

# International Painful Bladder Foundation

*The IPBF is a voluntary non-profit organization for interstitial cystitis/bladder pain syndrome/hypersensitive bladder*  
[www.painful-bladder.org](http://www.painful-bladder.org)

## **IPBF e-Newsletter and Research Update Issue 54, February 2020**

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

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

- Meeting Reviews
- Publications
- Upcoming meetings
- Calendar Overview
- Research Update
- Donations & Sponsoring

## **MEETING REVIEWS**

### **REVIEW OF ESSIC ANNUAL SCIENTIFIC MEETING, AMSTERDAM, 5-7 DECEMBER 2019**

The **ESSIC 2019 annual scientific meeting (International Society for the Study of BPS/IC)**, held at the DoubleTree by Hilton Hotel in Amsterdam and enthusiastically chaired by Dick Janssen MD (NL), was attended by some 170 participants from no fewer than 33 countries around the world including doctors, nurses, physiotherapists and patient advocates and all these groups were well represented among the speakers.

The meeting 5-7 December coincided with the Feast of St Nicholas which is celebrated in the Netherlands on 5 December. The opening day was consequently a festive occasion with a personal visit by St Nicholas ("Sinterklaas" in Dutch) who took time off from his busy 5 December gift-delivery schedule to wish the delegates and speakers every success!

A successful innovation this year was the organization of 3 interactive workshops on the Saturday morning: for physiotherapists, nurses and the new ESSIC committees.

This 2019 meeting was remarkable for its great atmosphere, high level of interaction and particularly the tremendous enthusiasm from everyone. It was encouraging to see younger generations of health professionals, including nurses and physiotherapists, participating to the full. The meeting was also attended by far more patient advocates than ever before, many of whom had travelled long distances, including from South Africa, Israel, Canada, USA and India as well as many different European countries. Some are new to the field and ESSIC 19 therefore provided a perfect learning and networking opportunity.

The theme of the ESSIC 19 meeting was "the right multidisciplinary treatment for the individual patient". The meeting also emphasized the need for appropriate phenotyping/subtyping with many speakers recommending that Hunner lesion should be split off or at the very least that lesion patients should not be combined with non-lesion patients in drug trials or studies.

An important message was that progress means sorting out the patients into relevant groups so that each group gets appropriate treatment, while at the same time ensuring that in a clinical setting each patient receives individual, personalized, usually empiric treatment.

This review is also only able to pick out a few highlights, an unenviable task bearing in mind that there were many excellent speakers at this meeting. [Click here to read the full review.](#)

#### **INTERNATIONAL PATIENT ADVOCATE NETWORKING MEETING HELD FOLLOWING ESSIC MEETING, SATURDAY 7 DECEMBER 2019 WAS A GREAT SUCCESS**

The Dutch IC patient association (ICP) took the opportunity to host and organize an international patient advocacy lunch and networking meeting directly after the ESSIC meeting finished on Saturday 7 December. This was a huge success and in addition to patient advocates from many countries was also attended by a number of medical professionals who support patient organizations in medical advisory boards as well as ESSIC Board members. Hopefully this will ultimately lead to some kind of global alliance of patient support groups. Many thanks are due to the ICP and especially Mathilde Scholtes for their hard work in organizing this event and to Dick Janssen MD for kindly chairing the meeting. [Click here to read more.](#)

#### **IPBF PARTICIPATED IN IMI-PAINCARE RESEARCH CONSORTIUM GENERAL ASSEMBLY 15-16 JANUARY 2020, WINDLESHAM, SURREY, UNITED KINGDOM**

IMI ([www.imi.europa.eu](http://www.imi.europa.eu)) – Innovative Medicines Initiative – is a public/private partnership aiming to improve the competitive situation of the European Union in the field of pharmaceutical research.

The IMI-PainCare Research Consortium comprises patients, academia and industry. The main hypothesis to be tested is that endometriosis-associated pain (EAP) and interstitial cystitis/bladder pain syndrome (IC/BPS) are primarily chronic pain conditions featuring similarities in mechanisms underlying pain generation and maintenance, albeit associated with specific pathological lesions and end-organ symptoms. IMI-Paincare comprises 3 sub-projects: PROMPT, Bio-Pain and TRiPP.

The focus of TRiPP is on two indications with common pain symptoms: endometriosis and IC/BPS. The key concepts of TRiPP are that:

- Women with chronic pelvic pain due to endometriosis or IC/BPS can be stratified into mechanistically and/or prognostically relevant clusters.
- Women show biomarker profiles associated with vulnerability to develop pain and/or to maintain pain, independent of the underlying peripheral disease.
- Pre-clinical models that fully reflect human phenotypes will have enhanced translational value.

A main objective is to improve disease understanding and optimize animal models to identify new treatment options for patients.

There are three patient representatives actively participating in this research consortium spanning several years: Jane Meijlink (IPBF) for IC/BPS, together with Judy Birch (Pelvic Pain Support Network, UK) and Lone Hummelshoj (Endometriosis.org) both for endometriosis. They also participate in monthly TRiPP-update telephone conferences. The patient perspective and the grass roots expertise of the patient representatives can play an important and valuable role in research projects such as this.

