

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 58, March 2021

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

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

- COVID-19 impact continues
- Webinars
- News from IMI-PainCare
- New Books
- Patient Education - EUPATI
- COVID-19: Information About COVID-19 And Useful Online Resources
- Overview of upcoming events
- Research Update
- Donations & Sponsoring

COVID-19 IMPACT CONTINUES

It is, alas, beginning to look as though the COVID-19 pandemic crisis is likely to continue for quite a while yet. Congresses have been cancelled for the second year running and transformed once again into virtual congresses. International conference travel is not going to be possible in the coming months and possibly considerably longer. While virtual meetings have made it possible for many people to participate who would otherwise not have been able to do so, including patient advocates, what everyone misses is the personal contact, the networking, and indeed the exhibitions where you can personally examine and discuss the latest developments and treatments from the pharma world. However, societies and other organisations have taken up the challenge not only with regard to virtual congresses but also continuous online education. Since software for online meetings and complete congresses is continually developing and greatly improving, we can look forward to innovative virtual congresses in 2021 including virtual networking and exhibitions.

WEBINARS

There have been innumerable webinars in the past months. In the field of IC/BPS and chronic pelvic pain we have been spoilt for choice, especially with the many educational and discussion webinars organized from India by the Global Interstitial Cystitis Bladder Pain Society (GIBS) (<https://gibsociety.com/>) and attended by hundreds of healthcare providers and patients worldwide. A welcome development is that GIBS has taken the initiative to involve many gynaecologists as speakers in their educational sessions. This will be of great value to patients. Many of these webinars have been organised in association with other institutes and societies, including recently a Chronic Pelvic Pain Symposium with the South African Urological Association (SAUA). These webinars have clearly revealed the great confusion felt by physicians everywhere concerning the multiple different names and definitions for this disease and total lack of any consensus worldwide. Steps really have to be taken to rectify this for the sake of the patients. It cannot wait any longer.

NEWS FROM IMI-PAINCARE

The IMI-PainCare Research Consortium held its Annual General Assembly on 2-4 March 2021, conducted as a virtual meeting due to the Covid-19 pandemic. With the project now approximately halfway into the funding period, more than 70 consortium members, including the patient representatives for chronic pelvic pain, endometriosis and IC/BPS, together with IMI scientific officer Elisabetta Vaudano and the external ethics and

scientific advisors, discussed exciting achievements and ongoing activities as well as the valuable input of the patient representatives Judy Birch, Lone Hummelshoj and Jane Meijlink.

Read more: <https://www.imi-paincare.eu/NEWS/>

NEW BOOKS

Diagnosis and Management in Patients with Chronic Pelvic Pain Syndrome

Authors: Jörgen Quaghebeur, Jean-Jacques Wyndaele

ISBN-13: 978-1-5275-6450-3 - ISBN-10: 1-5275-6450-9

Date of Publication: 27/01/2021 – Pages: 178

Published by: Cambridge Scholars Publishing

<https://www.cambridgescholars.com/product/978-1-5275-6450-3>

This book is an update for students and practitioners. Chronic pelvic pain (CPP) involves a list of deviations with persistent pain in the pelvic area as the main factor. Multiple pain syndromes exist, and after assessment, often the reason for the chronic symptoms remains unclear. The exclusion of curable pathology that causes pain is of the highest importance. When no reasons for the pain are found, or when the pain cannot be cured, symptomatic treatment will be necessary. The most successful treatment is a multidisciplinary approach. Doctors, nurses, physical therapists, osteopaths, psychologists and other disciplines can be of help. Chronic pain has an essential impact on the quality of life and substantial negative consequences on these patients' psychological and emotional state. The success of the treatment is not easy to predict. Usually, it will be long term. After a general discussion, most parts of the small pelvis's pain-related abnormalities are described, and specific treatments are discussed separately.

Cystitis UNMASKED

Author: James Malone-Lee

Date of Publication: February 2021 - Pages: 350 - Published by: TFM Publishing Ltd

ISBN: 978-1-910079-63-8

<https://www.tfmpublishing.com/catalog/product/view/id/275/s/cystitis-unmasked/>

This book covers the history of the medicine of urinary tract infection (UTI); the urinary microbiome and what the microbes are really up to; the battles between the pathogens and the innate immune system; the truth about the tests and the criteria used to define UTI; antimicrobial resistance and the importance of Darwinian evolution; the science and ground-breaking research on UTIs; the use of antibiotics; successful treatment; supportive and other related treatments; ethics; the future; and, above all, the experiences of the patients. Professor James Malone-Lee's research group in London made discoveries that challenged numerous strongly held beliefs about lower urinary tract disease, particularly infection. For many years this new knowledge was rejected by many, but in the wake of corroborative evidence from others around the world, this new thinking is becoming more widely accepted.

Good Research Practice in Non-Clinical Pharmacology and Biomedicine

Editors: Anton Bespalov, Martin C. Michel, Thomas Steckler

Date of publication: 2020

Published by: SpringerOpen, EQIPD.

Open Access

This open access book, published under a CC BY 4.0 license in the Pubmed indexed book series Handbook of Experimental Pharmacology, provides up-to-date information on best practice to improve experimental design and quality of research in non-clinical pharmacology and biomedicine. Provides a good insight into how research is done. Further information: <https://link.springer.com/book/10.1007/978-3-030-33656-1#about>

PATIENT EDUCATION

EUPATI (EUROPEAN PATIENTS' ACADEMY ON THERAPEUTIC INNOVATION)- OPEN CLASSROOM

Patient education initiative EUPATI has launched the EUPATI Open Classroom, an e-learning platform that will expand access to the EUPATI Patient Expert Training Programme. The course started life under the IMI project EUPATI as a 14-month course on medicines research and development combining online and face-to-face

learning. Graduates receive a certificate and are known as EUPATI Fellows, and the skills and knowledge gained allow them to contribute to medicines R&D in a wide range of ways. EUPATI received additional funding from EIT (European Institute for Innovation and Technology) Health to transform the training content into smaller units following a MOOC ('massive open online course') format. This new version of the programme is now available via the EUPATI Open Classroom. Access to the EUPATI Open Classroom is open to anyone in the world. Those who want to become a EUPATI Fellow can still do so by registering as a learner and following the full programme and attending two training events. However, it is now also possible to register as a learner and choose and complete individual courses. There is no fee for accessing the courses, however those who want to complete the assessment (and receive a certificate if they pass) will have to pay a small fee. Registered learners can follow courses at their own pace and track their progress via a personalised dashboard. The EUPATI expert training programme (<https://learning.eupati.eu/>) is specially designed for patients, patient advocates and other stakeholders working in patient engagement activities in the private and/or public sector. The EUPATI Open Classroom is accessible [here](#).

COVID-19: INFORMATION ABOUT COVID-19 AND USEFUL ONLINE RESOURCES

- The International Alliance of Patients' Organizations (IAPO) has put together a very extensive COVID-19 resources hub at <https://www.iapo.org.uk/covid-19-resources-hub> which patients and their support groups around the world may find useful.
- Latest information is also available from the National Institutes of Health (NIH) at <https://www.coronavirus.gov/>
<https://covid19.nih.gov/>
<https://combatcovid.hhs.gov/>
- United Kingdom National Health Service (NHS): <https://www.nhs.uk/conditions/coronavirus-covid-19/>
- WHO Coronavirus disease (COVID-19) <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>
- CDC (Centers for Disease Control and Prevention): Things to Know about the COVID-19 Pandemic. <https://www.cdc.gov/coronavirus/2019-ncov/your-health/need-to-know.html>
- CDC (Centers for Disease Control and Prevention), USA: symptoms of coronavirus <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>
- CDC (Centers for Disease Control and Prevention), USA: risk of reinfection <https://www.cdc.gov/coronavirus/2019-ncov/your-health/reinfection.html>
- European Medicines Agency (EMA) <https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19#what's-new-section>
<https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines-covid-19>
- For speakers of Dutch, Dr Joop P. van de Merwe in the Netherlands is continually updating a very interesting and highly informative, well-documented overview of all aspects of COVID-19 (in Dutch). The introductory page with a link to the overview can be found at: <https://www.jpvandemerwe.nl/corona>

OVERVIEW OF UPCOMING EVENTS:

Many conferences that were rescheduled for this year have now been cancelled as physical meetings and are now virtual. These include the following events, but with so much uncertainty regarding the Covid-19 crisis it is wise to keep checking the websites for updates.

EULAR EUROPEAN CONGRESS OF RHEUMATOLOGY – 2-5 JUNE 2021

With the aim of protecting everyone's health and safety, EULAR has decided that the EULAR 2021 Congress will be virtual. The EULAR 2021 Virtual Congress will address a wide range of topics including clinical, translational and basic science. Sessions dedicated to People with Arthritis and Rheumatism in Europe (PARE), Health Professionals in Rheumatology (HPR) will feature prominently. Further information: www.congress.eular.org/about.cfm

IASP VIRTUAL WORLD CONGRESS ON PAIN 2021

The IASP Virtual World Congress on Pain organized by the International Association for the Study of Pain will take place 9-11 June and 16-18 June 2021. For further information: www.iaspworldcongress.org/

AMERICAN UROLOGICAL ASSOCIATION – AUA ANNUAL MEETING 2021

AUA2021 is offering extended programming this year. Virtual programs will be available from May to August, providing education on timely topics: May Kick-off: May 21 – 23; Summer School: June – August; Las Vegas: September 10 – 13: this is currently planned as a physical meeting. Further information: www.aua2021.org/

36th EAU ANNUAL CONGRESS 2021 NOW VIRTUAL

The European Association of Urology (EAU) has decided that with too many uncertainties about the current situation, it can best serve our members and congress delegates with an online-only EAU21 Virtual Congress. The EAU21 Virtual congress will take place from 8- 12 July 2021 with 5 days of pioneering urological research from key opinion leaders. The [congress website](#) will be continually updated over the coming weeks.

51st ICS ANNUAL SCIENTIFIC MEETING 2021 ONLINE

In order to provide its international audience with the safest and most accessible meeting experience during a time of continued travel restrictions and health concerns, the ICS has made the difficult decision to move the 2021 meeting Online. Originally planned for 12-15 October, there may be some changes to these dates. Further information will follow. Please note that the abstract submission deadline has moved to Tuesday 4th May 2021. Further information will become available at www.ics.org/2021

RESEARCH UPDATE

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

Most of these have a direct link to the PubMed abstract if you click on the title. An increasing number of scientific articles “In Press” or “Early View” are being published early online (on the Journal website) as “Epub ahead of print” sometimes long before they are published in the journals. While abstracts are usually available on PubMed, the pre-publication articles can only be read online if you have online access to that specific journal. However, in some cases there may be free access to the full article online. Click on the title to go to the PubMed abstract or to the full article in the case of free access.

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

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

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

TEMPORAL RELATIONSHIPS BETWEEN PAIN, MOOD AND URINARY SYMPTOMS IN UROLOGIC CHRONIC PELVIC PAIN SYNDROME (UCPPS): A MAPP NETWORK STUDY

Bruce D Naliboff, Andrew D Schrepf, Alisa J Stephens-Shields, J Quentin Clemens, Michael A Pontari, Jennifer Labus, Bayley J Taple, Larissa V Rodriguez, Eric Strachan, James W Griffith. J Urol. 2021 Feb 4;101097JU0000000000001595. doi: 10.1097/JU.0000000000001595. Online ahead of print. PMID: 33535797 DOI: 10.1097/JU.0000000000001595

The purpose of this MAPP study was to determine the time-lagged, bidirectional relationships among clinical variables of pelvic pain, urinary symptoms, negative mood, non-pelvic pain and quality of life (QOL) in men and women with UCPPS, incorporating IC/BPS and CP/CPSPS. 204 female and 166 male patients were assessed up to 24 times over a 48-week period on the five primary outcomes. A lagged autoregressive analysis was applied to determine the directional relationship of one variable to another two weeks later, beyond that of the concurrent relationships at each time point and autocorrelations and trends over time. The results show clear evidence for a bidirectional positive relationship between changes in pelvic pain severity and urinary symptom severity. Increases in either variable predicted significant increases in the other two weeks later, beyond that explained by their concurrent relationship at each time point. Pelvic pain and to a lesser degree urinary frequency also showed similar bidirectional relationships with negative mood and decreased QOL. Interestingly, neither pelvic pain nor urinary symptom severity showed lagged relationships with non-pelvic pain severity. It was concluded that the results document for the first time specific short-term positive feedback between pelvic pain and urinary symptoms, and between symptoms of UCPPS, mood, and QOL. The feedforward aspects of these relationships can facilitate a downward spiral of increased symptoms and worsening psychosocial function and suggest the need for multifaceted treatments and assessment to address this possibility in individual patients.

COMPARISON OF DEEP PHENOTYPING FEATURES OF UCPPS WITH AND WITHOUT HUNNER LESION: A MAPP-II RESEARCH NETWORK STUDY

H Henry Lai, Craig Newcomb, Steve Harte, Dina Appleby, A Lenore Ackerman, Jennifer T Anger, J Curtis Nickel, Priyanka Gupta, Larissa V Rodriguez, J Richard Landis, J Quentin Clemens, MAPP Research Network. Neurourol Urodyn. 2021 Feb 19. doi: 10.1002/nau.24623. Online ahead of print. PMID: 33604963 DOI: 10.1002/nau.24623

The aim of this study from the MAPP Network was to use the phenotyping data from the MAPP-II Symptom Patterns Study (SPS) to compare the systemic features between urologic chronic pelvic pain syndrome (UCPPS) with Hunner lesion (HL) versus those without HL. The authors performed chart review on 385 women and 193 men with UCPPS who enrolled in the MAPP-II SPS. 223 had cystoscopy and documentation of HL status. Among them, 12.5% had HL and 87.5% did not. UCPPS participants with HL were older, had increased nocturia, higher Interstitial Cystitis Symptom and Problem Indexes, and were more likely to report "painful urgency" compared with those without HL. On the other hand, UCPPS without HL reported more intense non-urologic pain, greater distribution of pain outside the pelvis, greater numbers of comorbid chronic overlapping pain conditions, higher fibromyalgia-like symptoms, and greater pain centralization, and were more likely to have migraine headache than those with HL. UCPPS without HL also had higher anxiety, perceived stress, and pain catastrophizing than those with HL. There were no differences in sex distribution, UCPPS symptom duration, intensity of urologic pain, distribution of genital pain, pelvic floor tenderness on pelvic examination, quality of life, depression, pain characteristics (nociceptive pain vs. neuropathic pain), mechanical hypersensitivity in the suprapubic area during quantitative sensory testing, and 3-year longitudinal pain outcome and urinary outcome between the two groups. It was concluded that UCPPS with HL displayed more bladder-centric symptom profiles, while UCPPS without HL displayed symptoms suggesting a more systemic pain syndrome. The MAPP-II SPS phenotyping data showed that Hunner lesion is a distinct phenotype from non-Hunner lesion.

