Bladder, Bowel and Sexual Dysfunction In Peripheral Neuropathy and Cauda Equina Lesions

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### Affiliations to disclose:

_Broaden view of common neurological disorders in the context of an aging population._

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Pelvic organ dysfunction is caused by peripheral nervous system (PNS) lesions

Sexual and lower urinary tract dysfunction (and less obviously anorectal dysfunction) may occur as a symptom

- of a **PNS disease**; they may occur in isolation, or in combination, and without other disturbances of the autonomic nervous system (*e.g.*, **ED in amyloid neuropathy**);

- of a **localized nerve injury** (*e.g.*, **painful clitoral dysesthesia after a pudendal nerve lesion**).
Pelvic organ dysfunction is caused by peripheral nervous system (PNS) lesions

Sexual and lower urinary tract dysfunction (and less obviously anorectal dysfunction) may occur

- as the **presenting symptom** of a developing **PNS disease**

- as an **isolated** phenomenon after **localized nerve injury**.
Knowledge of the anatomy and physiology of sexual, bladder and bowel function, as well as of the PNS disorders is essential to understand peripheral neurogenic „pelvic“ dysfunctions.
Knowledge of the anatomy and physiology of sexual, bladder and bowel function, as well as of the PNS disorders is essential to understand peripheral neurogenic dysfunctions.

Knowledge of the **topographic anatomy** is particularly important for surgeons to achieve **preservation** of the peripheral nerves related to sexual, bladder and bowel function during abdominal and pelvic surgery.

*Careful surgical technique, and specific intraoperative “mapping” and “monitoring” procedures are needed to preserve relevant neural structures.* (Rodi and Vodušek, 2008).
The importance of peripheral innervation

The *peripheral sensory and motor branches* of the respective reflex arcs are constitutional to *reflex control* of pelvic organ function, but also the final common *links to* CNS neural control.

The necessity of *motor innervation* for effector activation is obvious.

The role of *sensory information* on the state of fullness of bladder and anorectum, and the importance of *sensory feedback* of motor actions are also obvious.
Less appreciated:

Primary erotic stimuli are mainly derived from the genitals themselves (the role of sensation in producing the individual’s awareness of sexual excitement).

Genital afferents also elicit phasic and tonic reflex responses, which induce and help maintain the genital responses throughout intercourse, and lead to orgasm.
Peripheral nervous system (PNS) disorders are an important cause of lower urinary tract (LUT) dysfunction.

LUT dysfunction caused by PNS involvement typically causes bladder and sphincter hypoactivity with poor bladder emptying, and incontinence; paradoxically, it may also cause bladder overactivity.

LUT symptoms may be a guide to the localization of nervous system pathology in the lumbosacral spinal canal, and in the pelvis.
LUT dysfunction due to PNS involvement is rarely a medical and surgical emergency (as in acute cauda equina syndrome).

More prevalently, LUT dysfunction is a chronic condition presenting a health hazard due to possible recurrent urinary infections and upper urinary tract complications.

LUT dysfunction also significantly affects the quality of life of patients.
Destructive lesions of the nerves to the bladder cause a silent, painless distension of the bladder (i.e., detrusor atonia). (Pavlakis et al., 1983)

Urinary **retention** is the resulting symptom and difficulty eliminating urine is the most common primary dysfunction in symptomatic peripheral neuropathic lesions.
Destructive lesions of the nerves to the bladder cause a silent, painless distension of the bladder (i.e., detrusor atonia).

(Pavlakis et al., 1983)

Urinary *retention*

If retention is complete, the *accompanying incontinence* is of the “overflow” type, although in the case of a denervated urinary sphincter the patient may also suffer from stress incontinence.
Destructive lesions of the nerves to the bladder cause a silent, painless distension of the bladder (i.e., detrusor atonia).

(Pavlakis et al., 1983)

**Continuous incontinence** is the consequence of severe sphincter denervation, particularly in women.
Other consequences of lesions of LUT peripheral innervation:

Paradoxically, in patients with presumed isolated PNS involvement (for instance, in Guillain–Barre’s syndrome) urodynamics has occasionally demonstrated
detrusor overactivity,
both with and without sphincter dyssynergia.

