Interstitial Cystitis/Bladder Pain Syndrome 2021

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1

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† All financial ties (over the last year) that you may have with any business organisation with respect to the subjects mentioned during your presentation

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2

Evidence Acquisition

755 publications in English reviewed, published since last Consultation

Level of evidence and grade of evidence according to Oxford Scale

Diagnosis, aetiology, pathophysiology open to interpretation as to use of Oxford system, which is primarily relevant for treatment only

3

Nomenclature

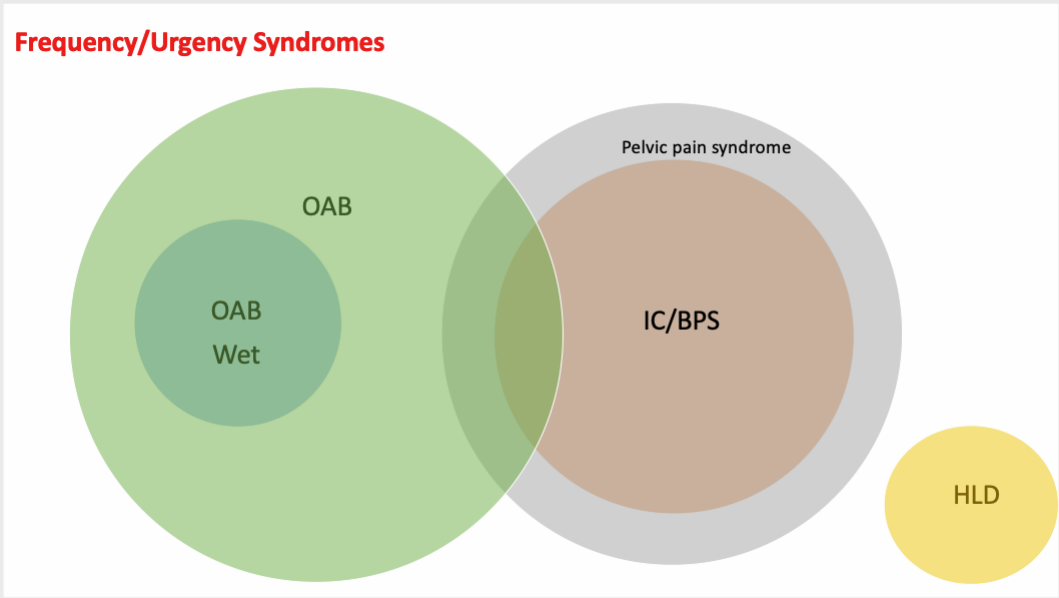
Interstial Cystitis/Bladder Pain Syndrome IC/BPS

- Interstitial cystitis and bladder pain syndrome are essentially interchangeable as there is no accepted definition that clearly delineates the interstitial cystitis syndrome from bladder pain syndrome.

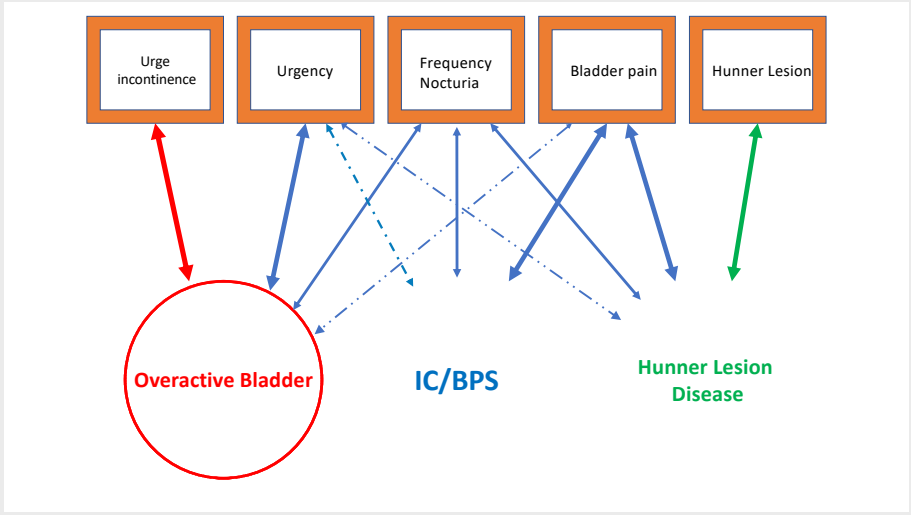
Hunner lesion disease (HLD)

