

International Painful Bladder Foundation

The IPBF is a voluntary non-profit organization focused on interstitial cystitis/bladder pain syndrome/Hunner lesion
<https://www.painful-bladder.org/>

RESEARCH UPDATE – January 2026

A REVIEW OF SELECTED RECENT SCIENTIFIC LITERATURE ON INTERSTITIAL CYSTITIS, BLADDER PAIN SYNDROME, HUNNER LESION, HYPERSENSITIVE BLADDER, CHRONIC INFLAMMATORY BLADDER DISEASES, KETAMINE CYSTITIS, CHRONIC (PELVIC) PAIN, URINARY TRACT INFECTION AND ASSOCIATED DISORDERS

Most of these entries include a direct link to the PubMed abstract when you click on the title. An increasing number of scientific articles are published online ahead of print as “In Press,” “Early View,” or “Epub ahead of print,” often well before their appearance in the print journal. While abstracts for these articles are usually available on PubMed, the full pre-publication articles can typically be accessed only through the journal’s website and may require a subscription. In some cases, however, the full article is available as open access. Click on the title to access the PubMed abstract or, where applicable, the full open-access article.

Also included are so-called “preprints.” These are preliminary reports that have not yet undergone peer review and therefore should not be relied upon to guide clinical practice or health-related behaviour. For further information, see: <https://www.medrxiv.org/content/about-medrxiv>.

Terminology: Published articles use varying terminology, including interstitial cystitis, painful bladder syndrome, (primary) bladder pain syndrome, hypersensitive bladder, chronic pelvic pain (syndrome), or combinations of these terms. Hunner Lesion Disease, Hunner’s ulcer, Hunner IC (HIC), and Classic IC are synonymous.

GLOBAL CONSENSUS MEETING ON IC/BPS, Wake Forest University, Winston Salem, US, 23-24 April 2025.

Below are publications by sub-committees in *Neurourology & Urodynamics: Volume 45, Issue 1, Special Section on Global Consensus on IC/BPS*.

[GLOBAL CONSENSUS MEETING ON IC/BPS APRIL 2025: SUMMARY REPORT.](#)

G. Badlani. *Neurourol Urodyn*. 2026 an;45(1):9-10. doi: 10.1002/nau.70126. Epub 2025 Aug 17. PMID: 40819288.

[A REVIEW OF THE ETIOPATHOLOGY OF PHENOTYPES IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME](#)

Maxwell L. Sandberg, Laura Santurri, David Klumpp, Larissa V. Rodriguez, Daniel Clauw, Henry Lai. *Neurourol Urodyn*. 2026 Jan;45(1):11-18. doi: 10.1002/nau.70097. Epub 2025 Jun 29. PMID: 40581873 Review.

Open Access

The aim of this manuscript was to provide a narrative review of the etiopathology of three different interstitial cystitis/bladder pain syndrome (IC/BPS) phenotypes: Hunner lesion, widespread pain, and low bladder capacity. IC/BPS literature was reviewed by the authors specific to the three phenotypes, focusing on etiopathology. Evidence was condensed and summarized on the different causes of each phenotype, emphasizing papers and abstracts dealing with basic science research, symptoms, and treatment options for patients afflicted with the three different IC/BPS phenotypes. Hunner lesion

patients are marked by a distinct, visible inflammatory lesion in the bladder, inflammatory serum and urinary biomarkers, and respond well to bladder-centric treatments targeted specifically at the Hunner lesions. Widespread pain patients have diffuse pain attributed to central nervous system changes manifesting in the bladder, often with co-occurring non-bladder chronic pain conditions such as fibromyalgia and seem to respond better to systemic therapies. Low bladder capacity patients have a marked decrease in anaesthetic bladder capacity during therapeutic hydrodistension of the bladder. They also tend to have higher pain scores, symptoms specifically concentrated at the bladder, and respond to localized treatments, constituting another bladder centric phenotype. IC/BPS should not be thought to represent one unique type or pathophysiology, but rather a diverse group of patients, each with their own etiopathology and phenotypic manifestations.

INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PATIENT PHENOTYPING.

Wolff DT, Tranchina S, Schrepf A, Christopher Doiron R, Chai TC, Walker SJ. Neurourol Urodyn. 2026. PMID: 40566827 DOI: 10.1002/nau.70098

Open Access

In April of 2025, the Wake Forest Institute for Regenerative Medicine hosted a Global Consensus meeting on IC/BPS in Winston-Salem, NC. The goal of this meeting was to establish global consensus regarding diagnostic criteria, phenotyping, treatment outcome assessment, and etiopathology in interstitial cystitis/bladder pain syndrome (IC/BPS). Our sub-committee was tasked with developing a consensus document on patient phenotyping in IC/BPS. Patients with IC/BPS populate broad groups that have been characterized as having a bladder-focused disease phenotype (bladder-centric), a widespread pain and symptoms phenotype (systemic), or by other variable phenotypes including those with myofascial pelvic pain. In this review, the authors discuss the published evidence supporting each of these patient phenotypic groups. Future clinical trials and treatment development in IC/BPS should include patient phenotyping efforts with, at minimum, a focus on stratification into bladder-centric vs systemic and efforts to refine discriminative thresholds (cut-off points) that may influence differential treatment outcomes. It is important to continue to investigate the importance of patient phenotypes on treatment strategy selection, outcomes, and our understanding of the underlying pathophysiology for this disease spectrum.

INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME IN MEN.

Snipes M, Whitman W, Pontari M, Anger J, Samarinas M, Taneja R. Neurourol Urodyn. 2026. PMID: 40605567. DOI: 10.1002/nau.7010

Open Access

In April 2025, the Wake Forest Institute for Regenerative Medicine hosted a Global Consensus meeting on interstitial cystitis/bladder pain syndrome (IC/BPS) in Winston-Salem, NC. The goal of this meeting was to establish attainable targets in phenotyping, diagnosis, and biomarkers for IC/BPS. This subcommittee focused on developing a consensus document addressing IC/BPS in men. Within this document, the authors discuss prevalence, clinical characteristics, evaluation/investigation, and treatment of IC/BPS in men. There is limited literature specifically addressing IC/BPS within the male population, as IC/BPS has traditionally been considered a disease of women. Thus, prevalence data varies widely. Diagnosis of IC/BPS in men is fraught with difficulty, as there is much overlap with other chronic pelvic pain syndrome, specifically chronic prostatitis. Key clinical features specific to IC/BPS are pain with bladder filling and relief with voiding. Painful ejaculation may be indicative of pelvic floor dysfunction. Physical exam, including extensive pelvic exam with analysis of pelvic floor tenderness, is critical in correct diagnosis. Ultrasound +/- urodynamics may be used to rule out obstructive disease, and urinalysis +/- culture must be used to rule out infection. There are no treatments specific to men with IC/BPS. The authors conclude that there is a significant need for more sex-specific research of IC/BPS with consideration for hormonal and anatomical factors that may differentiate the disease in men.

INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME (IC/BPS) DIAGNOSIS: CURRENT LIMITATIONS AND A PRAGMATIC CLINICAL DIAGNOSTIC DEFINITION.

Werneburg GT, Moldwin R, Lowell Parsons C, Shivam Priyadarshi M, Sinha S, Quentin Clemens J. Neurourol Urodyn. 2026 Jan;45(1):32-38. doi: 10.1002/nau.70112. Epub 2025 Jul 8. PMID: 40626422.

Open Access

The purpose was to develop a consensus on diagnostic criteria for interstitial cystitis/bladder pain syndrome (IC/BPS). A subcommittee was identified based on expertise in IC/BPS diagnostic criteria. An outline was generated and iteratively modified until it was found to be acceptable by subcommittee members as the basis for manuscript generation. The manuscript was presented and revised in two iterations according to feedback from international key opinion leaders at the Global Consensus on IC/BPS and the AUA Annual Meeting, respectively. The patient history and physical examination are necessary components in the diagnosis of IC/BPS. Urinalysis and urine culture are necessary laboratory tests to rule out exclusionary conditions including active infection. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) criteria, which were established in 1988 for research purposes, pose several limitations and result in the exclusion of a large proportion of IC/BPS patients when applied clinically. Thus, the authors put forth a pragmatic and streamlined definition that is aligned with existing clinical guidance and standard diagnostic workup. The clinical diagnosis of IC/BPS is based on history, physical examination, and urine studies. IC/BPS is clinically defined as an unpleasant sensation (e.g. pain, discomfort, pressure, burning) that worsens with bladder filling and improves with bladder emptying, of 3 or more months duration, in the absence of exclusionary diagnoses that would likely account for the symptomatology. A substantial number of IC/BPS patients have comorbid pelvic disorders (e.g., pelvic floor dysfunction, vulvodynia, endometriosis) which require separate treatment.

ROLE OF GYNECOLOGIC FINDINGS IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: A CONSENSUS.

Sullivan ME, El Haraki A, Padoa A, Vincent K, Whitmore KE, Cervigni M. Neurourol Urodyn. 2026 Jan;45(1):39-45. doi: 10.1002/nau.70099. Epub 2025 Jun 27. PMID: 40575937.

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The purpose was to evaluate the role of gynecologic findings in Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) by reviewing current international guidelines and identifying relevant gynecologic co-morbidities. This consensus statement was developed through a systematic four-phase process: (1) comprehensive literature review across PubMed/MEDLINE, Embase, Cochrane Library, and Web of Science databases (inception-January 2025) using predefined search terms related to IC/BPS and gynecologic conditions; (2) assembly of a 6-member multidisciplinary expert panel including urologists, urogynecologists, gynecologists and pain specialists; (3) consensus development via modified Delphi technique comprising several electronic rating rounds and a face-to-face meeting, with consensus defined as $\geq 80\%$ agreement; and (4) manuscript preparation with iterative review. A number of associated gynecologic disorders may overlap with IC/BPS, our consensus committee identified five main co-morbid disorders: Endometriosis/Adenomyosis, Genito-Pelvic Pain Penetration Disorder/Sexual Dysfunction, Overactive Pelvic Floor Muscles, Hormone- Associated Genitourinary Changes, Vulvodynia/Vestibulodynia. While not exhaustive, this consensus highlights the most prevalent gynecologic co-morbidities supported by current literature. Clinical evaluation should prioritize a detailed medical history and pelvic examination to identify these overlapping conditions. Future directions include developing a multidisciplinary diagnostic and treatment algorithm to guide clinicians—including urologists, gynecologists, urogynecologists, physical therapists—in comprehensive IC/BPS care.

GLOBAL CONSENSUS ON INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: AN UPDATE ON THERAPEUTIC TREATMENTS.

Buford K, Peters KM, Riedl C, Nath Mishra N, Jacques WJ, Lovasz S, Pinto RA, Birder L. Neurourol Urodyn. 2026 Jan;45(1):46-53. doi: 10.1002/nau.70106. Epub 2025 Aug 10. PMID: 40783827

Open Access

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic condition marked by chronic pain and voiding dysfunction, often without a clear cause. Management of which often requires a multidisciplinary approach, as well as multiple therapeutic interventions. This review characterizes mechanisms and limitations of currently available treatment modalities for IC/BPS, as well as novel and investigational therapies. Conservative and supportive therapies include cognitive therapies, dietary and fluid management, pelvic floor exercises and bladder training. Additionally, pelvic floor directed therapies such as physical therapy, injections and nerve blocks should be considered. Cystoscopy with hydrodistension is both a diagnostic and therapeutic intervention. Currently available oral therapies include: pentosan polysulfate, amitriptyline, hydroxyzine, silodosin, and non-opioid medications such as cyclobenzaprine. Immunotherapies include cyclosporine and tacrolimus. Available intravesical therapies include dimethyl sulfoxide, lidocaine, oxybutynin, and glycosaminoglycan substitution treatment. Neuromodulation is also available including sacral and pudendal neuromodulation. Finally, they explore emerging therapies and drug delivery systems. In this review, the authors present currently available treatment options for IC/BPS. These include conservative therapies, oral medications, intravesical therapies, and neuromodulation. Novel and investigational therapies are presented as well as promise for future directions.

GENOMICS AND HISTOPATHOLOGY IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Ruetten H, , Crawford LK, De EJB, Li W, Akiyama Y. Neurourol Urodyn. 2026 Jan;45(1):54-59. doi: 10.1002/nau.70117. Epub 2025 Jul 16. PMID: 40671333.

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In April of 2025, a Global Consensus meeting on IC/BPS was held in Winston-Salem, NC. The goal of this meeting was to establish global consensus in diagnostic criteria, phenotyping, treatment outcome assessment, and possible etiopathology in interstitial cystitis/bladder pain syndrome (IC/BPS). This sub-committee focused on developing a consensus document on histopathology in IC/BPS. Herein they discuss histological and molecular distinctions of Hunner lesion disease (HLD) and non-Hunner lesion disease (non-HLD) in IC/BPS, including urothelial alterations, inflammatory changes, vascularization and fibrosis, and neurophysiological dysfunction. The molecular and histological characteristics of HLD make it distinct from non-HLD. HLD is histologically characterized by urothelial denudation and subepithelial chronic inflammation featured by B-cell dominant lymphoplasmacytic infiltration, while non-HLD shows subtle inflammatory changes with preserved urothelial layers. Some cases of non-HLD reflect a component of multi-systemic pain syndrome driven by altered neurophysiological networks within the central or peripheral nervous system. Molecular and histological characteristics revealed that HLD and non-HLD are distinct disease entities as the former is an inflammatory disease of the urinary bladder and the latter may be represented by systemic neurophysiological disorder, rather than pathology that is limited to the bladder. This concept could be useful in phenotyping, diagnosis, and development of biomarkers for IC/BPS.

THE ROLE OF BIOMARKERS IN THE DIAGNOSIS AND TREATMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: WHAT DOES CURRENT EVIDENCE REVEAL?

Chen YC, Tyagi P, Alperin M, Stern JNH, Lenore Ackerman A, Kuo HC. Neurourol Urodyn. 2026 Jan;45(1):60-70. doi: 10.1002/nau.70144. Epub 2025 Sep 11. PMID: 40931974.

This narrative expert review aims to elucidate the role of biomarkers in the diagnosis and treatment of interstitial cystitis/bladder pain syndrome (IC/BPS), highlighting their potential to enhance patient care by enabling more precise and individualized therapeutic strategies. The authors performed a comprehensive review of literature focused on biomarkers relevant to IC/BPS, including bladder capacity, symptom intensity, bladder wall thickness, as well as serum and urinary inflammatory cytokines and other biomarkers of inflammation, oxidative stress, and urothelial and extracellular

matrix remodelling. Evidence indicates that biomarkers such as TNF- α , IL-8, and bladder capacity can differentiate between Hunner lesion and non-Hunner lesion IC subtypes, predict treatment responses, and guide effective interventions. Furthermore, advanced statistical methods and machine learning applications show promise in improving diagnostic accuracy and treatment outcome predictions through clustering of the biomarker data. Reliable biomarkers are vital for improving diagnostic precision and tailoring therapies for IC/BPS patients. Ongoing research and validation of these biomarkers are essential for advancing understanding, guiding treatment decisions, and enhancing the quality of life for individuals affected by this complex syndrome. The need for integrated biomarker profiles and multipronged research approaches is crucial for the future of IC/BPS management.

INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: WHY A GLOBAL PATIENT REGISTRY IS CRITICALLY NEEDED.

Mezes C, Niimi A, Kasyan G, Dobberfuhr AD, Malde S. Neurourol Urodyn. 2026 Jan;45(1):71-76. doi: 10.1002/nau.70114. Epub 2025 Jul 7. PMID: 40621787.

The purpose of this article is to establish expert consensus on the rationale for, and components of, a global patient registry for interstitial cystitis/bladder pain syndrome (IC/BPS). The goal is to highlight what a comprehensive international patient registry can add to the growing body of IC/BPS-focused research and summarize the committee's rationale for inclusion or exclusion of certain patient and diagnostic characteristics to identify sub-groups of patients who will benefit from targeted therapy. An expert working group was formed from members of the Global Consensus on IC/BPS meeting. The working group consisted of four Urologists and a Urogynaecologist, and held a series of meetings in 2025 to achieve consensus on the benefits, hurdles and practical aspects of developing a global registry for IC/BPS. Literature search of the PubMed database was also performed where relevant, and all members agreed on the final proposals. The framework for an IC/BPS global registry was developed inclusive of male and female patients ages 18 years and older, who have symptoms of pain, pressure or discomfort related to the bladder, along with lower urinary tract symptoms, that have persisted for 3 or more months, in the absence of confusable disorders. A comprehensive list of patient data points including demographic, history-related, and comorbid conditions was developed. Additionally, validated questionnaires were identified for inclusion that assess domains of pain, urinary symptoms and quality of life. Consensus was reached regarding collecting data on prior treatment, cystoscopy findings and biopsy results where applicable. Lastly, importance was placed on patient-reported questionnaire data that can be input longitudinally by patients to lessen the burden of data collection by providers. Technical, legal and financial aspects were addressed as potential barriers. A global registry for IC/BPS would overcome the limitations of current regional registries by including large numbers of patients from varied geographical locations, allowing for more efficient recruitment of patients for clinical trials. Understanding epidemiological trends and global variation in practice would enable optimization of care and quality

PATIENT RELATED OUTCOMES FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME RECOMMENDATIONS FOR CLINICAL TRIALS AND GENERAL UROLOGY PRACTICE.

Hayes B, Namugosa M, Evans RJ, Hajebrahimi S, Janssen D, King C, Pandey S, Curtis Nickel J. Neurourol Urodyn. 2025 Sep;44(7):1455-1465. doi: 10.1002/nau.70107. Epub 2025 Jul 7. PMID: 40621808; PMCID: PMC12319472.

Open access

The goal of this committee of the Interstitial Cystitis/Bladder Pain (IC/BPS) Consensus Group was to address the use of patient related outcomes (PROs) in IC/BPS. Priority areas of concern and related PICO (Population, Intervention, Comparison, Outcome) questions were addressed based on literature review, committee discussion and consensus group feedback. Consensus recommendations were developed regarding PROs and PRO Measures (PROMs) for the critical PICO questions. PICO questions addressed 4 critical areas of concern: PROs, clinical trial primary endpoints, secondary endpoint

PROMs and questionnaires for general practice management. The committee made 12 recommendations regarding outcomes in IC/BPS research and clinical practice. The most important recommendation was the unmet need to develop and validate a better IC/BPS specific PRO, based on unbiased patient qualitative research methodology. At the present time, the Numerical Rating/VAS pain scales, voiding diaries and global response assessment are recommended for primary endpoint outcomes in clinical trials. The suggested composite IC/BPS specific PROM is the Genito Urinary Pain Index (GUPI) while the Interstitial Cystitis Symptom Index/Problem Index can be used for trial comparisons. If appropriate, generic PROMs that describe and measure pain, quality of life, sexual, and psychosocial parameters are suggested. Until a validated PRO is developed, the NIH GUPI or the Pain Urinary Frequency (PUF) questionnaire provides reasonable clinical evaluation of patients in standard urology practice. PROMs are currently available for use in clinical trials and general practice, but more research is required to create better IC/BPS PRO-based outcome measures.

INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME

COMPARATIVE RISK OF DEVELOPING INTERSTITIAL CYSTITIS WITH CHILDHOOD GASTROINTESTINAL, UROLOGICAL, AUTOIMMUNE, OR PSYCHIATRIC DISORDERS

Alipour-Vaezi M, McNamara RS, Rukstalis MR, Gentry EC, Rukstalis DB, Penzien DB, Tsui KL, Zhong H. *Neurourol Urodyn.* 2025 Sep;44(7):1448-1454. doi: 10.1002/nau.70104. Epub 2025 Jun 25. PMID: 40566828; PMCID: PMC12319504.

Open Access

Interstitial cystitis (IC) is a chronic urological condition associated with significant discomfort, posing diagnostic and therapeutic challenges. Although its etiology remains unclear, early-life conditions such as gastrointestinal (GI) disorders, urological anomalies (UA), psychiatric disorders (PD), and autoimmune diseases (AD) have been hypothesized as potential risk factors for developing IC in adulthood. This study from the USA aims to investigate these associations by conducting a retrospective cohort analysis utilizing data from the TriNetX US Collaborative Network, encompassing over 118 million patient records.

NRF2 DEFICIENCY IN BLADDER EPITHELIAL CELLS OWING TO UBIQUITINATION BY N6-METHYLADENOSINE-MODIFIED TRIM21 INDUCES OXIDATIVE STRESS AND INFLAMMATION TO AGGRAVATE IC/BPS.

Fan Z, Ge Q, Ni B, Zhang J, Du T, Xu H, Duan Z, Zhang S, Wang C, Xue J, Ling F, Chen Z, Shen B, Wei Z. *J Inflamm Res.* 2025 Aug 24;18:11577-11592. doi: 10.2147/JIR.S545880. eCollection 2025. PMID: 40896536

Open Access

Interstitial cystitis/bladder pain syndrome (IC/BPS) has become a pressing clinical issue due to its unclear etiology and severe, persistent pelvic pain. Despite extensive research, the pathogenesis of IC/BPS remains unresolved, and current treatments primarily target symptom relief rather than addressing underlying disease mechanisms. This study from China aimed to investigate the effects of nuclear factor erythroid 2-related factor 2 (NRF2) on IC/BPS and the potential molecular mechanisms. Bladder mucosal biopsies from IC/BPS patients were subjected to RT-qPCR and immunoblotting to quantify NRF2 mRNA/protein expression. In vivo modelling, WT and NRF2 gene knockout mice received intraperitoneal cyclophosphamide to induce cystitis. Bladder function was assessed via Void Spot Assays, and Urodynamic. In vitro validation, LPS-stimulated SV-HUC-1 cells were transduced with NRF2 knockdown or overexpression, and oxidative stress and inflammation levels were evaluated. Then, the molecular mechanism of NRF2 in IC/BPS was determined by conducting Western blot, mass spectrometry, co-immunoprecipitation, and RT-qPCR analyses. This study identified markedly reduced expression of NRF2 in the lesional bladder mucosa of patients with IC/BPS. By employing NRF2 knockout mice and cellular models of bladder inflammation, the essential role of NRF2 in modulating oxidative stress and inflammation was underscored. Furthermore, tripartite motif-containing 21

(TRIM21) interacted with NRF2, promoting its degradation via ubiquitination in bladder epithelial cell lines, thus elucidating TRIM21's regulatory role in bladder inflammation. Additionally, N6-methyladenosine (m⁶A) modifications recognized by IGF2BP2 enhanced TRIM21 expression by stabilizing TRIM21 mRNA. This study positions the TRIM21-NRF2 axis as a key regulator of oxidative stress and inflammation in IC/BPS and suggests it as a promising therapeutic target for future IC/BPS interventions.

USING STRUCTURAL EQUATION MODELLING TO EXPLORE THE RELATIONSHIP BETWEEN INSOMNIA, ANXIETY AND DEPRESSION TO THE SEVERITY OF BPS/IC: A CROSS-SECTIONAL STUDY IN CHONGQING, CHINA.

Wu C, Wang L, Zhou X, Zhou Y, Han S, Dong X, Liu H. *BMJ Open*. 2025 Dec 17;15(12):e099604. doi: 10.1136/bmjopen-2025-099604.PMID: 41407415

Open Access

Despite the high prevalence of insomnia, anxiety and depression in patients with bladder pain syndrome/interstitial cystitis (BPS/IC), their clinical impact is often overlooked. To address this gap, this study from China systematically investigated whether these three comorbidities impact BPS/IC severity. This cross-sectional study included 237 patients with BPS/IC recruited via convenience sampling from Shapingba Hospital affiliated to Chongqing University (Shapingba District People's Hospital of Chongqing) and Chongqing Liangjiang Minsheng Hospital in Chongqing, China, between 24 August 2023 and 21 November 2023. Apart from demographic characteristics, BPS severity was assessed using the O'Leary-Sant interstitial cystitis questionnaire, insomnia was assessed using the Athens Insomnia Scale and anxiety and depression were assessed using Zung's Self-rating Anxiety Scale and Zung's Self-rating Depression Scale, respectively. The structural equation model (SEM) was used to analyse the role of insomnia, anxiety and depression on the severity of BPS/IC. The proportion of severe disease, insomnia, anxiety and depression in participants was 49.37%, 70.89%, 43.88% and 47.26%, respectively. The analysis of SEM indicated that insomnia ($\beta=0.294$, $p<0.001$) and anxiety ($\beta=0.364$, $p<0.001$) were associated with BPS severity, but depression showed no significant association ($\beta=0.042$, $p=0.674$). According to the mediating analysis, the association between insomnia and the disease was attributable to both direct effects of insomnia (55.5%) and indirect effects involving anxiety conditions (44.5%). The authors conclude that their findings indicate that insomnia is associated with BPS/IC severity both directly and indirectly through anxiety in patients with BPS/IC. These results further support the use of psychological and sleep interventions for BPS/IC.

UROLOGIC CHRONIC PELVIC PAIN SYNDROME 3-YEAR SYMPTOM TRAJECTORIES: THE MULTIDISCIPLINARY APPROACH TO THE STUDY OF CHRONIC PELVIC PAIN (MAPP) SYMPTOM PATTERNS STUDY.

Bradley CS, You M, Guo W, Afari N, Gupta P, Kreder KJ, Krieger JN, Lai HH, Lutgendorf SK, Naliboff BD, Sutcliffe S, Tu F, Williams DA, McWilliams T, Rodriguez L, Landis JR; Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network. *BJU Int*. 2025 Dec 2. doi: 10.1111/bju.70087. Online ahead of print. PMID: 41328479

The aim of this study from the USA was to characterise 3-year pelvic pain and urinary symptom trajectories and to identify baseline factors associated with urologic chronic pelvic pain syndrome (UCPPS) improvement. The Trans-Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Symptom Patterns Study was a multicentre, prospective cohort study of UCPPS, including interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome. Patients completed four weekly run-in assessments, baseline visit, and quarterly visits up to 3 years, providing clinical and patient-reported data. A functional clustering approach, applied separately to Pelvic Pain Severity (PPS) and Urinary Symptom Severity (USS) longitudinal change scores, was used to generate symptom trajectory clusters dichotomised as Group 0 'improvers' vs Groups 1-3 'non-improvers'. Logistic regression models explored baseline factors associated with improvement and included run-in period average and baseline scores to adjust for regression to the mean effects. A total

of 545 patients (66% female) were followed for a median (interquartile range) of 34 (23-35) months. Four trajectory clusters were identified for each of PPS and USS, consistent with moderate improvement (Group 0), slight improvement (Group 1), no change (Group 2), and slight worsening (Group 3). In all, 18% and 19% of patients were in the moderately improved PPS and USS groups, respectively, representing 30% of patients overall. Female sex, better sleep, and less opioid use were associated with PPS improvement (Group 0); younger age and baseline cystoscopic treatment were associated with USS improvement (Group 0). In all, 30% of patients with UCPPS demonstrated improvement in pain and/or urinary symptoms over 3 years. Baseline factors associated with improvement may represent markers of a milder or localised phenotype and/or treatment effects.

[INTEGRATIVE DIAGNOSTIC MODEL COMBINING URINARY BIOMARKERS AND CLINICAL PARAMETERS TO IMPROVE DIAGNOSTIC PERFORMANCE IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.](#)

Chen YC, Tian JH, Kuo HC. Eur Urol Open Sci. 2025 Nov 13;82:192-200. doi: 10.1016/j.euros.2025.10.021. eCollection 2025 Dec. PMID: 41322958.

Open Access

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic condition characterized by pelvic pain and urinary symptoms that overlap with other urological disorders, making diagnosis challenging. Current diagnostic approaches are often subjective and inconsistent. This study from Taiwan develops and internally validates a multivariable diagnostic prediction model that combines urinary biomarkers and clinical parameters to improve the diagnostic accuracy for IC/BPS. Data from 385 participants (344 IC/BPS patients and 41 controls) who underwent cystoscopic hydrodistension and videourodynamic studies were analyzed. Urine samples were analyzed for inflammatory cytokines and oxidative stress markers using multiplex and enzyme-linked immunosorbent assays. Clinical parameters included bladder pain (visual analog scale [VAS]) and functional bladder capacity (3-d voiding diary). The participants were randomly divided into training (70%) and testing (30%) sets. Logistic regression with stepwise selection was used to develop diagnostic models.

Urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) showed the highest discriminative ability among individual biomarkers (area under the receiver operating characteristic curve [AUROC] = 0.838). The two-marker model combining 8-OHdG and tumor necrosis factor-alpha (TNF- α) yielded AUROC values of 0.958 (training) and 0.952 (testing). The final integrative model incorporating 8-OHdG, TNF- α , and VAS achieved near-perfect diagnostic performance (AUROC = 0.997 in training and 0.997 in testing), with 96% accuracy, 96% sensitivity, and 92% specificity. This integrative, noninvasive diagnostic model demonstrates excellent diagnostic performance and offers a scalable, objective, and patient-friendly alternative to traditional invasive testing. Incorporation of urinary oxidative stress and inflammatory biomarkers into clinical pain scores may facilitate earlier and more accurate IC/BPS diagnosis in routine practice.

Patient summary: We found that combination of specific urine markers with pain scores can diagnose interstitial cystitis/bladder pain syndrome accurately, without invasive tests. This diagnostic model reduces reliance on patients' subjective symptom reporting, helping doctors confirm the disease earlier and more confidently, while making the diagnostic process more comfortable for patients.

[PLATELET-RICH PLASMA IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS.](#)

Hajebrahimi S, Tahmasbi F, Jahantabi E, Hosseinpour G, Taneja R, Salehi-Pourmehr H. Adv Pharm Bull. 2025 Sep 3;15(3):521-532. doi: 10.34172/apb.025.45444. eCollection 2025 Sep. PMID: 41403738

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This systematic review from Iran and India aims to critically evaluate the safety and efficacy of PRP therapy in managing interstitial cystitis/bladder pain syndrome (IC/BPS). Two researchers independently searched related Databases and collected all studies from inception to December 5,

2023. Outcome indicators of symptom relief were pain scores self-assessment using the VAS system, IC symptoms using the O'Leary-Sant score (OSS), urinary frequency, nocturia, post-void residual (PVR), voided volume, and functional bladder capacity. Among 372 retrieved articles, 13 studies, including 426 patients, were included. The pain of patients decreased significantly after treatment with platelet-rich plasma (PRP) compared to the baseline values (MD: -1.93, 95% CI: -2.28, -1.58). All subgroup analyses revealed a decrease in VAS scores after PRP injection. IC symptoms using OSS, and ICSI decreased significantly after treatment. PRP therapy as a new and successful course of treatment may be a novel therapeutic approach in IC/BPS cases. More study with the control arm is required to enhance treatment regimens for this difficult condition and to better understand the mechanisms of action of PRP in IC/BPS.

UNCOVERING THE MOLECULAR MECHANISM OF SOLASONINE IN TREATING INTERSTITIAL CYSTITIS VIA NETWORK PHARMACOLOGY AND MOLECULAR DOCKING.

Ma Y, Miao J, Cheng C, Liang Y, Xu Z, Zhou J, Tao T. Naunyn Schmiedebergs Arch Pharmacol. 2025 Dec 27. doi: 10.1007/s00210-025-04930-1. Online ahead of print. PMID: 41454953

The purpose of this study from China was to search for potential targets and pathways of solasonine acting on Interstitial cystitis using network pharmacology and molecular docking methods, and to explore the potential mechanism of solasonine in the treatment of IC. Potential therapeutic targets of solasonine were retrieved from three databases: Pharmmapper, Targetnet, and SEA. GO and KEGG analyses were performed. IC-related genes were retrieved from the GEO and Genecards databases, and GO and KEGG analyses were performed. The STRING database combined with Cytoscape was used to map the protein interaction network (PPI) of IC-related targets and screen the core targets. The potential targets of solasonine and IC disease targets were intersected to obtain solasonine-IC common targets. Molecular docking techniques were utilized to confirm the binding of solasonine to primary targets. There are four common core targets of solasonine -IC, HMOX1, B2M, MUC1, and FAS, and molecular docking showed that solasonine binds stably to these four proteins. The analysis of these four gene pathways showed that solasonine regulated several inflammatory and cellular immune pathways, mainly involving the IL-18, apoptosis, and cytokine signalling pathway in the immune system. This study demonstrated that solasonine can inhibit polarization of M1 macrophages and M1-type inflammation. Solasonine may treat IC by targeting HMOX1, B2M, MUC1, FAS and affecting pathways such as the IL-18 signaling pathway, regulation of the apoptosis signalling pathway, and cytokine signalling pathways in the immune system.

ROLE OF PSYCHOSOCIAL FACTORS OF SYMPTOM FLARES IN A COHORT OF PATIENTS WITH CHRONIC UROLOGIC PELVIC PAIN SYNDROME: A COGNITIVE-AFFECTIVE APPROACH.

Lackner JM, Xiong Y, Rogers AH, Radziwon CD, Gudleski GD, Sutcliffe S, Wang J, Naliboff BD, Clemens JQ, Danforth TL. Behav Res Ther. 2025 Dec 18;196:104942. doi: 10.1016/j.brat.2025.104942. Online ahead of print. PMID: 41442954

Little is known about cognitive-affective factors associated with symptom exacerbations ("flares") in individuals with Urologic Chronic Pelvic Pain Syndrome (UCPPS) even though pain is its cardinal feature and a defining attribute of flares which are regarded as a global marker of illness severity. Disease activity is unable to explain UCPPS flares because its pathophysiology involves altered pain modulation in the central nervous system independent of peripheral pain input. The authors from the USA sought to characterize how different psychosocial factors correspond with distinct flare attributes in UCPPS patients. Subjects included 92 formally diagnosed UCPPS (Interstitial Cystitis/Bladder Pain Syndrome or Chronic Prostatitis/Chronic Pelvic Pain Syndrome) patients ($M_{age} = 43$, $SD = 14$, 82 % female) with refractory pelvic pain. Data, completed as part of baseline evaluation of an NIH clinical trial, included the Pain Discomfort Scale (pain-related suffering), Coping Strategies Questionnaire, Catastrophizing subscale, revised McGill Pain Inventory-Short Form (pain quality), Positive and Negative Affect Scale, Childhood Trauma Questionnaire, as well as flare and UCPPS symptom measures. Regression analyses were applied to characterize the association between psychosocial factors and flare dimensions.

Psychosocial factors were broadly associated with multiple flare attributes. Their combined effect was strongest for flare severity with mood, and pain-related suffering, as significant predictors. This investigation breaks new ground by linking psychosocial risk factors to multiple dimensions of UCPPS flares. Further studies are needed to leverage this line of research to develop behaviourally-based flare management programs that strengthen patients' self-regulatory capacity for reducing flares, thereby decreasing the public health burden of UCPPS.

SUCCESSFUL TREATMENT OF CHRONIC SPONTANEOUS URTICARIA AND BLADDER PAIN SYNDROME WITH MONTELUKAST AND/OR OMALIZUMAB: A CASE REPORT.

Bulut G.J Med Case Rep. 2025 Dec 24;19(1):640. doi: 10.1186/s13256-025-05549-9.PMID: 41444680

Open Access

Bladder pain syndrome (BPS) is a chronic condition characterized by pelvic pain, frequency, and urgency lasting more than 6 months without a urinary tract infection. It is a devastating condition that affects both sexes and is often confused with other conditions that cause pelvic pain. Diagnosis is difficult, and effective treatment options are limited. In this article from Turkey, the author presents a 59 year-old Turkish male patient with chronic spontaneous urticaria with typical clinical symptoms of bladder pain syndrome. Common etiologies that could cause increased urinary frequency, urgency or nocturia, urinary tract infection, and overactive bladder were excluded. The patient's symptoms improved significantly with omalizumab and montelukast. This case not only provides new insight into the management of BPS, but also highlights the potential roles of mast cell-mediated mechanisms in the etiology and treatment of this complex condition.

LOW-ENERGY EXTRACORPOREAL SHOCK-WAVE THERAPY WITH OR WITHOUT INTRAVESICAL BOTULINUM TOXIN A INSTILLATIONS FOR REFRACTORY INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: A RANDOMIZED DOUBLE-BLIND TRIAL OF CLINICAL AND BIOMARKER OUTCOMES.

