

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 49, October 2018

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:

- Upcoming ESSIC Meeting 2018
- German Interstitial Cystitis Guideline
- Global Interstitial Cystitis Bladder Pain Syndrome Society of India 3rd Annual Meeting + Clinical Guideline
- Dutch IC Support Group celebrates 20th anniversary
- Patients on oral PPS may need regular eye checks
- EAU ELUTS 2018 included IC/BPS
- Review of ICS 2018
- Publications
- Calendar of Upcoming Events
- Research Update
- Donations & Sponsoring

UPCOMING ESSIC MEETING - 29 NOVEMBER-1 DECEMBER 2018, FLORENCE, ITALY

The ESSIC 2018 Annual Meeting will be held at the Auditorium al Duomo Conference Centre located in the historic Via de' Cerretani, a few steps from the central railway station and the Duomo cathedral in Florence, Italy. Address: Via de' Cerretani, 54/R, 50123 Florence. Meeting Chair is Professor Giulio del Popolo, ESSIC Coordinator Professor Mauro Cervigni. Save the date in your diary as this is an important meeting on the IC/BPS calendar and there is much to be discussed. For registration and further information, go to www.essicmeeting.eu

GERMAN INTERSTITIAL CYSTITIS GUIDELINE: DIAGNOSTIK UND THERAPIE DER INTERSTITIELLEN CYSTITIS (IC/BPS)

An immense amount of work by a multidisciplinary team, with the German IC support group ICA Deutschland playing a leading role, has produced a new German Guideline on IC/BPS. The present version is in German but it is hoped to produce an English language version also. For those with a knowledge of German, the guideline can be found at: https://www.awmf.org/uploads/tx_szleitlinien/043-050l_S2k_Diagnostik_Therapie_Interstitielle_Cystitis_2018-10.pdf

GLOBAL INTERSTITIAL CYSTITIS BLADDER PAIN SYNDROME SOCIETY (GIBS) OF INDIA 3RD ANNUAL MEETING + CLINICAL GUIDELINE

The Global Interstitial Cystitis Bladder Pain Syndrome Society (GIBS) of India (<https://gibsociety.com/>) held a successful 3rd Annual Scientific Conference on IC/BPS, held on 1-2 September 2018, at Hotel Orchid, Mumbai, India. Many congratulations are due to the organizing chairman Dr Rajesh Taneja and organizing secretary Dr Sanjay Pandey. Patients were fully involved and IC patient advocate Balaka Basu also gave a wonderful presentation. A review of the meeting can be found at: <https://gibsociety.com/wp-content/uploads/2018/09/Post-Event-Report.pdf>. The Indian clinical guideline can be found at: <https://gibsociety.com/wp-content/uploads/2017/11/GIBS-Guidelines.pdf>
The next GIBS conference is to be held 24-25 August 2019 in Mumbai.

DUTCH INTERSTITIAL CYSTITIS SUPPORT GROUP (ICP) CELEBRATES 20 YEARS

While the Dutch IC patient movement began 25 years as just 2 patients in a sitting room, the patient association ICP was set up 20 years ago. Every reason for a celebration! Chair Hilde Andriess and her committee organized a great anniversary meeting in Amersfoort on Saturday 8 October with interviews with a panel of guests including first ICP chair and co-founder Jane Meijlink, urologist Dr Erik Arendsen, gynaecologist Dr Bram ter Harmsel and pathologist Dr Roel Veldhuizen, against a background of lighthearted music and serious discussions. Congratulations ICP!

PATIENTS ON ORAL PENTOSAN POLYSULFATE SODIUM (PPS) MAY NEED TO HAVE REGULAR EYE CHECKS.

A study by ophthalmologists revealed a possible association between pigmentary maculopathy and long-term use of oral PPS. While further studies are needed, it may be advisable for patients to be alert to this possibility and to seek a regular eye-check, particularly if they are experiencing any vision problems.

(See: Pearce WA, Chen R, Jain N. Pigmentary maculopathy associated with chronic exposure to pentosan polysulfate sodium. *Ophthalmology*. 2018 Nov;125(11):1793-1802.)

EUROPEAN ASSOCIATION OF UROLOGY (EAU) ELUTS 2018 PROGRAMME INCLUDES IC/BPS

A concerning development in the past few years has been that too few urology trainees are interested in specialising in IC/BPS and chronic urogenital pain, finding e.g. oncology a more attractive field. If steps are not taken now, there will be a massive shortage of urologists to treat IC and bladder pain conditions in the years ahead. There is also an urgent need for expert training in diagnosing different kinds of Hunner lesion. The EAU made a start this year with its newly restructured ELUTS18 which included IC/BPS.

IC/BPS patients in many countries around the world are already facing great difficulty in finding urologists or urogynaecologists willing or able to diagnose and treat them. This trend needs to be reversed before it is too late.

REVIEW OF THE INTERNATIONAL CONTINENCE SOCIETY ANNUAL MEETING, 28-31 AUGUST 2018 PHILADELPHIA

The International Continence Society (ICS) annual scientific meeting attracts a multidisciplinary group including urologists, gynaecologists, neurologists, nurses, physiotherapists, basic scientists and physiologists as well as patient advocates from around the world. This year's meeting was held in Philadelphia, renowned as the birthplace of the United States of America. Topics this year included pathophysiology, diagnosis and treatment in the fields of urinary incontinence and lower urinary tract and pelvic floor dysfunction (e.g. interstitial cystitis/bladder pain syndrome, prolapse, overactive and underactive bladder). There was also a focus this year on nocturia (urination at night) and tremendous interest in neurological aspects and current research in this field. The fact that the meeting was held in the USA provided the possibility of hearing more about the work of the National Institutes of Health in a Round Table session on Innovation in LUTS Clinical Research Networks.

In recent years we have seen a steady increase in interest in chronic pelvic and bladder pain at ICS. This has been a very welcome development for everyone in the IC/BPS field. The recently established "ICS Institute", which comprises "Schools" to serve the e-learning needs of members and provide training in designated centres of excellence, also includes a School of Pelvic Pain, the Director of which is Professor Kristene Whitmore. This interest is now also reflected in the number of abstracts submitted for the conference related to IC/BPS, in the scientific programme as a whole and in the fact that top doctors and researchers in our field from around the world attended the meeting in Philadelphia. This year's programme included two podium oral abstract sessions dedicated to IC/BPS, a workshop on intravesical treatment, another workshop on chronic pelvic pain and sexual dysfunction and much more besides.

ICS is well-known for its standardisation of terminology and definitions. However, doctors and researchers around the world are still using a variety of different terms/definitions, and this particularly applies in our field of IC/BPS/PBS/HSB! It was stressed that we need common terminology and definitions, using the same terms to mean the same thing. This will also promote better international cooperation, research and data exchange. But at a patient level in today's bureaucratic, electronic healthcare world, it is also vital for the right diagnosis, right treatment and reimbursement of that treatment. A major problem in our IC/BPS field is that medical societies have omitted to address this widespread non-reimbursement issue. For the sake of the patients, action is needed.

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PUBLICATIONS

REVIEW ICICJ 2018

A review of the 4TH International Consultation on Interstitial Cystitis Japan (ICICJ) and the annual meeting of the Society of Interstitial Cystitis of Japan (SICJ), held 17-18 April 2018, Kyoto, Japan is available on the IPBF website: http://www.painful-bladder.org/pdf/2018_ICICJ4_Kyoto.pdf

BOOK ON INTERSTITIAL CYSTITIS, INDIA

Author: Dr Rajesh Taneja, New Delhi, India
Contributing authors: Prof. Jorgen Nordling, Prof. Philip Hanno
Published 2014 by Kontentworx
ISBN: 978-93-83988-00-6
contact@kontentworx.com

An IC book for India comprising a history of IC, definitions and nomenclature, pathology and pathogenesis, clinical presentation, evaluation and diagnosis, management, future trends and directions.

SJÖGREN'S SYNDROME: INFORMATION FOR PATIENTS AND PROFESSIONALS

Stay updated with Sjögren's syndrome and associated disorders, including its relationship with disorders of the lower urinary tract such as IC/BPS, with Dr Joop P. van de Merwe's continually evolving online book: http://www.painful-bladder.org/pbs_ic_ass_dis.html. Available in two versions: English and Dutch.

CALENDAR OF UPCOMING EVENTS

ESSIC ANNUAL MEETING 2018

29 November – 1 December
Auditorium al Duomo, Florence, Italy.
<https://www.essicmeeting.eu/>

THE THIRD ANNUAL MEETING OF THE SOCIETY FOR PELVIC RESEARCH 2018

December 1-2, 2018 (Main Meeting), November 30, 2018 (Trainee Workshop)
Hilton New Orleans/St. Charles Avenue, 333 St. Charles Avenue, New Orleans, LA, USA
<https://www.pelvicresearch.com/spr-2018-meeting.html>

SUFU 2019 WINTER MEETING

February 26 – March 2, 2019
InterContinental Miami Hotel
Miami, Florida
<https://sufu.org.com/meetings/upcoming-sufu/meeting-information.aspx>

EAU 2019

15-19 March 2019 Barcelona, Spain
<https://eaucongress.uroweb.org/>

AUA 2019

3-6 May, Chicago, USA
<http://www.aa2019.org/>

Global Interstitial Cystitis Bladder Pain Society (GIBS) of India

Annual Conference, 24-25 August 2019. Theme: "Beyond Horizon",
Mumbai, India
<https://gibsociety.com/#>

ICS 2019

3-6 September 2019
Gothenburg, Sweden
<https://www.ics.org/2019>

EFIC CONGRESS: PAIN IN EUROPE XI

4-7 September 2019, VALENCIA, SPAIN
<https://efic-congress.org/welcome-messages/>

RESEARCH UPDATE

A REVIEW OF SELECTED RECENT SCIENTIFIC LITERATURE ON INTERSTITIAL CYSTITIS, BLADDER PAIN SYNDROME, 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.

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

If you would like to know more about the MAPP Research Network and its work, [click here](#) to go to the home page.

[SENSORY SENSITIVITY AND SYMPTOM SEVERITY REPRESENT UNIQUE DIMENSIONS OF CHRONIC PAIN: A MAPP RESEARCH NETWORK STUDY.](#)

Schrepf A, Williams DA, Gallop R, Naliboff B, Basu N, Kaplan C, Harper DE, Landis R, Clemens JQ, Strachan E, Griffith JW, Afari N, Hassett A, Pontari MA, Clauw DJ, Harte SE; [MAPP Research Network](#). *Pain*. 2018 May 28. doi: 10.1097/j.pain.0000000000001299. [Epub ahead of print] PMID: 29863527

Chronic Overlapping Pain Conditions (COPCs) are characterized by aberrant central nervous system processing of pain. This 'centralized pain' phenotype has been described using a large and diverse set of symptom domains, including the spatial distribution of pain, pain intensity, fatigue, mood imbalances, cognitive dysfunction, altered somatic sensations, and hypersensitivity to external stimuli. Here, Schrepf and colleagues used three cohorts, including patients with Urologic Chronic Pelvic Pain Syndrome (UCPPS), a mixed pain cohort with other COPCs, and healthy individuals (total 1039) from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network to explore the factor structure of symptoms of centralized pain. Using exploratory and confirmatory factor analysis, they identified two general factors in all three cohorts, one characterized by a broad increased sensitivity to internal somatic sensations and environmental stimuli, and diffuse pain, termed Generalized Sensory Sensitivity (GSS), and one characterized by constitutional symptoms - Sleep, Pain, Affect, Cognition, Energy (SPACE). Longitudinal analyses in the UCPPS cohort found the same two factor structure at month six and one year, suggesting that the two-factor structure is reproducible over time. In secondary analyses, they found that GSS particularly is associated with the presence of comorbid COPCs, while SPACE shows modest associations with measures of disability and urinary symptoms. These factors may represent important and distinct continuum of symptoms that are indicative of the centralized pain phenotype at high levels. Future research of COPCs should accommodate the measurement of each factor.

