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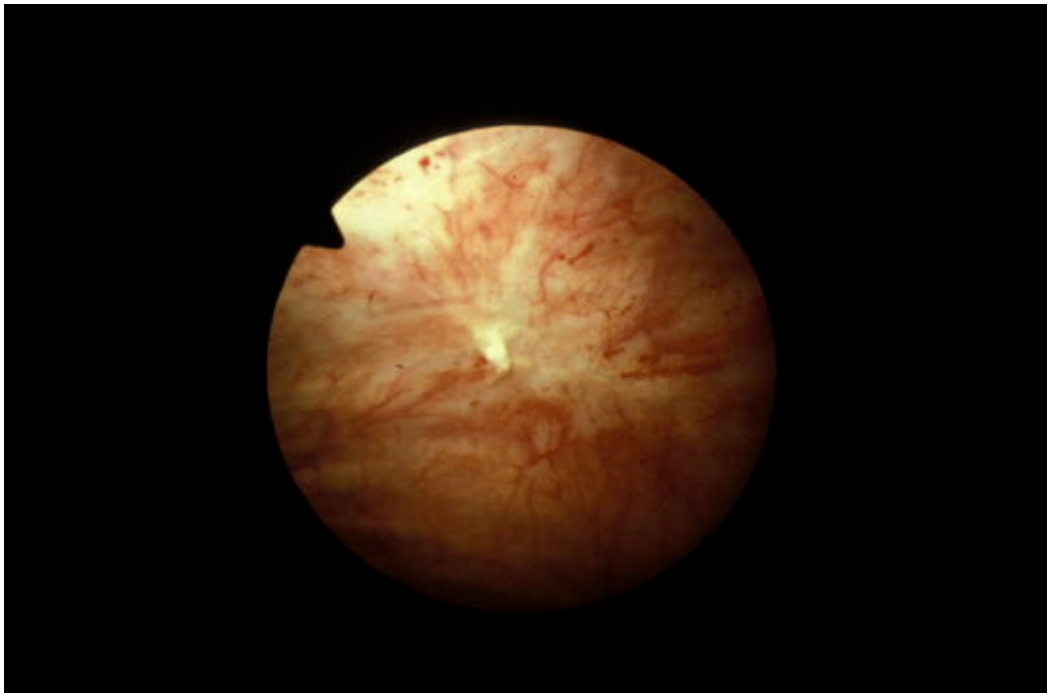

Interstitial Cystitis/Bladder Pain Syndrome
IC/BPS Clinical Guideline

Rigorous, evidence- based clinical practice guidelines

AUA GUIDELINES

A Department within the Health Policy Division

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Background: Why Now?

- AUA first attempted IC guideline in 1998, but after an exhaustive literature review it became apparent that the existing knowledge base could not support it.
- Interest, research, publications increasing world-wide in last decade.
- AUA determined that the time was right to provide a clinical framework for Dx and Management with thought leaders from the urologic, gynecologic, neurologic, nursing, and patient advocacy fields.

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Panel Members

- David Burks
- Quentin Clemens
- Roger Dmochowski
- Debora Erickson
- Mary Pat Fitzgerald
- John Forrest
- Barbara Gordon
- Mikel Gray
- Philip Hanno
- Robert Mayer
- Diane Newman
- Leroy Nyberg
- Christopher Payne
- Ursula Wesselmann

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Methodology

- **Systematic Review**
  - *Rigorous,* of high quality conducted by a methodologist
  - *Transparent* and *replicable*

- **Literature Search and Study Selection**
  - MedLINE Literature search – 1/1/1983 – 7/22/2009
  - Study inclusion and exclusion criteria applied
  - Evidence base of 86 treatment articles

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Methodology

- **Determination of Study Quality**
  - Cochrane Risk of Bias tool
  - Levels of Evidence
    - A – well-conducted RCTs or exceptionally strong observational studies
    - B – RCTs with some weaknesses of procedure or generalizability, or strong observational studies
    - C – observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data

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Methodology

- **Development of Guideline Statements for Treatment**
  - **Level of Evidence linked to Type of Statement**
  - **Standard** – evidence statement where the benefits are > **or** < than the risks/burdens. **Level of evidence A or B**
  - **Recommendation** – evidence statement where the benefits are > **or** < than the risks/burdens. **Level of evidence C**
  - **Option** – evidence statement where the benefits are equal to the risks or there is a question about the benefits vs. risks. (=/?) **Level of evidence A or B or C**

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Methodology

- **Development of Initial Management Strategies and Diagnosis Statements**
- Insufficient evidence
- Based on expert opinion and clinical principles.
  - **Clinical Principle** – is a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature
  - **Expert Opinion** – refers to a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence.

