

International Painful Bladder Foundation

The IPBF is a voluntary non-profit organization for interstitial cystitis/bladder pain syndrome/hypersensitive bladder
www.painful-bladder.org

IPBF e-Newsletter and Research Update Issue 56, August 2020

An IPBF update, including Research Highlights, for patient support groups, healthcare professionals and friends around the world in the field of interstitial cystitis, bladder pain syndrome/painful bladder syndrome, hypersensitive bladder, Hunner lesion, ketamine cystitis, chronic pelvic pain and associated disorders.

This issue of the IPBF e-Newsletter includes the following topics:

- COVID-19 Impact
- EAU Virtual Meeting 2020: prize for IC/BPS abstract
- NVA: valuable source of information on vulvovaginal disorders
- IASP announces revised definition of pain
- Overview of rescheduled upcoming events
- Information about COVID-19: online resources
- Research Update
- Donations & Sponsoring

COVID-19 IMPACT

At the beginning of this year, no-one could have imagined how our lives would be turned upside down in 2020 with the COVID-19 crisis. Everyone around the world has been affected in many ways, and some very dramatically. In March we thought it would be over in a few months, but now it seems difficult to foresee when it will all end. Much of our life has moved online and has become a “virtual” life. Will it ever become “normal” again? Doubtless in the years to come psychologists will be writing shelves of books about how people and society were affected by this devastating virus. Hopefully, however, the lockdown will have opened many people’s eyes to the social isolation experienced every day of every year by many people with chronic diseases, including many patients with IC/BPS. Let us also hope that this experience will lead to more empathy and understanding for people who have difficulty in leaving their home every day, not just in the COVID-19 crisis.

In the medical world and patient advocacy, meetings and conferences this year have moved online. For us as patients, even our hospital appointments are currently online or by phone, a change which is likely to remain to a certain extent even after COVID. Will this be enough for the chronically ill? Will more professional counsellors and more helplines be needed?

On the positive side, we are becoming more experienced at online meetings and have been able to take advantage of the many educational webinar opportunities organised by societies or individuals, with many more to come this year, as you can see from the list of events in this Newsletter, including a Masterclass by ESSIC covering a number of webinars this autumn.

We need much more of this virtual information and education for patients, their support groups and patient advocates. It is an ideal way to educate and train IC/BPS patient advocates to play a full and valuable role, nationally and internationally, including in research projects.

Although IC/BPS research has experienced some disruptions during the past difficult months, publications in our field have continued, as you can see from the Research Update in this Newsletter which will hopefully bring you up to date.

EAU VIRTUAL MEETING 2020: IC/BPS IN THE PRIZES THANKS TO JAPANESE RESEARCH TEAM

With the cancellation of the annual congress this year due to the COVID-19 crisis, the European Association of Urology opted for a virtual meeting 17-19 July followed by a theme week 20-26 July.

Asst Professor Yoshiyuki Akiyama and colleagues from the University of Tokyo, Japan won second prize in the category Best Abstract Awards Non-Oncology for their study on glomerulations as a marker for IC/BPS: “Are

glomerulations still characteristic marker for interstitial cystitis/bladder pain syndrome? Biological evidence from global gene expression and comprehensive immunohistochemical quantification analyses”.

The Japanese research team’s conclusion was that no significant differences in the gene expression profile and degree of inflammation and neovascularization between patients with and without glomerulations. Furthermore, this biological evidence supports the recent scepticism towards the role of glomerulations in the diagnosis of IC/BPS.

European Urology Today volume 32 No 3 June/July 2020 devoted a full page review article to this best abstract, noting that “it may be time to revisit the definition, diagnosis and future research progress. Proper subtyping and an accurate understanding of the pathophysiology based on clinical and basic research findings is the only way to achieve better clinical management and future research progress.”

Our congratulations to authors Yoshiyuki Akiyama, Daichi Maeda, Hiroto Katoh, Aya Niimi, Haruki Kume and Yukio Homma.

USA NATIONAL VULVODYNIA ASSOCIATION (NVA): VALUABLE SOURCE OF INFORMATION ON VULVOVAGINAL DISORDERS

Founded in 1994, the National Vulvodynia Association (NVA) in the United States has for years been a valuable source of information in the field of vulvodynia/vulvovaginal pain disorders for patient, healthcare professionals and scientists. Many women with IC/BPS also suffer from different types of vulvodynia. The NVA website (www.nva.org) offers a great deal of information, while its Research Update Newsletter keeps everyone up to date with the latest research developments and insights.

IASP ANNOUNCES REVISED DEFINITION OF PAIN

For the first time since 1979, the International Association for the Study of Pain (IASP) has introduced a revised definition of pain, the result of a two-year process that the association hopes will lead to revised ways of assessing pain. After several years of deliberation and discussion, the task force has now finally published its recommendation that the definition of pain be revised to “An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage”.

See further:

https://journals.lww.com/pain/Citation/2020/09000/The_revised_International_Association_for_the.6.aspx

This development can also be seen as an “infographic” (= in pictures!) at http://s3.amazonaws.com/rdcms-iasp/files/production/public/images/Infographic_20200708_5_5_Final.pdf

Overview of Rescheduled Upcoming Events:

With conferences this year cancelled due to COVID-19, many are being rescheduled for 2021 and some have been replaced in 2020 by educational webinars. These include the following upcoming events:

VIRTUAL GIBS-USI ONLINE MEETING 2020 ON INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME

The Global Interstitial Cystitis Bladder Pain Society (GIBS) and the Urological Society of India (USI) are holding a collaborative online meeting 5 September 2020 [IST 5pm – 8pm] & 6 September [IST 2pm & 5pm] with an international faculty. The theme of the meeting is “Conquering Bladder Pain with You”. For further information, [click here](#) or go to <https://gibsociety.com/>. Email info@gibsociety.com

IAPO ONLINE EVENT FOR PATIENTS

The International Alliance of Patients’ Organizations (IAPO) is holding a virtual event online 16-17 September 2020 based on the theme of ‘Co-creation in Innovative Healthcare during COVID-19’. For further information, [click here](#) or go to <https://www.iapo.org.uk/global-patients-congress>

ESSIC ONLINE 2020 IC/BPS MASTERCLASS: 6 WEBINARS

The International Society for the Study of Bladder Pain Syndrome (ESSIC) is to hold a 2020 online Masterclass on IC/BPS comprising 6 educational webinars with expert speakers on 18/9, 24/9, 27/10, 4/11, 12/11, 13/11. [Click here](#) for more information or go to <https://www.essic.org/masterclass-2020> where you will find the [Programme](#) and a trailer.

EFIC ONLINE VIRTUAL PAIN SUMMIT 6-8 NOVEMBER 2020

The European Pain Federation (EFIC) is presenting a virtual pain educational summit 6-8 November 2020 with some 40 hours of teaching spread over 3 days. For further information, [click here](#) or go to <https://europeanpainfederation.eu/news/join-our-virtual-pain-education-summit/>

50th ICS ANNUAL MEETING GOES ONLINE IN 2020

The International Continence Society (ICS) which had to cancel its planned 50th annual congress is now presenting a virtual meeting online 19-22 November 2020 with an outstanding programme of educational exchanges, scientific news and best practice updates. For further information, [click here](#) or go to <https://www.ics.org/2020>

EAU ANNUAL CONGRESS 2021 MILAN, ITALY

The European Association of Urology (EAU) is planning to hold its rescheduled annual congress 19-23 March 2021, in Milan, Italy. For further information, [click here](#) or go to <https://www.prmedicalevents.com/congress/eau-2021>

INTERNATIONAL SYMPOSIUM ON SJOGREN'S SYNDROME 2021

An international symposium on Sjogren's syndrome will be held 14-17 April 2021 in Rome, Italy. For further information, [click here](#) or go to <http://www.sjogren2021.com/>

AUA 2021 ANNUAL MEETING, LAS VEGAS, UNITED STATES OF AMERICA

The American Urological Association (AUA) is planning to hold its rescheduled annual meeting 24 – 27 May, 2021, in Las Vegas, Nevada, United States. For further information, [click here](#) or go to <https://www.aua2021.org/>

IASP WORLD CONGRESS ON PAIN

The World Congress on Pain organized by the International Association for the Study of Pain has been rescheduled and is now planned for 27 June – 1 July 2021 in Amsterdam, the Netherlands. For further information, [click here](#) or go to <https://www.iaspworldcongress.org/>

ICS ANNUAL SCIENTIFIC MEETING 2021

The 51st annual scientific meeting of the International Continence society (ICS) will be held 12-15 October 2021 in Melbourne, Australia. For further information, [click here](#) or go to <https://www.ics.org/2021>

INFORMATION ABOUT COVID-19 AND USEFUL ONLINE RESOURCES

- The International Alliance of Patients' Organizations (IAPO) has put together a now very extensive COVID-19 resources hub at <https://www.iapo.org.uk/covid-19-resources-hub> which patients and their support groups around the world may find useful.
- Useful information is also available at <https://www.coronavirus.gov>.
- Latest research information is available from the National Institutes of Health (NIH) at <https://www.nih.gov/coronavirus> .
- For speakers of Dutch, Dr Joop P. van de Merwe in the Netherlands is continually updating a very interesting and highly informative article about all aspects of COVID-19 (in Dutch). The introductory page with a link to the detailed article (currently at 80 pages) can be found at: <https://www.jpvandemerwe.nl/corona>

RESEARCH UPDATE

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

Most of these have a direct link to the PubMed abstract if you click on the title. An increasing number of scientific articles "In Press" or "Early View" are being published early online (on the Journal website) as "Epub ahead of print" sometimes long

before they are published in the journals. While abstracts are usually available on PubMed, the pre-publication articles can only be read online if you have online access to that specific journal. However, in some cases there may be free access to the full article online. Click on the title to go to the PubMed abstract or to the full article in the case of free access.

Terminology: different published articles use different terminology, for example: interstitial cystitis, painful bladder syndrome, bladder pain syndrome, hypersensitive bladder, chronic pelvic pain (syndrome) or combinations of these. Hunner's ulcer, Hunner lesion, Hunner IC and Classic IC are synonymous. When reviewing the article, we generally use the terminology used by the authors.

NIH MULTIDISCIPLINARY APPROACH TO THE STUDY OF CHRONIC PELVIC PAIN (MAPP) RESEARCH NETWORK

(For about the MAPP Research Network, [click here](#))

THE MULTIDISCIPLINARY APPROACH TO THE STUDY OF CHRONIC PELVIC PAIN (MAPP) RESEARCH NETWORK: DESIGN AND IMPLEMENTATION OF THE SYMPTOM PATTERNS STUDY (SPS)

J Quentin Clemens, Jason J Kutch, Emeran A Mayer, Bruce D Naliboff, Larissa V Rodriguez, David J Klumpp, Anthony J Schaeffer, Karl J Kreder, Daniel J Clauw, Steven E Harte, Andrew D Schrepf, David A Williams, Gerald L Andriole, H Henry Lai, Dedra Buchwald, M Scott Lucia, Adrie van Bokhoven, Sean Mackey, Robert M Moldwin, Michel A Pontari, Alisa J Stephens-Shields, Chris Mullins, J Richard Landis. *Neurourol Urodyn.* 2020 Jun 23. doi: 10.1002/nau.24423. Online ahead of print. PMID: 32578257.

The Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network initiated a second observational cohort study-the Symptom Patterns Study (SPS)-to further investigate the underlying pathophysiology of Urologic Chronic Pelvic Pain Syndrome (UCPPS) and to discover factors associated with longitudinal symptom changes and responses to treatments. This multisite cohort study of males and females with UCPPS features a run-in period of four weekly web-based symptom assessments before a baseline visit, followed by quarterly assessments up to 36 months. Controls were also recruited and assessed at baseline and 6 months. Extensive clinical data assessing urological symptoms, nonurological pain, chronic overlapping pain syndromes, and psychosocial factors were collected. Diverse biospecimens for biomarker and microbiome studies, quantitative sensory testing (QST) data under multiple stimuli, and structural and functional neuroimaging scans were obtained under a standardized protocol. Recruitment was initiated (July 2015) and completed (February 2019) at six discovery sites. A total of 620 males and females with UCPPS and 73 Controls were enrolled, including 83 UCPPS participants who re-enrolled from the first MAPP Network cohort study (2009-2012). Baseline neuroimaging scans, QST measures, and biospecimens were obtained on 578 UCPPS participants. The longitudinal follow-up of the cohort is ongoing. This comprehensive characterization of a large UCPPS cohort with extended follow-up greatly expands upon earlier MAPP Network studies and provides unprecedented opportunities to increase our understanding of UCPPS pathophysiology, factors associated with symptom change, clinically relevant patient phenotypes, and novel targets for future interventions.

GUIDELINES, TERMINOLOGY, DEFINITIONS

AN URGENT CASE FOR SENSORY URGENCY: A PATIENT PERSPECTIVE

Meijlink J. *Neurourol Urodyn.* 2020 Sep;39(7):2008-2010. doi: 10.1002/nau.24457. Epub 2020 Jul 10. PMID: 32648972

Interstitial cystitis/bladder pain syndrome (IC/BPS) patients around the world are all too familiar with the immense stress and anxiety caused by an urgent and frequent need to void, leading to many patients with IC/BPS staying at home in social isolation since they are afraid that they will not find a public toilet when they urgently need it. It is therefore of great concern that for almost two decades the "sensory" type of urgency due to intolerable pain or unpleasant sensation as typically experienced by this group of patients has no longer been officially recognized, researched or treated as a symptom of IC/BPS. This official misrepresentation of IC/BPS symptoms needs to be addressed and rectified for the sake of patients and to ensure medical accuracy in research.