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

SINGLE-CELL TRANSCRIPTOMES OF MOUSE BLADDER UROTHELIUM UNCOVER NOVEL CELL TYPE MARKERS AND UROTHELIAL DIFFERENTIATION CHARACTERISTICS

Yan Li, Yaxiao Liu, Zhengdong Gao, Lekai Zhang, Lipeng Chen, Zonglong Wu, Qinggang Liu, Shuai Wang, Nan Zhou, Toby C Chai, Benkang Shi. Cell Prolif. 2021 Feb 3;e13007. doi: 10.1111/cpr.13007. Online ahead of print. PMID: 33538002 DOI: 10.1111/cpr.13007

Much of the information to date in terms of subtypes and function of bladder urothelial cells derives from anatomical location or by the expression of a small number of marker genes. To have a comprehensive map of the cellular anatomy of bladder urothelial cells, the authors from China and Boston performed single-cell RNA sequencing to thoroughly characterize mouse bladder urothelium. A total of 18,917 single cells from mouse bladder urothelium were analysed by unbiased single-cell RNA sequencing. The expression of the novel cell marker was confirmed by immunofluorescence using urinary tract infection models. Unsupervised clustering analysis identified 8 transcriptionally distinct cell subpopulations from mouse bladder urothelial cells. They discovered a novel type of bladder urothelial cells marked by *Plxna4* that may be involved with host response and wound healing. They also found a group of basal-like cells labelled by *ASPM* that could be the progenitor cells of adult bladder urothelium. *ASPM*⁺ urothelial cells are significantly increased after injury by UPEC. In addition, specific transcription factors were found to be associated with urothelial cell differentiation. At the last, a number of IC/BPS-regulating genes were found differentially expressed among different urothelial cell subpopulations. The authors concluded that their study provides a comprehensive characterization of bladder urothelial cells, which is fundamental to understanding the biology of bladder urothelium and associated bladder disease.

EFFECT OF GLYCOSAMINOGLYCAN REPLACEMENT ON MARKERS OF INTERSTITIAL CYSTITIS IN VITRO

Peadar Rooney, Christina Ryan, Barry J McDermott, Kapil Dev, Abhay Pandit, Leo R Quinlan. Front Pharmacol. 2020 Dec 3;11:575043. doi: 10.3389/fphar.2020.575043. eCollection 2020. PMID: 33390947 PMCID: PMC775665 DOI: 10.3389/fphar.2020.575043

The aim of this study from Ireland was to examine the effect of three commercial intravesical formulations of glycosaminoglycan on in vitro inflammatory models of IC/BPS to better understand their effect on specific markers of disease. Human urothelial cells (HTB-4) were cultured under four conditions in the presence or absence of commercial GAG formulations. Cells were cultured under a basal condition or pre-treated with protamine sulfate (100 ng/ml) (damages the endogenous glycosaminoglycan layer), hydrogen peroxide (1%) (a metabolic stressor) or TNF α (10 ng/ml) (creating an inflammatory environment). Each of these four culture

conditions was then treated with one of three GAG formulations, Cystistat®[®], iAluRil®[®] and Hyacyst®[®]. Assays were then performed to examine the effect of the exogenous GAGs on cell viability, cell migration, sGAG production, cytokine and gene expression. All GAG formulations were well tolerated by the HTB-4 cells and supported cell growth and migration. iAluRil®[®] was most effective at stimulating endogenous sGAG production under all conditions, increasing sGAGs by up to 15-fold. All GAG formulations significantly reduced the production of the pro-inflammatory cytokine IL-8 under basal conditions, while no GAG treatment suppressed cytokine production under any other condition. Only Cystistat®[®] had a significant effect on HA receptor expression, significantly increasing ICAM-1 expression at 3 h that returned to basal levels at 24 h. No GAG treatment significantly changed the expression of GAG synthesis enzymes (CSGALNACT1, CSGALNACT2) or markers of tissue remodelling (MMP2, TIMP1) and pain (COX-1/PTGS-1, NGF). The data presented in this study reveal that commercial intravesical formulation support cell viability and migration. In addition, the commercial GAG formulations have a mild anti-inflammatory effect in the in vitro model of interstitial cystitis/bladder pain syndrome.

GABAPENTIN REDUCES PAINFUL BLADDER HYPERSENSITIVITY IN RATS WITH LIPOPOLYSACCHARIDE-INDUCED CHRONIC CYSTITIS

Masaru Yoshizumi, Chizuko Watanabe, Hirokazu Mizoguchi. *Pharmacol Res Perspect*. 2021 Feb;9(1):e00697. doi: 10.1002/prp2.697. PMID: 33340266 PMCID: PMC7749515 DOI: 10.1002/prp2.697

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

Although IC/BPS is a chronic condition causing bladder pain and urinary symptoms, effective treatments have not been established. The aim of this study from Japan was to adapt a chronic cystitis model in rats using lipopolysaccharide (LPS), which reflects IC/BPS pathology, and characterize the model's histological and behavioral effects. Furthermore, the authors investigated the effect of an $\alpha 2 \delta$ subunit ligand, gabapentin (GBP), on bladder hypersensitivity of rats with chronic cystitis. Cystitis models were created by repeated intravesical injections of LPS. In the histological examination, the LPS-injected group had greater inflammatory response, fibrosis, and abnormally thick re-epithelialization. In the LPS-injected group, LPS prompted hyperalgesia in both the lower abdomen and hind paw regions after day 1 of the first injection compared with the saline-injected controls, without any recovery for 21 days at least. During cystometry, the LPS-injected group showed bladder hyperactivity at all times. Systemic administration of GBP reduced cystitis-related pain due to chronic inflammation and reduced the increased frequency of voiding in the LPS-injected group. These results suggest that repeated intravesical injections of LPS induce long-lasting bladder inflammation, pain, and overactivity in rats, while GBP is effective in the management of those symptoms in this chronic cystitis model. The current study identifies a relatively simple method to develop an animal model for chronic cystitis and provides evidence that GBP may be an effective treatment option for patients with IC/BPS.

EDITORIAL COMMENT: INTRAVESICAL INJECTIONS OF PLATELET-RICH PLASMA IS EFFECTIVE AND SAFE IN TREATMENT OF INTERSTITIAL CYSTITIS REFRACTORY TO CONVENTIONAL TREATMENT-A PROSPECTIVE CLINICAL TRIAL

Cássio L Z Riccetto. *Int Braz J Urol*. Mar-Apr 2021;47(2):456-457. doi: 10.1590/S1677-5538.IBJU.2021.02.04. PMID: 33284551 DOI: 10.1590/S1677-5538.IBJU.2021.02.04

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

In this study, the authors assessed the effects of four monthly intravesical injections of 10 mL of autologous platelet-rich plasma (PRP) in 40 patients (37 women and 3 men, aged 55.5 ± 11.1 years) with IC / BPS who had previously failed to conventional treatments, including lifestyle modifications, cystoscopic hydrodistention, non-steroid anti-inflammatory drugs, oral Pentosan Polysulfate, tricyclic antidepressants, intravesical instillation of hyaluronic acid, or botulinum toxin A injection. Diagnosis of IC/BPS was based on symptoms and cystoscopic findings. Patients with Hunner's injury were not included. The authors note that if we assume that one of the most relevant pathophysiological mechanisms of IC is the increase in urothelial permeability related to proteoglycan deficiency, the use of PRP has a consistent rationale and may be clinically useful, mainly if other researchers are able to reproduce such results.

QUALITATIVE ANALYSIS OF TREATMENT NEEDS IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: IMPLICATIONS FOR INTERVENTION

Lindsey C McKernan, Kemberlee R Bonnet, Michael T M Finn, David A Williams, Stephen Bruehl, W Stuart Reynolds, Daniel Clauw, Roger R Dmochowski, David G Schlundt, Leslie J Crofford. *Can J Pain*. 2020;4(1):181-198.

doi: 10.1080/24740527.2020.1785854. Epub 2020 Sep 1. PMID: 33367196 PMCID: PMC7751614 (available on 2021-01-01) DOI: 10.1080/24740527.2020.1785854

IC/BPS is a debilitating condition carrying substantial psychosocial burden. Psychological treatment for IC/BPS is little studied, and there are barriers to its use in clinical management. Whether psychological treatments benefit patients with IC/BPS is unclear and it is not known if such treatments would meet patient needs. Incorporating patient-reported needs and acknowledging diversity in pain experiences can inform patient-centred interventions for IC/BPS. This project characterized the experience of living with IC/BPS and patient perceptions of needs in its treatment, with the goal of informing patient-centred treatment for IC/BPS. Using both quantitative and qualitative methods, 27 females with IC/BPS participated in a focus group and completed validated self-report assessments evaluating urinary symptoms, pain, and emotional functioning. Focus groups were audio recorded and transcribed, then coded and analyzed using an iterative inductive/deductive approach. Linear regression models evaluated the relationship between psychological functioning and symptom severity. The authors conducted six focus groups between 8/2017-12/2017. Five major themes emerged from qualitative analysis: managing physical symptoms, emotional symptoms, impact on daily life and socio-contextual factors, responding to illness, and addressing needs in treatment. The physiological and emotional consequences of IC/BPS were reported, highlighting their impact on interpersonal relationships and challenges obtaining appropriate treatment for IC/BPS. Quantitative analysis showed depression levels were significantly associated with worsened IC/BPS symptomology, after controlling for known confounding factors. It was concluded that individuals with IC/BPS could benefit from tailored psychological interventions focusing on pain management, emotion regulation, communications skills, along with sexual dysfunction and intimacy fears.

CYSTOSCOPIC HYDRODISTENTION CHARACTERISTICS PROVIDE CLINICAL AND LONG-TERM PROGNOSTIC FEATURES OF INTERSTITIAL CYSTITIS AFTER TREATMENT

Wan-Ru Yu, Jia-Fong Jhang, Han-Chen Ho, Yuan-Hong Jiang, Cheng-Ling Lee, Yung-Hsiang Hsu, Hann-Chorng Kuo. *Sci Rep.* 2021 Jan 11;11(1):455. doi: 10.1038/s41598-020-80252-x. PMID: 33432045 DOI: 10.1038/s41598-020-80252-x

The purpose of this study from Taiwan was to evaluate the correlations of clinical symptoms, urodynamic parameters, and long-term treatment outcomes with different findings of cystoscopic hydrodistention (HD) in patients with IC/BPS. This retrospective analysis of 486 patients with IC/BPS investigated baseline clinical symptoms, disease duration, medical comorbidities, urodynamic findings, cystoscopic characteristics [including maximal bladder capacity (MBC) and the presence of glomerulations and Hunner's lesions], and outcomes according to the five IC/BPS HD subtypes based on the glomerulation grade, MBC, and the presence of Hunner's lesions. Receiver operation characteristic analysis identified an optimal cutoff value of MBC \geq 760 ml as a predictor of satisfactory outcomes. Glomerulation grade and MBC were significantly correlated ($r = -0.403$, $P < 0.001$), and both were significantly associated with IC Symptom Index scores. The rate of satisfactory outcomes was better for the patients with low glomerulation grade and MBC \geq 760 ml (64.2%), and significantly worse for those with Hunner's lesions (36.8%); no significant differences were noted among the other groups. The results suggested that IC/BPS patients can be classified into the following three distinct subgroups: (1) those with low glomerulation grade and MBC \geq 760 ml; (2) those with low glomerulation grade and MBC $<$ 760 ml, or with high glomerulation grade regardless of MBC; and (3) those with Hunner's lesions. The results showed that three IC/BPS subgroups had distinct bladder characteristics and treatment outcomes. The patients with high MBC and low glomerulation grade after HD had more medical comorbidities but a significantly higher rate of satisfactory treatment outcome.

INTRAVESICAL THERAPY FOR BPS/IC

Jean-Jacques Wyndaele. *Curr Bladder Dysfunct Rep* 16, 6–11 (2021). <https://doi.org/10.1007/s11884-020-00625-w>

This manuscript gives a recent overview of intravesical treatments in patients with bladder pain syndrome/interstitial cystitis (BPS/IC). The newest data on GAG replenishment therapy, intravesical local anaesthetics, DMSO, botulinum toxin, experimental drugs, and ways of application are discussed. The literature data show symptomatic therapeutic successes in a limited number of patients with most treatments discussed here. The heterogeneity of BPS/IC, the absence of clear knowledge of the cause in each patient, the different phenotypes included in the same research sample, the variability of dosage, and application frequency make interpretation of study results difficult. Treatment can aim at restoring a deficient GAG, to block the pain with local analgesics, and to lessen local inflammation, but it is uncertain from which treatment an individual patient will benefit most: trial and error are mostly used. Exclusion of many confusable diseases and Hunner lesions is the first step to indicate the treatment options with the most chance of success. The actual trial and error

approach is the only available way so far for intravesical treatment in patients with BPS/IC. The overall results are acceptable, but a better understanding of the symptom syndrome and better phenotyping of BPS/IC patients will most probably improve the outcome in individual patients.

BIOMARKERS FOR BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.

Charrua A, Mendes, P, Cruz C. Curr Bladder Dysfunct Rep 16, 12–18 (2021). <https://doi.org/10.1007/s11884-020-00626-9>

In this manuscript, the literature published in the past 5 years about BPS/IC biomarkers was reviewed. Topics include BPS/IC biomarkers, the classical BPS/IC diagnostic, clinical outcomes as a new concept of BPS/IC phenotyping biomarkers, BPS/IC urinary biomarkers, BPS/IC bladder tissue biomarkers and BPS/IC biomarkers outside the bladder. The importance of patients' phenotyping and sub-grouping emerged as a way of finding new BPS/IC biomarkers and treatment. Also, the use of non-invasive methodologies and of artificial intelligence approaches has been gaining momentum in BPS/IC biomarkers studies. Biomarker research points to the need of following an approach based on a systemic theory instead of a bladder-centred theory. Also, the importance of sample size and the choice of controls to validate BPS/IC biomarkers have been elevated.

COGNITION, EMOTION, AND THE BLADDER: PSYCHOSOCIAL FACTORS IN BLADDER PAIN SYNDROME AND INTERSTITIAL CYSTITIS (BPS/IC)

Sula Windgassen, Lindsey McKernan. Curr Bladder Dysfunct Rep. 2020 Mar;15(1):9-14. doi: 10.1007/s11884-019-00571-2. Epub 2020 Jan 31. PMID: 33456639 PMCID: PMC7810165 (available on 2021-03-01) DOI: 10.1007/s11884-019-00571-2

The purpose of this review from London and Nashville was to review findings from empirical studies assessing the role of psychosocial factors in bladder pain syndrome and interstitial cystitis (BPS/IC). There is a high rate of psychosocial comorbidity in BPS/IC, including elevated levels of anxiety and depression. Recent studies assessing the role of illness perceptions in BPS/IC relate poorer illness perceptions to more unhelpful illness coping patterns. Conversely, positive illness perceptions including self-efficacy in illness management are associated with more adaptive coping behaviors such as exercising and acceptance. New research is investigating the role of trauma in BPS/IC and the impact of suicidality. There is a paucity of psychosocial interventions for BPS/IC over the last 5 years. The three small-scale studies reviewed included a mindfulness-based stress reduction (MBSR) intervention tailored for BPS/IC, a brief self-management intervention designed to increase patient knowledge and symptom management techniques and a 90-minute interview aimed at increasing awareness about physiological-affective relationship in IC.