IC/BPS/HSB BASIC SCIENCE, DIAGNOSIS AND TREATMENT

[PRODROME AND NON-PRODROME PHENOTYPES OF BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.](#)

Warren JW, Jian N, Gallicchio L, Wu D, Clauw DJ. *Urology*. 2018 Jun 26. pii: S0090-4295(18)30458-8. doi: 10.1016/j.urology.2018.05.004. [Epub ahead of print] PMID: 29775697

The purpose of this study was to test the hypothesis that risk factors for bladder pain syndrome/interstitial cystitis (BPS/IC) in women differ between those with and without the BPS/IC prodrome. Incident cases of BPS/IC and healthy controls were recruited nationally. More than half the BPS/IC cases reported subsyndromal urinary symptoms for decades before onset of BPS/IC and were identified as having the prodrome. Risk factors for BPS/IC were examined separately for cases with and without the prodrome using a set of matched controls. Two risk factors distinguished 178 prodrome from 134 non-prodrome cases. One was "UTIs" in the year before BPS/IC onset, possibly a manifestation of the prodrome itself. The other was the presence of the maximal number of nonbladder syndromes (NBSs): prodrome cases were 12 times more likely than non-prodrome cases to have ≥ 4 NBSs. Additional risk factors for prodrome and/or non-prodrome cases were the direct association of exogenous female hormones, as well as 3 inverse associations: type 2 diabetes mellitus, multiple pregnancies, and current

daily smoking. Prodrome cases developed urinary symptoms in their early 20s (ie, the prodrome) and were at very high risk of numerous NBSs. Non-prodrome cases developed urinary symptoms in their early 40s (ie, full-blown BPS/IC) and were no more likely than controls to have the maximal number of NBSs. These findings are consistent with recent suggestions of two BPS/IC phenotypes: one with systemic and psychosocial manifestations and the other more specific to the bladder. Additionally, several risk factors identified here might be hints of related or causal nervous system pathophysiologies.

COMPARISON OF UROLOGIC AND NON-UROLOGIC PRESENTATION IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PATIENTS WITH AND WITHOUT HUNNER LESIONS.

Van Moh F, Vetter J, Lai HH. Neurourol Urodyn. 2018 Sep 6. doi: 10.1002/nau.23812. [Epub ahead of print] PMID: 30187950

This study compared severity and characteristics of urologic pain, other urinary symptoms, sexual pain, psychosocial health, and the distribution and intensity of non-urologic pain between men and women with and without Hunner lesions. All cystoscopies were performed and documented by the same clinician to ensure uniform recognition of Hunner lesions. Intensity of urologic and sexual pain, nocturia, frequency, urgency, and bladder hypersensitivity features were assessed using validated questionnaires and numeric rating scales. The distribution and intensity of non-urologic pain was assessed using self-reported history, a body map diagram, and numeric rating scales. Somatic symptom burden, depression, and anxiety were compared. Among the 150 participants, 27% (41) had Hunner lesions (36% men, 25% women). Close to half of Hunner IC patients had non-urologic pain outside the pelvis. There were no differences in bladder hypersensitivity features (eg, painful bladder filling) between the two groups. It was concluded that Hunner lesions can be identified in both men and women. There are significant overlaps in terms of their urologic and non-urologic presentation. Further investigation is needed on phenotypic and biological distinction between IC/BPS with and without Hunner lesions.

PIGMENTARY MACULOPATHY ASSOCIATED WITH CHRONIC EXPOSURE TO PENTOSAN POLYSULFATE SODIUM.

Pearce WA, Chen R, Jain N. Ophthalmology. 2018 Nov;125(11):1793-1802. doi: 10.1016/j.ophtha.2018.04.026. Epub 2018 May 22. PMID: 29801663

This study described the clinical features of a unique pigmentary maculopathy noted in the setting of chronic exposure to pentosan polysulfate sodium (PPS), a therapy for interstitial cystitis (IC) in 6 adult patients evaluated by a single clinician between May 1, 2015, and October 1, 2017. Patients were identified by query of the electronic medical record system. Local records were reviewed, including results of the clinical examination, retinal imaging, and visual function assessment with static perimetry and electroretinography. Molecular testing assessed for known macular dystrophy and mitochondrial cytopathy genotypes. Mean best-corrected visual acuity (BCVA; in logarithm of the minimum angle of resolution units), median cumulative PPS exposure, subjective nature of the associated visual disturbance, qualitative examination and imaging features, and molecular testing results. On fundus examination, nearly all eyes showed subtle paracentral hyperpigmentation at the level of the retinal pigment epithelium (RPE) with a surrounding array of vitelliform-like deposits. Four eyes of 2 patients showed paracentral RPE atrophy, and no eyes demonstrated choroidal neovascularization. Multimodal retinal imaging demonstrated abnormality of the RPE generally contained in a well-delineated area in the posterior pole. None of the 4 patients who underwent molecular testing of nuclear DNA returned a pathogenic mutation. Additionally, all 6 patients showed negative results for pathogenic variants in the mitochondrial gene MTTL1. The authors describe a novel and possibly avoidable maculopathy associated with chronic exposure to PPS. Patients reported symptoms of difficulty reading and prolonged dark adaptation despite generally intact visual acuity and subtle funduscopic findings. Multimodal imaging and functional studies are suggestive of a primary RPE injury. Additional investigation is warranted to explore causality further.

PAINFUL BLADDER SYMPTOMS RELATED TO SOMATIC SYNDROMES IN A CONVENIENCE SAMPLE OF COMMUNITY WOMEN WITH OVERACTIVE BLADDER SYMPTOMS.

Kowalik CG, Cohn JA, Delpo S, Kaufman MR, Wein A⁴, Dmochowski RR, Reynolds WS. J Urol 2018 Jul 11. pii: S0022-5347(18)43483-0. doi: 10.1016/j.juro.2018.06.070. [Epub ahead of print] PMID:30017963

This study investigated the relationship between painful bladder filling and urinary urgency with somatic and chronic pain symptoms in women with overactive bladder (OAB) without an interstitial cystitis/bladder pain syndrome (IC/BPS) diagnosis. Women meeting OAB criteria based on symptoms were recruited through the community or Urology clinic to complete validated questionnaires assessing urinary symptoms, somatic symptoms, and pain syndromes. Participants were categorized into 3 groups, (1) Neither (2) Either or (3) Both, based on their report of painful urinary urgency and/or painful bladder filling. Multivariable regression analyses

were performed to determine factors predictive of having either or both painful urgency and/or painful filling. Of 218 women with OAB, 46% had neither painful bladder filling nor urinary urgency, 43% had either, and 11% had both. Controlling for age, women with either or both urologic pain symptoms were more likely to have irritable bowel syndrome, chronic pelvic pain, and temporomandibular disorder compared to women in the neither group. Additionally, these women had higher pain intensity and somatic symptoms scores than women with neither symptom. The majority of women with OAB, without a diagnosis of IC/BPS, reported either painful urgency, painful filling, or both. Experiencing painful urgency and/or filling was associated with increased somatic symptom burden and pain intensity. These findings support the hypothesis that OAB and IC/BPS diagnoses may represent a continuum of bladder hypersensitivity.

[SYMPTOMATIC OVERLAP IN OVERACTIVE BLADDER AND INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME - DEVELOPMENT OF A NEW ALGORITHM.](#)

Ackerman AL, Lai HH, Parameshwar PS, Eilber KS, Anger JT. BJU Int. 2018 Sep 25. doi: 10.1111/bju.14568. [Epub ahead of print]

In order to address challenges in the diagnosis and classification of storage Lower Urinary Tract Symptoms (LUTS), Ackerman and colleagues sought to define the fundamental features of overactive bladder (OAB) and interstitial cystitis/bladder pain syndrome (IC/BPS), two conditions with considerable symptomatic overlap. Through retrospective comparison of self-reported symptoms in women with a range of clinical presentations and symptom severities, they have attempted to refine OAB and IC/BPS diagnostic features and develop a novel clinical nomogram to improve patient screening and classification. While all validated questionnaires used could distinguish between controls and storage LUTS, no combined symptom scores differed significantly between the IC/BPS and OAB patients. It was concluded that there is significant overlap of urinary tract symptoms between OAB and IC/BPS. The authors present a novel algorithm that provides a binary output capable of guiding clinical diagnosis. Future studies aimed at assessing the diagnostic value of novel classification schemes that address symptoms rather than specific diagnoses may improve patient prognosis.

[INTERSTITIAL CYSTITIS: AN UPDATE ON THE DISEASE PROCESS AND TREATMENT.](#)

Daniels AM, Schulte AR, Herndon CM. J Pain Palliat Care Pharmacother. 2018 Sep 13:1-10. doi: 10.1080/15360288.2018.1476433. [Epub ahead of print]

Interstitial cystitis (IC) is a chronic pain disorder of the bladder that is often underdiagnosed and mistreated. The difficulties in diagnosis stem from numerous theories regarding pathophysiology and etiology, including the breakdown of the glycosaminoglycan (GAG) layer, altered permeability of the urothelium, uroinflammation, and neural up-regulation. Dysfunction of the bladder increases the struggle for proper treatment and continues to prove difficult for health care providers to correctly diagnose and manage IC. If diagnosed and/or managed inappropriately, IC may contribute to increased symptom burden and decreased quality of life with respect to activities of daily living. When evaluating a patient's clinical presentation in combination with predefined risk factors, a health care provider can better establish a true diagnosis of IC, which, in turn, leads to better management of IC-associated symptoms. This review will help health care providers better understand the disease process by discussing pathophysiology, pain pathways, and common symptoms of IC, with the goal of better aiding them in the proper diagnosis and treatment of patients with IC.

[ELECTRON MICROSCOPIC CHARACTERISTICS OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AND THEIR ASSOCIATION WITH CLINICAL CONDITION.](#)

Jhang JF, Ho HC, Jiang YH, Lee CL, Hsu YH, Kuo HC. PLoS One. 2018 Jun 7;13(6):e0198816. doi: 10.1371/journal.pone.0198816. eCollection 2018. PMID: 29879217

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Electron microscopy (EM) characteristics of the urothelium in interstitial cystitis/bladder pain syndrome (IC/BPS) and their association with the clinical condition are unclear. Ten IC/BPS patients who were admitted for hydrodistension and 5 patients with stress urinary incontinence (control patients) were enrolled. All patients provided detailed clinical histories and underwent urodynamic studies. Cystoscopic bladder biopsies were obtained and processed for transmission EM (TEM) and scanning EM (SEM). The severity of the urothelium findings was graded on a 4-point scale (0: none, 1: mild, 2: moderate, and 3: severe). The EM findings between IC/BPS and control patients were compared; the results were analyzed using the chi-square test. Compared with the urothelium of control patients, the urothelium of IC/BPS patients had more severe defects of the urothelial cell layers and integrity of umbrella cells in TEM. In SEM, umbrella cell pleomorphism increased and microplicae of the cell membrane decreased in the IC/BPS group, and both were more severe than in the control group. The patients with moderate to severe defects of umbrella cell integrity had more severe bladder pain and smaller

maximal bladder capacity (MBC). Patients with moderate to severe defects in micropliae of the cell membrane had smaller cystometric bladder capacity and MBC. The results revealed significant urothelium defects in IC/BPS, especially in the umbrella cells. Defects of umbrella cells may play an important role in the pathogenesis of IC/BPS.