- Patients who meet the definition of IC/BPS and are found to have Hunner lesion(s) on cystoscopic examination

4


Frequency/Urgency Syndromes
OAB
OAB
Wet
Pelvic pain syndrome
IC/BPS
HLD

5


Urge incontinence
Urgency
Frequency Nocturia
Bladder pain
Hunner Lesion
Overactive Bladder
IC/BPS
Hunner Lesion Disease

6

Definitions

IC/BPS: Based on ESSIC and AUA guideline

- Pain, pressure or discomfort perceived to be related to the urinary bladder of 6 weeks (AUA) 6 months (ESSIC) duration when accompanied by at least one other urinary symptom in the absence of a confusable disorder
- No pathognomonic histopathological findings; essentially diagnosis of exclusion

HLD

- Patients meet IC/BPS diagnostic requirement and have Hunner lesion on cystoscopy confirmed by histopathology

7

Epidemiology

Reasonable prevalence estimation 300/100,000 women based on O'leary Sant surveys in Europe and Asia

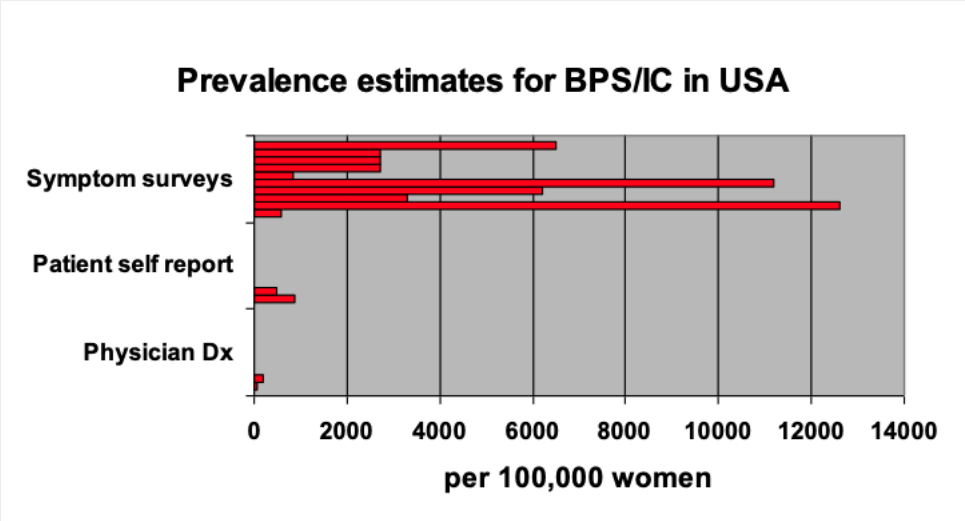
Male prevalence 10-20% of female estimate, potentially up to 60% based on Rand epidemiology survey

Prevalence of women and men with symptoms suggestive of IC/BPS could be 10X based on USA Rand Survey

Epidemiological data required to describe long term progression patterns of IC/BPS is lacking