_Pelvic nerve irritation was suggested as one possible underlying mechanism._

_(Fowler, 1999)_
The sensory dimension of the bladder dysfunction has been less attended to by clinical research.

**Sensation** is indispensable for appropriate LUT function, and sensory symptoms are an important complaint of patients.

In partial neurogenic lesions, **sensory symptoms may predominate**, with dysesthetic sensations attributed to bladder or urethra.
Peripheral nervous system (PNS) disorders are recognized as a cause of anorectal dysfunction.

Anorectal dysfunction caused by PNS involvement encompasses:

**defective evacuation** *(due to the lesion of anorectal somatic motor and sensory innervation, or sacral parasympathetic lesion causing slow colonic transit)*, and

**incontinence** *(apart from motor denervation, defective sensation of rectum and anal canal is an important factor in incontinence)*.

*(Bielefeldt et al 1990)*
Peripheral nervous system (PNS) disorders are an important cause of sexual dysfunction (SD).

Sexual symptoms – particularly erectile failure - may be a warning signal not only of cardiovascular disease, but also peripheral neuropathy.

Sexual dysfunction caused by PNS involvement typically presents as problems with the 

**genital response** (erection and vaginal lubrication, ejaculation, and sensation).

*Paradoxically, it may also cause spontaneous erection without erotic stimulation.*
A particular PNS lesion may cause a specific SD

Particular peripheral nerve lesions may cause a specific SD, limited to one specific part of the genital response (e.g., isolated ejaculation failure in lesions of the hypogastric plexus).

However, more often the PNS lesion is complex, or less well defined, or the consequences go beyond what can be expected from the affected anatomy.
Sexual dysfunction caused by PNS involvement typically presents as problems with the **genital response**.

While **desire** and **arousal** necessarily involve higher brain centers, they also depend on the overall “capability” of the subject to act as a sexual being.

*This is probably why desire may be affected* in patients with pure PNS lesions such as residual deficits after a cauda equina lesion.

(Podnar et al., 2002)

*This type of SD after a PNS lesion might be called “indirect neurogenic”.*
Pelvic organ dysfunction as part of PNS syndromes and PNS diseases

Pelvic organ innervation may be compromised by a localized lesion („anatomic syndromes“ of lower sacral nerve roots, the sacral plexus, the abdominal and pelvic autonomic nerves, and the pudendal nerve due to trauma, compression, inflammation,...).

Pelvic organ innervation may be compromised by a generalized PNS disease (ie. polyradiculoneuropathy, polyneuropathy of metabolic, inflammatory, genetic,...origin).

In case of polyneuropathy, pelvic organ dysfunction is as a rule part of a more generalized involvement of the peripheral autonomic nervous system.
Pelvic organ dysfunction as part of PNS syndromes ie. „anatomic syndromes“ of lower sacral nerve roots, the sacral plexus, the abdominal and pelvic autonomic nerves, and the pudendal nerve due to trauma, compression, inflammation,…

Pelvic organ „peripheral“ innervation may be compromised by

------ Lesions within the spinal canal:
- Conus syndrome
- Cauda equina syndrome

------ Lesions within the abdominal cavity / pelvis:
- Hypogastric and Sacral plexus lesion
- Pudendal nerve lesion
Pelvic organ dysfunction as part of Cauda equina/conus syndrome (CES)

Lower-back **pain**, **sacral sensory loss**, and **urinary symptoms** are the most robust presenting features of CES.

(Jalloh and Minhas, 2007)

CES has been classified (clinically) as “complete”, if associated with urinary retention, and “incomplete”, if other urinary symptoms (e.g., straining, loss of bladder sensation) are present.

(Gitelman et al., 2008)
Cauda equina/conus syndrome (CES)

Approximately 2% of operated herniated lumbar discs are because of CES.

(Gitelman et al., 2008)

A study at a national referral uro-neurophysiologic unit found for CES an annual incidence rate of 3.4 per 1,000,000 and a prevalence rate of 8.9 per 100,000

(Podnar, 2007)
Pelvic organ dysfunction as part of sciatica

Neurogenic pelvic organ (LUT...) dysfunction is not expected in “trivial” degenerative spinal/disc disease without any compromise of nervous structures, nor in a patient with lumbar or sacral monoradiculopathy (L4, L5, S1).