BLADDER PAIN SYNDROME: PREVALENCE AND ROUTINE CLINICAL PRACTICE IN WOMEN ATTENDING FUNCTIONAL UROLOGY AND URODYNAMICS UNITS IN SPAIN.

[Article in English, Spanish]

Morales-Solchaga G1, Zubiatur-Libano C2, Peri-Cusí L3, Adot-Zurbano JM4, Arlandis-Guzmán S5, Franco-de Castro A3, Castillejo C6; Grupo de Investigación de Resultados en Salud en Urología Funcional y Urodinámica (Grupo IFU). *Actas Urol Esp.* 2018 Sep 24. pii: S0210-4806(18)30154-2. doi: 10.1016/j.acuro.2018.06.004. [Epub ahead of print] PMID: 30262204

Bladder pain syndrome (BPS) is classified as a rare chronic debilitating disease and its diagnosis presents a challenge because its symptoms overlap with those associated with overactive bladder syndrome. The aim of the routine study was to estimate the prevalence of BPS and discover to study the profile of symptoms and clinical practice for patients attending functional urology and urodynamics units. An epidemiological study in which 37 functional urology and urodynamics units in Spain participated. The prevalence was studied in both sexes. Clinical practice was evaluated for 319 women with BPS (new diagnosis or under review). Clinical and sociodemographic data were collected retrospectively. The results were studied of urine tests, cystoscopy, biopsy, physical examination, bladder diary, and those of the four available questionnaires: Patient Perception of Bladder Condition; Bladder Pain/Interstitial Cystitis Symptom Score; EuroQoL-5 Dimensions-5L and Patient Global Impression of Severity. The authors found that the prevalence of BPS in functional urology and urodynamics units in Spain is low. No homogeneity was observed in terms of diagnosis between the different participating centres. Therefore, a common methodology is required for the management of patients with BPS in these units, with tools specific to this disorder.

SEX-ASSOCIATED DIFFERENCES IN BASELINE URINARY METABOLITES OF HEALTHY ADULTS.

Fan S1, Yeon A2, Shahid M2, Anger JT3, Eilber KS3, Fiehn O1,4, Kim J5,6,7,8. *Sci Rep.* 2018 Aug 8;8(1):11883. doi: 10.1038/s41598-018-29592-3. PMID: 30089834

The biological basis for gender variability among disease states is not well established. There have been many prior efforts attempting to identify the unique urine metabolomic profiles associated with specific diseases. However, there has been little advancement in investigating the metabolomic differences associated with gender, which underlies the misconception that risk factors and treatment regimens should be the same for both male and female patients. This present study aimed to identify biologically-meaningful baseline sex-related differences using urine samples provided by healthy female and male participants. Their findings indicate that there are baseline sex-related differences in urinary metabolism, which should be considered in biomarker discovery, diagnosis, and treatment of bladder diseases, such as interstitial cystitis.

COMPARISON OF OUTPATIENT REIMBURSEMENT FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AND RHEUMATOID ARTHRITIS TREATMENT IN TAIWAN: A NATIONWIDE POPULATION-BASED STUDY.

Lin HY, Lee MH, Chang KM, Wu HC. *Low Urin Tract Symptoms.* 2018 Aug 2. doi: 10.1111/luts.12238. [Epub ahead of print] PMID: 30073771

This observational study compared Taiwanese public health insurance outpatient reimbursements for interstitial cystitis (IC)/bladder pain syndrome (BPS) and rheumatoid arthritis (RA) treatment, using data from the Taiwan Longitudinal Health Insurance Database between 2002 and 2013. Patients with International Classification of Diseases, Ninth Revision, Clinical Modification codes for IC/BPS and RA were selected and matched in a ratio of 1 : 5 based on index year. After adjustment for possible confounders, including age, sex, income, hospital levels of care, and reimbursements for 24 comorbidities, yearly and per-visit pharmacy, non-pharmacy, and total claims were determined. In all, 1438 IC/BPS and 7190 RA patients were identified in the database. IC/BPS patients were significantly younger, and the proportion of females in this group was higher. Income levels were lower in the IC/BPS cohort, but not significantly. There were no significant differences between cohorts in terms of reimbursements for treatment for comorbidities, with the exception of end-stage renal disease, for which reimbursement was higher in the RA cohort. After adjusting for confounders, the regression coefficient for IC/BPS to RA was significantly lower for yearly total pharmacy claims, yearly total claims, per-visit pharmacy claims, and total claims per visit. It was found that outpatient reimbursement was significantly lower for IC/BPS than for RA treatment, primarily with regard to pharmacy costs. This indicates less medical utilization for IC/BPS,

possibly due to poor treatment outcomes and co-payment policies. Further advances in the treatment of IC/BPS and health budget reallocation are encouraged.

RISK OF URINARY TRACT CARCINOMA AMONG SUBJECTS WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS: A NATIONWIDE POPULATION-BASED STUDY.

Wu MP, Luo HL, Weng SF, Ho CH, Chancellor MB, Chuang YC. *Biomed Res Int.* 2018 Jun 28;2018:7495081. doi: 10.1155/2018/7495081. eCollection 2018. PMID: 30050942

The purpose of this study from Taiwan and the USA was to investigate the subsequent risks of urinary tract cancers among individuals with bladder pain syndrome/interstitial cystitis(BPS/IC), and gender differences, as well as the effect of associated comorbidity using a population-based administrative database in Taiwan. BPS/IC subjects (10192) and their age- and sex-matched non-BPS/IC control subjects (30576), who had no previous upper urinary tract cancer (UUC), bladder cancer (BC), and prostate cancer (PC), subsequently developed these disorders from the recruited date between 2002 and 2008 and the end of follow-up 2011. It was concluded that patients with BPS/IC are at risk of developing BC in both males and females, and UUC in females. This result reminds physicians to evaluate the potential risk of subsequent development of BC and UUC among individuals with BPS/IC.

IMPACT OF INTRAVESICAL HYALURONIC ACID TREATMENT ON BLADDER INFLAMMATION IN INTERSTITIAL CYSTITIS RAT MODEL.

Sahiner IF, Soylu H, Ates E, Acar N, Ustunel I, Danisman A. *Int Braz J Urol.* 2018 Apr 15;44. doi: 10.1590/S1677-5538.IBJU.2017.0713. [Epub ahead of print] PMID: 30044599

This study from Turkey evaluated the effect of intravesical hyaluronic acid (HA) treatment on inflammatory cells and the severity of inflammation in an interstitial cystitis rat model created with hydrogen chloride (HCL) via immunohistochemical studies and myeloperoxidase activity for the first time in the literature. It was concluded that a single dose intravesical hyaluronic acid instillation reduces inflammatory cell infiltration and the severity of bladder inflammation in the rat model of bladder pain syndrome/interstitial cystitis.

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF CERTOLIZUMAB PEGOL IN WOMEN WITH REFRACTORY INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Bosch PC. *Eur Urol.* 2018 Jul 30. pii: S0302-2838(18)30548-7. doi: 10.1016/j.eururo.2018.07.026. [Epub ahead of print] PMID: 30072210

The purpose of this study from the USA was to evaluate the efficacy and safety of certolizumab pegol, used to treat autoimmune diseases, compared with placebo in women with refractory IC/BPS. Eligible women, aged 18-65 yrs with moderate to severe IC/BPS, were enrolled in this randomized, double-blind, placebo-controlled pilot study. Women with moderate to severe refractory IC/BPS were more likely to experience significant improvement in symptoms with certolizumab pegol compared with placebo therapy. Further investigation of certolizumab pegol for the treatment of IC/BPS is warranted with a larger, longer, multicenter, randomized, placebo-controlled trial.

AN EVALUATION OF THE PHARMACOTHERAPY FOR INTERSTITIAL CYSTITIS.

Giusto LL, Zahner PM, Shoskes DA. *Expert Opin Pharmacother.* 2018 Jul 4:1-12. doi: 10.1080/14656566.2018.1491968. [Epub ahead of print] PMID: 29972328

Interstitial cystitis (IC) and bladder pain syndrome (BPS) are chronic conditions that can be debilitating for patients. There is no consensus as to their etiology, and there are many proposed treatment algorithms. Often multimodal therapy, such as combining behavioral modification and physical therapy alongside pharmacotherapies, will be utilized. With the various treatment options available to patients and providers, there is an ever-growing need to implement evidence-based therapies. The authors explore the different pharmacotherapies as commonly recommended in the American Urological Association (AUA) and European Association of Urology (EAU) multitiered guidelines for IC/BPS treatment as well as other investigational therapies. Pharmacotherapies targeting bladder, pelvic, and/or systemic factors in the overall treatment of IC/BPS are discussed with a particular focus on evidence-based guideline therapies. This article also looks at emerging therapies of interest. Expert opinion: IC/BPS is a syndrome that requires a multimodal approach, including clinical phenotyping and directed therapy based on the patient's symptoms. The AUA and EAU provide guidelines for practitioners to follow, but adequate treatment requires the therapy to be targeted toward the patient's phenotypic domain.

[DOWNREGULATION OF WNT11 IS ASSOCIATED WITH BLADDER TISSUE FIBROSIS IN PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME WITHOUT HUNNER LESION.](#)

Choi D, Han JY, Shin JH, Ryu CM, Yu HY, Kim A, Lee S, Lim J, Shin DM, Choo MS. *Sci Rep.* 2018 Jun 28;8(1):9782. doi: 10.1038/s41598-018-28093-7. PMID: 29955137

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This study from Korea assessed the functional role of WNT genes and the association between WNT signalling cascades and fibrosis in interstitial cystitis/bladder pain syndrome (IC/BPS) patients. Twenty-five patients (3 males, 22 females; mean age 59.7 ± 10.9 years), included 7 non-Hunner-type IC (NHIC), 18 Hunner-type IC (HIC), and 5 non-IC (control) groups. HIC patients had significantly shorter symptom duration, higher daily urinary frequency, and smaller bladder capacity than NHIC patients. Downregulation of WNT11 results in fibrotic changes of bladder epithelial cells and is associated with the pathogenesis and differential diagnosis of NHIC. Decreased expression of WNT11 is a potential biomarker for predicting NHIC.

[BRIDGING PHARMACOTHERAPY AND MINIMALLY INVASIVE SURGERY IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME TREATMENT.](#)

Dellis AE, Papatsoris AG. *Expert Opin Pharmacother.* 2018 Aug 3:1-5. doi: 10.1080/14656566.2018.1505865. [Epub ahead of print] PMID: 30074829

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a painful and debilitating clinical entity which is challenging to diagnose and even more difficult to treat. Unfortunately, none of the existing oral and intravesical medications have been established as effective and therefore relevant research is ongoing. In this review, the authors from Greece present established and emerging treatment options for IC/BPS in terms of medication and minimal invasive procedures. Both American and European Urological Association Guidelines recommend multimodal behavioral techniques alongside oral (e.g. amitriptyline and pentosan polysulfate sodium) or minimally invasive treatments (e.g. dimethyl sulfoxide, botulinum toxin, chondroitin sulfate, triamcinolone, hyaluronic acid, and lidocaine). Novel treatment modalities include immunomodulating drugs, stem cell therapy, nerve growth factor, and ASP6294. IC/BPS is still a pathophysiological enigma with multifactorial etiopathogenesis that may be controlled but not completely cured. Patient-tailored phenotype-directed multimodal therapy is the most promising treatment strategy. Combined phenotypic categorization with specific biomarkers could help toward better treatment.