Jhang JF, Kuo HC. *Int Urol Nephrol*. 2025 Dec 15. doi: 10.1007/s11255-025-04950-z. Online ahead of print. PMID: 41396358

Intravesical botulinum toxin A (BoNT-A) injection effectively alleviates symptoms of interstitial cystitis/bladder pain syndrome (IC/BPS) but remains invasive. Low-energy shock-wave therapy (LESW) has emerged as a novel, noninvasive alternative. This study from Taiwan investigated whether LESW could enhance BoNT-A penetration through the urothelium and improve therapeutic outcomes in patients with refractory IC/BPS. In this prospective, randomized, double-blind trial, 51 adults with refractory IC/BPS received four weekly suprapubic LESW sessions. Patients were then catheterized and instilled with either 100 U BoNT-A in 30 mL saline (LESW + BoNT-A, n = 25) or saline alone (LESW + NS, n = 26). The primary endpoint was the 4-week change in O'Leary-Sant symptom score (OSS). Secondary endpoints included pain visual analog scale (VAS), voiding diary parameters, urodynamic results, global response assessment, urinary biomarker levels, and safety during 8 weeks. The results for the total cohort, the LESW + BoNT-A group, and the LESW + NS group were reported separately. Across the cohort, LESW, with or without BoNT-A, significantly reduced IC problem index and pain VAS at week 1, maintaining VAS improvement to week 8. LESW + BoNT-A induced only transient ICPI reduction, whereas LESW + NS further improved OSS, voided volume, and nocturia. BoNT-A instillation after LESW offered no advantage over saline. Urinary eotaxin and prostaglandin E₂ increased after BoNT-A, while 8-isoprostane decreased after saline. No urinary retention, hematuria or infection occurred in both groups. It was concluded that LESW alone provides safe, short-term symptomatic relief for refractory IC/BPS. BoNT-A 100U weekly intravesical instillation after LESW modifies urinary biomarkers but lacks of additional clinical efficacy.

SACRAL NERVE STIMULATION AND CHRONIC BLADDER PAIN: META-ANALYSIS.

Husein R, Tavakkoli M, Abhari SA, Hutchinson L, Shah S, Thillainathan A, Baranowski A. *Neuromodulation*. 2025 Dec 6:S1094-7159(25)01103-1. doi: 10.1016/j.neurom.2025.09.318. Online ahead of print. PMID: 41353655

Chronic bladder pain syndrome (CBPS) is a debilitating condition with limited treatment efficacy. This meta-analysis from London, UK evaluates the effectiveness of sacral nerve stimulation (SNS) in the management of pain, urinary symptoms, and quality of life (QoL) in patients with CBPS. A systematic review was conducted across EMBASE, PubMed, and the Cochrane Library, adhering to Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines. Studies involving adult patients with bladder pain symptoms treated with SNS and reported pain scores were included. Pain scores were the primary outcome measure of interest. Secondary outcome measures included Interstitial Cystitis Problem Index (ICPI)/Interstitial Cystitis Symptom Index (ICSI), urinary frequency, nocturia, and QoL. Risk of bias was assessed using Risk Of Bias In Non-randomized Studies-of Interventions, and pooled effect estimates were calculated using random-effects meta-analysis models. A total of 15 studies (N = 494) were included in the meta-analysis. SNS was associated with a statistically significant reduction in pain scores (mean difference: -2.27 on a 0-10 scale, 95% CI: -2.94 to -1.60, $p < 0.001$), ICSI (-2.18, 95% CI: -2.99 to -1.37, $p < 0.001$), urinary frequency (-1.71 voids/d, 95% CI: -2.29 to -1.12), and nocturia (-1.49 episodes/night, 95% CI: -2.35 to -0.63). Changes in ICPI and QoL were not statistically significant. Complication rates ranged from 0% to 40.6%, and explantation rates from 0% to 18%. This meta-analysis suggests that SNS may offer clinically meaningful pain and urinary symptom relief in patients with CBPS. However, substantial methodological heterogeneity, moderate-to-high risk of bias, and the absence of randomized control trials limit the strength of conclusions. Larger, high-quality trials with standardized diagnostic criteria and outcome measures are essential to establish SNS as a validated treatment option for CBPS.

OPTIMAL DURATION OF HYDRODISTENSION FOR SYMPTOMATIC TREATMENT OF INTERSTITIAL CYSTITIS: A SYSTEMATIC REVIEW.

Lim S, Alhamdani Z, Qin KR, Nesbitt A, Manohar P, Harper M, Donnellan S, Brennan J, Ranasinghe W. Neurourol Urodyn. 2025 Nov 29. doi: 10.1002/nau.70190. Online ahead of print. PMID: 41318983

Interstitial cystitis (IC) is a chronic pelvic condition in the absence of other pathology leading to significant morbidity with limited available treatment options. Cystoscopic hydrodistension (HD) remains an offered intervention for diagnosis and management, providing temporary relief in some patients. There is no overall consensus regarding the optimal duration of HD. This systematic review aims to comprehensively assess the existing literature to identify if there is a relationship between HD time and treatment efficacy. A systematic search in MEDLINE, Embase, and PubMed between January 1969 to April 2024 was performed to identify relevant articles investigating the efficacy of HD as a sole treatment for IC. Two independent reviewers screened abstracts and full texts, and a third resolved conflicts. Quality assessment was performed by two independent blinded authors using The Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) assessment tool. Data regarding population characteristics, duration of HD, treatment number and method, outcome measurements and values were extracted. Included articles were subcategorized into standard (< 15 min) and prolonged (> 15 min) HD durations. A total of 1404 patients in 14 studies were included. Ten studies were prospective or retrospective cohort studies, and four were randomized controlled trials. Nine trials investigated the effect of HD for 15 min or less. Of these, four demonstrated no statistically significant differences in preoperative and post operative symptoms and voiding function between 1 month and 6 months. Four trials found significant improvement in subjective patient symptom scores. Of these, one study investigated two groups of different HD times via different surgeons, and found significant improvements in pain scores for patients in those undergoing HD for 2 min (Pre: 2.4 vs. Post: 5.5) and over 5 min (Pre: 1.3 vs. Post: 3.6). A final study found a time to therapeutic failure post 3 min HD of 25.2 months. Five trials performed prolonged HD between 30 min to 2 h in a total of 152 patients. All were older studies (1977-2003) and performed HD under spinal or local anaesthetic. These studies demonstrated long term symptomatic improvement in included participants (32.3%-67.3%) with follow up durations of 7 months to 3.2 years. Overall risk of bias across domains was assessed as high between included studies. HD remains a contentious treatment option for IC, with limited long-term results in the literature. This study suggests longer HD times may result in improved

efficacy and duration of symptom relief but in the setting of potentially increased risks of severe complications including bladder perforation. Risk of bias, observational study designs, heterogeneity, and lack direct comparisons in durations of HD limits conclusions. This review underscores the need for larger, prospective trials determining the effects of HD duration on treatment efficacy.

DISCRETE MATHEMATICAL NETWORK ANALYSIS BRIDGING CLINICAL VOCABULARY AND PATIENT DISCOURSE IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME ONLINE COMMUNICATIONS.

Okui N, Ichino K, Sakuma Y, Ikehata Y, Okui M, Horie S. Sci Rep. 2025 Nov 29. doi: 10.1038/s41598-025-30819-3. Online ahead of print. PMID: 41318822

Open Access

Interstitial cystitis/bladder pain syndrome is a chronic condition involving pelvic pain and urinary symptoms. A three-stage analytical framework examined the correspondence between vocabulary from validated clinical questionnaires and language used in patient discussions on social media. Stage 1 identified 19 symptom-related terms from three questionnaires, all consistent with international diagnostic criteria. Stage 2 analyzed over 500,000 words from online discussions, detecting 73.7% of these terms and revealing a central "pain-urgency-voiding" triad in patient discourse. Stage 3 mapped strong symptom-site links, including burning-urethra and pain-abdomen, which may indicate underrecognized comorbidities. Clinical terms occupied central positions in the discourse network and showed greater structural importance than general vocabulary. Findings highlight differences between clinical terminology and patient-preferred language, suggesting strategies to improve assessment tools, address terminology gaps, and enhance patient-centered care. The approach is adaptable to other chronic conditions, supporting integration of real-world patient expression into clinical practice.

CLINICAL FEATURES AND PROGNOSTIC SIGNIFICANCE OF PELVIC-PERINEAL PAIN IN WOMEN WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS: A RETROSPECTIVE STUDY.

Zhang Z, Zhang Z, Ling M, Zhang Z. Int Urogynecol J. 2025 Nov 27. doi: 10.1007/s00192-025-06422-5. Online ahead of print. PMID: 41307596

Research on female patients with bladder pain syndrome/interstitial cystitis (BPS/IC) who have urethral, vaginal, perineal, or anal pain (pelvic-perineal pain, PPP) remains limited. This retrospective study from China characterized their clinical features and treatment outcomes. From 2013 to 2023, a total of 130 female patients with BPS/IC were enrolled. Treatments included hydrodistension with Hunner lesion resection (when present), oral/intravesical medications, and pudendal nerve block for significant PPP. Recurrences were managed with repeat therapy or advanced options (platelet-rich plasma, botulinum toxin, sacral neuromodulation), with urinary diversion as the last resort. : Among the cohort, 24 patients (18.46%) were identified as having PPP. These patients were significantly older and had higher symptom scores than those without PPP (all $p < 0.05$). The PPP group exhibited a higher prevalence of cystoscopic grade 4 lesions and a smaller anaesthetic bladder capacity. Furthermore, within the PPP cohort, the presence of grade 4 lesions and a bladder capacity ≤ 400 ml were significant predictors of poor treatment outcome. Over a median follow-up of 74.8 months, although overall improvement was not statistically different from a severity-matched control group, treatment failure necessitating urinary diversion occurred exclusively in the PPP group (12.5% vs 0%, $p = 0.013$). Furthermore, the PPP group required significantly more therapeutic interventions per patient (1.96 vs 1.17, $p = 0.001$). A subset of female patients with BPS/IC presents who had concomitant PPP, which identifies a more severe disease phenotype characterized by objective markers of severity and a higher risk of treatment failure. The assessment of PPP serves as a straightforward and valuable prognostic marker in clinical practice.

BAICALIN AMELIORATES INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME BY INHIBITING THE TLR4/NF-KAPPAB PATHWAY.

Yang D, He Y, Alimu P, Cao D, Liu J. *Naunyn-Schmiedeberg's Arch Pharmacol.* 2025 Nov 26. doi: 10.1007/s00210-025-04824-2. Online ahead of print. PMID: 41296034

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic inflammatory bladder disorder characterized by pelvic pain and urinary symptoms, yet effective therapeutic options remain limited. Baicalin (BA), a bioactive flavonoid derived from *Scutellaria baicalensis*, exhibits anti-inflammatory and antioxidant properties, though its role in IC/BPS has not been fully elucidated. This study from China demonstrates that BA significantly ameliorates cyclophosphamide-induced urination frequency and bladder tissue damage and reduces serum levels of pro-inflammatory cytokines, including TNF- α , IL-6, and IL-1 β , in a rat model of IC/BPS. Integrated analysis of network pharmacology, metabolomics, molecular docking, and experimental validation elucidated the potential mechanism by which BA treats IC/BPS through regulation of the TLR4/NF- κ B signalling pathway. Network pharmacological analysis identified 13 core targets, and both KEGG pathway enrichment and metabolomics results indicated significant enrichment of the NF- κ B signalling pathway. Molecular docking confirmed strong binding affinities between BA and TLR4, MYD88, and NF- κ B p65, with binding energies below -7.0 kcal/mol. Western blot analysis further verified that BA treatment downregulated the expression of these key signalling molecules. These results indicate that BA alleviates IC/BPS primarily by suppressing the TLR4/NF- κ B pathway, thereby attenuating inflammation and restoring metabolic balance. These findings provide a mechanistic basis for the application of BA in IC/BPS treatment and support its potential for clinical translation.

BLADDER TRIGONE AS A SENSORY HUB: A NARRATIVE REVIEW.

Sadahira T, Maruyama Y, Mitsui Y, Sekito T, Watanabe T, Watanabe M. *Cureus.* 2025 Oct 19;17(10):e94951. doi: 10.7759/cureus.94951. eCollection 2025 Oct. PMID: 41267700

Open Access.

The bladder trigone is an anatomically and functionally distinct region within the lower urinary tract (LUT), characterized by a dense network of afferent sensory fibers, specialized urothelial interactions, and prominent mechanotransduction mechanisms. Its intricate neuroarchitecture enables precise detection of bladder filling and coordination of micturition, whereas dysregulation of these pathways contributes to lower urinary tract symptoms (LUTS), including urgency, frequency, and bladder pain. Despite its recognized clinical relevance, the structural and functional basis of trigonal sensory signaling - and its role - remain incompletely understood. This review from Japan synthesizes current evidence on trigonal afferent organization, integrating data from anatomical mapping, receptor profiling, electrophysiological characterization, and translational research. Seminal anatomical observations are combined with recent advances in mechanotransduction and purinergic, peptidergic, and transient receptor potential (TRP) signaling to provide a comprehensive perspective. The trigone exhibits three principal afferent classes: (1) intraepithelial fibers penetrating umbrella cells, marked by P2X purinoceptor 3 (P2X3), transient receptor potential vanilloid 1 (TRPV1), calcitonin gene-related peptide (CGRP), and substance P (SP); (2) subepithelial plexuses surrounding microvasculature, enriched in vasoactive neuropeptides and exhibiting plastic hypertrophy in overactive bladder (OAB) and interstitial cystitis/bladder pain syndrome (IC/BPS); and (3) encapsulated corpuscular endings at the lamina propria-detrusor junction, expressing PIEZO1/2 and acid-sensing ion channels (ASICs) for rapid adaptation. In trigeminal dorsal root ganglion (DRG) neurons, high expression of PIEZO2, P2RX3, and voltage-gated sodium channel, type 1.8 (Nav1.8) was observed, revealing their role as the foundation for multisensory information processing. Functional assays highlight distinct mechanotransductive and chemosensory pathways, with aging, inflammation, and neurotrophic factors driving afferent plasticity underlying abnormal bladder sensation, such as urgency, frequency, and pain. Early clinical trials of P2X3 antagonists and intravesical TRPV1 inhibitors demonstrate promising symptomatic benefits. Collectively, evidence positions the bladder trigone as a critical sensory hub where neuronal, urothelial, and immune signals converge to regulate bladder sensation. Understanding its molecular and structural specialization may inform the development of region-

specific neuromodulatory therapies targeting sensory urgency and afferent-driven bladder dysfunction.

INTEGRATED IDENTIFICATION OF IMMUNE-RELATED THERAPEUTIC TARGETS FOR INTERSTITIAL CYSTITIS VIA MULTI-ALGORITHM MACHINE LEARNING: TRANSCRIPTOMIC PROFILING AND IN VIVO EXPERIMENTAL VALIDATION.

Wang Y, Zhou C, Zhang F, Yang Y, Miao J, Hu X, Zhang X, Ji A, Zhang Q. *Front Immunol.* 2025 Jul 24;16:1636855. doi: 10.3389/fimmu.2025.1636855. eCollection 2025. PMID: 40777016

Open Access

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a complex urological disorder characterized by chronic pelvic pain and urinary dysfunction, with limited diagnostic biomarkers and therapeutic options. Emerging evidence implicates immune microenvironment dysregulation in its pathogenesis, yet the identification of key driver genes and cross-omics integration remains underexplored. This study from China integrated three transcriptomic datasets to identify immune-related gene modules via weighted gene co-expression network analysis (WGCNA). A diagnostic model was constructed using 113 machine learning algorithms. Immune cell infiltration was assessed via CIBERSORT, and single cell sequencing elucidated cellular heterogeneity. Drug candidates were predicted using DSigdb and validated through molecular docking and dynamics simulations. A cyclophosphamide (CYP)/lipopolysaccharide (LPS)-induced IC/BPS murine model was established to evaluate therapeutic efficacy of prioritized compounds (Resiniferatoxin and Acetohexamide) via histopathology, ELISA, and immunohistochemistry. Eight core immune-related genes were identified. The machine learning model achieved AUC >0.9 in both training and validation cohorts. Single-cell analysis revealed IFI27 overexpression in epithelial and immune cells, correlating positively with M1 macrophages and activated CD4+ T cells ($p < 0.05$). Molecular docking demonstrated strong binding affinity between IFI27 and Acetohexamide (-19.91 ± 0.98 kcal/mol) or Resiniferatoxin (-32.98 ± 1.74 kcal/mol), with dynamics simulations confirming structural stability. *In vivo*, both compounds significantly reduced bladder inflammation ($p < 0.05$), with Acetohexamide showing superior efficacy in downregulating IFI27 expression and systemic pro-inflammatory cytokines. This multi-omics study deciphered immune dysregulation in IC/BPS and established a robust diagnostic framework. The validation of IFI27-targeting compounds in alleviating inflammation highlights translational potential for repurposed therapeutics. These findings advance precision immunotherapy strategies for IC/BPS.

INTRAVESICAL SUBSTANCE P ENHANCES BLADDER AFFERENT NERVE ACTIVITY WITHOUT THE INFLUENCE OF THE MICTURITION REFLEX.

Natsuya H, Fujita T, Kojima Y, Aizawa N. *Naunyn Schmiedebergs Arch Pharmacol.* 2025 Aug 7. doi: 10.1007/s00210-025-04503-2. Online ahead of print. PMID: 40773011

Substance P (SP) is important in the physiological and pathophysiological functions of the bladder, including bladder sensory disorders like interstitial cystitis/bladder pain syndrome (IC/BPS) and overactive bladder (OAB). However, the impact of SP on sensory function is not fully understood. The aim of this study from Japan was to determine the effects of SP on bladder function in relation to capsaicin, specifically on bladder afferent nerve activity. Female Sprague-Dawley rats were used. The *in vitro* organ bath study assessed SP-induced detrusor contraction in intact and inside-out preparations of isolated whole bladders. *In vivo* cystometry and multi-unit bladder afferent nerve activity were measured before and after intravesical SP-instillation. Immunohistochemistry was used to locate the neurokinin-1 receptor (NK1R), an SP receptor, and transient receptor potential vanilloid 1 (TRPV1), a capsaicin receptor, in the urinary bladder. The organ bath study revealed that the intravesical pressure significantly increased in the intact preparation, but not in the inside-out preparation, by administering SP after capsaicin-desensitization. During intravesical SP-instillation, cystometric parameters remained unchanged, but bladder afferent nerve activities were significantly increased. Immunohistochemistry revealed that NK1R and TRPV1 were expressed differently throughout the bladder, but some of the expression was colocalized in the lamina propria. SP caused

detrusor contraction via the smooth muscle and increased bladder afferent activity via the urothelium. SP may influence such bladder function on its own rather than as a result of capsaicin exposure. These findings may shed new light on SP's pathophysiological roles and therapeutic strategies for IC/BPS and OAB.

