Neurogenic Bladder (NB)

5th year medical students' curriculum
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Neurogenic bladder is a term used to describe lower urinary tract (LUT) dysfunction resulting from a neurologic disease or process.

Up to 80% of neurological diseases develop Lower Urinary Tract Symptoms (LUTS)

Accurate diagnosis and proper management of LUT dysfunction in the neurogenic population consist of two main goals: (1) to preserve the safety of the bladder with low-pressure storage and adequate emptying and (2) to maintain a reasonable quality of life in relationship to the bladder.

NEURAL CONTROL OF THE LOWER URINARY TRACT (LUT)

Lower urinary tract (LUT) function represents a complex interplay of autonomic and somatic circuitry with the goal of maintaining a low-pressure bladder during filling and periodic voluntary bladder emptying. Normal neural circuitry allows an individual to voluntarily switch between storage and voiding phases, based on a perceived sense of bladder fullness and an assessment of the social appropriateness of the situation

The autonomic nervous system consists of parasympathetic and sympathetic innervation.

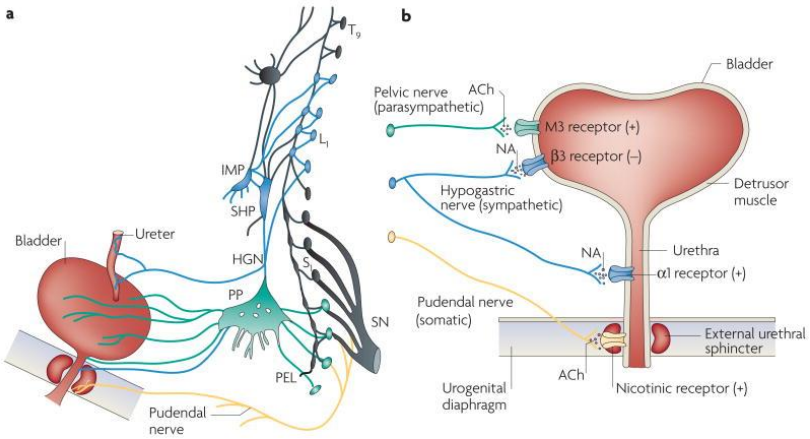
Sympathetic nerves originate from the thoracolumbar spinal cord segments T10/11 through L2 or L3. These nerves span the lumbar sympathetic ganglion and join the presacral nerve at the superior hypogastric plexus. Sympathetic postganglionic nerves release noradrenaline, which activates (1) β-adrenergic receptors, which inhibit the detrusor muscle, causing bladder relaxation; (2) α-adrenergic receptors in the bladder and bladder neck, causing outlet contraction.

Parasympathetic innervation originates from spinal cord segments S2–S4 as preganglionic nerve fibers that converge into the pelvic nerve

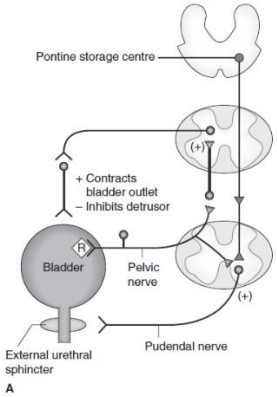
Parasympathetic postganglionic nerves release cholinergic (acetylcholine) and nonadrenergic noncholinergic transmitters. Detrusor contraction can be initiated by release of acetylcholine binding to M2 and M3 muscarinic receptors

The somatic nerve supply to the LUT arises from motor neurons in the anterior horn of S2, S3, and S4 in an area known as **Onuf's nucleus** and reaches the external urethral sphincter

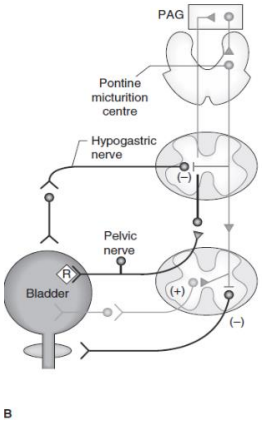
via the pudendal nerve. Somatic cholinergic motor nerves supply the striated external urethral sphincter and are under voluntary control.



