Bladder Pain Syndrome (Interstitial Cystitis)

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BPS/IC

- Chronic condition characterized by pelvic pain, pressure or discomfort accompanied by lower urinary tract symptoms
- International Society for the Study of BPS (ESSIC) definition
  - *"Chronic pelvic pain, pressure or discomfort of >6 months duration, perceived to be related to the urinary bladder, accompanied by at least one other urinary symptom as persistant urge to void or urinary frequency. Confusable diseases as the cause of the symptoms must be excluded."*
- The American Urological Association definition
  - *"An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in tha absence of infection or other identifiable causes."*

Incidence & Prevalance

- 5:1 felame-to-male dominance
- Mean average age of 51 years
- Estimated prevalence of 100-200/100.000
- Incidence varies in different populations worldwide

Pathogenesis

- Pathogenesis is unclear
- Unknown mutual effect triggers immune and neuroendocrine factors
- Provoking an inflammatory response in the urothelium

- Increased permeability
- Urothelial dysfunction

Patient with Possible Interstitial Cystitis

Patient with possible interstitial cystitis

History

Symptoms:
Urgency, frequency, suprapubic/pelvic pain, dyspareunia, flare-ups and remissions

Commonly associated conditions:
Migraine, vulvodynia, fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome

Triggers:
Diet
Sexual activity
Allergens

Physical examination:
Bladder neck tenderness on bimanual examination

Rule out:
Preinvasive and invasive lesions with urine cytology or cystoscopy and biopsy
Urinary tract infections with urine culture and sensitivity

Confirmation:
Cystoscopy and hydrodistention under anesthesia or office cystoscopy and trial of therapy; consider potassium sensitivity test

