripheral neuropathies:
- Porphyria — bladder dilatation in up to 12% of patients (6).
- Sarcoidosis — NLUTD rare (7).
- Lumbosacral (8) zone and genital (9) herpes — NLUTD transient in most patients.
- Guillain Barré — Urinary symptoms in 30% of patients, regressive in most (10).

2.1.2 Regional spinal anaesthesia

This may cause NLUTD (11) but no prevalence figures were found (12).

2.1.3 Iatrogenic

Abdominoperineal resection of rectum or uterus may cause lesions of the lower urinary tract innervation in 10-60% of patients (13,14). The extent of the resection is important: <8% after colostomy only, but 29% after posterior resection (15). Radical prostectomy is a risk factor also (16).

2.1.4 Demyelinization

Multiple sclerosis causes NLUTD in 50-90% of the patients (17-19). NLUTD is the presenting symptom in 2-12% of the patients (20).

2.1.5 Dementia

Alzheimer, Binswanger, Nasu and Pick diseases frequently cause non-specific NLUTD (21-25).

2.1.6 Basal ganglia pathology (Parkinson, Huntington, Shy-Drager, etc.)

Parkinson's disease is accompanied by NLUTD in 37.9-70% (26). In the rare Shy-Drager syndrome almost all patients have NLUTD (27).

2.1.7 Cerebrovascular pathology

This causes hemiplegia with remnant incontinence NLUTD in 20-50% of patients (28- 30) with decreasing prevalence in the post-insult period (30).

2.1.8 Frontal brain tumours

These tumours can cause LUTD in 24% of the patients (31).

2.1.9 Spinal cord lesions

Spinal cord lesions can be traumatic, vascular, medical, or congenital. An incidence of 30-40 new cases per million population is the accepted average for the USA. Most patients will develop NLUTD (32). For spina bifida and other congenital nerve tube defects, the prevalence in the UK is 8-9 per 10,000 aged 10-69 years with the greatest prevalence in the age group 25-29 years (33), and in the USA 1 per 1000 births (34). About 50% of these children will have detrusor sphincter dyssynergia (DSD) (35).

2.1.10 Disc disease

This is reported to cause NLUTD in 6-18% of the patients (36,37).

2.2 Standardization of terminology

2.2.1 Introduction

Several groups already presented guidelines for the care of patients with NLUTD for national or international urological community (38-41).These guidelines will evolve further as time goes by. They also contain definitions of various important terms and procedures. The ICS NLUTD standardization report (39) is addressed specifically at the standardization of terminology and urodynamic investigation in this patient group. Other relevant definitions are found in the general ICS standardization report (42).

The definitions from these references, partly adapted, and other definitions that are judged useful for the clinical practice in NLUTD, are listed in section 2.2.2. For specific definitions relating to the urodynamic investigation technique the reader is referred to the appropriate ICS report (39).

2.2.2 Definitions

Acontractility, detrusor — see below under voiding phase

Acontractility, urethral sphincter — see below under storage phase

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

Catheterization, indwelling — Emptying of the bladder by a catheter that is introduced (semi-)permanently

Catheterization, 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, and disinfecting lubricant is 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-catheterization (ISC) — IC performed by the patient

Compliance, detrusor — see below under storage phase
Condition — The presence of specific observations associated with characteristic symptoms or signs evidencing relevant pathologic processes
Diary, urinary — 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 (MTC) — Times of micturitions only
Filling rate, physiological — Below the predicted maximum: body weight (kg)/4 in ml/s (42, 43)
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 (LPP) — see below under storage phase
Lower motor neuron lesion (LMNL) — Lesion at or below the S1-S2 spinal cord level
Neurogenic lower urinary tract dysfunction (NLUTD) — Lower urinary tract dysfunction secondary to confirmed pathology of the nervous supply
Observation, specific — Observation made during specific diagnostic procedure
Overactivity, bladder — see below under symptom syndrome
Overactivity, detrusor — see below under storage phase
Rehabilitation, LUT — Non-surgical non-pharmacological treatment for LUT dysfunction
Sign — Observation by the physician including simple means (direct observation, bladder diary, pad weighing) 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 to seek help from health care professionals
Upper motor neuron lesion (UMNL) — Lesion above the S1-S2 spinal cord level
Voiding, balanced — In patients with NLUTD: 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

<u>Storage phase</u>

- Maximum anaesthetic bladder capacity — Maximum bladder filling volume under deep general or spinal anaesthesia
- Increased daytime frequency — Self-explanatory; the normal frequency can be estimated at about 8 times per day (44)
- Nocturia — Waking at night one or more times to void
- Urgency — The symptom of a sudden compelling desire to pass urine which is difficult to defer
- Urinary incontinence — Any involuntary leakage of urine. This can be specified:
  - Stress urinary incontinence — On effort or exertion, or on sneezing or coughing
  - Urge urinary incontinence — Accompanied by or immediately preceded by urgency
  - Mixed urinary incontinence — Associated with urgency and also exertion, effort, sneezing, or coughing
  - Continuous urinary incontinence
- Bladder sensation categorized as:
  - Normal — 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.
  - Increased — 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
  - Reduced — 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

Definitions valid after urodynamic confirmation only

- 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-anaesthetized 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
  Subgroups:
  - Phasic detrusor overactivity — Characteristic phasic contraction
  - Terminal detrusor overactivity — A single contraction at cystometric capacity
- High pressure detrusor overactivity — Maximal detrusor pressure >40 cm H_2O (39,45)
- Overactivity volume — Bladder volume at first occurrence of detrusor overactivity
- 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
- Detrusor compliance — Relationship between change in bladder volume (ΔV) and change in detrusor pressure (Δp_{det}): $C=\Delta V/\Delta p_{det}$ (ml/cm H_2O)
- Low detrusor compliance — $C=\Delta V/\Delta p_{det}$ <20 ml/cm H_2O (39)
- Break volume — Bladder volume after which a sudden significant decrease in detrusor compliance is observed
- Urethral sphincter acontractility — No evidence of sphincter contraction during filling, particularly at higher bladder volumes, or during abdominal pressure increase

Voiding phase
- 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

Definitions valid after urodynamic confirmation only
- Normal detrusor function — Voluntarily initiated detrusor contraction that causes complete bladder emptying within a normal time span
- Detrusor underactivity — Contraction of reduced strength and/or duration
- Acontractile detrusor — Absent contraction
- Non-relaxing urethral sphincter — Self-explanatory
- Detrusor sphincter dyssynergia (DSD) — Detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated musculature

Post micturition phase
- 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 lower urinary tract 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 urge incontinence, usually with frequency and nocturia

Synonyms: Urge syndrome, urgency-frequency syndrome
This syndrome is suggestive for LUTD

2.3 Classification

2.3.1 Introduction

The purpose of classification of NLUTD is to facilitate the understanding and management of NLUTD and to provide a standardized terminology of these disease processes. The normal LUT function depends on neural integration at and between the peripheral, spinal cord, and central nervous systems. The gross type of NLUTD is dependent on the location and the extent of the lesion: suprapontine or pontine, suprasacral spinal cord, or subsacral and peripheral (32,40).