THE REVISED INTERNATIONAL ASSOCIATION FOR THE STUDY OF PAIN DEFINITION OF PAIN: CONCEPTS, CHALLENGES, AND COMPROMISES

Srinivasa N Raja, Daniel B Carr, Milton Cohen, Nanna B Finnerup, Herta Flor, Stephen Gibson, Francis J Keefe, Jeffrey S Mogil, Matthias Ringkamp, Kathleen A Sluka, Xue-Jun Song, Bonnie Stevens, Mark D Sullivan, Perri R Tutelman, Takahiro Ushida, Kyle Vader. *Pain.* 2020 May 23. doi: 10.1097/j.pain.0000000000001939. Online ahead of print. PMID: 32694387

The current International Association for the Study of Pain (IASP) definition of pain as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" was recommended by the Subcommittee on Taxonomy and adopted by the IASP Council in 1979. This definition has become accepted widely by health care professionals and researchers in the pain field and adopted by several professional, governmental, and nongovernmental organizations, including the World Health Organization. In recent years, some in the field have reasoned that advances in our understanding of pain warrant a re-evaluation of the definition and have proposed modifications. Therefore, in 2018, the IASP formed a 14-member, multinational Presidential Task Force comprising individuals with broad expertise in clinical and basic science related to pain, to evaluate the current definition and accompanying note and recommend whether they should be retained or changed. This review provides a synopsis of the critical concepts, the analysis of comments from the IASP membership and public, and the committee's final recommendations for revisions to the definition and notes, which were discussed over a 2-year period. The task force ultimately recommended that the definition of pain be revised to "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage," and that the accompanying notes be updated to a bulleted list that included the etymology. The revised definition and notes were unanimously accepted by the IASP Council early this year.

INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: BASIC SCIENCE, DIAGNOSIS AND TREATMENT

CLINICAL MANAGEMENT OF BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS: A REVIEW ON CURRENT RECOMMENDATIONS AND EMERGING TREATMENT OPTIONS

Colemeadow J, Sahai A, Malde S. Res Rep Urol. 2020;12:331-343 <https://doi.org/10.2147/RRU.S238746>

Bladder pain syndrome (BPS) is a chronic condition characterized by pelvic pain or pressure which is perceived to be originating from the bladder, accompanied by one or more urinary symptoms, including frequency, urgency and nocturia. The precise etiology of BPS is not fully understood. Chronic bacterial infection, defective glycosaminoglycan (GAG) layer of the bladder urothelium, inappropriate activation of mast cells in the suburothelial layer of the bladder, autoimmune-mediated mechanisms and autonomic nervous system dysfunction have all been implicated. Treatments targeted at each of these mechanisms have been developed with mixed outcomes. High-quality research into the treatment options is lacking and it is difficult to draw definite conclusions. The treatment approach is multimodal and should be patient specific, targeting the symptoms which they find most bothersome. Conservative treatment, including patient education, behavioural modification, dietary advice, stress relief and physical therapy is an essential initial management strategy for all patients. If no response is observed, oral treatments such as amitriptyline are likely to offer the greatest response. Cystoscopy is essential to phenotype patients, and Hunner lesion directed therapy with fulguration or resection can be performed at the same time. Intravesical instillation of DMSO or lidocaine, detrusor injections of botulinum toxin A and neuromodulation can be used if initial management fails to improve symptoms. Oral cyclosporin can be trialled in those experienced with its use; however, it is associated with significant adverse events and requires intense monitoring. Lastly, radical surgery should be reserved for those with severe, unremitting BPS, in which quality of life is severely affected and not improved by previously mentioned interventions. Future work investigating exact aetiological factors will help target the development of efficacious treatment options, and several promising oral and intravesical treatments are emerging.

AN UPDATE ON TREATMENT OPTIONS FOR INTERSTITIAL CYSTITIS

Simone Garzon, Antonio Simone Laganà, Jvan Casarin, Ricciarda Raffaelli, Antonella Cromi, Davide Sturla, Massimo Franchi, Fabio Ghezzi. Review Prz Menopauzalny. 2020 Mar;19(1):35-43. doi: 10.5114/pm.2020.95334. Epub 2020 Apr 27. PMID: 32699542.

Interstitial cystitis or bladder pain syndrome (IC/BPS) is a chronic pelvic pain syndrome related to the urinary bladder. The ideal treatment should match as much as possible with the pathophysiologic causes of the IC/BPS, but the scarcely available evidence limits this approach, with the majority of available treatments that are primarily targeted to the control of symptoms. The treatment strategies have traditionally focused on the bladder, which is considered the primary end-organ and source of pain. Nevertheless, the growing body of evidence suggests a multifaceted nature of the disease with systemic components. In general, guidelines recommend the personalized and progressive approach, that starts from the more conservative options and then advances toward more invasive and combined treatments. The behavioural changes represent the first and most conservative steps. They can be combined with oral medications or progressively with intravesical instillation of drugs, up to more invasive techniques in a combined way. Despite the multiple available options, the optimal treatment is not easy to be found. Only further investigation on the etiopathogenetic mechanisms,

taking into account the differences among subgroups, and the interaction between central and peripheral factors may allow providing a real improvement in the treatment and management of these patients.

[\[INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME \(IC/BPS\)\]](#)

[Article in German]

Thomas Bschiepfer. *Urologe A*. 2020 Aug 25. doi: 10.1007/s00120-020-01309-3. Online ahead of print. PMID: 32840644

As an orphan disease interstitial cystitis/bladder pain syndrome (IC/BPS) is a frequently underdiagnosed and inadequately treated disease of the urinary bladder, often after years of symptoms. Caused by an unknown etiology, a high variability of symptoms, a lack of biomarkers and a gradual onset, IC/BPS is a diagnosis by exclusion and poses a special challenge to doctors and patients. In addition to conventional and complementary medical treatment, oral medication, intravesical and transurethral procedures are available as treatment options. Due to the invasiveness or irreversibility, however, interventional surgical procedures should only be used after careful consideration or as a last resort. In order to find a suitable individualized treatment, a classification of the patients according to the severity and type of symptoms can be advantageous.

[CLASSIFICATION OF THE URINARY METABOLOME USING MACHINE LEARNING AND POTENTIAL APPLICATIONS TO DIAGNOSING INTERSTITIAL CYSTITIS](#)

Feng Tong, Muhammad Shahid, Peng Jin, Sungyong Jung, Won Hwa Kim, Jayoung Kim. *Bladder (San Franc)*. 2020 Jun 2;7(2):e43. doi: 10.14440/bladder.2020.815. eCollection 2020. PMID: 32775485

[Free full article, click on title](#)

With the advent of artificial intelligence (AI) in biostatistical analysis and modelling, machine learning can potentially be applied into developing diagnostic models for interstitial cystitis (IC). In the current clinical setting, urologists are dependent on cystoscopy and questionnaire-based decisions to diagnose IC. This is a result of a lack of objective diagnostic molecular biomarkers. The purpose of this study was to develop a machine learning-based method for diagnosing IC and assess its performance using metabolomics profiles obtained from a prior study. To develop the machine learning algorithm, two classification methods, support vector machine (SVM) and logistic regression (LR), set at various parameters, were applied to 43 IC patients and 16 healthy controls. There were 3 measures used in this study, accuracy, precision (positive predictive value), and recall (sensitivity). Individual precision and recall (PR) curves were drafted. Since the sample size was relatively small, complicated deep learning could not be done. The authors achieved a 76%-86% accuracy with leave-one-out cross validation depending on the method and parameters set. The highest accuracy achieved was 86.4% using SVM with a polynomial kernel degree set to 5, but a larger area under the curve (AUC) from the PR curve was achieved using LR with a l 1-norm regularizer. The AUC was greater than 0.9 in its ability to discriminate IC patients from controls, suggesting that the algorithm works well in identifying IC, even when there is a class distribution imbalance between the IC and control samples. This finding provides further insight into utilizing previously identified urinary metabolic biomarkers in developing machine learning algorithms that can be applied in the clinical setting.

[THE ROLE OF BLADDER INSTILLATION IN THE TREATMENT OF BLADDER PAIN SYNDROME: IS INTRAVESICAL TREATMENT AN EFFECTIVE OPTION FOR PATIENTS WITH BLADDER PAIN AS WELL AS LUTS?](#)

Digesu GA, Tailor V, Bhide AA, Khullar V. *Int Urogynecol J*. 2020 Jul;31(7):1387-1392. doi: 10.1007/s00192-020-04303-7. Epub 2020 May 1. PMID: 32358624

The aetiology of bladder pain syndrome/interstitial cystitis is still unknown. Numerous mechanisms have been proposed and treatments targeting various aspects of these are used. This review looks at the existing evidence on bladder instillations and whether they could be used in the treatment of lower urinary tract symptoms as well.

[PHYSICAL EXAM IN THE EVALUATION OF BLADDER PAIN SYNDROME \(BPS\): A KEY COMPONENT FOR DIFFERENTIAL DIAGNOSIS.](#)

[Article in English, Spanish; Abstract available in Spanish from the publisher]

Vicente Palacio E, Franco de Castro A, Adot Zurbano JM, Medina-Polo J, Salinas Casado J, Arlandis Guzmán S. *Arch Esp Urol*. 2020 May;73(4):281-292. PMID: 32379063

The purpose of this study from Spain was to describe in more detail the usual clinical practice regarding physical examination (PE) in Bladder Pain Syndrome (BPS) and to evaluate if the performance of PE relates to changes in severity of symptoms and in Health Related Quality of Life (HRQoL). Epidemiological, observational, national and multicentric study that included 319 patients with BPS (79 of new diagnosis and 240 in follow-up). Demographic

and clinical data were collected. The diagnostic study was performed according to the usual clinical practice, including as the case: PE and biopsy. The patients completed the "Bladder Pain/Interstitial Cystitis Symptom Score" (BPIC-SS) and "EuroQoL-5D-5L" (EQ-5D-5L) questionnaires. To describe the continuous variables, the mean, standard deviation (SD) and quartiles analyzed were used, and for categorical variables, number and percentage of patients by response category. The questionnaires' results were described according to the visual analog scale (VAS). Health status was evaluated in patients with myofascial pain. PE was performed in 296 cases. 28.4% of the patients presented pelvic myofascial pain. The variation of the BPIC-SS score in the explored patients was 7.77 points, compared to 1.73 in the unexplored ones. The variations in EQ-5D-5L were 0.13 and 0.04 points, respectively. Myofascial involvement was observed in 28.4% of the 296 cases of BPS who received a PE. It is important to implement a systematic, comprehensive method of PE at the national level in order to achieve a more precise characterization of BPS and a better evolution of the patient's symptoms and HRQoL.

[A COMPREHENSIVE REVIEW OF THE DIAGNOSIS, TREATMENT, AND MANAGEMENT OF UROLOGIC CHRONIC PELVIC PAIN SYNDROME.](#)

Adamian L, Urits I, Orhurhu V, Hoyt D, Driessen R, Freeman JA, Kaye AD, Kaye RJ, Garcia AJ, Cornett EM, Viswanath O. Curr Pain Headache Rep. 2020 May 6;24(6):27. doi: 10.1007/s11916-020-00857-9. PMID: 32378039

Urologic chronic pelvic pain syndrome (UCPPS) is a chronic, noncyclic pain condition which can lead to significant patient morbidity and disability. It is defined by pain in the pelvic region, lasting for greater than 3 to 6 months, with no readily identifiable disease process. The aim of this review from the USA was to provide a comprehensive update of diagnosis and treatment of UCPPS. UCPPS encompasses chronic pelvic pain syndrome or chronic prostatitis (CP/CPPS) in men and interstitial cystitis or painful bladder syndrome (IC/PBS) in women. Underlying inflammatory, immunologic, and neuropathic components have been implicated in the pathogenesis of UCPPS. For optimal patient management, an individualized and multimodal approach is recommended. Medical management and physical therapy are the mainstays of treatment. Injection therapy may offer additional relief in medically refractory patients. Further minimally invasive management may include spinal cord and peripheral nerve stimulation, though evidence supporting efficacy is limited.