PREVALENCE OF CHILDHOOD TRAUMA AND ITS ASSOCIATION WITH LOWER URINARY TRACT SYMPTOMS IN WOMEN AND MEN IN THE LURN STUDY

Julia Geynisman-Tan, Margaret Helmuth, Abigail R Smith, H Henry Lai, Cindy L Amundsen, Catherine S Bradley, Margaret G Mueller, Christina Lewicky-Gaupp, Steven E Harte, J Eric Jelovsek, Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN) Study Group. NeuroUrol Urodyn. 2021 Jan 28. doi: 10.1002/nau.24613. Online ahead of print. PMID: 33508156 DOI: 10.1002/nau.24613

The aim of this study from the USA was to describe the association between childhood traumas (death of a family member, severe illness, sexual trauma, parental separation) reported by women and men and lower urinary tract symptoms (LUTS). In this secondary analysis of the Lower Urinary Tract Research Network Observational Cohort Study, participants completed the LUTS tool, childhood trauma events scale (CTES), PROMIS depression and anxiety and perceived stress scale. LUTS tool responses were combined to quantify urinary urgency, frequency, incontinence, and overall LUTS severity. Multivariable linear regression tested associations between trauma and LUTS; mental health scores were tested for potential mediation. It was concluded that although total childhood trauma is not associated with LUTS, childhood sexual trauma is associated with urinary incontinence severity. For patients with childhood trauma, half the effect of CTE Impact score on overall LUTS severity is mediated through the association between trauma and the patient's mental health.

SUPERGAG BIOPOLYMERS FOR TREATMENT OF EXCESSIVE BLADDER PERMEABILITY

Rheal A Towner, Beverley Greenwood-Van Meerveld, Ehsan Mohammadi, Debra Saunders, Nataliya Smith, Grannum R Sant, Harrison C Shain, Thomas H Jozefiak, Robert E Hurst. Pharmacol Res Perspect. 2021 Feb;9(1):e00709. doi: 10.1002/prp2.709. PMID: 33540486 DOI: 10.1002/prp2.709

Few therapeutic options exist for treatment of IC/BPS. A novel high MW GAG biopolymer ("SuperGAG") was synthesized by controlled oligomerization of CS, purified by TFF and characterized by SEC-MALLS and 1H-NMR

spectroscopy. The modified GAG biopolymer was tested in an OVX female rat model in which bladder permeability was induced by a 10-minute intravesicular treatment with dilute (1 mg/ml) protamine sulfate and measured by classical Ussing Chamber TEER measurements following treatment with SuperGAG, chondroitin sulfate, or saline. The effect on abrogating the abdominal pain response was assessed using von Frey filaments. The SuperGAG biopolymer was then investigated in a second, genetically modified mouse model (URO-MCP1) that increasingly is accepted as a model for IC/BPS. Permeability was induced with a brief exposure to a sub-noxious dose of LPS and was quantified using contrast-enhanced MRI (CE-MRI). The SuperGAG biopolymer restored impermeability to normal levels in the OVX rat model as measured by TEER in the Ussing chamber and reduced the abdominal pain response arising from induced permeability. Evaluation in the URO-MCP1 mouse model also showed restoration of bladder impermeability and showed the utility of CE-MRI imaging for evaluating the efficacy of agents to restore bladder impermeability. The authors concluded that novel high MW SuperGAG biopolymers are effective in restoring urothelial impermeability and reducing pain produced by loss of the GAG layer on the urothelium. SuperGAG biopolymers could offer a novel and effective new therapy for IC/BPS, particularly if combined with MRI to assess the efficacy of the therapy.

EFFICACY OF CLORPACTIN IN REFRACTORY BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS: A RANDOMIZED CONTROLLED TRIAL

Kristina Cvach, Anna Rosamilia, Peter Dwyer, Yik Lim, Alison DeSouza, Linli Ow, Elizabeth Thomas, Christine Murray, Alison Leitch, Lore Schierlitz. Int Urogynecol J. 2021 Jan 16. doi: 10.1007/s00192-020-04652-3. Online ahead of print. PMID: 33452887 DOI: 10.1007/s00192-020-04652-3

Clorpectin is an antibacterial agent with limited evidence for its use as instillation therapy in patients with BPS/IC. This study from Australia was a multi-centre, single-blinded randomized controlled trial to investigate whether Clorpectin instillation results in symptom improvement in patients with refractory BPS/IC. Fifty women with refractory BPS/IC were randomized to undergo cystoscopy/hydrodistension (25) or instillation of Clorpectin 0.4% solution (25) under general anaesthesia. Primary outcome was based on Global Response Assessment (GRA) at 3 months; secondary outcomes were based on O'Leary Sant Symptom (OLSI) and Problem (OLPI) questionnaire scores, visual analogue scale (VAS) score for pain and bladder diary parameters. Complete follow-up data were available on 22 in the hydrodistension group and 16 in the Clorpectin group. GRA improvement was 4.5% for hydrodistension and 56% for Clorpectin ($p = 0.001$) at 3 months. Reduction in mean total scores for OLSI (14.1 to 9.1; $p = 0.004$) and OLPI (12.6 to 7.4; $p = 0.001$) was seen in the Clorpectin group only. VAS pain scores were reduced in the Clorpectin group only (7.4 to 3.3; $p < 0.001$). Post-treatment VAS pain scores did not differ between groups although 6/25 (24%) women in the Clorpectin group required admission for pain compared to 1/25 (4%) in the hydrodistension group. It was concluded that Clorpectin treatment results in significant improvement in BPS/IC symptoms, bother and pain based on the GRA, OLSI/OLPI and VAS pain scores at 3 months post-treatment compared to cystoscopy/hydrodistension. These conclusions are limited by the high loss to follow-up in both groups.

URINE BIOMARKERS IN ESSIC TYPE 2 INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME AND OVERACTIVE BLADDER WITH DEVELOPING A NOVEL DIAGNOSTIC ALGORITHM

Yuan-Hong Jiang, Jia-Fong Jhang, Yung-Hsiang Hsu, Han-Chen Ho, Ya-Hui Wu, Hann-Chorng Kuo. Sci Rep. 2021 Jan 13;11(1):914. doi: 10.1038/s41598-020-80131-5. PMID: 33441752 PMCID: PMC7806856 DOI: 10.1038/s41598-020-80131-5

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This study from Taiwan aimed to investigate the diagnostic values of urine cytokines in IC/BPS and OAB patients, and to develop a novel diagnostic algorithm. Urine samples were collected from 40 IC/BPS, 40 OAB patients, and 30 controls. Commercially available multiplex immunoassays were used to analyze 31 targeted cytokines. Urine cytokine profiles were significantly different among study groups and controls. MIP-1 β showed the highest sensitivity (92.2%) for identifying diseased study patients from controls. The cytokines with high diagnostic values for distinguishing between IC and OAB included IL-10, RANTES, eotaxin, CXCL10, IL-12p70, NGF, IL-6, IL-17A, MCP-1, and IL-1RA. The diagnostic algorithm was subsequently developed according to the diagnostic values obtained. MIP-1 β was selected for the initial screening test to diagnose diseased patients and controls with diagnostic rates of 81.6% and 68.4%, respectively. As confirmation tests for IC/BPS, the diagnostic rates of eotaxin, CXCL10, and RANTES were 73.3%, 72.7%, and 69.7%, respectively. As the confirmation test for OAB, the diagnostic rate of IL-10 was 60%. Urine cytokine profiles of IC/BPS and OAB patients differed from those of controls and might be useful as biomarkers for diagnosis. A novel pilot diagnostic algorithm was developed based on these profiles.

CYSTOSCOPIC HYDRODISTENTION CHARACTERISTICS PROVIDE CLINICAL AND LONG-TERM PROGNOSTIC FEATURES OF INTERSTITIAL CYSTITIS AFTER TREATMENT

Wan-Ru Yu, Jia-Fong Jhang, Han-Chen Ho, Yuan-Hong Jiang, Cheng-Ling Lee, Yung-Hsiang Hsu, Hann-Chorng Kuo. *Sci Rep.* 2021 Jan 11;11(1):455. doi: 10.1038/s41598-020-80252-x. PMID: 33432045 PMCID: PMC7801576 DOI: 10.1038/s41598-020-80252-x

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The purpose of this study from Taiwan was to evaluate the correlations of clinical symptoms, urodynamic parameters, and long-term treatment outcomes with different findings of cystoscopic hydrodistention (HD) in patients with IC/BPS. This retrospective analysis of 486 patients with IC/BPS investigated baseline clinical symptoms, disease duration, medical comorbidities, urodynamic findings, cystoscopic characteristics [including maximal bladder capacity (MBC) and the presence of glomerulations and Hunner's lesions], and outcomes according to the five IC/BPS HD subtypes based on the glomerulation grade, MBC, and the presence of Hunner's lesions. Receiver operation characteristic analysis identified an optimal cutoff value of MBC \geq 760 ml as a predictor of satisfactory outcomes. Glomerulation grade and MBC were significantly correlated ($r = -0.403$, $P < 0.001$), and both were significantly associated with IC Symptom Index scores. The rate of satisfactory outcomes was better for the patients with low glomerulation grade and MBC \geq 760 ml (64.2%), and significantly worse for those with Hunner's lesions (36.8%); no significant differences were noted among the other groups. The results suggested that IC/BPS patients can be classified into the following three distinct subgroups: (1) those with low glomerulation grade and MBC \geq 760 ml; (2) those with low glomerulation grade and MBC $<$ 760 ml, or with high glomerulation grade regardless of MBC; and (3) those with Hunner's lesions. The results showed that three IC/BPS subgroups had distinct bladder characteristics and treatment outcomes. The patients with high MBC and low glomerulation grade after HD had more medical comorbidities but a significantly higher rate of satisfactory treatment outcome.

WOMEN'S EXPERIENCES OF INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME

Angela Kirkham, Katherine Swainston. *West J Nurs Res.* 2021 Jan 29;193945921990730. doi: 10.1177/0193945921990730. Online ahead of print. PMID: 33514302 DOI: 10.1177/0193945921990730

The aim of this UK study was to explore the lived experience of IC/PBS. A phenomenological approach with emphasis on reflection and openness was adopted. Twenty women diagnosed with IC an average of nine years prior to data collection produced a written account of their experiences. The textual data was analyzed using thematic analysis. Four themes were derived from data analysis: diagnostic uncertainty; restrictions and limitations on life; self-management; and interpersonal relationships and social support. Women reported issues in receiving a diagnosis of IC, undergoing numerous diagnostic tests, and experiencing multiple referrals. Having undergone numerous treatments with limited success, women sought information and management strategies outside of standard medical care and reported a negative impact on sexual and social relationships. The findings illustrate the complex nature of women's experiences and the physical and psychological impacts and effects of IC/PBS on women's daily lives.

COMPARISON OF INTRAVESICAL HYALURONIC ACID, CHONDROITIN SULFATE AND COMBINATION OF HYALURONIC ACID-CHONDROITIN SULFATE THERAPIES IN ANIMAL MODEL OF INTERSTITIAL CYSTITIS

Yavuz Onur Danacioglu, Bulent Erol, Seyma Ozkanli, Asif Yildirim, Ramazan Gokhan Atis, Mesur Selcuk Silay, Turhan Caskurlu. *Int Neurourol J.* 2021 Jan 19. doi: 10.5213/inj.1938176.088. Online ahead of print. PMID: 33504136 DOI: 10.5213/inj.1938176.088

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In this study from Turkey, three different intravesical treatment agents were compared by the effectiveness; chondroitin sulphate, hyaluronic acid and hyaluronic acid-chondroitin sulphate combination in a rat interstitial cystitis model. Thirty-five female rats were divided into five groups by and control (group I), isotonic (group II), chondroitin sulphate (group III), hyaluronic acid (group IV), hyaluronic acid-chondroitin sulphate combination (group V). Chemical cystitis was induced in all groups by intravesical instillation of hydrogen peroxide (H₂O₂) via transurethral route except sham control group. 1 ml of 5% H₂O₂ was instilled intravesically for 15 min to create chemical cystitis. The treatment protocol was administered every other day for a total of three sessions in all the groups two days after the formation of chemical cystitis except the group I. All the animals in the group II, III, IV and V were treated with 1 ml 0.9% NaCl, 1 ml 0.2% sodium chondroitin sulfate, 1 ml low molecular weight hyaluronic acid, 1 ml 2% sodium chondroitin sulfate + 1.6% sodium hyaluronic acid, respectively. On the seventh day, the animals were sacrificed and the bladders were removed for histopathological and immunohistochemical assessment. Based on histopathological examinations, there was a significant difference between the groups in terms of vascular congestion ($p=0.006$). The grade of submucosal edema in the group II

and group IV were found significantly higher than group I ($p=0.006$; $p=0.006$). In the group I, the grade of granulation tissue was lower than the other four groups, but no significant difference was found between these four groups ($p=0.016$). The intensity of neutrophil cell infiltration in group II and group IV were higher than group I ($p=0.006$; $p=0.006$; respectively). According to the analysis of leukocyte and mast cell count; significant differences were detected between the groups ($p<0.001$; $p<0.001$). Immunohistochemical evaluation revealed that the abnormal immunoreactivity of ZO-1 and UP-III in the group II were higher than group I, group III and group V ($p=0.002$, $p=0.010$). The level of IL-8 expression was lower in group V than I group II ($p=0.001$). The authors conclude that single treatment of chondroitin sulphate and combination treatment of hyaluronic acid-chondroitin sulphate agents provides treatment efficacy by suppressing inflammatory process and achieving improvement in the urothelium.

LONG-TERM OUTCOMES OF SACRAL NERVE STIMULATION IN PELVIC FLOOR DYSFUNCTIONS

David Hernández-Hernández, Bárbara Padilla Fernánd, Milagros Castro Romera, Stephany Hess Medler, David Castro-Díaz. Int Neurourol J. 2021 Jan 27. doi: 10.5213/inj.2040364.182. Online ahead of print. PMID: 33504121 DOI: 10.5213/inj.2040364.182

The aim of this study from Spain was to analyse the long-term outcomes of SNS at a reference centre in both idiopathic and neurogenic pelvic floor disorders. Retrospective observational study analysing the records of 106 tested patients in our department from December 1999 to January 2017. Efficacy variables evaluated were Global Response Assessment (GRA) (range from 0 to 100%) and, according to clinical indication, other specific variables such International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF), number of catheterizations or pads/day and numerical pain scale (NPS). Safety variables analysed were complications (pain, migration, infection), reinterventions and explants. The quality of life (QoL) and satisfaction with the procedure were evaluated through a telephone interview. Clinical indications: OAB ($n=36$), urinary retention (UR) ($n=37$), BPS/IC ($n=19$), faecal incontinence (FI) ($n=8$), double incontinence (DI) ($n=6$). Implant rates: OAB 55.6%, UR 56.8%, BPS/IC 63.15%, FI 87.5% and DI 66.7%. Clinical and/or statistically significant improvements in all efficacy variables studied were observed. The loss of therapeutic effect at 75 months follow-up was 34%. Device-related pain appeared in 25 patients (39%), 20 resolved by reprogramming and 5 required device removal. An overall improvement in QoL and high levels of satisfaction with the procedure were observed. More than 90% of patients would recommend SNS to a friend or relative. It was concluded that SNS is a minimally invasive procedure that offers a real alternative to patients with refractory pelvic floor dysfunctions. Its safety profile is very favourable and provides a long-lasting improvement in symptoms and QoL.

SPONTANEOUS MISCARRIAGES IN PATIENTS WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS - EFFECT OF STRESS ON INFLAMMATION?

