Neurogenic bladder

**Definition**
- **Neurogenic bladder (NB)** refers to the disturbance of lower urinary tract storage and voiding function. It originates in the nervous system (brain, spinal cord and peripheral nerves), but has no psychogenic factors. It has recently been renamed neurogenic lower urinary tract dysfunction (NLUTD) based on ICS (International Continence Society) terminology.

**Neurological control of micturition** (Fig 1)

- **Sympathetic nucleus** (hypogastric nerve):
  - Alpha stimulus: bladder neck contraction.
  - Beta stimulus: detrusor relaxation.
- **Parasympathetic nucleus** (pelvic nerve): detrusor contraction.
- **Pudendal nucleus** ( pudendal nerve): voluntary contraction of the external sphincter.

**Brain injuries**
- **Causes:** stroke, Alzheimer's, Parkinson's, multiple sclerosis, senility, tumors.
- **Urodynamics:** overactivity due to lack of brain control over medullary nuclei, with **detrusor sphincter dyssynergia** (the pontine nucleus continues to exercise its function over the medullary nuclei).
- **Symptoms:** urge incontinence with a loss of voluntary voiding control. There is a desire to urinate that cannot be inhibited. Tends not to affect the UUT.

**Spinal cord injuries**
- **Causes:** spinal injuries, multiple sclerosis (MS), spinal channel stenosis, spinal cord ischemia, spina bifida (myelomeningocele), spinal disc herniations, tumors, tethered cord, spondylolysis, arachnoiditis, tabes dorsalis, poliomyelitis, iatrogeny (e.g. after spinal anesthesia).
- **Urodynamics:**
  - **High spinal cord injuries** (cervical and thoracic spine): the control exerted by the pontine nucleus over the three medullary nuclei is lost, producing uncoordinated actions in the bladder and urethra. Leads to overactivity with **detrusor sphincter dyssynergia** (DSD).
  - **Low spinal cord injuries** ( lumbar and sacral spine): the voiding medullary nuclei are injured, interrupting the reflex arc. The detrusor is acontractile and the urethra underactive, unless the sympathetic nucleus is intact (active internal sphincter).
- **Symptoms:**
  - **High injuries:** incontinence without the patient's awareness. Residual urine is significant and high pressure is generated in the bladder, putting the UUT at risk.
  - **Low injuries:** incontinence due to lack of urethral resistance. Even in cases in which the sympathetic nucleus is conserved and the urethra is active, if the patient is able to empty the bladder well, the risk of UUT complications is less than in high injuries.
Peripheral nerve injuries

• **Causes:** diabetic, uremic, or alcoholic neuropathy, collagen diseases, porphyria, pharmacological or surgical iatrogeny (rectal, gynecological, or radical urological surgery), VZV or HIV infections, **Guillain-Barré syndrome** (reversible), sacral agenesis.

• **Urodynamics:** detrusor underactivity or acontractility in pelvic nerve injuries; underactivity of the external sphincter in pudendal injuries; underactivity of the internal sphincter in hypogastric nerve injuries + detrusor overactivity/low compliance.

• **Symptoms:** obstructive syndrome in pelvic nerve injuries, UI in pudendal and hypogastric nerve injuries.

**Diagnosis**

• **Medical history:**
  - **General:** urological, neurological, endocrinial, and systemic diseases; congenital abnormalities; urological, abdominopelvic, or spinal surgery; and drugs used.
  - **Specific:** voiding history (current LUT symptoms, previous voiding patterns, bladder sensation), digestion history (changes associated with bowel habits), sexual history (impaired erection, ejaculation, or orgasm; previous sexual function), neurological history (start/evolution of symptoms, treatment, presence of spasticity or dysreflexia).
  - **Assessment of physical and mental limitations of the patient:** important before performing diagnostic tests and deciding upon therapeutic possibilities.

