Chronic Bladder Discomfort

Healthed
Sydney
2017

So common
So confusing
So poorly managed

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Chronic Bladder Discomfort

Abstract:

- Chronic bladder discomfort is not uncommon and may be difficult to diagnose and treat.
- Pain is regarded as a normal response to a noxious stimulus.
- In many patients this is not the case but clearly **local pathology needs to be excluded.**
- Perception of pain may depend on:
  - the actual source/cause/origin of the pain.
  - May vary depending on many other circumstances.

Chronic Bladder Pain

Abstract:

- The **origins of pain** and **neural pathways** are important.
- The neural circuitry that controls the process of pain is **complex and highly distributed**.
- Involves pathways at many levels of the:
  - brain,
  - spinal cord
  - peripheral nervous system
  - is mediated by multiple neurotransmitters.
- Through these central and spinal cord connections, pain may be influenced, chronicised and catastrophised.
- The hypothalamo-pituritary axis may also be involved.

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Abstract:

Comorbidities:

- **Comorbidities** and other pain orientated problems are **common.**
- Patients will often **move from one to another comorbidity or have more than one.**

Chronic Bladder Discomfort

Abstract:

Symptoms related to Chronic Bladder Discomfort include:

- **Frequency** (Needing to go often to the toilet).
- **Nocturia** (Needing to get up to the toilet at night).
- **Urgency** (Needing to rush to the toilet and finding it difficult to 'hold on').
- **Pain** Which gets worse as the bladder distends, and improves once the bladder empties.
- **Pain with intercourse in women** Especially in positions that put pressure on the front wall of the vagina (near the bladder).
- May mimic UTI.

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Abstract:

- **Treatment** [After exclusion and/or treatment of local pathology]:
- **1st-line treatments –**
  - **Behavioral techniques** (healthy lifestyle habits, diet modification, biofeedback, bladder retraining, pelvic muscle exercises).
  - **Oral medications** (Elmiron, anticholinergics, antispasmodics, muscle relaxants or tricyclic antidepressants).
  - **Intravesical medi**cations – DSMO.
  - Success will often be **short-lived.**

Chronic Bladder Discomfort
Abstract:

- **2nd line treatment –**
  - Sacral Neuromodulation
  - ??? Botox
- **3rd line treatments -**
  - Ablative surgical procedures.

Chronic Bladder Discomfort

Chronic bladder discomfort:

- The perception of low abdominal 'bladder' discomfort in response to bladder filling and/or emptying . It includes **Painful Bladder Syndrome** [Interstitial Cystitis].

Incidence:

- Incidence unknown
- Up to prevalence of **12,600 cases of PBS/IC per 100,000 of the population**.
- Chronic bladder discomfort has a higher incidence than this.

Chronic Bladder Discomfort

Quality of life:

- Highlighted by the **1st International Consultation on Incontinence** sponsored by the World Health Organization as a **major health issue**.
- Problems contributing to QoL issues include:

Debilitating pain	Frequency and urgency
Depressive disorders	Urge incontinence
Anxiety	Fear / embarrassment
Sleep disturbance	Inability to work

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Symptoms:

The common symptoms include:

- 'Bladder' pain
- Frequency
- Nocturia
- Urgency Pain - Urge incontinence
- Pain with intercourse in women
- Mimic UTI
- Occasionally, pelvic/vaginal pain/discomfort.

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'Causes' of Chronic Bladder Discomfort:

- Situations which cause pain in any circumstance.
- the pathological sieve should be followed.

Inflammatory causes:

- Infection [incl diverticular abscess &/or fistula]
- Tumours [bladder - but remember ovarian etc.]
- Polyps
- Stones
- Reactions to medications
- Post surgical sutures/tape/mesh.
- 'Interstitial Cystitis'

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Non-inflammatory:

- Detrusor Muscle spasm.
- **Overactive detrusor - over 45% of patients with Chronic Bladder Discomfort/pain will have OAD.**
  - Systolic contractions
  - Reduced compliance
- Detrusor sphincter dyssinergia.
- Neurogenic bladder.
- Bladder overdistension.

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Medications contributing to bladder discomfort:

- Methotrexate
- Cyclophosphamide.
- Surgam.