[NEW INSIGHTS INTO INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AT SINGLE-CELL RESOLUTION.](#)

Kuret T, Kreft ME. *BJUI Compass*. 2025 Aug 4;6(8):e70051. doi: 10.1002/bco2.70051. eCollection 2025 Aug. PMID: 40765664

Open Access

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic inflammatory bladder disorder with unknown aetiology and limited treatment options. Single-cell RNA-sequencing (scRNA-seq) has provided unprecedented insights into cellular heterogeneity in IC/BPS. This review from Slovenia summarizes recent scRNA-seq findings on bladder cell populations, emphasizing urothelial, interstitial and immune cells. A comprehensive analysis of published scRNA-seq studies was conducted to compare bladder cell subtypes in healthy and IC/BPS-affected bladders. Differences between IC/BPS patients and mouse models, as well as sex-specific cellular variations, were examined. IC/BPS bladders exhibit significant urothelial alterations, including a reduction in UPK3A + umbrella cells and an expansion of progenitor-like cells with impaired regenerative capacity, linked to TLR3-NR2F6 signalling. Interstitial cells include three fibroblast subtypes (PDGFRA+, RGS5+ and pro-inflammatory IL6-producing fibroblasts), which contribute to fibrosis and inflammation. The immune landscape is characterized by a Th1-biased response, exhausted CD8 + T cells and reduced regulatory T cells, with HPV infection detected in most IC/BPS patients, suggesting a possible viral aetiology. Cell-to-cell interactions are compromised, with enhanced macrophage-endothelial signalling via CXCL8-ACKR1 and CXCL2/3-ACKR1 pathways, highlighting potential therapeutic targets. Notably, sex-based differences reveal stronger immune activation in females and increased urothelial proliferation in males, potentially explaining the higher IC/BPS prevalence in females. scRNA-seq has advanced our understanding of IC/BPS by identifying disease-associated cell types, signalling pathways and intercellular interactions. Future research should integrate multi-omics approaches and explore non-invasive urine-based scRNA-seq for improved diagnosis and therapy.

[ANALYSIS OF THE DIAGNOSTIC VALUE OF PERIPHERAL BLOOD IMMUNE INFLAMMATORY INDICATORS OF FEMALE BLADDER PAIN SYNDROME.](#)

Wang Y, Liu S, Shi H, Xie C, Li P, Jia K, Tang Y, Hu H. *Front Surg*. 2025 Oct 31;12:1685098. doi: 10.3389/fsurg.2025.1685098. eCollection 2025. PMID: 41245799

Open Access

Numerous research indirectly prove that Female bladder pain syndrome (FBPS) is associated with immune-related inflammation. According to the correlation analysis between peripheral blood immune-inflammatory markers and disease diagnosis, this research from China further verifies the potential diagnostic value of peripheral blood inflammatory markers in FBPS. A total of 149 women with bladder pain syndrome who visited the urology department of the authors' hospital from January 2013 to December 2024 and 149 healthy controls Patients who underwent health examinations at the physical examination centre of the authors' hospital from January 2022 to January 2023 were screened. All patients' peripheral blood inflammatory markers at admission included Neutrophil-to-Lymphocyte ratio (NLR), Systemic Immune Inflammation index (SII), et al. The maximum bladder capacity (MBC) during surgery served as the bladder volume. Multivariate binary regression was used to calculate the correlation between these indicators and disease diagnosis as well as MBC. The correlation between these indicators and MBC is secondary outcomes. The optimal cut-off value for the parameters was identified using the receiver operating characteristic (ROC) curve and its area under the curve (AUC) over time. Compared with the control group, patients in the observation group demonstrated significantly higher SII, NLR, PLR, neutrophil count, whereas peripheral blood platelet

count (PLT) and absolute lymphocyte count decreased, with statistically significant differences (all $P < 0.05$). Multivariate binary logistic regression analysis revealed increased NLR as an independent risk factor for FBPS. Compared with the normal bladder capacity group, patients with small bladder capacity demonstrated significantly lower SII, PLR, PLT, with statistically significant differences (all $P < 0.05$). Multivariate binary logistic regression analysis revealed decreased PLT as an independent risk factor for reduced bladder capacity. Peripheral blood inflammation indicators can be employed as an auxiliary diagnostic standard for FPBS, and NLR can be used as an independent diagnostic indicator for FBPS. However, further prospective studies are warranted to identify the causal relationship of these indicators with patient symptoms.

[THE ROLE OF URINARY SECRETORY IMMUNOGLOBULIN A IN THE PATHOPHYSIOLOGY OF INTERSTITIAL CYSTITIS.](#)

Ozdemir T, Aliyev B, Ergun KE, Kalemci S, Kizilay F, Azarsiz E, Sirmsir A. Int Neurourol J. 2025 Sep;29(3):181-187. doi: 10.5213/inj.2550048.024. Epub 2025 Sep 30. PMID: 41077791

Open Access

This study from Turkey aimed to determine whether urinary secretory immunoglobulin A (sIgA) levels differ between patients with bladder pain syndrome/interstitial cystitis (BPS/IC) and healthy controls, and to assess whether urinary sIgA is linked to mucosal immune mechanisms that may contribute to BPS/IC pathophysiology. A single-centre, cross-sectional study was conducted between April and June 2020 at the Department of Urology, Ege University Faculty of Medicine. Forty female patients with BPS/IC and 40 healthy controls were enrolled. Symptom severity in the BPS/IC group was evaluated using the O'Leary-Sant Interstitial Cystitis Symptom and Problem Index. Patients with active urogenital infections, a history of bladder cancer, or prior pelvic radiotherapy were excluded. Urine samples were collected in sterile containers, centrifuged, and stored at -80°C before sIgA measurement using a commercial enzyme-linked immunosorbent assay kit. Correlations between continuous variables were examined with Spearman rank correlation coefficients. Urinary sIgA levels were not significantly different between the BPS/IC group (mean \pm standard deviation: 0.96 ± 1.5 $\mu\text{g}/\text{mL}$) and healthy controls (0.53 ± 0.7 $\mu\text{g}/\text{mL}$) ($P=0.173$). Subgroup analyses within the BPS/IC cohort showed that smokers had significantly lower urinary sIgA levels (median [range], 0.001 [0.000 - 0.082] $\mu\text{g}/\text{mL}$) compared with nonsmokers (median [range], 0.720 [0.000 - 6.850] $\mu\text{g}/\text{mL}$) ($P=0.004$). Conversely, patients with cardiac comorbidities had significantly higher urinary sIgA levels (median [range], 0.820 [0.100 - 6.850] $\mu\text{g}/\text{mL}$) than those without cardiac disease (median [range], 0.213 [0.000 - 2.300] $\mu\text{g}/\text{mL}$) ($P=0.015$). Although no significant differences in urinary sIgA levels were observed between BPS/IC patients and healthy controls, subgroup analyses identified associations with smoking and cardiac comorbidities. These findings suggest that sIgA may be relevant to BPS/IC pathophysiology and highlight the potential of mucosal immune biomarkers. Larger studies are warranted to further clarify the role of sIgA in BPS/IC.

[NERVE GROWTH FACTOR-TARGETING NANOCLUSTER-ANTIBODY-DRUG CONJUGATES FOR INTRAVESICAL PRECISION THERANOSTICS OF INTERSTITIAL CYSTITIS.](#)

Lin Z, Wang W, Liu D, Liu Q, Xu Z, Zhou X, Zhang X, Huang Y, Zhao Q, Wu Z, Yang J. Biomaterials. 2025 Nov 5;328:123840. doi: 10.1016/j.biomaterials.2025.123840. Online ahead of print. PMID: 41223715

Interstitial cystitis (IC) is a chronic inflammatory bladder disorder lacking timely diagnostic and therapeutic options. Here, the authors from China and USA propose a unitary theranostic nanocluster-antibody-drug conjugate (NADC) by covalently attaching dihydroorotate dehydrogenase inhibitors (DHODHi) and ultrasmall gold quantum clusters (AuQCs) to a nerve growth factor (NGF) antagonistic antibody, with multimodality imaging contrasts. Combining anti-inflammatory effects from all individual components, intravesical NADC specifically homed to mucosal lesions with tissue-residing NGF overexpression in the voided bladder, where it neutralized and formed immunocomplexes with secreted NGF to be intracellularly internalized by inflammatory macrophages for payload release through the Fc γ R-mediated pathway. NADC alleviated inflammation in chronic, acute, and prophylactic IC models of rats, as revealed by behavioural and pathological evaluations.

Transcriptomics unveiled cytokine modulation and concomitant inhibition of perturbed IL-17, NF- κ B, TNF, and JAK-STAT signaling pathways. Notably, NADC indirectly remodeled the host bladder microbiota by differentially varying anti-inflammatory and pro-inflammatory bacterial diversities. Distinct from conventional nanoparticles conjugated with antibodies or drugs, NADC relies on the antibody framework, outperforms clinical standard-of-care agents, and represents emerging precision medicine with translational potential for IC theranostics in clinical practice.

EFFECTS OF INTRAVESICAL COCKTAIL INSTILLATION ON OUTCOMES AND SERUM PAIN FACTORS OF PATIENTS WITH BLADDER PAIN SYNDROME.

Jia Y, Zhang Y, Wang B, Shi J. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2025 Nov 11. doi: 10.5507/bp.2025.029. Online ahead of print. PMID: 41222218

Jia and colleagues from China aimed to assess the effects of intravesical cocktail instillation on the outcomes and serum pain factors of patients with bladder pain syndrome (BPS). The clinical data of 86 female BPS patients hospitalized between March 2017 and March 2024 were collected for retrospective analysis. All patients were treated with oral medication (amitriptyline) + local intravesical instillation of drugs, and then assigned to a control group (sodium hyaluronate intravesical instillation) and a research group [intravesical instillation of dimethyl sulfoxide (DMSO) + chondroitin sulfate (CS) + low-molecular-weight heparin (LMWH) cocktail]. The research group (n=43) had lower urination frequency in 24 h, Pelvic Pain and Urgency/Frequency Patient Symptom Scale score, and O'Leary-Sant interstitial cystitis symptom index and interstitial cystitis problem index, as well as larger single urination volume than those of the control group (n=43) after 3 and 6 months of treatment ($P < 0.05$). In the serum, the levels of substance P (SP), 5-hydroxytryptamine (5-HT), prostaglandin E2 (PGE2), neuropeptide Y (NPY), β -endorphin (β -EP), and dopamine (DA) declined in the two groups after 1 month of treatment in comparison to the pre-treatment levels. The levels of SP, 5-HT, PGE2, and NPY were lower, while the levels of β -EP and DA were higher in the research group than those in the control group ($P < 0.05$). The intravesical instillation of DMSO + CS + LMWH cocktail is superior in long-term outcomes. It is more conducive to improving the levels of serum pain factors, with a good safety profile and without increasing adverse reactions.

THE USE OF INTRAVESICAL HYALURONIC ACID FOR THE TREATMENT OF REFRACTORY INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME IN TAIWAN: A REVIEW OF THE LITERATURE.

Yang E, Liu CK, Tsai CP, Liao YH, Ying TH, Hung MJ. Taiwan J Obstet Gynecol. 2025 Nov;64(6):971-977. doi: 10.1016/j.tjog.2024.04.023. PMID: 41213788

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic bladder disease characterized by pelvic pain, irritative urinary symptoms and typical cystoscopic findings in the absence of other identifiable pathology. Intravesical hyaluronic acid (HA) instillation, which is a glycosaminoglycan replenishment therapy, has been indicated for the treatment of refractory IC/BPS in Taiwan since 2008. To assess treatment outcomes, the authors conducted a thorough literature review and EMBASE, PubMed and The Cochrane Library were used to retrieve relevant studies. Eight studies with a total of 428 patients were included in the review. A standard 6-month therapy with four weekly followed by five monthly bladder instillations was used in these studies. All studies reported statistically significant ($p < 0.05$) improvements of bladder symptoms, bother and overall bladder conditions after treatment via the pain-Visual Analogue Scale, the O'Leary-Sant Interstitial Cystitis Symptom and Problem Index, a three-day voiding diary and the Global Response Assessment. Hyaluronic acid instillation also significantly ($p < 0.05$) improved urodynamic parameters, sexual function scores, and mental health scores. However, some bladder pain and storage symptoms persisted, and cystoscopic abnormality was not improved after treatment in most patients. No significant adverse events from the treatment were reported. In conclusion, intravesical HA therapy is a safe and effective treatment for refractory IC/BPS. The persistence of some bladder pain, storage symptoms, and cystoscopic abnormalities after treatment verifies the chronicity of the disease. Further studies on maintenance and additional

therapy for refractory IC/BPS with longer-term follow-up are necessary to further improve treatment outcomes.

[HYALURONIC ACID AND CHONDROITIN SULPHATE INSTILLATION IN CHRONIC BLADDER DISEASES: A META-ANALYSIS.](#)

Corona G, Capogrosso P, Baldini S, Rastrelli G, Vignozzi L, Romero-Otero J, Salonia A, Reisman Y, Bettocchi C, Maggi M, Fode M. BJU Int. 2026 Jan;137(1):36-48. doi: 10.1111/bju.70016. Epub 2025 Oct 26. PMID: 41139434

The purpose of this study from Italy and Spain was to systematically summarise and meta-analyse all uncontrolled and controlled studies evaluating the role of intravesical instillation of hyaluronic acid (HA), with or without chondroitin sulphate (ChS), in the treatment of bladder pain syndrome (BPS), recurrent urinary tract infection (rUTI) and post-radiation cystitis (pRC). A systematic review was conducted, and a protocol was registered with PROSPERO (CRD42025640480). Studies published between 1 January 1969 and 31 August 2024 were retrieved from multiple databases. Data were analysed using random-effects and common-effects models with subgroup and sensitivity analyses. A total of 131 studies were retrieved, of which 30, 10 and three investigated the use of HA/ChS in patients with BPS and rUTI or pRC, respectively, and were included in the analyses. The use of HA/ChS resulted in a significant improvement in pain as well as voiding and irritative symptoms in all the investigated conditions. In addition, the treatment reduced the risk of rUTI when compared to standard care. Although limited data were available, when randomised controlled trials were investigated, the combined use of HA/ChS resulted in better outcomes and a lower infection rate compared to either placebo or standard of care (odds ratio 0.42 [95% CI 0.25; 0.49]; $P < 0.0001$). Finally, an improvement in sexual function and quality of life was also observed.

[ENHANCED THERAPEUTIC EFFICACY OF CATIONIC LIPOSOME-DELIVERED NERVE GROWTH FACTOR ANTISENSE OLIGONUCLEOTIDE FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.](#)

Gao Y, Zhao Y, Zhu L, Ke H, Li W, Bolaji SG, Wang H, Xu K, Wang L. J Mater Chem B. 2025 Sep 24;13(37):11663-11673. doi: 10.1039/d5tb00820d. PMID: 40878215

The pathogenesis of interstitial cystitis/bladder pain syndrome (IC/BPS) remains unclear, and there is no definitive treatment for this condition. Studies have shown that antisense oligonucleotide (asODN) targeting nerve growth factor (NGF) can downregulate the level of NGF in the bladder, however, the uptake of NGF asODN by the body is limited. Therefore, this study from China constructed cationic liposomes (CLs) as a delivery system to carry NGF asODN and evaluated its functional efficacy on the bladder. The results indicated that the optimized CLs/asODN delivery system had an average particle size of approximately 200 nm, an average zeta potential of around +53 mV, and an encapsulation efficiency of over 90% with good stability. Additionally, CLs/asODN significantly facilitated the uptake of asODN fluorescence by the urothelium, with an uptake rate of 14.6%, which was 40.2 times free asODN. In a rat model of IC/BPS, treatment with CLs/asODN reduced voiding frequency, significantly increased maximum cystometric capacity, prolonged inter-contraction interval of the bladder, and improved bladder compliance. Furthermore, hematoxylin-eosin staining and immunohistochemical analysis revealed significantly reduced expression levels of NGF, PACAP, Piezo2, CCL2, IL-6, and TGF- β factors after treatment, indicating that the overexpression of NGF in the bladder could be indirectly blocked by complexing NGF asODN with cationic liposomes. The CLs/asODN prepared in this study improved the adhesion and penetration of the drug at the bladder mucosa site, effectively alleviated bladder dysfunction in rats, and further enhanced the inhibitory effect of asODN on NGF, which may provide a new strategy for the treatment of IC/BPS.

[INTRAVESICAL INSTILLATION WITH VIVO-MORPHOLINO NERVE GROWTH FACTOR ANTISENSE THERAPY AMELIORATES ACUTE INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME-RELATED URINARY FREQUENCY IN A RAT MODEL.](#)

Chen YH, Chen WC, Liu PL, Chen HY. *Int Urogynecol J.* 2025 Oct 25. doi: 10.1007/s00192-025-06394-6. Online ahead of print. PMID: 41137924

Increased nerve growth factor (NGF) expression in the bladder is known to contribute to the hyperexcitability of C-fiber bladder afferent pathways in interstitial cystitis/painful bladder syndrome (IC/PBS). Chen and colleagues from Taiwan hypothesized that intravesical administration of vivo-morpholino NGF antisense oligonucleotide (OND) would downregulate NGF expression and alleviate IC/PBS-associated urinary frequency. Eighteen virgin female rats were randomly divided into three groups: (1) saline-injected control, (2) cyclophosphamide (CYP) plus intravesical instillation with normal saline, and (3) CYP plus intravesical instillation with vivo-morpholino NGF antisense OND (2 mg/kg). Female rats received an intravesical instillation of vivo-morpholino NGF antisense oligonucleotide once daily for three consecutive days, with a 30-min dwell time. Cystometric and histological evaluations were performed 24 h after the last instillation. Cystometry was used to evaluate voiding interval values under anaesthesia, while NGF expression was measured. Immunohistochemistry demonstrated a ~ 26% increase in bladder NGF expression in CYP-induced IC/PBS rats compared with controls, particularly in the urothelium and suburothelium, whereas intravesical NGF antisense therapy reduced NGF levels by ~ 28%, approaching control values. Cystometric analysis revealed that CYP treatment reduced voiding intervals by ~ 61% at 24 h and ~ 40% at 48 h compared to controls, consistent with bladder overactivity. NGF antisense therapy markedly prolonged voiding intervals, increasing them by ~ 113% at 24 h and ~ 80% at 48 h compared with CYP, indicating progressive functional improvement. Baseline and maximal bladder pressures were not significantly different among groups. Intravesical administration of vivo-morpholino NGF antisense OND significantly prolonged voiding intervals and attenuated bladder NGF expression in CYP-induced acute IC/PBS female rats. These results highlight the potential of NGF antisense OND as a novel intravesical therapy for IC/PBS.