Basic Constructs

- **Name**: Interstitial Cystitis / Bladder Pain Syndrome – abbreviated to IC/BPS
- **Definition**: (SUFU) An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than 6 weeks duration, in the absence of infection or other identifiable causes*

*Neurourol Urodyn. 2009;28(4):274-86.

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Guideline Statements: Diagnosis

- Principles
  - Baseline assessment: history, physical exam, laboratory exam to exclude other disorders commonly associated with IC/BPS in the differential diagnosis
  - Obtain baseline symptom and pain levels
- Expert Opinion
  - Cystoscopy and Urodynamics unnecessary for diagnosis in *uncomplicated* presentations when diagnosis is clear

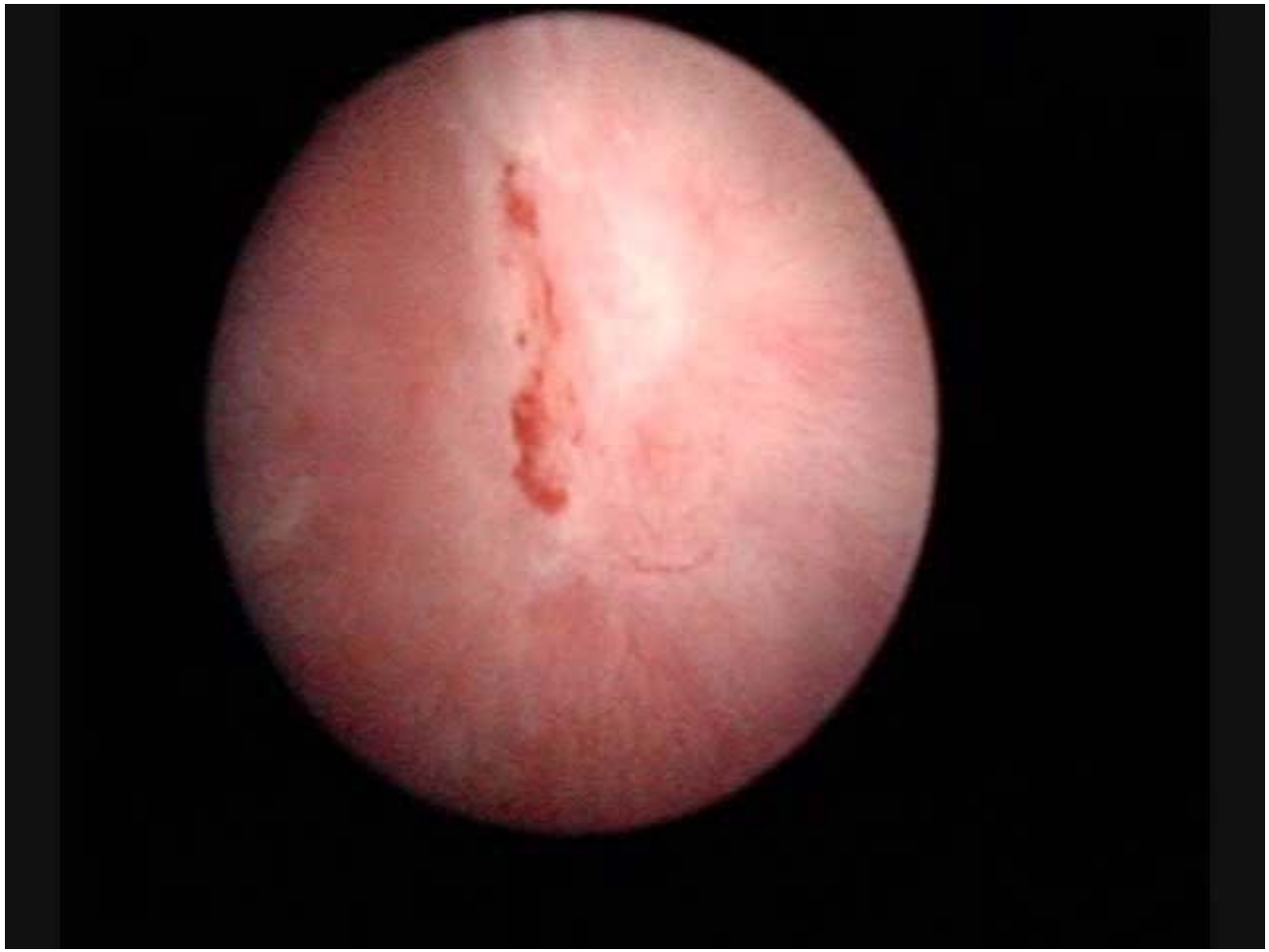
Diagnosis

- Cystoscopy and urodynamic testing are appropriate when after the basic assessment the diagnosis remains in doubt
  - Hematuria, incontinence, overactive bladder, gastrointestinal symptoms, gynecologic symptoms, pyuria, etc
- The potassium sensitivity test should not be used as a diagnostic tool in clinical practice because its outcome changes neither management nor the treatment approach