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Diagnosis:

- A thorough history and examination are important
  - vaginal inspection and pelvic examination must be carried out.
  - associated urinary and bowel symptoms,
  - family history,
  - co-morbidities,
  - menopause,
  - surgery – particularly pelvic surgery and medications.
- Urinalysis for blood, leukocytes, culture [and cytology] must be carried out.
- Ultrasound imaging – renal, pelvic and bladder scans.
- Urodynamic studies.
- Cystoscopy.

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Treatment:

- Treat any **underlying pathology** – UTI Tumours stones foreign bodies etc.
- Much treatment deals with the local issues – eg Anticholinergics/muscle relaxants for OAD urgency and hypersensitivity
- Many treatments have **little evidence** : Botulinum Toxin, pentosan polysulphate sodium [Elmiron], Dimethylsulphoxide [DMSO].

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Lifestyle Changes

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Lifestyle changes:

- Reducing bladder stimulants such as: caffeinated beverages.
- Pelvic Floor Exercises.
- Bladder re-training.
- Tens

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When urgency and Detrusor overactivity present:

2nd Line Treatment:

- **Pharmacology**
  - Antimuscarinics
  - Anticholinergics

NOW:

- **Beta 3 agonists**

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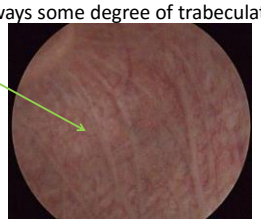
Cystoscopic findings with detrusor overactivity:

- Almost always some degree of trabeculation

Trabeculation



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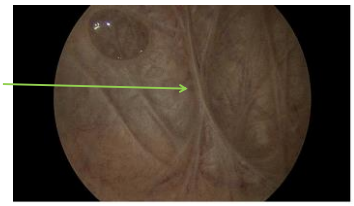
Cystoscopic findings with detrusor overactivity:

- Severe trabeculation

Trabeculation



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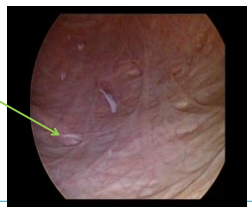
Cystoscopic findings with detrusor overactivity:

- Almost always some degree of trabeculation.
- In severe causes – diverticular formation.

More severe Trabeculation + Early Diverticulum



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Detrusor Overactivity

Treatment of OAD:

- Lifestyle changes
- Medication
- Sacral nerve stimulation [+/- medication]
- Botox
- Ablative procedures

Dry out with drugs!

Medications: [alone or in combination]

Propantheline	15-30mg tds
Endep	25 - 50mg nocte
Oxybutynin	2.5-5mg bd-tds
Trans-dermal Oxybutynin	1 patch twice a week
Solifenacin	5-10mg daily [or divided dose]
Darifenacin	7.5-15mg daily [or divided dose]
Detrusitol	1-2mg bd
Fesoterodine [not available in Australia]	
Mirabegron	25-100mg daily
Combinations often appropriate	

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Beta 3 agonists:

- **Mirabegron [Betmiga]**
  - Stimulate the Beta 3 sympathetic nerves.
  - These nerves keep the detrusor muscle relaxed.
  - Generally less side effects.
  - No anticholinergic side effects.
  - ? May increase blood pressure.
  - May take a month to work.
  - Often used in combination with another medication.
  - Occasional patient with headaches.
  - Occasional patient with itching.

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Overactive Detrusor

Beta 3 agonist [Mirabegron]
- Has transformed the medical management of OAD.
- Often used in combination with anticholinergic medication.

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Overactive Detrusor

3RD Line Treatment for OAD
- **Sacral neuromodulation [S3]**
- Botox
- Ablative surgery

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Painful Bladder Syndrome:
When other pathologies have been excluded, **Painful Bladder Syndrome** [aka interstitial cystitis] may be the problem.
- Not uncommon
- Cause unknown
- NB. Similarities with Ulcerative colitis and Crohn's disease.

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Painful Bladder Syndrome [interstitial cystitis]**:**
The painful bladder syndrome (PBS) is a spectrum of urological symptoms characterised by bladder pain with typical cystoscopic features.
- Hunners lesions - [inflammatory areas]
- Petechial haemorrhages on emptying.

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Causes of PBS:
- ?????
- ? Local causes
  - Damaged Glycosaminoglycan layer - **GAG layer .**
  - Thought to function as an antibacterial coating for the bladder by retarding the adhesion of pathogens.
  - ?triggered by infections, toxic substances auto-immune disorders or
  - **Complex sensitisation** of pain.

