

## Review Article

# Interstitial Cystitis/Painful Bladder Syndrome as a Cause of Sexual Pain in Women: A Diagnosis to Consider

Tess Crouss<sup>1\*</sup>, Xibei Jia<sup>2</sup> and Kristene Whitmore<sup>3,4</sup><sup>1</sup>Department of Obstetrics and Gynecology, Cooper University Healthcare, USA<sup>2</sup>Department of Obstetrics and Gynecology, UMass Memorial Medical Center/University of Massachusetts Medical School, USA<sup>3</sup>Department of Urology and Obstetrics and Gynecology, Drexel University College of Medicine, USA<sup>4</sup>Virtua Female Pelvic Medicine, USA**\*Corresponding author**

Tess Crouss, Division of Female Pelvic Medicine and Reconstructive Surgery, Department of Obstetrics and Gynecology, Cooper University Healthcare, Camden, NJ, 428 N 13th St Apt 6C, Philadelphia, PA 19123, USA, Tel: 207-751-9964; Email: crousst@gmail.com

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**Abstract**

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a complex disorder with a high degree of overlap with additional inflammatory and chronic pain syndromes. In women presenting with dyspareunia, especially with concomitant irritative voiding symptoms, IC/BPS should be strongly considered as a diagnosis. As a clinical diagnosis of exclusion, history and physical exam are integral to establishing a diagnosis of IC/BPS. Patients with IC/BPS are also at a higher risk for additional causes of dyspareunia such as endometriosis, high tone pelvic floor dysfunction and vulvodynia. Management of IC/BPS is best accomplished with multimodal therapy in a multidisciplinary setting. If dyspareunia is secondary to IC/BPS, symptoms will often improve with management of IC/BPS. Comorbid disorders should be managed simultaneously.

**ABBREVIATIONS**

IC/BPS: Interstitial Cystitis/Bladder Pain Syndrome; HTPFD: High Tone Pelvic Floor Dysfunction; UTI: Urinary Tract Infection; BI: Bladder Instillation; PFPT: Pelvic Floor Physical Therapy; PPS: Pentosan Polysulfate Sodium

**INTRODUCTION**

Interstitial cystitis or bladder pain syndrome (IC/BPS) is a chronic inflammatory condition of the bladder. It can be difficult to diagnose and manage as it is a diagnosis of exclusion with significant overlap with other inflammatory disorders [1-3]. It is estimated that a high proportion of gynecologic patients with chronic pelvic pain have IC/BPS, which is often misdiagnosed for a significant period of time.[4] While bladder pain and irritative voiding are the more common presenting symptoms for those with IC/BPS, studies suggest that anywhere from 46 to 80% will report dyspareunia as a presenting symptom [4-9].

Dyspareunia refers to pain associated with sexual intercourse. [10,11] There are several classification systems that consider the onset of the symptoms (primary vs. secondary or acquired), as well as the location of pain (initial or entry vs. deep dyspareunia) [11-14]. When symptoms are persistent for at least 6 months, cause significant distress, and cannot be better explained by another disorder, relationship distress or substances, the

diagnosis of genito-pelvic pain/penetration disorder is used [10,15]. Dyspareunia as a symptom is prevalent, with research suggesting over 20% of females worldwide are affected [16]. The cause is often multifactorial and can involve gynecologic, urologic, gastrointestinal, musculoskeletal, neurologic, rheumatologic and psychosocial systems [17]. Examples of gynecologic causes of dyspareunia include endometriosis, vulvodynia, and vulvovaginal atrophy, infection or dermatoses [11,12]. Musculoskeletal disorders including high tone pelvic floor dysfunction (HTPFD) can be implicated. Psychosocial factors, such as a history of sexual abuse, can manifest as dyspareunia [11]. An important and commonly overlooked cause of dyspareunia pertaining to the urologic system is IC/BPS [8,12,17-19].

**INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME**

A widely used definition for IC/BPS is the clinical definition proposed by the Society for Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction, "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" [2,20]. IC/BPS is thought to affect between 3 to 7% of women, yet remains poorly understood [3]. When symptoms are not well controlled, IC/BPS has been shown

to negatively impact quality of life and can lead to disabling pain [3,6,21]. Work from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network showed that almost half of women with IC/BPS will have at least one additional chronic pain condition, such as irritable bowel syndrome, fibromyalgia and vulvodynia [3]. Women who suffer from IC/BPS are also more likely to have a history of abuse, and suffer from anxiety and depression [3,7].

## DYSPAREUNIA AND INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME

The causes of dyspareunia are often multifactorial and IC/BPS should be considered in the differential diagnosis [8]. Several studies have identified dyspareunia as a key presenting symptom in IC/BPS patients [4,22]. One particular study that assessed the prevalence of female sexual dysfunction in this population found that 90% of patients experienced more than one IC/BPS-specific sexual dysfunction symptom within the previous month [23], of these patients, 18.9% experienced bladder pain during sexual intercourse, and 19.4% after intercourse [23]. IC/BPS is also associated with sexual distress [24]. Research has shown that patients with IC/BPS are more likely to report pelvic pain, fear of pain during sexual intercourse, and dyspareunia [24]. Furthermore, studies show a higher prevalence of decreased sexual desire and orgasm in those with IC/BPS [9]. A study by Yoon et al. found that symptoms of urinary frequency and urgency in IC/BPS patients were positively correlated with discomfort during sexual activity [25].

Patients with IC/BPS are known to have higher rates of several of the more common causes of dyspareunia [26]. One case-control study showed that those with IC/BPS were 10.5 times more likely to have endometriosis compared to the general population [26]. Additionally, patients with IC/BPS have a higher prevalence of HTPFD than the general population [27,28]. In one particular study on IC/BPS patients, 70% reported dyspareunia and nearly 90% had levator tenderness on vaginal exam [28]. Furthermore, in a retrospective study that included 186 IC/BPS patients, nearly 80% were found to have levator pain with at least one trigger point on exam [27]. There is also an association between vulvodynia and IC/BPS [21,29]. Studies show that patients with IC/BPS have a higher prevalence of vulvodynia (approaching 75%), and significantly impaired sexual function as compared to controls [29,30].

The urinary bladder and the female reproductive tract are embryologically related. Conditions that affect one system such as the bladder may produce symptoms in the vagina or vulva [8,31]. The bladder and pelvic floor also share the same sacral nerve roots S2, S3 and S4. One of the theories to explain the high degree of overlap of IC/BPS with chronic pelvic pain disorders is that of neural and organ “cross-talk” [5,31-33]. Through both animal and human studies, there is growing evidence that noxious afferent stimulation of an organ can lead to “cross-talk” with another via both central and peripheral sensitization [32,33]. This theory also explains the high degree of overlap of bladder and bowel symptoms, as well as the fact that stimulation of the 3<sup>rd</sup> sacral nerve root improves both bowel and bladder symptoms [33].

Studies have shown both peripheral and central sensitization

play a role in the heightened pain response in patients with IC/BPS and other chronic pelvic pain syndromes [5,34]. Recurrent painful stimulation leads to a reduced pain threshold and increased nociceptor response of peripheral nerves, a phenomenon called peripheral sensitization, which is limited to the site of injury [35]. In contrast, central sensitization leads to changes in the sensory response of normal stimuli, which produces pain hypersensitivity in normal tissue, and persists even after painful stimuli has disappeared [35]. For example, a study using functional magnetic resonance imaging showed increased frontal cortex activation in women with vulvodynia who perceived touch to the posterior vulvar vestibule as painful compared to controls [36]. In other studies, increased peripheral nerve densities were noted on histologic analysis in patients with vulvodynia when compared to controls [37,38]. Similarly, elevated expression of nerve growth factor [NGF], and increased transient receptor potential vanilloid receptor subtype 1 [TRPV-1], nerve fiber density were found to correlate with pain scores in IC/BPS patients [39]. While there is still much to be confirmed, this research offers insight into explanations for the high degree of comorbid chronic pelvic pain syndromes in those with IC/BPS [27].