[THE EFFICACY OF BOTULINUM TOXIN A AND SACRAL NEUROMODULATION IN THE MANAGEMENT OF INTERSTITIAL CYSTITIS \(IC\)/BLADDER PAIN SYNDROME \(BPS\), WHAT DO WE KNOW? ICI-RS 2017 THINK TANK, BRISTOL.](#)

Rahnama'i MS, Marcelissen T, Apostolidis A, Veit-Rubin N, Schurch B, Cardozo L, Dmochowski R. *Neurourol Urodyn.* 2018 Jun;37(S4):S99-S107. doi: 10.1002/nau.23493. Epub 2018 Jan 24. PMID: 29363792

This manuscript aims to address the evidence available in the literature on the efficacy of Botulinum Toxin A (BoNT-A) and sacral neuromodulation (SNM) in patients suffering from Interstitial Cystitis (IC)/BPS and propose further research to identify mechanisms of action and establish the clinical efficacy of either therapy. Both intravesical BoNT-A treatment and SNM have been shown to have positive effects in patients with IC/BPS. However, firm conclusions cannot yet be drawn. Patient-reported outcomes and quality of life should be assessed in addition to urinary and pain symptoms. Since current treatments mainly focus on symptomatic relief, future research should also focus on clarifying the pathogenic mechanisms involved in IC/BPS.

[NOVEL APPLICATIONS OF ONABOTULINUMTOXINA IN LOWER URINARY TRACT DYSFUNCTION.](#)

Jhang JF, Kuo HC. *Toxins (Basel).* 2018 Jun 26;10(7). pii: E260. doi: 10.3390/toxins10070260. PMID: 29949878

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OnabotulinumtoxinA (BoNT-A) was first used to treat neurogenic lower urinary tract dysfunction (LUTD) 30 years ago. Recently, application of BoNT-A in LUTD have become more common since the approval of intravesical BoNT-A injection for patients with both overactive bladders (OAB) and neurogenic detrusor overactivity (NDO) by regulatory agencies in many countries. Although unlicensed, BoNT-A has been recommended to treat patients with interstitial cystitis/bladder pain syndrome (IC/BPS) under different guidelines. BoNT-A delivery with liposome-encapsulation and gelation hydrogel intravesical instillation provided a potentially less invasive and more convenient form of application for patients with OAB or IC/BPS. BoNT-A injections into the urethral sphincter for spinal cord injury patients with detrusor-sphincter dyssynergia have been used for a long time. New evidence revealed that it could also be applied to patients with non-neurogenic dysfunctional voiding. Previous studies and meta-analyses suggest that BoNT-A injections for patients with benign prostate hyperplasia do not have a better therapeutic effect than placebo. However, new randomized and placebo-controlled trials

revealed intraprostatic BoNT-A injection is superior to placebo in specific patients. A recent trial also showed intraprostatic BoNT-A injection could significantly reduce pain in patients with chronic prostatitis. Both careful selection of patients and prudent use of urodynamic evaluation results to confirm diagnoses are essential for successful outcomes of BoNT-A treatment for LUTD.

VIDEOURODYNAMIC CHARACTERISTICS OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME-THE ROLE OF BLADDER OUTLET DYSFUNCTION IN THE PATHOPHYSIOLOGY.

Kuo YC, Kuo HC. Neurourol Urodyn. 2018 Mar 5. doi: 10.1002/nau.23542. [Epub ahead of print] PMID: 29504632

This study investigated the characteristics of videourodynamic study (VUDS) in females with interstitial cystitis/bladder pain syndrome (IC/BPS) focusing on the etiologies of bladder outlet dysfunction (BOD) and their associations with clinical and urodynamic parameters. IC/BPS females with complete data on symptom assessment, VUDS, the potassium sensitivity test, and cystoscopic hydrodistention were reviewed retrospectively. Diagnoses of bladder dysfunction (hypersensitive bladder, HSB) and BOD including dysfunctional voiding (DV), poor relaxation of the external urethral sphincter (PRES), and bladder neck dysfunction (BND) were made by VUDS. The clinical and urodynamic parameters between patients with normal and abnormal VUDS diagnoses were analyzed. They found that HSB and BOD are common findings on VUDS in IC/BPS females. BOD is associated with duration and hypersensitive bladder. A $Q_{max} \leq 11$ mL/s predicts BOD in IC/BPS.

PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA AGONIST AS A NOVEL TREATMENT FOR INTERSTITIAL CYSTITIS: A RAT MODEL.

Mahal A, Young-Lin N, Dobberfuhr A, Estes J, Comiter CV. Investig Clin Urol. 2018 Jul;59(4):257-262. doi: 10.4111/icu.2018.59.4.257. Epub 2018 Jun 15. PMID: 29984341

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The aim of this study from the USA was to understand the therapeutic potential of pioglitazone, a peroxisome proliferator-activated receptor gamma (PPAR- γ) agonist with a propensity to cause bladder mucosal proliferation, on interstitial cystitis (IC) in a rat model. Pioglitazone, a PPAR- γ agonist, improved bladder function in cyclophosphamide-induced cystitis by both observed urinary frequency and measured cystometric capacity. Urothelial structural integrity was also improved. Pioglitazone, due to a propensity to cause bladder mucosal proliferation, may prove useful for treating IC, and deserves further investigation.

EPSTEIN-BARR VIRUS AS A POTENTIAL ETIOLOGY OF PERSISTENT BLADDER INFLAMMATION IN HUMAN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Jhang JF, Hsu YH, Peng CW, Jiang YH, Ho HC, Kuo HC. J Urol. 2018 Apr 11. pii: S0022-5347(18)42926-6. doi: 10.1016/j.juro.2018.03.133. [Epub ahead of print] PMID: 29653163

Interstitial cystitis/bladder pain syndrome is characterized by bladder inflammation without bacterial infection. Although viral infection is a potential etiological cause, few studies have been reported. Bladder specimens were obtained from patients with interstitial cystitis/bladder pain syndrome and from patients with stress urinary incontinence as controls. Bladder specimens were tested for Epstein-Barr encoded RNAs by in situ hybridization and for Epstein-Barr DNA by quantitative real-time polymerase chain reaction, serology and immunohistochemical staining. Enrolled in study were 16 patients with interstitial cystitis/bladder pain syndrome and Hunner lesions, 23 without interstitial cystitis/bladder pain syndrome or Hunner lesions and 10 controls. It was concluded that bladder Epstein-Barr infection in T cells may be linked to the pathogenesis of persistent inflammation in patients with interstitial cystitis/bladder pain syndrome.

CROSSTALK BETWEEN THE IMMUNE SYSTEM AND NEURAL PATHWAYS IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Duh K, Funaro MG, DeGouveia W, Bahlani S, Pappas D, Najjar S, Tabansky I, Moldwin R, Stern JNH. Discov Med. 2018 May;25(139):243-250. PMID: 29906407

[Free full text, click on title.](#)

Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) is a condition causing intense pelvic pain and urinary symptoms. While it is thought to affect millions of people and significantly impair quality of life, difficulty with diagnosis and a lack of reliably effective treatment options leave much progress to be made in managing this condition. Duh and colleagues describe what is currently known about the immunological and neurological basis of this disease, focusing on the interactions between the immune and nervous system. Evidence for immune involvement in IC/BPS comes from its high co-occurrence with known autoimmune diseases, altered cytokine profiles, and immune cell infiltration in patients. These cytokines have the ability to cross-talk with the nervous system via NGF signalling, resulting in hyper-sensitization of pain receptors, causing them to release substance

P and creating a positive feedback loop of neuroinflammation. While it seems that the crosstalk between the immune and nervous system in IC is understood, much of the information comes from studying other diseases or from animal models, and it remains to be confirmed in patients with the disease. Identifying biomarkers and confirming the mechanism of IC/BPS are ultimately important for selecting drug targets and for improving the lives of patients with this disease.

HEALTH EDUCATION AND SYMPTOM FLARE MANAGEMENT USING A VIDEO-BASED M-HEALTH SYSTEM FOR CARING WOMEN WITH IC/BPS.

Lee MH, Wu HC, Tseng CM, Ko TL, Weng TJ, Chen YF. Urology. 2018 Jun 10. pii: S0090-4295(18)30547-8. doi: 10.1016/j.urology.2018.05.027. [Epub ahead of print] PMID: 29894774

The purpose of this study from Taiwan was to assess effectiveness of the video-based m-health system providing videos dictated by physicians for health education and symptom self-management for patients with IC/BPS. An m-health system was designed to provide videos for weekly health education and symptom flare self-management. O'Leary-Sant index and VAS scale as well as SF-36 health survey were administered to evaluate the disease severity and quality of life (QoL), respectively. A total of 60 IC/BPS patients were recruited and randomly assigned to either control group (30 patients) or study group (30 patients) in sequence depending on their orders to visit this urological clinic. Patients in both control and study groups received regular treatments, while those in the study group received additional video-based intervention. Statistical analyses were conducted to compare the outcomes between baseline and post-intervention for both groups. The outcomes of video-based intervention were also compared with the text-based intervention conducted in a previous study. After video-based intervention, patients in the study group exhibited significant effect manifested in all disease severity and QoL assessments except the VAS pain scale, while no significance was found in the control group. Moreover, the study group exhibited more significant net improvements than the control group in 7 SF-36 constructs, except the mental health. The limitations include short intervention duration (8 weeks) and different study periods between text-based and video-based interventions. The authors concluded that video-based intervention is effective in improving the QoL of IC/BPS patients and outperforms the text-based intervention even in a short period of intervention.

URINARY AND PSYCHOLOGICAL OUTCOMES IN WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME FOLLOWING HYALURONIC ACID TREATMENT.

Liang CC, Lin YH, Hsieh WC, Huang L. Taiwan J Obstet Gynecol. 2018 Jun;57(3):360-363. doi: 10.1016/j.tjog.2018.04.006. PMID: 29880165

This study from Taiwan investigated urinary and psychological symptoms in patients with interstitial cystitis/bladder pain syndrome (IC/BPS) after intravesical hyaluronic acid (HA) treatment. 30 patients newly diagnosed with IC/BPS undergoing 4 weekly intravesical HA instillations followed by 5 monthly instillations were recruited. Pre-treatment evaluation included a urinalysis and urinary culture, a 3-day voiding diary, and cystoscopy with hydrodistension of the bladder. Questionnaires containing hospital anxiety and depression scale (HADS), O'Leary-Sant score, Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire (PISQ-12), and a pain visual analog scale were completed before and after treatment. Frequency, nocturia, bladder capacity, IC symptom and problem index scores, and pain score improved after 6 months of intravesical HA treatment. After HA treatment, 73% of patients showed improvement in their urological symptoms, but no significant changes were found in their HADS and PISQ-12 scores. It was concluded that bladder pain and lower urinary tract symptoms in patients with IC/BPS may improve after a 6-month intravesical HA treatment. However, no significant changes in their psychological and sexual functional scores were found.