But opiate medication may be necessary to control pain, and constipation and impaired bladder emptying (even urinary retention) may occur as side-effects of treatment in such patients.

(Holzer, 2012)
LUT dysfunction as part of chronic Cauda equina/conus syndrome (CES)

LUT symptoms **persist** in many patients after an acute cauda equina lesion.

Symptoms interfere with daily life

in 88% of men and 92% of women. 21% wear pads continuously, 14% occasionally.

(Podnar et al., 2006)
LUT dysfunction as part of Cauda equina/conus syndrome (CES)

Symptoms of **disturbed bladder emptying** were reported by 95% of men and 92% of women; **urinary incontinence** by 56% and 71%, respectively; **urgency** and **frequency** by 40% and 56%, respectively.

On cystometry, subjective reports were supported by the finding of **detrusor overactivity** in 21% of men, and no woman; **a reduced bladder capacity** was found in 9% of men and 15% of women.

(Podnar et al., 2006)
Pelvic organ dysfunction as part of Cauda equina/conus syndrome (CES)

In about 10% of patients with long-standing CES there is significant pelvic organ dysfunction **without** uro-ano-genital sensory loss.

*The mechanism of preserved touch and pinprick sensation in these patients, in spite of significant motor fiber damage to the same segments, is not clear.*

(Podnar, 2007)
Anorectal dysfunction as part of Cauda equina/conus syndrome (CES)

Flatus and fecal incontinence are frequent symptoms in chronic CES
(80% in our study had incontinence of flatus).

Changes in lifestyle due to anal incontinence were reported in 60% of patients.

Constipation was reported by 68% men and 93% women.

(Podnar, 2006)
Sexual dysfunction in patients with Cauda equina/conus syndrome (CES)

A complete lesion of the cauda equina damages the **parasympathetic erectile pathways to the penis**.

Approximately one-fourth of men are still able to achieve a „psychogenic“ erection.

Vaginal lubrication in women is under same type of neural control.

(The „preserved“ response in patient with CES is considered to be mediated by the sympathetic erectile pathway traveling in the hypogastric plexus).

(Podnar et al., 2002)
In patients with “stable” chronic CES (a consequence of some past disorder or trauma) sexual dysfunction causes significant frustration.

Genital sensory loss is often accompanied by paresthesias and dysesthesias. Pain syndromes are commonly reported as disruptive for sexual function, particularly if patients suffer from coital pain.

In men, ED is the major problem, and can vary from complete inability to obtain an erection, to inability to sustain adequate erection, to complete sexual activity.

(Podnar et al., 2002)
Sexual dysfunction in men with Cauda equina/conus syndrome (CES)

Ejaculation may be delayed or absent, although occasionally premature ejaculation is reported. Bilateral damage to all S2–5 roots results in dribbling ejaculation, since seminal emission is preserved, but bulbo- and ischiocavernosus muscles are paretic. Ejaculation may also be painful.

**Orgasmic dysfunction** was the most common SD in men with CES, and was associated with impaired genital sensation.

(Podnar et al., 2002)
Sexual dysfunction in women with Cauda equina/conus syndrome (CES)

**Women** with CES report diminished vaginal lubrication in response to genital stimulation. They also report loss of erotic sensation, dyspareunia, loss of lubrication, loss of sensation during vaginal intercourse, difficulties in achieving orgasm, and changes in the feeling of orgasm.

(Sipski et al., 2001)
Lesions of the sacral plexus and pudendal nerves can be caused by pelvic fractures, hip surgery, malignant infiltration, local radiotherapy, and by the use of orthopedic traction tables.

**Sacral plexus** lesions are usually unilateral and do not result in significant pelvic organ dysfunction, unless the sensory symptoms are disruptive.

(Amarenco et al., 2001)
Pelvic organ dysfunction as part of PNS syndromes

**Trauma** may cause pudendal nerve injury, leading to loss of perineal sensation, dysesthesias, pain syndromes, and dribbling ejaculation due to perineal muscle denervation.

In one study, 22% of long-distance cyclists had penile sensory symptoms, and 13% had ED with symptoms that persisted for up to 8 months.

(Andersen and Bovim, 1997)

Pudendal nerve lesion induced by bicycling may also cause ejaculatory dysfunction.