8

Epidemiology related to methodology

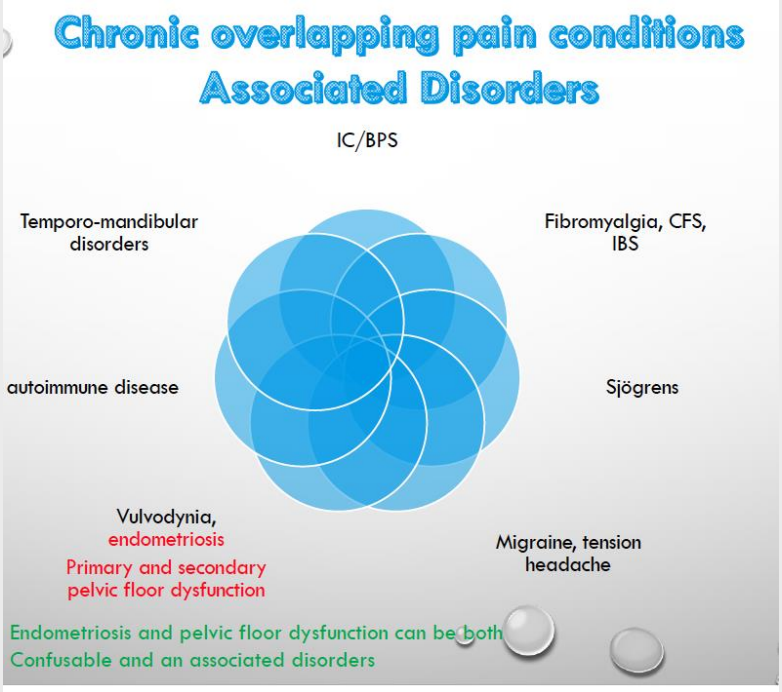


9

Disease Impact

1. Long delay from symptom onset to diagnosis
2. Symptom can be refractory to treatment
3. Lowers quality of life physically and mentally with impact similar to rheumatoid arthritis and renal dialysis
4. Direct medical costs double compared to non-IC/BPS patients
5. Indirect costs are 84% higher
6. 10% unable to work at all due to IC/BPS symptoms
7. 19% experience loss of wages in preceding 3 months

10



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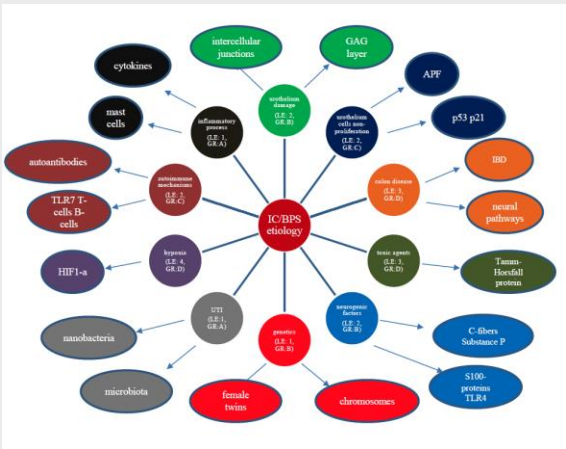
- The etiology of IC/BPS remains a wide-open field for investigation.
- Study of Hunner lesion disease etiology awaits its recognition as a specific entity apart from IC/BPS.

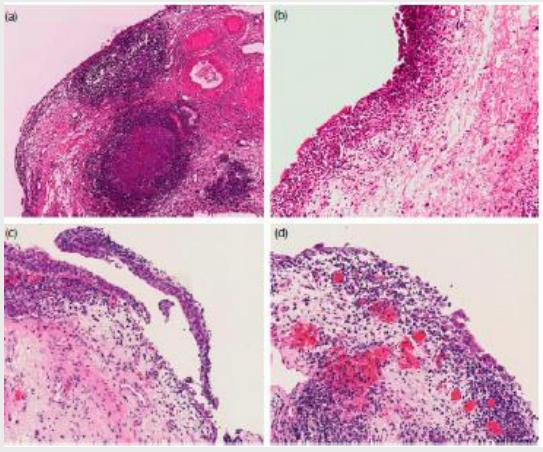


12

Pathology

Hunner Lesion Histopathology

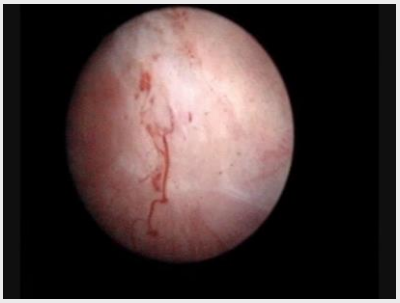
- Bladder histopathology plays a supportive diagnostic role at best
- Hunner-lesion disease not only is different clinically from IC/BPS, but also exhibits histological differences such as significant inflammation and denudation in the bladder, which are clinically and pathologically distinct from IC/BPS



13

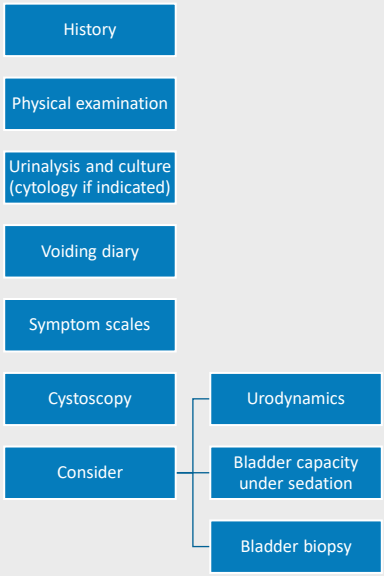
expert opinion: level evidence 4, grade C