Hunner's Lesion

- A positive finding that can confirm the diagnosis in patients who meet the definition criteria
- acute phase (inflamed, friable, denuded area)
- chronic phase (blanched, non-bleeding area)
- Provides a therapeutic option

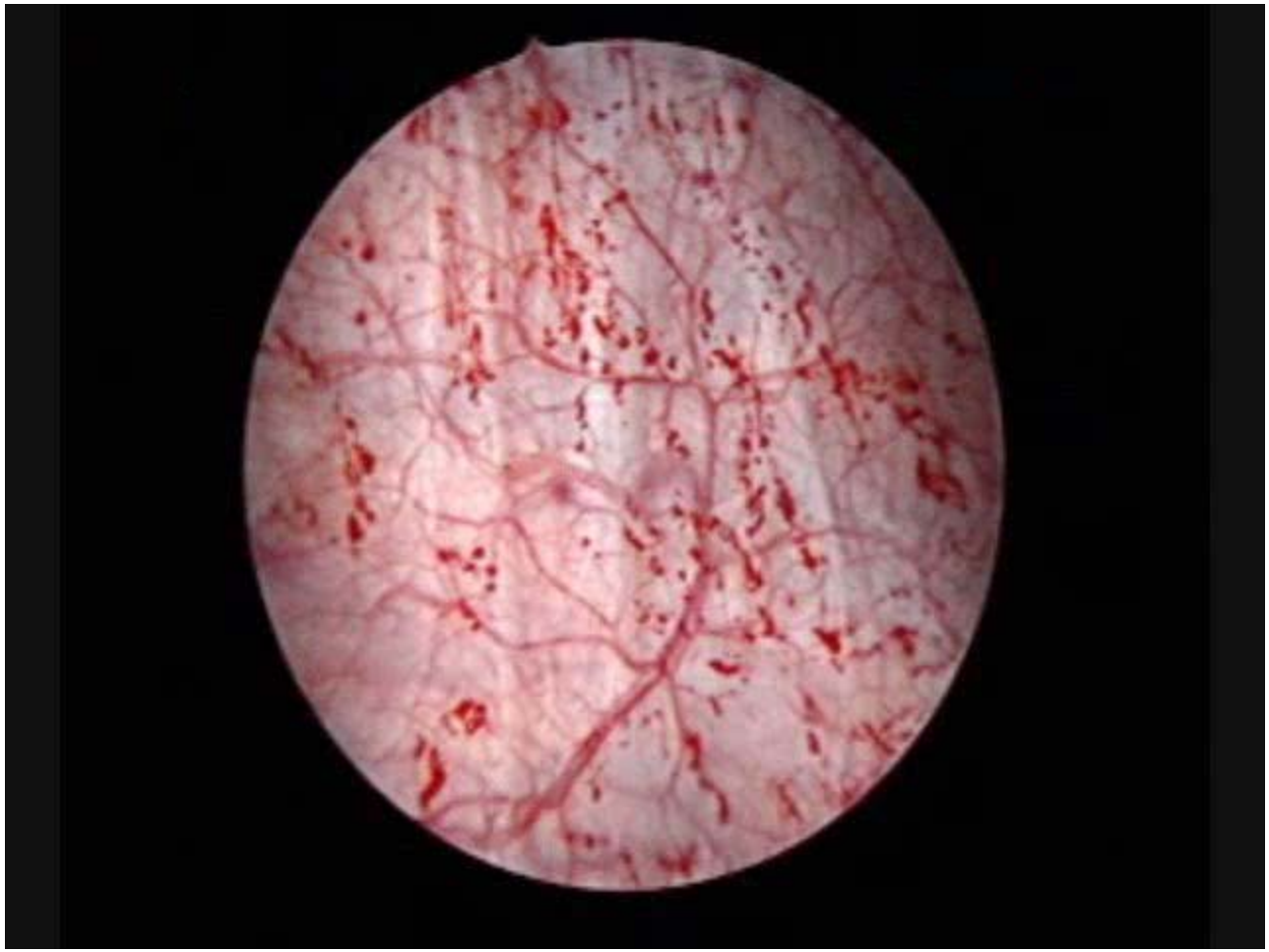
Hunner's lesion



Glomerulations

- The finding of glomerulations on hydrodistention is variable and not consistent with clinical presentation
- Absence of glomerulation can lead to false negative assessment of patients who present with clinical findings consistent with IC/BPS
- Seen in many clinical situations
  - Radiation therapy, defunctionalized bladders, bladder cancer, chemotherapeutic or toxic drug exposure, normal bladders

Glomerulations



Chronic prostatitis/chronic pelvic pain syndrome; NIH type 3 prostatitis

- Pain in the perineum, suprapubic region, testicles or tip of the penis.
- The pain is often exacerbated by urination or ejaculation.
- Voiding symptoms such as sense of incomplete bladder emptying and urinary frequency are also commonly reported, but pain is the primary defining characteristic

Male IC/BPS vs CP/CPPS

- If a man fulfills the criteria established by the definition of IC/BPS, he can be assumed to have the disorder
- The clinical characteristics which define CP/CPPS are similar to IC/BPS.
- The diagnosis of IC/BPS should be strongly considered in men whose pain is perceived to be related to the bladder.
- Both conditions can occur together, and treatment should reflect this when appropriate.

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Guideline Statements: Treatment

- Clinical Principles of Management
  - Begin with more conservative therapies reserving less conservative therapies for inadequate control of symptoms
  - Surgery (other than fulguration of Hunner's lesions) should be reserved for end-stage, small fibrotic bladders or when more conservative measures have been exhausted and quality of life is poor
  - Initial Rx type and level depend on symptom severity, clinician judgement, and pt. preference
