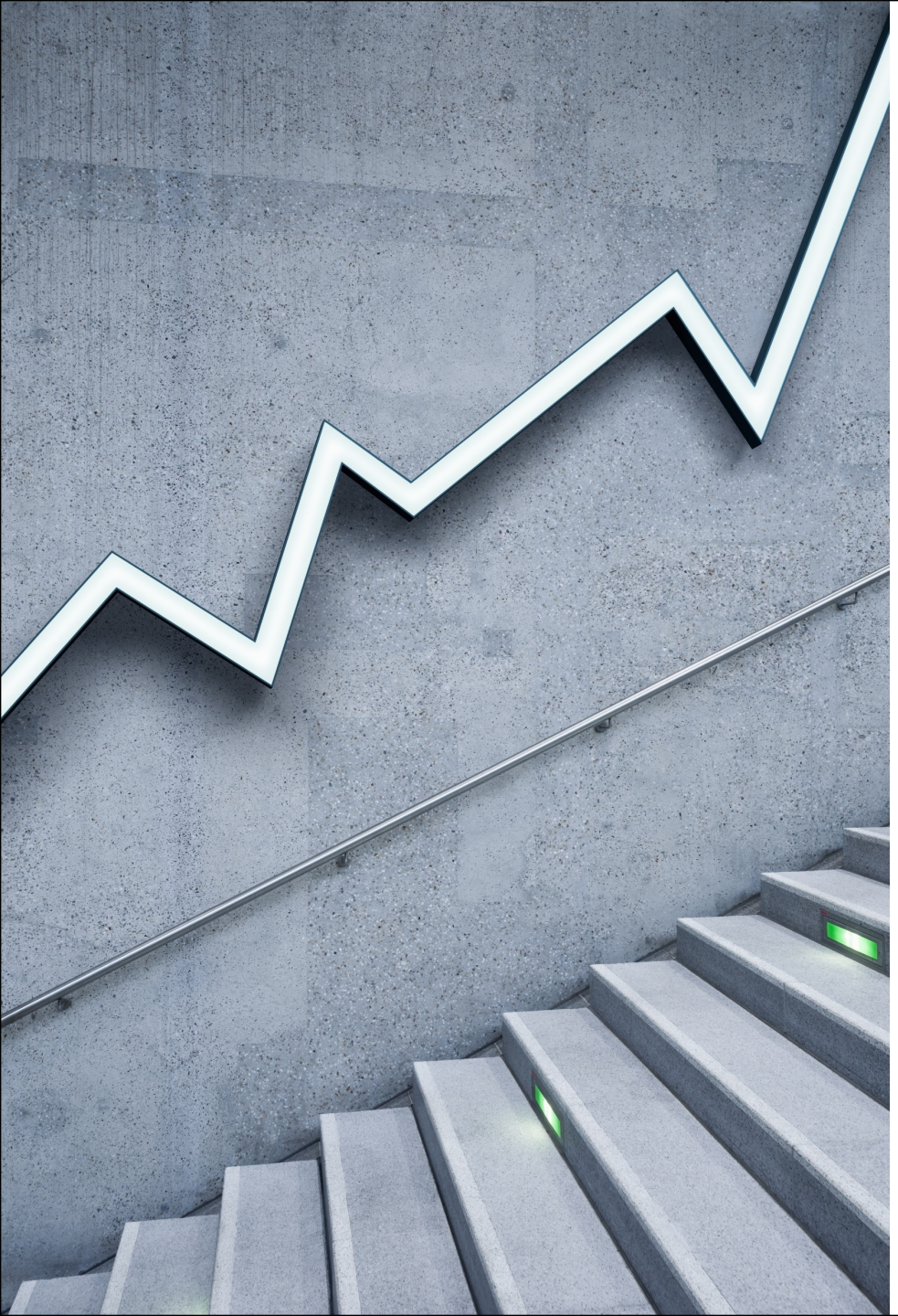


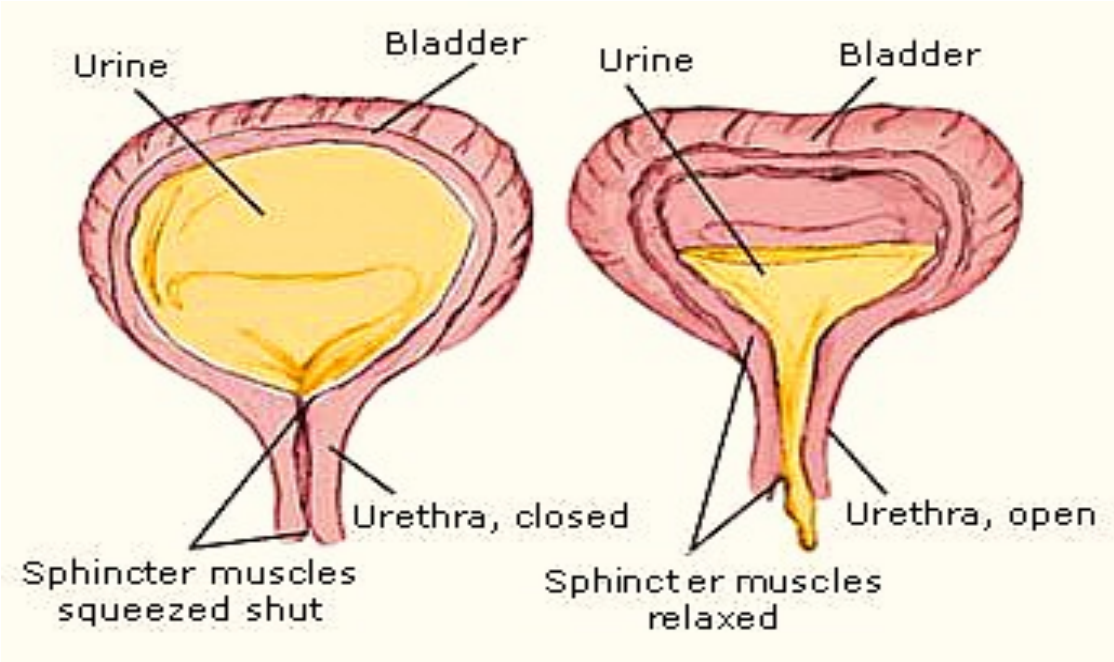
Neurogenic Bladder (NB)

Dr. Fadi Sawaqed
Assistant Professor of Urology
Functional & Neuro-Urology

Introduction

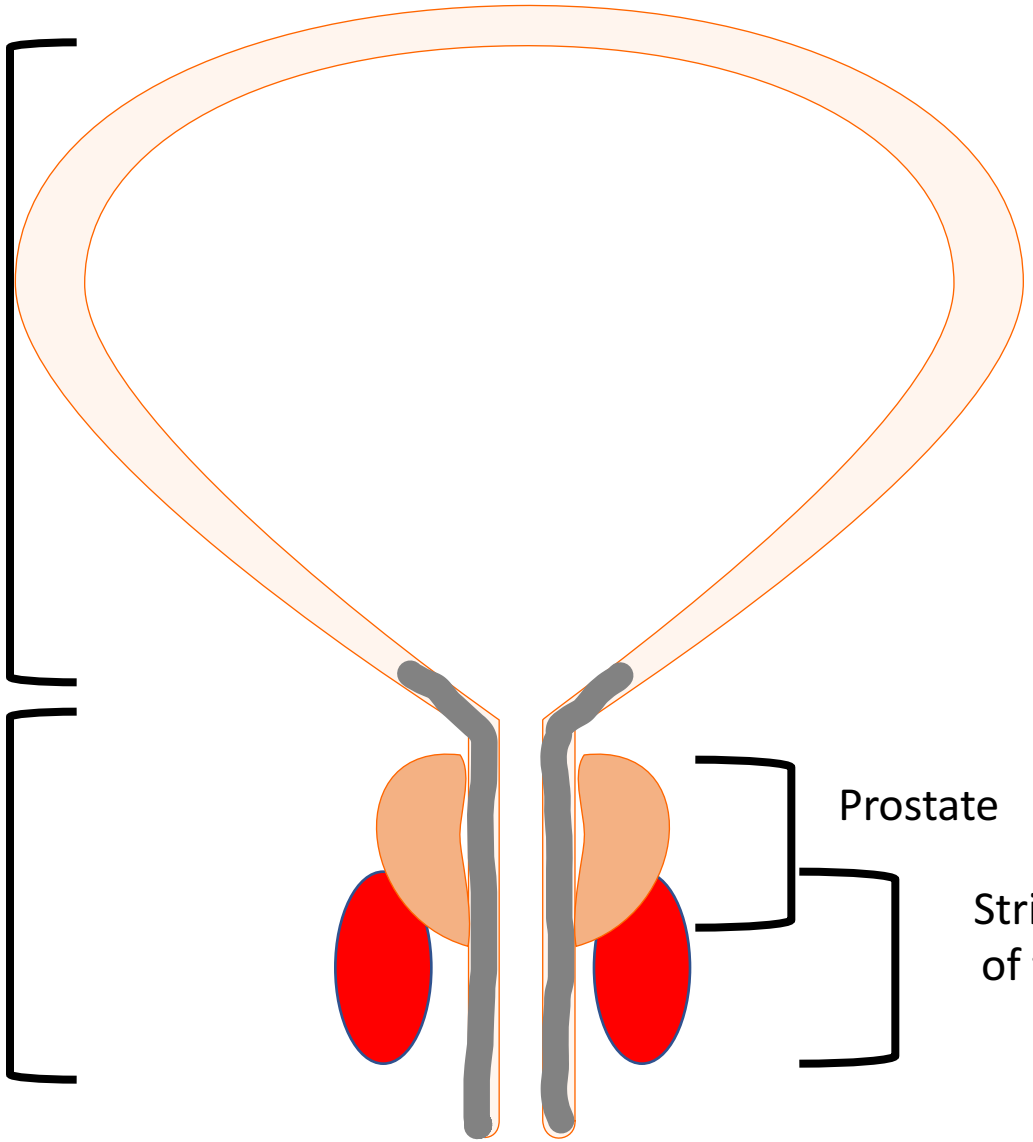
- **Neurogenic bladder** is a term used to describe lower urinary tract (LUT) dysfunction resulting from a neurologic disease or process.
- Up to 80% of neurological diseases develop Lower Urinary Tract Symptoms (LUTS)
- Accurate diagnosis and proper management of LUT dysfunction in the neurogenic population consist of two main goals:
- (1) to preserve the safety of the bladder with low-pressure storage and adequate emptying, consequently, preserve the upper Urinary Tract
- (2) to maintain a reasonable quality of life in relationship to the bladder.