- IC/BPS diagnosis of exclusion based on symptoms and exclusion of confusable disorders
- HLD symptoms plus presence of Hunner lesion



14

Diagnostic Steps



Goal to rule out common confusable conditions

- pelvic floor dysfunction
- overactive bladder
- infection
- pudendal neuropathy
- endometriosis
- vulvodynia

Goal to identify associated disorders

15

Principles of Management: Expert Opinion

- Decision on management should be evidence based
- We should be guided by patient perceived and driven outcomes
- Many patients prefer noninvasive therapies
- Early diagnosis of HLD is critical (engages separate Rx algorithm)
- Natural history of IC/BPS
  - Up to 50% patients improve regardless of treatment or follow up
  - Symptom duration generally not associated with symptom severity
  - Symptom duration not associated with risk for overlapping pain comorbidities or mental health comorbidities
  - Catastrophizing increases morbidity

16

Principles of Management Continued

- ❑ Tailor treatment to symptoms
- ❑ Consider multidisciplinary approach
- ❑ Time can be the ally of patient and provider
- ❑ Add to initial therapy if necessary, substitute if ineffective
- ❑ Generally proceed from conservative therapy to invasive therapy

17

Initial Management

- ➢ Education

Internet Sites

(1)The Interstitial Cystitis Association (ICA)

web site: https://www.ichelp.org/

(2)Taiwan interstitial cystitis Association (TICA)

web site:http://www.ticataiwan.org/ContentAspx/index.aspx

(3) International Painful Bladder Foundation (IPBF)

web site: http://www.painful-bladder.org/IPBFwho_are_we.html

(4) Society of Interstitial cystitis Japan (SICJ)

web site: http://sicj.umin.jp/

(5) Netherlands Interstitial Cystitis Patients Organization (ICP)

web :https://www.sip-platform.eu/sip-platform/endorsers/details/netherlands-interstitial-cystitis-patients-organization-icp

(6) Interstitial Cystitis Network.

Web: htpp://www.ic-network.com

18

Conservative therapy

- Behavioral modification: Level Evidence 2; Grade B
- Physical therapy: Level of Evidence 1; Grade A
- Stress reduction: Level of Evidence 4; Grade C
- Dietary Manipulation: Level of Evidence 2; Grade B
- Early Identification of nonurological symptoms and psychosocial dysfunction as separate and exacerbating clinical factors: Hypothesis