## **PUBLICATIONS**

#### **IPBF UPDATE OF INFORMATION ON ASSOCIATED DISEASES IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME**

Dr Joop P. van de Merwe from the Netherlands has updated the IPBF information on associated diseases in IC/BPS. These include allergy, fibromyalgia, irritable bowel syndrome, Crohn's disease, ulcerative colitis, systemic lupus erythematosus, rheumatoid arthritis and Sjögren's syndrome. Good cooperation between various medical specialists in a multidisciplinary approach is essential for optimal management of patients with IC/BPS and associated diseases. [Click here for direct link.](#) Or via home page: [www.painful-bladder.org](http://www.painful-bladder.org)

#### **RECIPE & DIET BOOKS FOR IC/BPS**

Adjusting your diet as an IC/BPS patient is a mainstay of self-help. However, every patient is different and not all IC/BPS patients appear to be affected by diet or by the same items, but by eliminating items known to cause irritation based on their own experience, a patient can at least avoid unnecessary exacerbation of the bladder symptoms. Patients with very mild IC/BPS may even find that diet adjustment is the only treatment they need. Basic items to try avoiding include food/drink containing caffeine, citrus fruit and juices, other acidic food such

as tomatoes, vinegar etc., artificial sweeteners, alcoholic drinks, carbonated drinks/soda, highly spiced food especially containing hot pepper. It should be stressed, however, that not all patients are affected by all of these. It is therefore great to see two new books produced for IC/BPS patients: a cookbook from Israel and a book on diet from India.

- The Israeli Association for Bladder Syndromes, Chair Yafit Shoval, has published an Israeli kosher cookbook for IC/BPS patients "Delicious with IC" by Elinoar Rabin and Yafit Shoval with medical input by Professor Kobie Stav and Dr Ilan Eldar and an introduction by Professor Yoram Abramov. Packed with delicious recipes! [www.shalpuchit.co.il](http://www.shalpuchit.co.il)

- "Indian Diet for Interstitial Cystitis (Eat Healthy and Protect your Bladder)" by Neelanjana Singh and Rajesh Taneja, published by Avichal Publishing Company ( [www.apcbooks.co.in](http://www.apcbooks.co.in)) is a book about diet therapy for IC/BPS patients in India, a country renowned for its highly spiced foods. Also includes a chapter on lifestyle.

(See more on effects of diet:

- *Effects of Comestibles on Symptoms of Interstitial Cystitis*, Barbara Shorter, Martin Lesser, Robert M. Moldwin, Leslie Kushner. *Journal of Urology*, July 2007, vol. 178, 145-152.

- *Diet and its role in interstitial cystitis/bladder pain syndrome (IC/BPS) and comorbid conditions*. Friedlander JJ, Shorter B, Moldwin RM. *BJU Int.* 2012 Jun;109(11):1584-91)

#### **MORE PUBLICATIONS ON POSSIBILITY OF A LINK BETWEEN ORAL PENTOSAN POLYSULFATE AND PIGMENTARY MACULOPATHY**

In the research update, you will find more publications on the possibility of a link between long-term oral pentosan polysulfate and pigmentary maculopathy. While it should be emphasized that this is still under investigation and needs further studies, it would be wise for patients already taking oral PPS to err on the safe side and have an annual eye check, and for patients contemplating taking this treatment to have their eyes checked before starting. It goes without saying that any patient who has been taking oral PPS for several years and is experiencing vision problems should immediately undergo ophthalmic screening.

#### **UPCOMING MEETINGS**

##### **9<sup>TH</sup> GLOBAL PATIENTS CONGRESS 2020 – SAVE THE DATE!**

The International Alliance of Patients' Organizations (IAPO) has announced that IAPO's 9<sup>th</sup> Global Patients Congress will be held 16-18 April 2020 at the Surgeons Quarter in Edinburgh, Scotland. At the 2020 Global Patient Congress, members, patients and partners will share their experiences of working and promoting global health. Delegates will also have the opportunity to build their capacity through a series of talks, interactive discussions and expert workshops. More information can be found at: [www.globalpatientscongress.org](http://www.globalpatientscongress.org)

#### **CALENDAR OVERVIEW**

##### **2020**

###### **EAU 2020**

20-24 March 2020, RAI Amsterdam, Europaplein 24, 1078 GZ Amsterdam, The Netherlands  
<https://eaucongress.uroweb.org/eau20/>

###### **9<sup>TH</sup> GLOBAL PATIENTS CONGRESS**

16-18 April 2020  
Surgeons Quarter, Edinburgh, Scotland.  
[www.globalpatientscongress.org](http://www.globalpatientscongress.org)

###### **AUA (AMERICAN UROLOGICAL ASSOCIATION) 2020**

15-18 May 2020.  
Walter E. Washington Convention Center,  
801 Mt Vernon Pl., NW, Washington, DC 20001.  
<https://www.aua2020.org/>

###### **VII MIPS ANNUAL MEETING**

4-6 June 2020, Athens  
<https://www.mipsnet.org/mips-2020>

**18TH WORLD CONGRESS ON PAIN**

August 4-8, 2020, Amsterdam, The Netherlands  
<https://www.iaspworldcongressonpain.org/amsterdam/>