Introduction:
The LUT functions:



Storage of urine ***Emptying***

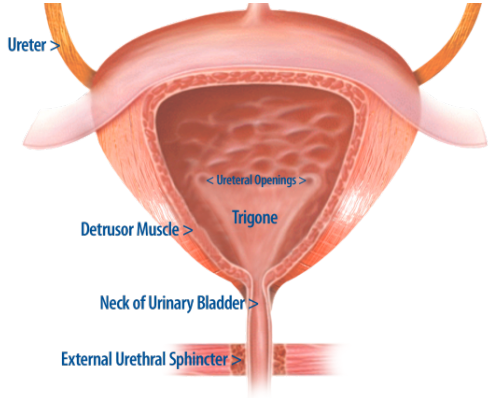
Bladder


Smooth muscle of the detrusor
Smooth muscle of the bladder neck & urethra
Prostate
Striated muscle of the external sphincter

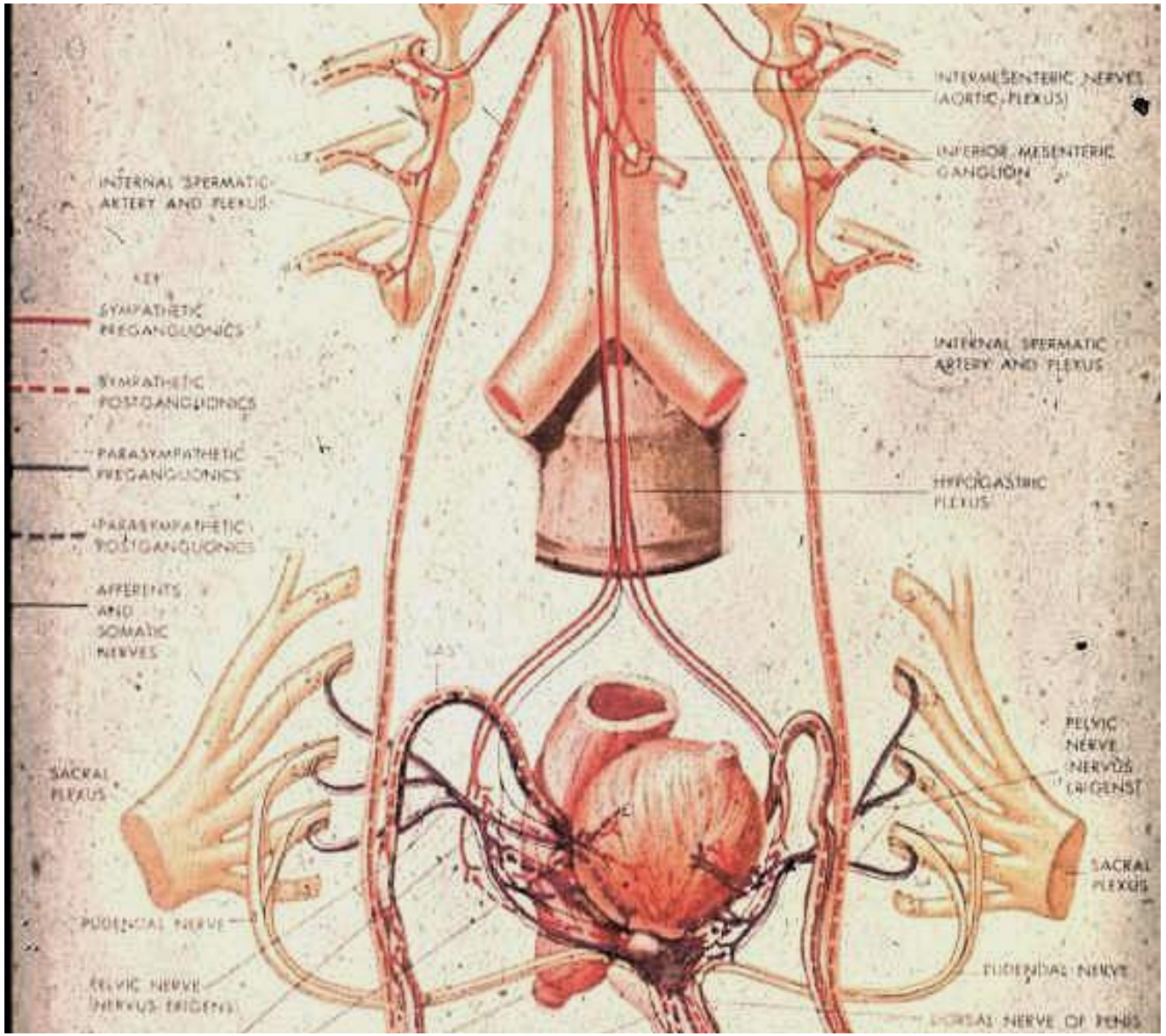
The Lower Urinary Tract (LUT)

- Urine storage and micturition depend on the coordination of the bladder, bladder neck, urethra, and urethral sphincter[1]
- Coordination between the muscles of the LUT is mediated by neural pathways in the brain, spinal cord, and peripheral nerves[1]

" ability to void or inhibit voiding…**sets humans apart** from all **other mammals"**



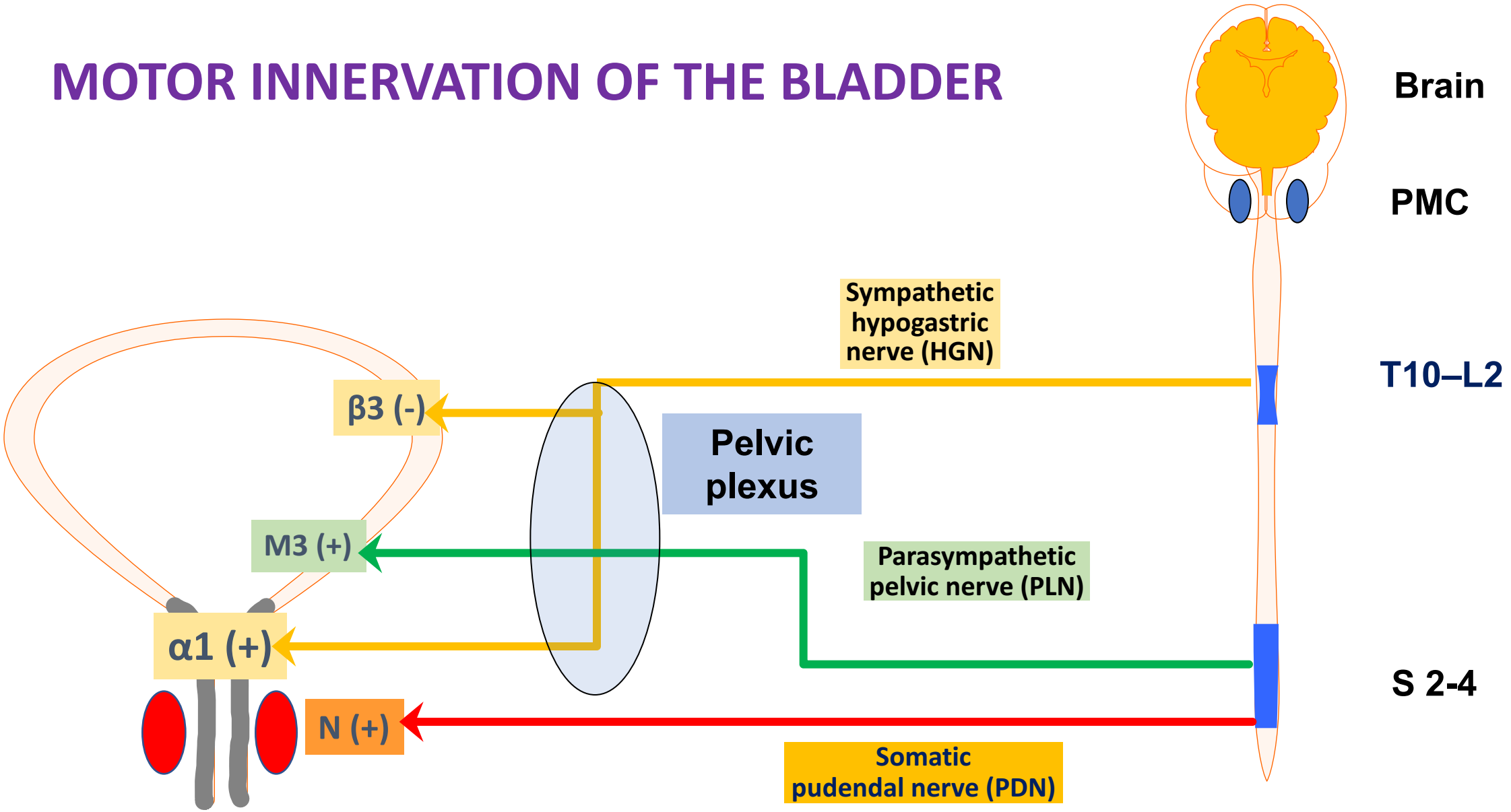
Reference: 1. Fowler CJ, Griffiths D, de Groat WC. *Nat Rev Neurosci*. 2008;9(6):453-466.



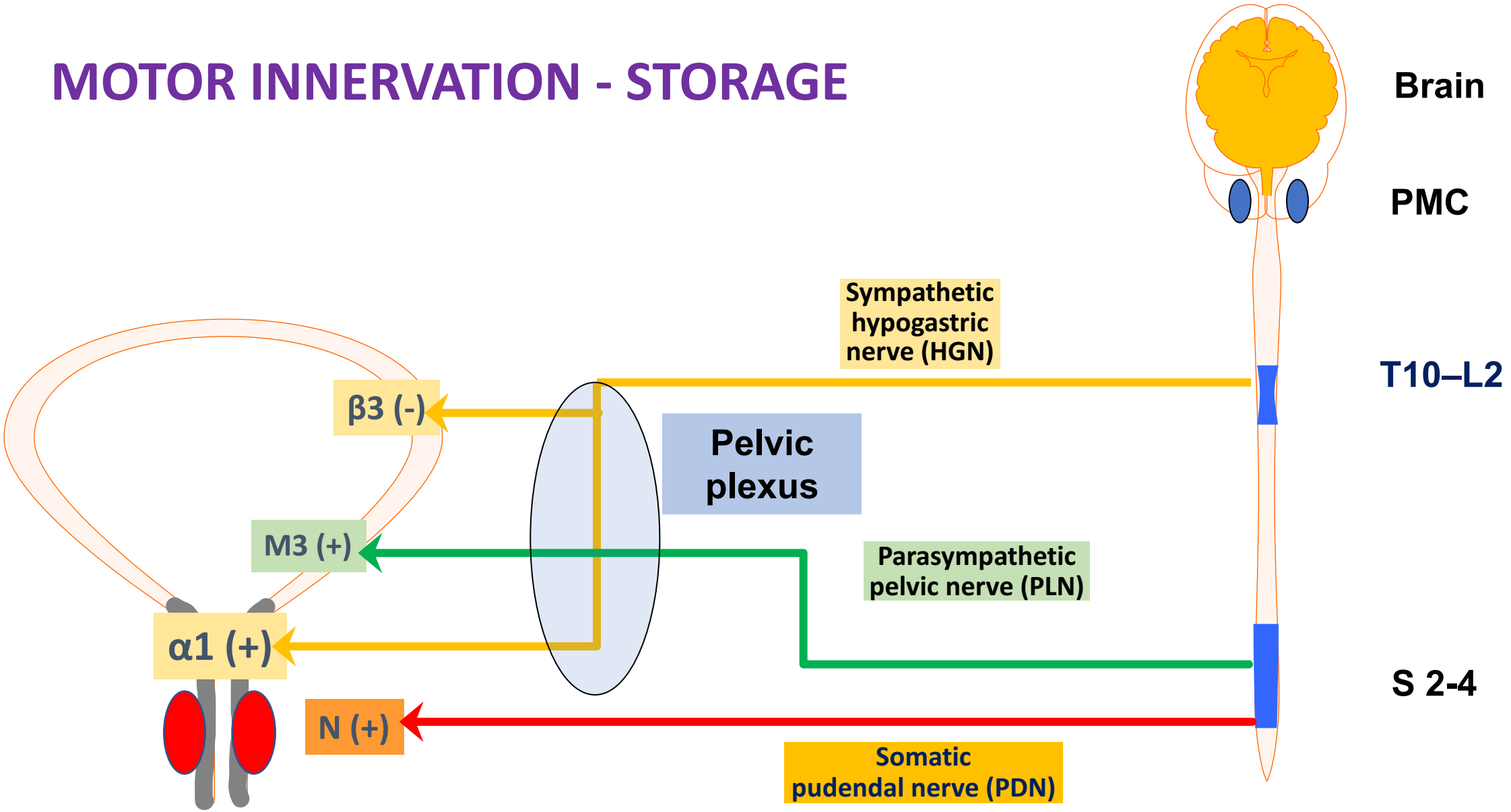
Bladder Peripheral Innervation

- Bilateral
- One site is usually dominant
- The sacral roots **S2 to S4**
- **T10-L2**
- Run from ***both sides*** of the sacrum to the bladder forming the sacral plexus
- Under CNS control