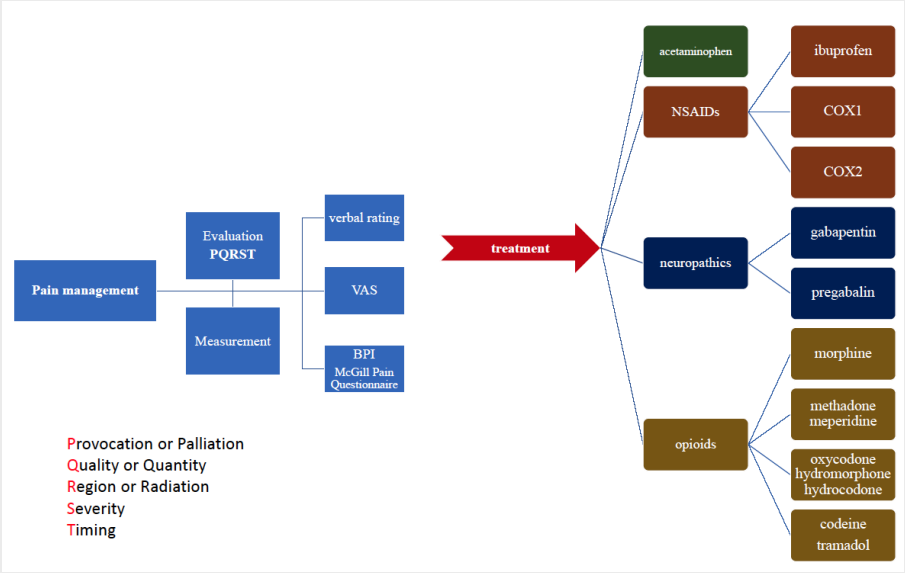
19

Oral Therapy

Modality	Representatives	Level of Evidence	Recommendation
Analgesics	Acetaminophen NSAIDs Neuropathics Opioids	4	C
Tricyclic Antidepressants	Amitriptyline	2	B
Antihistamines	Pyribenzamine Hydroxyzine Cimetidine	3	C
Immunosuppressants	Cyclosporine	2	C
	IPD-1151T Prednisone	1 4	Not recommended
Permeability regulators	Pentosan polysulfate	1	D
Other treatments	Quercetin	4	D
	Antibiotics	2	Not recommended
	Methotrexate	4	Not recommended
	Montelukast	4	Not recommended
	Nifedipine	4	Not recommended
	Misoprostol	4	Not recommended
	Sildenafil	2	D
	L-Arginine	2	Not recommended
	Adalimumab	1	Not recommended
Cannabinoids	Palmitoylethanolamide	2	D

20

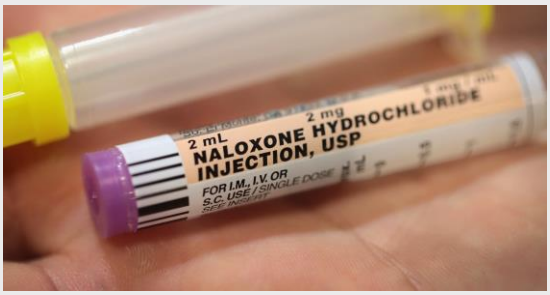
Analgesics



21

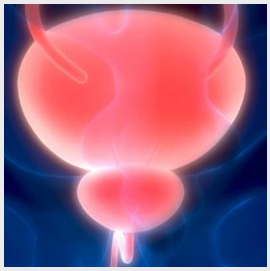
Use of Narcotics

- Chronic opioids are best considered in patients not responsive to nonopioid analgesics or standard therapies.
- Consult a pain management expert and move this portion of care to a pain clinic where available that will be responsible for all prescribed analgesic and can institute a pain contract with patient.
- Educate patients and their families on the use of rescue medication in the event of overdose and have such medications available



22

Intravesical Therapy

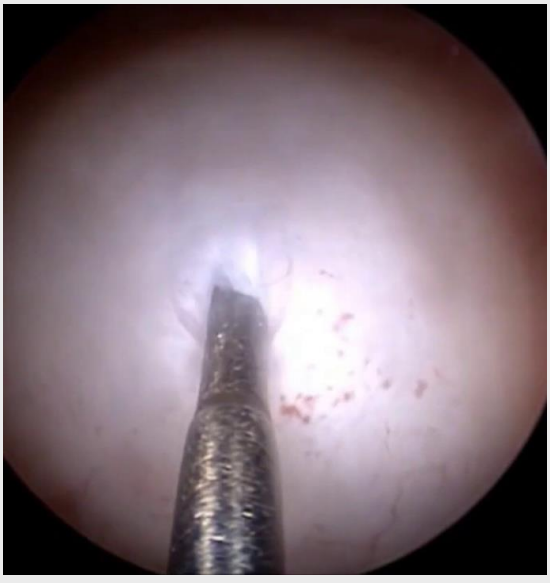


MEDICATION	RECOMMENDATION	LEVEL OF EVIDENCE
Dimethyl Sulfoxide 50%	B	1
Heparin	C	3
Hyaluronic Acid	C	1
Chondroitin Sulfate	C	1
Hyaluronic Acid plus Chondroitin Sulfate	C	2
Lidocaine	C	1
Silver nitrate	Not recommended	3
Chlorpactin WCS90	C	3
Pentosan Polysulfate	D	4
Vanilloids	Not recommended	1
BCG	Not recommended	1
Oxybutinin	D	4