  - Ineffective Rx should be stopped once a clinically meaningful interval has elapsed

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Guideline Statements: Treatment

- Clinical Principles of Management
  - Multiple, simultaneous treatments may be considered if it is in the best interests of the patient. Reassessment to document efficacy is essential
  - Continuously assess pain management for effectiveness, consider multidisciplinary approach if necessary
  - Reconsider diagnosis if no improvement after multiple treatment approaches

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Guideline Statements: First-Line Treatment

- Clinical Principle: Education
  - Review normal bladder function, IC/BPS knowledge base, risk/burdens of available treatments, potential need to try multiple therapeutic options over time
- Clinical Principle: Self-care practices
  - behavioral modifications that can improve symptoms should be discussed and implemented as feasible
  - Stress management to improve coping and manage stress-induced symptom exacerbations

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Guideline Statements: Second-Line Treatments

- Clinical Principle: Manual Physical Therapy if appropriately trained clinicians are available
  - Maneuvers that resolve pelvic, abdominal and/or hip muscular trigger points and connective tissue restrictions; avoid pelvic floor strengthening exercises
- Expert Opinion: Multimodal pain management approaches
  - Pharmacological, stress management, manual therapy if available should be initiated

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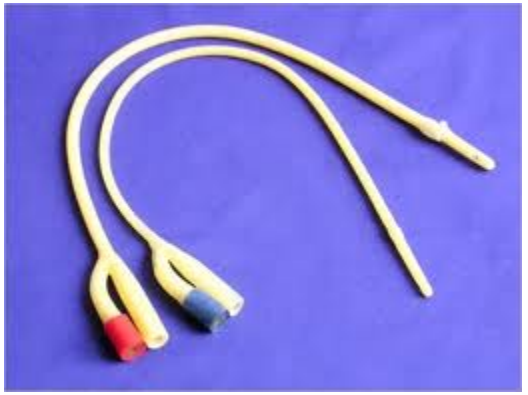
Guideline Statements: Second-Line Treatments



- Option: Oral Medications
  - Amitriptyline, cimetidine, hydroxyzine, pentosanpolysulfate (alphabetical order, no hierarchy implied)
- Option: Intravesical Medications
  - DMSO, heparin, lidocaine (alphabetical order, no hierarchy implied)

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Guideline Statements: Third-Line Treatments