MOTOR INNERVATION OF THE BLADDER



MOTOR INNERVATION - STORAGE



Urine Storage Reflex

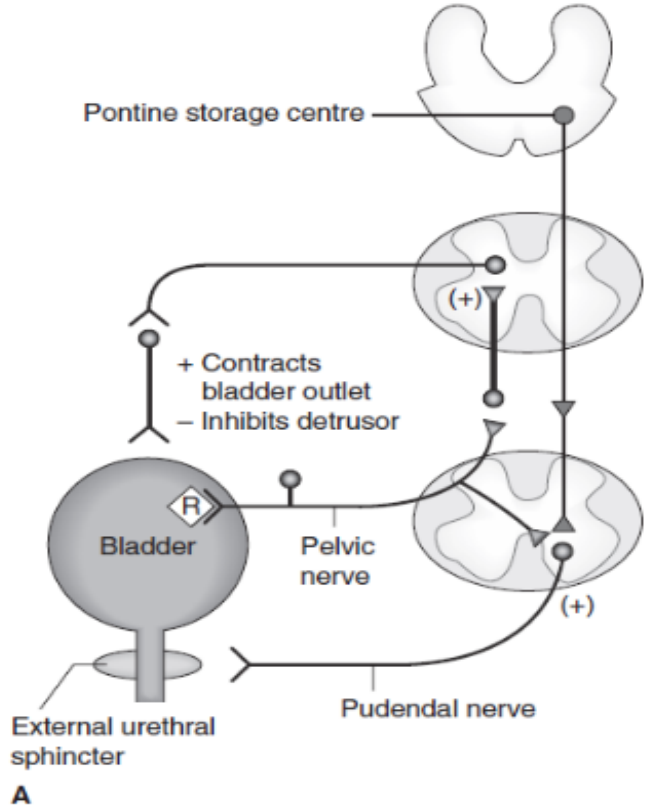
- Low-level afferent signals are organized in the spinal cord and promote urine storage via efferent signals from the CNS[1,2]

References: 1. Fowler CJ, Griffiths D, de Groat WC. *Nat Rev Neurosci*. 2008;9(6):453-466.
2. de Groat WC. *Br J Pharmacol.* 2006;147:S25-S40.

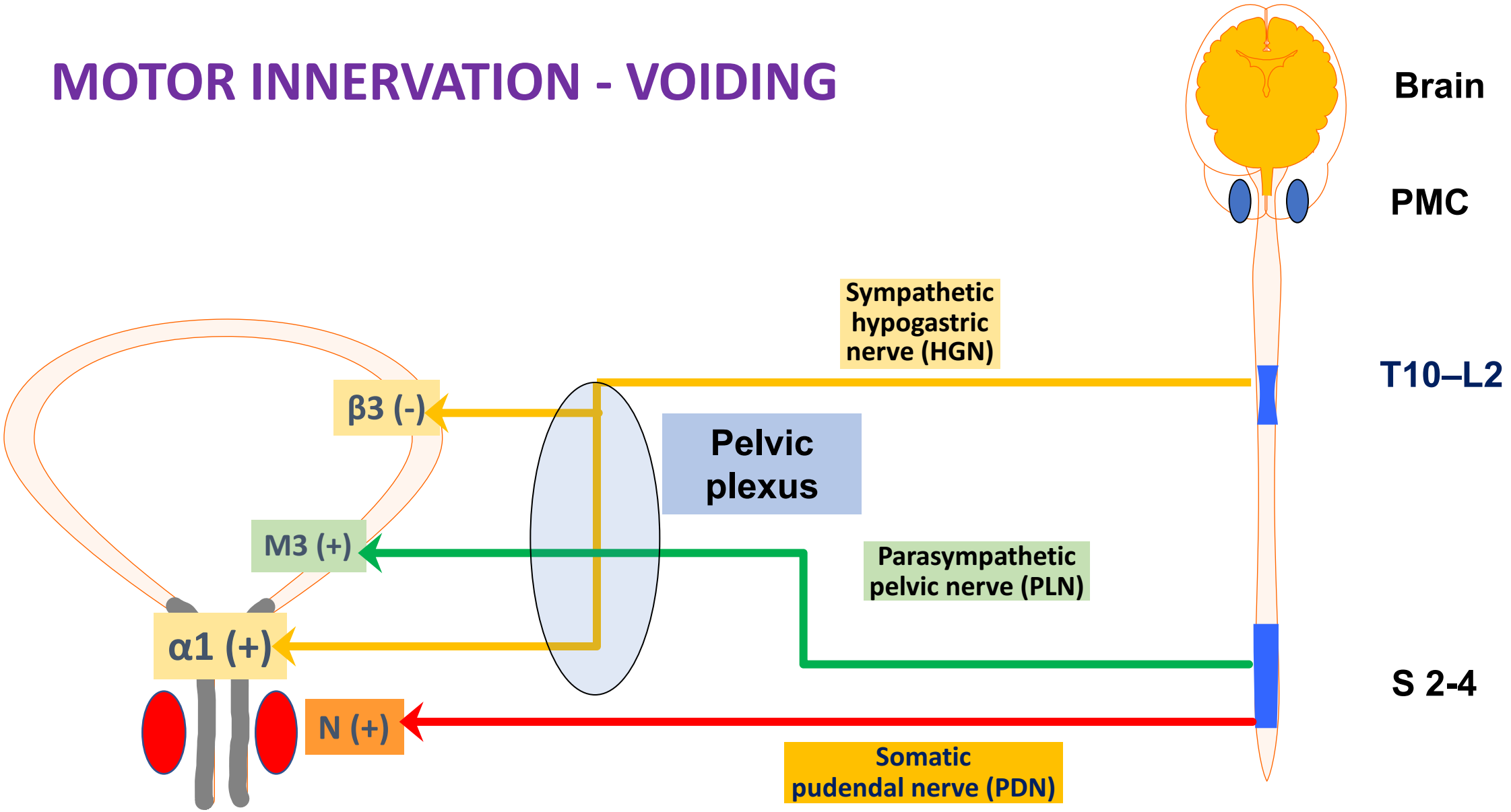
Urine Storage Reflex

- 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



MOTOR INNERVATION - VOIDING



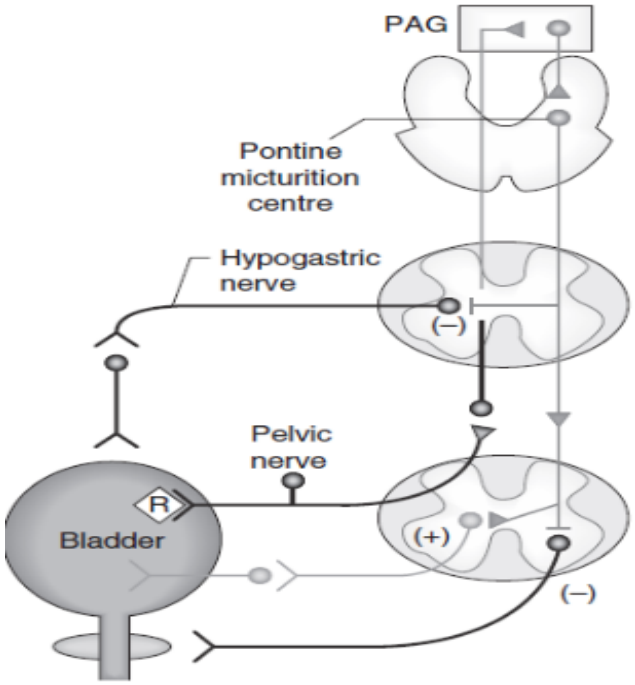
Urine Voiding Reflex – A Positive Feedback Loop

- High-level afferent signals are stimulated by intravesical pressure, resulting in increased activity to the brain[1]
- Descending efferent pathways then cause voluntary bladder contraction and the flow of urine[2]
- Normal voiding is, therefore, a function of a positive feedback mechanism[3]

References: 1. Andersson KE. *Nat Clin Pract Urol*. 2004;1(2):103-108. **2.** Fowler CJ, Griffiths D, de Groat WC. *Nat Rev Neurosci*. 2008;9(6):453-466. **3.** Leng WW, Morrisroe SN. *Urol Clin N Am.* 2006;33:491-501.

Urine Voiding Reflex – A Positive Feedback Loop

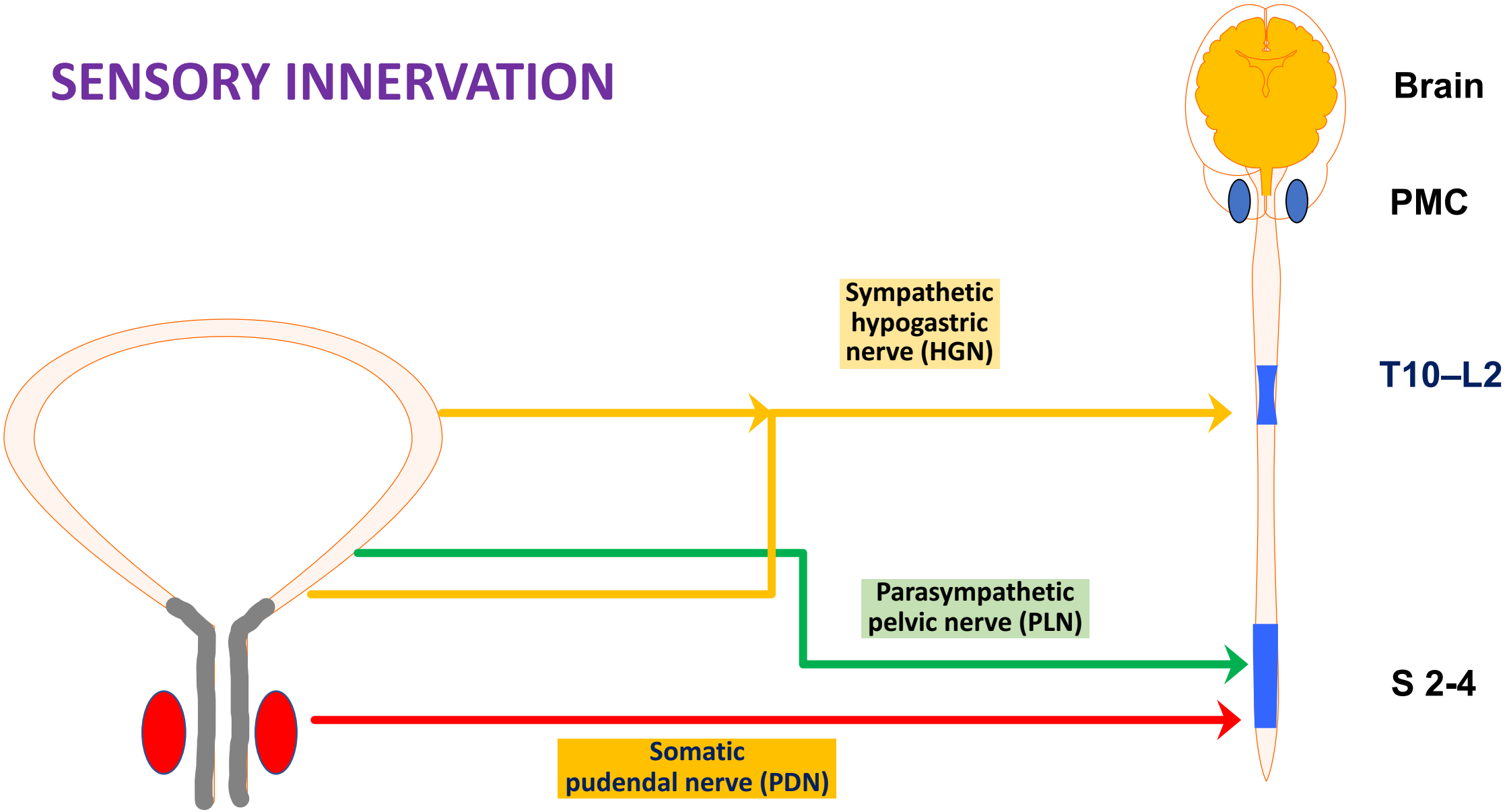
- When an individual decides that it is time to urinate
- The pontine micturition center (PMC) is released from tonic inhibitory control of the higher cortical and subcortical centers of the brain, initiating the voiding process.
- The parasympathetic system then switches "on," stimulating a detrusor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