(Leibovitch and Mor, 2005)
Pelvic organ dysfunction as part of PNS syndromes

**Pudendal neuralgia** is considered a syndrome, with pudendal nerve entrapment as one of the possible etiologies.

The leading symptom is pain, although pelvic organ dysfunction has also been reported.

(Stav et al., 2009)
Sacral plexus lesions due to complicated vaginal delivery

Rarely, complicated vaginal delivery causes a severe sacral plexus lesion with obvious severe sensory and motor deficits in lower sacral segments.

*These are occasionally not associated with LUT dysfunction!*

(Feasby et al., 1992)
Lesions due to uneventful vaginal delivery?

The **uneventful vaginal delivery** may cause some mechanic and neurogenic pelvic floor and sphincter muscle lesions, as a rule mild and not associated with gross structural damage to nervous structures.

(Mallet et al., 1993)

In the EAS muscle neurogenic changes are minimal after uncomplicated deliveries.

(Podnar et al., 2000)

*Lesions associated with vaginal delivery are suggested as relevant in the pathogenesis of stress urinary incontinence and pelvic organ prolapse in women.*
Pelvic organ dysfunction due to **polyneuropathy**

**Polyneuropathies** involving autonomic nerve fibers are the most frequent cause of LUT symptoms.

There are many causes of polyneuropathy, but relatively few of them cause prominent bladder dysfunction.

(Burakgazi et al., 2012)

*In patients with LUTD and without “urologic” pathology, polyneuropathy should be among the suspected neurogenic causes.*

*The causal link to LUTD is strengthened if other symptoms of autonomic nervous system involvement are present.*
Polyneuropathies affecting autonomic nerve fibers and causing lower urinary tract dysfunction

**Primary autonomic neuropathies**
- Transthyretin amyloid polyneuropathy
- AL amyloid polyneuropathy
- Hereditary sensory autonomic neuropathies
- Fabry’s disease
- Porphyrias

**Secondary autonomic neuropathies**
- Diabetes mellitus
- Alcohol, chemotherapeutics
- Guillain–Barre´ syndrome
- Paraneoplastic autonomic neuropathy
- Lambert–Eaton myasthenic syndrome
- HIV-associated polyneuropathy
- Tabes dorsalis
- Neurosarcoidosis
Genetic disorders affecting autonomic nerve fibers and causing pelvic organ dysfunction

The most common **genetic disorders** presenting with autonomic dysfunction include

*Familial amyloid polyneuropathy*

*Hereditary sensory autonomic neuropathies (HSAN)*

*Fabry’s disease*

*Porphyrias*

(Freeman, 2005)
Diabetic neuropathy is by far the commonest polyneuropathy in the developed world and by far the commonest polyneuropathy to be associated with bowel, bladder, and sexual dysfunction.

(Wessells et al., 2011)

A large US epidemiologic study found that the prevalence of diabetics in the whole population with ED was 20%.

(Sun et al., 2006)
Diabetic cystopathy *(the term used initially for LUTD in diabetics)* has been described on its own right, meaning “involvement of the LUT by diabetic neuropathy.” *(Decreased bladder sensation, increased bladder capacity, impaired detrusor contractility).*

(Frimodt-Moller, 1980)

The prevalence of detrusor underactivity in insulin-dependent diabetics is estimated to be 43–87% *(without sex or age differences).*

(Gomez et al., 2011)
Onset of diabetic LUTD is in most patients *insidious* and often not recognized until it has reached an advanced stage.

LUT symptoms in diabetics often begin with *diminished sensation of bladder filling*, resulting in decreased frequency of voiding.

Patients complain of *difficulty in voiding* and a poor stream, accompanied by incomplete emptying of the bladder.

*(Postvoid dribbling may also occur, mimicking bladder neck obstruction. Urinary tract infections may lead to detrusor fibrosis, further worsening LUT function).*

*(Daneshgari et al., 2009)*
Some studies show that \textbf{nicturia} and \textbf{urinary frequency} are the most common LUT symptoms in diabetics complaining of LUTD. (Thus detrusor overactivity is actually more common than detrusor underactivity).

(Hill et al., 2008)
Sexual dysfunction in diabetes

ED in diabetic men usually begins insidiously with a **progressive decline in erection rigidity** and duration, to the point where penetration and intercourse become impossible.