The classification systems for NLUTD are based on either the neurological substrate (type and location of the neurological lesion), the neuro-urological substrate (neurological lesion and LUTD), the type of LUTD, or are

strictly functional. Many descriptive terms were derived from these classification systems, but they are standardized only within any specific system and have little meaning outside the system and can sometimes be confusing.

A perfect classification system is not yet available. Neurologic classification systems, by nature, cannot describe the LUTD completely and vice versa. Individual variations exist in the NLUTD caused by a specific neurologic lesion. Thus for any particular patient the description of the NLUTD should be individualized.

2.3.2 Neuro-urological classification

Bors and Comarr's (46) classic neuro-urological classification system was deduced from clinical observations of patients with traumatic spinal cord injury. It specifies three elements: location of lesion, completeness of lesion, and co-ordination of LUT.

Hald and Bradley (47) reduced the number of categories in Bors and Comarr's classification. The authors describe their system as a simple neurotopographic classification.

Burgdörfer completed Bors and Comarr's system with information on the LUTD, broken down for detrusor, sphincter, and residual urine. This classification is published elsewhere (48).

2.3.3 Neurological classification

Bradley (49) presented four control loops for the LUT. Loop I are the connections between the central nervous system and the pontine micturition center, loop II the intraspinal pathways between the detrusor to the micturition center (afferent) and the sacral spinal cord (efferent), loop III the sensory axons pathways from the detrusor and the striated urethral sphincter to the sacral spinal cord, and loop IV describes the suprasacral and segmental innervation of the periurethral striated muscles.

2.3.4 Urodynamic classification

Lapides (50) classifies the clinical and urodynamic findings into five categories: sensory neurogenic bladder, motor paralytic bladder, autonomous neurogenic bladder, uninhibited neurogenic bladder, and reflex neurogenic bladder.

Krane and Siroky (51) present a descriptive classification of detrusor and sphincter co-ordination observed during urodynamic evaluation in patients with NLUTD, focussed on the functional interaction between detrusor and urethral sphincter.

2.3.5 Functional classification

Quesada et al. (52) suggested that a classification based on the functional aspects of the LUT might be more practicable for clinical decision making.

Wein (53) provides a practical approach towards the diagnosis and therapy of LUTD by classifying against the storage and voiding functions of the LUT, and the activity of the detrusor and the urethra.

Fall et al. (54) proposed a more detailed classification of the overactive detrusor. This is included in the ICS classification.

The ICS (42) separates the storage and voiding phases and describes the detrusor and urethral functions in each phase by specific designations (cf. 2.2.).

Madersbacher (40,55) presented a very simple classification that basically is focussed on the therapeutic consequences (fig. 2.1). It is based on the clinical concept that the important differentiation in the diagnosis exists between the situations of high and low detrusor pressure during the filling phase and urethral sphincter relaxation and non- relaxation or DSD during the voiding phase. A non-relaxed sphincter or DSD will cause high detrusor pressure during the voiding phase. This classification is the easiest one for general use in clinical diagnosis of NLUTD.

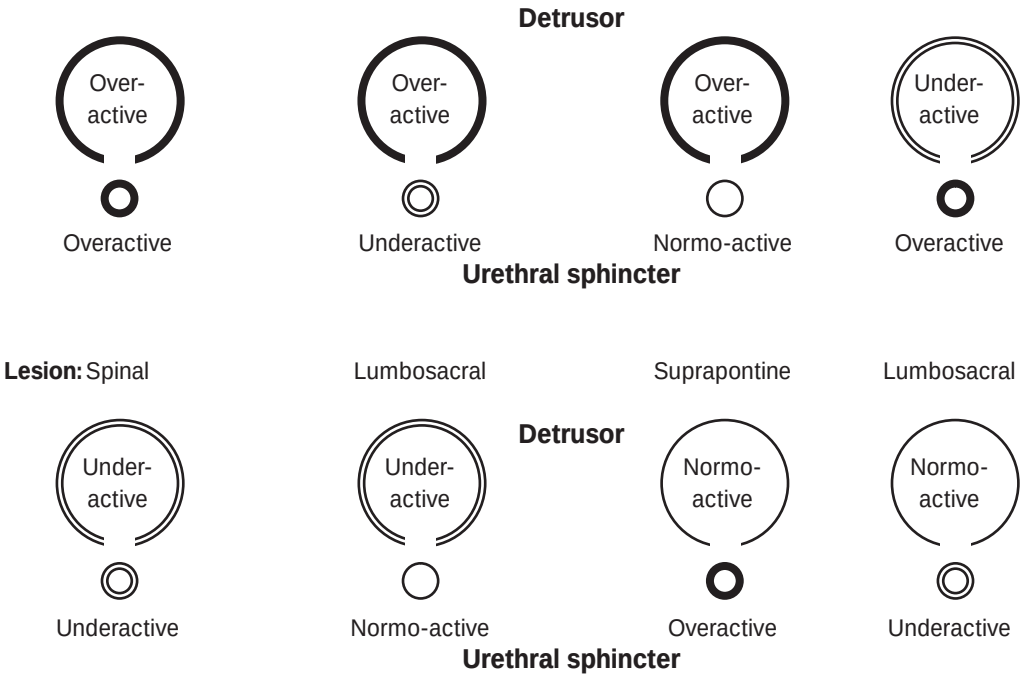

Figure 2.1. Madersbacher classification system (40) with typical neurogenic lesions

2.3.6 RECOMMENDATION FOR CLASSIFICATION

The Madersbacher classification system (40) (fig. 2.1) is recommended for clinical practice.

2.4 Timing of diagnosis and treatment

Both in congenital and in acquired NLUTD, early diagnosis and treatment is essential as irreversible changes may occur in particular in children with myelomeningocele (56-61), but also in patients with traumatic spinal cord injury (62-64), even if the related neuropathological signs may be normal (65).

The fact must also be considered that LUTD by itself may be the presenting symptom for neurological pathology (20,66).

2.4.1 GUIDELINE FOR TIMING OF DIAGNOSIS AND TREATMENT

1. Diagnosis and treatment in NLUTD should be performed as soon as possible.

2.5 References

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3. DIAGNOSIS

3.1 Introduction

Before any functional investigation is planned, an extensive general and specific diagnosis should be performed. Part of this diagnosis is specific for neurogenic pathology and its possible sequelae. The clinical assessment of patients with NLUTD includes and extends that for other LUTD. The latter should consist of a detailed history, bladder diary and a physical examination. In urinary incontinence, leakage should be demonstrated objectively.

These data are indispensable for reliable interpretation of the findings in diagnostic investigations performed subsequently in NLUTD.

3.2 History

3.2.1 General history

The general history should include relevant questions to neurological and congenital abnormalities, information on the previous occurrence and frequency of urinary infections and on relevant surgery. Information must be

obtained on medication with known or possible effects on the lower urinary tract (1-3). The general history should also include the assessment of menstrual, sexual and bowel function, and obstetric history (3).

