

IN THE NAME OF GOD

Bladder pain syndrome

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SUMS

- ▶ Bladder pain syndrome/interstitial cystitis (BPS/IC) is a **condition diagnosed on a clinical basis and requiring a high index of suspicion on the part of the clinician.**
- ▶ Simply put, it should be considered in the **differential diagnosis of the patient presenting with chronic pelvic pain that is often exacerbated by bladder filling and associated with urinary frequency.**
- ▶ It is a **diagnosis of exclusion in a patient who has experienced the symptoms for at least 6 weeks**
- ▶ To embrace all patients suffering from bladder pain, the terms **painful bladder syndrome (PBS) or BPS have been suggested as more accurate when referring to pain in the bladder region**

Definition

- ▶ **Persistent or recurrent pain perceived in the urinary bladder region.**
- ▶ **Accompanied by at least one other symptom, such as pain worsening with bladder filling and day-time and/or nighttime urinary frequency**
- ▶ **Absence of any proven infection or other obvious local pathology.**

nature of pain

The nature of pain is key to disease definition

- ❖ Pain, pressure or discomfort perceived to be related to the bladder, increasing with increasing bladder content.
- ❖ Located suprapubically, radiating to the groins, vagina, rectum or sacrum.
- ❖ Relieved by voiding but soon returns
- ❖ Aggravated by food or drink

Prevalence

- ▶ Symptoms compatible with the diagnosis are now thought to affect up to 3% of the female population
- ▶ The lack of accepted definition, the absence of validated diagnostic marker and questions regarding etiology and pathophysiology make much of the literature difficult to interpret.
- ▶ 1.2- 4.5 per 100,000 females in Japan , to a questionnaire-based study that suggests a figure in American women of 20,000 per 100,000