P C Theoharides, S Christodoulou, A Athanasiou. J Biol Regul Homeost Agents. 2020 Dec 30;35(1). doi: 10.23812/20-528-E. Online ahead of print. PMID: 33494583 DOI: 10.23812/20-528-E

IC/PBS affects mostly women and is characterized by pelvic pain or pressure and frequency of voiding in the absence of urinary tract infection. Acute stress worsens IC/PBS symptoms and bladder inflammation associated with increased number of activated mast cells. The authors investigated retroactively the incidence of spontaneous miscarriages and any related stress in IC/PBS patients. A questionnaire was posted on an IC/PBS website and patients visiting the site were invited to complete and file it electronically. Limitations include the lack of defined diagnosis of those responding, and of a validated stress questionnaire. There were 193 respondents (mean age = 37.3 years) over two weeks. Of those responding, 87% (mean age = 33.2 years) had received a diagnosis of IC/PBS. Of those respondents with IC/PBS, 76% reported having had miscarriages: (a) 55% had one miscarriage, (b) 26% had two, and (c) 23% had three or more. These rates are much higher than those of in the general population: 10-20% with one and 1-2% with habitual spontaneous miscarriages. The majority of patients (78%) reported experiencing significant stress. IC/PBS patients appear to have a much high incidence of spontaneous miscarriages compared to the general population. Most patients reported experiencing stress that has been associated with miscarriages. This finding may be explained via stress stimulating bladder and uterine immune cells, especially mast cells, inhibition of which by the natural flavonoid luteolin may be beneficial.

LIFESTYLE AND BEHAVIORAL MODIFICATIONS MADE BY PATIENTS WITH INTERSTITIAL CYSTITIS

Krystal Bay-San Lin, Ming-Ping Wu, Yen-Kuang Lin, Yu-Chun Yen, Yao-Chi Chuang, Hung-Yen Chin. Sci Rep. 2021 Feb 4;11(1):3055. doi: 10.1038/s41598-021-82676-5. PMID: 33542405 DOI: 10.1038/s41598-021-82676-5

IC/BPS negatively affects the quality of life. In this study, the authors investigated the lifestyle behavioral changes patients with IC/BPS make to cope with their symptoms. This prospective study from Taiwan and China was

conducted between August 2018 and June 2019. All patients had a primary symptom of suprapubic pain with a full bladder and other lower urinary tract symptoms for more than 6 weeks as well as cystoscopic findings. All participants completed our self-developed questionnaire, which included information about their living and work environment, occupational garments, dietary habits, and personal habits. Continuous variables were compared using an independent sample t test, and categorical variables were compared using a chi-square test. The authors recruited 86 patients with IC/BPS and age-matched 86 controls without IC/BPS. In our study, patients with IC/BPS had more cranberry intake (45.34% vs. 5.81%, $P < 0.05$) than non-IC/BPS controls; the IC/BPS group had decreased consumption of coffee and spicy food; and wore less makeup or special work garments. In conclusion, patients with IC/BPS tend to make several lifestyle behavioral changes to cope with their symptoms.

[ADENOSINE A 2A RECEPTOR AGONIST POLYDEOXYRIBONUCLEOTIDE ALLEVIATES INTERSTITIAL CYSTITIS-INDUCED VOIDING DYSFUNCTION BY SUPPRESSING INFLAMMATION AND APOPTOSIS IN RATS](#)

Il-Gyu Ko, Jun-Jang Jin, Lakkyong Hwang, Sang-Hoon Kim, Chang-Ju Kim, Kyu Yeoun Won, Yong Gil Na, Khae Hawn Kim, Su Jin Kim. J Inflamm Res. 2021 Feb 15;14:367-378. doi: 10.2147/JIR.S287346. eCollection 2021. PMID: 33623409 PMCID: PMC7894910 DOI: 10.2147/JIR.S287346

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Interstitial cystitis (IC) is a chronic disorder that indicates bladder-related pain or discomfort. Patients with IC often experience urination problems, such as urinary frequency and urgency, along with pain or discomfort in the bladder area. Therefore, new treatments based on IC etiology are needed. Polydeoxyribonucleotide (PDRN) is a biologic agonist of the adenosine A2A receptor, and PDRN has anti-inflammatory effect and inhibits apoptosis. In this study from Korea, the effect of PDRN on a cyclophosphamide-induced IC animal model was investigated using rats. To induce the IC animal model, 75 mg/kg of cyclophosphamide was injected intraperitoneally once every 3 days for 10 days. The rats in the PDRN-treated groups were intraperitoneally injected with 0.5 mL physiological saline containing 8 mg/kg PDRN, once a day for 10 days after IC induction. Induction of IC by cyclophosphamide injection caused voiding dysfunction, bladder edema, and histological damage. Cyclophosphamide injection increased secretion of pro-inflammatory cytokines and enhanced apoptosis. In contrast, PDRN treatment alleviated voiding dysfunction, bladder edema, and histological damage. Secretion of pro-inflammatory cytokines and expressions of apoptotic factors were suppressed by PDRN treatment. These changes indicate that treatment with PDRN improves voiding function by ultimately promoting the repair of damaged bladder tissue. The conclusion of this experiment suggests the possibility that PDRN could be used as an effective therapeutic agent for IC.

[ISOTONIC ION REPLACEMENT CAN LOWER THE THRESHOLD FOR SELECTIVE INFRARED NEURAL INHIBITION](#)

Junqi Zhuo, Zihui Ou, Yuhan Zhang, Elizabeth M Jackson, Sachin S Shankar, Matthew T McPheeters, Jeremy B Ford, E Duco Jansen, Hillel J Chiel, Michael W Jenkins. Neurophotonics. 2021 Jan;8(1):015005. doi: 10.1117/1.NPh.8.1.015005. Epub 2021 Feb 19. PMID: 33628860 PMCID: PMC7893321 DOI: 10.1117/1.NPh.8.1.015005

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Infrared (IR) inhibition can selectively block peripheral sensory nerve fibers, a potential treatment for autonomic-dysfunction-related diseases (e.g., neuropathic pain and interstitial cystitis). Lowering the IR inhibition threshold can increase its translational potentials. The authors hypothesized that the IR dose threshold could be reduced by combining it with isotonic ion replacement. They tested the IR inhibition threshold on the pleural-abdominal connective of *Aplysia californica*. Using a customized chamber system, the IR inhibition was applied either in normal saline or in isotonic ion-replaced saline, which could be high glucose saline, high choline saline, or high glucose/high choline saline. Each modified saline was at a subthreshold concentration for inhibiting neural conduction. They showed that isotonically replacing ions in saline with glucose and/or choline can reduce the IR threshold and temperature threshold of neural inhibition. Furthermore, the size selectivity of IR inhibition was preserved when combined with high glucose/high choline saline. The present work of IR inhibition combined with isotonic ion replacement will guide further development of a more effective size-selective IR inhibition modality for future research and translational applications.

[EFFICACY AND SAFETY COMPARISON OF PHARMACOTHERAPIES FOR INTERSTITIAL CYSTITIS AND BLADDER PAIN SYNDROME: A SYSTEMATIC REVIEW AND BAYESIAN NETWORK META-ANALYSIS](#)

Xing-Peng Di, De-Yi Luo, Xi Jin, Wan-Yu Zhao, Hong Li, Kun-Jie Wang. Int Urogynecol J. 2021 Feb 27. doi: 10.1007/s00192-020-04659-w. Online ahead of print. PMID: 33638677 DOI: 10.1007/s00192-020-04659-w

The objective of this study from China was to compare the clinical efficacy and safety of pharmacological interventions for IC/BPS with direct and indirect evidence from randomized trials. PubMed, the Cochrane library, and EMBASE were searched for randomized controlled trials (RCTs) that assessed the pharmacological therapies for IC/BPS. Primary efficacy outcomes included ICSI (O'Leary Sant Interstitial Cystitis Symptom Index), ICPI (O'Leary Sant Interstitial Cystitis Problem Index), 24-h micturition frequency, visual analog scale (VAS), and Likert score for pain. Safety outcomes are total adverse events (AEs, intravesical instillation, and others), gastrointestinal symptoms, headache, pain, and urinary symptoms. A systematic review and Bayesian network meta-analysis were performed. A total of 23 RCTs with 1,871 participants were identified. The ICSI was significantly reduced in the amitriptyline group (MD = -4.9, 95% CI: -9.0 to -0.76), the cyclosporine A group (MD = -7.9, 95% CI: -13.0 to -3.0) and the certolizumab pegol group (MD = -3.6, 95% CI: -6.5 to -0.63) compared with placebo group. Moreover, for ICPI, cyclosporine A showed superior benefit compared to placebo (MD = -7.6, 95% CI: -13 to -2.3). VAS score improved significantly in cyclosporine A group than pentosan polysulfate sodium (MD = 3.09, 95% CI: 0.13 to 6.07). None of the agents revealed a significant alleviation of 24-h micturition frequency. In terms of safety outcomes, the incidence rate on urinary symptoms for botulinum toxin A was the only variate higher than chondroitin sulfate (MD = -2.02, 95% CI: -4.99 to 0.66) and placebo (MD = -1.60, 95% CI: -3.83 to 0.17). No significant difference was found among the other treatments. It was concluded that Cyclosporine A might be superior to other pharmacological treatments in efficacy. Amitriptyline and certolizumab pegol were capable of lowering the ICSI as well.

COGNITION, EMOTION, AND THE BLADDER: PSYCHOSOCIAL FACTORS IN BLADDER PAIN SYNDROME AND INTERSTITIAL CYSTITIS (BPS/IC)

Sula Windgassen, Lindsey McKernan. Curr Bladder Dysfunct Rep. 2020 Mar;15(1):9-14. doi: 10.1007/s11884-019-00571-2. Epub 2020 Jan 31. PMID: 33456639 PMCID: PMC7810165 DOI: 10.1007/s11884-019-00571-2

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The purpose of this study from London and Nashville was to review findings from empirical studies assessing the role of psychosocial factors in BPS/IC. There is a high rate of psychosocial comorbidity in BPS/IC, including elevated levels of anxiety and depression. Recent studies assessing the role of illness perceptions in BPS/IC relate poorer illness perceptions to more unhelpful illness coping patterns. Conversely, positive illness perceptions including self-efficacy in illness management are associated with more adaptive coping behaviors such as exercising and acceptance. New research is investigating the role of trauma in BPS/IC and the impact of suicidality. There is a paucity of psychosocial interventions for BPS/IC over the last 5 years. The three small-scale studies reviewed included a mindfulness-based stress reduction (MBSR) intervention tailored for BPS/IC, a brief self-management intervention designed to increase patient knowledge and symptom management techniques and a 90-minute interview aimed at increasing awareness about physiological-affective relationship in IC.

SELECTIVE BLOCKADE OF TRANSIENT RECEPTOR POTENTIAL VANILLOID 4 REDUCES CYCLOPHOSPHAMIDE-INDUCED BLADDER PAIN IN MICE

Shiori Kawasaki, Masahiko Soga, Yusuke Sakurai, Isamu Nanchi, Miyuki Yamamoto, Sunao Imai, Tatsuya Takahashi, Naoki Tsuno, Toshiyuki Asaki, Yasuhide Morioka, Masahide Fujita. Eur J Pharmacol. 2021 Mar 15;174040. doi: 10.1016/j.ejphar.2021.174040. Online ahead of print. PMID: 33737012 DOI: 10.1016/j.ejphar.2021.174040

Transient receptor potential vanilloid 4 (TRPV4) is a non-selective cation channel activated by various physical stimuli such as cell swelling and shear stress. TRPV4 is expressed in bladder sensory nerves and epithelium, and its activation produces urinary dysfunction in rodents. However, there have been few reports regarding its involvement in bladder pain. Therefore, the authors investigated whether TRPV4 is involved in bladder pain in mouse cystitis model. Intraperitoneal injection of cyclophosphamide (CYP; 300 mg/kg) produced mechanical hypersensitivity in the lower abdomen associated with a severe inflammatory bladder in mice. The mechanical threshold was reversed significantly in Trpv4-knockout (KO) mice. Repeated injections of CYP (150 mg/kg) daily for 4 days provoked mild bladder inflammation and persistent mechanical hypersensitivity in mice. Trpv4-KO mice prevented a reduction of the mechanical threshold without an alteration in bladder inflammation. A selective TRPV4 antagonist also reversed the mechanical threshold in chronic cystitis mice. Although expression of Trpv4 was unchanged in the bladders of chronic cystitis mice, the level of phosphorylated TRPV4 was increased significantly. These results suggest involvement of TRPV4 in bladder pain of cystitis mice. A TRPV4 antagonist might be useful for patients with irritable bladder pain such as those with interstitial cystitis/painful bladder syndrome.

EXAMINATION OF PELVIC FLOOR MUSCLE ELASTICITY IN PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME USING REAL-TIME TISSUE ELASTOGRAPHY

Yui Abe-Takahashi, Takeya Kitta, Mifuka Ouchi, Hiroki Chiba, Madoka Higuchi, Mio Togo, Nobuo Shinohara. Int Urogynecol J. 2021 Mar 19. doi: 10.1007/s00192-021-04761-7. Online ahead of print. PMID: 33740121 DOI: 10.1007/s00192-021-04761-7

The aim was to compare pelvic floor muscle (PFM) elasticity between IC/BPS patients and healthy women using real-time tissue elastography. The subjects were 17 IC/BPS female patients (IC/BPS group; age 34-84 years), 10 healthy middle-aged women (middle-aged group; 50-80 years), and 17 healthy young adult women (young group; 23-37 years). The target sites of elastography were the striated urethral sphincter (SUS) and adipose tissue as the reference site; muscle elasticity was calculated as the strain ratio (SR) of the SUS to the reference site. Evaluations were performed at rest and during PFM contraction. The IC/BPS group completed lower urinary tract symptom and pain questionnaires. SUS SR was compared among the three groups. SUS SR at rest and during PFM contraction was compared among the three groups with the t-test and the Wilcoxon test. Associations between questionnaire results and SUS SR were evaluated by correlation analysis. There was no significant difference in age between the IC/BPS and middle-aged groups, but the young group was significantly younger than the other groups ($p < 0.001$). SUS SR at rest was significantly higher in the IC/BPS group than in the middle-aged ($p = 0.014$) and young groups ($p = 0.002$). Furthermore, in the IC/BPS group, there was no significant difference in SUS SR between at rest and during PFM contraction. SUS SR was not significantly correlated with questionnaire results for lower urinary tract symptoms. It was concluded that SUS SR at rest was significantly higher in the IC/BPS group than in the young and middle-aged groups.

THE CHICKEN OR THE EGG: LONGITUDINAL CHANGES IN PAIN AND CATASTROPHIZING IN WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME

Alison Crawford, Abi Muere, Dean A Tripp, J Curtis Nickel, R Christopher Doiron, Robert Moldwin, Laura Katz. Can Urol Assoc J. 2021 Mar 18. doi: 10.5489/cuaj.7106. Online ahead of print. PMID: 33750522 DOI: 10.5489/cuaj.7106

Evidence-based psychological strategies are being used as clinicians look for helpful interventions for patients diagnosed with the enigmatic chronic urological pelvic pain condition of IC/BPS. Pain and pain catastrophizing are associated with chronic pelvic pain outcomes but the longitudinal role of catastrophizing on patient pain in IC/BPS remains unknown. Women with IC/BPS were recruited from tertiary care clinics across North America and completed a battery of questionnaires, including demographics, pain, depression, catastrophizing at baseline, six months, and one year. A total of 226 patients completed baseline, 183 completed the six-month survey, and 151 completed the one-year survey. Using a cross-lagged analysis, early changes in pain catastrophizing predicted later changes in pain, but not vice versa. Follow-up subscale analyses revealed that early changes in magnification predicted later changes in pain, early changes in pain predicted later changes in rumination, and that there was a recursive relationship between changes in helplessness and changes in pain across the study. The authors concluded that pain catastrophizing should be considered a prime target in psychological treatment for chronic pain in patients with IC/BPS, particularly those thinking styles associated with pain onset and maintenance. Future research should be conducted with constructs such as pain catastrophizing in samples prioritizing diversity of patients with IC/BPS and mechanisms as to how to effectively decrease catastrophizing.