23

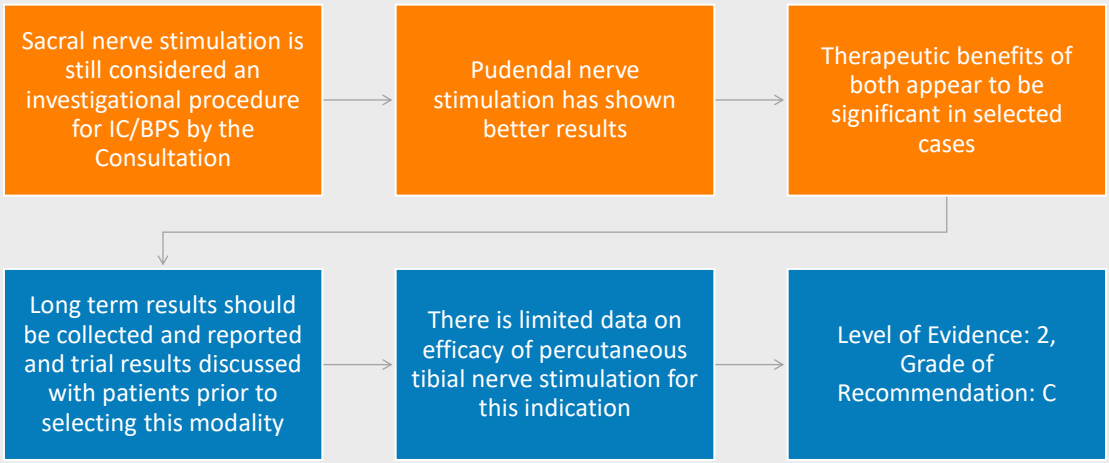
Intradetrusor Botox

- 100 unit total dose in 10unit aliquots
- Okay to limit to bladder base
- Can be effective in HLD and IC/BPS
- If successful, may need to be repeated in 6-9 months
- Level of evidence 2, grade of recommendation B



24

Neuromodulation



25

Surgical Approach to Treatment

- ❑ Hydrodistention under anesthesia
- ▪ Fulguration/Steroid Injection/ Resection of HLD
- ○ Bladder Augmentation-Cystoplasty
- • Cystoplasty with Supratrigonal Resection
- ❖ Cystoplasty with Subtrigonal Resection (Orthotopic continent bladder augmentation
- ➢ Urinary Diversion with or without cystectomy/urethrectomy

- ❑ LOE: 3; Grade of Recco: D
- ▪ LOE: 1; Grade of Recco: A
- ○ LOE: 3 ; Grade of Recco: C
- • LOE: 3 ; Grade of Recco: C
- ❖ LOE: 3 ; Grade of Recco: C
- ➢ LOE: 3; Grade of Recco: B

26

Outcome Assessment

- There are no accepted biologic disease markers for assessment of response to therapy
- The 5 question RICE IC/BPS case definition could be a screening tool for primary care providers J Urol **183**:5, 1848-52
- Multiple validated questionnaires exist to follow disease progression and response to therapy

27

Future Directions in Research

The committee believes that further basic research is needed in many broad areas:

1. Pathology of IC/BPS
2. Biomarker development
3. Immunology of IC/BPS
4. Neurological aspects with particular attention to the relationship of IC/BPS to overactive bladder
5. The relationship of IC/BPS to chronic prostatitis/ chronic pelvic pain syndrome in men