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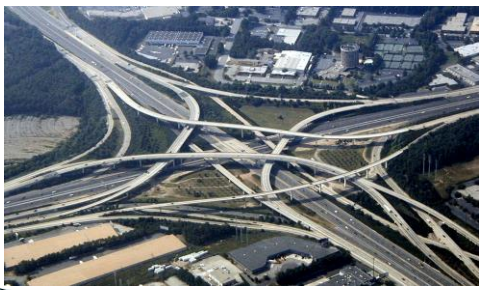
Like SPAGHETTI JUNCTION



Innervation of lower urinary tract

- So many different types of nerves.
- So many different nerve pathways.
- So many interactions between the nerves.

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Pain theoretically originates in sensory nerve receptors:

Nociceptors

- Nociceptors are the specialised sensory receptors responsible for the detection of noxious (unpleasant) stimuli.
- Transform the stimuli into electrical signals, which are then conducted to the central nervous system.
- They are the free nerve endings of primary afferent Aδ and C fibres.
- **Inflammatory mediators (eg bradykinin, serotonin, prostaglandins, cytokines, and H+) are released from damaged tissue stimulate the Nociceptors.**

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These inflammatory substances:

- Act to reduce the activation threshold of nociceptors.
- Then the stimulation required to cause activation is **less**.
- This process is called **primary sensitisation.**

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Primary afferent fibres:

- **Aβ fibres** are **highly myelinated** and of large diameter.
  - respond to light touch and transmit non-noxious stimuli.
- **Aδ fibres** are **lightly myelinated** and smaller diameter.
  - respond to mechanical and thermal stimuli.
  - responsible for the initial reflex response to acute pain.
- **C fibres** are **unmyelinated** and are also the smallest type of primary afferent fibre.
  - C fibres are polymodal, responding to chemical, mechanical and thermal stimuli.
  - C fibre activation leads to slow, burning pain.

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What happens to these nerves?

- Aδ and C fibres **synapse** with **secondary afferent neurones in the dorsal horn** of the spinal cord.
- **Complex interactions** occur in the dorsal horn between afferent neurones, interneurones and descending modulatory pathways.
- These interactions determine **activity of the secondary afferent neurones.**
- There are **two main pathways** that carry nociceptive signals to higher centres in the brain.

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Ascending Tracts:

2 main tracts –

- **The spinothalamic tract**:
  - Secondary afferent neurones decussate within a few segments of the level of entry into the spinal cord and ascend in the contralateral spinothalamic tract to **nuclei within the thalamus**.
  - **Third order neurones** then ascend to terminate in the **somatosensory cortex**. There are also projections to the **periaqueductal grey matter (PAG).**
  - Transmits signals that are important for **pain localisation**.
- **The spinoreticular tract.**

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- **The spinoreticular tract:**
  - Fibres also decussate and ascend the contralateral cord to reach the **brainstem reticular formation, before projecting to the thalamus and hypothalamus.**
  - Many further **projections to the cortex.**
  - This pathway is involved in the **emotional aspects of pain.**

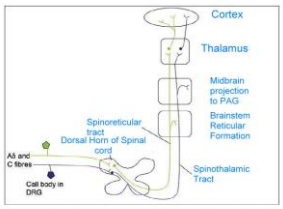

Figure 1 Ascending pain pathways. DRG dorsal root ganglion, PAG periaqueductal grey matter

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Pain processing in the brain:

- The experience of pain is **complex and subjective**,
- It is affected by factors such as **cognition (eg distraction or catastrophising), mood, beliefs and genetics**.
- The somatosensory cortex is important for the **localisation of pain**.
- Insular, anterior cingulate cortex and prefrontal cortex, and the thalamus also important.

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Why is all this important:

Visceral pain:

- Arises from the **internal organs**.
- The viscera are largely innervated by **C fibres** but also Aδ fibres.
- Visceral pain is **typically diffuse and poorly localised,** often described as deep, dull or dragging.
- It can be associated with **autonomic changes such as nausea, vomiting, and changes in heart rate or blood pressure.**
- It can also evoke **strong emotional responses**.

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Why is all this important:

Visceral pain:

- is triggered by **smooth muscle distension or contraction,**
- **stretching of the capsule** surrounding an organ,
- **ischaemia and necrosis**, irritation by chemicals produced during inflammatory processes.
- **These are factors involved in PBS!**

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But - there is more!!!