[PAIN REDUCTION REALIZED WITH EXTRACORPOREAL SHOCK WAVE THERAPY FOR THE TREATMENT OF SYMPTOMS ASSOCIATED WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME-A PROSPECTIVE, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY.](#)

Chuang YC, Meng E, Chancellor M, Kuo HC. Neurourol Urodyn. 2020 Jun;39(5):1505-1514. doi: 10.1002/nau.24382. Epub 2020 May 11. PMID: 32394478

Extracorporeal shock wave therapy (ESWT) inhibited bladder inflammation and pain in preclinical studies. Chuang and colleagues from Taiwan and Michigan (USA) assessed ESWT for the treatment of refractory interstitial cystitis/bladder pain syndrome (IC/BPS). This double-blind, randomized, placebo-controlled physician-initiated study enrolled 54 patients with IC/BPS. The patients were assigned to ESWT (N = 24; 2000 shocks, frequency of 3 Hz, and maximum total energy flow density 0.25 mJ/mm²) once a week for 4 weeks at suprapubic bladder area or placebo (N = 25; shock wave setting without energy transmission). The primary endpoint was the average changes in O'Leary-Sant symptom scores (OSS) between baseline and 4 weeks after treatment. Secondary endpoints included visual analog scale (VAS, 0-10) for pain, the average changes of variables in a 3-day voiding diary, and global response assessment of patient satisfaction. At 4 weeks posttreatment, both groups were associated with a statistically significant decrease in OSS and VAS pain scale. However, there were no difference in mean change between ESWT vs placebo groups. A significantly higher proportion of patients on ESWT responded as improved in the VAS ≥ 3 vs placebo (P = .035). At 12 weeks posttreatment, improvement in the VAS ≥ 3 was 57.1% vs 19.0% (ESWT vs placebo; P = .011). The finding was associated with an improvement in frequency - 1.0 ± 2.3 vs 0.7 ± 3.2 (ESWT vs placebo; P = .065). No significant adverse events were found in either group. A reduction in pain was discovered in this trial assessing ESWT in patients with IC/BPS but OSS, which was the primary outcome parameter, was not improved.

[PERCUTANEOUS TIBIAL NERVE STIMULATION FOR THE TREATMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: A PILOT STUDY](#)

Neha T Sudol, Noelani Guaderrama, Emily Adams-Piper, Emily Whitcomb, Felicia Lane. Int Urogynecol J. 2020 Aug 13. doi: 10.1007/s00192-020-04481-4. Online ahead of print. PMID: 32789810.

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic pain condition that requires multimodal management. The American Urologic Association includes sacral neuromodulation in the treatment algorithm for refractory IC/BPS. Sudol and colleagues sought to determine the rate of overall symptom improvement of

IC/BPS symptoms, using validated measures, after treatment with percutaneous tibial nerve stimulation (PTNS), a form of peripheral neuromodulation. This was a single-arm, dual-centre, pilot study examining a standard PTNS protocol in subjects with IC/BPS. The primary outcome was subject response of "moderately" or "markedly improved" on the Global Response Assessment (GRA) scale after 12-weekly PTNS sessions. Assuming a 60% response rate, 24 subjects were needed to detect a response rate between 40 and 80% with 95% confidence. Secondary objectives included change in urinary frequency on a 24-h bladder diary, bladder pain as measured by VAS and responses to validated questionnaires for pelvic pain and IC/BPS. Of 21 subjects enrolled, 16 initiated and 10 completed the PTNS treatment course. The GRA response rate was 40% at week 6 and 30% at week 12. Seventy percent of the cohort had some degree of improvement. There were no adverse events. While only a minority of subjects with IC/BPS were responders to PTNS per GRA criteria, 70% of the cohort had some degree of improvement. Due to low recruitment and loss to follow-up, the authors did not achieve our predetermined significance. However, their promising findings add to the limited literature on this subject.

RELIABILITY AND VALIDITY OF TURKISH VERSIONS OF THE INTERSTITIAL CYSTITIS SYMPTOM INDEX AND INTERSTITIAL CYSTITIS PROBLEM INDEX

Bariş Esen, Khaled Obaid, Evren Süer, Mehmet İlker Gökçe, Derya Gökmen, Yaşar Bedük, Ömer Gülpınar. Neurourol Urodyn. 2020 Aug 26. doi: 10.1002/nau.24492. Online ahead of print. PMID: 32846036

The aim of this study was to validate the Turkish versions of the interstitial cystitis symptom index (ICSI) and interstitial cystitis problem index (ICPI) for use in Turkish speaking patients with bladder pain syndrome/interstitial cystitis (BPS/IC). After translation of the original ICSI and ICPI into the Turkish language, Turkish versions of ICSI and ICPI were self-administered to all participants. Test-retest reliability (intraclass correlation coefficient) was evaluated at 2 weeks intervals in the BPS/IC group. Internal consistency was evaluated using Cronbach's alpha. Scores of ICSI and ICPI was compared between BPS/IC and control groups to examine discriminant validity. Criterion validity was examined via investigating the correlations between bladder diary data (24-hour frequency and nocturia), visual analogue scale (VAS) scores, and results to the corresponding questions in ICSI and ICPI. Results of 79 patients with BPS/IC and 50 control patients were analyzed. Both indices showed high internal consistency (Cronbach's α for ICSI and ICPI was 0.879 and 0.923, respectively). The test-retest reliability of ICSI and ICPI was high for total scores and subdomains of both indices (intraclass correlation coefficient was 0.722 for ICSI and 0.777 for ICPI). Scores of both indices were significantly higher in BPS/IC group than the control group. Statistically significant correlations were found between 24-hour frequency, nocturia, VAS scores, and corresponding questions in the indices. A statistically significant and strong correlation was observed between ICSI and ICPI scores. It was concluded that Turkish versions of ICSI and ICPI are reliable, consistent, and valid instruments to evaluate symptoms of Turkish speaking patients with BPS/IC.

HIGH-DENSITY SURFACE ELECTROMYOGRAPHIC ASSESSMENT OF PELVIC FLOOR HYPERTONICITY IN IC/BPS PATIENTS: A PILOT STUDY

Nicholas Dias, Chuan Zhang, Christopher P Smith, H Henry Lai, Yingchun Zhang. Int Urogynecol J. 2020 Aug 6. doi: 10.1007/s00192-020-04467-2. Online ahead of print. PMID: 32761375.

The purpose of this study was to assess the feasibility of objectively assessing pelvic floor hypertonicity (PFH) in women with interstitial cystitis/bladder pain syndrome (IC/BPS) using an intra-vaginal high-density surface electromyography (HD-sEMG) probe. Seven female subjects (mean age 44 ± 13 years) with a prior diagnosis of IC/BPS were recruited. A full digital pelvic examination was administered to identify hypertonic muscles. Intra-vaginal HD-sEMG was acquired during rest. Root-mean-squared (RMS) amplitude during rest was calculated for each channel to define a hypertonicity index and hypertonic zone. Innervation zones (IZs) were identified from the bipolar mapping of decomposed HD-sEMG signals and summarized into an IZ distribution mapping. Of the seven subjects recruited, five had normal pelvic floor muscle tone and two exhibited hypertonicity upon muscle palpation. Subjects with PFH demonstrated a higher hypertonicity index (12.6 ± 3.5 vs. 4.5 ± 1.2) in sessions 1 and 2. The hypertonic zone defined by the 64-channel RMS mapping coincided with the digital pelvic examination findings. The corresponding IZs were localized for each motor unit. The hypertonicity indices between two consecutive sessions were well correlated ($CC = 0.95$). This study represents the first effort to employ intra-vaginal HD-sEMG to assess PFH in women with IC/BPS. The authors believe that their results demonstrate the feasibility of HD-sEMG to provide a quantitative diagnosis of PFH and the precise localization of hypertonic muscles and IZs. The proposed HD-sEMG-based techniques provide promising tools for clinical diagnosis and treatment of PFH, such as the personalized guidance of BoNT injections.

CULTIVABLE BACTERIA IN URINE OF WOMEN WITH INTERSTITIAL CYSTITIS: (NOT) WHAT WE EXPECTED

Kristin M Jacobs, Travis K Price, Krystal Thomas-White, Thomas Halverson, Abigail Davies, Deborah L Myers, Alan J Wolfe. Female Pelvic Med Reconstr Surg. 2020 Apr 6. doi: 10.1097/SPV.0000000000000854. Online ahead of print. PMID: 32265402.

Multiple studies show cultivatable bacteria in urine of most women. The existence of these bacteria challenges interstitial cystitis (IC)/painful bladder syndrome (PBS) diagnosis, which presumes a sterile bladder. The aims of this study were (1) to compare the female bladder microbiomes in women with IC/PBS and unaffected controls and (2) to correlate baseline bladder microbiome composition with symptoms. This cross-sectional study enrolled 49 IC/PBS and 40 controls. All provided catheterized urine samples and completed validated questionnaires. A subset of the IC/PBS cohort provided voided and catheterized urine samples. All samples from both cohorts were assessed by the expanded quantitative urine culture (EQUC) protocol; a subset was assessed by 16S rRNA gene sequencing. Of the IC/PBS cohort, 49.0% (24/49) were EQUC positive; in these EQUC-positive samples, the most common urotypes were *Lactobacillus* (45.8%) and *Streptococcus* (33.3%). Of the controls, 40.0% were EQUC positive; of these EQUC-positive samples, the most common urotype was *Lactobacillus* (50.0%). The urotype distribution was significantly different ($P < 0.05$), as 16% of the IC/PBS cohort, but 0% of controls, were *Streptococcus* urotype ($P < 0.01$). Symptom-free IC/PBS participants were less likely to be EQUC positive (12.5%) than IC/PBS participants with moderate or severe symptoms (68.8% and 46.2%) and the control cohort (60%; $P < 0.05$). *Lactobacillus* was the most common urotype. However, the presence of *Lactobacillus* did not differ between cohorts, and it did not impact IC/PBS symptom severity. Bacteria were not isolated from most participants with active IC/PBS symptoms. These findings suggest that bacteria may not be an etiology for IC/PBS.

ANALYSIS OF VIRUSES PRESENT IN URINE FROM PATIENTS WITH INTERSTITIAL CYSTITIS

Maria Teresa Sáenz Robles, Paul G Cantalupo, Alexis M Duray, Melissa Freeland, Michelle Murkowski, Adrie van Bokhoven, Alisa J Stephens-Shields, James M Pipas, Michael J Imperiale. Virus Genes. 2020 Aug;56(4):430-438. Epub 2020 May 23. PMID: 32447589.

The question of whether some cases of interstitial cystitis may have an infectious etiology has been debated for some time. Previous studies have looked for the presence of certain specific viruses, but generally did not use the types of sensitive and unbiased approaches that are currently available. As part of the MAPP (Multidisciplinary Approach to the Study of Chronic Pelvic Pain) Research Network, this team examined urine specimens from interstitial cystitis patients who provided specimens over time and also reported various symptoms at the time of urine collection. They first performed next-generation sequencing to look for the presence of viruses in urines and detected two human polyomaviruses that are known to be excreted into urine, BKPyV and JCPyV. They were especially interested in BKPyV because it is a known cause of another bladder disease, hemorrhagic cystitis, in bone marrow transplant recipients. Further analysis of individual samples indicates a trend toward higher excretion of polyomaviruses in patients experiencing increased symptoms.

HYPERSENSITIVITY OF BLADDER LOW THRESHOLD, WIDE DYNAMIC RANGE, AFFERENT FIBRES FOLLOWING TREATMENT WITH THE CHEMOTHERAPEUTIC DRUGS CYCLOPHOSPHAMIDE AND IFOSFAMIDE

Kylie A Mills, Eleanor J West, Luke Grundy, Catherine McDermott, Donna J Sellers, Roselyn B Rose'Myer, Russ Chess-Williams. Arch Toxicol. 2020 Aug;94(8):2785-2797. doi: 10.1007/s00204-020-02773-8. Epub 2020 May 22. PMID: 32444959.

The cytotoxic drugs cyclophosphamide (CPO) and ifosfamide (IFO) cause toxic urological effects due to the production of urinary metabolites that cause bladder inflammation. This study aimed to identify changes in the bladder afferent system following treatment with these drugs that might explain reported urological adverse effects. Intravesical pressure and afferent nerve activity were recorded during bladder distension and drug administration in isolated bladders from mice, 24 h after intraperitoneal treatment with cyclophosphamide (100 mg/kg), ifosfamide (200 mg/kg) or saline (control). In isolated bladders, total afferent nerve activity at maximum bladder distension was increased from 182 ± 13 imp/s in control animals, to 230 ± 14 imp/s in CPO-treated ($p < 0.05$) and 226 ± 17 imp/s in IFO-treated ($p < 0.001$) mice. Single fibre analysis revealed the increase resulted from an enhanced activity in low threshold, wide dynamic range fibres (23.3 ± 1.9 imp/s/fibre in controls to 31.5 ± 2.5 ($p < 0.01$) in CPO and 29.9 ± 2.0 imp/s/fibre ($p < 0.05$) in IFO treated). CPO treatment was accompanied by an increase in urinary frequency in vivo but was not associated with increases in urothelial release of ATP or acetylcholine, bladder compliance or spontaneous muscle activity. Also, CPO-treatment did not affect afferent nerve responses or pressure responses to purinergic, muscarinic or nicotinic agonists. This is the first report of CPO and IFO-induced changes in specific populations of bladder afferents, namely an increase

in low threshold, wide dynamic range fibres. These effects appear to be direct and not secondary to increases in smooth muscle activity or the release of urothelial mediators.

MEDICATIONS USED TO TREAT BLADDER DISORDERS MAY ALTER EFFECTS OF NEUROMODULATION

Timothy J Ness, Jamie McNaught, Buffie Clodfelder-Miller, Xin Su. NeuroUrol Urodyn. 2020 Jun;39(5):1313-1320. doi: 10.1002/nau.24373. Epub 2020 Apr 24. PMID: 32330365.