B

Nerves	Receptors	Storage	Voiding
HGN Sympathetic	α , β	+	-
PLN Parasympathetic	M	-	+
PDN Somatic	N	+	-

SENSORY INNERVATION



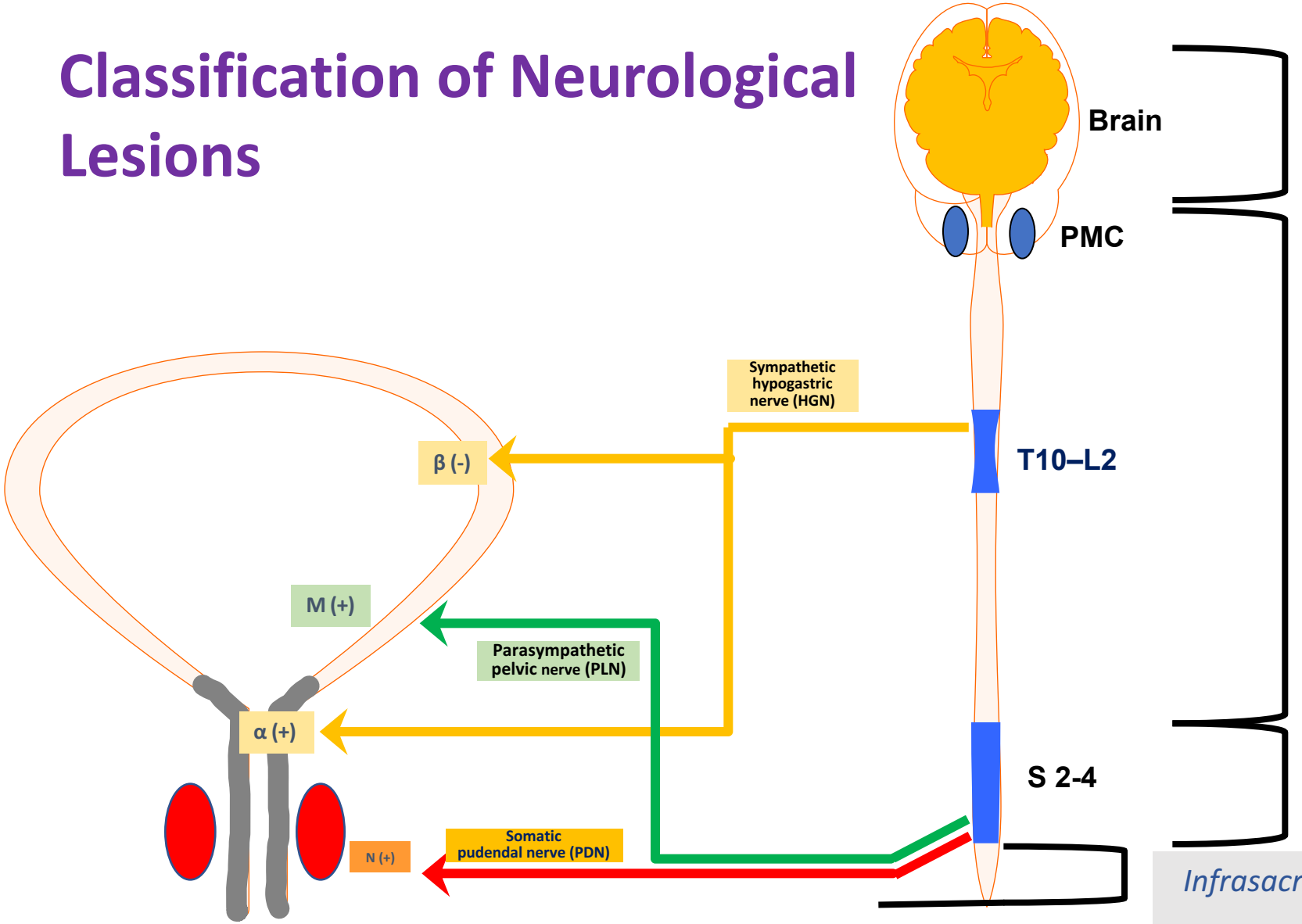
SENSORY INNERVATION

- The pelvic nerve - most important afferents for initiating micturition
- The pelvic nerve afferents,
  - monitor the volume of the bladder and
  - the amplitude of the bladder contraction.
- These afferents are small myelinated (Aδ) and unmyelinated (C) fibres
- In NLUTD and possibly inflammatory conditions, there is recruitment **of C fibers** that form a new functional afferent pathway
  - that can cause urgency incontinence and
  - possibly bladder pain.

Neurogenic Lower Urinary Tract Dysfunction (NLUTD)

- **NLUTD** can be diagnosed in the presence of neurological disease only.
- the dysfunction(s) may involve not only the bladder but also the urethral sphincter competence or relaxation
- Therefore older terminology of “Neurogenic Bladder” or “Neurogenic Bladder Dysfunction” are misleading

Classification of Neurological Lesions



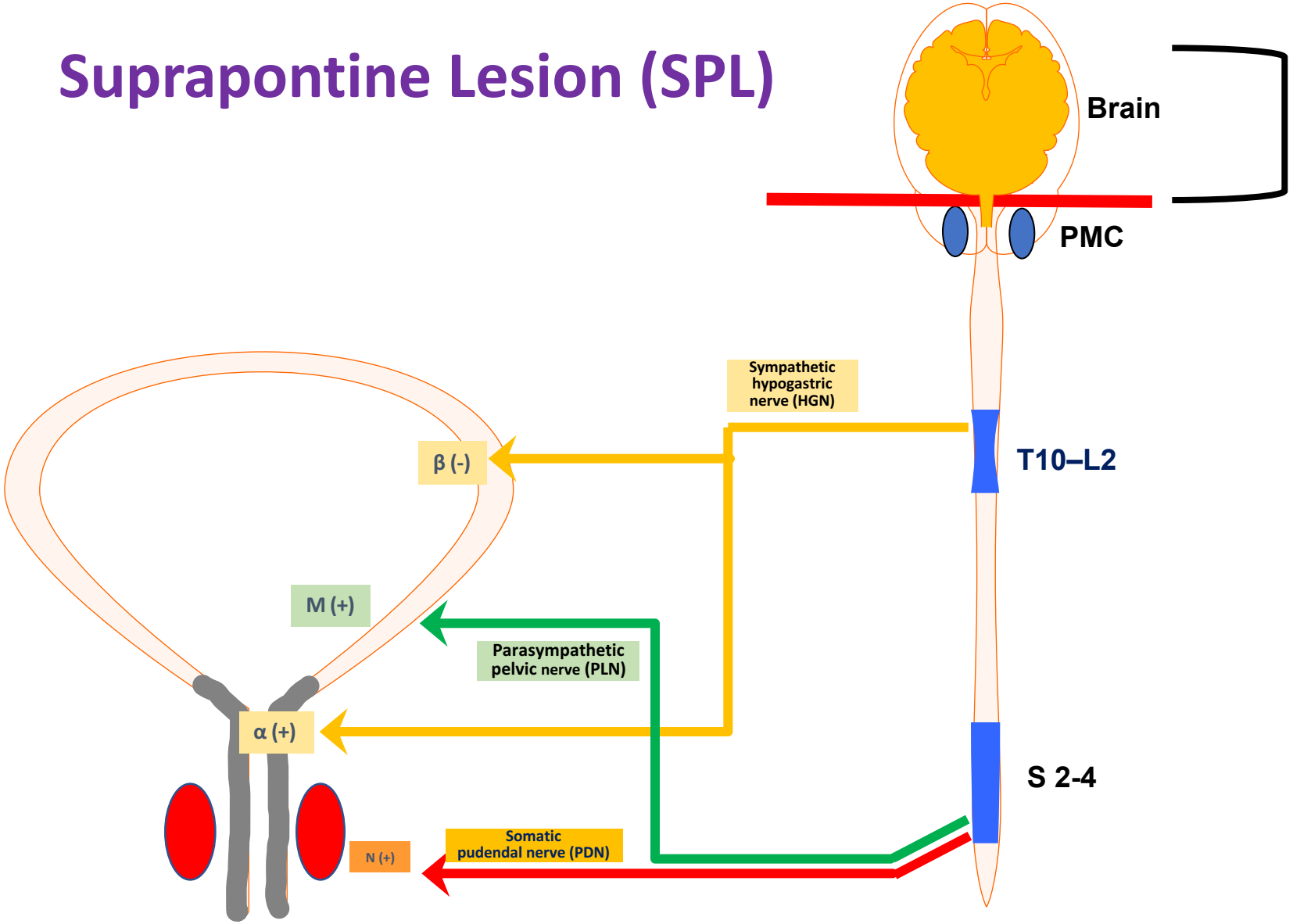
Suprapontine lesion (SPL)

Suprasacral spinal cord/ pontine lesion (SSL)

Sacral Spinal Cord Lesion (SSCL)

Infrasacral (cauda equina and peripheral nerves) Lesion (CEPNL)