During normal bladder filling, sympathetic (hypogastric nerve) and somatic (pudendal nerve) neural mechanisms mediate the contraction of the internal smooth and external striated urethral sphincters, respectively. As the bladder fills, sympathetic-mediated inhibition of the detrusor allows for the bladder to accommodate increasing volumes at low intravesical pressures.



When an individual decides that it is time to urinate, the pontine micturition center (PMC) is released from tonic inhibitory control of the higher cortical and subcortical centers of the brain, initiating the voiding process. The parasympathetic system then switches “on,” stimulating a detrusor contraction and relaxation of the pelvic floor and external and internal urethral sphincters



NERVOUS SYSTEM DAMAGE AND LUT DYSFUNCTION

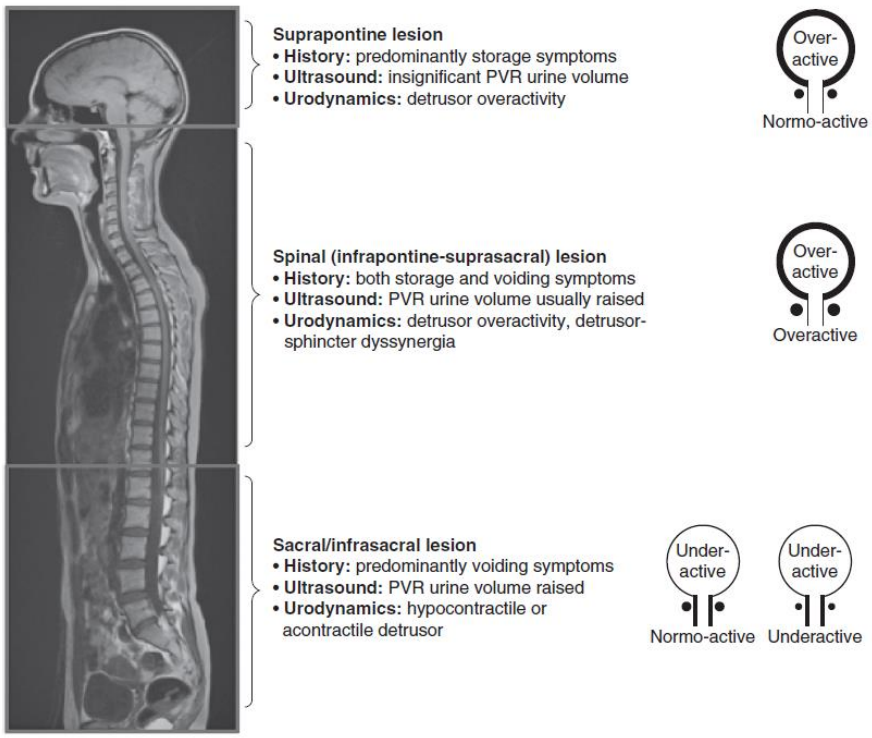
The level and extent of damage to the nervous system often correlates with patterns of LUT dysfunction.

Damage to the suprasacral and suprapontine nervous systems each results in signs of detrusor overactivity (which can be demonstrated on urodynamics) and symptoms of varying degrees of overactive bladder (urinary urgency, frequency, urgency urinary incontinence, and nocturia).

While the signs and symptoms may be similar between both types of neurologic lesions, the underlying pathophysiology behind these symptoms differs. In cases of damage to the suprapontine regions, there is a lack of inhibitory control on the PMC, causing spontaneous and involuntary detrusor contractions. In cases of suprasacral spinal cord lesions, on the contrary, the same symptoms are caused by the emergence of a segmental reflex at the level of the spinal cord that arises after a period of spinal shock.

Suprasacral spinal cord lesions are also noted to have a loss of coordination between the bladder and the sphincter during voiding, resulting in detrusor sphincter dyssynergia (DSD). In DSD, instead of relaxing, the urethral sphincter contracts during voiding, resulting in incomplete bladder emptying and potentially dangerously high bladder pressures during voiding.

Unlike lesions of the suprapontine and suprasacral nervous system, lesions of the sacral nervous system result in the opposite findings of detrusor hypo- or acontractility. These findings can cause poor or incomplete bladder emptying.