Option:
cystoscopy + hydrodistention

Under anesthesia; short duration, low pressure distention

Recommendation:
If Hunner's Lesion

Fulgeration (laser or electrocautery) or triamcinolone injection into lesion

Guideline Statements: Fourth-Line Treatment

Option: Neurostimulation

Permanent implantation if trial is successful

Consider if other therapies have not provided adequate symptom control

Guideline Statements: Fifth-Line Treatments

Option: Cyclosporine A

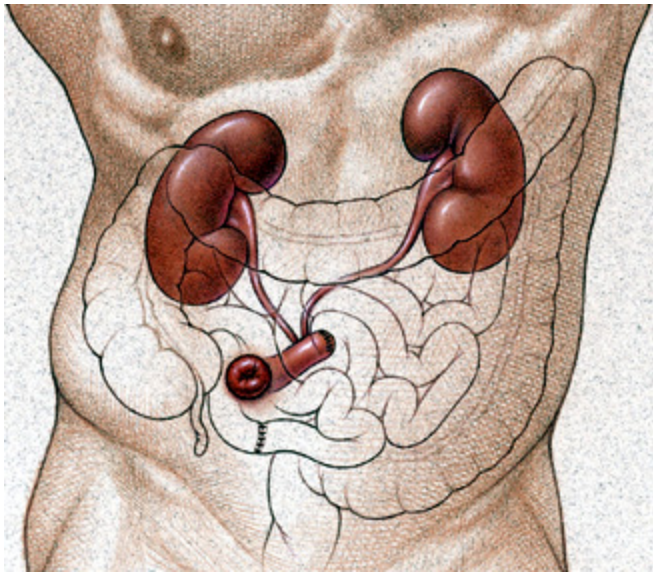
- Administered orally if other treatments have not provided adequate symptom control

Option: Intradetrusor botulinum toxin A

- Patient must be willing to accept possibility of need for intermittent catheterization for unknown period of time after treatment

The evidence supporting the use of Neuromodulation, Cyclosporine A, and BTX for IC/BPS is limited by many factors including study quality, small sample sizes, and lack of durable follow up. None of these therapies have regulatory approval (FDA) for this indication. The panel believes that none of these interventions can be recommended for generalized use for this disorder, but rather should be limited to practitioners with experience managing this syndrome and willingness to provide long term care of these patients post intervention.

Guideline Statements: Sixth Line Treatments



- Option: Major Surgery (substitution cystoplasty, urinary diversion with or without cystectomy) may be undertaken in carefully selected patients for whom all other therapies have failed to provide adequate symptom control and quality of life

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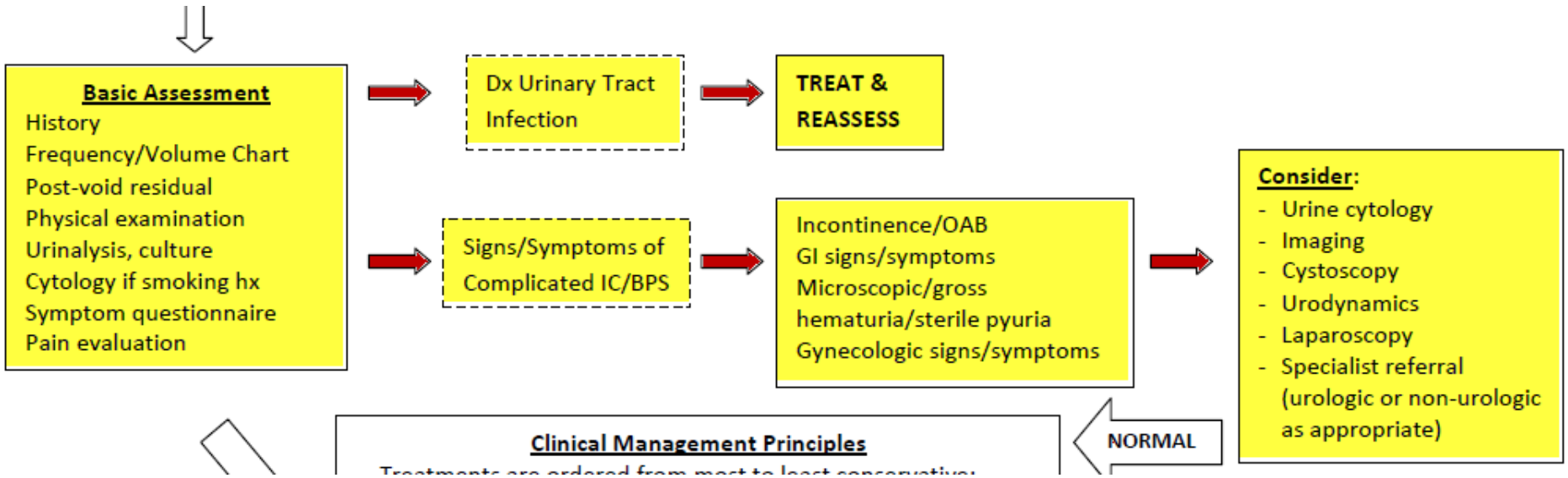
Guideline Statements:
Therapies to Avoid