Central sensitization:

- Defined operationally as '***an amplification of neural signaling within the spinal cord & CNS that elicits pain hypersensitivity'*** **.**
- Can contribute to **inflammatory, neuropathic and dysfunctional pain disorders** in patients.
- **The pain we experience might not necessarily reflect the presence of a peripheral noxious stimulus.**

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Central Sensitisation

Central sensitization introduces another dimension:

- **one where the CNS can:**
  - change, distort or amplify pain,
  - increasing its degree, duration, and spatial extent in a manner **that no longer directly reflects the specific qualities of peripheral noxious stimuli,**
  - but **affects the particular functional states of circuits in the CNS.**

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What does this mean?

The **overwhelming conclusion** from these diverse epidemiological studies is:

- **Chronic pain hypersensitivity** in the absence of inflammation or nerve damage **results in apparently phenotypically different syndromes** depending on the tissue/organs affected.
- The **overall similarity** of the sensitivity changes may reflect a **common contribution of central sensitization**, and this may account for the **unexpectedly high comorbid rate of apparently different syndromes.**

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This comorbidity list is extensive:

migraine	rheumatoid arthritis
primary headache	premenstrual syndrome
chronic fatigue symptom	chronic urticaria
systemic lupus erythematosus	Temporomandibular disorders
irritable bowel syndrome	fibromyalgia
cervical myofascial pain syndrome	chronic prostatitis and vulvodynia
chronic pelvic pain	? U/C, Crohn's, I/C

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Can central sensitisation cause inflammation in organs?

Probably:

Magdy Hassouna, M.D., Ph.D., senior scientist, Division of Applied and Interventional Research, Toronto Western Research Institute:

- High expression of **NOS** in rats **with interstitial cystitis.**
- **NOS** has ability to send nerve impulse **backwards down sensory nerves.**
- This **releases inflammatory substances** at the origins of he sensory nerves.
- **Sacral nerve stimulation reduced the expression of the NOS and the interstitial cystitis in these rats.**

[NOS – Nitric oxide synthase]

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What can we conclude?

- This complex central sensitisation brings into question the **origins of PBS and many other conditions**.
- While there may be some initial insult, **the sensitisation in an individual may explain the pain's chronicity.**
- Explains why **most treatments are 'bandaids'.**
- **IC/PBS Patients** are universally **dissatisfied with treatment.**
- One large-scale longitudinal investigation of actively treated IC/PBS patients (n= 637, median follow-up 31 months) found **no detectable improvement in symptom severity over the period of observation** (Propert et al., 2000).

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Treatment Options:

Diet– Avoid:

- **Foods high in acid** such as citrus fruit, cranberries, strawberries, vitamin C, some herbal or green teas or tomatoes. A plain mint/chamomile tea or just water is best.
- **Foods that stimulate nerves** such as caffeine, chocolate or cola drinks.
- **Foods high in sodium or potassium** such as bananas.
- **Artificial Sweeteners** including aspartamine etc.
- **Fizzy drinks** (including mineral water). Diet cola drinks are probably the worst as they contain acid.
- **? Cigarettes.**

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Treatment of PBS

- Tricyclics [Amitriptyline]
- Pentosan polysulphate sodium [Elmiron]
- Pregabolin [Lyrica]
- Dimethylsulphoxide [DSMO]
- **Anticholinergics**
- **Muscle relaxants [beta 3 sympathomimetics - Mirabegron]**
- **Combinations of the above**
- **Sacral Nerve Stimulation**
- Ablative Surgery

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Summary:

- Chronic bladder discomfort is **not uncommon** and may be **difficult to diagnose and treat.**
- There **may be an initial insult/physical process** to set up a pain response but the **chronicity is more likely related to sensitisation in the spinal cord** and other factors in the individual.
- Whether this implies some **genetic susceptibility or situational cause is unclear.**
- After excluding remedial causes, **treatment is difficult and usually short-lived.**

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Remember:

- Chronic Pain is more about **sensitivity** than about **injury**.
- **Treatment** is about finding the **appropriate stressor**.
- The patient is an **active participant in their own care**.
- Pain is [**not necessarily**] a normal response to a noxious stimulus.
- Perception of pain **may vary**.
- Perception will depend on **many other coexisting physical and emotional circumstances**.
- Will also depend on the **actual source/origin of the pain**.