History and Physical Examination

A detailed history should factor in urinary tract symptoms, neurologic symptoms and diagnosis (if known), the clinical course of the neurologic disease, bowel symptoms, sexual function, comorbidities, and use of prescription and other medication and therapies. In order to assess the impact of the underlying neurological disease and to help determine what bladder management strategies might be appropriate, assessment of patient mobility, hand function, cognitive function and social support are also important. Other factors to consider are risk and history of urinary tract infections, decubitus ulcers, and other urologic factors that may contribute to LUT dysfunction such as prostate enlargement in men and urethral hypermobility in women.

A general physical examination should include blood pressure measurement, an abdominal examination, an external genitalia examination in males and a vaginal examination if clinically indicated to look for pelvic floor prolapse in women along with a rectal exam to look for fecal loading or alteration in anal tone. A focused neurological examination is also recommended. This may include assessment of cognitive function, ambulation and mobility, hand function, and lumbar and spinal segment function, including testing sensation and reflexes in the urogenital area.

Investigations

A. Urine Testing
B. Measurement of Renal Function
C. Upper Tract Evaluation
D. Urodynamic Investigations

MANAGEMENT OF NEUROGENIC BLADDER

Management of Storage Dysfunction

A. Behavioral and Conservative Treatments

Lifestyle interventions

1. Moderation of fluid intake to 1–1.5 litres per day
2. Avoid alcohol, caffeine
3. Drug regimens avoiding diuretics,
4. control of chronic cough and constipation,
5. cessation of smoking,
6. exclusion or treatment of urinary tract infection,
7. weight reduction is desirable.

Behavioral therapy

8. Timed voiding
9. Pelvic floor muscle training and exercise (including pelvic floor relaxation),
10. Delayed voiding,
11. Double voiding,
12. Biofeedback

B. Pharmacotherapy

- **Anticholinergic drugs**

Anticholinergic medications are the mainstay of pharmacotherapy for individuals with neurogenic detrusor overactivity (level of evidence 1a) and are considered to be first-line therapy, at times in combination with clean intermittent catheterization (CIC).

Anticholinergic medications aim to increase bladder capacity and reduce episodes of urinary incontinence secondary to neurogenic detrusor overactivity.

These medications act by competitively antagonizing the muscarinic acetylcholine receptors in the detrusor, causing detrusor relaxation, lower intravesical pressures, and decreased storage symptoms.

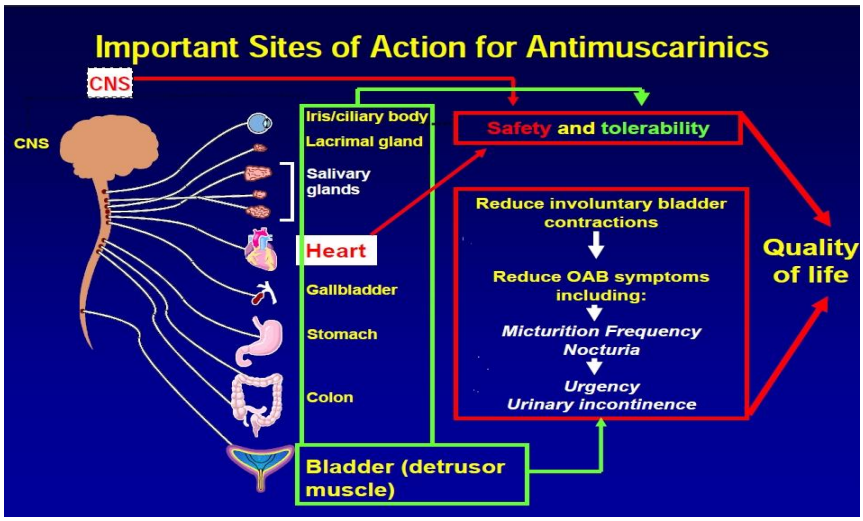
There are two types of muscarinic receptors in the bladder: M2 and M3. M2 receptors are most abundant, but M3 receptors are functionally more relevant to bladder relaxation.