• **Physical examination:**
  - **Urological:** suprapubic palpation, examination of genitals, DRE.
  - **Neurological:** sensory and motor nerves, reflexes.
  - **Neurourological:** perineal and genital sensitivity, anal sphincter tone, bulbocavernosus and cremasteric reflexes, voluntary contraction of the anal sphincter and pelvic floor.

• **Lab work:**
  - **Urinalysis and urine culture.**
  - **Blood:** glucose, kidney function, electrolytes.

• **Radiology:**
  - **KUB X-ray:** useful in diagnosing bladder stones, which are common in retentive neurogenic bladders.
  - **Ultrasound:** of the bladder (to detect presence of stones and measure PVR); of the kidney (to assess state of the UUT and presence of stones).
  - **IVP/CT scan:** to assess the morphology and function of the UUT.
  - **VCUG:** to assess the LUT and diagnose vesicoureteral reflux.

• **Urodynamic studies:** necessary for characterizing voiding or storing dysfunction and choosing the most suitable treatment. Urodynamic findings must be reported according to the recommendations and terminology of the **International Continence Society.** For a description of each test, see chapter on **Urodynamic Studies.**
  - Uroflowmetry and ultrasound measurement of postvoid residual urine.
  - Filling cystometry.
  - Pressure-flow study.
  - Detrusor leak point pressure.
  - Electromyography.
  - Urethral pressure profile.
  - Video-urodynamics: in combination with a filling cystometry and pressure-flow study, this constitutes the gold standard for studying the urodynamics of NLUTD.
  - Ambulatory urodynamics.

• **Neurophysiological studies:** EMG of the pelvic floor and external and anal sphincters, pudendal nerve conduction studies, latency studies of the RBC and anal reflex, evoked potentials of the glans penis or clitoris, sensory testing of the bladder and urethra.

• **Other explorations for the etiological diagnosis of NLUTD:** CT, MRI, spinal X-ray, CSF analysis, EEG, cerebral and spinal angiography.
Madersbacher classification system

- Urodynamic studies help distinguish between a normoactive, overactive, or underactive detrusor and urethra. These distinct combinations are used in the Madersbacher Classification System for NLUTD. (Fig 2)
- Recommended for clinical practice by the EAU Guidelines as a simple and useful tool for identifying situations of UUT risk (dysynergia) and for choosing a suitable treatment.

<table>
<thead>
<tr>
<th>Detrusor</th>
<th>Sphincter</th>
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<tbody>
<tr>
<td>Spinal injury</td>
<td>Overactive</td>
</tr>
<tr>
<td>Lumbo-sacral injury</td>
<td>Underactive</td>
</tr>
<tr>
<td>Supra-pontine injury</td>
<td>Normoactive</td>
</tr>
<tr>
<td>Lumbo-sacral injury</td>
<td>Sphincter only</td>
</tr>
<tr>
<td>Subsacral injury</td>
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<tr>
<td>Sphincter only</td>
<td>Sphincter only</td>
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Fig 2. Madersbacher Classification

Treatment overview

- **Support**: psychological help and family collaboration due to patient’s physical limitations.
- **Objectives of treatment**:
  - To protect the UUT by keeping intravesical pressure low during filling and voiding.
  - To improve continence.
  - To restore LUT function as much as possible.
  - To improve the patient’s quality of life.
- **Treatment modalities**: treatment should be individualized and can combine:
  - Conservative treatment.
  - Minimally invasive treatment.
  - Surgical treatment: only if other approaches fail.

Conservative treatments

- **Dietary measures**: control the amount and timing of fluid intake.
- **Measures to enhance urine storage**:
  - **LUT rehabilitation**: limited efficacy; only useful in incomplete injuries.
    - Training of pelvic floor (Kegel exercises).
    - Biofeedback.
    - Behavior modification: scheduled voiding, bladder training.
  - **Electrostimulation**: application of electrical energy to induce response.
  - **Drugs**: anticholinergics, Desmopressin (MINIRIN®). Adrenergic drugs for ↑ urethral resistance are not useful.

