



Interstitial cystitis/bladder pain syndrome: when part of the posterior fornix syndrome is potentially curable surgically

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Abstract: Interstitial cystitis/bladder pain syndrome (IC/BPS) is defined as chronic pelvic pain plus a bladder symptom, usually urge. Evidence is offered to show IC/BPS forms part of the posterior fornix syndrome (PFS), which was defined in 1993 as: chronic pelvic pain (CPP), urge, frequency, nocturia, abnormal emptying, post-void residual urine, caused by uterosacral ligament (USL) laxity and cured or improved by USL repair. The IC/BPS definition implies that the urge and pain of IC/BPS is from a single (as yet unknown) pathogenic origin. However, when urge and pain are viewed from the perspective of the PFS, though both have the same lax USL origin, the anatomical pathway from lax USL to symptom manifestation is very different manifestation. For CPP the anatomical pathway is the inability of loose USLs to support pelvic visceral plexuses (VPs); it is hypothesized that inability of weak USLs to mechanically supports VPs, the afferent nerve synapse from end organs may fire off autologous afferent impulses to the brain which interprets them as pain from end organs such as urothelium, vulva, lower abdomen. For urge, the anatomical pathway is very different: lax USLs weaken the directional pelvic muscle forces which stretch the vagina to support the urothelial stretch receptors. The receptors fire off afferent impulses to the cortex at a lower bladder volume, and these are interpreted as “urge to go”. Mechanical support of USLs relieves both pain and urge, as does USL repair.

Keywords: Interstitial cystitis (IC); bladder pain syndrome (BPS); posterior fornix syndrome (PFS); chronic pelvic pain (CPP)

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Introduction

The key points of the article are summarized in the video abstract (Video S1) which shows the relationship of interstitial cystitis/bladder pain syndrome (IC/BPS) to posterior fornix syndrome (PFS).

Though IC/BPS is considered a chronic pelvic pain (CPP) syndrome (1), the International Continence Society (ICS) defines IC/BPS more precisely as “*persistent or recurrent CPP, pressure, or discomfort perceived to be related to the urinary bladder accompanied by at least one other urinary*

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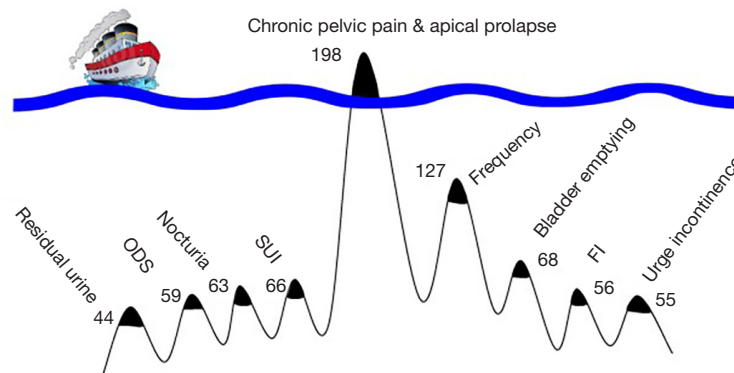


Figure 1 The Pescatori Iceberg. The symptom prevalence of 198 women presenting with CPP is graphically indicated in the iceberg diagram, with latent bladder pelvic symptoms below the waterline. All symptoms were derived from the ITSQ. Numbers indicate combined total of the hysterectomy and non-hysterectomy cohorts. Reused from Goeschen K, Gold D. Surgical cure of chronic pelvic pain, associated bladder & bowel symptoms by posterior sling in 198 patients validates the Pescatori Iceberg principle of pelvic symptom co-occurrence. *Pelvipereineology* 2017;36:84-88, Copyright 2017, with permission from *Pelvipereineology*. ODS, obstructive defecation syndrome; SUI, stress urinary incontinence; FI, fecal incontinence; CPP, chronic pelvic pain; ITSQ, Integral Theory Symptom Questionnaire.

symptom such as an urgent need to void or urinary frequency, diagnosed in the absence of any identifiable pathology which could explain these symptoms” (2).