## DIAGNOSIS

Diagnosing IC/BPS can be challenging as it is a clinical diagnosis of exclusion with several associated syndromes [7,20,40]. This requires providers to take a thorough medical history that covers multiple systems [11]. Paramount to this process is developing trust with patients, especially given the high prevalence of sexual trauma and psychosocial issues in this population [7]. All aspects of a patient's pain should be assessed, including the timeline, nature, severity, exacerbating and alleviating factors, and associated symptoms [11]. It is important to collect information on dietary, menstrual, and sexual patterns [7,41]. One classic presentation for IC/BPS is a patient reporting multiple urinary tract infections (UTI) with primarily negative urine cultures [8,40]. A patient with both IC/BPS and dyspareunia may complain of positional pain with intercourse, especially in the suprapubic region, that can exacerbate their urinary symptoms [8].

Physical exam is the next step to establishing the diagnosis of IC/BPS as a cause for dyspareunia. The exam should focus on the abdominal and pelvic regions, making sure to assess the skin, muscles, nerves, bony pelvis and lower back, and pelvic/abdominal organs [11,18]. The pelvic exam should start with inspection to look for any dermatologic abnormalities including atrophy, scar tissue, or signs of infection. A Q-tip touch test for pain mapping should be used, with gentle and systematic palpation involving all aspects of the external genitalia, including the vestibular, Skene's and Bartholin's glands [11,29,42,43]. The provider should assess for neurologic sensation and the bulbocavernosus reflex [11]. Next, a gentle speculum exam to assess the vagina and cervix should be performed. One study suggests that performance of a speculum exam prior to a bimanual exam may result in decreased pain during speculum exam [44].

An internal vaginal exam should be performed to assess the vagina and pelvic floor muscles.[42,45] After assessment of

the pelvic floor muscles for spasm and trigger points, muscle function should be assessed by asking the patient to contract and then relax her pelvic floor muscles to test for coordination and dysfunction.[45] Vaginal palpation of the bladder should be performed, which often results in tenderness or discomfort for IC/BPS patients [11]. Lastly, a bimanual exam is performed to assess for abnormalities such as uterine or cervical tenderness, enlargement, masses and nodularity particularly along the uterosacral ligaments. Throughout this process it is important to gauge whether any part of the exam reproduces their symptoms [8].

Patients presenting with dyspareunia with concomitant urinary symptoms should undergo a urinalysis to rule out a UTI [40,46]. Additional evaluations such as completing a voiding diary, post-void residual, urine culture, vaginal wet mount, vaginal yeast and bacterial cultures, cystoscopy with or without biopsy, urine cytology, imaging or urodynamic studies should be performed only if indicated by abnormal history and exam findings. [19,40] If the pelvic exam findings are not straightforward, but there is a high suspicion for IC/BPS, a bladder instillation (BI) with alkalinized lidocaine, or an “anesthetic challenge,” can be performed to help with pain mapping and diagnosis [11,14,47].

Screening questionnaires are also useful in evaluating for IC/BPS [40]. Two particularly useful questionnaires are the O’Leary Sant Interstitial Cystitis Symptom and Problem Indices and the Pelvic Pain and Urgency/Frequency questionnaire [48,49]. The Female Sexual Function Index is useful for screening for sexual dysfunction [50]. It is important to remember that patients can find questionnaires burdensome, particularly if too many are used, and if the questions are repetitive or irrelevant to their condition [51,52]. Anecdotally, explaining the utility of the questionnaires as baseline measures of their pain that can be repeated throughout treatment to assess for progress often mitigates frustrations associated with excess paperwork.