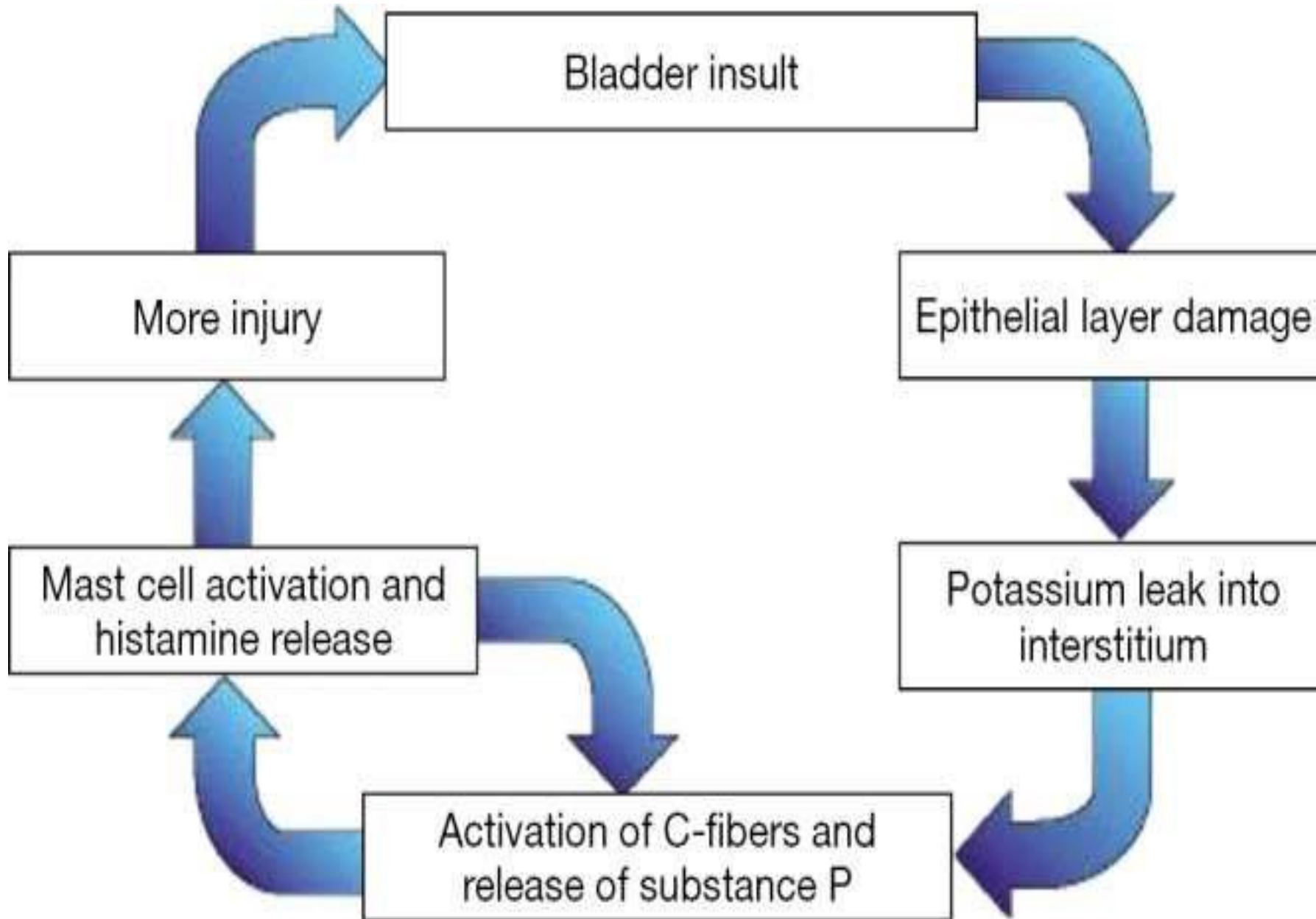
Etiology

- ▶ BPS has no known single aetiology.
- ▶ Initial unidentified insult to the bladder >>> Urothelial damage >>> neurogenic inflammation >>> Pain.

OR

- ▶ Local manifestation of a systemic disorder.
- ▶ Urinary infection is significantly more frequent during childhood and adolescence, in patients with BPS in adulthood

Cystoscopic and biopsy findings in both lesion and non-lesion BPS are consistent with defects in the urothelial glycosaminoglycan (GAG) layer, which might expose submucosal structures to noxious urine components and a consequent cytotoxic effect.



Association with other diseases

An association has been reported between BPS and non-bladder syndromes (NBSs) such as:

fibromyalgia(FM), chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), vulvodynia, depression, panic disorders, migraine, sicca syndrome, temporomandibular joint disorder, allergy, asthma and systemic lupus erythematosus,

DIAGNOSIS

- ▶ It has now morphed largely into a diagnosis of chronic pain, pressure, or discomfort associated with the bladder, usually accompanied by urinary frequency in the absence of any identifiable cause
- ▶ Diagnostic approaches vary widely, and general agreement on a diagnostic algorithm remains a **future goal**

- ▶ A presumptive diagnosis can be made merely by ruling out known causes of frequency, pain, and urgency in a patient with compatible chronic symptoms
- ▶ Often this will involve a complete history, physical examination, appropriate cultures, and local cystoscopy.
- ▶ A finding of tenderness on examination of the anterior vaginal wall with an empty bladder at the initial examination can lead one to suspect BPS.

Lab tests

- ▶ Urine dipstick and urine culture (including culture for TB if sterile pyuria) are recommended in all patients suspected of having BPS.
- ▶ Urine cytology is also recommended in risk groups (as in patients older than 40 and those with a smoking history)

it must be recognized that one may sacrifice a certain level of confidence in the diagnosis without the supporting evidence that can be furnished by additional studies. In a long-term illness such as BPS/IC, many patients and physicians ultimately want to base a diagnosis and treatment plan on the most complete data set possible.