Anticholinergic medications act on these receptors and include oxybutynin (immediate release [IR], extended release [ER], patch, topical gel), tolterodine (IR, ER), trospium chloride (IR, ER), solifenacin, darifenacin, and fesoterodine

Adverse effects of anticholinergic medications most commonly include dry mouth, blurred vision, constipation, tachycardia, and confusion, some or all of which may already be present in the neurogenic patient.

Difficulty emptying the bladder is another potential adverse event of these medications, which should be considered in any individual who has an elevated PVR and in individuals with multiple sclerosis, stroke, or Parkinson's disease

It is also recommended to monitor PVRs after starting treatment with an anticholinergic medication and to take into account that these medications can cross the blood-brain barrier, can reduce bladder emptying increasing the risk for urinary tract infection, and can precipitate or exacerbate constipation



- **Beta-AR agonists**

Over 97% of β-adrenergic receptors in the bladder are of the β3 type, representing the main method of bladder relaxation in humans .

These receptors serve to relax the detrusor muscle, making them an ideal therapeutic target. The selective β3-adrenoceptor agonist mirabegron was approved in by the Food and Drug Association (FDA) in 2012 for clinical use as an additional medication used to treat overactive bladder symptoms.

This medication has limited evidence in the neurogenic bladder population, but like many medications, it has been adopted for use in these patients.

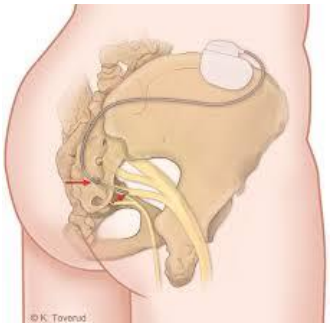
The main side effects of this medication are cardiovascular with a mean rise in blood pressure of up to 2.4 mm Hg and small increases in heart rate

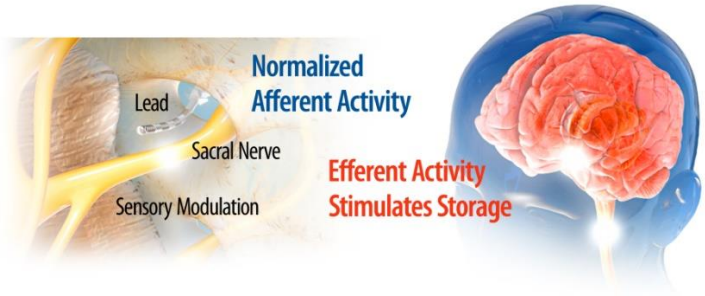
C. **Neuromodulation**

Neuromodulation is a well-established third-line treatment for nonneurogenic overactive bladder, but its use in neurogenic bladder is relatively less established. Neuromodulation

is currently performed in two varieties: sacral neuromodulation (SNM) and percutaneous tibial nerve stimulation (PTNS),

The mechanism behind neuromodulation is not clearly understood. The current leading hypothesis is that neuromodulation works by stimulating peripheral somatic afferent nerves, or C-fibers. SNM stimulates the pudendal afferent nerves, and PTNS stimulates the sensory component of the tibial nerve. It is assumed that this stimulation blocks competing abnormal visceral afferent signals from the bladder and prevents reflex bladder hyperactivity





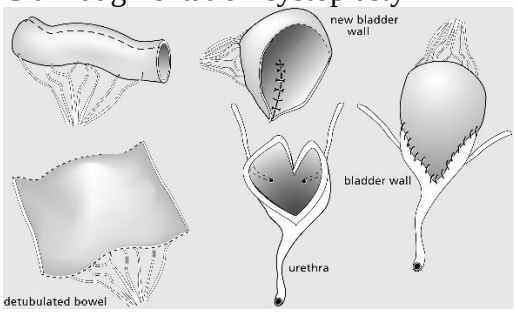
D. Onabotulinumtoxin A

Onabotulinumtoxin A works by blocking the release of acetylcholine from nerve endings (exocytosis), resulting in the blockage of neural transmission and alteration of afferent sensory input.

It is important to consider that these injections may increase the PVR among individuals who void, introducing the need for CIC or other more invasive bladder management strategies.

E. Surgical

- Clam augmentation cystoplasty



- Detrusor myectomy
- Denervation procedures
- Urinary diversion

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