CORRELATES OF POSITIVE RESPONSE TO THERAPEUTIC HYDRODISTENSION IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Wolff DT, Langefeld CD, Call JT, Badlani G, Evans RJ, Walker SJ. *Neurourol Urodyn.* 2026 Jan;45(1):169-176. doi: 10.1002/nau.70170. Epub 2025 Oct 17. PMID: 41104643

The objective of this study from the USA was to assess the duration and clinical correlates of positive response in interstitial cystitis/bladder pain syndrome patients undergoing therapeutic bladder hydrodistension (HOD) or HOD with electrofulguration (for those with Hunner lesions). One hundred and twenty four women were enrolled in this prospective IRB-approved study. Participants answered a set of validated questionnaires at intake including chronic overlapping pain conditions (COPCs), brief pain index (BPI), and IC/BPS symptomatic questionnaires. These were repeated at 1, 2-, 3-, 6-, and 12-months posttreatment, together with a global response assessment (GRA). The primary outcome measure was the GRA score. A secondary analysis of patients who were strong responders to treatment was used to identify clinical correlates of positive response. At 1-month post-HOD, 62 patients (53.9%) were responders (i.e., reported persistent positive response to treatment). Further, 21/49 (42.9%) respondents continued to report a positive response at 12 months. Logistic regression analyses identified several correlates of strong response to therapy including absence of Hunner lesions (odds ratio (OR) = 3.629), lack of diagnosis of fibromyalgia (OR = 0.31), lower number of total sites of pain on BPI pain map (OR = 0.91), fewer total number of COPCs (OR = 0.36), and lower complex medical symptom inventory scale (CMSI; OR = 0.91). After false discovery rate correction, only the CMSI remained statistically significant. Therapeutic hydrodistension results in a clinically meaningful and sustained improvement in associated symptoms and pain for many patients. However, having higher scores on markers of a widespread pain/non-bladder centric phenotype was associated with a lower treatment success rate.

THE ROLE OF CLINICAL NURSE SPECIALISTS IN THE MANAGEMENT OF PATIENTS WITH BLADDER PAIN SYNDROME.

Hillery S. *Br J Nurs.* 2025 Oct 9;34(18):S14-S20. doi: 10.12968/bjon.2025.0471.PMID: 41085368

Bladder pain syndrome (BPS) is a complex and chronic condition with no known cure. Diagnosis is generally based on the elimination of other identifiable disorders, and symptom management often involves a plethora of behaviour and lifestyle modifications. Consequently, BPS can have a profound effect on a patient's psychosocial wellbeing and quality of life. Clinical nurse specialists (CNSs) are core members of multidisciplinary teams that care for patients with BPS and aim to provide them with improvements in their symptoms, which can be challenging. By assessing, treating and supporting patients with personalised symptom management and treatment strategies, CNSs can help to improve the quality of life for individuals experiencing this often-debilitating condition.

EFFICACY AND SAFETY OF SUBMUCOSAL INTRAVESICAL INJECTION OF PLATELET-RICH PLASMA IN THE TREATMENT OF INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME.

Mourad MS, Tawfick A, Kotb M, Saleh IM, Salim MS, Samir YR. *Int Urogynecol J.* 2025 Oct 8. doi: 10.1007/s00192-025-06324-6. Online ahead of print. PMID: 41060442

The aim of this study from Egypt was to assess the effectiveness of a single session of submucosal intravesical injections of autologous platelet-rich plasma in the treatment of IC/PBS resistant to conventional methods of treatment. This is a prospective one-arm clinical trial that was conducted from April 2021 to April 2023 on 30 patients ranging from 30 to 50 years old with Interstitial Cystitis/Painful Bladder Syndrome symptoms (IC/PBS) not relieved by medical treatment. They were assessed by the O'Leary-Sant Interstitial Cystitis Symptom Index and problem indexes (ICSI) (ICPI). They received a single session of 20 submucosal injections of PRP and were assessed after 1, 3, and 6 months. Four patients declined to show in the follow-up visits (13.3%) due to personal reasons and were excluded from the final analysis due to incomplete outcome data. Out of 26 patients, 16 patients (61.54%) were considered to have successful results, while treatment failed in 10 patients (38.46%). There was a highly statistically significant decrease in ICPI, ICSI, pain VAS score, frequency, nocturia, and functional bladder capacity (FBC) with a p value of < 0.001. Hematuria was observed in three patients (11.5%), while urinary tract infection (UTI) was detected in four patients (15.4%). A single session of submucosal intravesical injections of platelet-rich plasma (PRP) presents a promising therapeutic option for patients with IC/PBS. The constraints of this research encompass the absence of a placebo arm, further randomized controlled trials are needed to prove its efficacy.

MAST CELLS AND INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME REVISITED.

Ruetten, H., Ritts, R., Namugosa, M. et al. *Int Urogynecol J* **36**, 2305–2312 (2025). <https://doi.org/10.1007/s00192-025-06213-y>

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There is significant variation in interstitial cystitis/bladder pain syndrome (IC/BPS) biopsy processing and reporting. The objective of this study from the USA was to review pathology reports from a large IC/BPS patient cohort to identify differences in findings. The authors hypothesize that variation in IC/BPS bladder biopsy reporting might be most frequent when it comes to mast-cell counts. They performed a retrospective analysis of 461 diagnostic pathology reports collected from their IRB-approved prospective study of patients diagnosed with IC/BPS at the Urology Clinic at Wake Forest Baptist Hospital from October 2011 to July 2023 (IRB00018552). Data were assigned as continuous or categorical variables. Groups were compared using Student's *t* test, Mann–Whitney, or Chi-squared tests. Staining strategy for mast-cell visualization differed between pathologists and included in order of frequency mast-cell tryptase (TPSAB1), CD117 (KIT), unspecified stain, a combination of stains, and toluidine blue. Mast-cell count was reported as a single number, range, or qualitatively. Pathologists used units of high-powered field (HPF), mm², or did not specify. As expected, average mast-cell count per HPF was significantly lower than per mm² across all stains ($p < 0.0001$). Average count with KIT was significantly lower than TPSAB1 ($p < 0.0001$). This trend remained significant when considering only KIT and TPSAB1 counts per HPF ($p = 0.0007$). Additionally, reports identified squamous metaplasia, acute inflammation, and/or chronic inflammation.

There is a lack of standardization regarding histological analysis of bladder biopsies from patients with IC/BPS, leading to inconsistent data and confusion surrounding the significance of pathology report findings.

UNSTIMULATED INFLAMMATORY ACTIVITY IS ASSOCIATED WITH TREATMENT RESPONSE TO COGNITIVE-BEHAVIORAL THERAPY FOR UROLOGIC CHRONIC PELVIC PAIN.

McKernan LC, Crofford LJ, Bruehl S, McGonigle TW, Kelly AG, Ryden AM, Sutherland SL, Clauw DJ, Williams DA, Dmochowski RR, Schrepf AD. *Front Pain Res (Lausanne)*. 2025 Sep 17;6:1593807. doi: 10.3389/fpain.2025.1593807. eCollection 2025. PMID: 41041602

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Interstitial cystitis/bladder pain syndrome (IC/BPS) is a debilitating urologic chronic pelvic pain condition characterized by pelvic pain and urinary symptoms. Evidence suggests that in chronic pain conditions such as IC/BPS, inflammatory markers are associated with heightened symptom severity and widespread pain. Non-pharmacological treatments such as cognitive-behavioural therapy are recommended as a core component of IC/BPS treatment. There is limited and mixed evidence as to whether inflammatory markers are affected by non-pharmacological treatments or their relationship to treatment response. This exploratory study from the USA considered how inflammatory characteristics may both predict and explain treatment response in a sample of females with interstitial cystitis. Participants were randomized to receive either 8-weeks of telemedicine-delivered cognitive-behavioural therapy (CBT) or an active attention control. Six cytokine/chemokines in whole blood plasma (IL-6, IL-8, IL-10, IL-1 β , and TNF- α) were assessed in a subset of trial participants at baseline, post-treatment, and at five months. The authors assessed relationships between baseline plasma inflammatory cytokine levels and self-reported symptoms, changes in cytokines over time, and how baseline cytokine levels may relate to clinically meaningful indicators of change following CBT. Cytokine/chemokine levels did not significantly change over time. Higher levels of unstimulated IL-1 β were associated with significantly worse clinical pain characteristics and greater degree of CBT treatment response. This suggests that individuals with greater degrees of inflammation may derive more benefit from the self-regulation training, pain coping strategies, and cognitive reframing offered in CBT for pain.

PHENOTYPE VARIABILITY IN INTERSTITIAL CYSTITIS CLINICAL TRIAL RECRUITMENT.

Wong R, Woodworth E, Wood C, Adelstein SA, Vollstedt AJ. *Urogynecology (Phila)*. 2025 Sep 29. doi: 10.1097/SPV.0000000000001759. Online ahead of print. PMID: 41025942

There is a need to understand phenotype-specific therapies for interstitial cystitis/bladder pain syndrome (IC/BPS) at the clinical trial level to move beyond trial-and-error treatment approaches. The objective of this study from the USA was to characterize IC/BPS clinical trials that incorporate patient phenotype into the eligibility criteria in accordance with the American Urological Association (AUA) guidelines. Registered IC/BPS clinical trials were identified from ClinicalTrials.gov. Trials were included if they enrolled patients with IC/BPS and addressed pain-related outcomes. Trials were assessed for phenotype recognition and categorized by intervention type, funding source, and registration date relative to the AUA's 2015 IC/BPS guidelines for initial phenotype recognition. Out of 170 trials, 37 (21.8%) included phenotype stratification. The majority focused on bladder-centric presentations. Men were underrepresented in IC/BPS clinical trials. Phenotypic stratification was more frequently reported in industry-funded trials compared with those without industry support (40.5% vs 16.5%, $P = 0.0031$). Trials registered after the 2015 AUA guideline update showed greater phenotype inclusion, though this was not statistically significant (26.6% vs 15.8%). Therapeutic trials comprised the majority of trials. Stratification appeared more often in physical therapy and psychosocial trials at 40% and in drug studies at 34.3%. Intravesical instillation and injection trials showed lower rates at 19.6% and 13.0%, respectively. Failure to incorporate IC/BPS phenotypes into trial design limits the ability to evaluate treatments within the context of real-world symptom

variability. Bridging this methodological gap is essential to ensure that clinical research supports the development of more targeted and effective therapies.

SEX DIFFERENCES IN CYSTOSCOPIC FINDINGS AMONG VETERANS WITH INTERSTITIAL CYSTITIS.

*Dolendo I, Chen A, Bresee C, Pacheco JAC, De Hoedt A, Kim J, Freedland S, Anger JT. *NeuroUrol Urodyn.* 2025 Nov;44(8):1602-1606. doi: 10.1002/nau.70142. Epub 2025 Sep 28. PMID: 41015899*

Previous studies have found significant sex differences in symptoms among patients with interstitial cystitis/bladder pain syndrome (IC/BPS). However, whether this translates into differences in pathology as observed on cystoscopy is unknown. The authors from the USA and Puerto Rico sought to assess cystoscopic findings in veterans diagnosed with IC/BPS and to identify possible sex differences in cystoscopic findings. This was a retrospective study of all hospital visits in the Veteran Health Affairs Hospital System between October 2004 and July 2016. Patients with IC/BPS were identified from the Veteran Informatics and Computing Infrastructure (VINCI) system using appropriate ICD codes. Patients older than 18 years of age with a confirmed diagnosis of IC/BPS who underwent cystoscopy were included. Rates of cystoscopic findings of ulceration, glomerulation, inflammation, trabeculation, and tumors adjusted for patient demographics were analyzed. A total of 570 patients met inclusion criteria and underwent analysis (57.9% female). The female cohort was of younger age (48.0 vs. 63.0 years). After adjusting for age, men and women had a similar likelihood of presenting with Hunner lesions (8.2% for men and 3.7% for women, $p > 0.05$). They also had a similar likelihood of glomerulation (11.4% in men vs. 15.2% in women, $p = 0.05$) and inflammation (19.6% vs. 15.8%, $p > 0.05$). Men were significantly more likely to present with trabeculation (15.4% vs. 8.1%, $p = 0.03$). Urothelial tumors on cystoscopy were rare in both groups. The proportion of patients with ulceration on cystoscopy in this study is consistent with previously published studies, and this study showed a similar prevalence of Hunner lesions between men and women. Cystoscopic identification of Hunner lesions is an important aspect of IC/BPS management given that treatment directed at these lesions is relatively successful compared to other treatments.

TGF-BETA1 MEDIATES EPITHELIAL-MESENCHYMAL TRANSITION IN INTERSTITIAL CYSTITIS THROUGH THE REGULATION OF ROCK.

*Long X, Yu B, Chen M, Zhang Q, Wang Y, Huang Y, Wu J, Cen P, Lan H, Long J, Zhang Z, Zhong J, Duan X, Yu Q, Gu D. *Eur J Pharmacol.* 2025 Nov 5;1006:178184. doi: 10.1016/j.ejphar.2025.178184. Epub 2025 Sep 18. PMID: 40975471*

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Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic condition characterised by bladder pain, urinary frequency, and urgency, which impacts quality of life. The pathogenesis remains unclear, though bladder fibrosis resulting from epithelial-mesenchymal transition (EMT) plays a key role. Transforming growth factor- β 1 (TGF- β 1) is a critical inducer of EMT and has been implicated in IC/BPS, although the molecular mechanisms are not fully understood. Rho-associated kinase (ROCK), a downstream effector of TGF- β 1, may be involved in this process. This study from China aimed to explore the role of TGF- β 1 in regulating EMT through ROCK in IC/BPS. An interstitial cystitis model in rats was established by intraperitoneal injection of cyclophosphamide (CYP). EMT in SV-HUC-1 cells was induced with recombinant TGF- β 1 and modulated by treatment with the TGF- β receptor inhibitor SB505124 and the ROCK inhibitor Y-27632. Mechanical pain sensitivity was assessed using the Von Frey test, and serum TGF- β 1 levels were measured by ELISA. Fibrosis markers in bladder tissue and cell were analyzed by H&E staining, Masson's trichrome, Western blotting, immunohistochemistry, and immunofluorescence. Results showed CYP-induced rats exhibited mechanical pain, elevated serum TGF- β 1, and aggravated bladder fibrosis. In addition, TGF- β 1, ROCK, and fibrosis-related proteins (vimentin, N-cadherin, fibroblast-specific protein 1, α -smooth muscle actin) were upregulated, while E-cadherin was reduced. Inhibition of TGF- β 1 and ROCK reversed these changes, though the ROCK inhibitor did not affect TGF- β 1 levels. This study demonstrates that TGF- β 1 mediates

EMT in bladder epithelial cells via ROCK, contributing to IC/BPS pathogenesis, and suggests that TGF- β 1 and ROCK inhibitors may offer potential therapeutic strategies for IC/BPS.

[CHARACTERIZATION OF ACTIONS OF THE NOVEL GABAPENTINOID DRUG MIROGABALIN ON PAINFUL BLADDER HYPERSENSITIVITY IN RATS WITH LIPOPOLYSACCHARIDE-INDUCED CHRONIC CYSTITIS.](#)

Yoshizumi M, Kitano Y, Watanabe C, Sakurada S, Mizoguchi H. Life Sci. 2025 Nov 1;380:123942. doi: 10.1016/j.lfs.2025.123942. Epub 2025 Aug 27. PMID: 40882699

Gabapentin reduces bladder pain and overactivity in lipopolysaccharide (LPS)-induced chronic cystitis in a rat model. This study from Japan evaluated the role of the spinal cord and the descending noradrenergic pathway in the effects of mirogabalin (MGB), a novel gabapentinoid drug on painful bladder hypersensitivity in this model. Chronic cystitis was induced in female Sprague-Dawley rats via repeated intravesical LPS instillation. von Frey filaments and continuous cystometry were used to assess bladder pain-related behaviors and micturition function, respectively. Changes in voltage-gated calcium channel $\alpha_2\delta$ -1 subunits expression in the spinal dorsal horn (SDH) and locus coeruleus (LC) were analyzed using western blotting. Gabapentinoid effects were evaluated after systemic, intracerebroventricular, and intrathecal administration. Additionally, rats were treated with N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine (DSP-4) to deplete noradrenergic nerves, in order to investigate the involvement of the descending noradrenergic system in the LC. MGB, as well as other gabapentinoids, reduced LPS-induced increases in cystitis-related pain and voiding frequency after systemic, intrathecal, or intracerebroventricular administration. Notably, MGB exhibited longer-lasting analgesic effects than other gabapentinoids. LPS-induced cystitis rats showed up-regulation of the $\alpha_2\delta$ -1 subunit in the SDH and LC. Pretreatment with DSP-4 reversed the analgesic effects of gabapentinoids but did not affect their inhibitory effect on micturition. The therapeutic effects of MGB in hypersensitivity associated with cystitis, similar to other gabapentinoids, are mediated by spinal and supraspinal actions, likely via the $\alpha_2\delta$ -1 subunit. Additionally, MGB exerts its analgesic effects through a supraspinal mechanism via the descending noradrenergic pathway, whereas a different mechanism regulates micturition.

[LIVING WITH INTERSTITIAL CYSTITIS: A QUALITATIVE STUDY OF WOMEN'S EXPERIENCES.](#)

Olaussen C, Jansen TL. West J Nurs Res. 2025 Nov 6;48(1):1939459251387205. doi: 10.1177/01939459251387205. Online ahead of print. PMID: 41195537

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Interstitial cystitis is a complex, highly challenging chronic inflammatory condition that is most predominant in women. It is characterised by persistent pain in the bladder and pelvis area and an urgent and frequent need to urinate during the day and at night. Despite the chronic and burdensome nature of interstitial cystitis, the lived experiences of women suffering from it have been inadequately explored. The authors from Norway sought to acquire in-depth knowledge and insights into the experiences of Norwegian women living with interstitial cystitis. A qualitative approach was used with an exploratory descriptive design, using the participants' own written stories of living with interstitial cystitis. The data were analysed using a reflective thematic analytic method. Three main themes came to the fore: (1) interstitial cystitis impacts every aspect of life, (2) struggling to be believed and heard, and (3) struggling to access personalised treatment for symptom alleviation. Interstitial cystitis is a complex condition that negatively impacts women's physical, mental, and sexual health. Women with interstitial cystitis may face disbelief and medical gaslighting compounded by a lack of awareness about the condition, which hinders their access to tailored treatment and care. The findings emphasise the need for competence and empathy among healthcare professionals and underscore the importance of an increased focus on conditions predominantly affecting women.

[\[PAIN SYNDROME IN UROLOGY: FEATURES OF CLASSIFICATION AND PATHOGENETIC ASPECTS\].](#)

Plekhanova O A, Pushkar D Y. Urologiia. 2025 Sep;(4):130-135. PMID: 40937806. Article in Russian.