It is widely believed that the pathogenesis of IC/BPS is unknown and that no cure is possible. Treatment usually consists of bladder distension or installations with various drugs with varied reports of efficacy. The Integral Theory Paradigm (ITP) views the pain and urge components of IC/BPS as different phenotypes of uterosacral ligament (USL) weakness, and not necessarily co-occurring as one condition. The ITP’s view of IC/BPS being one and the same condition as the PFS is further analysed below.

Highlight box

Key findings

- Interstitial cystitis/bladder pain syndrome (IC/BPS), as defined by the International Continence Society, is likely part of the posterior fornix syndrome (PFS) and therefore, potentially curable surgically.

What is known and what is new?

- IC/BPS has no known pathogenesis and is not considered curable.
- Cure of IC/BPS without Hunner’s lesion by uterosacral/cardinal ligament repair.

What is the implication, and what should change now?

- Following diagnostic and treatment protocols of PFS can help many women who have IC/BPS.

Evidence for IC/BPS and PFS being the one and the same condition

In 2021, Scheffler *et al.* reported a histologically validated cure of Hunner’s lesion in a 73-year-old woman (3). The report was highly disruptive to existing concepts of IC/BPS, not only because Hunner’s lesion is considered incurable, but also, the patient was managed according to the protocols of the PFS. The PFS comprises CPP, urge, frequency, nocturia, abnormal emptying, post-void residual urine, caused by USL laxity and cured or improved by repair thereof (4). Scheffler *et al.* repaired the cardinal ligament (CL) and USLs with the Tissue Fixation System (TFS) minisling; Hunner’s ulcer cure was a serendipitous finding. Scheffler *et al.* hypothesized that IC/BPS was likely part of the PFS.

Goeschen *et al.* (5) tested the Scheffler hypothesis, that IC/BPS could be part of PFS, for truth or falsity. They revisited clinical data from 198 women who had presented with CPP plus varying degrees of uterine/apical prolapse. The women were treated with a posterior intravaginal slingplasty (IVS), an operation which repaired the USLs using a collagen-producing polypropylene tape (5). Goeschen *et al.* had applied the same PFS diagnostic and treatment protocols as Scheffler *et al.* (3), including the diagnostic algorithm and speculum test (*Figure 1*) (6). Excluding stress urinary incontinence (66 cases), Goeschen

Table 1 Co-occurrence of CPP and several bladder symptoms conforms to the definition of ICS/BPS and posterior fornix syndrome

Variables	Incidences before surgery, n [%]	Incidences 12 months after surgery, n [%]	Comparisons (pre- versus post-incidences) (Z values)	Odds ratios (95% CI)	Cure rates 12 months after surgery, %
Pelvic pain (main symptom)	198 [100]	52 [26]	8.690***	n.d.	74.00
Urinary frequency	127 [64]	26 [13]	6.000***	0.085 (0.051–0.140)	79.69
Nocturia	63 [32]	13 [7]	3.690**	0.151 (0.135–0.493)	78.13
Bladder emptying difficulties	68 [34]	32 [16]	3.198**	0.369 (0.228–0.595)	52.94
SUI	66 [33]	4 [2]	4.266***	0.041 (0.015–0.116)	93.94
ODS	59 [30]	12 [6]	3.596**	0.152 (0.079–0.294)	80.00
Urge incontinence	55 [28]	11 [6]	3.412**	0.153 (0.077–0.303)	78.57
Residual urine >50 mL	44 [22]	20 [10]	2.490*	0.393 (0.222–0.696)	54.55

Reused from (5). Copyright 2022, with permission from Karger. *, P<0.05; **, P<0.01; ***, P<0.001. CPP, chronic pelvic pain; ICS, International Continence Society; BPS, bladder pain syndrome; CI, confidence interval; n.d., not detected; SUI, stress urinary incontinence; ODS, obstructive defecation syndrome.

et al. found that the 198 women had 313 bladder symptoms (*Figure 1*) (4). The diagnosis was in accord with descriptions for both IC/BPS and PFS, except that, CPP and bladder symptoms were cured (*Table 1*). Pain and multiple bladder symptoms were cured (variously) by the USL sling (5), confirming Scheffler *et al.*'s hypothesis that IC/BPS may be one and the same condition as PFS. Hunner's ulcer was absent in all 198 of Goeschen *et al.*'s patients.