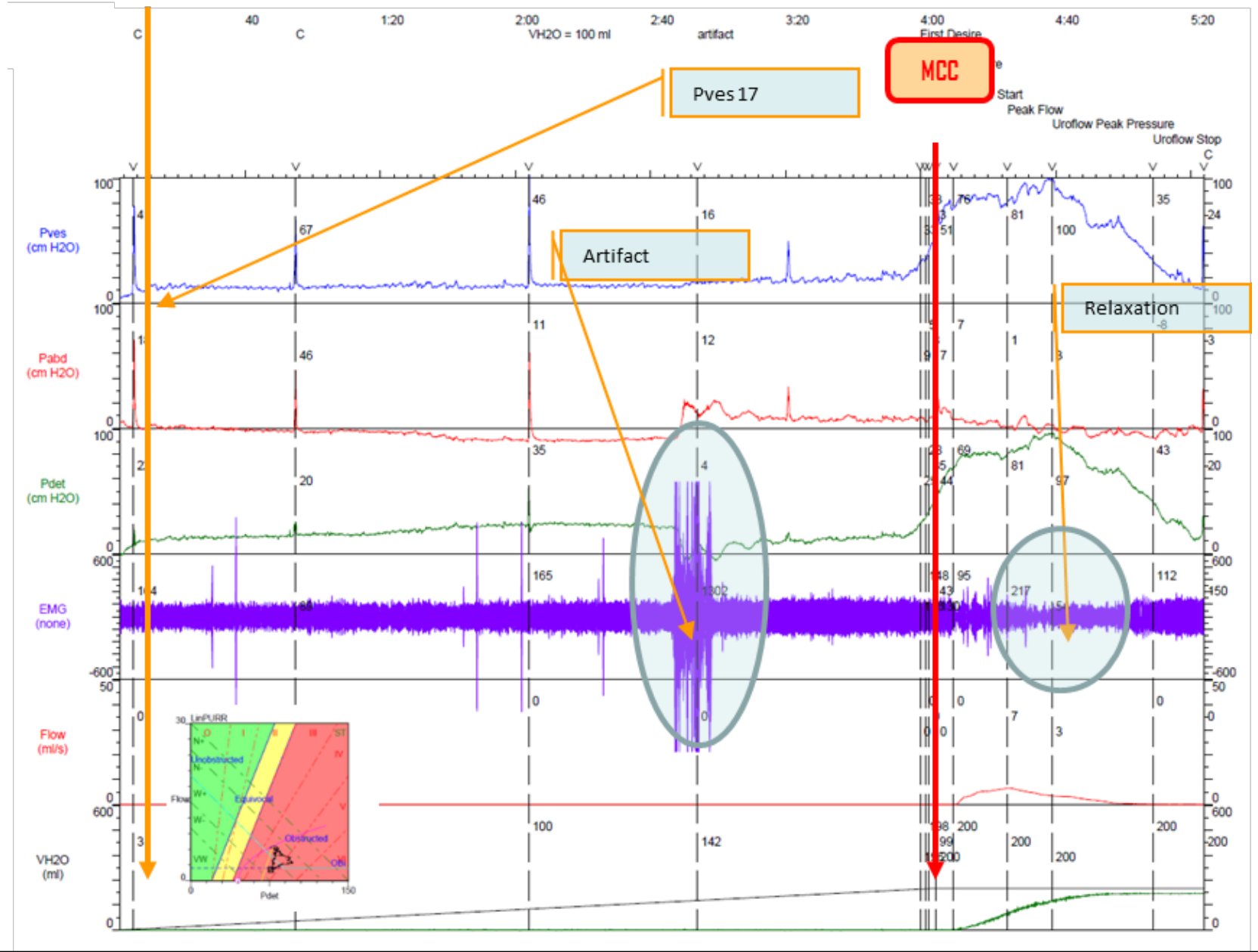
Suprapontine Lesion (SPL)



Suprapontine Lesion (SPL)

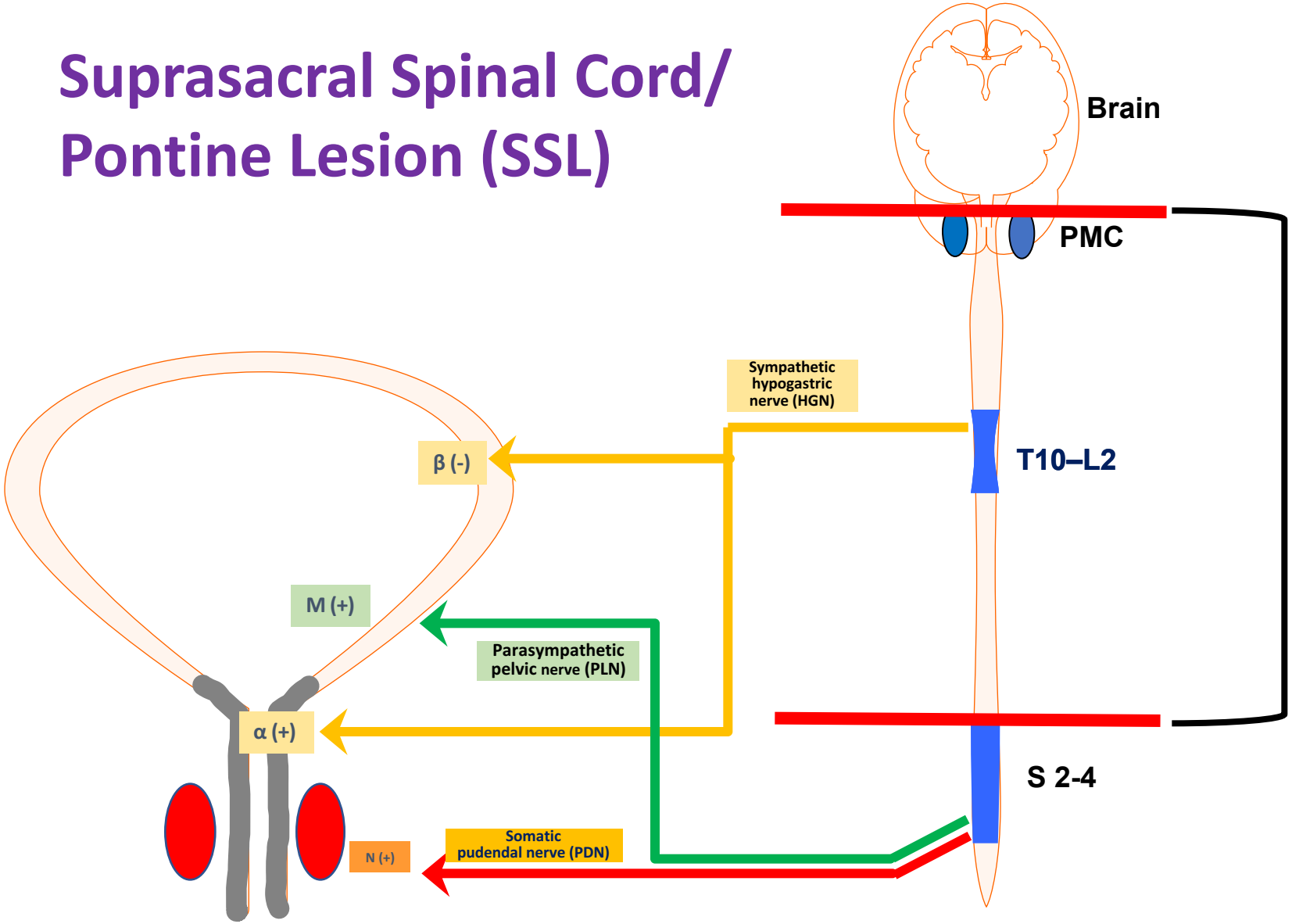
- Is a lesion above the pons (forebrain or midbrain)
- NLUTD in SPL:
  - impaired cerebral regulation and central inhibition
  - reflex contraction of the detrusor (DO) +/- DO incontinence
  - usually synergistic voiding/bladder emptying.
- Lesions resulting from cerebral or brainstem lesion with preservation of the pontine micturition center (PMC)
  - cerebrovascular disease
  - degenerative disease
  - hydrocephalus
  - intracranial neoplasms
  - traumatic brain injury (the list is incomplete)

START



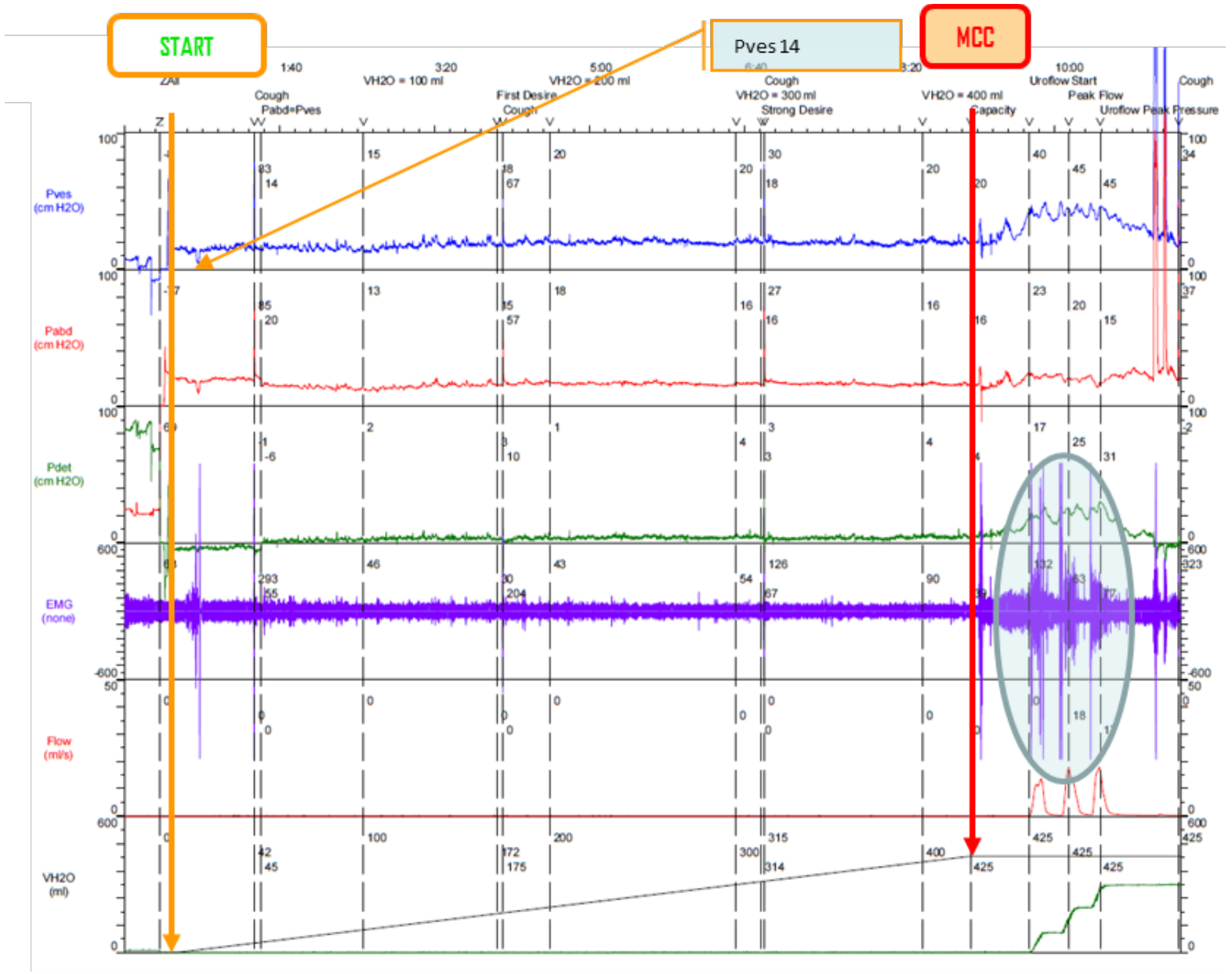
68 M CVA

Suprasacral Spinal Cord/ Pontine Lesion (SSL)