Neuromodulation (nerve stimulation) can produce analgesia. One form, bilateral pudendal nerve stimulation (bPNS), suppresses responses to urinary bladder distension (UBD) in hypersensitive rats. Drugs can modify this effect (eg, benzodiazepines, but not opioids, suppress bPNS effects). Prior to a clinical trial of bPNS effects on bladder pain, the authors felt it was prudent to survey the effects of medications commonly used in patients with bladder disorders. Bladder hypersensitivity was produced by neonatal bladder inflammation in rat pups coupled with a second inflammatory insult as an adult. Antimuscarinic (oxybutynin), β_3 -adrenoceptor agonist (mirabegron, CL316243), α_1 -adrenoceptor antagonist (tamsulosin), antidepressant (amitriptyline), muscle relaxing (baclofen), and sedative (propofol) agents were administered and effects of bPNS on responses to UBD assessed. bPNS consisted of bilateral biphasic electrical stimulation of the mixed motor/sensory component of the pudendal nerves. Visceromotor responses (VMRs; abdominal muscle contractile responses) were used as nociceptive endpoints. Many of these drugs directly inhibited the VMRs to UBD, but only mirabegron, at the doses employed, significantly reduced inhibitory effects of bPNS. In the presence of the other drugs, bPNS continued to produce statistically significant inhibition of VMRs to UBD. This study suggests that concurrent therapy with drugs used to treat bladder disorders could affect assessment of the effects of bPNS on bladder hypersensitivity. This study gives guidance to clinical trials using bPNS for the treatment of painful bladder syndromes and suggests potential clinical use of some of these medications in the treatment of these same disorders.

ROLE OF URINARY CATIONS IN THE ETIOLOGY OF INTERSTITIAL CYSTITIS: A MULTISITE STUDY

C Lowell Parsons, Sulabha Argade, Robert J Evans, Jeffrey Proctor, J Curtis Nickel, Matt T Rosenberg, Philip C Bosch. Int J Urol. 2020 Jul 17. doi: 10.1111/iju.14293. Online ahead of print. PMID: 32677166.

The purpose of this study was to determine whether patients with interstitial cystitis have elevated levels of toxic urinary cations, to identify and quantify these cationic metabolites, and to assess their cytotoxicity. Isolation of cationic fraction was achieved by solid phase extraction using an Oasis MCX cartridge on urine specimens from interstitial cystitis patients and controls. C18 reverse phase high-performance liquid chromatography was used to profile cationic metabolites, and they were quantified by the area under the peaks and normalized to creatinine. Major cationic fraction peaks were identified by reverse phase high-performance liquid chromatography and liquid chromatography-mass spectrometry. HTB-4 urothelial cells were used to determine the cytotoxicity of cationic fraction and of individual metabolites. The reverse phase high-performance liquid chromatography analysis was carried out on cationic fraction metabolites isolated from urine samples of 70 interstitial cystitis patients and 34 controls. The mean for controls versus patients was 3.84 (standard error of the mean 0.20) versus 6.71 (0.37) mAU*min/ μ g creatinine, respectively. The cationic fraction cytotoxicity normalized to creatinine for controls versus patients in mean percentage was -7.79% (standard error of the mean 3.32%) versus 20.03%. The major toxic cations were 1-methyladenosine, 1-methylguanine, N₂,N₂-dimethylguanosine and L-tryptophan. It was concluded that these data confirm significant elevation of toxic cations in the urine of interstitial cystitis patients. These toxic cations likely represent a primary cause of interstitial cystitis, as they can injure the bladder mucus and initiate an epithelial leak.

A PROTOCOL OF SYSTEMATIC REVIEW AND META-ANALYSIS OF NEUROMUSCULAR ELECTRICAL STIMULATION FOR INTERSTITIAL CYSTITIS

Da-Yin Chen, Ying-Xue Guo, Long-Xin Dong, Wen-Jie He, Hui-Feng Cao, Ping Wang, Cai-Fang Yue. Medicine (Baltimore). 2020 Jul 10;99(28):e21088. PMID: 32664129

The purpose of this study from China is to examine the effectiveness and safety of neuromuscular electrical stimulation (NMES) for the treatment of patients with interstitial cystitis (IC). The authors will retrieve the following electronic databases from their commencement to 1 March, 2020 to discover all related potential studies: MEDLINE, EMBASE, Cochrane Library, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), China National Knowledge Infrastructure, Chinese Biomedical Literature Database, Chinese Scientific Journal Database, and WANFANG Database. Randomized controlled trials related to the NMES for the treatment of patients with IC will be included, regardless publication status and language. Literature selection, data collection, and study quality assessment will be independently performed by 2 authors. The extracted data will be expressed as risk ratio and 95% confidence intervals for dichotomous data, and mean difference or

standard mean difference and 95% confidence intervals for continuous data. RevMan V.5.3 software will be employed for statistical analysis. This study will summarize current high quality randomized controlled trials to appraise the effectiveness and safety of NMES for the treatment of patients with IC. The findings of this study will provide helpful evidence to determine whether NMES is an effective treatment for patients with IC or not.

UREASE-POWERED POLYDOPAMINE NANOMOTORS FOR INTRAVESICAL THERAPY OF BLADDER DISEASES

Hyunsik Choi, Seong Hwi Cho, Sei Kwang Hahn. ACS Nano. 2020 Jun 23;14(6):6683-6692. doi: 10.1021/acsnano.9b09726. Epub 2020 Jun 8. PMID: 32491832.

The intravesical therapeutic delivery has been extensively investigated for various bladder diseases such as bladder cancer, overactive bladder, urinary incontinence, and interstitial cystitis. However, conventional drug carriers have a low therapeutic delivery efficiency because of the passive diffusion of drug molecules in bladder and the rapid clearance by the periodic urination. Here, the authors report biocompatible and bioavailable enzyme-powered polymer nanomotors which can deeply penetrate into a mucosa layer of bladder wall and remain for a long-term period in the bladder. The successful fabrication of nanomotors was confirmed by high resolution - transmission electron microscopy (HR-TEM), energy-dispersive X-ray (EDX) mapping, zeta-particle analysis, Fourier transform - infrared (FT-IR) spectroscopy, and urease activity and nanomotor trajectory analyses. After injection into the bladder, urease immobilized nanomotors became active moving around in the bladder by converting urea into carbon dioxide and ammonia. The nanomotors resulted in the facilitated penetration to the mucosa layer of bladder wall and the prolonged retention in the bladder even after repeated urination. The enhanced penetration and retention of the nanomotors as a drug delivery carrier in the bladder would be successfully harnessed for treating a variety of bladder diseases.

BOTULINUM TOXIN IN LOW URINARY TRACT DISORDERS - OVER 30 YEARS OF PRACTICE (REVIEW)

Arsenie Dan Spinu, Ovidiu Gabriel Bratu, Camelia Cristina Diaconu, Ana Maria Alexandra Stanescu, Simona Bungau, Ovidiu Fratila, Roxana Bohiltea, Dan Liviu Dorel Mischianu. Review Exp Ther Med. 2020 Jul;20(1):117-120. doi: 10.3892/etm.2020.8664. Epub 2020 Apr 15. PMID: 32509003

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Botulinum toxin is a substance produced by Clostridium Botulinum and is responsible for human botulism. This substance is a poison, a neurotoxin, but used in limited quantities it can be a cure for some diseases. It is well connected to a large variety of medical applications. The mechanism of action relies on blocking the acetylcholine at the neuromuscular junction, which blocks the transmission of the nervous impulse with secondary flaccid paralysis. In urology, its role in idiopathic overactive bladder and neurogenic bladder is well known. The authors performed a thorough review using PubMed and other databases, revising the mechanisms of botulinum toxin action in urologic pathology, treatment procedures and other options. Botulinum toxin is a well-studied substance with a large number of applications in medicine. In urologic pathology, overactive bladder and neurogenic bladder are backed by robust studies that support the therapeutic role of this substance. The toxin has multiple effects, such as inhibition of the nerve growth factor, blocking the bladder sensory afferent pathway and apoptotic effect on the prostate tissue, by inhibiting the substance P, altering the nociceptive pathways. Interstitial cystitis and other rare pathologies show promising results, but further studies are needed. The role of botulinum toxin in benign prostatic hyperplasia is still not elucidated.

PLATELET-RICH PLASMA AMELIORATES CYCLOPHOSPHAMIDE-INDUCED ACUTE INTERSTITIAL CYSTITIS /PAINFUL BLADDER SYNDROME IN A RAT MODEL

Yung-Hsiang Chen, Kee-Ming Man, Wen-Chi Chen, Po-Len Liu, Kao-Sung Tsai, Ming-Yen Tsai, Yu-Tzu Wu, Huey-Yi Chen. Diagnostics (Basel). 2020 Jun 8;10(6):E381. doi: 10.3390/diagnostics10060381. PMID: 32521683.

Interstitial cystitis/painful bladder syndrome (IC/PBS) could be treated to ameliorate urothelial injury. Here, the authors investigated the efficacy of intravesical instillation with platelet-rich plasma (PRP) and hyaluronic acid for acute IC/PBS. The effects of PRP and hyaluronic acid on the proliferation of normal human fibroblast cells (HFCs) were assessed. Additionally, thirty virgin female rats were randomized into five groups: group 1, saline-injected control; group 2, cyclophosphamide (CYP) plus intravesical instillation with normal saline; group 3, CYP plus intravesical instillation with hyaluronic acid (1 mg/mL); group 4, CYP plus intravesical instillation with PRP; and group 5, CYP plus intravesical instillation with PRP plus hyaluronic acid. A cystometry and histological assessments were performed. The expression of cell junction-associated protein zonula occludens-2 (ZO-2) and inflammatory cytokine interleukin 6 (IL-6) was also measured. Low dose PRP increased proliferation in HFCs. The acute IC/PBS rats showed significantly lower voiding interval values. Voiding interval values were significantly higher in the CYP plus intravesical instillation with PRP group than in the CYP-induced acute IC/PBS group. Additionally, the expression of ZO-2 was increased and IL-6 was decreased in the CYP plus intravesical instillation

with PRP group compared with the CYP-induced acute IC/PBS group. These findings suggest that PRP modulate urothelial repair, which ameliorate the increase in urination frequency in rats treated with CYP. Overall, PRP may confer potential benefits by acting as urothelial repair modulators.

ROLE OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS

Porru Daniele, Regina Cesare, Oworae Howardson Bright, Fiorello Nicolo, Gardella Barbara, Manzoni Federica, Klersy Catherine, Sala Maria Gabriella, La Fianza Alfredo, Ballerini Daniela, Preda Lorenzo, Simeone Claudio, Spinillo Arsenio, Jallous Hussein. Urology. 2020 Jul;141:55-59. doi: 10.1016/j.urology.2020.03.019. Epub 2020 Apr 8. PMID: 32277992

Some recent studies evaluated the introduction of diffusion-weighted magnetic resonance imaging (DW-MRI) in the diagnosis of bladder pain syndrome/interstitial cystitis (BPS/IC). The purpose of this study was to evaluate whether DW-MRI can contribute to noninvasive diagnosis of BPS/IC. The agreement between two raters (2 radiologists involved in the study) was also evaluated, the relevance of the "operator-dependent" factor defined. Twenty-two female patients with a diagnosis of BPS-IC were recruited and performed DW-MRI. The same investigation was also performed in 20 patients with pelvic gynecological diseases and no BPS-IC. A significant difference was found between BPS-IC and no-BPS-IC since 17 out of 22 subjects of the first group were positive, compared to 3 out of 20 no-IC subjects, with a P value of .001 to highlight the statistical significance. The sensitivity of the exam was 77%, while the specificity was 85%. There was good agreement between the 2 raters in the evaluation of MRI results. It was concluded that DW-MRI helps to obtain a noninvasive diagnosis of BPS/IC, by providing useful information on the choice of which patients may be more appropriately submitted to cystoscopy and bladder biopsy.

INTERSTITIAL CYSTITIS OR PAINFUL BLADDER SYNDROME IN A PREMENOPAUSAL FEMALE PRECIPITATED BY ORAL COMBINED CONTRACEPTIVES

Anna Thompson, Ashley E Siegel, Zachery Thompson, John M Tramont Sr. Case Reports Cureus. 2020 May 29;12(5):e8348. doi: 10.7759/cureus.8348. PMID: 32617221.

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It has been well documented that female sex is a significant risk factor for the development of various autoimmune diseases. While the reason for this has been debated, one well-regarded theory is that increased estrogen and decreased testosterone play a role in this predisposition. Interstitial cystitis (IC), also known as painful bladder syndrome (PBS), is an autoimmune disorder that affects over nine million women in the United States. It presents with pelvic and bladder pain and urinary symptoms, both of which significantly and negatively affect the quality of life. Even so, very few studies have examined the pathophysiologic relationship between autoimmune disorders and hormonal contraceptives. In this report, the authors present a case of IC likely precipitated by oral contraceptives (OCPs) in a premenopausal female. Shortly after beginning OCPs, this patient developed symptoms of severe pelvic pain and increased urinary frequency. Over the course of a year, the patient was diagnosed and treated for a variety of conditions, such as urinary tract infection (UTI), fungal vaginitis, and nephrolithiasis. After consultation with a gynecologist, a normal abdominal CT scan, and unsuccessful cystoscopy due to pain, she was finally diagnosed with IC. The patient independently learned of a potential link between hormonal contraceptive pills and IC and decided to discontinue this method of birth control. Following this, her symptoms completely resolved within several months. The timing of her initiation and discontinuation of OCPs, alongside her symptomatology, suggest a connection to the development of IC. A literature review was performed, which supports this association. The authors, therefore, highlight this case as an important example of IC precipitated by OCPs.