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION FOR CHRONIC NEUROPATHIC PAIN IN PATIENTS WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.

Cervigni M, Onesti E, Ceccanti M, Gori MC, Tartaglia G, Campagna G, Panico G, Vacca L, Cambieri C, Libonati L, Inghilleri M. NeuroUrol Urodyn. 2018 May 24. doi: 10.1002/nau.23718. [Epub ahead of print] PMID: 29797500

The purpose of this study from Rome, Italy was to evaluate the efficacy, safety, and tolerability of repetitive Transcranial Magnetic Stimulation (rTMS) associated with standard drug therapies for neuropathic pain that does not respond to pharmacological treatment alone in patients with Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC). Secondary goals were to assess the effects of rTMS on Lower Urinary Tract Symptoms (LUTS) and Quality of Life (QOL). Fifteen patients with BPS/IC were enrolled in this randomized, double-blind, sham stimulation-controlled, crossover study. Patients were treated for 2 weeks with either real-rTMS (for five consecutive days in 20-min sessions) or sham-rTMS (for five consecutive days in 20-min sessions). After a 6-week washout period, the patients who had previously undergone real-rTMS underwent sham-rTMS, and vice versa.

The results of this study show that rTMS applied with an H-coil over the M1 in the area corresponding to the pelvic region in patients with BPS/IC appears to improve chronic pelvic pain (CPP) and associated urinary disorders.

ASSESSMENT OF TREATMENT OUTCOMES OF INTERSTITIAL CYSTITIS WITH HYDRODISTENTION AND BLADDER TRAINING BY O'LEARY-SANT INTERSTITIAL CYSTITIS SYMPTOM AND PROBLEM INDICES.

Huang MC, Hsieh CH, Chang WC, Chang ST, Lee MS. *Taiwan J Obstet Gynecol.* 2018 Oct;57(5):718-721. doi: 10.1016/j.tjog.2018.08.019. PMID: 30342658

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The authors investigated whether the O'Leary-Sant Interstitial Cystitis Symptom Index (ICSI) and Interstitial Cystitis Problem Index (ICPI) is efficacy measure tool for interstitial Cystitis (IC) treatment with hydrodistention (HD) and bladder training (BT). From January 2003 to March 2006, 108 consecutive IC patients were treated by HD and BT after HD. This study evaluated the efficacy of treatment with the specific questionnaire for IC, the ICSI and ICPI. Each patient filled out the questionnaire before HD and three months after HD and BT. The efficacy of the treatment was evaluated using the average scores of ICSI and ICPI. It was concluded that O'Leary-Sant ICSI and ICPI is not only a screening tool for IC but also a useful assessment tool for IC treatment outcomes.

PROTEASE ACTIVATED-RECEPTOR 4 ACTIVATION AS A MODEL OF PERSISTENT BLADDER PAIN: ESSENTIAL ROLE OF MACROPHAGE MIGRATION INHIBITORY FACTOR AND HIGH MOBILITY GROUP BOX 1.

Ma F, Hunt DE, Leng L, Bucala R, Meyer-Siegler KL, Vera PL. *Int J Urol.* 2018 Oct;25(10):887-893. doi: 10.1111/iju.13778. Epub 2018 Aug 15. PMID: 30112848

Ma and colleagues developed a rodent model of persistent non-inflammatory bladder pain and to test macrophage migration inhibitory factor and high mobility box group 1 as mediators of bladder pain and found that repeated intravesical protease activated receptor 4 instillations produce persistent bladder pain without inflammation. Macrophage migration inhibitory factor and high mobility group box 1 are possible effective target molecules for bladder pain alleviation.

POSTTRAUMATIC STRESS DISORDER IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: RELATIONSHIP TO PATIENT PHENOTYPE AND CLINICAL PRACTICE IMPLICATIONS.

McKernan LC, Johnson BN, Reynolds WS, Williams DA, Cheavens JS, Dmochowski RR, Crofford LJ. *Neurourol Urodyn.* 2018 Oct 23. doi: 10.1002/nau.23861. [Epub ahead of print] PMID: 30350890

This study aimed to assess the prevalence and impact of posttraumatic stress disorder (PTSD) in patients with IC/BPS, including their relation to genitourinary symptom presentation and widespread pain phenotype. The authors recruited 202 participants with chronic pain from an academic medical center and classified 64 individuals as IC/BPS based on validated epidemiological criteria. Participants completed self-reported questionnaires assessing trauma exposure, PTSD symptoms, emotional distress, pain, and urinary symptoms. Wilcoxon rank-sum tests assessed study aims comparing IC/BPS to other chronic pain. The authors recommend that patients with IC/BPS and widespread pain have ongoing screening and monitoring of PTSD, using trauma-informed care practices with these patients to increase trust and safety, which could improve treatment compliance and follow-up.

SENSORY PUDENDAL NERVE STIMULATION INCREASES BLADDER CAPACITY THROUGH SYMPATHETIC MECHANISMS IN CYCLOPHOSPHAMIDE-INDUCED CYSTITIS RATS.

Gonzalez EJ1, Grill WM1,2,3,4. *Neurourol Urodyn.* 2018 Oct 23. doi: 10.1002/nau.23860. [Epub ahead of print] PMID: 30350879

Neuromodulation has emerged as a therapeutic option to treat IC/BPS patients refractory to standard care. The objective of this study was to determine the efficacy and mechanism(s) of sensory pudendal nerve stimulation on bladder function in cystitis rats. The authors found that sympathetic reflex activity mediates sensory pudendal nerve stimulation in CYP treated but not control rats. These studies demonstrate an alternative approach to neuromodulation in cystitis and establish mechanistic changes during stimulation that may enable the development of novel therapeutics.

HISTORICAL

AVICENNA'S POINT ABOUT BLADDER GAS AS A CAUSE OF INTERSTITIAL CYSTITIS.

Tabarrai M, Niktabe Z, Masoudi N, Eftekhaar T. *Iran J Public Health.* 2018 Sep;47(9):1436-1437. PMID: 30320024

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Interstitial cystitis (IC) or bladder pain syndrome (BPS) is considered a devastating condition of chronic nature which can have negative impact on the patients' quality of life. The level of distress can be variable from abdominal tenderness to severe bladder spasm. The diagnosis of this condition is still not very clear and depends on ruling out other diseases. The etiology of BPS is still undetermined mainly due to disagreement on its classification. Recent studies show the significant association of environmental factors such as diet, drinking behavior, physical activity and smoking with occurrence of BPS/IC. In this article, the authors present an interesting and important etiology, which may justify some types of pain in interstitial cystitis. A fascinating glimpse of Avicenna's historical view from Iran.

TERMINOLOGY REPORTS/GUIDELINES

[PATHOLOGY AND TERMINOLOGY OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: A REVIEW.](#)

Akiyama Y, Homma Y, Maeda D. Histol Histopathol. 2018 Jul 17:18028. doi: 10.14670/HH-18-028. [Epub ahead of print] PMID: 30015351

Interstitial cystitis/bladder pain syndrome (IC/BPS) is an umbrella term for chronic debilitating conditions of unknown etiology characterized by symptoms of lower urinary tract hypersensitivity such as bladder pain/discomfort, urgency, and urinary frequency. The pathological features of IC/BPS have been generally reported as non-specific chronic inflammatory changes, with mast cell infiltration as a potential key finding. However, growing evidence reveals a histological distinction between IC/BPS with Hunner lesions and IC/BPS without Hunner lesions, and also sheds doubt on the diagnostic value of the mast cell count. Specifically, IC/BPS with Hunner lesions is an inflammatory disorder characterized by pancystitis with B cell abnormalities and epithelial denudation, while IC/BPS without Hunner lesions shows minimal histological changes. The umbrella term "IC/BPS" connects totally distinct clinical entities. Pathological evaluation thus plays an important role in the precise subtyping and clinical management of IC/BPS. In addition, terminology should be developed to refer separately to IC/BPS with Hunner lesions and IC/BPS without Hunner lesions.

[CURRENT BEST PRACTICE MANAGEMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.](#)

Han E, Nguyen L, Siris L, Peters K. Ther Adv Urol. 2018 Mar 19;10(7):197-211. doi: 10.1177/1756287218761574. eCollection 2018 Jul. PMID: 30034539

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Over the last 100 years, the terminology and diagnosis criteria for interstitial cystitis have evolved. Many therapeutic options have changed, but others have endured. This article reviews the idea of separating 'classic' Hunner lesion interstitial cystitis (HL IC) from non-Hunner lesion interstitial cystitis and bladder pain syndrome (N-HL IC/BPS) and their respective treatment algorithms. In this study from the USA, a literature search was performed to identify articles and research on HL IC and N-HL IC/BPS including definitions, etiological theories, and treatments. This article is an overview of the existing literature. Han and colleagues also offer insight into how HL IC and N-HL IC/BPS are approached at their tertiary referral centre. Additionally, American Urological Association guidelines have been integrated and newer treatment modalities and research will be introduced at the conclusion. The AUA guidelines have mapped out a stepwise fashion to treat IC/BPS; at the authors' institution they separate patients with HL IC from those with N-HL IC/BPS prior to them entering a treatment pathway. They identify the rarer patient with HL as having classic 'IC': this cystoscopic finding is critical in guiding treatment. They believe HL IC is a distinct disease from N-HL IC/BPS and therapy should focus on the bladder. The vast majority of patients with N-HL IC/BPS need management of their pelvic floor muscles as the primary therapy, complemented by bladder-directed therapies as needed as well as a multidisciplinary team to manage a variety of other regional/systemic symptoms. Ongoing research into IC/BPS will help better understand the pathophysiology and phenotypes of this complex disease while exciting and novel research studies are developing promising treatments.

CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME

[EVALUATION OF THE MALE WITH CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME.](#)

Doiron RC, Nickel JC. Can Urol Assoc J. 2018 Jun;12(6 Suppl 3):S152-S154. doi: 10.5489/cuaj.5322. PMID: 29875039

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Chronic prostatitis/chronic pelvic pain syndrome is a symptom complex associated with chronic pelvic pain in men after the exclusion of other confusable diseases, such as infection, malignancy, and benign prostatic hyperplasia (BPH). Prostatitis symptoms are a common reason for outpatient referral to the urologist, as up to

9% of Canadian men will experience some type of prostatitis symptoms (1/3 of these will report very bothersome symptoms to their physician) over the course of a year. These cases can constitute up to 2% of a urologist's outpatient practice. According to the authors, a proper diagnosis and evaluation in these men use the general urologic skills and tools available in the outpatient clinic. The evaluation and workup need not be overly complex, but rather follow an organized approach while keeping in mind a few general principles that will aid in organizing an efficient and potentially successful management strategy.

MANAGEMENT OF CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME.

Doiron RC, Nickel JC. Can Urol Assoc J. 2018 Jun;12(6 Suppl 3):S161-S163. doi: 10.5489/cuaj.5325. PMID: 29875042

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Prostatitis can refer to host of urologic diagnoses with a spectrum of etiologies and varying natural histories. Acute and chronic bacterial prostatitis have clear bacterial etiologies and are managed as infectious diseases. Chronic prostatitis/ chronic pelvic pain syndrome (CP/CPPS), characterized by chronic pelvic pain and voiding symptoms in the absence of a clear bacterial etiology, can be a more challenging entity to manage and is the focus of this article. CP/CPPS is a common condition afflicting 2–6% of men and is a common reason for referral to the community urologist. Furthermore, symptoms persisting for >1 year predict a dismal quality of life. Several previously published guidelines describe the evaluation and management of CP/CPPS, however, recommendations based on level 3 and 4 evidence are pervasive, and the guidelines often fail to address the sometimes idiosyncratic approach required to manage this enigmatic condition.