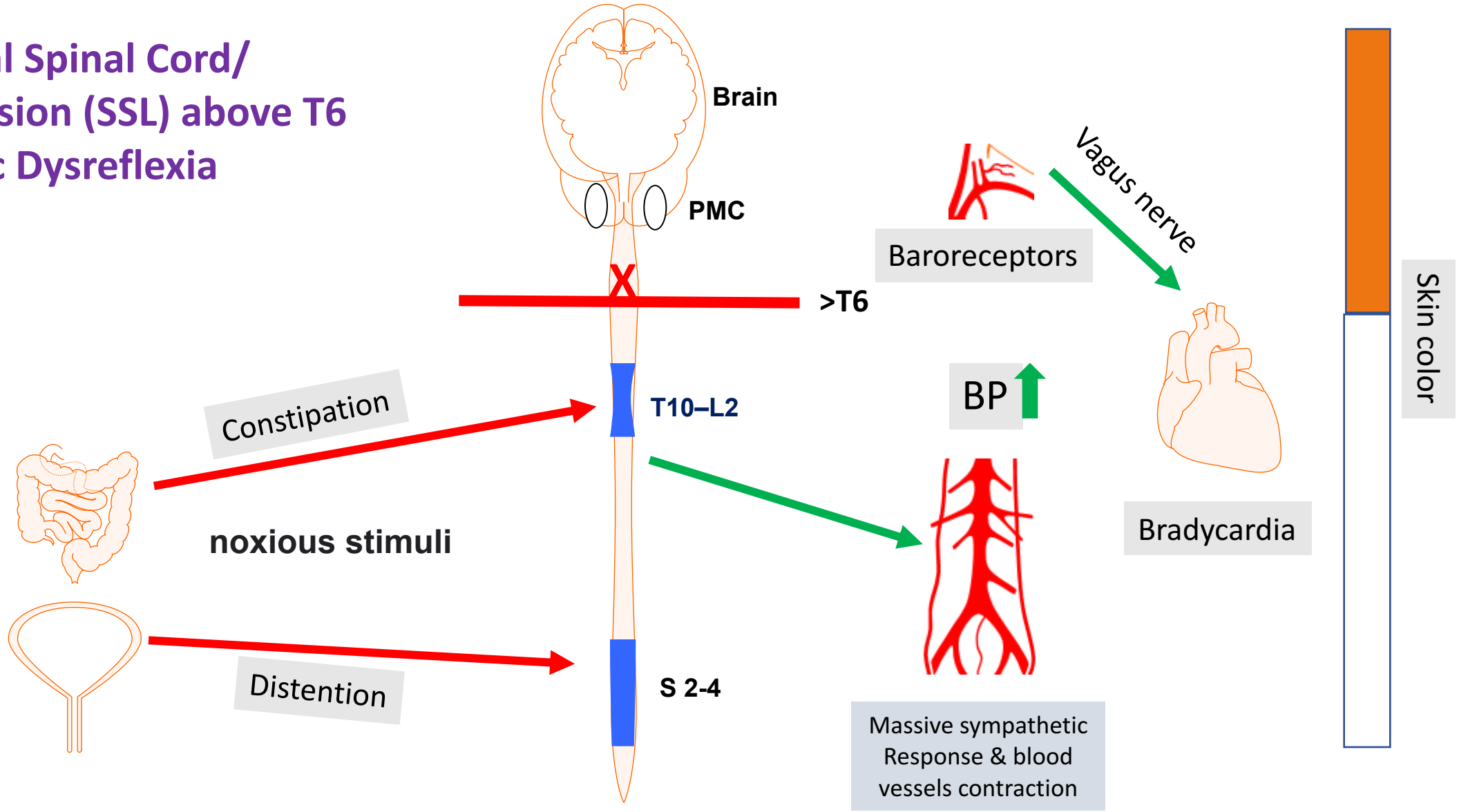
Suprasacral Spinal Cord/Pontine Lesion (SSL)

- Is a lesion in suprasacral spine and/or pons.
- NLUTD in SSL:
  - Detrusor overactivity (DO)
  - DO incontinence is common,
  - With or without detrusor-urethral sphincter dyssynergia (DSD),
    - often resulting in a significant post void residual (PVR)
    - and “high pressure” bladder
  - Bladder sensation may be somewhat preserved (incomplete lesions) but voluntary control of the micturition reflex arc is lost.
  - Complete SSL above T6 may be associated with autonomic dysreflexia



Suprasacral Spinal Cord/ Pontine Lesion (SSL)
28 M, SCI ASIA B T5

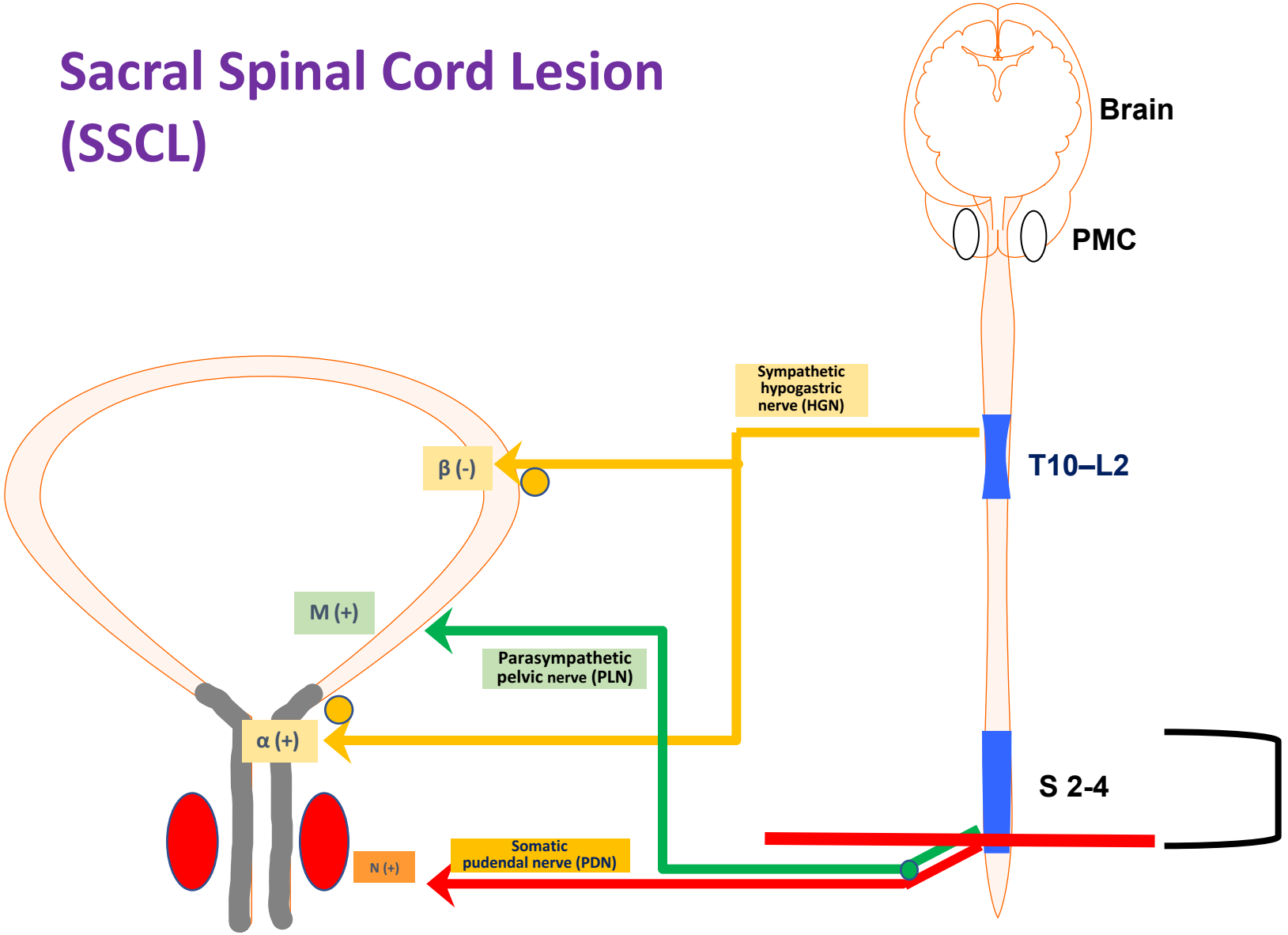
Suprasacral Spinal Cord/ Pontine Lesion (SSL) above T6 Autonomic Dysreflexia



Autonomic Dysreflexia

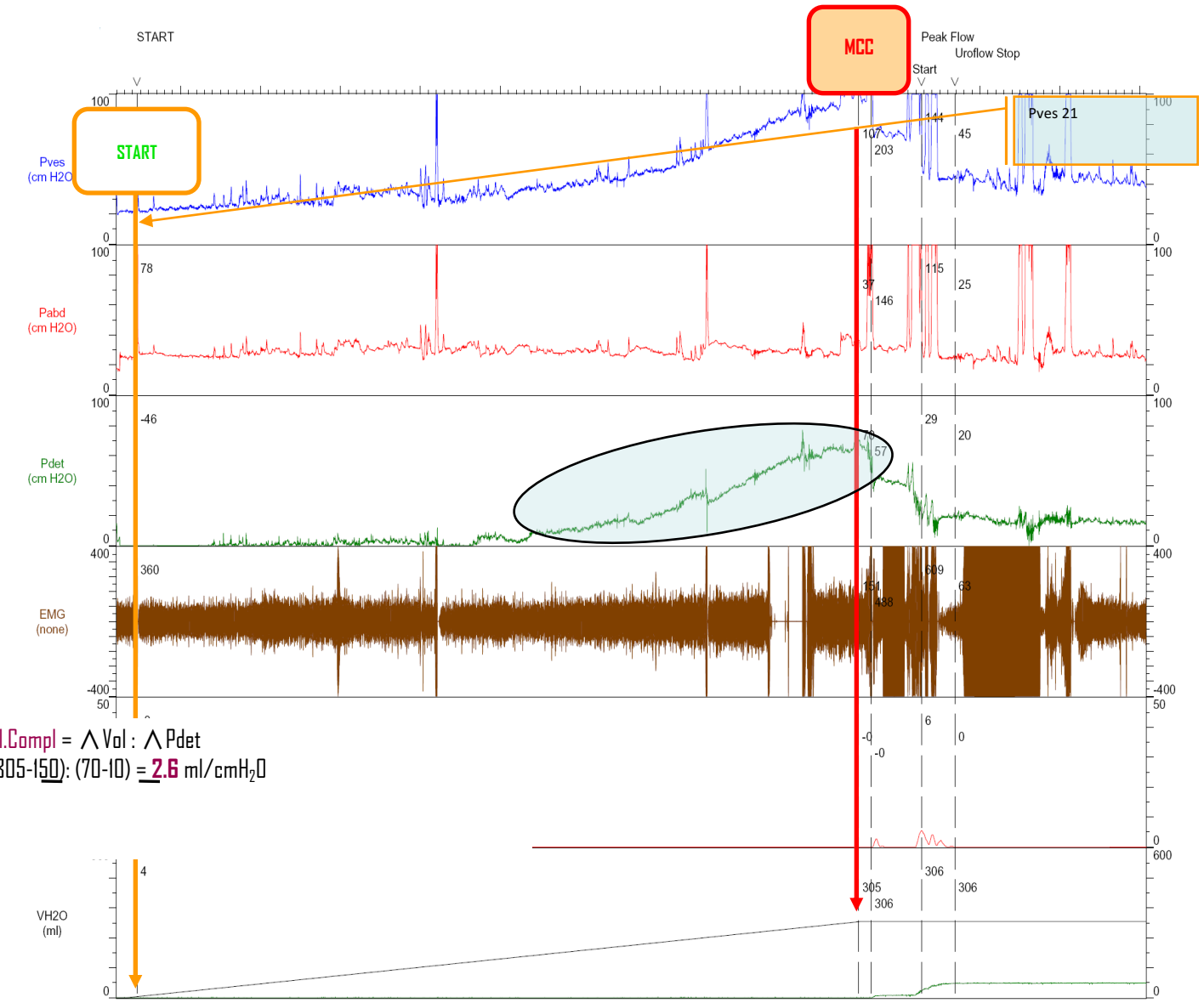
- It is potentially a medical emergency characterized by hypertension, bradycardia, severe headaches, and flushing above, with pallor below the cord lesion, and sometimes convulsions.
- An increase of blood pressure without any other symptoms is called Asymptomatic Autonomic Dysreflexia.