RELEVANCE OF THE ENDOSCOPIC EVALUATION IN THE DIAGNOSIS OF BLADDER PAIN SYNDROME /INTERSTITIAL CYSTITIS

Alessandro Morlacco, Mariangela Mancini, Matteo Soligo, Fabio Zattoni, Arturo Calpista, Giuseppe Vizzielli, Rosario Patti, Francesco Gerardo Mandato, Andrea Celeste Barneschi, Filiberto Zattoni, Massimo Iafrate, Fabrizio Dal Moro, European Reference Network for rare UROGENital disease and complex conditions (ERN eUROGEN). Urology. 2020 Jun 30;S0090-4295(20)30787-1. doi: 10.1016/j.urology.2020.06.032. Online ahead of print. PMID: 32619597.

In 2008, the European Society for the Study of Interstitial Cystitis (ESSIC) established the diagnostic criteria and classification of Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC), based on clinical features and cystoscopy results. The present study assess the relevance of the endoscopic evaluation in clinically suspected cases of BPS/IC, using ESSIC criteria. The authors included all patients who underwent endoscopic evaluation between

01/01/2015 and 31/10/2019 for clinical suspicion of BPS/IC. Collected data included demographic and baseline clinical features, endoscopic appearance (prior and after hydrodistension) and bladder wall biopsy results, both defined according to ESSIC criteria. Data were cross tabulated to define ESSIC phenotypes, while subgroups and multivariate analyses were carried out to assess the influence of clinical variables on ESSIC phenotypes. Fifty-two subjects were included, mainly women (92%). Median age at evaluation was 45 (32.9-58.2) years. At hydrodistension, 21 patients (42%) had positive and 29 (58%) had negative findings. Grade 2-3 glomerulations were found in 18 patients, while Hunner lesions were reported only in 1 patient. Positive results at biopsy were found in 24 pts (51.1%), while negative in 23 (48.9%). Overall, the positive and negative concordance between hydrodistension and biopsy results was 78%. No significant differences in ESSIC subtypes were found after stratification based on clinical features and at multivariate analysis. Retrospective design is the main limitation. Cystoscopy with hydrodistension and biopsy do have a role in the diagnostic pathway of BPS/IC. However, results should be considered in the clinical context of the individual patient.

INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AND RECURRENT URINARY TRACT INFECTION AND THE POTENTIAL ROLE OF THE URINARY MICROBIOME

Alka Bhide, Visha Tailor, Vik Khullar. Post Reprod Health. 2020 Jun;26(2):87-90. doi: 10.1177/2053369120936426. PMID: 32627695.

Interstitial cystitis/bladder pain syndrome and recurrent urinary tract infections carry significant burden for those affected. As women enter the menopause, other factors may influence how these conditions manifest. The urinary microbiome has shown that the urine contains extensive numbers of bacteria. There is some evidence to suggest that it is altered depending on the menopausal state of the individual. It is possible that this alteration may go on to influence how the disease course of interstitial cystitis/bladder pain syndrome and recurrent urinary tract infections runs in the post-menopausal group. The review will explore these two conditions and the potential role of the urinary microbiome.

HIGH-DENSITY SURFACE ELECTROMYOGRAPHY ASSESSMENT OF PELVIC FLOOR DYSFUNCTION IN WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME

Nicholas Dias, Chuan Zhang, Theresa Spitznagle, H Henry Lai, Yingchun Zhang. J Urol. 2020 Jul 6;101097JU0000000000001237. doi: 10.1097/JU.0000000000001237. Online ahead of print. PMID: 32628100.

Up to 85% of women with interstitial cystitis/bladder pain syndrome (IC/BPS) have pelvic floor dysfunction and hypertonicity. Current evaluation methodologies lack objective measures of pelvic floor muscle (PFM) activity. The authors examined the ability of utilizing intravaginal high-density surface electromyography (HD-sEMG) to quantitatively, objectively and non-invasively map PFM activity and innervation zone (IZ) locations in IC/BPS patients. Fifteen IC/BPS women and fifteen controls underwent two sessions of digital pelvic exams and HD-sEMG assessments. The root mean squared (RMS) amplitude of HD-sEMG was first calculated, and the resting RMS ratio was then calculated by normalizing the resting EMG RMS to the peak EMG amplitude during maximum voluntary contraction. IZ distributions were obtained from decomposed HD-sEMG signals. The correlation between the RMS ratio and IC/BPS symptom scores and PFM alignment were investigated in IC/BPS patients and healthy controls. IC/BPS Women demonstrated significantly increased resting RMS ratios compared to controls (0.155±0.048 vs. 0.099±0.041, p=0.0019). Significant correlations were found between resting RMS ratio and patient-reported pain (rs=0.523, p=0.003), IC symptom (rs=0.521, p=0.003) and problem indices (rs=0.60, p<0.001). In addition, women with IC/BPS were more likely to have shortened PFMs (80% (12/15) vs. 13.3% (2/15), p<0.01). Women with shortened PFMs demonstrated significantly higher resting RMS ratio compared to those with normal PFM length (0.155±0.046 vs. 0.107±0.040, p=0.0058). It was concluded that intravaginal HD-sEMG offers an objective and quantitative strategy to non-invasively assess PFM dysfunction in women with IC/BPS. Abundant spatiotemporal muscle activity information captured by HD-sEMG allows for mapping IZ distributions for major PFMs.

CYSTITIS-RELATED BLADDER PAIN INVOLVES ATP-DEPENDENT HMGB1 RELEASE FROM MACROPHAGES AND ITS DOWNSTREAM H2S/CA V 3.2 SIGNALING IN MICE

Shiori Hiramoto, Maho Tsubota, Kaoru Yamaguchi, Kyoko Okazaki, Aya Sakaegi, Yuki Toriyama, Junichi Tanaka, Fumiko Sekiguchi, Hiroyasu Ishikura, Hidenori Wake, Masahiro Nishibori, Huy Du Nguyen, Takuya Okada, Naoki Toyooka, Atsufumi Kawabata. Cells. 2020 Jul 22;9(8):E1748. doi: 10.3390/cells9081748. PMID: 32707767.

Cystitis-related bladder pain involves RAGE activation by HMGB1, and increased Cav3.2 T-type Ca²⁺ channel activity by H₂S, generated by upregulated cystathionine-γ-lyase (CSE) in mice treated with cyclophosphamide (CPA). We, thus, investigated possible crosstalk between the HMGB1/RAGE and CSE/H₂S/Cav3.2 pathways in the bladder pain development. Bladder pain (nociceptive behaviour/referred hyperalgesia) and immuno-

reactive CSE expression in the bladder were determined in CPA-treated female mice. Cell signalling was analyzed in urothelial T24 and macrophage-like RAW264.7 cells. The CPA-induced bladder pain was abolished by pharmacological inhibition of T-type Ca²⁺ channels or CSE, and genetic deletion of Cav3.2. The CPA-induced CSE upregulation, as well as bladder pain was prevented by HMGB1 inactivation, inhibition of HMGB1 release from macrophages, antagonists of RAGE or P2X4/P2X7 receptors, and N-acetylcysteine, an antioxidant. Acrolein, a metabolite of CPA, triggered ATP release from T24 cells. Adenosine triphosphate (ATP) stimulated cell migration via P2X7/P2X4 and caused HMGB1 release via P2X7 in RAW264.7 cells, which was dependent on p38MAPK/NF- κ B signalling and reactive oxygen species (ROS) accumulation. Together, our data suggest that CPA, once metabolized to acrolein, causes urothelial ATP-mediated, redox-dependent HMGB1 release from macrophages, which in turn causes RAGE-mediated CSE upregulation and subsequent H₂S-targeted Cav3.2-dependent nociceptor excitation, resulting in bladder pain.

UNDERSTANDING BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS

Visha Tailor 1, Marco Torella 2, Valentin Manriquez 3, Giuseppe Alessandro Digesu 4. *Int Urogynecol J* 31, 1495–1496 (2020). <https://doi.org/10.1007/s00192-020-04232-5>. PMID: 32095957. Editorial.

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EVALUATION OF THE EFFICACY OF CHINESE HERBAL MEDICINE AND ACUPUNCTURE FOR THE PREVENTION OF MENTAL DISORDERS IN INTERSTITIAL CYSTITIS PATIENTS: A NATIONWIDE POPULATION-BASED STUDY

Hao-Hsiu Hung, Wen-Chi Chen, Yung-Hsiang Chen, Lu-Ting Chiu, Huey-Yi Chen *Medicine (Baltimore)*. 2020 Jul 24;99(30):e21422. PMID: 32791761.

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Traditional Chinese medicine (TCM) is commonly used for urinary symptoms in Eastern countries. Since there are few effective treatments available for patients with interstitial cystitis/bladder pain syndrome (IC/BPS), the psychological burden leads to increased healthcare-seeking behavior. Some patients may therefore seek TCM treatment for related urinary symptoms. Due to limited clinical research evaluating the effects of TCM on IC/BPS, Hao-Hsiu Hung and colleagues conducted a nationwide population-based cohort study to investigate the relationship between TCM and mental disorders among these patients. The IC/BPS cohort and its matched non-IC/BPS comparison cohort were recruited from the National Health Insurance (NHI) Research Database between 2000 and 2011. Patients with the use of Chinese herbal medicine (CHM) granules or acupuncture over 90 days per year were enrolled as the TCM users. Multivariable Cox proportional hazards models were used to evaluate the hazard ratio (HR) of mental disorders related to interstitial cystitis. The incidence of mental disorders in the 2 cohorts was assessed with Kaplan-Meier curves. A total of 1123 patients with IC/BPS and 4492 matched non-IC/BPS subjects were included in this study. The IC/BPS cohort demonstrated higher incidence rate of mental disorders than the cohort without IC/BPS (adjusted HR: 2.21, 95% confidence interval [CI]: 1.73-2.81). There was no statistically significant difference in the risk of mental disorders between IC/BPS patients with and without CHM granules or acupuncture treatment (adjusted HR: 0.99, 95% CI: 0.58-1.68). Their results indicated that CHM and acupuncture showed insignificant efficacy in the prevention of mental disorders in IC/BPS patients.

HUNNER LESION

CLINICAL CHARACTERIZATION OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME IN WOMEN BASED ON THE PRESENCE OR ABSENCE OF HUNNER LESIONS AND GLOMERULATIONS

Daiji Watanabe, Yoshiyuki Akiyama, Aya Niimi, Akira Nomiya, Yuta Yamada, Yusuke Sato, Masaki Nakamura, Taketo Kawai, Daisuke Yamada, Motofumi Suzuki, Yasuhiko Igawa, Haruki Kume, Yukio Homma. *Low Urin Tract Symptoms*. 2020 Aug 23. doi: 10.1111/luts.12344. Online ahead of print. PMID: 32830459

The purpose of this study from Japan was to compare the clinical characteristics of three groups of female patients with interstitial cystitis/bladder pain syndrome (IC/BPS) classified according to the presence or absence of Hunner lesions (HL) and glomerulations. The clinical records of 100 female patients with IC/BPS who underwent their first bladder hydrodistension at our institution were retrospectively reviewed. They were divided into patients having (HL-IC; n = 57) or lacking (BPS; n = 43) HL. BPS patients were further classified as those with (29) and without (14) glomerulations. Among these three subtypes, demographics, comorbidities, symptom parameters including a visual analog scale for pain scores, O'Leary and Sant Symptom and Problem (OSSI/OSPI) Indices, frequency volume chart variables, and bladder capacity at hydrodistension were compared. The authors found that HL-IC patients were older and had higher OSSI/OSPI scores, greater daytime frequency and nocturia, reduced maximum and average voided volumes, and smaller bladder capacity at hydrodistension compared with BPS patients. Pain intensity and illness duration were comparable among the three groups. HL-

IC patients had autoimmune disorders as comorbidities more often but had psychiatric disorders and irritable bowel syndrome less often compared with BPS patients. No discernible differences in clinical characteristics of symptom severity and comorbid disorders were evident between BPS patients with and without glomerulations. They concluded that the presence of HL is associated with distinctive clinical characteristics, while glomerulations are not in female patients with IC/BPS. The presence of HL, but not glomerulations, is a robust phenotypic feature of IC/BPS in women.

CHANGES IN UROPLAKIN EXPRESSION IN THE UROTHELIUM OF PATIENTS WITH ULCERATIVE INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Cho KJ, Lee KS, Choi JB, Koh JS, Kim JC. *Investig Clin Urol.* 2020 May;61(3):304-309. doi: 10.4111/icu.2020.61.3.304. Epub 2020 Apr 20. PMID: 32377607

Cho and colleagues from Korea evaluated changes in the expression of uroplakin (UP) in the urothelium of patients with ulcerative interstitial cystitis/bladder pain syndrome (IC/BPS). Bladder samples were collected from 19 patients with ulcerative IC/BPS who were treated with augmentation ileocystoplasty and from 5 control patients. Frequency-volume charts, the pain visual analogue scale (VAS), and the O'Leary-Sant interstitial cystitis symptom index (ICSI) and problem index (ICPI) were used to evaluate the patients' symptoms preoperatively. The expression levels of UP-Ib and UP-III in the urothelium were compared between the IC/BPS patients and control patients. Sixteen women and three men with IC/BPS were evaluated. Their values for preoperative mean voiding frequency, number of nocturia episodes, and functional bladder capacity as recorded in frequency-volume charts were 21.1 ± 12.8 , 5.9 ± 4.2 , and 151.1 ± 62.7 mL, respectively. The mean pain VAS, ICSI, and ICPI scores were 8.4 ± 1.3 , 17.7 ± 2.2 , and 14.7 ± 1.8 , respectively. Immunofluorescence staining showed that UP-Ib and UP-III were localized in the urothelium. Upon Western blot analysis, the expression of UP-III was significantly increased in the IC/BPS group compared with the control group. However, expression of UP-Ib did not differ significantly between the IC/BPS and control groups. It was concluded that UP-III was significantly upregulated in patients with ulcerative IC/BPS. UP-III is a potential biomarker for the diagnosis of ulcerative IC/BPS.