24-hour voiding log

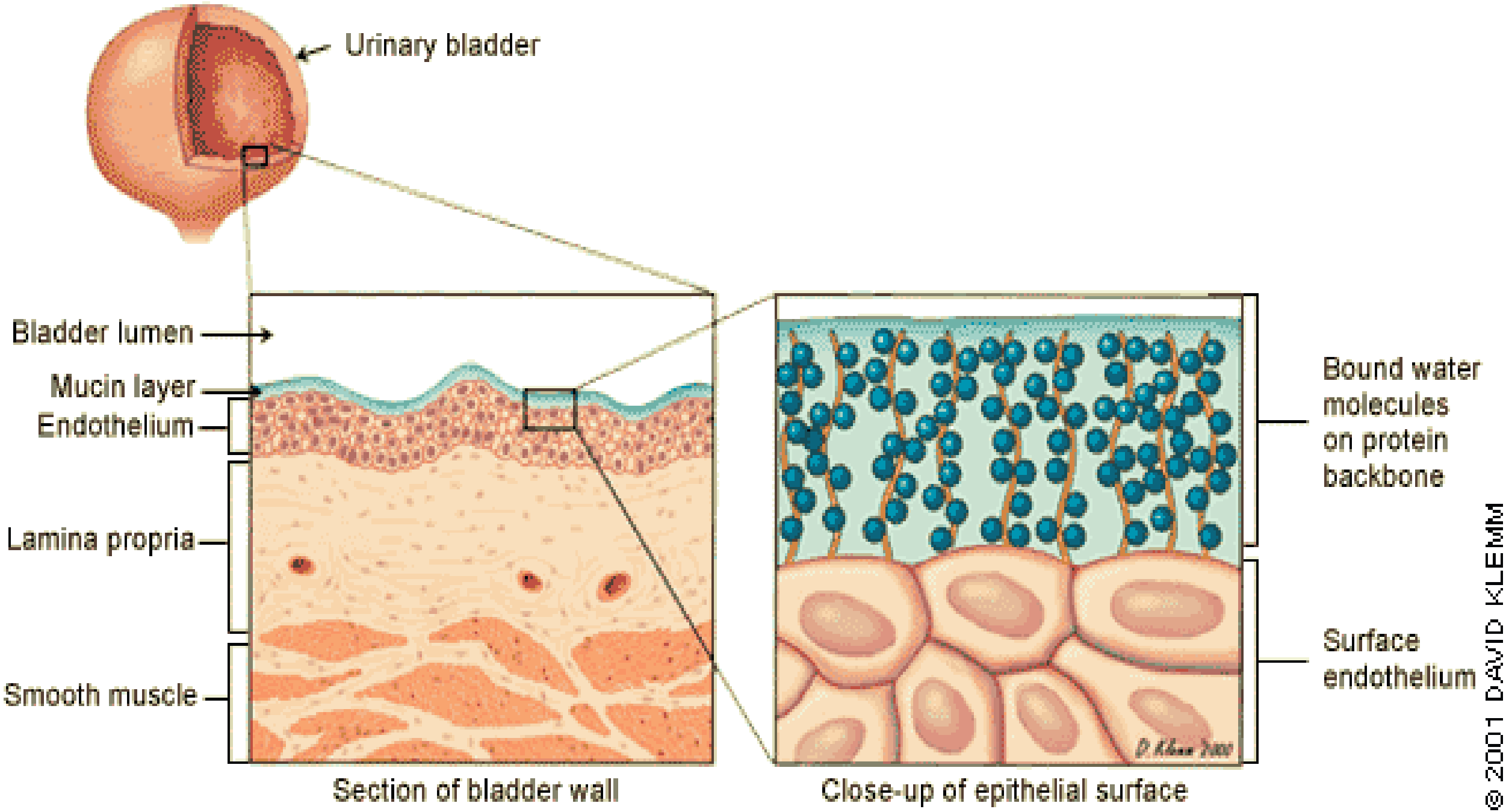
Interstitial cystitis

Etiological Factors

- Urinary toxic substances
- Infections
- Immune cell activation(mast cell)
- Autoimmune mechanisms
- Autonomic nerve changes
- Inhibition of bladder urothelial cell proliferation
- Decreased microvascular density resulting in hypoxia
- Genetic predisposition

The Importance of Urothelium

- Barrier to irritants in urine
- Glycosaminoglycans, chondroitin sulfate and sodium hyaluronate
- Intercellular junctions


Urinary bladder
Bladder lumen
Mucin layer
Endothelium
Lamina propria
Smooth muscle
Bound water molecules on protein backbone
Surface endothelium
Section of bladder wall
Close-up of epithelial surface
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Diagnosis

- No objective tool nor a pathognomonic finding
- Criteria differ among international societies
- Medical history including questions about suprapubic pain related to bladder filling
- Voiding diaries
- Validated questionnaires
- Physical examination
- Neurological examination and pelvic muscle strength assessment
- Urinary dipstick and urine culture
- Urodynamic tests (not routine) may allow detrusor over activity or reduced bladder capacity
- Cystoscopy

European Association of Urology (EAU) Guidelines 2020

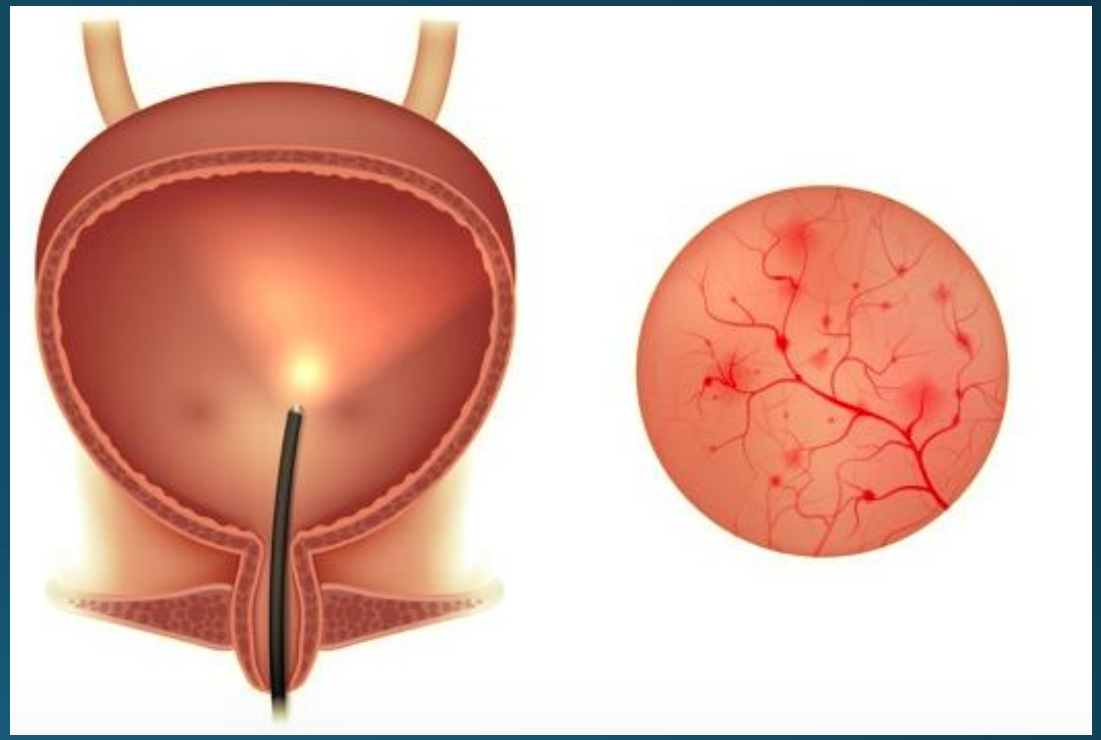
4.5.2 ***Diagnostic evaluation of BPS***