NOCTURIA/NIGHT-TIME URINATION

CLINICAL CHARACTERISTICS OF SELF-REPORTED NOCTURIA IN PATIENTS WITH INTERSTITIAL CYSTITIS, AND EFFECTS OF BLADDER HYDRODISTENSION (WITH FULGURATION OF HUNNER LESIONS) ON NOCTURIA.

Otsuka A, Suzuki T, Aki R, Matsushita Y, Tamura K, Motoyama D, Ito T, Sugiyama T, Miyake H. Low Urin Tract Symptoms. 2018 Jul 16. doi: 10.1111/luts.12235. [Epub ahead of print] PMID: 30010251

The aim of this study from Japan was to investigate the clinical characteristics of nocturia in patients with interstitial cystitis (IC), and the effects of bladder hydrodistension (with fulguration of Hunner lesions) on nocturia. Significant differences in nocturia were observed between Hunner- and non-Hunner-type IC. Nocturia was positively correlated with age, urgency score (ICSI and VAS), mean number of urgency episodes per 24 hours and the nocturnal polyuria (NP) index, and negatively correlated with average voided volume. Age, NP index, average voided volume, and the presence of Hunner lesions were independent factors associated with nocturia. Bladder hydrodistension significantly decreased nocturia in non-Hunner type IC without NP. In addition, regardless of the presence or absence of NP, bladder hydrodistension with fulguration of Hunner lesions significantly decreased nocturia in Hunner-type IC. The severity of nocturia is associated with age, NP, average voided volume, and the presence of Hunner lesions in IC patients. Bladder hydrodistension (with fulguration of Hunner lesions) has the potential to decrease nocturia.

DEVELOPMENT OF THE IMPACT OF NIGHTTIME URINATION (INTU) QUESTIONNAIRE TO ASSESS THE IMPACT OF NOCTURIA ON HEALTH AND FUNCTIONING.

Abrams S, Martin S, Gillard KK, Cheng L, Fein S. Neurourol Urodyn. 2018 Jun;37(5):1686-1692. doi: 10.1002/nau.23453. Epub 2018 Mar 22. PMID: 29566269

This study describes development of the Impact of Nighttime Urination (INTU) questionnaire to assess nocturia impacts on health and functioning. Development of the questionnaire followed an iterative patient-directed process as recommended by current guidance for patient-reported outcome (PRO) measures. An initial 15-item questionnaire was devised based on reviewing the published literature, and then modified through four rounds of semi-structured interviews of 28 individuals with nocturia. In each round, open-ended concept elicitation, followed by cognitive debriefing, was used to assess the questionnaire. Items were modified based on participants' responses and incorporated into the next round of interviews. In all rounds, participants reported that their experiences were easy to recall and report on a daily basis and that the burden of completing the questionnaire was low. Development of the 10-item INTU, a nocturia-specific PRO measure, was based on direct input and feedback from patients and has demonstrated that it captures the patient-reported impacts of nocturia.

MICROBIOME, MICROBIOTA

THE URINARY TRACT MICROBIOME: THE ANSWER TO ALL OUR OPEN QUESTIONS?

Magistro G, Stief CG. *Eur Urol Focus*. 2018 Jul 2. pii: S2405-4569(18)30159-7. doi: 10.1016/j.euf.2018.06.011. [Epub ahead of print] PMID: 30042043

The dogma of a sterile urinary tract persisted for over a century. With the advances in new high-throughput sequencing technologies and modified culture protocols for microbiome research, we have discovered a variable microbial spectrum in the urinary tract. Its relevance for health and disease is now under investigation. The purpose of this study was to present the latest insights into the role of the urinary tract microbiome in functional disorders. The urinary tract is not sterile. Every individual harbours a complex microbial network in the urinary tract that is exposed to internal and external factors. Any imbalance in this network is likely to contribute to the development of lower urinary tract symptoms. Functional disorders such as interstitial cystitis, urinary urge incontinence, and chronic prostatitis/chronic pelvic pain syndrome, none of which include a bacterial origin for diagnosis, show features of an altered microbiome with specific dominating urotypes in contrast to urine from asymptomatic healthy individuals. The growing insights into the impact of the urinary microbiome on these entities may help in gaining a deeper understanding of the condition and may provide guidance for optimised management. The urinary tract is naturally colonised with a specific microbial spectrum for which impairment may cause bothersome symptoms.

IS THE MICROBIOME INFLUENCING PATIENT CARE IN LOWER URINARY TRACT DYSFUNCTION? REPORT FROM THE ICI-RS 2017.

Ford AA, Veit-Rubin N, Cardozo L, Khullar V. *Neurourol Urodyn*. 2018 Jun;37(S4):S93-S98. doi: 10.1002/nau.23708. PMID: 30133786

This report sets out to consider the role of the microbiome within the bladder to provide clinicians with knowledge on this specific area of research and recommend potential topics for further studies. There appear to be complex associations between microbial presence in the bladder and lower urinary tract symptoms. There appears to be a greater role of bacteria in the development of overactive bladder symptoms than previously thought with bacteria such as Gardnerella highlighted to be more prevalent in women with urgency urinary incontinence. Some species of Lactobacillus have also been found to play a protective role in both overactive bladder syndrome and bladder pain syndrome. The bladder is a reservoir for bacterial colonization and what was previously thought to be a sterile environment now seems to be a complex interaction of both multiple protective and pathogenic bacterial species than can give rise to lower urinary tract symptoms. While most clinicians use antibacterial agents as part of treatment regimens, and evidence does suggest a role of antibacterial therapies in treatment of LUTS, this remains a far from an ideal solution.

THE ROLE OF URINARY MICROBIOTA IN LOWER URINARY TRACT DYSFUNCTION: A SYSTEMATIC REVIEW.

Antunes-Lopes T, Vale L, Coelho AM, Silva C, Rieken M, Geavlete B, Rashid T, Rahnama'i SM, Cornu JN, Marcelissen T; EAU Young Academic Urologists (YAU) Functional Urology Working Group. *Eur Urol Focus*. 2018 Sep 27. pii: S2405-4569(18)30283-9. doi: 10.1016/j.euf.2018.09.011. [Epub ahead of print] PMID: 30270128

Until 2012, the urinary tract of healthy individuals was considered to be sterile. The advent of metagenomic sequencing revealed a unique urinary microbiota (UM). This paradigm shift appears to have prolific implications in the etiology of several functional lower urinary tract (LUT) disorders. This study systematically summarized recent data on the role of UM in LUT dysfunction. Analysis by 16S rRNA sequence and expanded quantitative urine culture provided evidence for the presence of live bacteria in urine, nondetectable by standard culture protocols. Moreover, differences in the UM between healthy individuals and patients with LUT dysfunction were demonstrated. In the near future, urologists must consider urinary dysbiosis as a possible cause of different functional LUT disorders, with potential clinical implications in their diagnosis and treatment.

ABNORMAL VAGINAL MICROBIOMA IS ASSOCIATED WITH SEVERITY OF LOCALIZED PROVOKED VULVODYNIA. ROLE OF AEROBIC VAGINITIS AND CANDIDA IN THE PATHOGENESIS OF VULVODYNIA.

Donders GGG, Bellen G, Ruban KS. *Eur J Clin Microbiol Infect Dis*. 2018 Jun 22. doi: 10.1007/s10096-018-3299-2. [Epub ahead of print] PMID: 29934834

Localized provoked vulvodynia (LPV) causes introital dyspareunia in up to 14% of premenopausal women. Vaginal infections like candidosis may play a initiating role. The aim of this study was to test a possible association of vaginal microbiota alternations such as Candida vaginitis (CV), aerobic vaginitis (AV) and bacterial vaginosis (BV) with severity of vulvodynia and painful intercourse. Detailed study of the vaginal microflora in patients demonstrates that the most severe patients suffer more from AV and less from Candida. These abnormalities need to be actively looked for and corrected before considering surgery or other therapies.

THE GUT MICROBIOME AND IRRITABLE BOWEL SYNDROME.

Menees S, Chey W. *F1000Res.* 2018 Jul 9;7. pii: F1000 Faculty Rev-1029. doi: 10.12688/f1000research.14592.1. eCollection 2018. PMID: 30026921

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Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders encountered in clinical practice. It is a heterogeneous disorder with a multifactorial pathogenesis. Recent studies have demonstrated that an imbalance in gut bacterial communities, or "dysbiosis", may be a contributor to the pathophysiology of IBS. There is evidence to suggest that gut dysbiosis may lead to activation of the gut immune system with downstream effects on a variety of other factors of potential relevance to the pathophysiology of IBS. This review will highlight the data addressing the emerging role of the gut microbiome in the pathogenesis of IBS and review the evidence for current and future microbiome-based treatments.

MARIJUANA/CANNABIS AND CHRONIC PAIN MANAGEMENT

EUROPEAN PAIN FEDERATION (EFIC) POSITION PAPER ON APPROPRIATE USE OF CANNABIS-BASED MEDICINES AND MEDICAL CANNABIS FOR CHRONIC PAIN MANAGEMENT.

Häuser W, Finn DP, Kalso E, Krcevski-Skvarc N, Kress HG, Morlion B, Perrot S, Schäfer M, Wells C, Brill S. *Eur J Pain.* 2018 Oct;22(9):1547-1564. doi: 10.1002/ejp.1297. Epub 2018 Sep 4. PMID: 30074291

Cannabis-based medicines are being approved for pain management in an increasing number of European countries. There are uncertainties and controversies on the role and appropriate use of cannabis-based medicines for the management of chronic pain. EFIC convened a European group of experts, drawn from a diverse range of basic science and relevant clinical disciplines, to prepare a position paper to empower and inform specialist and nonspecialist prescribers on appropriate use of cannabis-based medicines for chronic pain. The expert panel reviewed the available literature and harnessed the clinical experience to produce these series of recommendations. Therapy with cannabis-based medicines should only be considered by experienced clinicians as part of a multidisciplinary treatment and preferably as adjunctive medication if guideline-recommended first- and second-line therapies have not provided sufficient efficacy or tolerability. The quantity and quality of evidence are such that cannabis-based medicines may be reasonably considered for chronic neuropathic pain. For all other chronic pain conditions (cancer, non-neuropathic noncancer pain), the use of cannabis-based medicines should be regarded as an individual therapeutic trial. Realistic goals of therapy have to be defined. All patients must be kept under close clinical surveillance. As with any other medical therapy, if the treatment fails to reach the predefined goals and/or the patient is additionally burdened by an unacceptable level of adverse effects and/or there are signs of abuse and misuse of the drug by the patient, therapy with cannabis-based medicines should be terminated. This position paper provides expert recommendations for nonspecialist and specialist healthcare professionals in Europe, on the importance and the appropriate use of cannabis-based medicines as part of a multidisciplinary approach to pain management, in properly selected and supervised patients.