Other evaluations

- ▶ Cystoscopy with or without hydrodistension under G/A (optional)
- ▶ Urodynamics(optional) (nl function ,the exception being decreased bladder capacity and hypersensitivity)
- ▶ Bladder biopsy (optional) (to R/O other disorders that might be suggested by the cystoscopic appearance)

Cystoscopy

- ▶ reddened mucosal areas often associated with small vessels radiating towards a central scar, sometimes covered by a small clot or fibrin deposit (**Hunner lesion**) **About 10% patients have Hunner`s ulcer**
- ▶ **Glomerulations** after hydrodistension is considered to be a positive diagnostic sign. **Pinpoint petechial hemorrhage that developed throughout the bladder after distension. Are not specific for BPS**
- ▶ **NI cystoscopy 8.7 %**
- ▶ **Distended twice to 80 cm of H2O for 1-2 min**

Cystoscopy view

Hunner Ulcer



Glumerulation



Treatment Options

A) Conservative Therapy

B) Interventions:

1. Oral pharmacologic agents
2. Intravesical therapy
3. Surgical therapies

Conservative Therapies

If the patients symptoms are tolerable and do not significantly impact quality of life, a policy of withholding treatment is reasonable.

▶ Behavioral and physical therapy:

- Biofeedback
- pelvic floor rehabilitation
- bladder training programs (progressively increasing the voiding interval over the course of weeks to months)
- Stress reduction, exercise, warm tub baths
- ▶ They are excellent initial interventions and have been used by some authors with some success.
- ▶ The **urinary frequency and urgency components seem to respond better** to these interventions than the pelvic pain component.

Dietary Therapy

- ▶ Dietary restrictions are unsupported by any literature (Campbell) , but EAU guideline stated that consider diet avoidance of triggering substances (GR C).
- ▶ Many patients do find their symptoms are adversely affected by specific foods and would do well to avoid them.
- ▶ Often this includes caffeine, alcohol, artificial sweeteners, hot pepper, and beverages that might acidify the urine such as cranberry juice.

Medical Treatment

Amitriptyline

- ▶ (EAU) Amitriptyline is effective for pain and related symptoms of BPS (LE 1b)
- ▶ Mechanism: blockade of acetylcholine receptors, inhibition of serotonin and noradrenalin reuptake, and blockade of histamine H1 receptors. It is also an anxiolytic agent.
- ▶ Median preferred dose is 50 mg in a range of 25 to 150 mg/day. The speed of onset of effect is 1 to 7 days.
- ▶ Drowsiness is a limiting factor with amitriptyline, and thus, nortriptyline is sometimes considered instead.

Anti-Histamins

- ▶ **Hydroxyzine:** No significant response was found in an NIDDK placebo-controlled trial. It has **limited efficacy** in BPS (LE 3).
- ▶ **Cimetidine:**
 - **(Campbell)** Uncontrolled studies show improvement of symptoms in two thirds of patients taking it in divided doses totaling 600 mg. Cimetidine is a common treatment in the United Kingdom, where over a third of patients reported having used it.
 - **(EAU)** Limited data exist on effectiveness of cimetidine in BPS (LE 2b) and it can be considered as a valid oral option before invasive treatments (GR B)

Pentosan Polysulphate Sodium

- ▶ Oral PPS is effective for pain and related symptoms of BPS (LE 1a) and could be offered oral pentosanpolysulphate sodium for the treatment of BPS (GR A).
- ▶ It is thought to repair defects in the GAG layer.
- ▶ 150-200 mg twice daily between meals

- ▶ Subjective improvement of pain, urgency, frequency, but not nocturia, has been reported.
- ▶ PPS had a **more favorable effect in BPS with lesion** than in non-lesion disease.
- ▶ **Approved dosage is 100mg TDS.**
- ▶ At 32 weeks, about half the patients responded. So
- ▶ **a 3- to 6-month treatment trial is generally required to see symptom improvement.**

Antibiotics

- ▶ **Antibiotics have no role in BPS due to the lack of evidence (EAU).**
- ▶ There is no evidence to suggest that antibiotics have a place in the therapy for BPS in the absence of a culture-documented infection.
- ▶ Nevertheless, it would not be unreasonable to treat patients with **one empirical course of antibiotic (Doxy is recommended)** if they have never been on an antibiotic for their urinary symptoms (Campbell).