Hereditary or familial risk factors should be recorded. Symptoms of any metabolic disorder or neurological disease that may induce neurogenic lower urinary tract dysfunction must be checked particularly. Specific signs such as pain, infection, hematuria, fever, etc., may justify further particular diagnosis.

A list of items of particular importance is:

- Congenital anomalies with possible neurological impact
- Metabolic disorders with possible neurological impact
- Preceding therapy, including surgical interventions
- Present medication
- Lifestyle factors such as smoking, alcohol, or addictive drug use
- Infections of the urinary tract
- Quality of life

3.2.2 Specific history

Urinary history: This consists of symptoms related to both the storage and the evacuation functions of the lower urinary tract. The onset and the nature of the NLUTD (acute or insidious) should be determined. Specific symptoms and signs must be assessed in NLUTD and if appropriate be compared with the patients' condition before the NLUTD developed. The separate diagnostic fields items should be diagnosed as detailed as possible (3).

- LUTS
- Previous voiding pattern
- Urinary incontinence
- Bladder sensation
- Mode and type of voiding (catheterization!)

The urinary diary gives (semi-)objective information about the number of voidings, daytime and nighttime voiding frequency, volumes voided, and incontinence and urge episodes.

Bowel history: Patients with NLUTD may suffer from a related neurogenic condition of the lower gastro-intestinal tract. The bowel history also must address symptoms related to the storage and the evacuation functions and specific symptoms and signs must be compared with the patients' condition before the neurogenic dysfunction developed. Again, the diagnostic items should be detailed (3).

- Ano-rectal symptoms
- Previous defecation pattern
- Faecal incontinence
- Rectal sensation
- Mode and type of defecation

Sexual history: The sexual function may also be impaired because of the neurogenic condition. The details of this history of course differ between men and women (3).

- Genital or sexual dysfunction symptoms
- Previous sexual function
- Sensation in genital area and for sexual functions
- Erection or arousal
- Orgasm
- Ejaculation

Neurological history: This should concentrate on the following information.

1. Acquired or congenital neurologic condition
2. Neurological symptoms (somatic and sensory), with onset, evolution, and performed therapy
3. Spasticity or autonomic dysreflexia (lesion level above Th6)

3.2.3 GUIDELINES FOR HISTORY TAKING

1. An extensive general history is mandatory, concentrating on past and present symptoms and conditions for urinary, bowel, sexual, and neurologic functions, and on general conditions that might impair any of these.
2. Special attention should be paid to the possible existence of alarm signs, such as pain, infection, hematuria, fever, etc., that warrant further specific diagnosis.
3. Specific history should be taken for each of the four mentioned functions.

3.3 Physical examination

3.3.1 General physical examination

Attention should be paid to the patient's physical and possible mental handicaps with respect to planned diagnostic investigations. Impaired mobility, particularly in the hips, or extreme spasticity may lead to problems in patient positioning in the urodynamics laboratory. Patients with very high neurological lesions may suffer from a significant drop in blood pressure when moved in a sitting or standing position. Subjective indications of bladder filling sensations may be impossible in retarded patients.

Prostate palpation or observation of pelvic organ descensus is made.

3.3.2 Neuro-urological examination

General neurological examination: This investigates the motor and sensory functions of the body, the limbs and the hand function. A suprapubic globe is searched for and an appreciation of the skin condition in the genital and perineal regions is made.

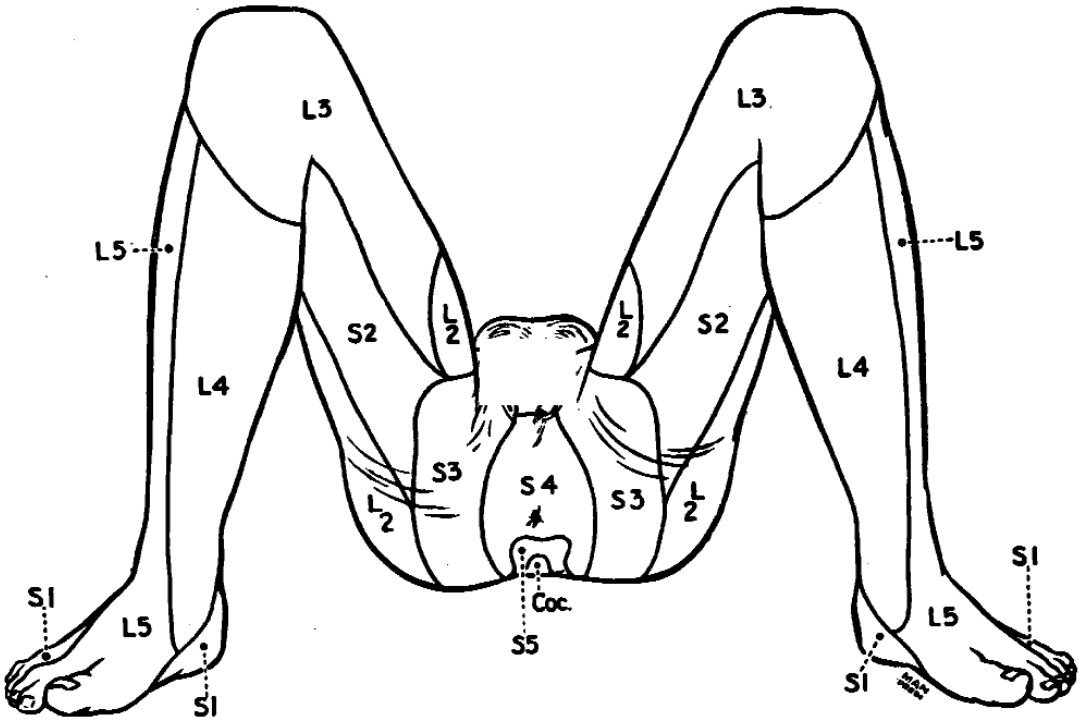

Figure 3.1. Dermatomes of spinal cord levels L2-S4.