SYSTEMATIC REVIEWS WITH META-ANALYSIS ON CANNABIS-BASED MEDICINES FOR CHRONIC PAIN: A METHODOLOGICAL AND POLITICAL MINEFIELD

Häuser W, Finnerup NB, Moore RA. *Pain.* 2018 Oct;159(10):1906-1907. doi: 10.1097/j.pain.0000000000001295. PMID: 29847473

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Public interest in cannabis products for medical purposes has been widely advocated, with legalization for recreational and medical use in North America and some European countries. Legalization of cannabis-based medicines (CBMs) (medical cannabis, plant-based cannabinoids [tetrahydrocannabinol, cannabidiol, and combinations], and synthetic tetrahydrocannabinol analogues) has bypassed usual drug regulatory procedures. Systematic reviews with meta-analyses of randomised controlled trials (RCTs) with CBM for chronic pain conditions help determine "post hoc" whether the preconditions of drug agencies for approval were met and to guide physicians and patients. A systematic review of systematic reviews on CBM highlighted the uncertainty about whether CBMs improve pain, with only low or very low quality evidence available. Individual systematic reviews generally avoided issues of trial quality, usually had some flaws, and included different drugs, doses, durations, conditions, and outcomes. Most reviews agreed that there was no, or no clinically relevant, effect.

MEDICAL MARIJUANA FOR UROLOGIC CHRONIC PELVIC PAIN.

Nickel JC. *Can Urol Assoc J.* 2018 Jun;12(6 Suppl 3):S181-S183. doi: 10.5489/cuaj.5331. PMID: 29875048

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It is generally acknowledged that many patients are not satisfied with the contemporary medical approach to the management of urologic chronic pelvic pain syndrome (UCPPS). Many have turned to marijuana or cannabis because of its strong anecdotal reputation of providing benefit to patients with chronic pain. In a condition in which patients are struggling to cope, the marijuana story appears to offer hope. The author explains that they have been prescribing medical marijuana for a number of years and are slowly figuring out how to do this properly. It was really trial and error, with our patients teaching us the optimal strategies for the use of marijuana in UCPPS. In this article Nickel shares the seven most important lessons they have learned.

CANNABIS AND CANNABINOIDS FOR THE TREATMENT OF PEOPLE WITH CHRONIC NONCANCER PAIN CONDITIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF CONTROLLED AND OBSERVATIONAL STUDIES.

Stockings E, Campbell G, Hall WD, Nielsen S, Zagic D1, Rahman R, Murnion B, Farrell M, Weier M, Degenhardt L. Pain. 2018 Oct;159(10):1932-1954. doi: 10.1097/j.pain.0000000000001293. PMID: 29847469

This review examines evidence for the effectiveness of cannabinoids in chronic noncancer pain (CNCP) and addresses gaps in the literature by: considering differences in outcomes based on cannabinoid type and specific CNCP condition; including all study designs; and following IMMPACT guidelines. The authors found that there were no significant impacts on physical or emotional functioning, and low-quality evidence of improved sleep and patient global impression of change. Evidence for effectiveness of cannabinoids in CNCP is limited. Effects suggest that number needed to treat to benefit is high, and number needed to treat to harm is low, with limited impact on other domains. It seems unlikely that cannabinoids are highly effective medicines for CNCP.

CHRONIC PELVIC PAIN/CHRONIC UROLOGIC PAIN/CHRONIC PAIN

INVOLVEMENT OF VOLTAGE-GATED CALCIUM CHANNELS IN INFLAMMATION AND INFLAMMATORY PAIN.

Sekiguchi F, Tsubota M, Kawabata A. Biol Pharm Bull. 2018;41(8):1127-1134. doi: 10.1248/bpb.b18-00054. PMID: 30068860

Sekiguchi and colleagues from Japan report that voltage-gated calcium channels (VGCCs) are classified into high-voltage-activated (HVA) channels and low-voltage-activated channels consisting of Cav3.1-3.3, known as T ("transient")-type VGCC. There is evidence that certain types of HVA channels are involved in neurogenic inflammation and inflammatory pain, in agreement with reports indicating the therapeutic effectiveness of gabapentinoids, ligands for the $\alpha 2\delta$ subunit of HVA, in treating not only neuropathic, but also inflammatory, pain. Among the Cav3 family members, Cav3.2 is abundantly expressed in the primary afferents, regulating both neuronal excitability at the peripheral terminals and spontaneous neurotransmitter release at the spinal terminals. The function and expression of Cav3.2 are modulated by a variety of inflammatory mediators including prostanoids and hydrogen sulfide (H₂S), a gasotransmitter. The increased activity of Cav3.2 by H₂S participates in colonic, bladder and pancreatic pain, and regulates visceral inflammation. Together, VGCCs are involved in inflammation and inflammatory pain, and Cav3.2 T-type VGCC is especially a promising therapeutic target for the treatment of visceral inflammatory pain in patients with irritable bowel syndrome, interstitial cystitis/bladder pain syndrome, pancreatitis, etc., in addition to neuropathic pain.

WHAT MAKES A CHRONIC PELVIC PAIN PATIENT SATISFIED?

Wygant JN, McGuire LJ, Bush NM, Burnett TL, Green IC, Breilkopf DM. J Psychosom Obstet Gynaecol. 2018 May 31:1-4. doi: 10.1080/0167482X.2018.1476486. [Epub ahead of print] PMID: 29848157

Caring for women with chronic pelvic pain (CPP) is challenging. There have been few studies on what factors patients consider to be important when being treated for their pelvic pain. This study sought to identify the key factors of the health care visit that contribute to patient's overall satisfaction with their care in a CPP clinic. Between January 2015 and December 2016, new patients visiting a tertiary care CPP clinic were recruited to complete a patient satisfaction survey. Inductive thematic analysis was performed on response data regarding important factors that impact patient satisfaction with their visit/care. Five themes of patient satisfaction identified included: providers with a compassionate and caring attitude, being listened to, clear communication with collaboration when needed, quality time spent with patient, and having a plan of care with recommendations. The theme regarding provider's compassion and listening skills was the most frequently identified. Pain relief was seldom mentioned as a source of patient satisfaction. The data suggest that a focus on empathic communication may make a meaningful difference in meeting the needs of women with CPP as well as strengthening the provider/patient relationship.

PHYSIOTHERAPY PROVIDES SIGNIFICANT BENEFITS FOR PATIENTS WITH CHRONIC UROLOGIC PAIN.

Faghani N. Can Urol Assoc J. 2018 Jun;12(6 Suppl 3):S171-S174. doi: 10.5489/cuaj.5328. PMID: 29875045

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Symptoms of urinary urgency, frequency, and bladder/pelvic pain debilitate a staggering number of people around the world. Many are left frustrated with symptoms of unknown cause and go through years of ineffective treatments, leaving them scared and without hope. The average patient has been seeking treatment for at least 3–5 years and has seen about 5–7 specialists during this time. Chronic urologic pain is much more prevalent than previously thought and patients present to us with multiple debilitating comorbidities that significantly impact their quality of life. A physiotherapist with the appropriate training to treat pelvic dysfunction can help many of your patients.

[**DOES EVIDENCE SUPPORT PHYSIOTHERAPY MANAGEMENT OF ADULT FEMALE CHRONIC PELVIC PAIN? A SYSTEMATIC REVIEW.**](#)

Loving S, Nordling J, Jaszczak P, Thomsen T. Scand J Pain. 2012 Apr 1;3(2):70-81. doi: 10.1016/j.sjpain.2011.12.002. PMID: 29913781

Chronic pelvic pain (CPP) is a debilitating condition among women with a major impact on health-related quality of life, work productivity and health care utilisation. The exact prevalence of chronic pelvic pain is not known, but 3.8% is commonly suggested. Musculoskeletal dysfunction is frequently cited as a possible aetiology. Physiotherapy is therefore recommended as one treatment modality. The aim of this systematic review was to source and critically evaluate the evidence for an effect of physiotherapy on pain, physical activity and quality of life in the treatment of female CPP. There seems to be some evidence to support the use of a multidisciplinary intervention in the management of female chronic pelvic pain. Somatocognitive therapy is a new approach that appears to be promising and randomised clinical trials are underway in order to establish its evidence base. Based on the findings of this review, recommendations for physiotherapy in chronic pelvic pain clinical guidelines, textbooks and narrative reviews should be interpreted with caution due to the lack of a sufficient evidence base. Only small and largely non-randomised studies have been undertaken of physiotherapeutic interventions and this greatly limits the available evidence on which to base clinical practice. High quality randomised clinical trials are therefore urgently needed.

[**FEMALE CHRONIC PELVIC PAIN IS HIGHLY PREVALENT IN DENMARK. A CROSS-SECTIONAL POPULATION-BASED STUDY WITH RANDOMLY SELECTED PARTICIPANTS.**](#)

Loving S, Thomsen T, Jaszczak P, Nordling J. Scand J Pain. 2014 Apr 1;5(2):93-101. doi: 10.1016/j.sjpain.2013.12.002. PMID: 29913678

A recent systematic review reported worldwide prevalence rates for female chronic pelvic pain ranging from 2.1% to 24%. The aim of this study was to assess the prevalence, characteristics, and factors associated with chronic pelvic pain among women living in Denmark, and to compare these findings with a pain-free reference group. Secondly, the authors evaluated the impact of pain on daily life in women suffering from chronic pelvic pain. This study was cross-sectional and relied on association-based analyses. Consequently, causality between age groups, country of birth, former pelvic surgeries and pelvic traumas and experiences of chronic pelvic pain remains unknown. In order to improve prevention and treatment of chronic pelvic pain in Denmark, high quality, population-based cohort studies and randomised clinical trials are essential. The demand for trustworthy chronic pelvic pain prevalence estimates might also inspire political attention and hereby facilitate funding for further development of treatment and research.

[**MRI VERSUS LAPAROSCOPY TO DIAGNOSE THE MAIN CAUSES OF CHRONIC PELVIC PAIN IN WOMEN: A TEST-ACCURACY STUDY AND ECONOMIC EVALUATION.**](#)

Khan KS, Tryposkiadis K, Tirapur SA, Middleton LJ, Sutton AJ, Priest L, Ball E, Balogun M, Sahdev A, Roberts T, Birch J, Daniels JP, Deeks JJ. Health Technol Assess. 2018 Jul;22(40):1-92. doi: 10.3310/hta22400. PMID: 30045805

Chronic pelvic pain (CPP) symptoms in women are variable and non-specific; establishing a differential diagnosis can be hard. A diagnostic laparoscopy is often performed, although a prior magnetic resonance imaging (MRI) scan may be beneficial. The purpose of this study in 291 women with CPP was to estimate the accuracy and added value of MRI in making diagnoses of (1) idiopathic CPP and (2) the main gynaecological causes of CPP. To quantify the impact MRI can have on decision-making with respect to triaging for therapeutic laparoscopy and to conduct an economic evaluation. The accuracy of laparoscopy appeared to be able to rule in these diagnoses. Using MRI to identify women who require therapeutic laparoscopy would lead to 369 women in a cohort of 1000 receiving laparoscopy unnecessarily, and 136 women who required laparoscopy not receiving it. The economic analysis highlighted the importance of the time horizon, the prevalence of CPP and the cut-off values to inform the sensitivity and specificity of MRI and laparoscopy on the model results. MRI was not found to be a cost-effective

diagnostic approach in any scenario. It was concluded that MRI was dominated by laparoscopy in differential diagnosis of women presenting to gynaecology clinics with CPP. It did not add value to information already gained from history, examination and ultrasound about idiopathic CPP and various gynaecological conditions.

INJECTION THERAPY FOR UROLOGIC CHRONIC PELVIC PAIN: LESSONS LEARNED.