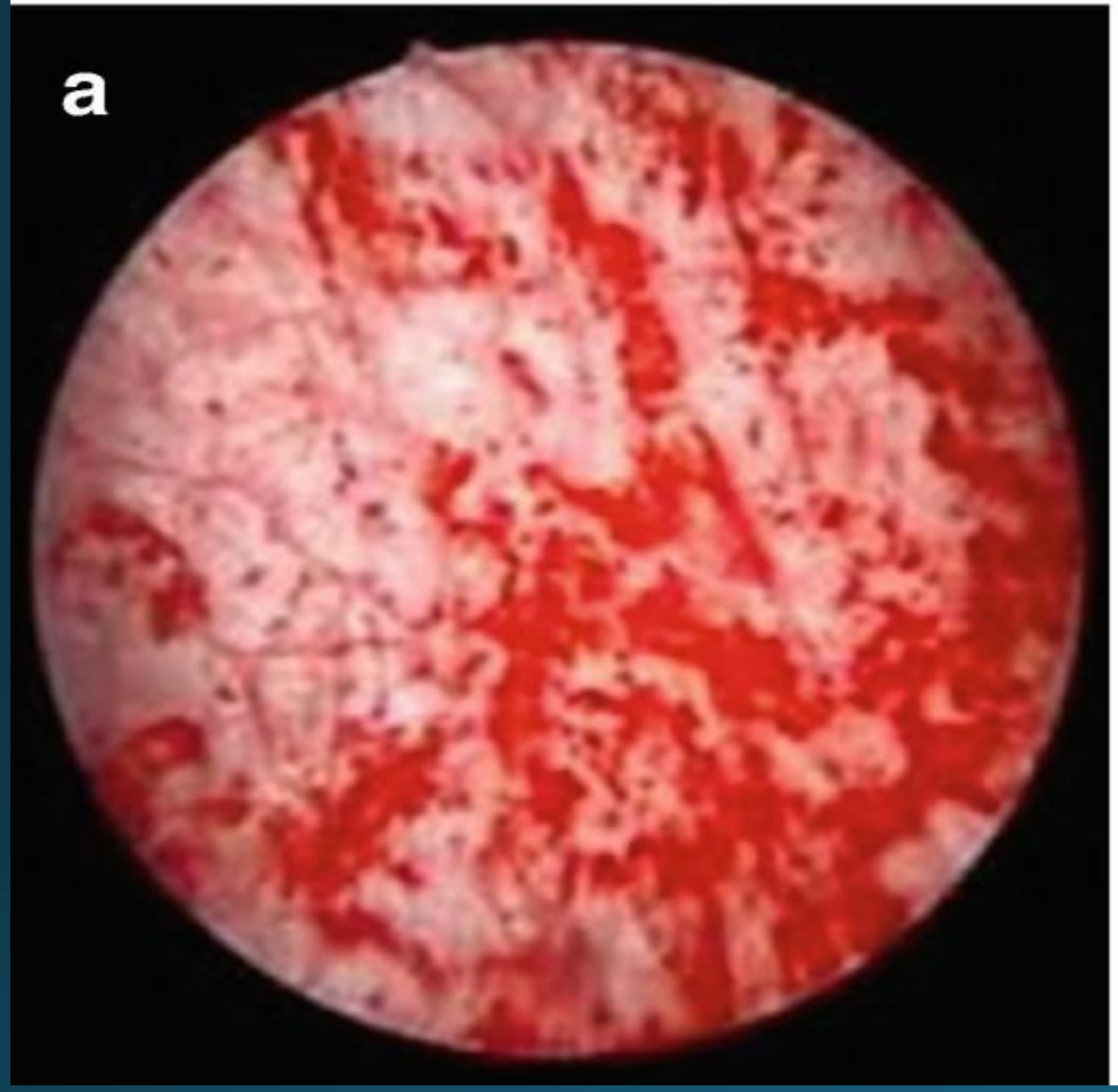
Summary of evidence	LE
BPS has no known single aetiology.	3
Pain in BPS does not correlate with bladder cystoscopic or histologic findings.	2a
BPS Type 3 C can only be confirmed by cystoscopy and histology.	2a
Lesion/non-lesion disease ratios of BPS are highly variable between studies.	2a
The prevalence of BPS-like symptoms is high in population-based studies.	2a
BPS occurs at a level higher than chance with other pain syndromes.	2a
BPS has an adverse impact on QoL.	2a
Reliable instruments assessing symptom severity as well as phenotypical differences exist.	2a