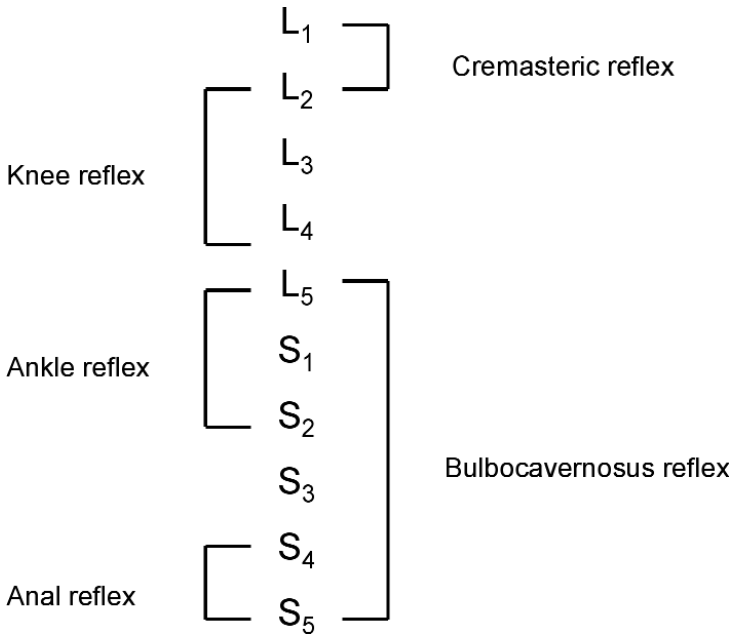

Figure 3.2. Urogenital and other reflexes in lower spinal cord

Specific neuro-urological examination: This investigation is necessary in patients with NLUTD. It includes several tests for sacral reflex activity and an evaluation of the sensation in the perineal area. Fig. 3.1 shows the different dermatomes and fig. 3.2 the associated reflexes in this area.
Specified information should become available on:

- Sensation S_2-S_5 on both sides of the body
- Reflexes
- Anal sphincter tone
- Volitional contraction of anal sphincter and pelvic floor

A high correlation exists between the clinical neurological findings and the NLUTD in some types of neuropathy, but less so in other types (4-9). The correspondence is low, for instance, in myelomeningocele patients (6) and in combined traumatic spinal cord lesions, but high in single-level traumatic spinal cord lesions (9).

3.3.3 Laboratory tests

Besides urinalysis and blood chemistry other tests are specifically indicated in patients with NLUTD. The results of these tests should be detailed (3).

- Imaging studies (sonography, X-ray, MRI)
- Free flowmetry with assessment of residual urine. Because of natural variations, multiple estimations (at least 2-3) are necessary (3,10,11).
- Quantification of urine loss by pad testing if appropriate

3.3.4 GUIDELINES FOR PHYSICAL EXAMINATION

1. Individual patient handicaps should be acknowledged in planning further investigations.
2. The neurological status should be described as completely as possible. Sensations and reflexes in the urogenital area must all be tested.
3. The anal sphincter and pelvic floor functions must be tested extensively.
4. Urinalysis, blood chemistry, imaging, free flowmetry and residual, and incontinence quantification should be performed.

3.4 Urodynamics

3.4.1 Introduction

Urodynamic investigation is the only method to objectify the (dys-)function of the LUT. This investigation is of pivotal interest to describe the status of the LUT in patients with NLUTD.

In these patients, particularly when detrusor overactivity might be present, the invasive urodynamic investigation is even more provocative than in other patients. Any technical source of artefacts must be critically considered. The quality of the urodynamic recording and its interpretation must be ensured (12).

In patients at risk for autonomic dysreflexia, blood pressure assessment during the urodynamic study is advisable.

In many patients with NLUTD, assessment of maximum anaesthetic bladder capacity may be useful.

The rectal ampulla should be empty of stool before the start of the investigation. Medication by drugs that influence the lower urinary tract function should be abandoned at least 48 hours before the investigation (if feasible) or otherwise be taken into account for the interpretation of the data.
All urodynamic findings must be reported in detail and performed according to the ICS technical recommendations and standards (3,12,13).

3.4.2 Urodynamic tests

Bladder diary: This semi-objective qualification of the LUT is a highly advisable diagnostic tool. For reliable interpretation it should be recorded over at least 2-3 days (3,14). Possible pathologic findings: High voiding frequency, very low or very high voided volumes, nocturnal voidings, urgency, incontinence.

Free uroflowmetry and assessment of residual urine: This gives a first impression of the voiding function. It is mandatory before any invasive urodynamics is planned. For reliable information it should be repeated at least 2-3 times (3,10,11). Possible pathological findings: Low flow rate, low voided volume, intermittent flow, hesitancy, residual urine.

Care must be taken in judging the results in patients who are not able to void in a normal position. Both the flow pattern and the flow rate may be modified by this inappropriate position and by any constructions to divert the flow.

Filling cystometry: The only method to quantify the filling function has limited significance as a solitary procedure. It is much more powerful if combined with bladder pressure measurement during micturition and even more in video urodynamics. This investigation is necessary to document the status of the LUT function

during the filling phase. 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 (3). Possible pathologic findings: Detrusor overactivity, low detrusor compliance, abnormal bladder and other sensations, incontinence, incompetent or relaxing urethra.

Detrusor leak point pressure: This specific investigation is important to estimate the risk for the upper urinary tract or for secondary bladder damage. When the DLPP is >40 cm H_2O the upper tract is endangered (3,15). The DLPP is a screening test only, because it gives no impression of the duration of the high pressure during the filling phase, which can be expected to have even more impact on the upper urinary tract (16). A high DLPP thus warrants further testing by video urodynamics to document the reflux also.

Pressure flow study: This measurement reflects the co-ordination between detrusor and urethra or pelvic floor during the voiding phase. It is even more powerful in combination with filling cystometry and with video urodynamics. It is necessary to document the function of the lower urinary tract function during the voiding phase. Possible pathological findings: Detrusor underactivity/acontractility, DSD, non-relaxing urethra, residual urine.

Most types of obstructions caused by NLUTD are due to DSD (17,18), non-relaxing urethra, or non-relaxing bladder neck (3,19,20). 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 neurogenic lower urinary tract dysfunction.

Electromyography: Registration of the activity of the external urethral sphincter, the peri-urethral striated musculature, the anal sphincter, or the striated pelvic floor muscles. The correct interpretation may be difficult due to artefacts introduced by other equipment used. In the urodynamic setting useful as a gross indication of the patient's ability to control the pelvic floor. Possible pathologic findings: Inadequate recruitment on specific stimuli (bladder filling, hyperreflexive contractions, onset of voiding, coughing, Valsalva, etc.).

More detailed analysis (motor unit potentials, single fibre EMG) only possible as part of a neurophysiologic investigation.

Urethral pressure measurement: This investigation has only a very limited place in NLUTD. There exists no basic consensus on parameters indicating pathological findings (21).

Video urodynamics: This combination of filling cystometry and pressure flow study with imaging is the gold standard for urodynamic investigation in NLUTD (3,22,23). Possible pathological findings: All as described under cystometry and pressure flow study, plus morphological pathology of the LUT and the upper urinary tract.

Ambulatory urodynamics: Functional investigation of the urinary tract utilizing predominantly natural filling of the urinary tract and reproducing normal subject activity (24).

This type of study should be considered when office urodynamics do not reproduce the patient's symptoms and complaints. Possible pathologic findings: as under filling cystometry and pressure flow study provided the flow is measured also. It should be kept in mind that during this study the actual bladder volume is unknown.

Provocative tests during urodynamics: The LUT function can be provoked by coughing, triggered voiding, or anal stretch.

Fast filling cystometry with cooled saline (the "ice water test") is considered a discriminative test between UMNL and LMNL (25-30). Patients with UMNL will develop a detrusor contraction if the detrusor muscle is intact, patients with lower lesions will not. It gives false positive results in young children (27) and seems not fully discriminative in other patients (28,29)

A positive bethanechol test (31) (detrusor contraction >25 cm H_2O) was presumed to proof detrusor denervation hypersensitivity and the muscular integrity of an acontractile detrusor, but it turned out to give equivocal results. Recently a variation of this method was reported with intravesical electromotive administration of the bethanechol (32). This test turned out to be both selective and predictive for successful oral bethanechol treatment.