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Brand name®</th>
<th>Dose</th>
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<tbody>
<tr>
<td>Oxybutynin</td>
<td>DITROPA 5 mg tablets</td>
<td>5 mg/8h oo</td>
</tr>
<tr>
<td>Trospium chloride</td>
<td>SPASMEX 20 mg tablets</td>
<td>1 tab/12 h</td>
</tr>
<tr>
<td>Tolterodine</td>
<td>DETRUSITOL 4 mg prolonged release capsules</td>
<td>4 mg/24 h oo (2 mg/24 h RI or HI)</td>
</tr>
<tr>
<td>Solifenacin</td>
<td>VESICARE 5 and 10 mg tablets</td>
<td>5-10 mg/24 h oo</td>
</tr>
<tr>
<td>Fesoterodine</td>
<td>TOVIAZ 4 and 8 mg tablets</td>
<td>4 mg/24 h oo</td>
</tr>
<tr>
<td>Desmopressin</td>
<td>MINIRIN nasal drops</td>
<td>10-40 µg/night</td>
</tr>
<tr>
<td></td>
<td>MINIRIN 120 µg orodispersable tablets</td>
<td>Initial 120 µg sl/night (max 240 µg)</td>
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- **Sacro neuromodulation**: only useful in overactive bladder due to incomplete injuries.
• **Measures to facilitate bladder voiding:**
  - *Credé* (pressure on the suprapubic area) and *Valsalva* maneuvers:
    - Useful in patients with ancontractile bladder and hypoactive urethra.
    - There is a risk for the UUT if excessive intravesical pressure is generated (use only if urodynamics indicate a safe pressure).
  - **Stimulation of reflexogenic areas** (pubis, scrotum, clitoris, anus, thighs):
    - Stimulate voiding reflex in patients with neurogenic overactivity.
  - **Drugs:**
    - $\alpha_1$-blockers are useful for ↓ urethral resistance, ↓ PVR, and ↓ autonomic dysreflexia.
    - Drugs that ↑ bladder contractility (e.g. *Betanecol*) are generally not effective.

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<tr>
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<th>Dose</th>
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<tbody>
<tr>
<td>Terazosin</td>
<td>HYTRIN 2 and 5 mg capsules</td>
<td>Initial: 2 mg/night 3-4 d Maintenance: 5 mg/night</td>
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<tr>
<td>Doxazosin</td>
<td>CARDURA 4 and 8 mg prolonged-release tablets</td>
<td>4-8 mg/24 h oa</td>
</tr>
<tr>
<td>Alfuzosin</td>
<td>XATRAL 10 mg prolonged-release tablets</td>
<td>1 tablet/24h oa</td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>OMNIC OCAS 0.4 mg prolonged-release tablets</td>
<td>1 tablet/24 h oa</td>
</tr>
<tr>
<td>Silodosin</td>
<td>SILODYX 4 and 8 mg capsules</td>
<td>8 mg/24 h oa*</td>
</tr>
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</table>

- **Aseptic intermittent catheterization** (*self-catheterization* or *assisted catheterization*):
  - Between the sterile catheterization (fewer UTIs and bacteriuria, more costly) and the Lapides’ *clean catheterization*.
  - Performed with a sterile catheter, genital disinfection, and disinfectant lubricant.
  - Useful in hypo- or ancontractil bladders or in overactive bladders if anticholinergics work well.
  - 4-6 catheterizations/day must be performed; volume drained should be <400 mL; adjust number of daily catheterizations to PVR (1 for approx. every 100 mL).
  - *Silicon* is preferred over latex (less encrustation/fewer allergies); caliber=12-14 Ch.