Key aspects of pain syndrome in urology, including its classification, pathogenesis, and current treatment approaches, are discussed in the article. Special attention is given to the phenomenon of chronic pelvic pain, defined as persistent pain lasting at least three months, accompanied by dysfunction of the genitourinary system and emotional disorders. The main pathogenetic mechanisms underlying pain syndrome determine its complex multisystem nature, which requires a comprehensive approach to both diagnosis and treatment. Various etiologies of urologic chronic pain syndrome are described. Particular emphasis is given on urological causes such as bacterial cystitis and interstitial cystitis/bladder pain syndrome (IC/BPS). Clinical phenotypes of IC/BPS are discussed, along with individualized treatment approaches for each phenotype. The impact of pain syndrome in bacterial cystitis on quality of life and the role of phenazopyridine in pain relief are also highlighted. The importance of an interdisciplinary approach and the combination of different therapeutic methods to achieve good outcomes in the management of pain syndrome is emphasized.

[EXPLORING PROMISING BIOMARKERS BASED ON PATHOGENIC MECHANISMS IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.](#)

Xin K, Wu S, Li R, Tan C, Jiang Y, Yu J, Liu X, Li S, Li Z, Chen X. Nat Rev Urol. 2025 Sep 11. doi: 10.1038/s41585-025-01078-8. Online ahead of print. PMID: 40935927

Interstitial cystitis/bladder pain syndrome (IC/BPS), characterized by bladder discomfort and lower urinary tract symptoms, is often either overtreated or undertreated owing to the complexity and variability of symptoms and the lack of reliable diagnostic tools, leading to reduced quality of life and prolonged illness. The pathophysiology of IC/BPS remains unclear, with multiple hypotheses - such as autoimmune inflammation, oxidative stress and urothelial dysfunction - offering potential explanations. Consequently, a diverse range of urinary biomarkers has emerged, although their diagnostic reliability remains inconsistent. As technology advances, biomarkers are increasingly shifting towards multiplex assays, encompassing genomics, transcriptomics, proteomics and cell-based methods; however, cutting-edge research and clinical validation are not yet integrated into the limited diagnostic tools available. Clinical phenotypes from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research Network studies provide multi-level biomarker research - including molecular, imaging and other modalities - to support the diagnosis of IC/BPS. Integrating these observations will advance the development of precision medicine for the diagnosis of IC/BPS, thereby improving management of this complex condition.

[SYSTEMIC OZONE THERAPY IMPROVES THE QUALITY OF LIFE IN PATIENTS WITH BLADDER PAIN SYNDROME.](#)

Martinelli M, Glielmo A, Licci MR, Romanello D. Bladder (San Franc). 2025 Aug 1;12(3):e21200054. doi: 10.14440/bladder.2025.0002. eCollection 2025. PMID: 40933473

Open Access

Bladder pain syndrome (BPS), also known as interstitial cystitis, is a chronic condition characterized by pelvic pain and urinary symptoms that severely impair patients' quality of life (QoL). The current therapeutic options often yield suboptimal results, prompting interest in complementary treatments. Systemic ozone therapy, known for its anti-inflammatory, immunomodulatory, and analgesic effects, may represent a promising adjunctive treatment for BPS. This study from Italy aimed to evaluate the efficacy and safety of systemic ozone therapy in improving the self-perceived QoL in patients with BPS. The retrospective observational study included 40 patients diagnosed with BPS according to ESSIC criteria. All patients underwent systemic ozone therapy administered through hemotransfusion, following a standardized protocol. Outcomes were assessed using the Short Form (SF)-36 questionnaire for QoL and the Global Response Assessment (GRA) for subjective treatment efficacy. Statistical analyses evaluated changes in SF-36 domain scores and their correlation with GRA results. Patients demonstrated significant improvement across all domains of the SF-36 questionnaire, with the most notable gains observed in physical functioning and mental health. The mean GRA score confirmed patient-perceived effectiveness, showing a strong positive correlation with SF-36

improvements ($p < 0.05$). No adverse events or complications were found during the study. Systemic ozone therapy appears to be a safe and effective complementary treatment for BPS, significantly enhancing patients' QoL across multiple domains. While these findings are promising, randomized controlled trials are needed to validate the results and further explore underlying mechanisms, such as the role of ozone in modulating inflammatory and neural pathways.

THE ROLE OF BIOMARKERS IN THE DIAGNOSIS AND TREATMENT

OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: WHAT DOES CURRENT EVIDENCE REVEAL?

Chen YC, Tyagi P, Alperin M, Stern JNH, Lenore Ackerman A, Kuo HC. Neurourol Urodyn. 2026 Jan;45(1):60-70. doi: 10.1002/nau.70144. Epub 2025 Sep 11. PMID: 40931974

This narrative expert review from Taiwan and the USA aims to elucidate the role of biomarkers in the diagnosis and treatment of interstitial cystitis/bladder pain syndrome (IC/BPS), highlighting their potential to enhance patient care by enabling more precise and individualized therapeutic strategies. The authors performed a comprehensive review of literature focused on biomarkers relevant to IC/BPS, including bladder capacity, symptom intensity, bladder wall thickness, as well as serum and urinary inflammatory cytokines and other biomarkers of inflammation, oxidative stress, and urothelial and extracellular matrix remodelling. Evidence indicates that biomarkers such as TNF- α , IL-8, and bladder capacity can differentiate between Hunner lesion and non-Hunner lesion IC subtypes, predict treatment responses, and guide effective interventions. Furthermore, advanced statistical methods and machine learning applications show promise in improving diagnostic accuracy and treatment outcome predictions through clustering of the biomarker data. Reliable biomarkers are vital for improving diagnostic precision and tailoring therapies for IC/BPS patients. Ongoing research and validation of these biomarkers are essential for advancing understanding, guiding treatment decisions, and enhancing the quality of life for individuals affected by this complex syndrome. The need for integrated biomarker profiles and multipronged research approaches is crucial for the future of IC/BPS management.

THE EFFICACY AND SAFETY OF INTRAVESICAL PLATELET-RICH PLASMA INJECTIONS INTO THE BLADDER FOR THE TREATMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Li HR, Wang T, Shen SH, Peng L. Minerva Urol Nephrol. 2025 Oct;77(5):605-617. doi: 10.23736/S2724-6051.25.06232-9. Epub 2025 Sep 5. PMID: 40910759

Interstitial cystitis/bladder pain syndrome is a chronic bladder condition with a rising incidence that significantly impacts the lives of millions worldwide. The lack of understanding regarding the pathophysiology of this condition has resulted in a deficiency of effective treatment options. However, the development of regenerative medicine has brought platelet-rich plasma into our field of vision. Platelet-rich plasma may address unresolved inflammation in the interstitial cystitis/bladder pain syndrome bladder and facilitate the restoration of bladder and urethral barrier function through repeated injections, potentially reducing bladder pain. The aim of this study from China is to investigate the efficacy and safety of intravesical injection of platelet rich plasma in the treatment of interstitial cystitis/bladder pain syndrome. A comprehensive search was conducted across PubMed, EMBASE, MEDLINE, Cochrane Library, and Web of Science databases for studies on platelet-rich plasma injection for the treatment of interstitial cystitis/bladder pain syndrome, with a search cutoff date of August 7, 2024. A total of 11 studies with 391 participants were included. The combined statistics indicated that the baseline interstitial cystitis symptom index score was 11.20 ± 4.60 , the interstitial cystitis problem index score was 10.81 ± 3.51 , and the pain score was 4.37 ± 3.14 . The results showed that compared to pre-treatment, the interstitial cystitis symptom index score decreased by 3.56 (95% CI -4.39 to -2.72, $P < 0.00001$), the interstitial cystitis problem index score decreased by 3.24 (95% CI -3.90 to -2.58, $P < 0.00001$), and the pain score decreased by 1.84 (95% CI -2.19 to -1.48, $P < 0.00001$). Additionally, the average proportion of patients with a global response assessment score

of ≥ 2 after treatment was 48% (95% CI 0.37 to 0.58, $P < 0.00001$). Furthermore, the overall incidence of adverse events among patients was 2.9%.

THERAPEUTIC EFFECT OF A COMPOSITE ACELLULAR MATRIX/HYALURONIC ACID THERMOSENSITIVE HYDROGEL FOR THE INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME IN A RAT MODEL.

Liu H, Guo W, Zhang J, Tang W, Wang F, Zhang J, Zhang P. J Biomed Mater Res A. 2025 Sep;113(9):e37973. doi: 10.1002/jbm.a.37973. PMID: 40899624

This study from China investigated the therapeutic effects of a composite small intestinal submucosa decellularized extracellular matrix/hyaluronic acid (HA)-incorporated thermosensitive hydrogel (HA-Gel) on interstitial cystitis (IC) in rats. The HA-Gel was fabricated using rabbit small intestinal submucosa-derived extracellular matrix as a thermosensitive scaffold combined with HA, and an IC rat model was established using the UPK3A65-84 peptide. Rats were divided into five groups: IC group, IC + HA group, IC + Gel group, IC + HA-Gel group, and a non-modeled control group. After 14 days of treatment, urodynamic analysis revealed that the HA, IC + Gel, and IC + HA-Gel groups exhibited significantly increased interval voiding times and maximum bladder capacities compared to the IC group, with the most pronounced improvement observed in the IC + HA-Gel group ($p < 0.01$). Histopathological evaluation revealed reduced mucosal edema, inflammatory cell infiltration, and mucosal denudation in all treatment groups, particularly in the IC + HA-Gel group ($p < 0.01$). Mast cell infiltration was also markedly suppressed by HA-Gel ($p < 0.01$). Immunofluorescence and molecular analyses further indicated that HA, Gel, and HA-Gel effectively downregulated the expression levels of CD3, ICAM-1, TNF- α , IFN- γ , IL-1 β , IL-6, and TRPM8 in bladder tissues, with the most significant reductions observed in the IC + HA-Gel group ($p < 0.01$). Notably, both Gel and HA-Gel remained detectable in bladder tissues for over 14 days post-administration. In conclusion, HA-Gel not only improves voiding function and bladder capacity in IC rats but also suppresses inflammatory responses, demonstrating promising therapeutic potential and providing new insights for the clinical management of IC/bladder pain syndrome (BPS).

APPLICATION STUDY OF PRESSURE- AND VOLUME-CONTROLLABLE BALLOON IN DIRECT VISUALISATION INTERSTITIAL CYSTITIS DILATION SURGERY.

Wei W, Gao C, Wang H, Yang M, Wan G, Zhou S, Jiang X, Yang J. Int Urol Nephrol. 2025 Aug 16. doi: 10.1007/s11255-025-04706-9. Online ahead of print. PMID: 40818007

This study from China aimed to evaluate the efficacy and safety of pressure- and volume-controlled balloon dilation in the treatment of interstitial cystitis/bladder pain syndrome (IC/BPS) and to compare it with traditional bladder hydrodistension to explore a superior therapeutic approach. A prospective randomised-controlled trial was conducted, enrolling 50 women with IC/BPS aged 52-77 years, treated between July 2013 and June 2023. Patients were randomly assigned to a pressure- and volume-controlled balloon dilation group (experimental group, $n = 25$) or a traditional bladder hydrodistension group (control group, $n = 25$). The primary outcome measures included interstitial cystitis symptom index and interstitial cystitis problem index (ICSI/ICPI) scores, pelvic pain and urinary frequency (PUF) scores, bladder capacity, nocturnal urination frequency, maximum voided volume, and postoperative complications (bleeding and bladder rupture). Statistical analyses were performed using t tests, Wilcoxon rank-sum tests, and Chi-square tests, with $P < 0.05$ indicating statistical significance. At 6 months post-treatment, the experimental group showed significantly lower ICSI/ICPI scores than the control group ($P < 0.05$). The experimental group also exhibited significantly lower PUF scores at all time points ($P < 0.05$). Under non-anaesthetic conditions, the experimental group demonstrated significantly greater bladder capacity ($P < 0.05$), whereas no significant difference was observed under anaesthetic conditions ($P > 0.05$). The experimental group experienced significantly fewer episodes of nocturnal urination from 2 weeks to 6 months post-treatment ($P < 0.05$). Pressure- and volume-controlled balloon dilation demonstrated superior efficacy in alleviating IC/BPS symptoms and improving bladder function compared with traditional hydrodistension. Additionally, it was associated

with a lower complication rate, offering a safer and more effective therapeutic option for patients with IC/BPS.

VARIABILITY IN THE DIAGNOSIS AND TREATMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: INTERNET SURVEY.

Melkonian E, Garrett AL, Kline E, Smith P, Wiesenhahn M, Petit J, Swierczynski A, Zhou C, Bauer SB, Adam R, Barbour KE, Ziniel SI, Brownstein CA. JMIR Form Res. 2025 Aug 5;9:e70813. doi: 10.2196/70813.PMID: 40764047

Open Access

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a complex, chronic condition affecting the urinary bladder. Symptoms commonly associated with IC/BPS include painful urination, pain during intercourse, a persistent or recurrent sensation of bladder discomfort or pressure that often worsens as the bladder fills and eases after urination, urgency, frequent urination with little warning, nighttime urination disrupting sleep, and burning or other unusual urinary sensations. These symptoms can profoundly impact emotional and mental health, hinder participation in daily activities, disrupt social interactions, and strain personal relationships. This study from the USA aimed to compare the experiences of different races and ethnicities with IC/BPS regarding symptoms, diagnosis, treatment status, and treatment methods. It was hypothesized that there would be differences in racial and ethnic minority groups. A cross-sectional web-based survey was administered between June and August 2022 through the Interstitial Cystitis Association and the Inspire web-based health community. Eligible adults resided in the United States, self-reported IC/BPS symptoms, and completed the survey in English. The instrument gathered demographic information, details regarding age at symptom onset, formal diagnosis status, and treatment use. Validated symptom and problem indices (the O'Leary-Sant Interstitial Cystitis Symptom Index and Problem Index) captured symptom severity and quality-of-life impact. Comparative analyses, including Fisher exact and median tests, were conducted across racial or ethnic groups (minority or multiple-race vs White and Hispanic vs non-Hispanic), and multivariable logistic regression assessed predictors of race or ethnicity on IC/BPS diagnosis status and treatment outcomes. In total, 1631 individuals completed the survey. Racial or ethnic minority or multiple-race respondents constituted 11.6% (n=189) of the sample. Although IC/BPS symptom severity (Interstitial Cystitis Symptom Index or Interstitial Cystitis Problem Index scores) did not significantly differ by race or ethnicity, minority or multiple-race respondents were 50% less likely to have a formal medical diagnosis of IC/BPS than White respondents (adjusted odds ratio 0.50, 95% CI 0.30-0.83). Overall, 86.7% (n=1408) of participants reported having received a formal IC/BPS diagnosis, and the single strongest determinant of receiving any form of treatment was having a formal diagnosis (odds ratio 29.67, 95% CI 18.32-48.05). Over 25% (n=385) of all respondents reported using narcotic or opioid medications, indicating the challenging nature of IC/BPS symptom management. Minority or multiple-race participants were significantly less likely to have ever been diagnosed with IC/BPS by a health care professional, and those who were not diagnosed with IC/BPS were less likely to have used self-care behavioural and nonpharmacological treatments for their symptoms. Streamlining the diagnostic process and public health awareness campaigns outlining treatment options may help individuals manage IC/BPS symptoms.

AN ANALYSIS OF THE ACCURACY, QUALITY, AND READABILITY OF ONLINE HEALTH INFORMATION FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Moreland K, Souders CP, Marchese CR, Pautler B, Dennis J, Kowalik CG. Urology. 2025 Nov;205:46-51. doi: 10.1016/j.urology.2025.07.013. Epub 2025 Jul 14. PMID: 40669700.

The purpose of this study from the USA was to assess the accuracy, quality, and readability of online health information for interstitial cystitis/bladder pain syndrome (IC/BPS). Two search engines, Google and Bing, were queried using the search terms "interstitial cystitis treatment" and "bladder pain syndrome treatment." The first 20 websites from each search were recorded. Duplicate websites between searches were removed and a pre-determined set of inclusion and exclusion criteria were

applied to screen websites. Two Urogynecology and Reconstructive Pelvic Surgery fellowship-trained Urologists assessed the accuracy of websites on a 1-5 Likert scale. The quality of websites was assessed using the DISCERN tool. The readability of websites was assessed using the Flesch-Kincaid Reading Ease (FKRE), Flesch-Kincaid Reading Level (FKRL), and SMOG indexes. After screening, 25 individual websites were included for assessment. The accuracy of websites was high, with a median accuracy rating of 4 (accuracy of 75%-99%). The quality of the websites was fair, with a median score of 42 (scale: 1-75). The readability of websites was poor, with a median FKRE of 45.8 (scale: 1-100), median FKRL of 10.6, indicating a 10th-grade reading level, and SMOG of 13, indicating a college reading level. Accuracy and quality of the top searched IC/BPS websites are adequate, but readability is poor. Further efforts should ensure that online health information is formatted at a reading level of 6th grade or below.

"I CAN'T ENJOY MY FULL SEX LIFE": UNDERSTANDING THE SEXUAL EXPERIENCES OF WOMEN WITH INTERSTITIAL CYSTITIS.

Richardson HM, Kleinplatz PJ, Charest M, Rice EE, DiCaita H, D'souza K, Rosen LA. J Health Psychol. 2025 Jul 29;13591053251354906. doi: 10.1177/13591053251354906. Epub ahead of print. PMID: 40727966.

Open Access

Women who complain of bladder pain and urinary urgency and frequency wait years to receive the label of interstitial cystitis (IC), an "orphan disease" which has no known cause or cure. The current research used phenomenological research methods to understand the experiences of women who have IC as they affect their sexualities. Ten women with IC participated in individual, semi-structured interviews. Nine themes emerged from the interviews. Findings indicated that women who have IC experienced severely limited sexual relationships, negative physician-patient interactions, the necessity for self-management of symptoms and diminished quality of life. Their accounts underscore the profound impact IC has on sexuality, revealing how sexual experiences are deeply intertwined with the emotional, physical and medical challenges of the condition. These findings from Canada contribute to a deepened understanding of the experiences of women who have IC and help to increase physicians' understanding and awareness of the sexual effects that accompany IC.

HUNNER LESION DISEASE

LONG-TERM CLINICAL OUTCOMES OF TRANSURETHRAL RESECTION OF HUNNER LESIONS COMBINED WITH BLADDER HYDRODISTENSION FOR PATIENTS WITH INTERSTITIAL CYSTITIS AT A TERTIARY REFERRAL CENTER IN JAPAN.