28

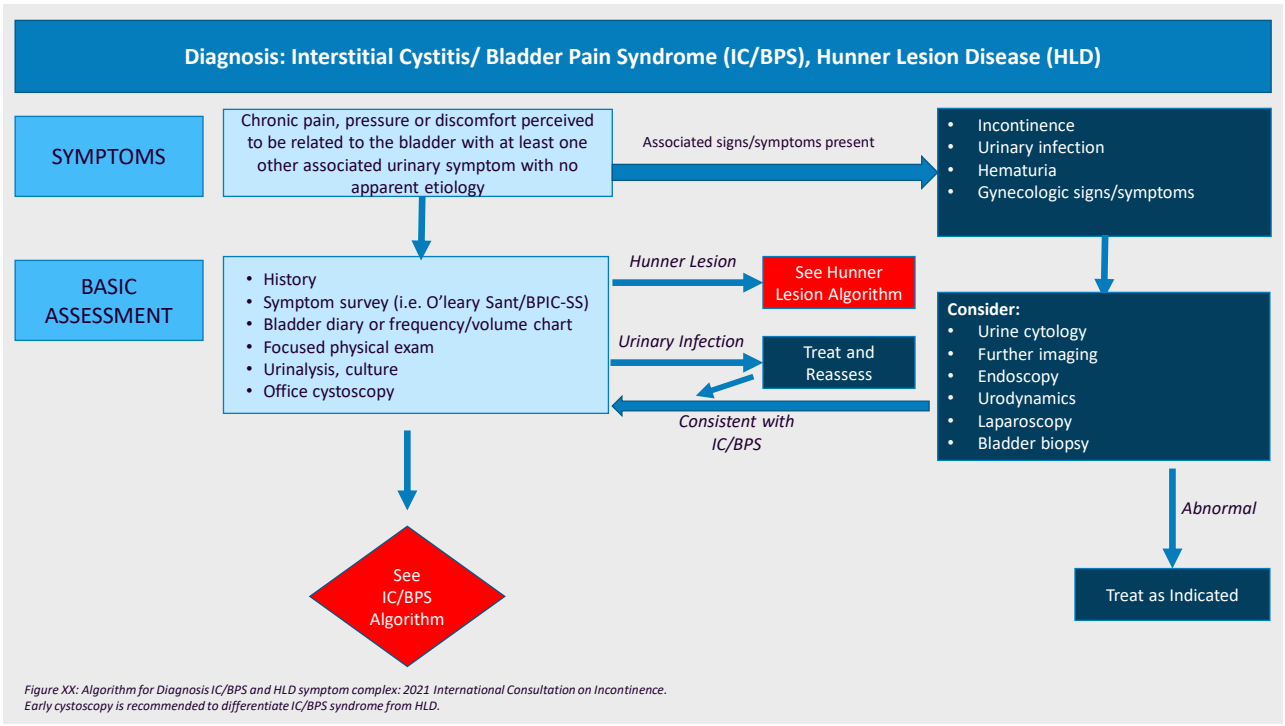
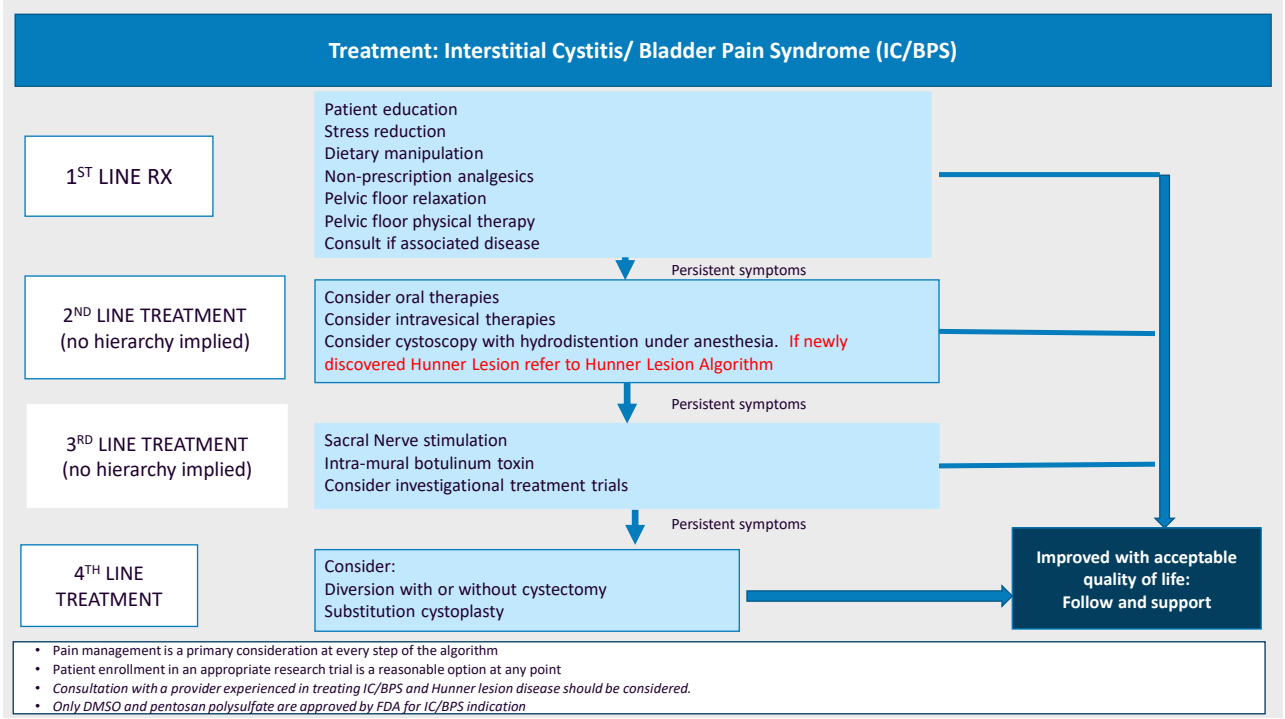


Figure XX: Algorithm for Diagnosis IC/BPS and HLD symptom complex: 2021 International Consultation on Incontinence. Early cystoscopy is recommended to differentiate IC/BPS syndrome from HLD.