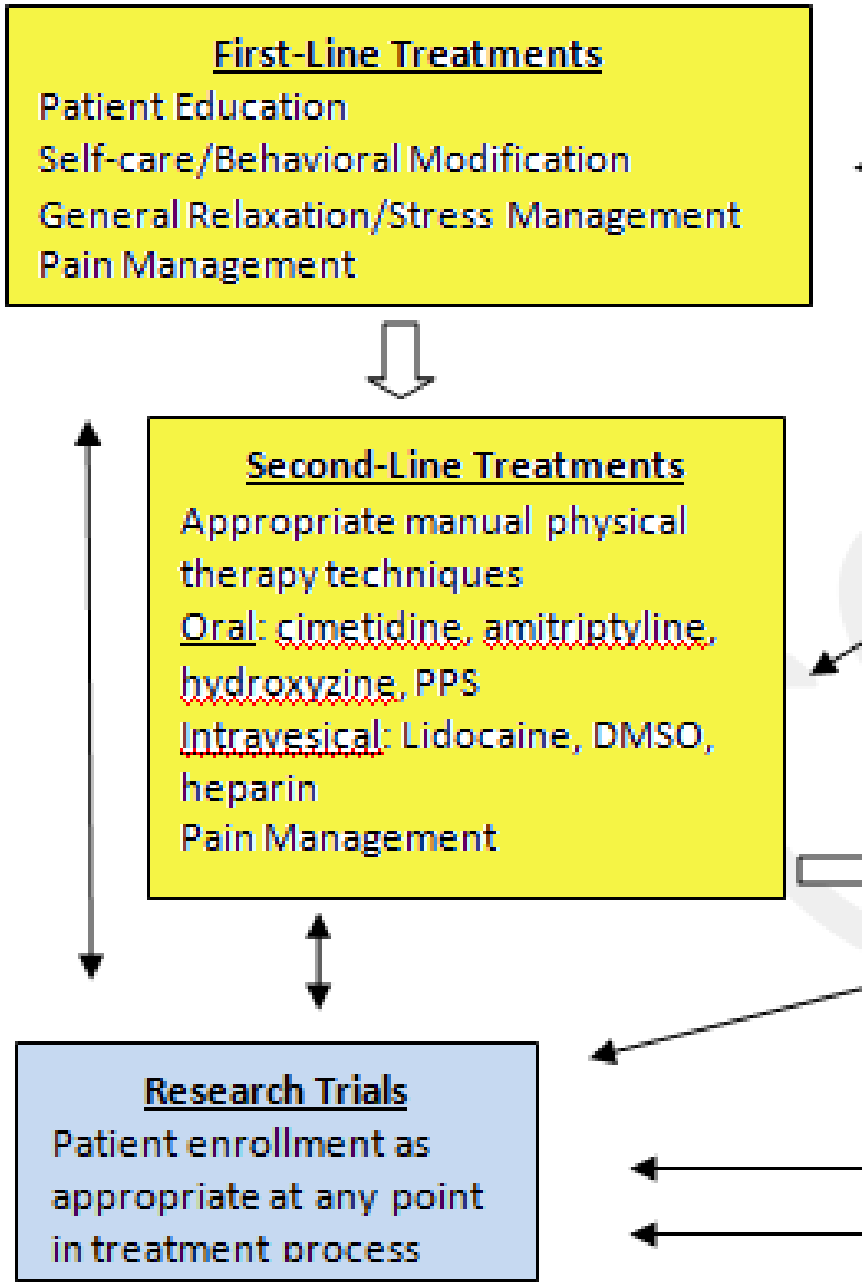
- **Standard**: long-term antibiotic administration
- **Standard**: intravesical bacillus Calmette-Guerin
- **Standard**: intravesical resiniferatoxin
- **Recommendation**: high pressure, long duration hydrodistention
- **Recommendation**: systemic (oral) long-term steroid administration