Akiyama Y, Hashimoto K, Niimi A, Homma Y, Kume H. Int J Urol. 2025 Dec;32(12):1834-1842. doi: 10.1111/iju.70227. Epub 2025 Sep 14. PMID: 40947757

Open Access

The aim of this study from Japan was to report the long-term clinical outcomes of transurethral resection of Hunner lesions with bladder hydrodistension in patients with Hunner lesion interstitial cystitis (HIC) at a tertiary referral center in Japan. A retrospective chart review was conducted to evaluate the treatment outcomes of 104 patients with HIC who underwent initial endoscopic surgery, including transurethral resection of Hunner lesions (ablation was kept to a minimum) and concomitant bladder hydrodistension between 2017 and 2023. Clinical outcomes were evaluated and compared between each follow-up visit and baseline over 12 months using a 7-graded global response assessment (GRA), O'Leary and Sant's symptom and problem indices (OSSI/OSPI), an 11-point pain intensity numerical rating scale, quality of life (QOL) score, and frequency volume chart variables. Patients with GRA scores $\geq +2$ (moderately/marked improved) and scores ≤ -1 (slightly/moderately/marked worse) were considered treatment responders and failures, respectively. Postoperative complications were also documented. The mean duration to treatment failure was 30.9 ± 21.0 months. The overall response rates at 1, 3, 6, 9, and 12 months were 78.8%,

80.8%, 76.0%, 69.2%, and 57.7%, respectively. Compared with the baseline, the OSSI/OSPI, pain intensity, QOL score, urinary frequency, and functional bladder capacity improved significantly after 1 month and were maintained over 12 months. One patient required a second surgery for postoperative bleeding and another developed distal urethral stenosis 6 months post-surgery. No other patients developed any postoperative complications. Transurethral resection of Hunner lesions combined with bladder hydrodistension offers long-term symptom relief without serious adverse events for treatment-naïve patients with HIC.

TREATMENT OUTCOMES OF PATIENTS WITH HUNNER INTERSTITIAL CYSTITIS WHO RECEIVED AUGMENTATION ENTEROCYSTOPLASTY OR BLADDER-PRESERVING THERAPY.

Lee YS, Chang TL, Chen SF, Jhang JF, Jiang YH, Kuo HC. Int Neurourol J. 2025 Sep;29(3):172-180. doi: 10.5213/inj.2550036.018. Epub 2025 Sep 30. PMID: 41077790

Open Access

The purpose of this study from Taiwan was to investigate the long-term therapeutic satisfaction after augmentation enterocystoplasty (AE) or non-AE bladder therapy in patients with Hunner interstitial cystitis (HIC). From 2013 to 2024, patients with cystoscopically confirmed HIC who received AE or non-AE bladder-preserving therapy were retrospectively analyzed. Treatment outcomes were analyzed using the subjective global assessment response, symptoms, and urodynamic parameters. The patients' symptoms and urodynamic parameters were compared between AE and non-AE groups from baseline to follow-up endpoint. A total of 54 patients (48 women and 6 men) were included with a mean age of 58.6±11.4 years at diagnosis and a mean follow-up period of 9.4±5.8 years. AE and non-AE therapy was performed in 17 (31.5%) and 37 patients (68.5%), respectively. A final satisfactory outcome was reported in 13 (76.5%) of the 17 HIC patients after AE and in 26 of the 37 patients (70.3%) after non-AE therapy. Compared with patients who had no improvement, patients who had improved outcomes after AE exhibited decreased interstitial cystitis symptom index (P=0.007) and visual analogue scale (P=0.013) scores and increased bladder fullness sensation (P=0.002) and cystometric bladder capacity (P=0.019). Patients who had no improved outcomes after AE did not experience pain relief or increased bladder fullness sensation or bladder capacity. Only 23.4% of the patients treated with AE required repeat surgery or intravesical therapy in the first 1-3 years. By contrast, patients treated with non-AE therapy required repeat intravesical therapy for the recurrence of Hunner lesions or bladder symptoms. Both AE or non-AE therapy can result in satisfactory outcomes in more than 70% of HIC patients. AE provides early relief of bladder pain and increases bladder capacity, and non-AE therapy can also relieve pain and improve functional bladder capacity, resulting in improved outcomes.

IMAGING MASS CYTOMETRY IMMUNE PROFILING OF HUNNER LESIONS IN A CONVENIENCE SAMPLE OF PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Cotechini T, Kim N, Hindmarch CCT, Berman DM, Nickel JC, Siemens DR, Simpson AL, Doiron RC. J Urol. 2026 Jan;215(1):70-80. doi: 10.1097/JU.0000000000004781. Epub 2025 Nov 18. PMID: 41252600

A comprehensive spatial immune profile of Hunner lesions (HLs) in interstitial cystitis/bladder pain syndrome (IC/BPS) is absent from the literature. Here, the authors from Canada leveraged imaging mass cytometry, a multiplex imaging platform, with novel computational pipelines to evaluate the immune in situ microenvironment of HL-IC/BPS. Formalin-fixed paraffin-embedded HL tissue samples retrospectively collected from 10 patients with HL-IC/BPS were stained using a cocktail of 20-metal conjugated antibodies designed to profile both the innate and adaptive immune system. Imaging data were acquired using the Hyperion Imaging System. Data were visualized and processed using computational machine learning pipelines to resolve general immune complexity and spatial relationships in HL. More than 174,000 cells were analyzed across these 10 patient samples. On average, macrophages were the most abundant cell type found in HL-IC/BPS, followed by CD4⁺ T cells, CD8⁺ T cells, and B cells. They observed distinct spatial neighborhoods of macrophage subtypes including tissue repair-like CD163⁺ macrophages and activated granzyme B⁺ macrophages within

lesions. Computational analysis also demonstrated quantifiable methods to differentiate HL-IC/BPS patients based on differences in immune cell agglomeration within a lesion. The authors demonstrate the use of highly multiplexed imaging in combination with novel analysis pipelines as a feasible method to understand the spatial organization of HLs. This pilot study suggests that these methods will be useful to prospectively characterize and evaluate the local immune microenvironment in HL-IC/BPS and could uncover mechanisms of disease pathogenesis.

[MULTI-OMICS ANALYSIS IDENTIFIES A MICROBIOTA-BILE ACID-TLR SIGNALING AXIS DRIVING BLADDER INJURY IN INTERSTITIAL CYSTITIS.](#)

Peng L, Chen JW, Chen YZ, Di XP, Lin LD, Li BY, Zhang C, Wang W, Gao XS, Ma YC, Shen SH, Li HR, Xu XF, Zeng X, Shen H, Sun Q, Jin T, Luo DY. *Nat Commun.* 2025 Dec 29. doi: 10.1038/s41467-025-68060-1. Online ahead of print. PMID: 41457077

Open Access

Hunner-type interstitial cystitis/bladder pain syndrome (HIC) is a debilitating condition defined by bladder pain and urinary urgency, yet its upstream drivers remain poorly understood. To identify upstream mechanisms that exacerbate urothelial injury, the authors from Chinba apply an integrative multi-omics framework combining metagenomic sequencing, targeted metabolomics of urine and serum, and single-cell RNA sequencing. This approach reveals a microbial signature enriched in *Enterococcus avium* and a marked alteration in bile acid metabolism, including increased taurochenodeoxycholic acid (TCDCA). Single-cell analysis indicates that these changes converge on Toll-like receptor 3 (TLR3) activation in urothelial cells. Further validations show that a microbiota-bile acid-TLR3 axis disrupts epithelial barrier integrity and triggers inflammatory responses in experimental models. Transplantation and metabolite administration confirm the causal role of *E. avium* and TCDCA, while TLR3 inhibition ameliorates injury. These findings uncover an upstream pathway linking gut-derived metabolites to bladder pathology and suggest opportunities for biomarker development and targeted therapies for HIC.

[HLA-DQB1-MEDIATED B CELL-EPITHELIAL CROSSTALK DRIVES EBV-ASSOCIATED INFLAMMATION IN HUNNER-TYPE INTERSTITIAL CYSTITIS.](#)

Thangameeran SIM, Jhang JF, Jiang YH, Kuo HC, Peng CW. *Mol Ther Nucleic Acids.* 2025 Nov 24;36(4):102783. doi: 10.1016/j.omtn.2025.102783. eCollection 2025 Dec 9. PMID: 41438366

Open Access.

Hunner-type interstitial cystitis (HIC) is a chronic condition marked by persistent pain and inflammation. To elucidate its immunogenetic drivers, the authors from Taiwan integrated bulk RNA sequencing and single-cell RNA sequencing datasets with targeted major histocompatibility complex (MHC) sequencing. Transcriptomic analysis revealed selective expansion of B cells and epithelial cells, with strong enrichment of Epstein-Barr virus (EBV) response signatures. CellChat and NicheNet modeling uncovered bidirectional communication wherein B cells secrete IL-1 β , FGF2, LIF, and TNFSF9, activating prostaglandin synthesis, matrix metalloproteinases, and stress genes in epithelial cells. In turn, epithelial BMP4, TGF- β 2, and SHH modulate B cell survival. SCENIC regulatory network analysis identified IRF8 as the top B cell regulator; its regulon controls HLA-DQB1, CD40, and CIITA, linking EBV latency to heightened antigen presentation. Among differentially expressed genes, HLA-DQB1 was the most strongly induced in EBV⁺ HIC (~1,000-fold), emerged as the most frequently mutated gene in targeted MHC sequencing, and ranked as a high-confidence IRF8 target. Notably, the evolutionarily constrained variant rs1049133 (A>G) lies within a low-entropy HLA-DQB1 domain, underscoring functional importance. According to the author, their integrated analysis supports a model where IRF8-driven, EBV-infected B cells perpetuate HIC via variant HLA-DQB1-mediated antigen presentation and epithelial cytokine loops, highlighting a tractable axis for precision therapy.

[ASSOCIATION OF SPECIFIC HLA ALLELES IN PATIENTS WITH INTERSTITIAL CYSTITIS SUGGESTING AUTOIMMUNITY.](#)

Tabansky Stern I, Wang J, Moldwin RM, Kim JM, Singh JH, Tran DC, Najjar S, Akinci M, Howard A, Duke-Cohan JE, Belhaj M, Stevens J, Lane WJ, Birder LA, Jackson EK, Keskin DB, Zhang G, Stern JNH. *Front Mol Med.* 2025 Dec 4;5:1712660. doi: 10.3389/fmmed.2025.1712660. eCollection 2025. PMID: 41424801

Open Access

Interstitial cystitis/bladder pain syndrome (IC/BPS) with Hunner Lesions (Hunner Type Interstitial Cystitis or HIC) is characterized by lesions on the bladder wall. Previous work on these lesions identified B cells and monocytes within the lesion. However, the overall role of the adaptive immune system in the disorder remains uncertain. In this study, the authors from the USA and Denmark performed HLA sequencing on 12 IC/BPS patients with HIC and 7 Non Hunner Type IC (NHIC) patients, and identified HLA-DQB1*02:02 and HLA-DRB1*07:01:01 have a significant association with HIC. This pilot study provides genetic evidence supporting a potential autoimmune component in HIC and may help define the pathogenesis of at least one subtype of IC/BPS, and lay the groundwork for identifying the etiology of IC/BPS as a disease complex. Identifying the mechanisms can also open new approaches to treatment. Identifying an HLA haplotype associated with HIC would indicate that it is autoimmune.

[EDITORIAL COMMENT ON LONG-TERM CLINICAL OUTCOME OF TRANSURETHRAL RESECTION OF HUNNER LESIONS COMBINED WITH BLADDER HYDRODISTENTION FOR PATIENTS WITH INTERSTITIAL CYSTITIS AT A TERTIARY CENTER IN JAPAN.](#)

Kuo HC. *Int J Urol.* 2025 Dec 7. doi: 10.1111/iju.70306. Online ahead of print. PMID: 41355317 No abstract available.

GUIDELINES, CLASSIFICATIONS, TERMINOLOGY, QUESTIONNAIRES

[VALIDATION OF THE ITALIAN VERSION OF THE O'LEARY-SANT QUESTIONNAIRE FOR PATIENTS WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.](#)

Natale F, Campagna G, Caramazza D, Panico G, Vacca L, Marturano M, Lombisani A, Mastrovito S, Cervigni M, Ercoli A, Scambia G. *Int Urogynecol J.* 2025 Nov 3. doi: 10.1007/s00192-025-06403-8. Online ahead of print. PMID: 41182338

The standard questionnaire for evaluated patients with bladder pain syndrome/interstitial cystitis (BPS/IC) is the O'Leary-Sant questionnaire, of which there is no validated Italian version. The objective of this study was to translate the O'Leary-Sant and validate it for Italian patients. The authors enrolled BPS/IC patients (aged over 18 years) alongside an age-matched control group without BPS/IC (healthy-volunteers). Inclusion criteria for BPS/IC patients: diagnosis of BPS/IC-according to the definition of the International Society for the study of bladder pain syndrome, ESSIC-and no specific treatment for BPS/IC. The study was approved by their institutional review board. They translated the questionnaire following the common guidelines for this process. All the enrolled women then answered the translated questionnaire at baseline and 2 weeks later. Cronbach's alpha; interclass correlation coefficient; Fisher-Freeman-Halton's exact test or Student's t-test when appropriate; Pearson's r. Between February 2022 and March 2023, they enrolled 102 BPS/IC patients and 51 healthy volunteers controls. Data analysis demonstrated: internal consistency between the two versions of the questionnaire; reproducibility for total scores and all single items in both indexes of O'Leary-Sant; discriminatory ability of the questionnaire between patients' mean scores and controls in both indexes and in single items; highly significant direct correlations between scores in the same domain and with the other domain (construct validity). The authors conclude that their study demonstrates that their Italian version of the O'Leary-Sant questionnaire is a reliable, consistent, and valid instrument to evaluate symptoms of Italian speakers with BPS/IC.

[HOW CAN WE MAKE PROGRESS IN THE MANAGEMENT OF BLADDER PAIN SYNDROME? ICI-RS 2025.](#)

Malde S, Sinha S, Dmochowski R, Samarinas M, Tyagi P, Carolina Ochoa D, Selai C, Charrua A, Wein AJ, Abrams P. *Neurourol Urodyn*. 2025 Dec 3. doi: 10.1002/nau.70195. Online ahead of print. PMID: 41334673

Management algorithms for Bladder Pain Syndrome (BPS) have remained stagnant over the past 20 years. Lack of high level evidence has hindered progress. Contributors to this have been the use of confusing and inconsistent terminology and failure to adequately phenotype participants entering clinical trials. At the International Consultation on Incontinence Research Society (ICI-RS) meeting in 2025 a Think Tank addressed the question of "How can we make progress in the management of Bladder Pain Syndrome," focussing on the non-Hunner lesion group. The Think Tank conducted a literature review and expert consensus meeting focusing on the current limitations in terminology and phenotyping, how we can improve identification of bladder-centric BPS, and how we can improve assessment of psychological comorbidity. Terminology needs to be standardised to enable more homogenous recruitment to clinical trials. Use of the term "interstitial cystitis" may be misleading, and the term is often inappropriately used. Classification based on the European Association of Urology guidelines should be favoured, using the term Primary Bladder Pain Syndrome. Participants entering clinical trials need to undergo thorough investigation to enable accurate phenotyping. The non-Hunner lesion BPS group need to be the focus of future research. Tools to aid identification of a bladder-centric phenotype (through biopsy and other techniques) need to be studied, including investigating the roles of inflammation, ischaemia and oxidative stress in this condition. A psychological assessment tool specific for BPS should be created to ensure earlier psychological intervention for those who would benefit most. The use of accurate terminology in describing this condition is the first step toward improving the quality of future research. The Think Tank overwhelmingly recommended that the term "Interstitial Cystitis" should not be used. Future studies should be focussed on understanding the BPS group, excluding those with Hunner lesion disease. Studying inflammation, ischaemia and oxidative stress will help to identify a bladder-centric phenotype, whereas improving our understanding of psychological mechanisms will help to direct psychological therapies more effectively.

PROVIDING CLARIFICATION ON THE USE OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Alperin M. *Urogynecology (Phila)*. 2026 Jan 1;32(1):1-2. doi:

10.1097/SPV.0000000000001769. PMID: 41411303

No abstract available. See:

https://journals.lww.com/fpmrs/citation/2026/01000/providing_clarification_on_the_use_of_interstitial.1.aspx

IC/BPS AND ARTIFICIAL INTELLIGENCE (AI)

ARTIFICIAL INTELLIGENCE FOR DIAGNOSING BLADDER PATHOPHYSIOLOGY: AN UPDATED REVIEW AND FUTURE PROSPECTS.

Mahapatra C. *Bladder (San Franc)*. 2025 Apr 10;12(2):e21200042. doi: 10.14440/bladder.2024.0054. eCollection 2025. PMID: 40747464

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Bladder pathophysiology encompasses a wide array of disorders, including bladder cancer, interstitial cystitis, overactive and underactive bladder, and bladder outlet obstruction. It also involves conditions such as neurogenic bladder, bladder infections, trauma, and congenital anomalies. Each of these conditions presents unique challenges for diagnosis and treatment. Recent advancements in artificial intelligence (AI) have shown significant potential in revolutionizing diagnostic methodologies within this domain. This review from France provides an updated and comprehensive examination of the integration of AI into the diagnosis of bladder pathophysiology. It highlights key AI techniques, including machine learning and deep learning, and their applications in identifying and classifying bladder conditions. The review also assesses current AI-driven diagnostic tools, their accuracy, and

clinical utility. Furthermore, it explores the challenges and limitations confronted in the implementation of AI technologies, such as data quality, interpretability, and integration into clinical workflows, among others. Finally, the paper discusses future directions and advancements, proposing pathways for enhancing AI applications in bladder pathophysiology diagnosis. This review aims to provide a valuable resource for clinicians, researchers, and technologists, fostering an in-depth understanding of AI's roles and potential in transforming bladder disease diagnosis. While AI demonstrates considerable promise in enhancing the diagnosis of bladder pathophysiology, ongoing progresses in data quality, algorithm interpretability, and clinical integration are essential for maximizing its potential. The future of AI in bladder disease diagnosis holds great promise, with continued innovation and collaboration opening the possibility of more accurate, efficient, and personalized care for patients.