Immunosuppressants

- ▶ **Cyclosporin A**: might be used in BPS but adverse effects are significant and should be carefully considered (GR B).
- ▶ Initial evaluation of **cyclosporin A** and **methotrexate** showed good analgesic effect but limited efficacy for urgency and frequency.
- ▶ **Azathioprine** treatment has resulted in disappearance of pain and urinary frequency.
- ▶ In an aborted multicenter randomized placebo-controlled NIDDK trial, **mycophenolate mofetil** (Cellcept 1 to 2 g/day in divided doses) failed to show efficacy in the treatment of symptoms of refractory BPS/IC.

Analgesics

- ▶ Urologists should preferably use analgesics in collaboration with pain clinics.
- ▶ **The long-term, appropriate use of pain medications forms an integral part of the treatment of a chronic pain condition such as IC.**
- ▶ Many non-opioid analgesics including **acetaminophen** and the **NSAIDs** and even **antispasmodic agents** have a place in therapy along with agents designed to specifically treat the disorder itself.

Others

- ▶ **Corticosteroids** are not recommended in the management of patients with BPS because of a lack of evidence (GR C).
- ▶ **Gabapentin** might be considered for oral treatment of BPS (GR C).
- ▶ **Prostaglandins (e.g. misoprostol)**: are not recommended. Insufficient data on BPS, adverse effects are considerable (GR C).
- ▶ **Duloxetine**: *inhibits both serotonin and noradrenaline reuptake.* **Duloxetine shows no efficacy, and tolerability is poor (LE 2b)**

- ▶ ***L-Arginine***: The body of evidence does not support the use of L-arginine for the relief of symptoms of IC.
- ▶ ***Nifedipine***. inhibits smooth muscle contraction and cell-mediated immunity. In one pilot study, with use of 30 mg daily within 4 months, 50% of patients showed at least a 50% decrease in symptom scores and 3 of the 5 were asymptomatic. No further studies have been reported.
- ▶ ***Montelukast***: In a pilot study, with 10 mg of montelukast daily for 3 months, frequency, nocturia, and pain improved dramatically in 80% of the patients.

Intravesical treatment

- ▶ Intravesical drugs are administered due to poor oral bioavailability establishing high drug concentrations at the target, with few systemic side-effects.
- ▶ Dimethyl sulfoxide (DMSO), glycosaminoglycans
- ▶ Disadvantages include the need for intermittent catheterization, which can be painful in BPS patients, cost, and risk of infection.



Bladder Hydrodistention

- ▶ Following diagnostic hydrodistention, therapeutic hydrodistention may be performed.
- ▶ **This is usually performed at 80-100 cm water for 8-10 minutes.**
- ▶ Although bladder hydrodistension is a common treatment for BPS, the scientific justification is scarce. It can be a part of the diagnostic evaluation, but **has a limited therapeutic role.**
- ▶ **Any efficacy is probably related to damage to mucosal afferent nerve endings**
- ▶ **Bladder distension should only be used as diagnostic (LE 3) and is not recommended as a treatment of BPS (GR C).**

Interventional treatments

- ▶ ***Bladder distension:*** it is a good diagnostic tool, but has a limited therapeutic role.
- ▶ ***TUR:*** *eliminate* urothelial, mostly Hunner, lesions.
- ▶ ***Botulinum toxin A (BTX-A):*** *may have an antinociceptive effect on bladder afferent pathways, producing symptomatic and urodynamic improvements*

Surgical treatment

When all efforts fail to relieve disabling symptoms, surgical removal of the diseased bladder is the ultimate option, for which three major techniques are common:

- ❖ supratrigonal cystectomy
- ❖ subtrigonal cystectomy
- ❖ radical cystectomy + excision of the urethra.



باغ ارم - شیراز