Review of other studies of women who were treated by posterior slings according to PFS protocols (7-16) and who were cured of CPP, urgency, other bladder symptoms, reached the same conclusions as Scheffler *et al.* (3) and Goeschen *et al.* (5): IC/BPS and PFS were likely to be the one and the same condition, mainly caused by USL laxity, and could be cured or improved by USL repair.

Unsupported visceral plexus—a likely pathogenesis for CPP and IC/BPS

Reported surgical cure of CPP symptoms by many studies (7-16), support the 1996 hypothesis of Petros (17), that CPP “of unknown origin” may be caused by autonomous afferent impulses originating from visceral nerve axon junctions in the pelvic visceral plexuses (VPs) because of weak USLs. VPs are anatomically supported by USLs. If USLs are weak, the force of gravity or muscle movements acting on the VP junctions may activate autonomous impulses which the cortex interprets as pain originating from the end organ, bladder, rectum, vagina/vulva/muscles, and other sites such

as coccyx, lower abdomen. In support of this hypothesis is the common observation that pelvic pain is relieved on lying down, and by multiple different pain manifestations being relieved by USL support by a speculum test (*Figure 2*) (3,5,6).

The hypothesis of visceral nerve etiology for pain (17) is consistent with the anatomical studies of Butler-Manuel: the T11–L2 and parasympathetic S2–4 VPs were closely involved with, and supported by, the USLs (18). These visceral nerves carry afferent signals from the organ to the cortex and transmit efferent instructions back to the organ. In normal situations, an injury or infection at the end organ sends afferent signals to the brain. The brain responds by sending efferent signals to hypothesized “sleeper cells” via the visceral efferent pathways; these secrete mast cells, leukocytes and other inflammatory cells to “heal” the perceived injury or infection (19).

The Integral Theory concept for IC and other pain causation in the absence of infection or injury is diagrammatically indicated in *Figure 2*: unsupported VPs which contain afferent axons from various end organ sites, bladder “B”, vagina/vulva “V”, rectum “R”, muscles “M” are stimulated by gravity “G”, or muscle movement to send autologous signals to the brain via T11–L2 and S2–4 afferent visceral nerves; the brain (wrongly) interprets these signals as coming from the end organs and responds appropriately; it sends efferent signals to hypothesized “sleeper cells” sited in the end organs.