[QUALITY OF PATIENT INFORMATION ON INTERSTITIAL CYSTITIS FROM ARTIFICIAL INTELLIGENCE CHATBOTS.](#)

Santucci J, Stapleton P, Ibrahim J, Johns-Putra L, Elmer S, Sathianathen N. BJU Int. 2025 Oct 13. doi: 10.1111/bju.70035. Online ahead of print. PMID: 41083921

The purpose of this study from Australia was to evaluate the quality (DISCERN), understandability and actionability (Patient Education Materials Assessment Tool for Printable Materials [PEMAT-P]), readability (Flesch-Kincaid), and misinformation of patient-facing information on interstitial cystitis generated by four publicly available artificial intelligence (AI) chatbots: ChatGPT-4.0, Perplexity, ChatSonic, and Bing AI. A total of 10 queries derived from Google Trends and Hopkins Medicine content were submitted to each chatbot. Responses were evaluated by two blinded reviewers using validated tools: the DISCERN instrument (reliability/quality), PEMAT-P (understandability/actionability), and Flesch-Kincaid Grade Level (readability). Word count and citation inclusion were also recorded. Across chatbots, information quality was moderate with a median (interquartile range [IQR]) DISCERN score of 3/5 (2-3), with Perplexity performing best and Bing AI worst. Understandability was moderate (median [IQR] PEMAT-P score 75% [66.7-83.3%]), highest for ChatSonic with Hopkins Medicine-derived prompts and lowest for ChatGPT with Google Trends inputs. Actionability was consistently poor (median [IQR] score 40% [20-60%]), with ChatSonic performing best and Bing AI lowest. Responses averaged 256 words and college-level readability (median [IQR] Flesch-Kincaid score 25.4 [20.89-28.50]) across all platforms, limiting accessibility. Misinformation was minimal across all platforms. Chatbots referencing clinically curated prompts (Hopkins Medicine) scored higher in understandability and completeness than those responding to public search trends. Artificial intelligence chatbots offer generally accurate and understandable information about interstitial cystitis but lack actionable guidance and generate content at reading levels above typical patient comprehension. Enhancing readability, actionability, and personalisation may increase their utility as adjunct tools for patient education in functional urology.

MICROBIOTA

[MICROBIOTA IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: EVIDENCE AND OPPORTUNITIES.](#)

Klumpp DJ. J Clin Invest. 2025 Sep 2;135(17):e197858. doi: [10.1172/JCI197858](https://doi.org/10.1172/JCI197858). No abstract

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PENTOSAN POLYSULFATE

[PIGMENTARY MACULOPATHY IN PATIENTS WITH INTERSTITIAL CYSTITIS: ASSOCIATION WITH PENTOSAN POLYSULFATE AND OTHER THERAPIES.](#)

Qin S, Evans JK, Jeong C, Havunjian M, Jain N, Greven MA, Ong SS. *Ophthalmol Sci.* 2025 Aug 7;6(1):100909. doi: 10.1016/j.xops.2025.100909. eCollection 2026 Jan. PMID: 41049115 Free PMC article.

The aim of this study from the USA was to examine the association between the development of pigmentary maculopathy and exposure to pentosan polysulfate sodium (PPS) and other therapies in patients with interstitial cystitis (IC) in a single-center retrospective study with patients diagnosed with IC who had ≥ 2 eye examinations at Wake Forest School of Medicine between January 2011 and August 2021. Two masked retina specialists evaluated available multimodal imaging for pigmentary maculopathy using the established criteria, with any disagreements adjudicated by a third reviewer. Cases were categorized by severity and analyzed for associations with medication exposure. Main outcome measures: association between the development of pigmentary maculopathy with PPS exposure duration and cumulative dose, and concurrent IC medication use. A total of 336 patients with IC (176 with PPS exposure, 160 without) were included. Patients with PPS exposure had increased odds of exposure to hydroxyzine (odds ratio [OR]: 4.76, $P < 0.0001$), amitriptyline (OR: 2.62, $P < 0.0002$), phenazopyridine or pyridium (OR: 1.68, $P = 0.036$), narcotics (OR: 2.68, $P < 0.0001$), oxybutynin (OR: 1.93, $P = 0.041$), cystoscopy with hydrodistention (OR: 4.001, $P < 0.0001$), bladder instillation (OR: 6.83, $P < 0.0001$), and vaginal valium (OR: 9.515, $P = 0.033$). Of the 122 patients with retinal imaging (71 with PPS exposure, 51 without), 8 patients (16 eyes) were graded to have pigmentary maculopathy and all 8 patients had PPS exposure. The median duration of PPS exposure in patients with moderate/severe maculopathy was 121 months (interquartile range [IQR] 117, 121) with a median cumulative dose of 929 200 mg (IQR 799 200; 1 109 100), which were significantly higher than patients with mild or no maculopathy (median duration 35 months [IQR 10, 63], $P = 0.002$ and median dose 166 800 mg [IQR 44 600; 569 100], $P = 0.004$). Higher proportions of patients with pigmentary maculopathy than those without had concurrent exposure to PPS and amitriptyline/nortriptyline (75% vs. 34.9%, $P = 0.015$) or PPS and cyclosporine (37.5% vs. 1.6%, $P = 0.003$). Pentosan polysulfate sodium exposure, and not IC itself, was associated with the development of pigmentary maculopathy. Longer duration and higher cumulative dose were associated with worse maculopathy. Patients on PPS were more likely to be on multiple other therapies for IC. Concurrent exposure to PPS and amitriptyline/nortriptyline or cyclosporine may increase the risk of developing maculopathy but these results should be validated by larger prospective studies.

BPS SYMPTOM LOAD DURING PENTOSANE POLYSULFATE SODIUM TREATMENT IN REAL LIFE IN FRANCE.

Saussine C, Gamé X, Levesque A, Chartier-Kastler E, Meyer F, Gaillet S, Waltenberger C. *Fr J Urol.* 2025 Dec;35(12):102972. doi: 10.1016/j.fjurol.2025.102972. Epub 2025 Sep 17. PMID: 40972775

Oral pentosane polysulfate sodium (PPS) is a symptomatic treatment for bladder pain syndrome (BPS), a rare, chronic and incurable inflammatory disease of the bladder leading to pelvic pain, frequent micturition, urgency, nocturia and reduced quality of life (QoL). As population, treatment practice and outcomes are insufficiently understood in France, data were collected in line with French Health authorities. ELMIRON was a national, multicentre, prospective, uncontrolled, observational study aiming to include up to 100 patients. Patients receiving PPS in clinical routine under ANSM were observed until discontinuation or study end. Endpoints included drug survival, demographics, BPS symptoms, QoL, and safety. Ninety-five patients were included, i.e., up to 29% of the BPS population in France under PPS treatment. Among the patients, 92.6% were female, with an age of 20-87 years. Among the patients, 83.2% reported at least one medical history. On average, 9.4 ± 7.7 years had passed since first symptoms, all but one patient had received pre-treatment, 47.4% were PPS naive. Patients started treatment with 2.9 doses of 100mg PPS, subsequently reduced to 2.4. After baseline, 58.3% reported improvement of pain, especially bladder pain, urinary frequency and of the O'Leary Sant problem score. Associated diseases and QoL changed little. Thirty-six patients (37.9%) experienced 71 new findings, one unrelated finding was assessed as serious by the investigator. Safety of PPS was confirmed. PPS treatment was associated with improvement of BPS symptoms like urinary

frequency, pain and patient perception of BPS-related problems. Monitoring every 6 months was confirmed to enable timely treatment modifications.

PENTOSAN POLYSULFATE MACULOPATHY: CLINICAL CONSIDERATIONS, PATHOBIOLOGY, AND CAUSALITY.

Hall BP, Shiromani S, Vanderbeek BL, Datta S, Girardot PE, Rajagopalan A, Nickerson JM, Boatright JH, Jain N. Prog Retin Eye Res. 2025 Nov;109:101400. doi: 10.1016/j.preteyeres.2025.101400. Epub 2025 Sep 15. PMID: 40962246

Pentosan polysulfate (PPS) maculopathy is a progressive, vision-threatening retinal disorder linked to prolonged use of PPS, a heparin-like sulfated polysaccharide prescribed for interstitial cystitis/bladder pain syndrome. Affected individuals often experience impaired dark adaptation and progressive central vision loss. Fundus imaging commonly reveals hyperpigmented macular clumps at the level of the retinal pigment epithelium (RPE), and a distinctive pattern of autofluorescence abnormality in the posterior fundus. This degenerative maculopathy may continue to progress even after drug cessation, with some patients developing macular atrophy years later. While the underlying pathogenic mechanism remains unclear, mounting evidence supports a causal relationship between PPS use and the macular pathology. Studies have repeatedly demonstrated the strength of the association; the dose-response relationship; and the lack of confounding by indication. Furthermore, laboratory studies demonstrate that such a toxicity is biologically plausible, suggesting a direct toxicity to the RPE and/or choroid. Given the widespread use of PPS over many decades, tens of thousands of individuals are already at risk for toxicity, with no known treatment available. However, screening rates remain low; prescribing rates continue to rise in certain regions; and novel applications for the drug, such as subcutaneous injection for osteoarthritis, are under clinical investigation. Consequently, there is a pressing need for increased recognition of PPS toxicity and further understanding of disease mechanisms. This review summarizes the clinical characteristics of PPS maculopathy, evaluates its public health impact, explores potential pathogenic mechanisms, and presents a compelling case for causality using clinical, laboratory, and epidemiological evidence.

COLOPATHY ASSOCIATED WITH PENTOSAN POLYSULFATE USE.

Jung EH, Zheng W, Weiss RJ, Mathew NE, Meyer BI, Nizam A, Iskandar H, Jain N. Front Pharmacol. 2025 Jul 28;16:1494467. doi: 10.3389/fphar.2025.1494467. eCollection 2025. PMID: 40792210

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Jung and colleagues from the USA describe a novel colopathy associated with pentosan polysulfate (PPS) use and assess the strength of the drug-disease association in a two-part investigation. 1. Cohort Study: They studied individuals with a history of long-term PPS use. Case histories concerning gastrointestinal disease were obtained with review of endoscopy records and histopathology specimens. Findings were summarized with descriptive statistics. 2. Cross-Sectional Study: They evaluated patients with interstitial cystitis at a single clinical center. They obtained data on drug exposure and medical histories and measured the strength of association between PPS use and diagnosis of inflammatory bowel disease (IBD) using multivariate logistic regression. Results were as follows: 1. Cohort Study: Among 13 participants, the median PPS exposure was 2.04 kg (range 0.99-2.54 kg). Eleven participants (84.6%) developed IBD symptomatology after initiating PPS therapy, and 9 (69.2%) were diagnosed with IBD. Two others (18%) were diagnosed with irritable bowel syndrome. Of the 10 participants with endoscopic and histopathologic data, six had abnormal colonic mucosa on endoscopy, and all 10 had histologic abnormalities. Clinical and histologic improvement was noted after PPS cessation, though two (18%) required colectomy for colitis-associated dysplasia. 2. Cross-Sectional Study: Among 219 subjects with interstitial cystitis, PPS use was a statistically significant predictor of an IBD diagnosis, with an adjusted odds ratio of 3.3 (95% confidence interval, 1.2-8.8, $p = 0.02$). The authors conclude that their study identifies a strong association between PPS use and clinical diagnosis of IBD. Histopathologic findings suggest a novel drug-associated colopathy, with

some subjects necessitating colectomy for dysplasia. Further investigation into the causality of this association is warranted.

EFFICACY AND SAFETY OF PENTOSAN POLYSULFATE THERAPY IN PATIENTS WITH INTERSTITIAL CYSTITIS FOR RELIEF OF LOWER URINARY TRACT SYMPTOMS: 15-YEAR SINGLE CENTER EXPERIENCE.

Song SH, Song B, Jung G, Kim H, Park JH, Jeong SJ, Hong SK. Prostate Int. 2025 Dec;13(4):207-213. doi: 10.1016/j.pnrl.2025.05.001. Epub 2025 May 19. PMID: 41472923

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Benefit of pentosan polysulfate sodium (PPS) for reducing chronic pain and lower urinary tract symptoms in patients with interstitial cystitis/bladder pain syndrome (IC/BPS) remains inconclusive with modest effect. The authors from Korea aimed to evaluate the impact of PPS on improvement of lower urinary tract symptom based on the International Prostate Symptom Score (IPSS), quality of life (QoL), and uroflowmetry (UFM) in patients with IC/BPS. A total of 204 patients who were prescribed oral PPS for IC/BPS from October 2006 to May 2021 were retrospectively reviewed. Patients were divided by age for treatment effect comparison. Linear mixed models were utilized to evaluate improvements in IPSS, QoL, and UFM parameters after PPS treatment. There were significant gains in total IPSS (-0.335 , $P < 0.001$) and QoL (-0.061 , $P < 0.001$) over time, achieving stable phase within 3 months from the initiation of PPS treatment. For UFM parameters, postvoid residual decreased significantly over time (-1.052 , $P = 0.029$), while maximum flow rate (0.093 , $P = 0.334$) and voiding volume (0.751 , $P = 0.586$) showed no significant differences. Compared to patients older than 65 years, those younger than 65 years showed significantly better improvements in the IPSS (-0.492 vs. -0.184 , $P = 0.018$) but worse in voiding volume (-2.481 vs. 5.032 , $P = 0.006$). PPS provides clinical benefits in urinary symptoms voiding symptoms and QoL over time, arriving plateau within 3 months. Such benefits based on the IPSS tend to be more evident in younger patients, suggesting that PPS mostly benefits early treatment if suspected for IC/BPS.

CHRONIC PAIN SYNDROMES, PAIN DISORDERS, PELVIC PAIN, PELVIC DISORDERS

COEXISTENCE OF PELVIC PAIN, BLADDER, AND BOWEL SYMPTOMS IN WOMEN WITH PELVIC ORGAN PROLAPSE: THE EFFECT OF TRANSVAGINAL SURGERY.

Schmidbauer L, Liedl B, Goeschen K, Antoniewicz A, Kurtzman J, Wenk MJ. Int Urogynecol J. 2025 Nov 8. doi: 10.1007/s00192-025-06348-y. Online ahead of print. PMID: 41204973

The purpose of this study from Germany was to investigate the coexistence of pelvic pain, bladder, and bowel symptoms in women with pelvic organ prolapse (POP) and possible surgical symptom cure. A secondary analysis of the PROPEL study (gov-identifier: [NCT00638235](https://clinicaltrials.gov/ct2/show/study/NCT00638235)) data was conducted to compare symptom prevalence preoperatively vs. 6 months after transvaginal prolapse repair with Elevate anterior and/or posterior. Symptoms were assessed with the pelvic floor distress inventory questionnaire (PFDI). Two hundred seventy-seven women with symptomatic II-IV stage POP underwent mesh-supported vaginal sacrospinous ligament fixation. Of these women, 187 (67%) reported at least one pain symptom of moderate or quite a bit severity preoperatively (anterior $n = 105$, visceral $n = 129$, posterior $n = 122$). Of these women reporting pain, approximately 40-64% had coexisting symptoms of urinary urgency, daytime urinary urgency, urinary urgency-incontinence, and nocturia of moderate or quite a bit severity. A smaller part reported coexisting symptoms of underactive bladder (UAB), fecal incontinence (FI), and/or obstructive defecation (OD). Six months postoperatively, a significant reduction in the prevalence of almost all symptoms was observed. Cure rates for symptoms of overactive and underactive bladder were 65-85%, for symptoms of FI and OD 51-71%, and 58% (posterior), 85% (visceral), and 82% (anterior) for pain, respectively. The coexistence of bothersome pain, bladder, and bowel symptoms is common in women with POP. Therefore, POP should always be ruled out as a differential diagnosis before classifying the symptoms as interstitial

cystitis/bladder pain syndrome. Women with POP and the co-existing symptoms described should be advised that surgical POP repair can resolve these symptoms in a high percentage.

ASSOCIATED DISORDERS – FIBROMYALGIA

[PREVALENCE AND PHENOTYPE OF LOWER URINARY TRACT SYMPTOMS IN FIBROMYALGIA: A RETROSPECTIVE OBSERVATIONAL STUDY AT A SINGLE TERTIARY MEDICAL CENTER.](#)

McClain J, Capo G, Terris M, Santamaria P, Rolle NA. *J Clin Med.* 2025 Aug 7;14(15):5584. doi: 10.3390/jcm14155584.PMID: 40807201

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Fibromyalgia syndrome (FMS) is a complex condition with poorly understood pathophysiology, characterized by widespread pain and an increasing recognition of its associations with genitourinary symptoms. The objective of this study from the USA was to characterize the prevalence, phenotype, and common comorbidities of lower urinary tract symptoms (LUTS) in women with FMS. A retrospective observational study was conducted using electronic medical records of 440 women diagnosed with FMS at a single institution between 1 January 2018, and 1 January 2024. Study subjects were evaluated for diagnoses associated with LUTS, including interstitial cystitis (IC), overactive bladder (OAB), and stress urinary incontinence (SUI), alongside comorbidities such as irritable bowel syndrome (IBS), generalized anxiety disorder (GAD), and major depressive disorder (MDD). Multivariate analyses were performed to assess predictors of conditions associated with LUTS. LUTS were identified in 37.0% of FM patients. GAD and IBS were significantly associated with conditions associated with LUTS (OR = 4.62; OR = 8.53, $p < 0.001$). SUI was present in 17.05% of patients, falling between survey-based and confirmed prevalence rates in the general population. IC was diagnosed in 2.95% of FMS patients. OAB was observed in 6.8% of patients and associated with GAD (OR = 5.98, $p < 0.001$). This study highlights a substantial burden of diagnoses associated with LUTS in patients with FMS. There is relatively high prevalence of SUI and IC in this dataset. IBS and GAD were commonly found to co-occur with one or more LUTS-associated condition. Future prospective studies are needed to investigate a multimodal approach to the treatment of LUTS in these patients.

VISCERAL PAIN

[MOLECULAR MECHANISMS AND PATHWAYS IN VISCERAL PAIN.](#)

Zhou Q, Verne GN. *Cells.* 2025 Jul 25;14(15):1146. doi: 10.3390/cells14151146.PMID: 40801578

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Chronic visceral pain, a significant contributor to morbidity in the United States, affects millions and results in substantial economic costs. Despite its impact, the mechanisms underlying disorders of gut-brain interaction (DGBIs), such as irritable bowel syndrome (IBS), remain poorly understood. Visceral hypersensitivity, a hallmark of chronic visceral pain, involves an enhanced pain response in internal organs to normal stimuli. Various factors like inflammation, intestinal hyperpermeability, and epigenetic modifications influence its presentation. Emerging evidence suggests that persistent colonic stimuli, disrupted gut barriers, and altered non-coding RNA (ncRNA) expression contribute to the pathophysiology of visceral pain. Additionally, cross-sensitization of afferent pathways shared by pelvic organs underpins the overlap of chronic pelvic pain disorders, such as interstitial cystitis and IBS. Central sensitization and viscerosomatic convergence further exacerbate pain, with evidence showing IBS patients exhibit hypersensitivity to both visceral and somatic stimuli. The molecular mechanisms of visceral pain involve critical mediators such as cytokines, prostaglandins, and neuropeptides, alongside ion channels like transient receptor potential vanilloid 1 (TRPV1) and acid-sensing ion channels (ASICs). These molecular insights indicate potential therapeutic targets and highlight the possible use of TRPV1 antagonists and ASIC inhibitors to mitigate visceral pain. This review from the USA explores the neurophysiological pathways of visceral pain, focusing on peripheral

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and central sensitization mechanisms, to advance the development of targeted treatments for chronic pain syndromes, particularly IBS and related disorders.

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