WEB-MEDIATED COUNSELING TO COUNTERACT THE EMOTIONAL IMPACT OF COVID-19 FOR WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME

G Marano, E Gaetani, M Marturano, G Sani, A Gasbarrini, G Scambia, M Mazza. Eur Rev Med Pharmacol Sci. 2021 Feb;25(4):2109-2113. doi: 10.26355/eurrev_202102_25116. PMID: 33660824 DOI: 10.26355/eurrev_202102_25116

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Interstitial Cystitis (IC) is a chronic and rare disease, more frequent in women. Symptoms of continuous pain can produce psychological disorders, such as anxiety and depression. The spread of COVID-19 pandemic added to distress experienced by patients with IC emotions, such as fear, sadness, boredom, frustration and anger. A research on very recent literature outlines the necessity for patients facing the complexity of IC during the COVID-19 outbreak to prevent the temporary crisis, to broaden perspectives, to deal with confusion, to support in struggling with unpleasant and unexpected events. People affected by IC have a psychological vulnerability that needs tailored support interventions, particularly in the COVID era. A multidisciplinary approach offers a personalized treatment through a web-mediated counselling intervention for patients and their caregivers: a

space for continuous discussion and reflection can favour a relationship-based process of change aimed at an improvement in quality of life.

IMPROVEMENT IN QUALITY OF LIFE WITH PELVIC FLOOR MUSCLE TRAINING AND BIOFEEDBACK IN PATIENTS WITH PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS

Pedro-Santiago Borrego-Jimenez, Javier Flores-Fraile, Bárbara-Yolanda Padilla-Fernández, Sebastián Valverde-Martinez, Agustín Gómez-Prieto, Magaly Teresa Márquez-Sánchez, José-Antonio Mirón-Canelo, María-Fernanda Lorenzo-Gómez. J Clin Med. 2021 Feb 19;10(4):862. doi: 10.3390/jcm10040862. PMID: 33669734 PMCID: PMC7922867 DOI: 10.3390/jcm10040862

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The purpose of this study was to prove the benefits of pelvic floor muscle training with biofeedback (BFB) as a complementary treatment in women with BPS/IC. Prospective, randomized study in 123 women with BPS/IC. Groups: BFB+ (n = 48): women with oral drug treatment (perphenazine and amitriptyline) plus intravesical instillations (sodium hyaluronate) plus pelvic floor muscle training with BFB; BFB-: (n = 75): women with oral drug treatment plus intravesical instillations. Variables: age, body mass index (BMI), time of follow-up, length of disease, time free of disease, diseases and health conditions concomitant, and responses to the SF-36 health-related quality of life questionnaire at the first consultation (SF-36 pre-treatment), and at the end of the study (SF-36 post-treatment). The treatment was considered successful when the SF-36 score reached values equal to or greater than 80 points or when the initial value increased by 30 or more points. Mean age was 51.62 years old (23-82). BMI was higher in BFB-. The mean length of BPS/IC condition was 4.92 years (1-20), shorter in BFB+ than in BFB-. Mean SF-36 score pre-treatment was 45.92 points (40-58), lower in BFB+ than in BFB-. Post-treatment SF-36 score was higher than pre-treatment SF-36 score both in BFB+ and BFB-. SF-36 values were higher in BFB+ compared to BFB- over the follow-up. It was concluded that BFB improves quality of life in women with BPS/IC as adjunct therapy to combined oral and intravesical treatment.

STEREOLITHOGRAPHY (SLA) 3D PRINTING OF A BLADDER DEVICE FOR INTRAVESICAL DRUG DELIVERY

Xiaoyan Xu, Alvaro Goyanes, Sarah J Trenfield, Luis Diaz-Gomez, Carmen Alvarez-Lorenzo, Simon Gaisford, Abdul W Basit. Mater Sci Eng C Mater Biol Appl. 2021 Jan;120:111773. doi: 10.1016/j.msec.2020.111773. Epub 2020 Dec 4. PMID: 33545904 DOI: 10.1016/j.msec.2020.111773

Intravesical instillation therapy is an alternative approach to oral medications for the treatment of severe bladder diseases, offering high drug concentrations at the site of action while minimising systemic side effects. However, therapeutic efficacy is often limited because of the short residence time of the drug in the bladder and the need for repeated instillations. This study from the UK and Spain reports, for the first time, the use of stereolithography (SLA) 3D printing to manufacture novel indwelling bladder devices using an elastic polymer to achieve extended and localised delivery of lidocaine hydrochloride. The devices were designed to be inserted into and retrieved from the bladder using a urethral catheter. Two types of bladder devices (hollow and solid) were prepared with a resilient material (Elastic Resin) incorporating three drug loads of lidocaine hydrochloride (10% w/w, 30% w/w and 50% w/w); a drug frequently used to treat interstitial cystitis and bladder pain. All of the devices showed acceptable blood compatibility, good resistance to compressive and stretching forces and were able to recover their original shape immediately once external forces were removed. In vitro drug release studies showed that a complete release of lidocaine was achieved within 4 days from the hollow devices, whereas the solid devices enabled sustained drug release for up to 14 days. SLA 3D printing therefore provides a new manufacturing route to produce bladder-retentive drug delivery devices using elastic polymers and offers a revolutionary and personalised approach for clinical intravesical drug delivery.

EFFICACY AND SAFETY OF INTRAVESICAL INSTILLATION OF KRP-116D (50% DIMETHYL SULFOXIDE SOLUTION) FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME IN JAPANESE PATIENTS: A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, CLINICAL STUDY

Naoki Yoshimura, Yukio Homma, Hikaru Tomoe, Atsushi Otsuka, Takeya Kitta, Naoya Masumori, Yoshiyuki Akiyama, Aya Niimi, Takahiko Mitsui, Masaharu Nanri, Takashige Namima, Mineo Takei, Akito Yamaguchi, Yuki Sekiguchi, Mitsuru Kajiwara, Shinya Kobayashi, Kaname Ameda, Yozo Ohashi, Sadaaki Sakamoto, Osamu Muraki, Toshihide Shishido, Shinji Kageyama, Koji Kokura, Homare Okazoe, Tomonori Yamanishi, Toyohiko Watanabe, Takashi Uno, Akira Ohinata, Tomohiro Ueda. Int J Urol. 2021 Feb 12. doi: 10.1111/iju.14505. Online ahead of print. PMID: 33580603 DOI: 10.1111/iju.14505

The purpose of this study from Japan was to evaluate the efficacy and safety of intravesical KRP-116D, 50% dimethyl sulfoxide solution compared with placebo, in IC/BPS patients. Japanese IC/BPS patients with an O'Leary-Sant Interstitial Cystitis Symptom Index score of ≥ 9 , who exhibited the bladder-centric phenotype of

interstitial cystitis/bladder pain syndrome diagnosed by cystoscopy and bladder-derived pain, were enrolled. Patients were allocated to receive either KRP-116D (n = 49) or placebo (n = 47). The study drug was intravesically administered every 2 weeks for 12 weeks. For the primary endpoint, the change in the mean O'Leary-Sant Interstitial Cystitis Symptom Index score from baseline to week 12 was -5.2 in the KRP-116D group and -3.4 in the placebo group. The estimated difference between the KRP-116D and placebo groups was -1.8 (95% confidence interval -3.3, -0.3; P = 0.0188). Statistically significant improvements for KRP-116D were also observed in the secondary endpoints including O'Leary-Sant Interstitial Cystitis Problem Index score, micturition episodes/24 h, voided volume/micturition, maximum voided volume/micturition, numerical rating scale score for bladder pain, and global response assessment score. The adverse drug reactions were mild to moderate, and manageable. According to the authors, this first randomized, double-blind, placebo-controlled trial shows that KRP-116D improves symptoms, voiding parameters, and global response assessment, compared with placebo, and has a well-tolerated safety profile in IC/BPS patients with the bladder-centric phenotype.

HUNNER LESION

[RELATIONSHIP BETWEEN THE FREQUENCY OF ELECTROCAUTERY OF HUNNER LESIONS AND CHANGES IN BLADDER CAPACITY IN PATIENTS WITH HUNNER TYPE INTERSTITIAL CYSTITIS](#)

Yoshiyuki Akiyama, Masayoshi Zaito, Daiji Watanabe, Itsuki Yoshimura, Aya Niimi, Akira Nomiya, Yuta Yamada, Yusuke Sato, Masaki Nakamura, Taketo Kawai, Daisuke Yamada, Motofumi Suzuki, Haruki Kume, Yukio Homma. *Sci Rep.* 2021 Jan 8;11(1):105. doi: 10.1038/s41598-020-80589-3. PMID: 33420263 DOI: 10.1038/s41598-020-80589-3

Electrocautery is a promising treatment option for patients with Hunner type interstitial cystitis (HIC), but frequently requires multiple sessions due to recurrence of the lesions. In this study from Japan, Akiyama and colleagues assessed the relationship between the frequency of electrocautery of Hunner lesions and changes in maximum bladder capacity (MBC) at hydrodistension in a large cohort of 118 HIC patients. Three mixed-effect linear regression analyses were conducted for MBC against (1) the number of sessions; (2) the number of sessions and the time between each session and the first session; and (3) other relevant clinical parameters in addition to the Model (2). The mean number of sessions was 2.8 times. MBC decreased approximately 50 mL for each additional electrocautery session, but this loss was offset by 10 mL for each year the subsequent session was postponed. MBC of < 400 mL at the first session was a significant risk factor for MBC loss with further sessions. No other clinical parameters were associated with MBC over time. This study demonstrates a significant relationship between the frequency of electrocautery of Hunner lesions and MBC changes in HIC patients. Low MBC at the first session is a poor prognostic marker for MBC loss over multiple sessions.

[MICRORNA-495 ALLEVIATES ULCERATIVE INTERSTITIAL CYSTITIS VIA INACTIVATING THE JAK-STAT SIGNALING PATHWAY BY INHIBITING JAK3](#)

Yi Hou, Hai Li 1, Wei Huo. *Int Urogynecol J.* 2021 Jan 8. doi: 10.1007/s00192-020-04593-x. Online ahead of print. PMID: 33416962 DOI: 10.1007/s00192-020-04593-x

As a notable chronic disorder, the incidence of interstitial cystitis (IC) has been documented to have increased among the female population with activity in microRNA-495 (miR-495) implicated in this disease. This study from China was aimed at elucidating the effects associated with miR-495 on the inflammatory response and bladder fibrosis in rats with ulcerative IC via the JAK-STAT pathway by targeting JAK3. Collectively, their key findings provide evidence supporting the notion that the overexpression of miR-495 ameliorates inflammatory response and bladder fibrosis in ulcerative IC rat models via inactivation of the JAK-STAT signaling pathway by inhibiting JAK3.

[AUTOIMMUNITY TO UROTHELIAL ANTIGEN CAUSES BLADDER INFLAMMATION, PELVIC PAIN AND VOIDING DYSFUNCTION: A NOVEL ANIMAL MODEL FOR HUNNER TYPE INTERSTITIAL CYSTITIS](#)

Yoshiyuki Akiyama, Jian-Rong Yao, Karl J Kreder, Michael A O'Donnell, Susan K Lutgendorf, Dan Lyu, Daichi Maeda, Haruki Kume, Yukio Homma, Yi Luo. *Am J Physiol Renal Physiol.* 2020 Dec 14. doi: 10.1152/ajprenal.00290.2020. Online ahead of print. PMID: 33308017 DOI: 10.1152/ajprenal.00290.2020

Recent evidence revealed that Hunner type interstitial cystitis (HIC) is a robust inflammatory disease potentially associated with enhanced immune responses and histologically characterized by epithelial denudation and lymphoplasmacytic infiltration with frequent clonal expansion of infiltrating B cells. To date, few animal models that reproduce the histological and clinical correlates of HIC have yet been established. In the present study, Akiyama and colleagues aimed to develop a novel animal model for HIC via autoimmunity to the bladder urothelium using the transgenic mouse model (URO-OVA) that expresses the membrane form of the model

antigen ovalbumin (OVA) as a self-antigen on the bladder urothelium. OVA-specific lymphocytes (splenocytes) were generated by immunization of C57BL/6 mice with OVA protein and injected intravenously into URO-OVA mice. The splenocytes from OVA-immunized C57BL/6 mice showed increased IFN- γ production in response to OVA stimulation in vitro. URO-OVA mice adoptively transferred with OVA-primed splenocytes developed cystitis exhibiting histological chronic inflammatory changes such as remarkable mononuclear cell infiltration predominantly composed of T and B lymphocytes, increased vascularity, and mucosal hyperemia in the bladder at days 7-28 with a peak at day 21 tested. No systemic inflammation was found in cystitis-induced URO-OVA mice, nor was any inflammation found in wild-type C57BL/6 mice adoptively transferred with OVA-primed splenocytes. Along with bladder inflammation, URO-OVA mice demonstrated significantly increased pelvic nociceptive responses, voiding dysfunction, and upregulated mRNA expression levels for IFN- γ , TNF- α and substance P precursor in the bladder. This model reproduces the histological and clinical features of human HIC, providing a novel model for HIC research.

COMPLEMENTARY, ALTERNATIVE AND TRADITIONAL THERAPY

[BENEFICIAL EFFECT OF BLETILLA STRIATA EXTRACT SOLUTION ON ZYMOSAN-INDUCED INTERSTITIAL CYSTITIS IN RAT](#)

Yi-Ching Liu, Wei-Ting Lee, Ching-Chung Liang, Tsia-Shu Lo, Wu-Chiao Hsieh, Yi-Hao Lin. NeuroUrol Urodyn. 2021 Feb 19. doi: 10.1002/nau.24630. Online ahead of print. PMID: 33604897 DOI: 10.1002/nau.24630

Interstitial cystitis (IC) is a chronic pain syndrome that is characterized by suprapubic pain upon bladder filling. Bletilla striata, a well-known traditional Chinese herb with established efficacy in wound healing and anti-inflammation, was hypothesized to improve the symptoms of IC possibly through forming a physical barrier that could isolate the bladder tissue from irritants. This study from Taiwan was conducted to evaluate the beneficial effects of intravesical treatment with B. striata extract solution (BSES) on visceral pain and bladder function of rats with zymosan-induced IC. Thirty female rats were randomly divided into control group, zymosan-induced cystitis rats treated with normal saline (Z + NS), and zymosan-induced cystitis rats treated with BSES (Z + BSES). All rats underwent evaluation for abdominal withdrawal reflex (AWR) scores to assess visceral hypersensitivity, cystometry, and electromyogram (EMG) of both external urethral sphincter and bladder detrusor. Data were analyzed by one way analysis of variance. The Z + NS group had an increased visceral hypersensitivity as compared to control group. Rats treated with BSES (Z + BSES group) had decreased AWR scores and amplitude of bladder detrusor-EMG. Besides, BSES treatment improved overactive bladder with significant effects on the extend of micturition interval and increase of storage of urine. It was concluded that intravesical instillation of BSES can significantly alleviate zymosan-induced visceral hypersensitivity and bladder overactivity associated with IC and that it might be a promising treatment for IC.