**Minimally invasive treatments**

• **Intravesical drugs:**
  - *Anticholinergics*: may be used at higher concentrations and with fewer SE.
  - *Vanilloids* (*Capsaicin* and *Resiniferatoxin*): desensitize C fibers.
  - *Botulinum toxin A*:
    - Produces reversible denervation in 9 m; needs to be repeated.
    - Requires various injections throughout the bladder mucosa.
    - SE: UTI, AUR, and (rarely) muscle weakness.
• **Intravesical stimulation**: useful in patients with incomplete peripheral injuries. ↑ the sensation of fullness; can restore voluntary voiding control.
• **Procedures for ↓ the resistance of the bladder neck and sphincter**: sometimes necessary to protect the UUT. Results in stress UI requiring collector or absorbent materials.
  - **Intrasphincteric botulinum toxin**:
    - Useful in dysynergia.
    - Lasts several months.
  - **Sphincterotomy**:
    - Staggered incisions can avoid the complete loss of the sphincter closure mechanism (laser gives the best results).
    - In many cases, procedure must be repeated with time.
    - Simultaneous incision in the bladder neck (if fibrotic) should be considered.
  - **Other**: intraurethral prostheses.
• **Injection of space-occupying agents**:
  - For early recurrences of UI.
  - Agents used: *collagen, dextranomer/hyaluronic acid* (DEFLUX®), etc.
Surgical treatments

• Surgery to ↑ bladder capacity:
  - **Detrusor myomectomy (self-augmentation of the bladder):** 20% of the detrusor surface is dissected to create a bladder diverticulum. Variations: laparoscopic myomectomy, simple myotomy.
  - **Denervation and neurostimulation:** posterior sacral rhizotomy + stimulation of the anterior sacral roots (SARS) in complete injuries (Brindley technique).
  - **Sacral root neuromodulation:** in incomplete injuries (See chapter on Neuromodulation).
  - **Augmentation or replacement cystoplasty:** to ↓ intravesical pressure. If possible, augmentation is preferable; substitution should be performed only in bladders with very thick and fibrotic walls. Problems: UTI, stones, metabolic disturbances, mucus production, malignization.
  - **Urinary diversion:** continent reservoir for patients who can catheterize the stoma; incontinent diversion (ileal conduit or vesicostomy) if self-catheterization is impossible.
  - **Diversion reversal:** may be indicated in long-standing diversions, if newer techniques can be applied to control detrusor pressure.

• Surgery to ↑ sphincter competence: reconstruction of the bladder neck (Young-Dees), cervical-urethral slings or suspension techniques, artificial sphincter (AMS-800® or Flow-secure®), functional autologous sphincter with transposition of gracilis muscle to the bladder neck, which is then electrically stimulated (experimental). These techniques are indicated only if bladder pressure is not high and there is no VUR. Often require self-catheterization.

• **Surgery to facilitate bladder emptying:** reduction surgery, striated muscle coating surgery (can be stimulated electrically; experimental).

• **Non-continent diversion procedures:** e.g. vesicostomy.

• **VUR treatment:** indicated if reflux persists after bringing high intravesical pressure under control. Standard techniques are used: subtrigonal injections or reimplantation.

Palliative treatments

• **Devices for incontinence:** collectors in men, absorbent pads in women/men. Penile clamps are contraindicated.

• **Permanent catheter:** only as a last resort. Preferably silicon, with replacement every 2-4 wk (latex 1-2 wk).

• **Suprapubic cystostomy:** in some cases preferable to permanent catheterization.

Follow-up

• **Frequency of specialized checkups:** carried out every 1-2 years, depending on the underlying neurological pathology and the stability of the NLUTD. In cases of MS, the beginning of acute spinal cord injury, or if there are warning signs, checkups should be more frequent.

• **Recommended complementary measures:**
  - Educate patient to identify signs of infection and self-check urine culture.
  - Annual kidney and bladder ultrasound with PVR measurements.
  - Annual physical exam and blood test.
  - Urodynamic study when complications or warning signs of risk to the UUT appear or when surgery is planned. Routinely, every 2-3 years.