In the case of the urothelium, hypothesized “sleeper

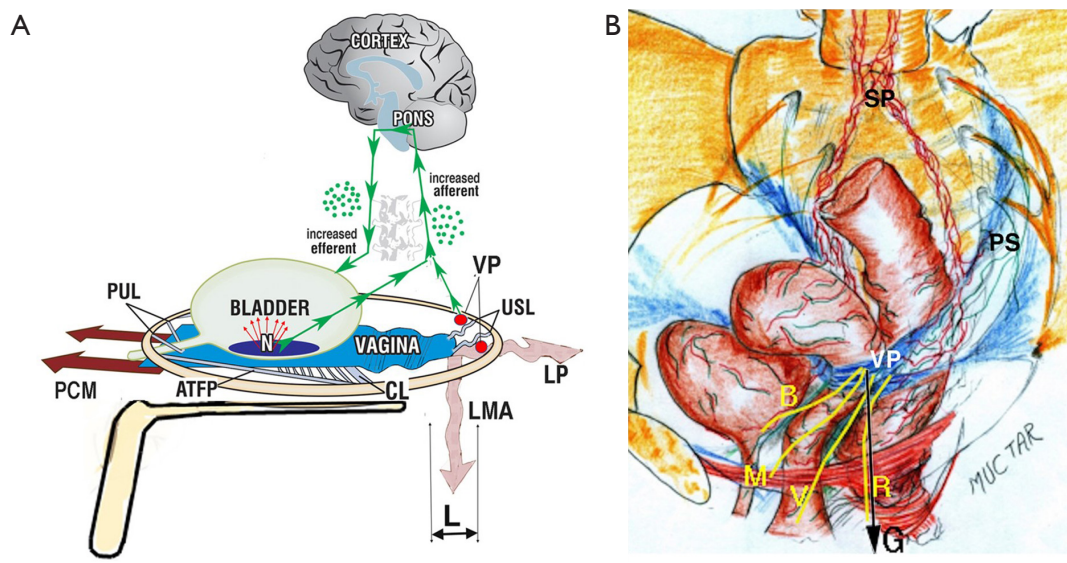


Figure 2 The speculum test relieves pain and urge by supporting uterosacral ligaments “USL”. (A) 3D view of PUL and USL attachments to the pelvic brim. A gently inserted speculum stretches the vagina to support the urothelial stretch receptors “N”, and mechanically supports USLs and pelvic visceral nerve plexuses “VP”. The test, if successful, decreases afferent pain and urge impulses (small green arrows); the patient reports lessening of urge and pain in multiple sites (e.g., “B”, “R”, “M”). “L” indicates USL laxity. Wavy lines in “LP” and “LMA” indicate weakened muscle forces, as “LP/LMA” require a firm insertion USL point to exert optimal force. The wavy form of the vagina indicates looseness; it cannot be stretched sufficiently to support “N” which fire off excess afferents to activate the micturition reflex prematurely. The cortex interprets these impulses as “urge”. (B) 3D view of pelvic organs. VP comprises sympathetic plexus “SP”, and parasympathetic plexus “PS”. The yellow lines represent visceral nerves to and from the end organs, M (muscles), V (vagina/vulva), B (bladder), R (rectum). “G” force of gravity acting on “VPs”. Reused from (5). Copyright 2022, with permission from Karger. PUL, pubourethral ligament; PCM, pubococcygeus muscle; VP, visceral plexus; USL, uterosacral ligament; ATFP, arcus tendineus fascia pelvis; CL, cardinal ligament; LMA, conjoint longitudinal muscle of the anus; LP, levator plate.

cells” create an inflammatory response sufficient to cause Hunner’s ulcer. We hypothesize that the fragility of the urothelium makes it vulnerable to the more florid inflammatory response seen in ulcerating Hunner’s ulcer and end-stage scarring, something not seen in the tissue inflammatory response seen with vulvodynia, which, like IC, exhibits inflammatory cells such as Mast cells and leucocytes and neuroproliferation (19) but no redness (20).

Testing for VP causation of CPP and IC/BPS

The hypothesis of the CPP, part of IC/BPS, being caused by unsupported visceral pelvic plexuses is testable and falsifiable by the speculum test (Figure 2) and the Bornstein local anesthetic (LA) test.

The speculum test

The speculum test (Figure 2) relieves pain and urge by supporting “USL” and stretching the vagina to support the urothelial stretch receptors “N”. The test, if successful, decreases afferent impulses (small green arrows), pain from VPs, and urge from “N”; the patient reports lessening of pain in multiple sites (e.g., “B”, “R”, “M”), and also, simultaneously, urge Figure 2.

The Bornstein test

The Bornstein test is considered the definitive test for VP causation of CPP. It comprises injection of LA into the lower end of the USLs to anesthetize the VPs. Bornstein

relieved the hyperesthesia of vulvodynia in 8/10 women bilaterally and 2/10 unilaterally (21). Petros injected LA into the USLs of three IC/BPS women who had multiple sites of CPP with LA. Relief of all the sites of pain was achieved in all three women (22).

Conclusions and future directions

The key research question now, as we see it, is, “What is the prevalence of PFS in IC/BPS women?”. If it is substantial, then it could reasonably be said, that IC/BPS, at least in such women, is part of PFS, and can potentially be improved or cured by mechanical or surgical support of the USLs.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All clinical procedures described in this study were performed in

accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients for the publication of this article and accompanying images. Human participation in the video was by patient permission on the basis it was deidentified.

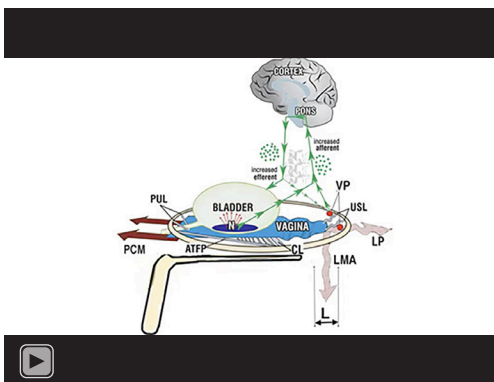
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Video S1 Shows the relationship of IC/BPS to posterior fornix syndrome.