Recommendations	Strength rating
Perform general anaesthetic rigid cystoscopy in patients with bladder pain to subtype and rule out confusable disease.	Strong
Diagnose patients with symptoms according to the EAU definition, after primary exclusion of specific diseases, with bladder pain syndrome (BPS) by subtype and phenotype.	Strong
Assess BPS associated non-bladder diseases systematically.	Strong
Assess BPS associated negative cognitive, behavioural, sexual, or emotional consequences.	Strong
Use a validated symptom and quality of life scoring instrument for initial assessment and follow-up.	Strong

Cystoscopic Evaluation

- Hunner's lesions (%10-15)
- Glomerulations
- Exclusion of malignancy
- Hydrodistension





a. Glomerulation b. Hunner's Ulcer

Table 4: ESSIC classification of BPS types according to results of cystoscopy with hydrodistension and biopsies [11]

	Cystoscopy with hydrodistension			
	Not done	Normal	Glomerulations[a]	Hunner's lesion[b]
Biopsy				
Not done	XX	1X	2X	3X
Normal	XA	1A	2A	3A
Inconclusive	XB	1B	2B	3B
Positive[c]	XC	1C	2C	3C

[a]*Cystoscopy: glomerulations grade 2-3.*

[b]*Lesion per Fall's definition with/without glomerulations.*

[c]*Histology showing inflammatory infiltrates and/or detrusor mastocytosis and/or granulation tissue and/or intrafascicular fibrosis.*

Management

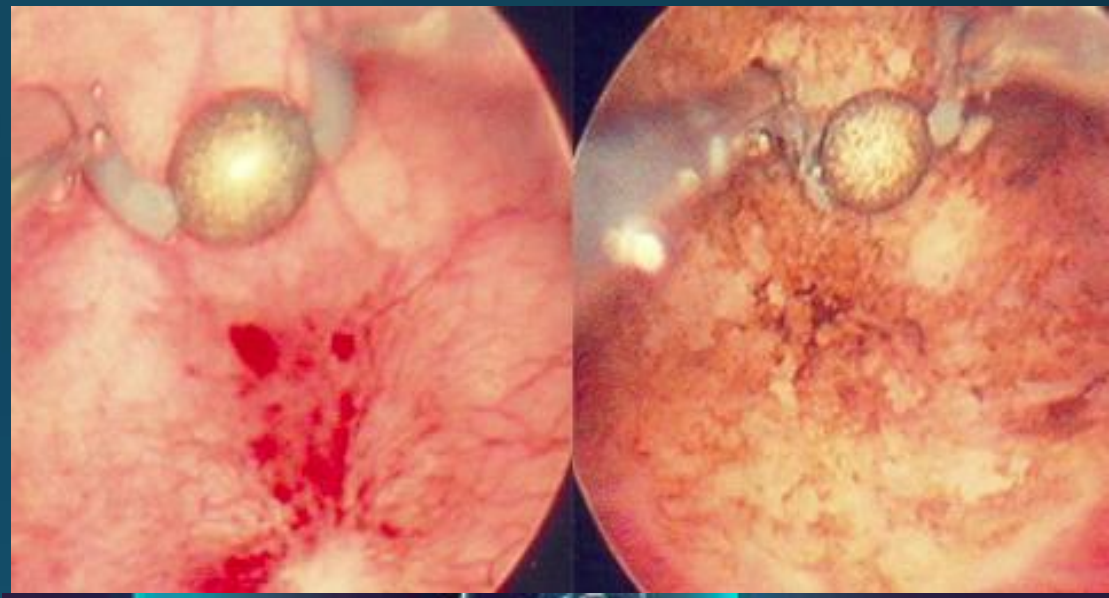
- Stepwise manner
- Conservative to more invasive treatment approaches

