1.1.1 Definition

Bladder Pain Syndrome (in the absence of a universally agreed definition, the International Society for the Study of Bladder Pain Syndrome—ESSIC definition is given [1]).

**ESSIC:** Chronic pelvic pain, pressure or discomfort of greater than 6 months duration perceived to be related to the urinary bladder accompanied by at least one other urinary symptom like persistent urge to void or urinary frequency. Confusatile diseases as the cause of the symptoms must be excluded.

There is no published data as to what duration of symptomatology indicates that early spontaneous resolution of symptoms is unlikely. While ESSIC arbitrarily uses a 6 month duration, the American Urological Association Guideline suggests 6 weeks is long enough to initiate diagnosis and treatment of BPS [2]. Without further data, the Consultation cannot make a recommendation and believes that it is up to the discretion of the physician and patient as to the proper interval between symptom onset and evaluation and diagnosis of a chronic condition.

1.1.2 Bladder Pain Syndrome (BPS)

1.1.2.1 Nomenclature

The scientific committee of the International Consultation voted to use the term “bladder pain syndrome” for the disorder that has been commonly referred to as interstitial cystitis (IC). The term painful bladder syndrome was dropped from the lexicon. The term IC implies an inflammation within the wall of the urinary bladder, involving gaps or spaces in the bladder tissue. This does not accurately describe the majority of patients with this syndrome. Painful Bladder Syndrome, as defined by the International Continence Society, is too restrictive for the clinical syndrome. Properly defined, the term Bladder Pain Syndrome appears to fit in well with the taxonomy of the International Association for the Study of Pain (IASP) (see below), and focuses on the actual symptom complex rather than what appears to be long-held misconception of the underlying pathology.

1.1.3 Bladder Pain Syndrome (XXIII-2) (per IASP)

Bladder pain syndrome is the occurrence of 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 night-time urinary frequency. There is no proven infection or other obvious local pathology. Bladder pain syndrome is often associated with negative cognitive, behavioral, sexual, or emotional consequences as
well as with symptoms suggestive of lower urinary tract and sexual dysfunction.

The Consultation believes that based on the pathology and endoscopic findings characteristic of the Hunner lesion, the epidemiologic pattern that distinguishes it from bladder pain syndrome, the clinical response to local treatment of the lesion by resection, fulguration, or steroid injection, the response to cyclosporine, and the absence of reports in the literature that non-Hunner patients go on to develop Hunner lesions (i.e., the finding of Hunner lesion does not represent a continuum in the natural history of bladder pain syndrome), the presence of a Hunner lesion should be considered a distinct disease. It therefore should drop out of the bladder pain syndrome construct, much like we do not consider other painful conditions like radiation cystitis, ketamine cystitis, or urinary tract infection a part of bladder pain syndrome.

The Consultation concludes that it would be reasonable to designate the Hunner lesion in symptomatic patients with the term “interstitial cystitis”, thus indicating a true interstitial inflammation. It would be defined much as Hunner defined it 100 years ago, and harmonize to a great extent the Asian, European, and North American concepts of interstitial cystitis. The Consultation will continue to refer to the symptom complex as “bladder pain syndrome”. Hunner lesion will be considered a distinct phenotype, but in the future may be classified as a separate disorder entirely, albeit with local symptoms that are difficult to differentiate from bladder pain syndrome in the absence of endoscopy. In other words, we may be coming full circle in the historical perspective (Fig. A1).

1.1.3.1 History/Initial Assessment

Males or females whose symptoms meet the requirements of the definition of bladder pain syndrome should be evaluated. The presence of commonly associated disorders including irritable bowel syndrome, chronic fatigue syndrome, and fibromyalgia in the presence of the cardinal symptoms of bladder pain syndrome also suggests the diagnosis. Abnormal gynecologic findings in women and well-characterized confusable diseases that may explain the symptoms must be ruled out.

The initial assessment consists of a frequency/volume chart, focused physical examination, urinalysis, and urine culture. In the absence of confusable disorders (uncomplicated disease), a
diagnosis can be made and treatment instituted. Urine cytology, cystoscopy, and urodynamic evaluation are recommended if clinically indicated and/or the diagnosis is in doubt (complicated disease). Patients with urinary infection should be treated and reassessed. Those with recurrent urinary infection, abnormal urinary cytology, and microscopic or gross hematuria are evaluated with appropriate imaging and endoscopic procedures, and only if findings are unable to explain the symptoms, are they diagnosed with BPS. Grade of recommendation: C

1.1.3.2 Initial Treatment

- Patient education,
- dietary manipulation,
- nonprescription analgesics,
- stress reduction,
- pelvic floor relaxation techniques comprise the initial treatment of BPS. In the patient with findings suggesting pelvic floor dysfunction, pelvic floor physical therapy with myofascial trigger point release and intravaginal Thiele massage is often an effective therapeutic intervention. The treatment of pain needs to be addressed directly, and in some instances referral to an anesthesia/pain center can be an appropriate early step in conjunction with ongoing treatment of the syndrome.