3.4.3 Specific uro-neurophysiological tests

These tests are advised as part of the neurological work-up of the patient. They comprise:

- 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 may be asked for specific conditions that became obvious during patient work-up and urodynamic investigations.

Possible pathological findings are dependent on the type of the test.

3.4.4 GUIDELINES FOR URODYNAMICS AND URO-NEUROPHYSIOLOGY

1. Urodynamic investigation is necessary to document the (dys-)function of the LUT.
2. The recording of a bladder diary is highly advisable.
3. Free uroflowmetry and assessment of residual urine is mandatory before invasive urodynamics is planned.
4. Video urodynamics is the gold standard for invasive urodynamics in patients with NLUTD. Should this not be available, then a filling cystometry continuing into a pressure flow study should be performed.
5. A physiological filling rate and body-warm saline must be used.
6. DLPP is an important investigation in patients with endangered upper tracts.
7. Specific uro-neurophysiological tests are elective procedures.

3.5 Typical manifestations of NLUTD

Typical findings in NLUTD are listed below.

Filling phase

- Hyposensitivity or hypersensitivity
- Vegetative sensations
- Low compliance
- High capacity bladder
- Detrusor overactivity, spontaneous or provoked
- Sphincter acontractility

Voiding phase

- Detrusor acontractility
- DSD
- Non-relaxing urethra
- Non-relaxing bladder neck

These signs warrant further neurological evaluation, as LUTD may be the presenting symptom of NLUTD (33-37).

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4. TREATMENT

4.1 Introduction

The primary aims for treatment of NLUTD and their priorities are (1-5):

1. Protection of the upper urinary tract
2. Improvement of urinary continence
3. Improvement of the patient's quality of life
4. Restoration of (parts of) the normal LUT function

Further considerations are the patient's disability, the cost effectiveness, the technical intricacy, and the possible complications (5).

Preservation of the upper tract function is of paramount importance (1-9). Renal failure was the main factor for mortality in the spinal cord injured patient surviving the trauma (6-9). This has lead to the golden rule in treatment of NLUTD: ensure that the detrusor pressure remains within safe limits during both the filling phase and the voiding phase (1-5). This approach has indeed significantly reduced the mortality from urological causes in this patient group (10).

The therapy of urinary incontinence is important for the social rehabilitation of the patient and thus contributes substantially to the quality of life, but is also pivotal in the prevention of urinary tract infection (UTI) (7-9). When no complete continence can be achieved, methods to attain a socially acceptable control of incontinence can be applied.

Complex procedures that might enable a satisfactory restoration or replacement of the LUT function often may limit the patient so much that the quality of life is unacceptably impaired (1).

In patients with high detrusor pressure during the filling phase (detrusor overactivity, low detrusor compliance) or during the voiding phase (DSD, other causes of bladder outlet obstruction) the therapy is aimed primarily at "the conversion of an active, aggressive high-pressure bladder into a passive low-pressure reservoir" despite the resulting residual urine (1).

4.2 Non-invasive conservative treatment

4.2.1 Assisted bladder emptying

Incomplete bladder emptying is a serious risk factor for UTI, for developing high intravesical pressure during the filling phase, and for incontinence. Therefore, methods to improve the voiding process are practised in patients with NLUTD.

Third party bladder expression (Credé): Regretfully, this method is still applied, foremost in infants and young children with myelomeningocele, and sometimes in tetraplegics. The suprapubic downwards compression of the lower abdomen leads to an increase in the intravesical pressure, but also causes a compression of the urethra and thus a functional obstruction (11,12), that may reinforce an already existing high bladder outlet resistance (13) and lead to inefficient emptying (12). Because of the high pressures that may be created during this procedure it is potentially hazardous for the urinary tract (14,15) and thus it is contra-indicated and its use should be discouraged unless urodynamics shows intravesical pressure to stay within the safe range (1,14-16).

Voiding by abdominal straining (Valsalva): The considerations mentioned under Credé above also hold for the

Valsalva manoeuvre (1,12,14,16). As most patients are unable to scale the pressure they exert on the bladder during Valsalva, the risk of exceeding the safe range is present.

For both methods of emptying long-term complications are hardly avoidable (12,14) and the already weak pelvic floor function may be further impaired, thus exacerbating the existing incontinence (16).

Triggered reflex voiding: Stimulation of the sacral or lumbar dermatomes in patients with UMNL can elicit reflex contraction of the detrusor (1,16). Morbidity occurs more often during the first decades of treatment (17-21). This method may be used in patients in whom it is urodynamically safe (1, 16).

4.2.2 Lower urinary tract rehabilitation

Behavioural modification: Prompted voiding, timed voiding (bladder training), and modification of the life pattern in patients with NLUTD are methods for improving the incontinence situation (2,22-25).

Pelvic floor muscle exercises: This training also aims at improving the incontinence. It has proven effective in stress incontinence treatment and for patients with NLUTD; it is mainly used in multiple sclerosis (26).

Pelvic floor electrostimulation: To improve the effect of pelvic floor muscle exercises, or to teach the patient how to contract the pelvic floor, or to improve the patient's compliance with the exercises, this may be supported by electrostimulation (16,27-29).

Biofeedback: This method can be used for supporting the voiding pattern modification (30-33).

4.2.3 Drug treatment

A medical therapy for NLUTD is not available. Most drugs used only resolve part of the problems, or are adjunct to other measures (34-40).

Detrusor overactivity: This can be treated effectively by anticholinergic substances (23,24,34-54). Their potentiality extends from a small reduction of detrusor overactivity to complete relaxation, depending on therapeutic regimen and individual tolerance. Increased drug tolerance during the basically life-long necessary therapy and the occurrence of adverse effects are topics of concern in patients with NLUTD in particular. Generally, these patients need a higher dose then other patients with overactive detrusor (41-46) and this may lead to an early discontinuation of the therapy because of adverse events (24,41,44-46).

Oxybutynin (36-41,46-49), trospium chloride (39,41,45,50,51), and propiverine (39,43,45,52), are established medical treatments. These drugs have diverse tolerance profiles and thus another anticholinergic may be prescribed if the patient experiences adverse effects on one. Tolteridine has been studied only in children with NLUTD (42). Various other drugs have been tested (16,36,38,47,48,53).

Additional treatment with desmopressin might improve the efficacy of the treatment (54-58).

Detrusor underactivity: No success had been attained with drugs for improving detrusor contractility (16,59-63), but Riedl et al. (64) have successfully applied oral bethanechol treatment in NLUTD patients with detrusor acontractility who responded positive to the electromotive intravesical bethanechol testing.

Decreasing bladder outlet resistance: Alpha-blockers have been used partly successfully for decreasing the bladder outlet resistance (16,65-70).