*The severity of ED depends on age, duration of DM, number of DM complications, and the vibration perception threshold.*

(Amano et al., 2011)

*Albuminuria, retinopathy, neuropathy, insulin therapy, calcium-channel blockers, and higher level of HbA1c correlated with severe ED.*

(Chuang et al., 2012)
Erectile dysfunction in diabetes

Typically, a prevalence of ED of 50% is reported in diabetic men.

(Thorve et al., 2011)

In an Italian cohort of 1503 newly diagnosed type 2 diabetics (mean age 59 years), 43% reported ED. Comorbidities were arterial hypertension (55%), coronary heart disease (8%), neuropathy (7%).

(Corona et al., 2013)
Sexual dysfunction in diabetes

**Diabetic neuropathy** is an independent predictor for erectile dysfunction (ED) in DM.

(Wessells et al., 2011)

Morphologic alterations have been demonstrated in unmyelinated nerve fibers of the penis.

(Faerman et al., 1973)

A preferential involvement of unmyelinated sensory fibers resulting in neuropathic pain and gastroparesis was reported in diabetic patients with ED.

(Wellmer et al., 1999)

The vibration perception threshold was also reported to be diminished in diabetic men and correlated with the severity of ED.

(Amano et al., 2011)
Erectile dysfunction in diabetes

The prevalence of ED in cohorts of diabetic men is generally reported as higher than that of neuropathy, indicating that, in addition to damage of nerves essential for erection, there are other important pathogenetic factors contributing to ED (vascular, elevated advanced glycation end products, impaired nitric oxide synthesis, increased endothelin B receptor binding sites, increased oxygen free radicals, upregulated RhoA / Rho-kinase pathway, and impaired cGMP-dependent protein kinase 1).

(Thorve et al., 2011)

The abovementioned metabolic defects block the vasodilator action of released nitric oxide in corporeal tissue and are probably the cause of the relatively poor response to sildenafil in diabetic men with ED.

In the long-term management of both neuropathy and ED, good glycemic control has always been stressed. Indeed, a period of intensive glycemic therapy significantly reduced the prevalence of ED 10 years later.

(Wessells et al., 2011)
ED is much more frequent than ejaculatory difficulties.

The latter usually involves retrograde ejaculation rather than total lack of ejaculation.

*Retrograde ejaculation in diabetic patients is a result of internal bladder sphincter paresis.*

(Hershlag et al., 1991)
Sexual dysfunction in diabetes

DM in men is significantly associated with **all aspects of sexual dysfunction**: erectile dysfunction, sexual desire, ejaculatory function, and sexual satisfaction were all affected in a cohort of 2115 men between 40 and 79 years of age.

(Burke et al., 2007)

In men with long-standing DM type 1 the prevalence of particular SD was as follows:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
</tr>
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<tbody>
<tr>
<td>ED</td>
<td>34%</td>
</tr>
<tr>
<td>orgasmic dysfunction</td>
<td>20%</td>
</tr>
<tr>
<td>decreased libido</td>
<td>55%</td>
</tr>
</tbody>
</table>

(Penson et al., 2009)
Pelvic organ dysfunction in Guillan-Barre syndrome

Autonomic features may be present in up to 50% of patients. *Labile blood pressure, extremity anhidrosis, paralytic ileus, lower urinary tract and sexual dysfunction*.

Hesitancy, poor and prolonged flow, urinary retention, urgency, nocturnal frequency, and urge incontinence have all been described. (Both storage and voiding can be affected).

(de Jager and Sluiter, 1991)
Pelvic organ dysfunction in Guillan-Barre syndrome

In the general GBS population, lower urinary tract dysfunction was reported in about 25% of patients, more often in patients with severe weakness.

(Naphade et al., 2012)

LUTD typically presents after the onset of weakness without correlation to sensory deficit, and to antibody titer against neuronal nAChRs.

(Sakakibara et al., 2009)
Iatrogenic neurogenic pelvic organ dysfunction
- abdominal and pelvic surgery

The **sympathetic thoracolumbar** fibers may be injured by retroperitoneal lymph node dissections.

**Pelvic plexus** and **cavernosal nerves** may be injured by abdominoperineal resection for carcinoma, hysterectomy, radical prostatectomy, or sphincterotomy, thus significantly impairing the quality of life in patients after otherwise successful surgery.
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