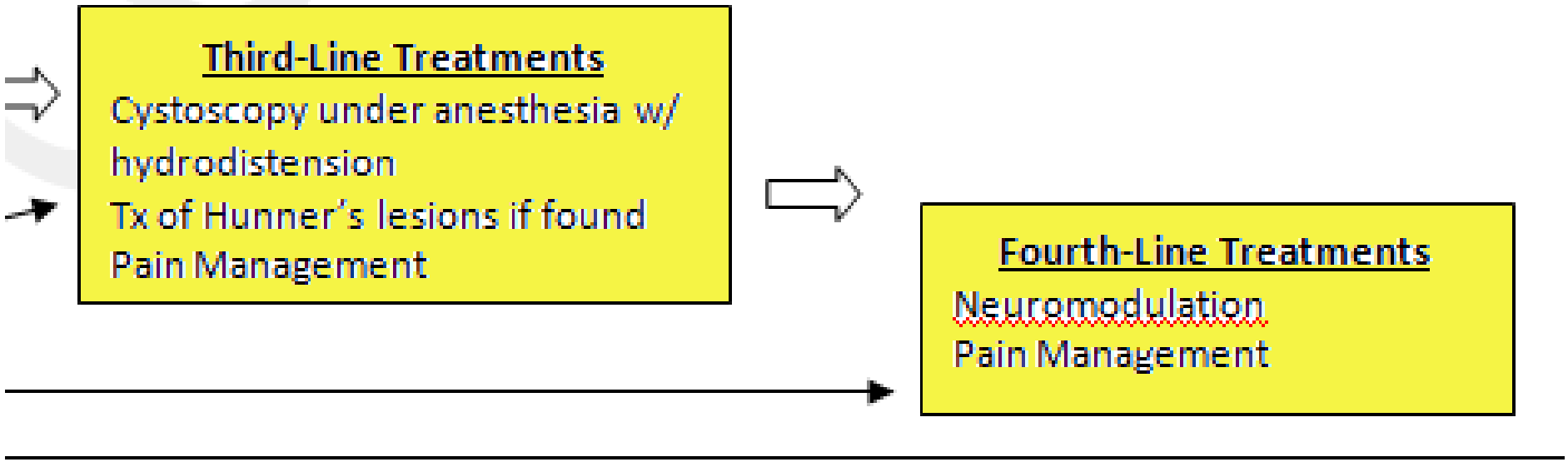
An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder associated with lower urinary tract symptoms of more than 6 weeks duration, in the absence of infection or other identifiable causes