Increasing bladder outlet resistance: Several drugs show efficacy in the treatment of selected cases of milder stress incontinence, but there are hardly any publications in patients with NLUTD (16,71,72).

4.2.4 Electrical neuromodulation

A strong contraction of the urethral sphincter and/or pelvic floor, but also anal dilatation, manipulation of the genital region, and physical activity reflexly inhibit the micturition (16,73). Whereas the first mechanism is affected by activation of efferent fibres, the latter ones are produced by activation of afferents (16). Electrical stimulation of the pudendal nerve afferents produces a strong inhibition of the micturition reflex and of the detrusor contraction (74). This stimulation then might support the restoration of the balance between excitatory and inhibitory inputs at the spinal or supraspinal level (16,75,76) and it might imply that patients with incomplete lesions will benefit (16,76,77), but patients with complete lesions will not (78).

Stimulation of the tibial nerve afferents has not been applied in patients with NLUTD.

4.2.5 External appliances

When incontinence cannot be resolved by any of the methods described above, the detrusor pressures are in the safe region, eventually after sphincterotomy or bladder neck incision, and furthergoing non-invasive therapy

is not feasible, social continence may be achieved by collecting the urine during the incontinence (1,16). Condom catheters with urine collection devices are a practical method for men. Otherwise incontinence pads may offer a reliable solution. In both cases the infection risk must be closely observed (16). Because of the risk of developing high intravesical pressure, the penile clamp is absolutely contra-indicated.

4.2.6 GUIDELINES FOR NON-INVASIVE CONSERVATIVE TREATMENT

1. The first aim of any therapy is the protection of the upper urinary tract.
2. The mainstay of the treatment for overactive detrusor is anticholinergic drug therapy.
3. Rehabilitation and neuromodulation may be effective in selected cases.
4. A condom catheter or pads may reduce the incontinence to a socially acceptable situation.
5. Any method of assisted bladder emptying should be used with the greatest caution.

4.3 Minimal invasive treatment

4.3.1 Catheterization

Intermittent self- or third party catheterization (79,80) is the gold standard for the management of NLUTD (1,16). It is effective in patients with detrusor underactivity or acontractility (1) and in patients with detrusor overactivity if the overactivity can be successfully suppressed for instance by anticholinergic treatment (1,16,34-40).

The catheters used are made from a diversity of materials and the discussions on re-usable or disposable catheters, use of lubricants, aseptic or clean technique are still going on (1,16,81). Sterile IC, as originally proposed by Guttmann and Frankel (79) significantly reduces the risk of UTI and/or bacteriuria (1,16,82,83), related to clean IC introduced by Lapides et al. (80), but the cost issue may be a limiting factor (16,83). Aseptic IC is believed to be in a mid position (1,84,85). Insufficient patient education and the inherent greater risk of UTI in patients with NLUTD are contributing factors (16,85-91).The average frequency of catheterizations per day is 4-6 times. Less frequent catheterization results in higher catheterization volumes and a higher risk of UTI (1,85-90). More frequent catheterization increases the risk of cross infections and other complications (1,85-90).

Other complications may include lower fertility in men and compromising the urethra (16,81), although the direct relation with the IC is discussed controversely. It appears however that the prevalence of these complications increases with the period that the IC has been practised and with the (temporary) use of indwelling catheterization (89).

The prevalence of complications can be limited by adequate patient education, use of non-traumatizing techniques, and adequate precautions to prevent cross-infections (16,91).

Indwelling transurethral catheterization and, although to a lesser extent, suprapubic cystostomy are significant and early risk factors for UTI and other complications (16,21,92-102). Silicone catheters are preferred because they are less susceptible for encrustation and because of the high incidence of latex allergy in the NLUTD population.

4.3.2 GUIDELINES FOR CATHETERIZATION

1. Intermittent catheterization is the standard treatment for patients who are unable to empty the bladder.
2. Patients should be well instructed on the technique and risks of IC.
3. Aseptic IC is the method of choice.
4. The catheter size is 12-14 Fr.
5. The frequency of IC is 4-6 times per day.
6. The bladder volume must remain below 400 ml and the post-IC residual low.
7. Indwelling transurethral and suprapubic catheterization should be used only exceptionally, under close control and the catheter should be changed frequently. Silicone catheters are preferred and should be changed every 2-4 weeks, (coated) latex catheters need to be changed every 1-2 weeks.

4.3.3 Intravesical drug treatment

For the reduction of the detrusor overactivity, anticholinergics can be applied also intravesically (103-112). This might reduce the adverse effects because it metabolizes differently (110) and a greater amount is sequestered in the bladder, even more so with electromotive administration (111,112).

The vanilloids capsaicin and resiniferatoxin desensitize the C-fibres and thereby reduce the detrusor overactivity for a period of a few months until the sensation of these fibres has restored (15,113-121). 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 an about 1000-fold potency compared to capsaicin, with less pain during the instillation, and was effective in patients refractory to capsaicin (121).

Botulinum toxin causes a long-lasting but reversible chemical denervation that lasts for about 9 months (122-126). The toxin injections are mapped over the detrusor in a dosage that depends on the preparation used. Generalized muscular weakness may be a seldom adverse effect (126).

4.3.4 Intravesical electrostimulation

Intravesical electrostimulation (127) enhances the sensation for bladder filling and urge to void and may restore the volitional control of the detrusor (16,128,129). Daily stimulation sessions of 90 minutes with 10 mA pulses of 2 ms duration at a frequency of 20 Hz (129,130) are used for at least one week (130). It appears that patients with peripheral lesions are the best candidates, that the detrusor muscle must be intact, and that at least some afferent connection between the detrusor and the brain must still be present (16,129,130). Also, the positioning of the stimulating electrodes and the bladder filling apparently are important parameters (131). With these precautions, the results in the literature are still not unequivocal: both positive (128,130,132-136) and negative (137,138) results are reported.

4.3.5 Bladder neck and urethral procedures

Reduction of the bladder outlet resistance is often necessary to protect the upper urinary tract. This can be achieved not only by surgical interventions (bladder neck or sphincter incision or urethral stent) but also by chemical denervation of the sphincter. Stress incontinence may result and can be managed by external devices (4.2.5).

Botulinum toxin sphincter injection: Detrusor sphincter dyssynergia can be treated effectively by injection with botulinum toxin in a dosage that depends on the preparation used. The dyssynergia is abolished for a few months, necessitating repeat injections. The efficacy of this treatment is high and few adverse effects have been recorded (139-145).

Balloon dilatation: Although favourable immediate results were reported (146), no further reports were found since 1994.

Sphincterotomy: By staged incision, the bladder outlet resistance can be reduced without completely losing the closure function of the urethra (1,14,147). The laser technique appears to be advantageous (1,148,149). Sphincterotomy also needs to be repeated at regular intervals in a substantial proportion of patients (150), but is efficient and without severe adverse effects (1,14,146-151). As secondary narrowing of the bladder neck may occur, combined bladder neck incision might be considered (1,152,153).