Conservative Treatment

- Behavioral modifications
- Physical therapy
- Stress reduction
- Dietary manipulations

Medical Treatments

- Systemic
- Intravesical
- Surgical

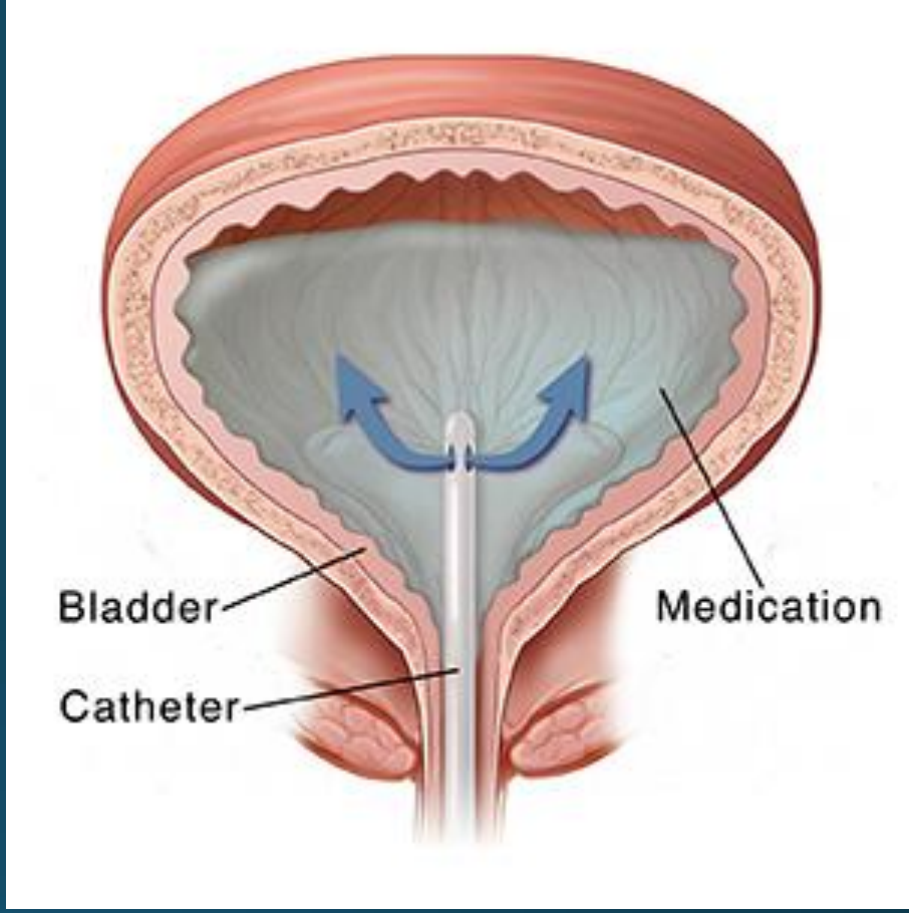


Systemic Treatment

- Non-steroidal anti-inflammatory drusg
- Anti-depressants (amitriptyline)
- Antihistamines (cimetidine, hydroxyzine)
- Immunosuppressants (cyclosporine)
- Sodium pentosan polysulfate