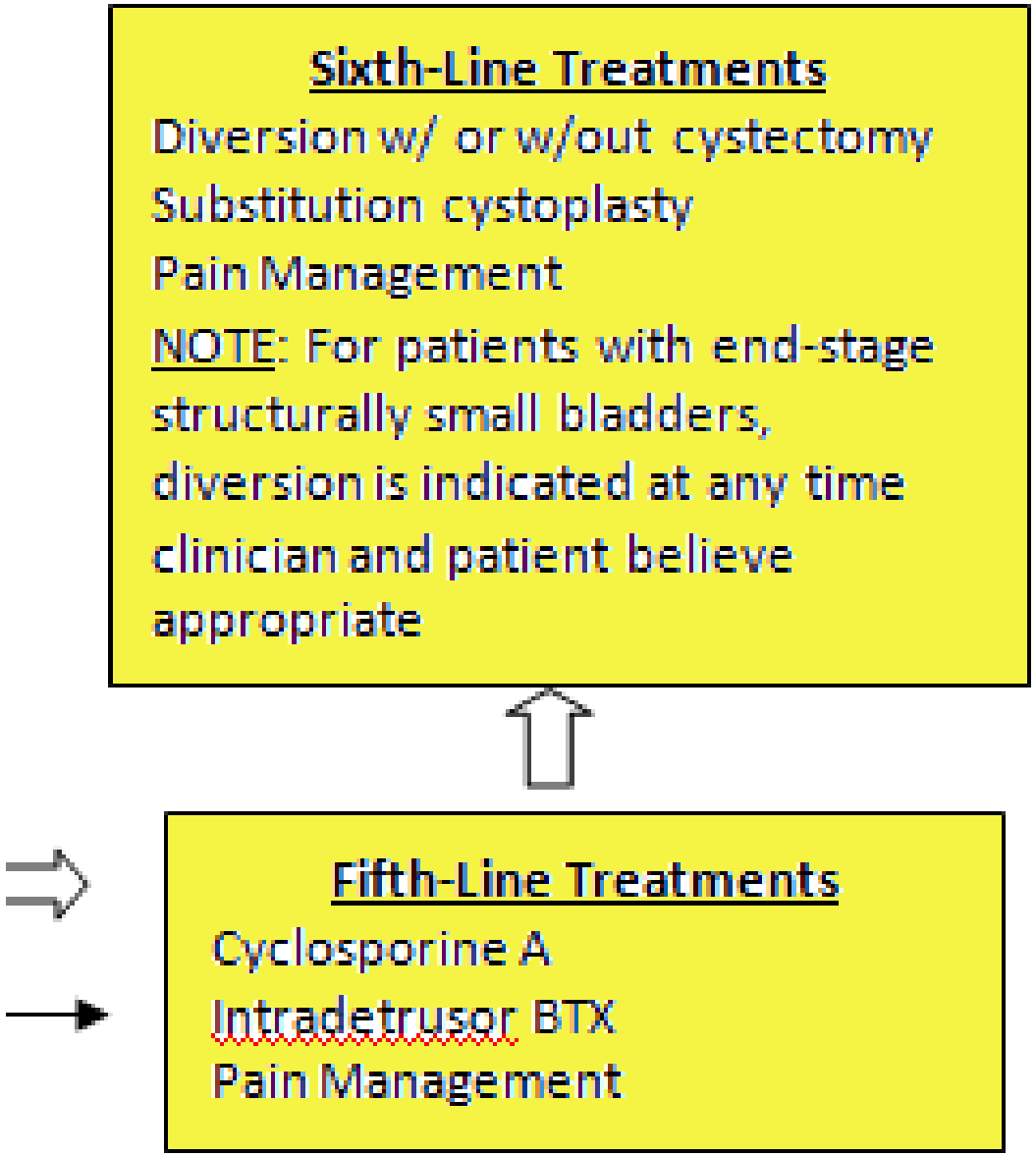


Clinical Management Principles

- Treatments are ordered from most to least conservative; surgical treatment is appropriate only after other treatment options have been found to be ineffective (except for treatment of Hunner's lesions if detected)
- Initial treatment level depends on symptom severity, clinician judgment, & patient preferences
- Multiple simultaneous treatments may be considered if in best interests of patient
- Ineffective treatments should be stopped
- Pain management should be considered throughout course of therapy with goal of maximizing function and minimizing pain and side effects
- Diagnosis should be reconsidered if no improvement w/in clinically meaningful time frame


First-Line Treatments
Patient Education
Self-care/Behavioral Modification
General Relaxation/Stress Management
Pain Management
Second-Line Treatments
Appropriate manual physical therapy techniques
Oral: cimetidine, amitriptyline, hydroxyzine, PPS
Intravesical: Lidocaine, DMSO, heparin
Pain Management
Research Trials
Patient enrollment as appropriate at any point in treatment process


Third-Line Treatments
Cystoscopy under anesthesia w/ hydrodistension
Tx of Hunner's lesions if found
Pain Management
Fourth-Line Treatments
Neuromodulation
Pain Management


Sixth-Line Treatments
Diversion w/ or w/out cystectomy
Substitution cystoplasty
Pain Management
NOTE: For patients with end-stage structurally small bladders, diversion is indicated at any time clinician and patient believe appropriate
Fifth-Line Treatments
Cyclosporine A
Intradetrusor BTX
Pain Management

IC/BPS: 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 the absence of infection or other identifiable causes

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Basic Assessment
History
Frequency/Volume Chart
Post-void residual
Physical examination
Urinalysis, culture
Cytology if smoking hx
Symptom questionnaire
Pain evaluation

Dx Urinary Tract Infection → **TREAT & REASSESS**

Signs/Symptoms of Complicated IC/BPS → Incontinence/OAB
GI signs/symptoms
Microscopic/gross hematuria/sterile pyuria
Gynecologic signs/symptoms → **Consider:**
- Urine cytology
- Imaging
- Cystoscopy
- Urodynamics
- Laparoscopy
- Specialist referral (urologic or non-urologic as appropriate)

NORMAL

ABNORMAL → **TREAT AS INDICATED**

Clinical Management Principles
- Treatments are ordered from most to least conservative; surgical treatment is appropriate only after other treatment options have been found to be ineffective (except for treatment of Hunner's lesions if detected)
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Second-Line Treatments
Appropriate manual physical therapy techniques
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NOTE: For patients with end-stage structurally small bladders, diversion is indicated at any time clinician and patient believe appropriate

Research Trials
Patient enrollment as appropriate at any point in treatment process

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Acknowledgements

- Martha Faraday, PhD: consulting methodologist
- Suzanne Pope, MBA: AUA panel manager
- Heddy Hubbard, PhD, MPH, RN, FAAN: Director AUA Guidelines Staff
- Panel Members
- External Reviewers
- As with all guidelines, these are a work in progress