BIOINFORMATICS APPROACH FOR IDENTIFYING NOVEL BIOMARKERS AND THEIR SIGNALING PATHWAYS INVOLVED IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME WITH HUNNER LESION

Subbroto Kumar Saha, Tak-Il Jeon, Soo Bin Jang, Se Jong Kim, Kyung Min Lim, Yu Jin Choi, Hyeong Gon Kim, Aram Kim, Ssang-Goo Cho. *J Clin Med.* 2020 Jun 21;9(6):E1935. doi: 10.3390/jcm9061935. PMID: 32575815.

The complexity of interstitial cystitis/bladder pain syndrome (IC/BPS) has led to considerable uncertainty in terms of diagnosis and prevalence of the condition. Here, the authors try to identify the IC/BPS-associated genes through an integrated analysis of Gene Expression Omnibus (GEO) datasets and confirm experimentally to predict the pathologic diagnosis of IC/BPS. Data mining analysis of GEO datasets (GSE621, GSE11783, GSE28242, and GSE57560) revealed a total of 53 (51 upregulated and two downregulated) common differentially expressed genes (DEGs) in IC/BPS. A protein-protein interaction (PPI) network was then constructed with the 53 common DEGs using Cytoscape v3.7.2, and subsequently, six hub genes (CD5, CD38, ITGAL, IL7R, KLRB1, and IL7R) were identified using cytoHubba v0.1 that were upregulated in IC/BPS. Enrichment analysis of common DEGs revealed that hematopoietic cell lineage, immune system, and T-cell receptor (TCR) signalling in naïve CD4+ T cell signalling pathways were prominently involved with the common 51 upregulated DEGs. The two common downregulated DEGs may enrich linoleic acid metabolism and synthesis of epoxy (EET) and dihydroxyeicosatrienoic acid (DHET) signalling pathways in IC/BPS. Moreover, they note that their RT-PCR data confirmed that the expression of the five hub genes (CD38, ITGAL, IL7R, KLRB1, and IL7R) was significantly augmented in IC/BPS patients' samples when compared with their normal counterparts. In this study, the authors systematically predict the significant biomarkers and possible signalling pathways involved in IC/BPS, confirming the differential expression of the hub genes in tissue samples from patients with IC/BPS. Thus, the hub genes might be used as potential diagnostic biomarkers of IC/BPS.

AN ADAPTIVE RANDOMIZED CLINICAL TRIAL IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME EVALUATING EFFICACY OF ASP3652 AND THE RELATIONSHIP BETWEEN DISEASE CHARACTERISTICS AND HUNNER'S LESIONS

Jos G A Houbiers, J W Olivier van Till, Mathilde Kaper, Yalcin Yavuz, Reynaldo V Martina, Dirk Cerneus, Joost Melis, Otto Stroosma, J Curtis Nickel, Phil M Hanno, Jørgen Nordling. *World J Urol.* 2020 Jul 30. doi: 10.1007/s00345-020-03372-z. Online ahead of print. PMID: 32734461

The primary purpose of this study was to evaluate the effect of the fatty acid amide hydrolase (FAAH) inhibitor ASP3652 on efficacy and safety in patients with Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS). The secondary purpose was to evaluate phenotyping based on Hunner's lesions (HL). In this randomized trial, adult

female patients with moderate/severe IC/BPS received 12 weeks of treatment with an oral dose of ASP3652 (50, 150, or 300 mg twice daily) or placebo. A Bayesian model was employed using accumulating data to adjust the randomization probability and to analyze the primary efficacy variable (change from baseline to end of treatment in Mean Daily Pain [MDP; range 0-10]). Study outcomes and patient characteristics of patients with and without HL (HL+ and HL-) were compared. In total, 287 patients were randomized. The 300 mg dose group (n = 97) showed the largest effect, i.e., a mean change from baseline to end of treatment of -1.73 in MDP. However, the mean difference from placebo was 0.02. The probability that this dose was better than placebo was 13.5%. Adverse event incidence was low and similar between study groups. HL+ patients were older and had more severe symptoms than HL-. An association was suggested in HL+ patients between changes in micturition frequency and MDP (R = 0.41 [95% CI 0.18, 0.63]), which was not observed in HL- (R = 0.04 [95% CI -0.16, 0.29]). It was concluded that ASP3652 was safe and well tolerated but did not show efficacy in IC/BPS. The observed differences between HL+ and HL- suggest that IC/BPS diagnosis and treatment may be approached differently in these two phenotypes.

[COMMENTS TO EDITORIAL BY J. CURTIS NICKEL. IT IS PREMATURE TO CATEGORIZE HUNNER LESION INTERSTITIAL CYSTITIS AS A DISTINCT DISEASE ENTITY. SCANDINAVIAN JOURNAL OF UROLOGY 2020, VOL. 54, NO. 2, 99-100; HTTPS://DOI.ORG/10.1080/21681805.2020.1744714.](https://doi.org/10.1080/21681805.2020.1744714)

Fall M, Nordling J, Cervigni M, Oliveira PD, Fariello J, Hanno P, Kabjörn-Gustafsson C, Logadottir Y, Meijlink J, Moldwin R, Nasta L, Quaghebeur J, Sairanen J, Taneja R, Tomoe H, Ueda T, Wennevik GE, Wyndaele JJ, Zaitcev A. Scand J Urol. 2020 Aug;54(4):355-356. doi: 10.1080/21681805.2020.1784269. Epub 2020 Jun 26. PMID: 32588705

[HUNNER LESION INTERSTITIAL CYSTITIS: THE BAD, THE GOOD, AND THE UNKNOWN](https://doi.org/10.1016/j.eururo.2020.04.067)

J Curtis Nickel, R Christopher Doiron. Editorial Eur Urol. 2020 Sep;78(3):e122-e124. doi: 10.1016/j.eururo.2020.04.067. Epub 2020 Jun 3. PMID: 32507337.

COCHRANE REVIEW

[INTERVENTIONS FOR TREATING PEOPLE WITH SYMPTOMS OF BLADDER PAIN SYNDROME: A NETWORK META-ANALYSIS](https://doi.org/10.1002/14651858.CD013325)

Mari Imamura, Neil W Scott, Sheila A Wallace, Joseph A Ogah, Abigail A Ford, Yann A Dubos, Miriam Brazzelli. Cochrane Database Syst Rev. 2020 Jul 30;7:CD013325. doi: 10.1002/14651858.CD013325.pub2. PMID: 32734597

Bladder pain syndrome (BPS), which includes the condition of interstitial cystitis, is a poorly understood clinical condition for which patients present with varying symptoms. Management of BPS is challenging for both patients and practitioners. At present, there is no universally accepted diagnosis and diverse causes have been proposed. This is reflected in wide-ranging treatment options, used alone or in combination, with limited evidence. This Cochrane network meta-analysis (NMA) simultaneously comparing multiple treatments may help to determine the best treatment options for patients with BPS. The aim was to conduct a network meta-analysis to assess the effects of interventions for treating people with symptoms of bladder pain syndrome (BPS). The authors searched the Cochrane Incontinence Specialised Register, which contains trials identified from the Cochrane Central Register of Controlled Trials (CENTRAL, in the Cochrane Library), MEDLINE, MEDLINE In-Process, MEDLINE Epub Ahead of Print, ClinicalTrials.gov, the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) and hand-searched journals and conference proceedings (searched 11 May 2018) and the reference lists of relevant articles. They conducted a further search on 5 June 2019, which yielded four small studies that were screened for eligibility but were not incorporated into the review. They included randomised controlled trials (RCTs) and quasi-RCTs of interventions for treating adults with BPS. All types of interventions (including conservative, pharmacological and surgical) were eligible. They assessed the risk of bias of included studies using Cochrane's 'Risk of bias' tool. Primary outcomes were the number of people cured or improved, pain, frequency and nocturia. For each outcome, random-effects NMA models were fitted using WinBUGS 1.4. They monitored median odds ratios (ORs) for binary outcomes and mean differences (MDs) for continuous outcomes with 95% credible intervals (CrIs). They compared results of the NMA with direct evidence from pairwise meta-analysis of head-to-head trials. They used the CINeMA tool to assess the certainty of evidence for selected treatment categories. They included 81 RCTs involving 4674 people with a median of 38 participants (range 10 to 369) per RCT. Most trials compared treatment against control; few trials compared two active treatments. There were 65 different active treatments, and some comparisons were informed by direct evidence from only one trial. To simplify, treatments were grouped into 31 treatment categories by mode of

action. Most studies were judged to have unclear or high risk of bias for most domains, particularly for selection and detection bias. Overall, the NMA suggested that six (proportion cured/improved), one (pain), one (frequency) and zero (nocturia) treatment categories were effective compared with control, but there was great uncertainty around estimates of effect. Due to the large number of intervention comparisons in this review, they focus on three interventions: antidepressants, pentosan polysulfate (PPS) and neuromuscular blockade. They selected these interventions on the basis that they are given 'strong recommendations' in the EAU Guidelines for management of BPS (EAU Guidelines 2019). They found very low-certainty evidence suggesting that antidepressants were associated with greater likelihood of cure or improvement compared with control (OR 5.91, 95% CrI 1.12 to 37.56), but it was uncertain whether they reduced pain (MD -1.27, 95% CrI -3.25 to 0.71; low-certainty evidence), daytime frequency (MD -2.41, 95% CrI -6.85 to 2.05; very low-certainty evidence) or nocturia (MD 0.01, 95% CrI -2.53 to 2.50; very low-certainty evidence). There was no evidence that PPS had improved cure/improvement rates (OR 0.14, 95% CrI 0.40 to 3.35; very low-certainty evidence) or reduced pain (MD 0.42, 95% CrI -1.04 to 1.91; low-certainty evidence), frequency (MD -0.37, 95% CrI -5.00 to 3.44; very low-certainty evidence) or nocturia (MD -1.20, 95% CrI -3.62 to 1.28; very low-certainty evidence). There was evidence that neuromuscular blockade resulted in greater cure or improvement (OR 5.80, 95% CrI 2.08 to 18.30) but no evidence that it improved pain (MD -0.33, 95% CrI -1.71 to 1.03), frequency (MD -0.91, 95% CrI -3.24, 1.29) or nocturia (MD -0.04, 95% CrI -1.35 to 1.27). The certainty of this evidence was always very low. They authors note that they are uncertain whether some treatments may be effective in treating patients with BPS because the certainty of evidence was generally low or very low. Data were available for a relatively large number of trials, but most had small sample sizes and effects of treatments often could not be estimated with precision. An NMA was successfully conducted, but limited numbers of small trials for each treatment category hampered their ability to fully exploit the advantages of this analysis. Larger, more focused trials are needed to improve the current evidence base.

"This article is based on a Cochrane Review published in the Cochrane Database of Systematic Reviews (CDSR) 2020, Issue 7, DOI: 10.1002/14651858.CD00 013325.pub2 (see www.cochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and the CDSR should be consulted for the most recent version of the review."

LOWER URINARY TRACT SYMPTOMS

RELATIONSHIP OF SYMPTOM SEVERITY AND BOTHER IN INDIVIDUALS SEEKING CARE FOR LOWER URINARY TRACT SYMPTOMS

Agochukwu-Mmonu N, Wiseman JB, Smith AR, Helmuth ME, Sarma AV, Cameron AP, Amundsen CL, Flynn KE, Cella D, Weinfurt KP, Kirkali Z, Clemens JQ. Eurourol Urodyn. 2020 Aug 6. doi: 10.1002/nau.24466. Online ahead of print. PMID: 32761962 DOI: 10.1002/nau.24466

Bother attributed to lower urinary tract symptoms (LUTS) drives care-seeking and treatment aggressiveness. The longitudinal relationship of LUTS severity and bother in a care-seeking cohort, however, is not well understood. This US study aimed to conduct a longitudinal evaluation of LUTS severity and bother and identify characteristics of patients with discordant LUTS bother relative to severity. Men and women with LUTS seeking care at six US tertiary care centers enrolled in the symptoms of lower urinary tract dysfunction research network study. Patients reporting at least one urinary symptom based on the LUTS Tool were prospectively enrolled from June 2015 to January 2017. Correlations were used to assess the relationship between LUTS severity and bother. Discordance scores (ie, the difference between bother and severity) were used to classify patients with high and low bother. Patients were classified as having high or low bother phenotypes if scores were one standard deviation above or below zero, respectively. Repeated measures multinomial logistic regression evaluated characteristics associated with high and low bother phenotypes. They found that LUTS severity and bother were at least moderately correlated for all symptom items and highly correlated for 13 out of 21 items. Correlations were highest for urgency, and lowest for daytime frequency and urinary incontinence. Odds of being in high bother phenotype were lowest at 3 and 12 months (3 months vs baseline odds ratio [OR] = 0.71, 95% confidence interval [CI] = 0.54-0.94; 12 months vs baseline OR = 0.66, 95% CI = 0.48-0.91), and highest for those who endorsed all urgency questions (OR = 3.65, 95% CI = 2.17-6.13). Odds of being in the low bother phenotype were lowest for patients who endorsed all urgency items (OR = 0.33, 95% CI = 0.26-0.42), and all frequency items (OR = 0.68, 95% CI = 0.53-0.88). It was concluded that LUTS severity and bother correlate highly and measurement of both in clinical practice is likely redundant. There are patient factors associated with discordance which may justify additional evaluation.