Nickel JC. *Can Urol Assoc J.* 2018 Jun;12(6 Suppl 3):S186-S188. doi: 10.5489/cuaj.5333. PMID: 29875050

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Pain is transmitted by afferent nerves from skin, organs, muscle, and other related structures in the lower abdomen and pelvis, while muscle spasm can be maintained by efferent nerves. These nerves are modulated centrally in the nervous system and can become upregulated with subsequent sensitization of the end organ. By injecting the nerves with local anesthetic, we effectively block this process. If we are accurate, the pain resolves, even if temporarily. This fact in itself allows for much better diagnosis of the cause of the patient's pain. However, a phenomenon that can occur by temporarily breaking this pain cycle is that when the pain returns, it may not be as severe as it was before the injection. With repeated injections, we may be able to downregulate or desensitize the chronic pain cycle.

FIBROMYALGIA

SYMPTOMS OF FIBROMYALGIA ACCORDING TO THE 2016 REVISED FIBROMYALGIA CRITERIA IN CHRONIC PAIN PATIENTS REFERRED TO MULTIDISCIPLINARY PAIN REHABILITATION: INFLUENCE ON CLINICAL AND EXPERIMENTAL PAIN SENSITIVITY.

Plesner KB, Vaegter HB. *J Pain.* 2018 Jul;19(7):777-786. doi: 10.1016/j.jpain.2018.02.009. Epub 2018 Mar 2. PMID: 29499328

Fibromyalgia (FM) is a condition with chronic widespread pain and signs of generalized pain hypersensitivity. FM has previously been classified according to the American College of Rheumatology-1990 criteria, where the presence of hypersensitivity is estimated by a tender point examination. Because of the limitations of these classification criteria, new diagnostic criteria have been proposed, abandoning this examination. This cross-sectional study investigated the prevalence of FM according to the revised 2016 FM criteria in a large cohort of chronic pain patients. More than one-third of patients were classified as FM, and patients classified showed increased clinical and experimental pain profiles.

PRIMARY AND SECONDARY FIBROMYALGIA ARE THE SAME: THE UNIVERSALITY OF POLYSYMPOMATIC DISTRESS.

Wolfe F, Walitt B, Rasker JJ, Häuser W. *J Rheumatol.* 2018 Jul 15. pii: jrheum.180083. doi: 10.3899/jrheum.180083. [Epub ahead of print] PMID: 30008459

Polysymptomatic distress (PSD) is the underlying metric of fibromyalgia (FM), and levels of PSD can identify criteria-positive FM with > 90% accuracy. Wolfe and colleagues used levels of the PSD scale to test whether symptom levels in primary FM (PFM) and secondary FM (SFM) were the same and whether symptoms were equivalent in persons not meeting FM criteria. They studied 1525 patients with a clinical diagnosis of FM and 12,037 patients with rheumatoid arthritis (RA), using regression models to compare patients with potential and actual PFM to RA patients with potential and actual SFM for 17 key clinical variables. They concluded that PFM and SFM are equivalent regarding symptom burden. PSD scores are more informative about severity and severity within diagnosis than dichotomization into FM/non-FM. Studies of FM versus "healthy individuals," or FM versus other diseases, are inherently defective, while studies of FM and PSD in RA offer the opportunity to have meaningful comparison groups, because there are no readily available unbiased appropriate controls for PFM.

PELVIC FLOOR DYSFUNCTION IN WOMEN WITH FIBROMYALGIA AND CONTROL SUBJECTS: PREVALENCE AND IMPACT ON OVERALL SYMPTOMATOLOGY AND PSYCHOSOCIAL FUNCTION.

Carrillo-Izquierdo MD1, Slim M2, Hidalgo-Tallon J3, Calandre EP4. *Neurourol Urodyn.* 2018 Jul 4. doi: 10.1002/nau.23723. [Epub ahead of print] PMID: 29974511

The aim of this study was to evaluate the prevalence, distress, and impact of pelvic floor dysfunction (PFD) symptomatology in women with fibromyalgia and control women and to evaluate the impact of PFD symptomatology on several psychosocial measures such as mood, sleep, pain, and quality of life. They found that PFD-related symptoms were significantly more frequent in women with fibromyalgia than in controls. PFD symptomatology, when present, negatively influenced mood, sleep quality, and quality of life of both patients with fibromyalgia and controls.

COMORBIDITIES

[RISK OF DEVELOPING COMORBIDITIES AMONG WOMEN WITH ENDOMETRIOSIS: A RETROSPECTIVE MATCHED COHORT STUDY.](#)

Surrey ES, Soliman AM, Johnson SJ, Davis M, Castelli-Haley J, Snabes MC. *J Womens Health (Larchmt)*. 2018 Aug 2. doi: 10.1089/jwh.2017.6432. [Epub ahead of print] PMID: 30070938

Endometriosis has been associated with higher rates of various chronic conditions, but its epidemiological data are fragmented and dated. This study sought to compare the incidence of developing commonly occurring comorbidities among patients with and without endometriosis in a large, contemporary patient cohort that reflects real-world clinical practice. The authors found that the incidence of developing many comorbidities was significantly higher among endometriosis patients compared with matched women without endometriosis. Additional research is needed to establish the implications for healthcare resource use.

PUDENDAL NEURALGIA

[CORRELATION BETWEEN ANATOMICAL SEGMENTS OF THE PUDENDAL NERVE AND CLINICAL FINDINGS OF THE PATIENT WITH PUDENDAL NEURALGIA.](#)

Pereira A, Pérez-Medina T, Rodríguez-Tapia A, Chiverto Y, Lizarraga S. *Gynecol Obstet Invest*. 2018 Jul 13:1-7. doi: 10.1159/000489497. [Epub ahead of print] PMID: 30007962

The objective was to describe clinical findings and outcomes of patients with pudendal neuralgia in relation with the anatomical segment affected. Chronic perineal pain and radiation of pain to lower limbs suggest a disorder at the second segment of PN. A positive Tinel sign in the third segment indicates a nerve entrapment. In terminal branches, pain was more frequent at the perineal nerve and more persistent at the DCN.

VULVODYNIA/VULVAL PAIN SYNDROME

[WOMEN'S EXPERIENCES OF VULVODYNIA: AN INTERPRETATIVE PHENOMENOLOGICAL ANALYSIS OF THE JOURNEY TOWARD DIAGNOSIS.](#)

Shallcross R, Dickson JM, Nunns D, Taylor K, Kiemle G. *Arch Sex Behav*. 2018 Jul 25. doi: 10.1007/s10508-018-1246-z. [Epub ahead of print] PMID: 30047005

Vulvodynia is the experience of idiopathic pain characterized by burning, soreness, or throbbing in the external female genitalia or vulva and is estimated to be experienced by 4-16% of the female population, yet only half of women seek help regarding their symptoms. Of the women who do seek help, only around 2% obtain a diagnosis. Therefore, the aim of the current study was to explore the experiences of women with vulvodynia on their journey toward diagnosis, by using semi-structured interviews and an interpretative phenomenological analysis (IPA) methodology. Overall, women perceived a healthcare system which was dismissive and shaming, with an inadequate knowledge of vulvodynia. This in turn impacted on women's psychological well-being. Psychological understanding, one-to-one therapy, and consultation and training for healthcare professionals may help to improve the psychological well-being of women with vulvodynia.

[VULVODYNIA AND CHRONIC PELVIC PAIN IN A GYNECOLOGIC OUTPATIENT CLINIC.](#)

Trutnovsky G, Plieseis C, Bjelic-Radisic V, BertholinyGalvez MC, Tamussino K, Ulrich D. *J Psychosom Obstet Gynaecol*. 2018 May 31:1-5. doi: 10.1080/0167482X.2018.1477753. [Epub ahead of print] PMID: 29848143

Vulvodynia and chronic pelvic pain are common but underdiagnosed chronic gynecologic pain syndromes. Insufficient knowledge regarding prevalence, typical pain patterns and associated factors contribute to delayed diagnosis. The present study explored the symptoms and characteristics of women presenting with vulvodynia and/or chronic pelvic pain to a gynecologic outpatient clinic. There is a need for increased awareness regarding vulvodynia and CPP among health care providers. A comprehensive history is important for adequate diagnosis.

[SYSTEMATIC REVIEW OF TREATMENT OUTCOME MEASURES FOR VULVODYNIA.](#)

Sadownik LA, Yong PJ, Smith KB. *J Low Genit Tract Dis*. 2018 Jul;22(3):251-259. doi: 10.1097/LGT.0000000000000406. PMID: 29933290

A systematic literature search on OVID, PubMed, and PsycINFO databases was conducted from inception until May 2016. Studies were included/excluded based on prespecified criteria. Reported outcome measures were organized into 6 core outcome domains recommended by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT): pain; physical functioning, emotional functioning, participant ratings of global improvement and satisfaction with treatment, symptoms and adverse events, and participant disposition.

Comparison of clinical trial results in vulvodynia is not possible because of a lack of standard treatment outcome measures. Vulvodynia researchers should apply the IMMPACT criteria to guide the development of a minimum core set of standard outcome measures that measure holistic health.

[PAIN, PSYCHOLOGICAL DISTRESS AND MOTOR PATTERN IN WOMEN WITH PROVOKED VESTIBULODYNIA \(PVD\) - SYMPTOM CHARACTERISTICS AND THERAPY SUGGESTIONS.](#)

Haugstad GK, Wojniusz S, Kirste UM, Kirschner RS, Lilleheie I, Haugstad TS. Scand J Pain. 2018 Apr 25;18(2):221-227. doi: 10.1515/sjpain-2017-0173. PMID: 29794291

Provoked vestibulodynia (PVD) represents a longstanding pain syndrome that affects large numbers of women worldwide. However, no standardized guidelines for PVD treatment exist. In a cross-sectional pilot study the authors examined 30 PVD patients on multidimensional parameters including pain, psychological distress and quality of movement, in order to obtain a broader understanding of the somatic and psychological symptoms in PVD, and for the future to develop better interventions. Additionally, they compared the findings to previously published results regarding the same parameters in women with chronic pelvic pain (CPP). They found that PVD women display reduced quality of movement, especially for gait and respiration patterns, increased level of anxiety and high average pain scores. These findings are similar to what they have previously reported in CPP patients. However, in contrast to CPP group, PVD women are on average younger, have higher work participation, higher education level and have not been subjected to surgical procedures. Since PVD women display similar, although somewhat less severe, symptom profile than CPP, they suggest that a multidimensional approach to treatment, such as "somatocognitive therapy" should be investigated in this group as it has previously been shown to be promising in treatment of CPP.

FEMALE SEXUAL DYSFUNCTION

[EVALUATION AND TREATMENT OF FEMALE SEXUAL PAIN: A CLINICAL REVIEW.](#)

Sorensen J, Bautista KE, Lamvu G, Feranec J. Cureus. 2018 Mar 27;10(3):e2379. doi: 10.7759/cureus.2379. PMID: 29805948

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Dyspareunia and vulvodynia are genital pain disorders that have devastating effects on women's quality of life. These disorders occur with high prevalence and place a significant financial burden on women and the health care system. Many women do not report genital pain, and most providers do not inquire about this type of pain. As a result, women also experience social isolation. Numerous treatments are thought to improve quality of life and decrease pain; however, more studies are needed. This review aims to provide an overview of clinical evaluation methods and to summarize treatment options for women suffering from dyspareunia and vulvodynia.

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