Intravesical Treatment

- Dimethyl sulfoxide
- Hyaluronic acid (HA)
- Chondrotin sulfate
- Lidocaine (effect on alkalisation)
- Heparin
- Combination of heparin, lidocaine and sodium bicarbonate



Surgical Treatments

- Hydrodistension
- Fulgarisation of Hunner ulcers
- Intravesical botulinum toxin A inj
- Sacral neuromodulation
- Cystoplasty or urinary diversion

Treatments of limited value for BPS/IC

- Cimetidine
- Prostaglandins
- L-Arginine
- Oxybutynin
- Duloxetine

5.4.2 *Management of BPS*

Summary of evidence	LE
There is insufficient data for the long-term use of corticosteroids.	3
Limited data exist on effectiveness of cimetidine in BPS.	2b
Amitriptyline is effective for pain and related symptoms of BPS.	1b
Oral pentosane polysulphate is effective for pain and related symptoms of BPS.	1a
Oral pentosane polysulphate plus subcutaneous heparin is effective for pain and related symptoms of BPS, especially in initially low responders to pentosane polysulphate alone.	1b
Intravesical lidocaine plus sodium bicarbonate is effective in the short term.	1b
Intravesical pentosane polysulphate is effective, based on limited data, and may enhance oral treatment.	1b
There are limited data on the effectiveness of intravesical heparin.	3
Intravesical chondroitin sulphate may be effective.	2b
There is insufficient data for the use of bladder distension as a therapeutic intervention.	3
Hydrodistension plus BTX-A is superior to hydrodistension alone.	1b
Intravesical BCG is not effective in BPS.	1b
Transurethral resection (coagulation and laser) may be effective in BPS type 3 C.	3
Sacral neuromodulation may be effective in BPS.	3
Pudendal nerve stimulation is superior to sacral neuromodulation for treatment of BPS.	1b
Avoidance of certain foods and drink may reduce symptoms.	3
Outcome of cystectomy for BPS is variable.	3

Recommendations	Strength rating
Offer subtype and phenotype-oriented therapy for the treatment of Bladder Pain Syndrome (BPS).	Strong
Always consider offering multimodal behavioural, physical and psychological techniques alongside oral or invasive treatments of BPS.	Strong
Offer dietary advice.	Weak
Administer amitriptyline for treatment of BPS.	Strong
Offer oral pentosane polysulphate for the treatment of BPS.	Strong
Offer oral pentosane polysulphate plus subcutaneous heparin in low responders to pentosane polysulphate alone.	Weak
Do not recommend oral corticosteroids for long-term treatment.	Strong
Offer intravesical hyaluronic acid or chondroitin sulphate before more invasive measures.	Weak
Offer intravesical lidocaine plus sodium bicarbonate prior to more invasive methods.	Weak
Offer intravesical heparin before more invasive measures alone or in combination treatment.	Weak
Do not use bladder distension alone as a treatment of BPS.	Weak
Offer submucosal bladder wall and trigonal injection of botulinum toxin type A (BTX-A) plus hydrodistension if intravesical instillation therapies have failed.	Strong
Offer neuromodulation before more invasive interventions.	Weak
Only undertake ablative organ surgery as the last resort and only by experienced and BPS-knowledgeable surgeons.	Strong
Offer transurethral resection (or coagulation or laser) of bladder lesions, but in BPS type 3 C only.	Strong
Offer intravesical bladder wall and trigonal injection of BTX-A if intravesical instillation therapies have failed.	Strong
Do not recommend oral corticosteroids for long-term treatment.	Strong
Do not use bladder distension as a treatment of BPS.	Weak

Physiotherapy in BPS

- Thiele massage (Transvaginal manuel therapy of the pelvic floor musculature)
- Levator ani trigger point injections
- Bupivacaine, lidocaine and triamcinolone
- %72 showed improvement with the first trigger point injection
- %33 completely pain-free
- Pelvic floor myofascial physical therapy vs. global therapeutic massage in women with BPS
  - Global response asessment rate was 59% vs 26% respectively
  - Pain urgency and frequency ratings, and symptoms decreased in both groups with no significant difference