[ADVERSE EFFECTS OF KAMPO MEDICINES](#)

Yutaka Shimada. Intern Med. 2021 Feb 8. doi: 10.2169/internalmedicine.6292-20. Online ahead of print. PMID: 33551404 DOI: 10.2169/internalmedicine.6292-20

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This review summarizes the adverse effects of Kampo medicines. These adverse effects in terms of immunoallergic reactions include interstitial pneumonia, liver injury, allergic cystitis, and drug eruption. Many cases of interstitial pneumonia, liver injury, and allergic cystitis associated with Kampo formulas have been reported to be caused by formulas containing Scutellariae Radix (Scutellaria root, ogon). The known adverse effects linked to overdose of Kampo formulas include pseudoaldosteronism (caused by Glycyrrhizae Radix [licorice, kanzo]), sympathomimetic symptoms (caused by Ephedrae Herba [ephedra, mao]), aconite poisoning (caused by Aconiti Tuber [processed aconite root, bushi and uzu]), and diarrhea (caused by Rhei Rhizoma [rhubarb, daio]). In recent years, mesenteric phlebosclerosis caused by the long-term administration of Gardeniae Fructus (gardenia fruit, sanshishi) has also been reported. It is necessary to consider these potential adverse effects when prescribing Kampo medicines in clinical practice.

SYMPTOMS MIMICKING IC/BPS

[MONOTYPIC PLASMA CELL PROLIFERATION OF UNCERTAIN CLINICAL SIGNIFICANCE MIMICKING INTERSTITIAL CYSTITIS: AN EARLY LESION OF MALT LYMPHOMA?](#)

Ana Cristina Vargas, Ivan Burchett, Jennifer Turner, Warick Delprado, Ross Brookwell, Venu Chalasani, Anthony J Gill, Fiona M Maclean. Am J Surg Pathol. 2021 Jan 4; Publish Ahead of Print. doi:

10.1097/PAS.0000000000001659. Online ahead of print. PMID: 33399339 DOI: 10.1097/PAS.0000000000001659

Vargas and colleagues from Australia prospectively studied their institutional experience of bladder extranodal marginal zone (mucosa-associated lymphoid tissue [MALT]) lymphoma including bladder biopsies in which the possibility of MALT lymphoma was considered. They identified a subset of cases primary to the urinary bladder, presenting with prominent plasma cell infiltrates and symptoms mimicking BPS/IC. These proliferations were designated for this study as "monotypic plasma cell proliferation of uncertain clinical significance" (MPCP-US), as the features were insufficient for diagnosis of MALT lymphoma. They identified 33 patients, consisting of 22 cases of MPCP-US (6 of which were associated with amyloid deposition) and 11 cases of MALT lymphoma. MPCP-US was more prevalent in men (73%), a mass lesion was not identified at cystoscopy, and only 1 case had an accompanying urinary tract infection (4.5%). Histologically, MPCP-US presented as monotypic plasma cells arranged in a superficial band-like distribution in the lamina propria, predominantly kappa restricted (68%) and IgA+ or IgM+ (64% and 23%, respectively) and without a histologic mass of atypical B cells or plasma cells, not diagnostic for established MALT lymphoma or plasmacytoma. Secondary involvement of the bladder by other lymphoproliferative disorders was excluded and there was no evidence of progressive disease. MALT lymphomas are presented for comparison and the authors' analysis demonstrated that MPCP-US represent a different clinicopathologic entity compared with classic MALT lymphoma. They present the first series of cases of MPCP-US. The recognition of this entity is fundamental to the development of management protocols to relieve intractable symptoms mimicking BPS/IC in these patients.

LOWER URINARY TRACT

[ACTIVATION OF MRGPRA3 AND MRGPC11 ON BLADDER-INNERVATING AFFERENTS INDUCES PERIPHERAL AND CENTRAL HYPERSENSITIVITY TO BLADDER DISTENSION](#)

Luke Grundy, Ashlee Caldwell, Sonia Garcia-Caraballo, David Grundy, Nick J Spencer, Xinzhong Dong, Joel Castro, Andrea M Harrington, Stuart M Brierley. *J Neurosci.* 2021 Mar 16;JN-RM-0033-21. doi: 10.1523/JNEUROSCI.0033-21.2021. Online ahead of print. PMID: 33727332 DOI: 10.1523/JNEUROSCI.0033-21.2021

Understanding the sensory mechanisms innervating the bladder is paramount to developing efficacious treatments for chronic bladder hypersensitivity conditions. The contribution of Mas-gene-related G protein-coupled receptors (Mrgpr) to bladder signalling is currently unknown. Using male and female mice, we show with single-cell RT-PCR that sub-populations of dorsal root ganglion (DRG) neurons innervating the mouse bladder express MrgprA3 (14%) and MrgprC11 (38%), either individually or in combination, with high levels of co-expression with Trpv1 (81-89%). Calcium imaging studies demonstrated MrgprA3 and MrgprC11 agonists (chloroquine, BAM8-22 and neuropeptide FF) activated sub-populations of bladder-innervating DRG neurons, showing functional evidence of co-expression between MrgprA3, MrgprC11 and TRPV1. In ex vivo bladder-nerve preparations chloroquine, BAM8-22 and neuropeptide FF all evoked mechanical hypersensitivity in sub-populations (20-41%) of bladder afferents. These effects were absent in recordings from Mrgpr-cluster Δ -/- mice. In vitro whole-cell patch clamp recordings showed that application of an MrgprA3/C11 agonist cocktail induced neuronal hyper-excitability in 44% of bladder-innervating DRG neurons. Finally, in vivo instillation of an MrgprA3/C11 agonist cocktail into the bladder of wild-type mice induced a significant activation of dorsal horn neurons within the lumbosacral spinal cord, as quantified by pERK-immunoreactivity. This MrgprA3/C11 agonist-induced activation was particularly apparent within the superficial dorsal horn and the sacral parasympathetic nuclei of wild-type, but not Mrgpr-cluster Δ -/- mice. This study demonstrates, for the first time, functional expression of MrgprA3 and MrgprC11 in bladder afferents. Activation of these receptors triggers hypersensitivity to distension, a critically valuable factor for therapeutic target development. Determining how bladder afferents become sensitized is the first step in finding effective treatments for common urological disorders such as OAB and IC/BPS. Here the authors show that two of the key receptors, MrgprA3 and MrgprC11, that mediate itch from the skin are also expressed on afferents innervating the bladder. Activation of these receptors results in sensitization of bladder afferents, resulting in sensory signals being sent into the spinal cord that prematurely indicate bladder fullness. Targeting bladder afferents expressing MrgprA3 or MrgprC11 and preventing their sensitisation may provide a novel approach for treating OAB and IC/BPS.

[CLINICAL GUIDELINES FOR FEMALE LOWER URINARY TRACT SYMPTOMS \(SECOND EDITION\)](#)

Satoru Takahashi, Mineo Takei, Hirotaka Asakura, Momokazu Gotoh, Osamu Ishizuka, Kumiko Kato, Masayasu Koyama, Masami Takeyama, Hikaru Tomoe, Tomonori Yamanishi, Osamu Yokoyama, Masaki Yoshida, Yasukuni

Yoshimura, Tsuyoshi Yoshizawa. *Int J Urol*. 2021 Mar 1. doi: 10.1111/iju.14492. Online ahead of print. PMID: 33650242 DOI: 10.1111/iju.14492

The present article is an abridged English translation of the Japanese Clinical Guidelines for Female Lower Urinary Tract Symptoms (second edition), published in September 2019. These guidelines consist of a total of 212 pages and are unique worldwide in that they cover female lower urinary tract symptoms other than urinary incontinence. They contain two algorithms for "primary treatment" and "specialized treatment," respectively. These guidelines, consisting of six chapters, address a total of 26 clinical questions including: (i) treatment algorithms; (ii) what are female lower urinary tract symptoms?; (iii) epidemiology and quality of life; (iv) pathology and illness; (v) diagnosis; and (vi) treatment. When the patient's symptoms mainly involve voiding and post-micturition symptoms, specialized treatment should be considered. In the event of voiding symptoms concurrent with storage symptoms, residual urine should be measured; if the residual urine volume is <100 mL, then diagnosis and treatment for storage symptoms is prioritized, and if the volume is ≥100 mL, then specialized treatment should be considered. When storage symptoms are the primary condition, then the patient is subject to the primary treatment algorithm. Specialized treatment for refractory overactive bladder includes botulinum toxin injection and sacral nerve stimulation. For stress urinary incontinence, surgical treatment is indicated, such as urethral slings. The two causes of voiding symptoms and post-micturition symptoms are lower urinary tract obstruction and detrusor underactivity (underactive bladder). Mechanical lower urinary tract obstruction, such as pelvic organ prolapse, is expected to improve with surgery.

UROBIOME

THE HUMAN UROBIOME

L Brubaker, C Putonti, Q Dong, A J Wolfe. *Mamm Genome*. 2021 Mar 2. doi: 10.1007/s00335-021-09862-8. Online ahead of print. PMID: 33651197 DOI: 10.1007/s00335-021-09862-8

Traditionally, the healthy urinary bladder has been considered to be sterile. Several teams have used metagenomic (DNA-dependent) and metaculturomic (culture-dependent) methods to debunk this longstanding dogma. In fact, resident microbial communities (urobiome) have been detected in both adult females and males. Although the field is young, several observations have been made. For example, the urobiome differs between men and women, likely due to anatomical and hormonal differences. Importantly, the urobiome has been associated with a variety of lower urinary tract disorders, including overactive bladder and post-operative urinary tract infection, raising the possibility that clinicians might one day treat symptoms by modifying the urobiome instead of killing the suspected uropathogen. Little is known concerning the relationship between the urobiome and host genetics; so far, only a single paper has reported such a study. However, major efforts have gone into understanding the genomics of the urobiome itself, a process facilitated by the fact that many urobiome studies have used metaculturomic methods to detect and identify microbes. In this narrative review, the authors introduce the urobiome with separate sections on the female and male urobiomes, discuss challenges specific to the urobiome, describe newly discovered associations between the urobiome and lower urinary tract symptoms, and highlight the one study that has attempted to relate host genetics and the urobiome. They finish with a section on how metagenomic surveys and whole genome sequencing of bacterial isolates are improving our understanding of the urobiome and its relationship to lower urinary tract health and disorders.

CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME

LOW-INTENSITY SHOCKWAVE THERAPY FOR THE MANAGEMENT OF CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

Ioannis Mykoniatis, Nikolaos Pyrgidis, Ioannis Sokolakis, Petros Sountoulides, Georgios Hatzichristodoulou, Apostolos Apostolidis, Dimitrios Hatzichristou. *BJU Int*. 2021 Jan 12. doi: 10.1111/bju.15335. Online ahead of print. PMID: 33434323 DOI: 10.1111/bju.15335

The purpose of this study from Greece and Germany was to perform a systematic review and meta-analysis aiming to improve the level of evidence and determine the efficacy and safety of low-intensity shockwave therapy (LiST) in patients with CP/CPPS. The authors searched PubMed, Cochrane Library and Scopus databases from inception to November 2020 for randomised controlled trials (RCTs) exploring the role of LiST for the management of CP/CPPS. They performed a random-effects meta-analysis of RCTs comparing LiST vs sham therapy on CP/CPPS symptoms at different time-points after treatment. Weighted mean differences (WMDs) with the corresponding confidence intervals (CIs) were estimated. Furthermore, they assessed the strength of evidence with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system

(International Prospective Register of Systematic Reviews [PROSPERO]: CRD42020208813). They included five sham RCTs and one non-sham RCT. In the meta-analysis of sham RCTs, both the National Institute of Health Chronic Prostatitis Symptom Index (NIH-CPSI) pain domain score and the numeric pain rating scale improved significantly after LiST vs sham therapy at the assessment directly after treatment protocol completion (WMD 3.2, 95% CI 0.88-5.52, I² = 90%; and WMD 1.43, 95% CI 0.85-2.01, I² = 32%, respectively), at 1 month (WMD 4.4, 95% CI 2.84-5.95, I² = 68%, and WMD 2.59, 95% CI 1.92-3.27, I² = 83%, respectively), and at 3 months after last treatment session (WMD 3.61, 95% CI 1.49-5.74, I² = 90%, and WMD 2.64, 95% CI 2.13-3.16, I² = 71%, respectively). Similarly, the NIH-CPSI total and quality-of-life domain scores improved significantly after LiST compared to sham therapy for the same time-points. Conversely, the long-term efficacy of LiST, as well as the effect of LiST on lower urinary tract symptoms and erectile function, was clinically insignificant. They concluded that iST is an effective treatment modality for the improvement of pain and quality of life in patients with CP/CPPS. Therefore, it should be recommended as a part of individualised treatment strategies in such patients.

PENTOSAN POLYSULFATE-ASSOCIATED MACULAR DISEASE

HEPARANASE DEFICIENCY IS ASSOCIATED WITH DISRUPTION, DETACHMENT, AND FOLDING OF THE RETINAL PIGMENT EPITHELIUM

Tine Van Bergen, Isabelle Etienne, Juan Jia, Jin-Ping Li, Israël Vlodavsky, Alan Stitt, Elke Vermassen, Jean H M Feyen. Curr Eye Res. 2020 Dec 29;1-5. doi: 10.1080/02713683.2020.1862239. Online ahead of print. PMID: 33372561 DOI: 10.1080/02713683.2020.1862239

Pentosan polysulfate sodium (PPS; Elmiron) is a FDA-approved heparanase inhibitor for the treatment of bladder pain and interstitial cystitis. The chronic use of PPS has been associated with a novel pigmentary maculopathy, associated with discrete vitelliform deposits that exhibit hyperfluorescence, macular hyper-pigmentary spots, and foci of nodular RPE enlargement. Therefore, this study aimed to investigate the retinal morphology of heparanase knockout mice. The retinal morphology of heparanase knock-out and age-matched control wild type mice of 3-, 9- and 15-weeks old was characterized by means of histological evaluation. Immuno-histological stains for RPE65, F4/80 and Ki67 were performed for investigating the RPE, inflammatory and proliferating cells, respectively. Histological analysis showed no changes in age-matched wild-type controls, whereas the eyes of heparanase null mice were characterized by alterations in RPE and neural retina, as manifest by RPE folds and choroidal thickening, detached RPE cells, thickening of the photoreceptor layer and retinal disorganization. The presence of discrete hyperfluorescent foci, however, was absent. The prevalence of the RPE/choroidal changes or protrusions seemed to progress over time and were correlated with more RPE65 signal rather than influx of F4/80- or Ki67-positive cells. These results indicate that the subretinal alterations were mostly RPE driven, without influx of inflammatory or proliferating cells. The authors conclude that their results indicate that heparanase deficiency in the mice leads to RPE folds, choroidal thickening, and retinal disorganization. The presence of discrete hyperfluorescent foci, a key characteristic of the human disease, was not observed. However, it can be concluded that some of the observations in mice are similar to those seen after chronic use of PPS in humans. These findings indicate that the toxicity observed in the presence of heparanase inhibitors is target-related and will preclude the clinical use of heparanase inhibition as a therapeutic intervention.