Sacral Spinal Cord Lesion (SSCL)



Sacral Spinal Cord Lesion (SSCL)

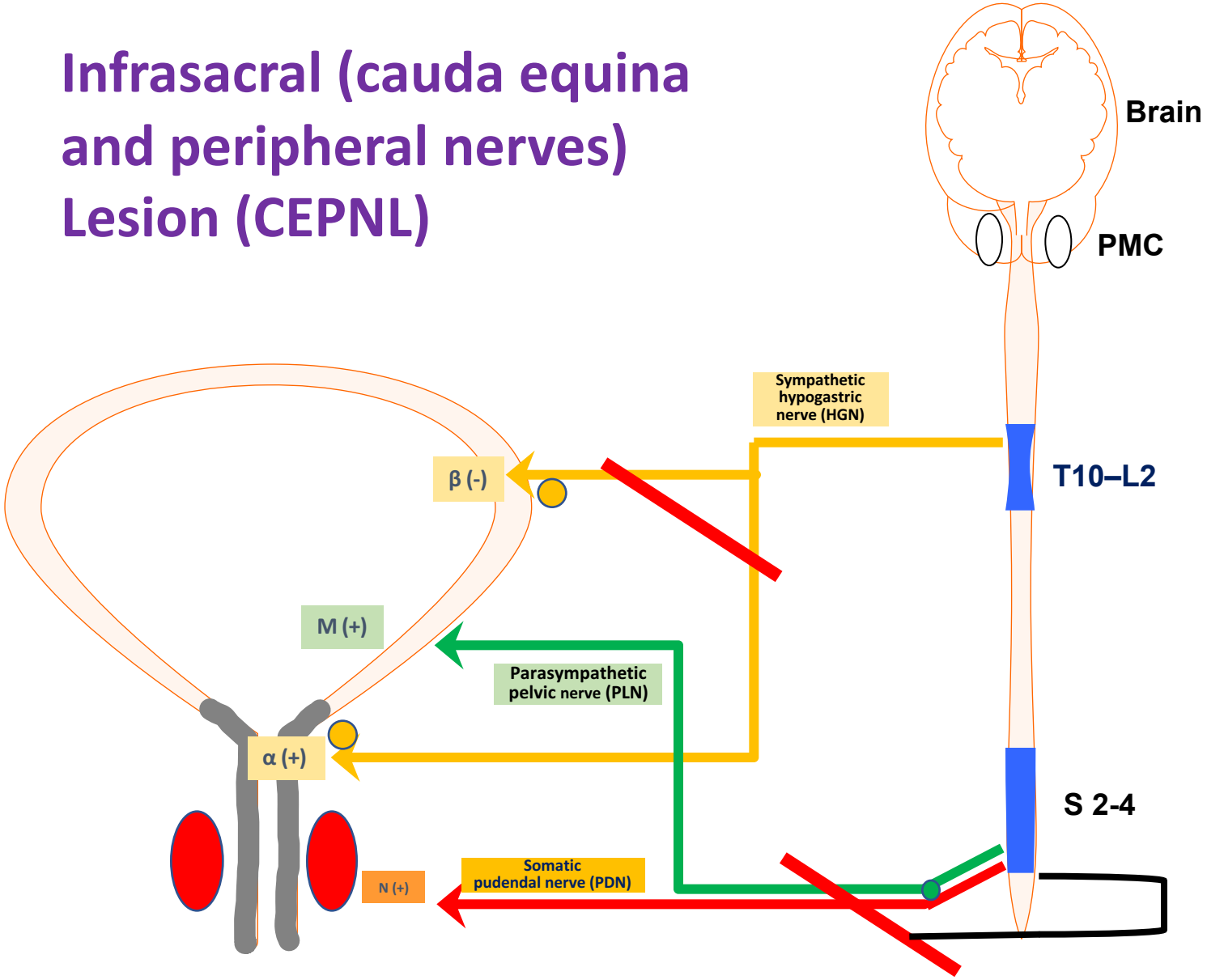
- is a lesion in the sacral spinal cord.
- NLUTD in SSCL
  - loss of parasympathetic control of the detrusor with acontractile detrusor with or without decreased bladder compliance
  - somatic deficiency (loss of Onuf's nuclei) of the external urethral sphincter usually with impaired sphincter activity & with stress urinary incontinence (SUI)
  - Sensory impairment is typically associated with a complete lesion. Some afferent pathways remain intact due to potential preservation of hypogastric afferents



Bl.Compl = ⋀Vol : ⋀Pdet
(305-150): (70-10) = 2.6 ml/cmH_2O

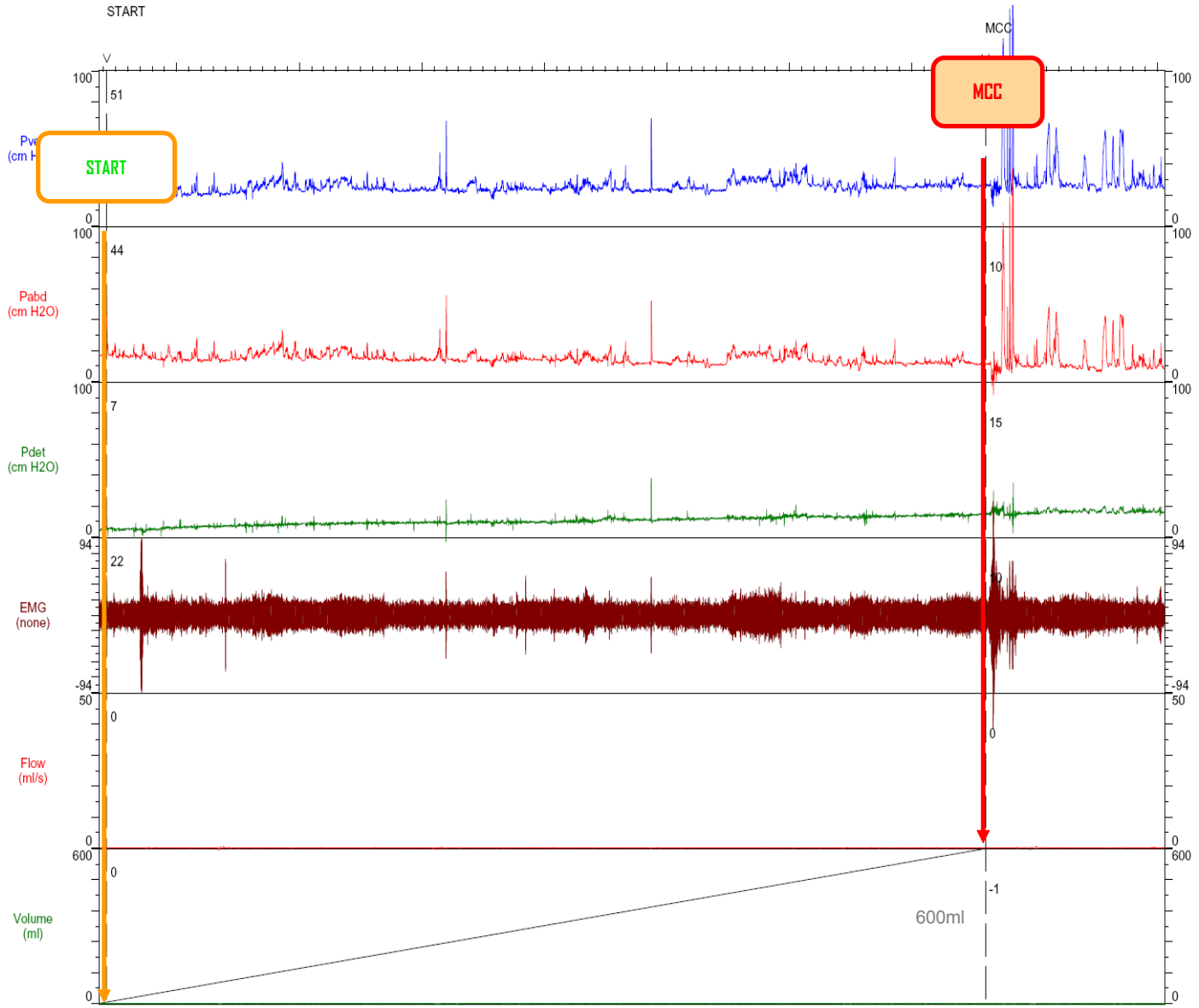
56 F, SCI, MVA, pelvis and lower back, L 2 incomplete, unable to void

Infrasacral (cauda equina and peripheral nerves) Lesion (CEPNL)



Infrasacral (cauda equina and peripheral nerves) Lesion (CEPNL)

- Is a neurological lesion affecting the cauda equina and/or peripheral nerves.
  - NLUTD in CEPNL:
    - acontractile detrusor
    - and/or SUI may be present.
    - In diabetic neuropathy, detrusor overactivity can be seen in combination with the above.



37 F with urinary retention post TAH for cervical ca
4 weeks post hysterectomy, CIC q6h, not voiding
No preoperative problems

Mixed Neuronal Lesion

- is resulting from lesions of the neural pathway at different levels of the central nervous system concurrently

Spinal Shock Phase

- Is usually temporary following acute neurologic insult or SCI that is characterized by
  - loss of sensory, motor, and reflex activity below the level of injury.
  - NLUTD in Spinal Shock is usually a temporary complete painless urinary retention.
  - 12 weeks

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

- 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.

History and physical examination

- 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

1. **Management of Storage Dysfunction (OAB)**

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

1. Timed voiding
2. Pelvic floor muscle training and exercise (including pelvic floor relaxation),
3. Delayed voiding,
4. Double voiding,
5. Biofeedback

Management of neurogenic bladder

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.

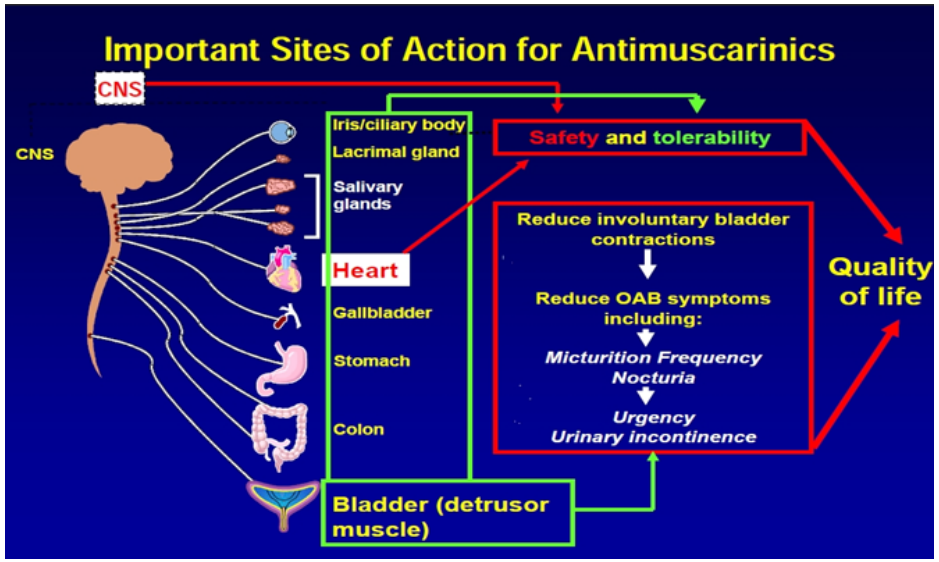
• There are two types of muscarinic receptors in the bladder: M2 and M3. M2 receptors are most abundant, but M3 receptors are functionally more relevant to bladder relaxation.

Management of neurogenic bladder

- 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



Oxybutynin (immediate release [IR], extended release [ER], patch, topical gel),

Tolterodine , Solifenacin, Fesoterodine (3ry)

Darifenacin (M3 Selective)

Trospium chloride (4ry)

Management of neurogenic bladder

- **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 .