When conservative therapy fails or symptoms are severe and conservative management is unlikely to succeed,
- oral medication or
- intravesical treatment can be prescribed. It is recommended to initiate a single form of therapy and observe results, adding other modalities or substituting other modalities as indicated by degree of response or lack of response to treatment. Grade of recommendation: C

1.1.3.3 Secondary Assessment

If initial oral or intravesical therapy fails, or before beginning such therapy based on clinician judgment, it is reasonable to consider further evaluation which can include Urodynamics, pelvic imaging, and cystoscopy with bladder distention and possible bladder biopsy under anesthesia.
- Findings of bladder overactivity suggest a trial of antimuscarinic therapy.
- The presence of a Hunner lesion suggests therapy with transurethral resection, fulguration of the lesion, or direct steroid injection into the lesion.
- Distention itself can have therapeutic benefit in 30–50% of patients, though benefits rarely persist for longer than a few months. Grade of recommendation: C

1.1.3.4 Refractory BPS

Those patients with persistent, unacceptable symptoms despite oral and/or intravesical therapy are candidates for more aggressive modalities. Many of these/ are best administered within the context of a clinical trial if possible. These may include
- neuromodulation,
- intradetrusor botulinum toxin,
- oral cyclosporine A, or
- clinical trials of newly described pharmacologic management techniques. At this point, most patients will benefit from the expertise of an anesthesia pain clinic.

The last step in treatment is usually some type of surgical intervention aimed at increasing the functional capacity of the bladder or diverting the urinary stream.
- Urinary diversion with or without cystectomy has been used as a last resort with good results in selected patients. Cystectomy and urethrectomy do not appear to add any additional efficacy to diversion alone [3–5].
- Augmentation or substitution cystoplasty seems less effective and more prone to recurrence of chronic pain in small reported series. Grade of recommendation: C
- Pain management is a primary consideration at every step of algorithm
- Patient enrollment in appropriate research trial is reasonable option at any point
- Evidence supporting neurostimulation, cyclosporine A, and botulinum toxin for BPS indication remains limited. These interventions are appropriate only for practitioners with experience treating BPS and willing to provide long-term care post-intervention.
Algorithm for diagnosis and treatment: 2016 International consultation on incontinence

Note: The only FDA approved therapies are DMSO and pentosan polysulfate. Consider CONTINENCE PRODUCTS for temporary support during treatment.

- Pain management is a primary consideration at every step of the algorithm
- Patient enrollment in appropriate research trial is a reasonable option at any point
- Evidence supporting SNS, cyclosporine A, and botulinum toxin for BPS remains limited. These interventions are appropriate only for practitioners with experience in treating BPS and who are willing to provide long-term care post-intervention


Addendum 2: AUA Guideline

**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.

### Signs/Symptoms of Complicated IC/BPS

- Incontinence/OAB
- GI signs/symptoms
- Microscopic/gross hematuria/sterile pyuria
- Gynecologic signs/symptoms

### First-Line Treatments
- General Relaxation/Stress Management
- Pain Management
- Patient Education
- Self-care/Behavioral Modification

### Second-Line Treatments
- Appropriate manual physical therapy techniques
- Oral: amitriptyline, cimetidine, hydroxyzine, PPS
- Intravesical: DMSO, Heparin, Lidocaine
- Pain Management

### Third-Line Treatments
- Cystoscopy under anesthesia w/ hydrodistention
- Pain Management
- Tx of Hunner’s lesions if found

### Fourth-Line Treatments
- Intradetrusor botulinum toxin A
- Neuromodulation
- Pain Management

### Fifth-Line Treatments
- Cyclosporine A
- Pain Management

### Sixth-Line Treatments
- Diversion w/ or w/out cystectomy
- Pain Management
- Substitution cystoplasty

Note: For patients with end-stage structurally small bladders, diversion is indicated at any time clinician and patient believe appropriate.

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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 been approved by the U.S. Food and Drug Administration for this indication. The panel believes that none of these interventions can be recommended for generalization 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.
Addendum 3: Asian Algorithm