WHAT DO WE REALLY KNOW ABOUT THE ROLE OF CAFFEINE ON URINARY TRACT SYMPTOMS? A SCOPING REVIEW ON CAFFEINE CONSUMPTION AND LOWER URINARY TRACT SYMPTOMS IN ADULTS

Mélanie Le Berre, Nancy Presse, Mélanie Morin, Maryse Larouche, Lysanne Campeau, Yu Xin Hu, Isabelle Reid, Chantale Dumoulin. Neurourol Urodyn. 2020 Jun;39(5):1217-1233. doi: 10.1002/nau.24344. Epub 2020 Apr 9. PMID: 32270903.

The purpose of this scoping review was to map out the existing literature on caffeine intake and lower urinary tract symptoms (LUTS) in adults. In this scoping review, the authors searched for all studies available until June 2019 in MEDLINE, Embase, CINAHL, Cochrane Central Register, PsycINFO, LILACS, LiSSa, Web of Science, and Joanna Briggs Institute electronic databases, in addition to a hand search of the bibliographies of all relevant articles and a grey literature search. Both intervention studies on the effects of caffeine reduction in adults with LUTS and observational studies on the association between caffeine intake and LUTS-related outcomes in adults were included and assessed for methodological quality by two independent reviewers. Fourteen intervention and 12 observational studies were included. Overall, there was a decrease in urgency episodes (level of evidence 2, grade of recommendation B) and nocturnal enuresis episodes (4, C) with caffeine reduction. Observational studies reported an unclear association between caffeine intake and LUTS-related outcomes. Most importantly, this present review highlighted high heterogeneity in the studied populations, caffeine measures, and reported outcomes. There was also unknown or high risk of bias in most identified studies. Caffeine reduction appears to reduce LUTS. Future studies on caffeine reduction interventions should target populations with urgency and urge urinary incontinence, which show the most promising results, and include valid and reliable measures of caffeine intake and LUTS. Finally, future studies should also use reporting guidelines to ensure lower risk of bias.

FEMALE LOWER URINARY TRACT SYMPTOM PREVENTION AND TREATMENT STRATEGIES ON SOCIAL MEDIA: MIXED CORRELATION WITH EVIDENCE

Claire Burton, Gabriela Gonzalez, Kristina Vaculik, Carine Khalil, Yuliya Zektser, Corey Arnold, Christopher V Almario, Brennan M R Spiegel, Jennifer T Anger. Urology. 2020 Jul 13;S0090-4295(20)30821-9. doi: 10.1016/j.urology.2020.06.056. Online ahead of print. PMID: 32673678.

This study evaluated the level of evidence behind recommendations on social media for disease prevention in five lower urinary tract symptoms. The authors conducted a digital analysis of anonymous online posts on social media sites collected by a social media data mining service. One thousand posts about pelvic organ prolapse (POP), stress urinary incontinence (SUI), overactive bladder (OAB), urinary tract infection (UTI), and interstitial cystitis / bladder pain syndrome (IC/BPS) were randomly selected. They analyzed these posts for recommendations regarding the prevention and treatment of these diseases, which were then compared to recommendations in available clinical guidelines and assessed for level of evidence. A total of 158/1000 posts contained 239 prevention strategies. For POP there were 41 strategies identified, 25 (61%) of which had no evidence. For UTI 14/58 (29%) had no evidence, including recommendations for dietary modifications and urinary alkalization. For OAB 8/28 (29%) had level 4 or no evidence. For SUI, 12/34 (36%) of prevention strategies had no evidence, such as laser rejuvenation and bladder training. IC had the highest number of prevention strategies, and most were low or non-evidence based (70/79, 89%). Prevention and treatment strategies are common in online discussions of pelvic floor disorders, but at least one third of these recommendations have no evidential support. There is a role for further online education and social media engagement by health care specialists to promote evidence-based practices.

MARIJUANA, LOWER URINARY TRACT SYMPTOMS, AND PAIN IN THE UROLOGIC PATIENT

Minh N Pham, Matthew T Hudnall, Robert B Nadler. Review Urology. 2020 May;139:8-13. doi: 10.1016/j.urology.2020.01.029. Epub 2020 Feb 4. PMID: 32027882

The purpose of this study was to describe marijuana's clinical role for urologic symptoms. Studies related to marijuana, voiding dysfunction, lower urinary tract symptoms (LUTS), and pain through January 2019 from PubMed were evaluated for relevance and quality. Forty-eight studies were reviewed. Cannabinoids have mixed efficacy for neurogenic LUTS and little evidence for non-neurogenic LUTS, chronic non-cancer-related and perioperative pain. For cancer-related pain, high-level studies demonstrate cannabinoids are well-tolerated with unclear benefit. Cannabinoids appear well-tolerated in the short-term, but their efficacy and long-term impact is unproven and unknown in urologic discomfort. Cannabinoids for urologic symptoms should be further explored with well-designed randomized controlled trials.

USE OF BOTULINUM TOXIN IN THE GENITOURINARY SYSTEM

Michael B Chancellor, Christopher P Smith. Handb Exp Pharmacol. 2020 Jun 20. doi: 10.1007/164_2019_308. Online ahead of print. PMID: 32562059.

Botulinum toxin injection has been widely accepted by the urology and urogynecology medical communities as a safe and effective treatment for refractory urinary incontinence. There are two approved genitourinary indications for botulinum toxin. OnabotulinumtoxinA (onaBoNTA) 200 U for the treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) in adults who have an inadequate response to or are intolerant of an anticholinergic medication. In addition, onaBoNTA 100 U is used for the treatment of overactive bladder with symptoms of urinary incontinence, urgency, and frequency, in adult patients who have an inadequate response to or are intolerant of an anticholinergic medication. The authors discuss the application of botulinum toxin for genitourinary indications with a focus on bladder injection and on potential use of BoNT use in the prostate and pelvic floor.

KETAMINE CYSTITIS

EFFICACY OF CYSTECTASIA IN THE TREATMENT OF KETAMINE-INDUCED BLADDER CONTRACTURE

Xue-Song Yang, Zheng Chen, Jian-Li Duan, Bin Pan, Xiao-Ping Qin, Bin Lei, Yang-Bai Lu, Yu-Tong Li, Yun Luo, Xiao-Long Xu, Cai-Yong Lai, Yu-Min Zhuo. *Transl Androl Urol.* 2020 Jun;9(3):1244-1251. doi: 10.21037/tau.2020.04.01. PMID: 32676407.

The treatment of ketamine-induced bladder contractures remains poorly studied. The authors from China therefore evaluated the efficacy of cystectomy with a sodium hyaluronate balanced solution in this kind of bladder contracture. Eighteen patients presenting with ketamine-induced bladder contracture between July 2010 and February 2018 were selected and analysed. Ketamine was discontinued in all patients, who were then treated with weekly cystectomy (0.09% sodium hyaluronate balanced solution) 3 times. The volume of the first perfusion was twice the preoperatively measured bladder capacity, and the volume of the subsequent two perfusions was increased by 100 mL each time. The Pelvic Pain and Urgency/Frequency (PUF) symptom score, O'Leary-Sant Interstitial Cystitis (IC) Symptom Index (ICSI), IC Problem Index (ICPI), Quality of Life (QOL) score, and bladder capacity were recorded before surgery and 3 and 12 months after the 3rd expansion. No significant complications were observed during the 3 expansions. Fourteen patients completed the full follow-up schedule. Preoperatively and at the 3- and 12-month follow-up evaluations performed after the 3rd expansion, the PUF symptom scores were 20.4±3.6, 11.5±3.1, and 13.2±3.3, respectively; the mean ICSI was 13.6±2.8, 7.7±2.3, and 8.2±2.5, respectively; the mean ICPI was 10.6±2.6, 7.3±2.1, and 7.7±2.5, respectively; and the mean QOL scores were 6.0±0, 2.1±0.5, and 2.7±0.8, respectively; and the mean bladder catheter volume was 83±27, 234±56, and 228±52 mL, respectively. There were significant differences between all preoperative and postoperative values. Cystectomy with a sodium hyaluronate balanced solution is an effective treatment modality for ketamine-induced bladder contracture.

PENTOSAN POLYSULFATE-ASSOCIATED MACULAR DISEASE

RETINAL TOXICITY IN A PATIENT ON PENTOSAN POLYSULFATE SODIUM

Maxwell J Wingelaar, Joseph J Raevs, Karina A Conlin, Kimberly E Stepien. *Urology.* 2020 Jul;141:e41-e42. doi: 10.1016/j.urology.2020.04.006. Epub 2020 Apr 17. PMID: 32305545.

Pentosan Polysulfate Sodium (PPS) is commonly used in the treatment of interstitial cystitis/bladder pain syndrome. Recently there have been reported cases of retinal toxicity associated with long-term PPS use. The authors present a case of a 42-year-old female taking PPS for the last 10 years who was found to have signs of retinal toxicity but was completely asymptomatic. PPS was discontinued after these retinal findings were discovered.

PENTOSAN POLYSULFATE SODIUM-INDUCED PIGMENTARY MACULOPATHY WITH NON-LEAKING CYSTOID MACULAR EDEMA SUCCESSFULLY TREATED WITH ANTI-VEGF THERAPY

Elianne De Larocheillère, Serge Bourgault. *Retin Cases Brief Rep.* 2020 Jun 5. doi: 10.1097/ICB.0000000000001013. Online ahead of print. PMID: 32541441.

The authors report a case of non-leaking cystoid macular edema (CME) associated with pentosan polysulfate sodium (PPS)-induced pigmentary maculopathy. Multimodal imaging, including optical coherence tomography, fundus photography, autofluorescence and fluorescein angiography, was used to substantiate their diagnosis, further characterize the CME showed by their patient and to monitor the response to treatment. A 59-year-old woman was referred for decreased visual acuity and bilateral macular edema. She had been treated for interstitial cystitis with PPS for 10 years. Multimodal imaging showed the characteristic features of PPS-induced

pigmentary maculopathy. Moreover, fluorescein angiogram showed non-leaking CME in both eyes. She was treated successfully with intravitreal injections of bevacizumab. The authors believe that this report is the first to demonstrate that PPS-associated CME can be non-leaking on fluorescein angiography and responds well to intravitreal anti-VEGF injections.

DISEASE COURSE IN PATIENTS WITH PENTOSAN POLYSULFATE SODIUM-ASSOCIATED MACULOPATHY AFTER DRUG CESSATION

Rachel Shah, Joseph M Simonett, Riley J Lyons, Rajesh C Rao, Mark E Pennesi, Nieraj Jain. JAMA Ophthalmol. 2020 Jul 9;e202349. doi: 10.1001/jamaophthalmol.2020.2349. Online ahead of print. PMID: 32644147.

Recent studies have linked a vision-threatening maculopathy with long-term use of pentosan polysulfate sodium (PPS). The purpose of this study was to evaluate the disease course in PPS-associated maculopathy after drug cessation. In this retrospective case series, patients diagnosed with PPS-associated maculopathy with at least 6 months of follow-up after drug cessation who were treated at the Emory Eye Center, Atlanta, Georgia, or the Casey Eye Institute, Portland, Oregon, were included. Data were collected from April 2014 through November 2019. Change in visual acuity and retinal imaging characteristics over time. Of the 11 included patients, all were female, and the median (interquartile range [IQR]) age was 53 (44-63) years. Participants had a baseline visit at a median (IQR) of 2 (0-4) months after drug cessation and were subsequently observed for a median (IQR) of 12 (8-26) months. The median (IQR) cumulative PPS exposure was 1.97 (1.55-2.18) kg. No eyes exhibited a demonstrable improvement in disease after discontinuing PPS. A total of 9 of 11 patients (82%) reported worsening visual symptoms at the final visit. The mean (SD) logMAR visual acuity was 0.14 (0.23) and 0.14 (0.34) at the baseline and final visit, respectively. Visual acuity improved by 2 or more Snellen lines in 1 eye (5%) and declined by 2 or more Snellen lines in 2 eyes of 1 patient (9%). There was evolution in the pattern of fundus autofluorescence changes and/or optical coherence tomography findings in all eyes. A total of 17 eyes (77%) exhibited expansion of the area of involved tissue. A total of 7 eyes (32%) had macular retinal pigment epithelium atrophy at the baseline visit, and atrophy enlarged after discontinuation of PPS in all 7 eyes, with a median (IQR) growth rate of 0.32 (0.13-0.38) mm per year. These retrospective data among 11 patients suggest PPS-associated maculopathy continues to evolve after drug cessation for at least 10 years. In some cases, progressive retinal pigment epithelium atrophy encroaches on the foveal center and thus may pose a long-term threat to central vision.