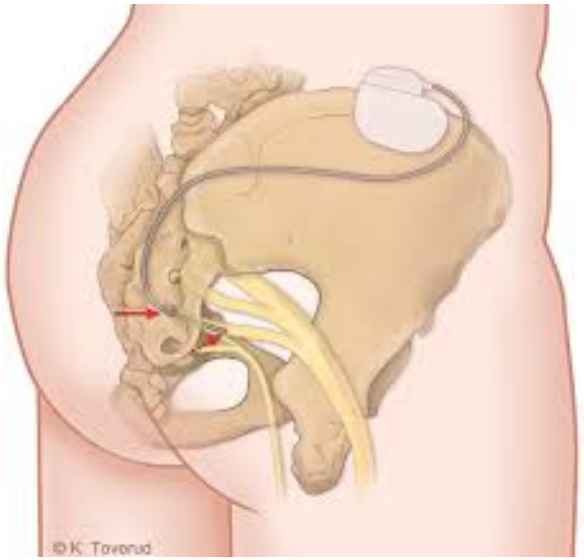
• These receptors serve to relax the detrusor muscle, making them an ideal therapeutic target. The selective β3-adrenoceptor agonist mirabegron was approved in by the Food and Drug Association (FDA) in 2012 for clinical use as an additional medication used to treat overactive bladder symptoms.

• 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

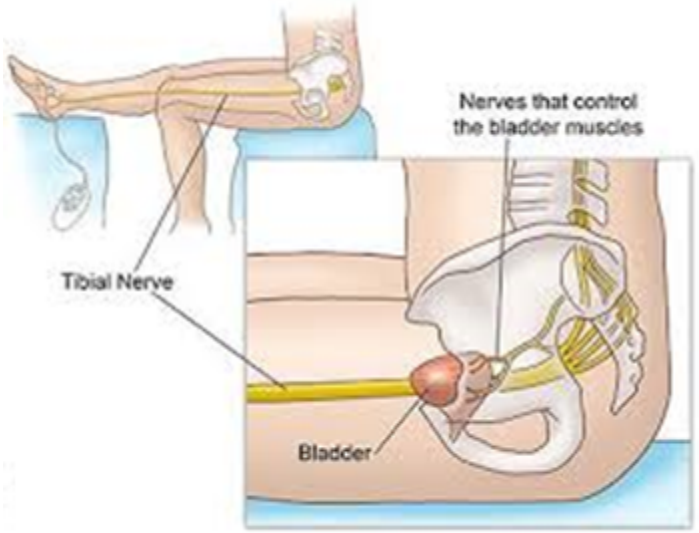
Management of neurogenic bladder

- **C. neuromodulation**

  sacral neuromodulation (SNM)



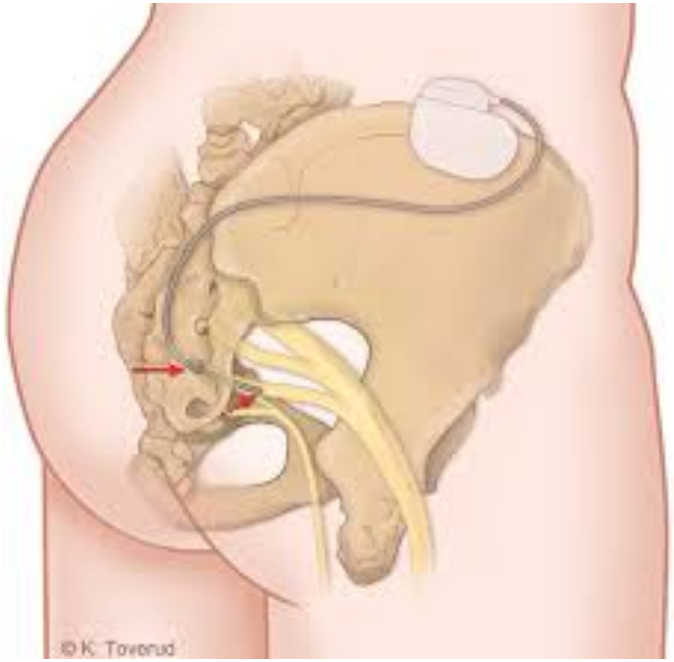
percutaneous tibial nerve stimulation (PTNS),



Sacral neuromodulation

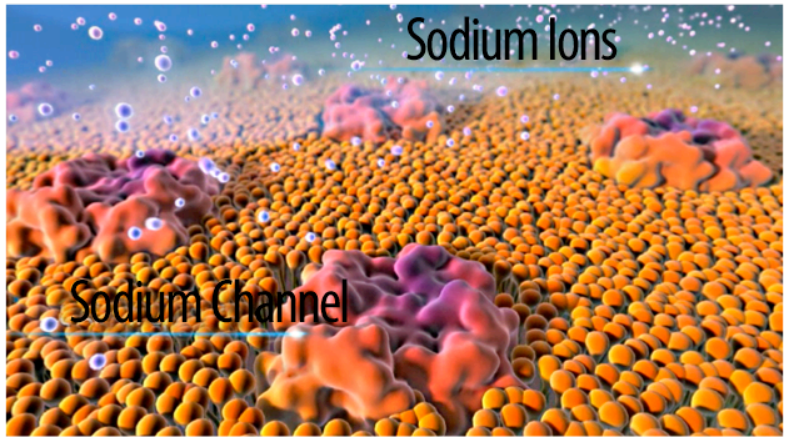
- Stimulation of the S3/S4 nerve root by an implanted electrical pulse generator

- The stimulator is a small electrical pulse generator, approximately the same size as a cardiac pacemaker, and is commonly implanted in the upper outer quadrant of the buttock.



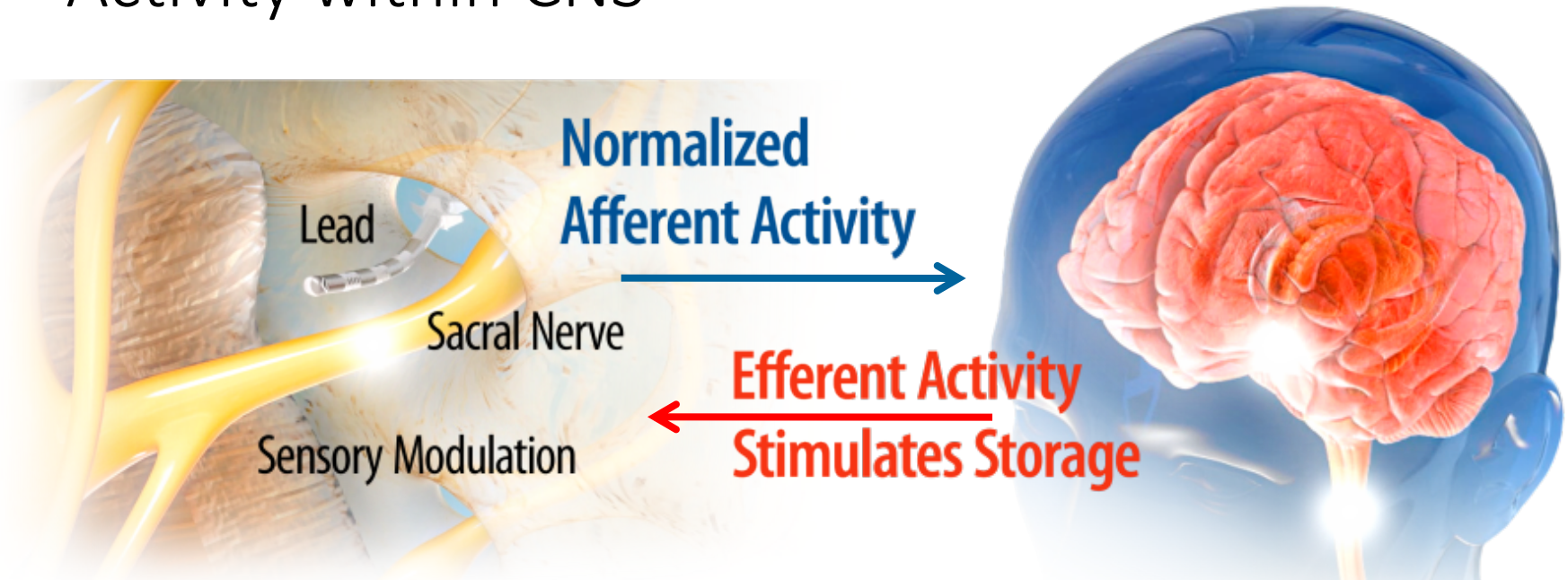
Production of Action Potentials Modulate CNS Processing of Bladder Afferent Input

- The neurostimulator provides an electrical charge to an area near the sacral nerve, resulting in altered neural activity
- This stimulation likely depolarizes the nerve, causing an action potential[1]
- The signal propagates impulses along the axon as if the neuron had naturally fired an action potential[1]



Reference: 1. Johnson M. Watson T, ed. *Electrotherapy: Evidence-Based Practice.* 12th ed. Elsevier; 2008:259-286.

Modulation of Abnormal Afferent Activity within CNS



- The action potentials induced by electrical stimulation are thought to alter abnormal sensory input from the bladder[1,2]
- Efferent pathways are uninhibited so as not to suppress voluntary voiding[3]
- Unlike other therapies that target the bladder, bladder regulation occurs without directly influencing the bladder or sphincter muscles[4]

Management of neurogenic bladder

D. botulinumtoxin A

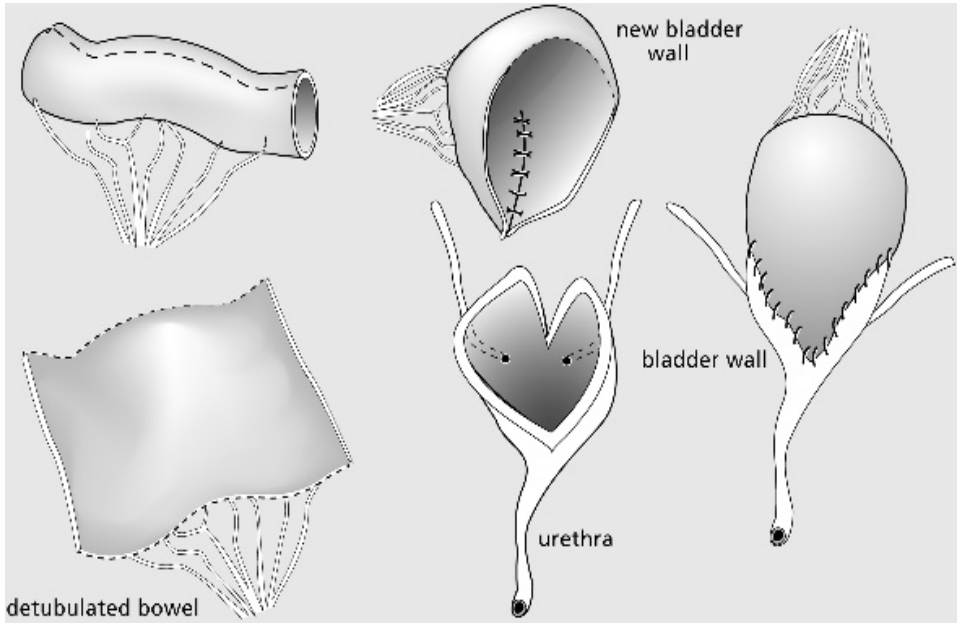
- botulinumtoxin A works by blocking the release of acetylcholine from nerve endings (exocytosis), resulting in the blockage of neural transmission and alteration of afferent sensory input.

- 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.

Management of neurogenic bladder

E. Surgical :

- Clam augmentation cystoplasty
- Detrusor myectomy
- Denervation procedures
- Urinary diversion



Management of neurogenic bladder

- 2- management of voiding dysfunction
- - Medications
- - Catheterization
-

Thank you