29



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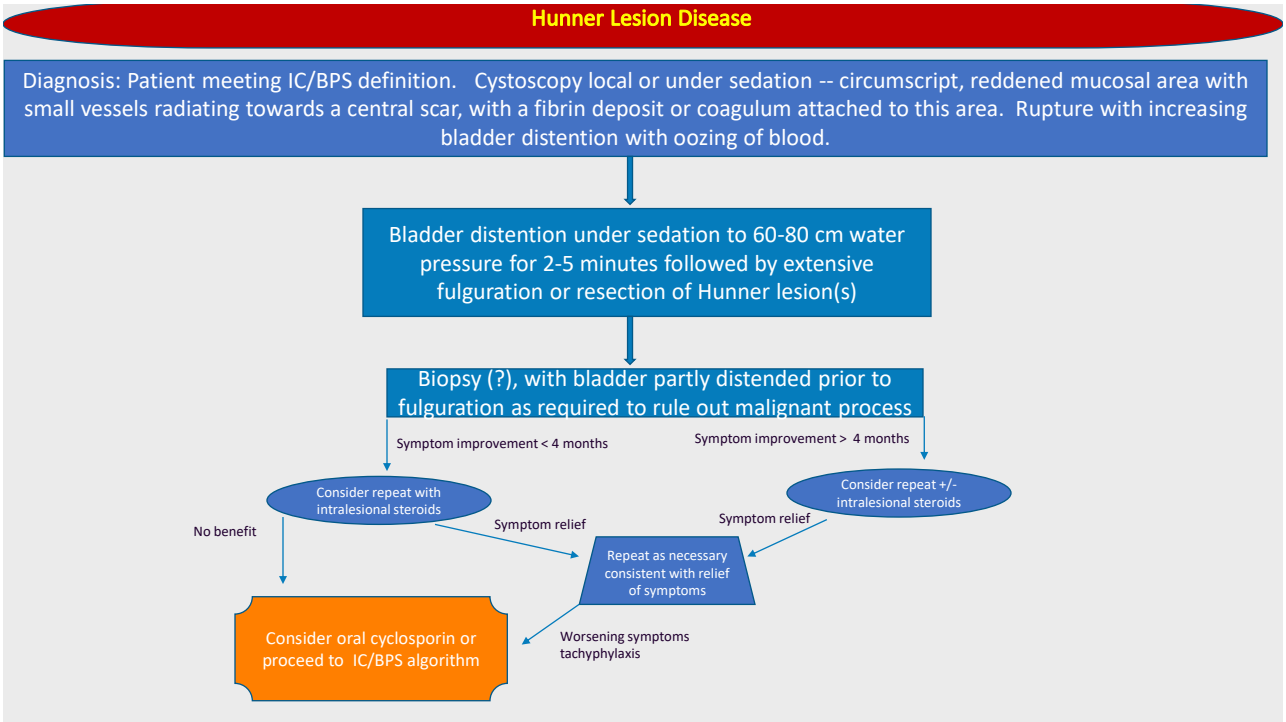
Hunner Lesion Disease
Diagnosis: Patient meeting IC/BPS definition. Cystoscopy local or under sedation -- circumscript, reddened mucosal area with small vessels radiating towards a central scar, with a fibrin deposit or coagulum attached to this area. Rupture with increasing bladder distention with oozing of blood.
Bladder distention under sedation to 60-80 cm water pressure for 2-5 minutes followed by extensive fulguration or resection of Hunner lesion(s)
Biopsy (?), with bladder partly distended prior to fulguration as required to rule out malignant process
Symptom improvement < 4 months
Symptom improvement > 4 months
Consider repeat with intralesional steroids
Consider repeat +/- intralesional steroids
No benefit
Symptom relief
Symptom relief
Repeat as necessary consistent with relief of symptoms
Consider oral cyclosporin or proceed to IC/BPS algorithm
Worsening symptoms tachyphylaxis

31