PENTOSAN POLYSULFATE AND VISION: FINDINGS FROM AN INTERNATIONAL SURVEY OF EXPOSED INDIVIDUALS

Ogul E Uner, Megha K Shah, Nieraj Jain. Retina. 2020 Dec 14; Publish Ahead of Print. doi: 10.1097/IAE.0000000000003078. Online ahead of print. PMID: 33332810 DOI: 10.1097/IAE.0000000000003078

The purpose of this study was to investigate patient-reported visual function in individuals taking pentosan polysulfate (PPS) for interstitial cystitis. A 27-item online survey was distributed to an international listserv of individuals with interstitial cystitis in November of 2018. Demographic characteristics, PPS exposure history, subjective visual function, and prior macular diagnoses were queried. Impact of PPS use, grouped by tertile of cumulative exposure, on visual function and macular diagnoses was assessed with multivariate logistic regression. The survey was completed by 912 respondents. 861 (96.4%) were female, and the median age was 55 (IQR, 45-64 years). Among PPS users, the median exposure was 547.5 grams (IQR, 219-1314 g). Respondents in the highest PPS exposure tertile were more likely to report difficulty with reading small print (adjusted OR 2.29, 95%CI 1.15-4.57) and to have a diagnosis of macular degeneration and/or pigmentary maculopathy (adjusted OR 2.41, 95%CI 1.44-4.03) than unexposed respondents. In this large sample of individuals with interstitial cystitis, those in the highest PPS exposure category were more likely to have difficulties reading small print and to report a prior diagnosis of macular disease. Further study of objective measures of visual function in PPS users is warranted.

IDENTIFICATION OF PATIENTS WITH PENTOSAN POLYSULFATE SODIUM-ASSOCIATED MACULOPATHY THROUGH SCREENING OF THE ELECTRONIC MEDICAL RECORD AT AN ACADEMIC CENTER

Kendall Higgins, R Joel Welch, Colin Bacorn, Glenn Yiu, Jennifer Rothschild, Susanna S Park, Ala Moshiri.

PMID: 33489347 PMCID: PMC7803106 DOI: 10.1155/2020/8866961 J Ophthalmol. 2020 Dec 17;2020:8866961. doi: 10.1155/2020/8866961. eCollection 2020.

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This chart review of a quaternary academic medical center electronic medical record (EMR) aimed to identify patients at risk of development of maculopathy with exposure to pentosan polysulfate sodium (PPS). A review of electronic medical records of a quaternary medical center of patients with either documented exposure to PPS or diagnosis of interstitial cystitis (IC) from 2007 to 2019 was performed for retinal imaging and visual acuity; the study was conducted in August of 2019. 216 charts were included for analysis, of which 96 had documented eye exams and 24 had retinal imaging done. The authors identified three patients with maculopathy in the context of long-term exposure to PPS via chart review, and one additional patient was identified by referral. The median PPS exposure duration was 11 years (range 7 to 19 years). Median logMAR BCVA OD 0.6 range was 0.0-1.9 (approximate Snellen equivalent 20/80 range (20/20-20/1600)) and OS 0.7 range was 0.1-1.9 (approximate Snellen equivalent 20/100 range (20/25-20/1600)). Ultrawidefield color fundus imaging and fundus autofluorescence revealed findings of pigmentary changes and patchy macular atrophy. Optical coherence tomography (OCT) demonstrated outer retinal thinning and increased choroidal transmission coincident with areas of atrophy seen on fundus imaging. The authors concluded that less than half of patients at risk for development of maculopathy due to exposure to PPS had received eye examinations, suggesting that those at risk are not receiving adequate screening. They found two patients with PPS maculopathy who had relatively preserved central vision, one patient with bitemporal vision loss, and one patient who developed vision loss in both eyes.

MACULOPATHY SECONDARY TO PENTOSAN POLYSULFATE USE: A SINGLE-CENTER EXPERIENCE

Neil S Kalbag, Nenita Maganti, Alice T Lyon, Rukhsana G Mirza. Clin Ophthalmol. 2021 Feb 11;15:513-519. doi: 10.2147/OPHTH.S285013. eCollection 2021. PMID: 33603329 PMCID: PMC7884940 DOI: 10.2147/OPHTH.S285013

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The aim of this study was to investigate the prevalence of retinal pathology in patients with a history of exposure to pentosan polysulfate sodium (PPS). Patients exposed to PPS and seen in the ophthalmology clinic at Northwestern University during 1/1/2002 to 1/1/2019 were identified from electronic health records (EHR) by an electronic data warehouse (EDW) search. Visual acuity (VA), reasons for clinic visit, ocular conditions, and duration of exposure to PPS were noted. Chart review was performed for fundus exam findings and ophthalmologic imaging, specifically fundus photography, fundus autofluorescence, and ocular coherence tomography (OCT) images. When OCT or fundus photography was available, studies were evaluated by two independent graders. A total of 131 patients who were exposed to PPS and seen at the Northwestern Ophthalmology clinic were identified in the EHR. Forty patients of 131 had imaging. Patients with imaging or fundus examination suspicious for PPS maculopathy were placed into the suspect group. Of the 40 patients that had imaging, 5 (12.5%) had features suspicious for PPS maculopathy. Of the remaining 91, 5 (5.4%) had macular pigmentary changes described on fundus exam. Among the 10 patients in the suspect group, the average duration of PPS use was 4.2 years (range 0.3-11.6 years, interquartile range 5.5 years) and the average cumulative dose was 380g (range 29-1092g, interquartile range 132g). A novel drug-induced maculopathy has been associated with PPS use with a distinct clinical constellation that can be accurately identified with multimodal imaging.

PENTOSAN POLYSULFATE MACULOPATHY VERSUS AGE-RELATED MACULAR DEGENERATION: COMPARATIVE ASSESSMENT WITH MULTIMODAL IMAGING

Joseph S Christiansen, Alexander C Barnes, Duncan E Berry, Nieraj Jain. Can J Ophthalmol. 2021 Mar 12;S0008-4182(21)00044-2. doi: 10.1016/j.cjco.2021.02.007. Online ahead of print. PMID: 33722504 DOI: 10.1016/j.cjco.2021.02.007

The purpose of this study was to evaluate whether pentosan polysulfate maculopathy manifests distinctive imaging features that can be differentiated from those found in age-related macular degeneration (AMD). Local databases were queried to identify patients with a diagnosis of interstitial cystitis who were seen at the Emory Eye Center between May 2014 and January 2019 and who had fundus imaging available for review. Ninety patients met the eligibility criteria. Masked graders categorized patients based on imaging characteristics as follows: category 1: pentosan polysulfate maculopathy; category 2: AMD or drusen; category 3: neither; and

category 4: unsure. Pentosan polysulfate exposure characteristics were compared among groups. Of the 90 subjects evaluated, 79 (88%) were female and the median age was 61.5 years (range, 30-89). Seventeen patients were placed in category 1; 25 in category 2; 47 in category 3, and; 1 in category 4. Among categories 1 to 4, respectively, 17 (100%), 15 (60%), 28 (60%), and 0 patients had exposure to pentosan polysulfate ($p = 0.007$). Mean cumulative exposure to pentosan polysulfate across the four categories was 2.1, 0.36, 0.34, and 0 kg, respectively ($p < 0.00001$). Eyes with pentosan polysulfate maculopathy did not have typical drusen in the macula. Although pentosan polysulfate maculopathy resembles some aspects of AMD, the 2 conditions can be differentiated with the use of multimodal fundus imaging.

CHRONIC PELVIC PAIN

[AN UPDATE ON THE MANAGEMENT OF CHRONIC PELVIC PAIN IN WOMEN](#)

K Vincent, E Evans. Anaesthesia. 2021 Apr;76 Suppl 4:96-107. doi: 10.1111/anae.15421. PMID: 33682093 DOI: 10.1111/anae.15421

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Chronic pelvic pain represents a major public health problem for women and impacts significantly on their quality of life. Yet it is under-researched and a challenge to manage. Women who suffer from chronic pelvic pain frequently describe their healthcare journey as long, via a variety of specialists and frustrating, with their pain often dismissed. Aetiological factors and associations are best conceptualised using the 'three P's' model of predisposing, precipitating and perpetuating factors. This integrates the numerous biological, psychological and social contributors to the complex, multifactorial nature of chronic pelvic pain. Overall management involves analgesia, hormonal therapies, physiotherapy, psychological approaches and lifestyle advice, which like other chronic pain conditions relies on a multidisciplinary team approach delivered by professionals experienced and trained in managing chronic pelvic pain.

PAINFUL SEXUAL INTERCOURSE

[DYSPAREUNIA](#)

Muhammad Tayyeb, Vikas Gupta. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan. 2021 Feb 6. PMID: 32965830 Bookshelf ID: NBK562159.

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Painful sexual intercourse is a common female health problem. In medical terminology, it is called dyspareunia. It is a complex disorder that often goes neglected. The prevalence of dyspareunia varies from 3 to 18% worldwide, and it can affect 10 to 28% of the population in a lifetime. dyspareunia can be further categorized into superficial or deep, and primary or secondary. Superficial dyspareunia is limited to the vulva or vaginal entrance, while deep dyspareunia means the extension of pain into the deeper parts of the vagina or lower pelvis. Deep Dyspareunia is frequently associated with deep penetration. Primary dyspareunia pain initiates at the start of sexual intercourse, while in secondary dyspareunia, pain begins after some time of pain-free sexual activity. Dyspareunia is sometimes intermixed with vulvodynia, a genital pain that lasts more than three months with or without the association of sexual intercourse. Dyspareunia can also lead to sexual difficulties, such as lack of sexual desire and arousal, and can cause trouble in sexual relationships. It can have a significant impact on physical as well as mental health. It can lead to depression, anxiety, hypervigilance to pain, negative body image, and low self-esteem. So prompt management is crucial to address this disorder. In this review, the authors focus on the etiology, epidemiology, evaluation, management, and prognosis of the dyspareunia.

ENDOMETRIOSIS

[ENDOMETRIOSIS](#)

Eleni S. Tsamantioti, Heba Mahdy. Review in StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan.11. PMID: 33620854 Bookshelf ID: NBK567777

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Endometriosis is a chronic gynecologic disease characterized by the development and presence of histological elements like endometrial glands and stroma in anatomical positions and organs outside of the uterine cavity. The main clinical manifestations of the disease are chronic pelvic pain and impaired fertility. The localization of endometriosis lesions can vary, with the most commonly involved focus of the disease the ovaries followed by the posterior broad ligament, the anterior cul-de-sac, the posterior cul-de-sac, and the uterosacral ligament.

Endometriotic nodules also affect the intestinal tract and the urinary system like the ureter, the bladder, and the urethra. Nevertheless, endometriosis is not limited to the pelvis but can damage extra pelvic structures like the pleura, the pericardium, or the central nervous system. The main theories utilized to explain the pathogenesis of endometriosis are Sampson's theory, the coelomic metaplastic theory, the stem cell theory, the Müllerian remnant theory, and the vascular and lymphatic metastasis theory.

MANAGEMENT OF URINARY TRACT ENDOMETRIOSIS PATIENTS BY GYNECOLOGISTS

Emsal Pinar Topdağı Yılmaz, Ömer Erkan Yapça, Gülşah Aynaoglu Yıldız, Yunus Emre Topdağı, Fatih Özkaya, Yakup Kumtepe. J Turk Ger Gynecol Assoc. 2021 Jan 4. doi: 10.4274/jtgga.galenos.2020.2020.0054. Online ahead of print. PMID: 33389930 DOI: 10.4274/jtgga.galenos.2020.2020.0054

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The authors aimed to report the postoperative outcomes of urinary tract endometriosis (UTE), which is a form of deep infiltrative endometriosis, and to contribute to the literature by presenting the obtained results. In the present study, 70 patients who underwent surgery for endometriosis at their clinic between 2005 and 2019 and had a diagnosis of UTE in the final pathological assessment were examined in detail. Patient information was retrospectively retrieved from the medical records. Data obtained pre-, peri-, and postoperatively were analyzed. Mean age of the 70 patients included according to the study criteria was 32.73 ± 7.09 years. Ureteral involvement alone was observed in 49% (n = 34) patients, bladder involvement alone was observed in 24% (n = 17) patients, and both bladder and ureteral involvement were observed in 27% (n = 19) patients. Microscopic hematuria was detected in 16% (n = 11) patients (16%), whereas preoperative urinary tract findings, such as recurrent urinary tract infections, were detected in 19% patients (n = 13). Of the patients, 56% (n = 39) were identified with dyspareunia, 56% (n = 39) with dysmenorrhea, and 30% (n = 21) with pelvic pain. Although postoperative results were typically considered positive, surgical method performed in deep infiltrative endometriosis should aim to preserve fertility, improve quality of life, and reduce the complication rate to a minimum.

BLADDER ENDOMETRIOSIS: PREOPERATIVE MRI ANALYSIS WITH ASSESSMENT OF EXTENSION TO URETERAL ORIFICES

Pascal Rousset, Elodie Bischoff, Mathilde Charlot, Flavia Grangeon, Gil Dubernard, Philippe Paparel, Jean-Christophe Lega, François Golfier. Diagn Interv Imaging. 2020 Dec 15;S2211-5684(20)30300-4. doi: 10.1016/j.diii.2020.11.011. Online ahead of print. PMID: 33339775 DOI: 10.1016/j.diii.2020.11.011

The purpose of this study was to retrospectively evaluate the performance of magnetic resonance imaging (MRI) in locating endometriosis implants within the bladder wall with assessment of ureteral orifice extension using surgical findings as standard of reference. MRI examinations of 39 consecutive women (mean age: 31.2 ± 5.5 [SD] years; age range: 22-42 years) operated in 3 university hospitals for bladder endometriosis over a 6-year period were reviewed by 2 independent readers. Interobserver agreement was assessed using Kappa tests. Results of consensus reading were used to calculate sensitivity, specificity and accuracy of MRI for the diagnosis, location and extent of endometriosis implants using surgical findings as the standard of reference. Mean bladder repletion volume was 134 ± 110 [SD] mL (range: 21-479 mL). The mean largest endometriosis implant diameter was 30 ± 7 [SD] mm (range: 19-41 mm). On MR images, 34/39 (87%) endometriosis implants were present in the two anterior thirds of the dome ($k=0.45$), 31/39 (79%) extended or were present in the posterior third pouch ($k=0.92$) and 25/39 (64%) extended into the bladder base ($k=0.84$) with sensitivities of 100% (31/31; 95% confidence interval [CI]: 89-100%), 100% (30/30; 95% CI: 88-100%) and 90% (19/21; 95% CI: 69-98%), respectively, specificities of 83% (5/6, 95% CI: 36-100), 88% (7/8, 95% CI: 47-100%), 87% (13/15; 95% CI: 52-96), respectively and accuracies of 97% (36/37, 95% CI: 86-100%), 97% (37/38; 95% CI: 86-100%), and 89% (32/36; 95% CI: 74-97%), respectively. In 9 (9/25; 36%) patients with bladder base involvement, a zero distance was reported between endometriosis implants and ureteral orifices, all but one presenting with low-to-moderate bladder volumes. In the two patients who needed ureteral resection-reimplantation, ureteral dilation was associated with a zero distance. External adenomyosis was reported in 26/39 (66%) patients ($k=0.94$). It was concluded that a dedicated preoperative MRI work-up for bladder endometriosis helps accurately depict and locate endometriosis implants. Adequate bladder filling is needed to improve appropriate estimate of the distance between endometriosis implants and ureteral orifices to better predict requirement of ureteral resection-reimplantation.