Bladder neck incision: This is indicated only for secondary changes at the bladder neck (fibrosis) (1,14,147,153). When the detrusor is hypertrophied and causes thickening of the bladder neck, this procedure makes no sense (1).

Stents: The implantation of urethral stents causes the continence to be dependent on the adequate closure of the bladder neck only (1,5). Although the results are comparable with sphincterotomy and the stenting procedure has a shorter surgery time and reduced hospital stay (154), the costs (1) and possible complications or re-interventions (154-160) are limiting factors in its use.

Increasing the 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 NLUTD (5,21,161-166).

Urethral inserts: Urethral plugs or valves for management of (female) stress incontinence have not been applied in patients with NLUTD. The experience with active pumping urethral prosthesis for treatment of the underactive or acontractile detrusor was disappointing (167).

4.3.6 GUIDELINES FOR MINIMAL INVASIVE TREATMENT

1. Guidelines for catheterization are listed separately under 4.3.2.
2. Botulinum toxin injections in the detrusor are the most promising intravesical drug application for reduction of detrusor overactivity.
3. Intravesical electrostimulation may be of value in specific patients.
4. (Laser) sphincterotomy is the standard treatment for DSD or other increased bladder outlet resistance at the sphincteric area. Botulinum sphincter injections will be the first choice in patients ineligible for interventional surgery. Bladder neck incision is effective in a fibrotic bladder neck. Urethral stents still have too many complications.
5. Urethral bulking agents have a disappointing long term effect.

4.4 Surgical treatment

4.4.1 Urethral and bladder neck procedures

Increasing the bladder outlet resistance has the inherent risk of causing high intravesical pressure during the

filling and even more during the voiding phase. These procedures to treat the sphincteric incontinence are suitable only when the detrusor activity is or can be controlled, when no significant reflux is present. Moreover they require a good condition of the urethra and bladder neck and will mostly lead to perform intermittent catheterization after the procedure (5,168).
Urethral sling: Various materials have been used for this procedure with enduring positive results (5,168-182). The procedure is established in women; for men the artificial sphincter is obviously the first choice (5).

Artificial urinary sphincter: This device stood the test of time in patients with NLUTD (5). It was introduced by Light and Scott (183) for this patient group and the need for revisions (184,185) have decreased significantly with the new generations of devices (175,186-192).

Functional sphincter augmentation: By transposing the gracilis muscle to the bladder neck (193) or to the proximal urethra (194,195) the possibility exists to create a functional autologous sphincter by electrical stimulation (193,195). This would open the possibility to restore the control over the urethral closure.

Bladder neck and urethra reconstruction: The classical Young-Dees-Leadbetter (196) procedure for reconstruction of the bladder neck in children with bladder exstrophy and the Kropp urethral lengthening (197) improved by Salle (198) are established methods to restore continence provided that intermittent catheterization is practised and/or bladder augmentation is performed (175,184,197-211).

4.4.2 Detrusor myectomy (auto-augmentation)

The idea of enlarging a shrunken bladder by removal of lateral detrusor tissue to free the entrapped ureter in a non-functional fibrotic detrusor was put forward by Couvelaire (212). Since its clinical introduction by Cartwright and Snow (213) in children and by Stöhrer (214,215) in adults, this procedure to reduce detrusor overactivity or to improve low detrusor compliance has gained popularity because of its acceptable long-term results, its low surgical burden, its low rate of long term adverse effects, its positive effect on the patient's quality of life, and because it does not preclude further interventions (1,5,45,213-244).

The procedure is performed extraperitoneally under general anaesthesia and consists of the dissection of about 20% of the detrusor tissue around the umbilicus, leaving the mucosa intact (1,213-215). A diverticulum will develop, but this may take 1-2 years in adults (1,213-215). The laparoscopic procedure (219,220,222,228,233), the covering of the mucosa at the detrusor defect (transperitoneal!) (217,229,232,234,238), supporting the bladder (213,216,238), or simple incision of the detrusor muscle (detrusor myotomy) (221,240-244) are proposed variations of the procedure but offer no essential advantages.

4.4.3 Denervation, deafferentation, neurostimulation, neuromodulation

Various procedures that were estimated to destroy the peripheral detrusor innervation have been abandoned because of poor long term results and severe complications (5). These procedures include bladder distension, cystolysis, transvaginal denervation (Ingelman-Sundberg procedure) and subtrigonal phenol injections.

Sacral rhizotomy, also known as sacral deafferentation (SDAF), has achieved some success in reducing detrusor overactivity (21,245-254), but it is used nowadays mostly as an adjuvant to sacral anterior root stimulation (255-269). Alternatives for the rhizotomy are sought in this treatment combination (270-273).

Sacral anterior root stimulation (SARS) is aimed at producing a detrusor contraction. The technique was developed by Brindley (274) and is applicable only in complete lesions above the implant location because of its stimulation amplitude over the pain threshold. The urethral sphincter efferents are also stimulated, but as the striated muscle relaxes faster than the smooth muscle of the detrusor, a so-called "post-stimulus voiding" will occur. This approach has been successful in highly selected patients (255-269). By changing the stimulation parameters this method can also induce defecation or erection.

The sacral nerve stimulation or sacral neuromodulation is based on the research by Schmidt and Tanagho (275). This technique stimulates the afferents and thereby probably restores the correct balance between excitatory and inhibitory impulses from and to the pelvic organs at a sacral and supra-sacral level, thus reducing the detrusor overactivity (75,276). It is used either as a temporary procedure using foramen electrodes with an external stimulator, with the expectation of perseverance of the changes after treatment, or as a chronic procedure with an implanted stimulator. In the latter case a test procedure, the percutaneous nerve evaluation (PNE), with an external stimulator is performed before the implant to judge the patient's response. This procedure also has considerable success in selected patients (230,277-283).

On the basis of the successful application of these systems, future developments towards a device that may be more integrated in the body are under research (284,285).

4.4.4 Bladder covering by striated muscle

When the bladder is covered by a (part of) striated muscle that can be stimulated electrically, or ideally could

be contracted volitionally, an acontractile bladder could be restored to perform a voiding function. The rectus abdominis (286) and the latissimus dorsi (287) have been used successfully in patients with NLUTD.

4.4.5 Bladder augmentation or substitution

Replacing or expanding the bladder by intestine or other passive expandable coverage will reduce the detrusor compliance and at least reduce the pressure effect of the detrusor overactivity. The inherent complications associated with these procedures include recurrent infection, stone building, perforation or diverticula, possible malignant changes, and for intestine metabolic abnormality, mucus production and impaired bowel function (5,288-290). As the NLUTD patient population's age when the surgery is performed is generally much lower than the patients with bladder malignancy who are elected for this surgery, the possible very long term complications must be appraised in particular. Thus the procedures should be used with caution in NLUTD patients, but may become necessary if all less invasive methods of treatment have failed.