## MANAGEMENT

Management of IC/BPS is best accomplished with multimodal therapy and a multidisciplinary team [7,19,40,46]. IC/BPS patients will often have more than one etiology for dyspareunia, reiterating the importance of a thorough history and physical exam. Pain management is an integral aspect of caring for IC/BPS patients at every stage, and should involve therapies for maintenance and breakthrough pain control [40]. Depending on the severity and chronicity, initial treatment should include education, stress management, behavioral modification, complementary alternative therapy, manual pelvic floor physical therapy (PFPT), BIs and pharmacologic medications [40]. Recommended medications include pentosan polysulfate sodium (PPS), tricyclic antidepressants such as amitriptyline, and anti-histamines such as hydroxyzine and cimetidine. BIs can be performed with different mixtures of local anesthetics, Heparin, or dimethyl sulfoxide. Third line treatment includes cystoscopy with hydrodistension under anesthesia, with or without treatment of Hunner’s lesions. Fourth line treatments include sacral neuromodulation and intradetrusor botulinum toxin A, and fifth line treatment involves immunosuppression

with cyclosporine A. Exceedingly rare today is the utilization of urinary diversion with or without cystectomy and substitution cystoplasty, considered sixth line therapies [40].

Depending on findings from history and exam, additional causes of dyspareunia such as vulvodynia, HTPFD, and/or endometriosis may also need to be addressed. Again, multimodal therapy with involvement of additional specialists as necessary is the recommendation for treatment [7,8,21,45]. Many of the initial treatments for IC/BPS overlap with treatments for vulvodynia and HTPFD [21]. Those with concomitant HTPFD should have a treatment plan with a focus on PFPT to target muscle dysfunction [45]. These patients may also benefit from low dose muscle relaxants such as cyclobenzaprine, or diazepam, either orally or by vaginal suppository [45]. Patients with palpable trigger points can undergo a series of pelvic floor muscle trigger point injections using a mixture of local anesthetic with corticosteroids. Injections are often prescribed congruent with PFPT sessions [7,14]. Those with refractory dysfunction may benefit from pelvic floor muscle injection of botulinum toxin A [7,53,54].

Patients with IC/BPS and vulvodynia may benefit from vulvar creams in addition to the previously mentioned multimodal therapy with education, behavioral modification and PFPT [42]. Postmenopausal patients with dyspareunia and IC/BPS who have concomitant vulvovaginal atrophy may benefit from any of the following treatments: vaginal estrogen, the selective estrogen receptor modulator Ospemifene, or the dehydroepiandrosterone vaginal suppository Prasterone [19]. IC/BPS patients with history or physical exam findings suggestive of other common comorbidities such as irritable bowel syndrome, endometriosis, fibromyalgia and psychosocial issues may require referral to specialists depending on the severity of their symptoms [7].

In patients with dyspareunia thought to be secondary to IC/BPS, management should proceed with the recommended multimodal therapy for IC/BPS. Several studies show improvement of sexual function with various treatments for IC/BPS [9,55-57]. In one such study, patients with IC/BPS underwent three weeks of three times weekly BIs that included a mixture of 2% lidocaine, heparin and sodium bicarbonate and were found to have significant improvements in the pain domain of their Female Sexual Function Index scores after the series. More so, over half of the patients reported complete resolution of their dyspareunia [55]. Similarly, results of a study in which IC/BPS patients were to take 300 mg of PPS daily for 32 weeks, there was significant improvement in sexual function scores and IC/BPS symptoms at the study’s conclusion [57]. A research group in Taiwan evaluated the efficacy of intravesical instillations of hyaluronic acid on sexual function in patients with IC/BPS. Patients in the study received weekly instillations of hyaluronic acid for four weeks, followed by monthly instillations to complete 6 months of therapy. At both 1 and 6 months there was a significant improvement in the dyspareunia subset of the Pelvic Organ Prolapse/Urinary incontinence Sexual Function Questionnaire compared to baseline scores [56].

## CONCLUSION

IC/BPS is a complex disorder with a high degree of overlap with additional inflammatory and chronic pain syndromes. For



this reason, multimodal therapy with a multidisciplinary team approach is the desired management strategy. Providers must maintain a high index of suspicion for IC/BPS when evaluating patients with dyspareunia and pelvic pain.

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