NATIONAL SURVEY OF BLADDER ENDOMETRIOSIS CASES IN JAPAN

Tetsuya Hirata, Kaori Koga, Fuminori Taniguchi, Naoko Takazawa, Ritsuo Honda, Toshiaki Tanaka, Masatoshi Kurihara, Jun Nakajima, Kotaro Yoshimura, Mari Kitade, Hisashi Narahara, Jo Kitawaki, Tasuku Harada, Hidetaka

Katabuchi, Shigeo Horie, Yutaka Osuga. J Obstet Gynaecol Res. 2021 Jan 4. doi: 10.1111/jog.14656. Online ahead of print. PMID: 33398892 DOI: 10.1111/jog.14656

The aim of this study was to describe the clinical presentation, operative or medical management, and postoperative recurrence of bladder endometriosis (BE). The authors conducted a national survey to investigate BE cases from 2006 to 2016 in Japan. Histologically diagnosed cases were extracted and then investigated for the following factors: age at diagnosis, body mass index, symptoms, imaging modalities, surgical therapy, hormonal therapy, follow-up period, and postoperative recurrence. Eighty-nine patients with pathologically benign BE were identified. Eighty patients underwent surgery, whereas nine did not. Moreover, 34 and 44 patients underwent transurethral resection (TUR) and partial cystectomy (PC), respectively. Cumulative recurrence rates were significantly higher with TUR than with PC ($p < 0.05$). The recurrence rate tended to be higher after laparoscopic PC ($n = 24$) than after open PC ($n = 20$), but the difference was not statistically significant ($p = 0.0879$). Of the nine nonsurgical patients, eight received hormonal therapy and one did not. Efficacy rates of dienogest, GnRH agonist, and OC were 85.7%, 66.7%, and 66.7%, respectively. Of five patients with BE extending to the ureter or ureteral orifices, two underwent PC and ureteroneocystostomy and one underwent total nephroureterectomy due to renal function loss. The authors believe this to be the first study to compare the postoperative recurrence of BE after TUR and PC. They found that cumulative recurrence rate is significantly lower after PC than after TUR. BE extending to the ureter or ureteral orifices is a very challenging condition. Further studies are required for the optimal management of BE.

VULVODYNIA

VULVODYNIA

Vanessa M Barnabei. Clin Obstet Gynecol. 2020 Dec;63(4):752-769. doi: 10.1097/GRF.0000000000000576. PMID: 33074981 DOI: 10.1097/GRF.0000000000000576

Vulvodynia is a heterogeneous, chronic pain condition of unknown etiology that affects 7% to 15% of women. It affects sexual function and quality of life. Vulvodynia can be primary or secondary, localized or generalized, and spontaneous or provoked. Contributing factors for provoked vulvodynia might include vulvovaginal infections, low estrogen states, and underlying anxiety disorder. Generalized vulvodynia likely arises from underlying connective tissue or neurological dysfunction. Vulvodynia treatment must be individualized on the basis of the patient's presentation and physical examination findings. Surgical excision of the vulvar vestibule has high success rates but other modalities showing success include pelvic floor physical therapy and cognitive-behavioral therapy.

IRRITABLE BOWEL SYNDROME

DOES IRRITABLE BOWEL SYNDROME INCREASE THE RISK OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME? A COHORT STUDY OF LONG TERM FOLLOW-UP

Kun-Min Chang, Ming-Huei Lee, Hsuan-Hung Lin, Shang-Liang Wu, Huei-Ching Wu. Int Urogynecol J. 2021 Feb 23. doi: 10.1007/s00192-021-04711-3. Online ahead of print. PMID: 33620539 DOI: 10.1007/s00192-021-04711-3

IC/BPS and irritable bowel syndrome (IBS) often occur concomitantly without an obvious reason. It is important to determine the relationship between these diseases. Chang and colleagues from Taiwan aimed to determine whether IBS increases the risk of IC/BPS. They identified newly diagnosed IBS patients between 2002 and 2013 from a nationwide database as the IBS cohort. Subjects diagnosed with IC/BPS before IBS were excluded. Cox's regression analysis with a hazard ratio (HR) of IC/BPS between IBS and the non-IBS cohort was applied to unmatched and matched (16 confounders of propensity scores) models. The time from diagnosis of IBS to IC/BPS was also calculated. In the unmatched group, which included 100,124 IBS (55% female) and 874,048 non-IBS patients, the IC/BPS adjusted HR was 1.292 (95% confidence interval [CI], 1.131-1.476; $p < 0.0001$) in the IBS cohort compared with the non-IBS cohort. In the matched group, there were 85,359 patients in each cohort, and the IC/BPS HR was 1.599 (95% CI, 1.344-1.903; $p < 0.0001$). The average numbers of years until the development of IC/BPS in the IBS cohort and non-IBS cohort were 4.60 ± 2.58 ($n = 253$) and 5.99 ± 3.49 ($n = 295$) years, respectively. IBS was shown to increase the risk of IC/BPS in this 12-year cohort study. The time from the diagnosis of IBS to IC/BPS was 5.35 ± 3.18 years. A common pathophysiology of IBS and IC/BPS is possible. Clinicians should be mindful of the association and promote collaborative care of these two elusive diseases.

THE COLONIC MUCOSAL MICRORNAS, MICRORNA-219A-5P AND MICRORNA-338-3P, ARE DOWNREGULATED IN IRRITABLE BOWEL SYNDROME AND ARE ASSOCIATED WITH BARRIER FUNCTION AND MAPK SIGNALING

Swapna Mahurkar-Joshi, Carl Robert Rankin, Elizabeth Jane Videlock, Artin Soroosh, Abhishek Verma, Ariela Khandadash, Dimitrios Iliopoulos, Charalabos Pothoulakis, Emeran A Mayer, Lin Chang. *Gastroenterology*. 2021 Feb 19;S0016-5085(21)00430-3. doi: 10.1053/j.gastro.2021.02.040. Online ahead of print. PMID: 33617890 DOI: 10.1053/j.gastro.2021.02.040

Alterations in microRNA (miRNA) and in the intestinal barrier are putative risk factors for irritable bowel syndrome (IBS). The authors aimed to identify differentially expressed colonic mucosal miRNAs, their targets in IBS compared to healthy controls (HCs), and putative downstream pathways. 29 IBS patients (15 IBS with constipation [IBS-C], 14 IBS with diarrhea [IBS-D]), and 15 age-matched HCs underwent sigmoidoscopy with biopsies. A nCounter array was used to assess biopsy associated miRNA levels. FDR<10% was considered significant. Real-time PCR (RT-PCR) was used to validate differentially expressed genes. To assess barrier function, trans-epithelial electrical resistance (TEER) and dextran flux assays were performed on Caco-2 intestinal epithelial cells that were transfected with miRNA-inhibitors or control inhibitors. Protein expression of barrier function associated genes was confirmed using western blots. Four out of 247 miRNAs tested were differentially expressed in IBS compared to HCs (FDR<10%). RT-PCR validation suggested decreased levels of miR-219a-5p and miR-338-3p in IBS (0.026 and p=0.004), and IBS-C (p=0.026 and 0.06) vs. HCs as the strongest associations. Inhibition of miR-219a-5p resulted in altered expression of proteasome/barrier function genes. Functionally, miR-219a-5p inhibition enhanced the permeability of intestinal epithelial cells as TEER was reduced (25-50%, p<0.05) and dextran flux was increased (p<0.01). Additionally, inhibition of miR-338-3p in cells caused alterations in the MAPK signaling pathway genes. Two microRNAs that potentially affect permeability and visceral nociception were identified to be altered in IBS patients. MiR-219a-5p and miR-338-3p potentially alter barrier function and visceral hypersensitivity via neuronal and MAPK signaling and could be therapeutic targets in IBS.

IRRITABLE BOWEL SYNDROME AND THE MENSTRUAL CYCLE

Girish K Pati, Chinmayee Kar, Jimmy Narayan, Kanishka Uthansingh, Manas Behera, Manoj K Sahu, Debakanta Mishra, Ayaskanta Singh. *Cureus*. 2021 Jan 14;13(1):e12692. doi: 10.7759/cureus.12692. PMID: 33614302 PMCID: PMC7883586 DOI: 10.7759/cureus.12692

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Irritable bowel syndrome (IBS) is a common gastrointestinal (GI) disorder. Female patients with bowel disease commonly report worsening of symptoms in the menstrual cycle. However, there is a paucity of data regarding IBS presentations' variation during different phases of the menstrual cycle. This study from India aimed to evaluate the same in female IBS patients. Consecutive premenopausal female patients with the diagnosis of IBS attending the outdoor (OPD) of Department of Gastroenterology and Gynaecology; IMS and SUM Hospital, Bhubaneswar, Odisha from June 2019 to December 2019 were included in the study and evaluated by a set of questionnaires regarding various presentations during all the three phases of the menstrual cycle. Consecutive 102 cases with the diagnosis of IBS were included in the study and evaluated. The mean age of presentation was in mid-30s. Most of the subjects suffered from IBS mixed (IBS-M) type. More patients significantly suffered from constipation (27.27%) during the luteal phase of their menstrual cycles than the menstrual period of their cycles (p - 0.009). More than 50% of all the cases suffered from abdominal bloating during all phases of the menstrual cycle, which was quite disturbing and affected the quality of life. These IBS patients were more symptomatic with more significant limitation of daily activities, suffered from low quality of life, and obtained physician consultation during the menstrual phase as compared to other cycle stages. Premenopausal female patients with IBS become much more symptomatic during the menstrual phase of the cycle than other stages of the cycle.

FIBROMYALGIA

FIBROMYALGIA PAIN AND DEPRESSION: AN UPDATE ON THE ROLE OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION

Abdul Haque Ansari, Ajay Pal, Aditya Ramamurthy, Maciej Kabat, Suman Jain, Suneel Kumar. *ACS Chem Neurosci*. 2021 Jan 4. doi: 10.1021/acchemneuro.0c00785. Online ahead of print. PMID: 33397091 DOI: 10.1021/acchemneuro.0c00785

Fibromyalgia is a musculoskeletal pain of different parts of the body, which is also associated with fatigue, lack of sleep, cognition deficits, family history, gender bias, and other disorders such as osteoarthritis and rheumatoid arthritis. It is generally initiated after trauma, surgery, infection, or stress. Fibromyalgia often

coexists with several other conditions or disorders such as temporomandibular joint disorders, bowel and bladder syndrome, anxiety, depression, headaches, and interstitial cystitis. While there is no permanent cure for fibromyalgia, some interventions are available with multiple side effects. rTMS (repetitive transcranial magnetic stimulation), a noninvasive management strategy is used widely for various pain-related etiologies including fibromyalgia in both the laboratory and clinical settings. In this review, the authors discuss the role and mechanism of action of rTMS in fibromyalgia patients and on associated comorbidities including anxiety, pain, depression, neurotransmitter alterations, sleep disorders, and overall quality of life of the patients suffering from this chronic problem. They also provide an update on the rTMS application in the clinical trials of fibromyalgia patients and prospective management therapy for multiple problems that these patients suffer.

CANNABIDIOL USE FOR FIBROMYALGIA: PREVALENCE OF USE AND PERCEPTIONS OF EFFECTIVENESS IN A LARGE ONLINE SURVEY

Kevin F Boehnke, Joel J Gagnier, Lynne Matallana, David A Williams. J Pain. 2021 Jan 2;S1526-5900(20)30117-6. doi: 10.1016/j.jpain.2020.12.001. Online ahead of print. PMID: 33400996 DOI: 10.1016/j.jpain.2020.12.001

Cannabidiol (CBD) is widely advertised as helpful for chronic pain management but research is limited. Using a cross-sectional, anonymous survey, the authors examined patterns of naturalistic CBD use among individuals with fibromyalgia (FM) and other chronic pain conditions. Their objective was to better understand rates of CBD use, reasons for use and discontinuation, communication with healthcare professionals about CBD, and perceptions of CBD effectiveness and safety among people with FM. After excluding incomplete surveys, their study population consisted of 2701 participants with fibromyalgia, primarily in the United States. Overall, 38.1% reported never using CBD, 29.4% reported past CBD use, and 32.4% reported current CBD use. Past-year cannabis use was strongly associated with past or current CBD use. Those using CBD typically did so due to inadequate symptom relief, while those not using CBD typically cited safety concerns as their reason for not using CBD. Two-thirds of participants disclosed CBD use to their physician, although only 33% asked for physician advice on using CBD. Participants used CBD for numerous FM-related symptoms (most commonly pain), and generally reported slight to much improvement across symptom domains. Around half of participants reported side effects, which were typically minor. The authors note that their findings are limited by selection bias and their cross-sectional design, which prevents causal associations. In conclusion, CBD use is common among individuals with FM and many individuals using CBD report improvements across numerous FM-related symptoms. The findings highlight the need for additional rigorous studies to better understand CBD's potential for FM management. This article indicates that that CBD use is common among people with fibromyalgia, and the results suggest that many derive benefit from using CBD across multiple symptoms domains. Clinicians should discuss CBD use with fibromyalgia patients, and future studies are needed to rigorously assess CBD's therapeutic value for fibromyalgia symptoms.

LUPUS CYSTITIS

VERY SEVERE AND REFRACTORY NONINFECTIOUS CYSTITIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: POTENTIAL ROLE OF RITUXIMAB THERAPY

Vanessa Ocampo-Piraquive, Inés Mondragón-Lenis, Juan G De Los Rios, Carlos A Cañas. Case Rep Rheumatol. 2021 Feb 27;2021:6610111. doi: 10.1155/2021/6610111. eCollection 2021. PMID: 33728086 PMCID: PMC7936892 DOI: 10.1155/2021/6610111

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Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease with various clinical manifestations, including, rarely, a form of interstitial cystitis (lupus cystitis, LC). LC can be asymptomatic and usually has discrete symptoms that improve with conventional therapies available for SLE and/or typical interstitial cystitis. A very severe and refractory form is rarely described. In this study from Colombia, the authors present four patients with SLE and a very severe form of noninfectious cystitis refractory to the different forms of treatment described. The clinical descriptions of the cases, demographic factors, manifestations associated with SLE, and clinical and paraclinical manifestations related to cystitis, treatments, and outcomes are provided. A proposal for the pathogenesis of this condition is based on the common findings of these patients, including the fact that three were in SLE remission and all four receiving rituximab as induction and/or maintenance therapy.

SJÖGREN'S SYNDROME

RENAL DISEASE IN PRIMARY SJÖGREN'S SYNDROME

Oshorenu Aiyegbusi , Laura McGregor, Lucy McGeoch, David Kipgen, Colin C Geddes, Kathryn I Stevens. Rheumatol Ther. 2020 Dec 24. doi: 10.1007/s40744-020-00264-x. Online ahead of print. PMID: 33367966 DOI: 10.1007/s40744-020-00264-x

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Primary Sjögren's syndrome (pSS) is a chronic autoimmune disorder characterised by lymphocytic infiltration of the exocrine glands, predominantly the salivary and lacrimal glands, leading to sicca symptoms. Patients may have extraglandular disease involving multiple organs, including the kidneys. 5% of patients with pSS can have renal involvement. Kidney disease in pSS presents a diagnostic challenge, as clinical symptoms are often insidious and can precede sicca symptoms. pSS affects the kidney through lymphocytic infiltration of renal tubules or immune complex deposition, leading to an array of clinical features. Tubulointerstitial nephritis is the most common histological pattern of kidney disease. Other tubular injuries include renal tubular acidosis with hypokalaemia, Fanconi's syndrome and diabetes insipidus. Glomerular disease is less common and typically involves an immune complex-mediated process. Optimal treatment for kidney diseases in pSS is not established, and treatment is guided by the pattern of disease. For tubulointerstitial nephritis, management involves electrolyte imbalance correction and the use of immunosuppression, including steroids. Treatment of glomerular disease is targeted to the histological pattern, and often requires a combination of immunosuppressive agents. The risk of end-stage kidney disease is low. Nevertheless, patients with pSS and kidney disease have significantly reduced quality of life.

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