Bladder augmentation, by procedures such as the clam cystoplasty, is a valid option to decrease detrusor pressure and increase bladder capacity whenever more conservative approaches have failed. A number of different techniques have been published. The results of the various procedures are very good and comparable (45,226,230-232,235-237,289-292). Bladder substitution to create a low pressure reservoir may be indicated in patients with severely thick and fibrotic bladder wall. Scaffolds, probably of tissue-engineered material for bladder augmentation or substitution or alternative techniques are promising future options (236,293-300).

4.4.6 Urinary diversion

When no other therapy has been successful urinary diversion must be considered for the protection of the upper tract and for the patient's quality of life (5,301).

Continent diversion: This should be the first choice for diversion. In patients for whom indwelling catheterization or suprapubic catheterization is the only feasible treatment option the change to a continent stoma may be a better prospect (5). Some patients with limited dexterity prefer a stoma above using the urethra for catheterization (5). The continent stoma is created following various techniques. All of them however do show frequent complications, including leakage or stenosis (5,302). The short term continence rates are over 80% and good protection of the upper urinary tract is achieved (5,18,301-317). For cosmetic reasons, the umbilicus is often used for the stoma site, but this may have a higher risk of stenosis (305,308,314).

Incontinent diversion: If catheterization is impossible, incontinent diversion with a urine collecting device is indicated. Fortunately, nowadays, this indication is seldom because many appropriate alternatives can be offered (5). Ultimately it could be considered in patients who are wheelchair bound or bed-ridden with intractable and untreatable incontinence, in devastated lower urinary tracts, when the upper urinary tract is severely compromised, and in patients who refuse other therapy (5). An ileal segment is used for the deviation in most cases (5,318-323). The rather poor long term results and the expected complications warrant a permanent follow-up (5).

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 the detrusor pressure and the incontinence (5). Also, in young patients the body image may play a role (311). The patient must be carefully counselled and must comply meticulously with the instructions (5). Successful undiversion than can be performed (324-326).

4.5 GUIDELINES FOR SURGICAL TREATMENT

1. Detrusor
   - 1.1. Overactive
     - 1.1.1. Detrusor myectomy is an acceptable option for the treatment of overactive bladder when more conservative approaches have failed. It is limited invasive and has minimal morbidity.
     - 1.1.2. Sacral rhizotomy with SARS in complete lesions and sacral neuromodulation in incomplete lesions are effective treatments in selected patients.
     - 1.1.3. Bladder augmentation is an acceptable option to decrease detrusor pressure whenever less invasive procedures have failed. For the treatment of a severely thick or fibrotic bladder wall a bladder substitution might be considered.
   - 1.2. Underactive
     - 1.2.1. SARS with rhizotomy and sacral neuromodulation are effective in selected patients.
     - 1.2.2. Restoration of a functional bladder by covering with striated muscle is still experimental.
2. Urethra
   - 2.1. Overactive (DSD) - refer to guidelines for minimal invasive treatment (4.3.6)
   - 2.2. Underactive
     - 2.2.1. The placement of a urethral sling is an established procedure.
     - 2.2.2. The artificial urinary sphincter is very effective.
     - 2.2.3. Transposition of the gracilis muscle is still experimental.

4.6 References

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5. TREATMENT OF VESICO-URETERAL REFLUX

5.1 Treatment options

The treatment options for vesico-ureteral reflux in patients with NLUTD do not differ essentially from those in other reflux patients. They become necessary when the abolishment of the high intravesical pressure during the filling phase or during the voiding phase have been treated successfully, but where the reflux did not resolve (1-4). Subtrigonal injections with bulking agents or ureteral re-implantation are the standard procedures.

Subtrigonal injections of bulking agents: This minimal invasive procedure has a relatively good effect with complete success in about 65% of patients (5-12). It can also be easily repeated if not effective and thereby the success rate can be increased to about 75% after the second or third session.

Ureteral re-implantation: This technique has an immediate and long-lasting result in over 90% of the patients (11-13).

In deciding which procedure will be offered to the patient, the relative risks of more invasive surgery and of less successful therapy should be considered.

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6. QUALITY OF LIFE

6.1 Considerations

The quality of life is a very important aspect in the treatment of patients with NLUTD. Apart from the limitations that relate directly to the neurologic pathology, the NLUTD can be treated adequately in the majority of patients and must not interfere with social independence. The life expectancy of the patients does not need to be impaired by the NLUTD. With adequate treatment and consequent neuro-urological care over a lifetime, the quality of life can be assured.

It is satisfying that this aspect is not neglected (1-12) in the recent medical literature.

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7. FOLLOW-UP

7.1 Considerations

NLUTD is an unstable condition and can vary considerably even within a relatively short period. Meticulous follow-up and regular checks are necessary (1-20). Depending on the type of the underlying neurological pathology and on the present stability of the NLUTD, the interval between the detailed investigations should not exceed 1-2 years. In patients with multiple sclerosis and in acute spinal cord injury this interval is of course much smaller. Urine dip sticks should be available for the patient and urinalysis should be performed at least every second month. The upper urinary tract, the bladder shape, and residual urine should be checked every 6 months. Physical examination and blood and urine laboratory should take place every year. Any sign indicating a risk factor warrants specialized investigation.

7.2 GUIDELINES FOR FOLLOW-UP

1. Possible UTI checked by the patient (dip stick).
2. Urinalysis every second month.
3. Upper urinary tract, bladder morphology, and residual urine every six months (ultrasound).
4. Physical examination, blood chemistry, and urine laboratory every year.
5. Detailed specialistic investigation every 1-2 years and on demand when risk factors emerge. The investigation is specified according to the patient's actual risk profile, but should in any case include a video urodynamic investigation and should be performed in a leading neuro-urological center.
6. All of the above more frequent if the neurological pathology or the NLUTD status demand this.

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8. CONCLUSION

NLUTD is a multi-facetted pathology. It needs an extensive and specific diagnosis before we can embark on an individualized therapy that takes into account the medical and physical condition of the patient, and the patient's expectations about his future social and physical situation with respect to the NLUTD.
The urologist or paediatric urologist can select from a wealth of therapeutical options, each with its specific pros and cons. Notwithstanding the success of any therapy embarked upon, a close surveillance is necessary for all of the patient's life.
With these guidelines we offer you expert advice on how to define the patient's NLUTD condition 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.

9. ABBREVIATIONS

This list is not comprehensive for the most common abbreviations

DLPP	Detrusor leak point pressure
DSD	Detrusor sphincter dyssynergia
EMG	Electromyography, electromyogram
FVC	Frequency volume chart
IC	Intermittent catheterization
ISC	Intermittent self-catheterization
ICS	International Continence Society
LPP	Leak point pressure
LMNL	Lower motor neuron lesion
LUT	Lower urinary tract
LUTD	Lower urinary tract dysfunction
LUTS	Lower urinary tract symptoms
MTC	Micturition time chart
NLUTD	Neurogenic lower urinary tract dysfunction
PNE	Percutaneous nerve evaluation test
SDAF	Sacral deafferentation
SARS	Sacral anterior root stimulation
UMNL	Upper motor neuron lesion
UTI	Urinary tract infection
VUR	Vesico-ureteral reflux