PENTOSAN POLYSULFATE MACULOPATHY-PRESCRIBERS SHOULD BE AWARE

Imran H Yusuf, Peter Charbel Issa, Andrew J Lotery. JAMA Ophthalmol. 2020 Jul 9. doi: 10.1001/jamaophthalmol.2020.2364. Online ahead of print. PMID: 32644128

In this issue of JAMA Ophthalmology, Shah and coauthors report progression of pentosan polysulfate (PPS) maculopathy after drug cessation in a series of 11 patients over a median follow-up interval of 11.5 months. Across this short follow-up period, 9 patients reported subjective worsening of visual symptoms. Fundus autofluorescence imaging identified an expansion of the affected area in 17 of 22 eyes and an enlargement of the area of retinal pigment epithelial (RPE) atrophy in all 7 eyes that exhibited RPE atrophy at baseline. These novel observations illuminate an important and concerning facet of the natural history of PPS maculopathy.

IC/BPS AND ENDOMETRIOSIS

NON-BLADDER CENTRIC INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PHENOTYPE IS SIGNIFICANTLY ASSOCIATED WITH CO-OCCURRING ENDOMETRIOSIS

Tyler L Overholt, Robert J Evans, Bruce A Lessey, Catherine A Matthews, Katherine N Hines, Gopal Badlani, Stephen J Walker. Can J Urol. 2020 Jun;27(3):10257-10262. PMID: 32544050.

Interstitial cystitis/bladder pain syndrome (IC/BPS) and endometriosis are coexistent diagnoses in 48%-65% of women with chronic pelvic pain (CPP), suggesting that dual screening may be warranted. To further investigate the clinical relationship and risk factors between these two conditions, the authors performed a retrospective review of their large IC/BPS patient data registry. They evaluated IC/BPS patients who were prospectively enrolled into their registry who completed validated questionnaires and underwent therapeutic hydrodistension, during which anesthetic bladder capacity (BC) and Hunner's lesion (HL) status were recorded. Demographic/medical history were reviewed. IC/BPS patients with co-occurring endometriosis diagnosis versus those without were compared using descriptive statistics as well as multivariate regression analyses to determine predictors of co-occurring disease. Of 431 IC/BPS participants, 82 (19%) were also diagnosed with endometriosis. These women were significantly younger, had increased prevalence of non-low BC (> 400 cc), and decreased prevalence of HL ($p < 0.05$). Patients with co-occurring endometriosis also had increased

prevalence of irritable bowel syndrome (IBS), CPP, fibromyalgia, and vulvodynia ($p < 0.05$). On multivariate analysis, non-low BC (OR 4.53, CI 1.004-20.42, $p = 0.049$), CPP (OR 1.84, CI 1.04-3.24, $p = 0.04$), and fibromyalgia (OR 1.80, CI 1.03-3.14, $p < 0.04$) were significantly associated with a diagnosis of endometriosis. It was concluded that patients with IC/BPS and co-occurring endometriosis were significantly more likely to carry a non-bladder centric IC/BPS phenotype as well as several comorbid, systemic pain diagnoses. This study characterizes features of a target IC/BPS phenotype that could potentially benefit from endometriosis and systemic pain syndrome screening.

CHRONIC PELVIC PAIN

[EVALUATING DISABILITY-RELATED QUALITY OF LIFE IN WOMEN WITH CHRONIC PELVIC PAIN](#)

Alice L Ye, William Adams, Lauren C Westbay, Colleen M Fitzgerald. *Female Pelvic Med Reconstr Surg.* 2019 Aug 15. doi: 10.1097/SPV.0000000000000771. Online ahead of print. PMID: 31425373.

The primary aim of this study was to describe quality of life (QOL) in women with chronic pelvic pain using the Pain Disability Index (PDI). A secondary goal was to assess the measurement properties and validity of the PDI for this population. This study was a cross-sectional retrospective chart review. In the setting of an outpatient female pelvic pain clinic, the authors included data from an initial evaluation of patients 16 years and older with chronic pelvic pain (N = 317) from 2012 to 2017. Quality of life was measured using the PDI and previously validated measures for depression and anxiety. The mean PDI score across all patients was similar to previously reported means for similar chronic pain populations. Patients experienced the most disability in their sexual activities. The most common cause of chronic pelvic pain was pelvic floor myofascial pain. Common diagnostic categories covered gynecologic, urologic, gastrointestinal, musculoskeletal, and neurological causes. The PDI was unable to discriminate between diagnoses. On average, patients qualified for mild depression and anxiety diagnoses. Results from a confirmatory factor analysis revealed the original factor structure for the PDI fits this population. The PDI shows promise as a questionnaire for QOL and could be a valuable clinician tool for tracking QOL in the chronic pelvic pain population. Additional research should be focused on assessing its ability to measure minimum clinically significant change over time.

[LAPAROSCOPIC PUDENDAL NEUROLYSIS : A VIDEO VIGNETTE](#)

Enrique Moncada Iribarren, Vincenzo Vigorita, Alberto San Ildefonso Pereira, Raquel Sánchez Santos. *Colorectal Dis.* 2020 Aug 27. doi: 10.1111/codi.15326. Online ahead of print. PMID: 32852135.

Pudendal Neuralgia is a chronic neuropathic pelvic pain that is disabling and often misdiagnosed. Its treatment includes analgesics, neuromodulator drugs and nerve block, nevertheless, the surgical decompression is an effective and safe treatment when conservative treatment fails. The Pudendal Nerve release by laparoscopic approach, has proven to be a minimally invasive, safe and a feasible technique that allows an excellent visualization of all the neurological structures of the presacral obturator region as well as an accurate dissection of the pudendal nerve.

[PAIN SYNDROMES SECONDARY TO CLUNEAL NERVE ENTRAPMENT](#)

Jay Karri, Mani Singh, Vwaire Orhurhu, Mihir Joshi, Alaa Abd-Elsayed. *Curr Pain Headache Rep.* 2020 Aug 21;24(10):61. doi: 10.1007/s11916-020-00891-7. PMID: 32821979.

The purpose of this review is to provide an overview of the cluneal nerves, present a summary of pain syndromes secondary to clunealgia, and evaluate current literature for diagnostic and treatment modalities. Multiple trials and studies have reported success with numerous modalities ranging from nerve blocks, neuroablation, and even peripheral neuromodulation with varying degrees of clinical benefit. Cluneal nerve entrapment or chronic impingement can cause buttock pain or referred pain to nearby areas including the lower back, pelvic area, or even the lower extremities. Clunealgias and associated pain syndromes can often be challenging to diagnose and differentiate. An appreciation of the pathophysiology of clunealgias can assist with patient selection for interventional pain strategies targeted towards the cluneal nerves, including nerve blocks, neuroablation, and peripheral neuromodulation. More research is needed to better delineate the efficacy of these procedures for clunealgias.

FIBROMYALGIA

[THE FIBROMYALGIA BLADDER INDEX IN 100 CONSECUTIVE WOMEN WITH FIBROMYALGIA](#)

Nouran Hamed, Mohamad Ali Rida, Imad Uthman, Lina El Taha, Mariam Assad, Elie Mikhael, Tony Bazi. *Int Urogynecol J.* 2020 Jan 9. doi: 10.1007/s00192-019-04199-y. Online ahead of print. PMID: 31919557.

The Fibromyalgia Bladder Index (FBI) is a validated instrument to quantify bothersome bladder symptoms specifically in women with fibromyalgia syndrome (FMS). The FBI includes two sub-scales: one addressing urinary urgency and bladder pain (UP), the other addressing urinary frequency and nocturia (FN). The objectives of this study are to evaluate the FBI in a cohort of patients with FMS, to correlate it with certain characteristics in this cohort, and to compare it with controls. The authors performed a case-control study of 100 women with FMS and 155 controls. Demographic data, comorbidities, and other characteristics were registered. Comparison between FBI scores of participants with and without FMS, as well as correlation of FBI scores with the characteristics of FMS patients, were undertaken using independent two-sample t test for continuous outcomes and Pearson's Chi-squared test for categorical outcomes. The mean UP subscale score of the FBI was significantly higher in the FMS group compared with the controls. The mean FN subscale score was significantly higher in the FMS group (9.93 ± 5.37) compared with the controls. FMS patients diagnosed >3 years ago had a higher UP subscale score and a higher FN subscale score compared with FMS patients diagnosed <3 years ago. Menopause and parity significantly increased the FBI scores. Smoking and a history of depression did not significantly affect any of the FBI subscale scores in the FMS group. It was concluded that women with FMS suffer from bothersome bladder symptoms that can be readily identified and quantified.

"NO ONE WANTS TO LOOK AFTER THE FIBRO PATIENT". UNDERSTANDING MODELS, AND PATIENT PERSPECTIVES, OF CARE FOR FIBROMYALGIA: REVIEWS OF CURRENT EVIDENCE.

Stefanie Doebel, Gary J Macfarlane, Rosemary J Hollick. Pain. 2020 Aug;161(8):1716-1725. doi: 10.1097/j.pain.0000000000001870. PMID: 32701832

Fibromyalgia is a common and complex long-term pain condition. Despite advancements in our understanding and treatment of fibromyalgia, patients report patchy health care provision and frustrating journeys through the health care system. To inform how best to deliver care, the authors undertook 2 narrative reviews examining existing evidence on (1) models of care for fibromyalgia and (2) patients' experiences, preferences, and unmet needs regarding their health care. Seven databases were systematically searched. Quantitative data was narratively synthesised and qualitative data thematically analysed. No evidence-based model of care covering the patient journey through the entire health care system was identified. Limited evidence suggests no clear benefit for ongoing care in secondary care settings. Patients with fibromyalgia report difficult interactions with the health care system that might equally be expressed by those with other long-term conditions, such as inconsistent and poorly coordinated care. However, they also face unique problems; fibromyalgia was often not viewed as a real condition, resulting in difficult encounters with health care staff, in particular not feeling believed or listened to. Significant delays in diagnosis were commonplace. Positive care experiences such as being listened to and shared decision-making made patients feeling better informed, well supported, and more satisfied. There is little evidence to inform how best to organise health care for patients with fibromyalgia and ensure care is delivered in a coordinated and consistent way. These findings provide a strong rationale for developing a new model of care for fibromyalgia.

VULVODYNIA

VULVODYNIA

Sophie Bergeron , Barbara D Reed , Ursula Wesselmann , Nina Bohm-Starke. Nat Rev Dis Primers. 2020 Apr 30;6(1):36. doi: 10.1038/s41572-020-0164-2. PMID: 32355269

Vulvodynia is a condition that occurs in 8-10% of women of all ages and is characterized by pain at the vulva that is present during sexual and/or non-sexual situations. Diagnosis is established through careful medical history and pelvic examination, including the cotton-swab test. The onset and maintenance of vulvodynia involves a complex interplay of peripheral and central pain mechanisms, pelvic floor muscle and autonomic dysfunction, anxiety, depression and childhood maltreatment as well as cognitive-affective, behavioural and interpersonal factors. Given the absence of empirically supported treatment guidelines, a stepwise approach of pelvic floor physical therapy and cognitive behavioural therapy as well as medical management is suggested, with surgery as the last option. Vulvodynia has a negative effect on the quality of life of women and their partners, and imposes a profound personal and societal economic burden. In addition, women with vulvodynia are more likely to report other chronic pain conditions, which further alters their quality of life. Future efforts should aim to increase girls', women's and healthcare professionals' education and awareness of vulvodynia, phenotype different subgroups of women based on biopsychosocial characteristics among more diverse samples, conduct longitudinal studies and improve clinical trial designs.

THE INTERNATIONAL CLASSIFICATION OF DISEASES, 11TH REVISION: A STEP-BACK FOR WOMEN WITH VULVODYNIA?

Gianluigi Radici, Mario Preti, Pedro Vieira-Baptista, Colleen K Stockdale, Jacob Bornstein. J Low Genit Tract Dis. 2020 Jul;24(3):332-333. PMID: 32068619

The aim of this study was to compare the International Classification of Diseases, 11th revision, (ICD-11) with current terminology of vulvodynia, approved by a broad-based consensus of the International Society for the Study of Vulvovaginal Disease (ISSVD), the International Society for the Study of Women Sexual Health (ISSWSH), and the International Pelvic Pain Society (IPPS). The diagnostic criteria and descriptions of vulvodynia as well as the definition and classification of chronic pain in ICD-11 were reviewed and compared with the Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia, endorsed in 2015 by the ISSVD, ISSWSH, and IPPS. Diagnostic criteria and descriptors of vulvodynia in the ICD-11 are outdated. Moreover, vulvodynia is not identified among chronic pain diagnoses, despite fulfilling the diagnostic criteria of chronic primary pain. Specifically, vulvodynia is a vulvar pain of at least 3-month duration, which is associated with significant emotional distress and functional disability and is not better accounted for by another specific condition. It was concluded that the ICD-11 is not aligned with current vulvodynia diagnostic criteria and terminology, approved by the ISSVD, ISSWSH, and IPPS. Collaboration among the International Association for the Study of Pain Task Force on Classification of Chronic Pain, ICD team, ISSVD, ISSWSH, and IPPS is needed to harmonize terminologies, codes, and clinical approach regarding vulvar pain and vulvodynia classification.

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