**50th INTERNATIONAL CONTINENCE SOCIETY ANNUAL MEETING 2020**

26-29 August, Las Vegas, USA  
<https://www.ics.org/2020>

**GIBS 2020 (GLOBAL INTERSTITIAL CYSTITIS BLADDER PAIN SOCIETY)**

Annual Congress on IC/BPS  
5-6 September 2020, Mumbai India  
<https://gibsociety.com/featured-image/#>

## 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.*

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

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

### [EXERCISE MODULATES NEURONAL ACTIVATION IN THE MICTURITION CIRCUIT OF CHRONICALLY STRESSED RATS: A MULTIDISCIPLINARY APPROACH TO THE STUDY OF UROLOGIC CHRONIC PELVIC PAIN SYNDROME \(MAPP\) RESEARCH NETWORK STUDY.](#)

*Holschneider DP, Wang Z, Guo Y, Sanford MT, Yeh J, Mao JJ, Zhang R, Rodriguez LV. *Physiol Behav.* 2019 Dec 26:112796. doi: 10.1016/j.physbeh.2019.112796. [Epub ahead of print] PMID: 31884113*

Rats exposed to water avoidance stress (WAS) show increased urinary frequency, increased somatosensory nociceptive reflex responses, as well as altered brain responses to bladder distension, analogous to similar observations made in patients with urologic chronic pelvic pain syndrome (UCPPS). Exercise has been proposed as a potential treatment option for patients with chronic urinary frequency and urgency. This MAPP research team examined the effects of exercise on urinary voiding parameters and functional brain activation during bladder distension in rats exposed to WAS. WAS exposure in sedentary animals (WAS/no-EX) increased voiding frequency and decreased urinary volumes per void. Exercise exposure in WAS animals (WAS/EX) resulted in a progressive decline in voiding frequency back to the baseline, as well as increased urinary volumes per void. WAS/EX showed a significantly greater positive brain functional connectivity compared to WAS/no-EX animals within regions of the extended reflex loop (PAG, Barrington's nucleus, intermediodorsal thalamic nucleus, pons), as well as within regions of the corticolimbic decision-making loop of the micturition circuit, with a strikingly negative correlation between these pathways. Urinary frequency was positively correlated with rCBF in the pons, and negatively correlated with rCBF in the cingulate cortex. Their results suggest that chronic voluntary exercise may decrease urinary frequency at two points of control in the micturition circuit. During the urine storage phase, it may diminish the influence of the reflex micturition circuit itself, and/or it may increase corticolimbic control of voiding. Exercise may be an effective adjunct therapeutic intervention for modifying the urinary symptoms in patients with UCPPS.

**[A MAPP NETWORK CASE-CONTROL STUDY OF UROLOGICAL CHRONIC PELVIC PAIN COMPARED WITH NONUROLOGICAL PAIN CONDITIONS.](#)**

Afari N, Buchwald D, Clauw D, Hong B, Hou X, Krieger JN, Mullins C, Stephens-Shields AJ, Gasperi M, Williams DA; MAPP Research Network. *Clin J Pain.* 2020 Jan;36(1):8-15. doi: 10.1097/AJP.0000000000000769. PMID: 31794439

Limited research suggests commonalities between urological chronic pelvic pain syndromes (UCPPS) and other non-urological chronic overlapping pain conditions (COPCs) including fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome. The goal of this case-control study was to examine similarities and differences between UCPPS and these other COPCs. As part of the Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research (MAPP) Network, the authors examined 1039 individuals with UCPPS, nonurological COPCs, and healthy controls. Validated standardized measures were used to assess urological symptoms, nonurological pain symptoms, and psychosocial symptoms and traits. Participants with UCPPS had more urological symptoms than nonurological COPCs or HCs; nonurological COPC group also had significantly worse urological symptoms than HCs. Participants with nonurological COPCs reported more widespread pain than those with UCPPS, yet both groups had similarly increased symptoms of anxiety, depression, negative affect, perceived stress, neuroticism, and lower levels of extraversion than HCs. Participants with UCPPS with and without COPCs reported more catastrophizing than those with nonurological COPCs. Findings are consistent with the hypothesis of common underlying biopsychosocial mechanisms and can guide the comprehensive assessment and treatment of these conditions regardless of the primary site of pain or diagnosis. Heightened catastrophizing in UCPPS should be examined to inform psychosocial interventions and improve patient care.

**[VOLUNTARY EXERCISE IMPROVES VOIDING FUNCTION AND BLADDER HYPERALGESIA IN AN ANIMAL MODEL OF STRESS-INDUCED VISCERAL HYPERSENSITIVITY: A MULTIDISCIPLINARY APPROACH TO THE STUDY OF UROLOGIC CHRONIC PELVIC PAIN SYNDROME RESEARCH NETWORK STUDY.](#)**

Sanford MT, Yeh JC, Mao JJ, Guo Y, Wang Z, Zhang R, Holschneider DP, Rodriguez LV. *Neurourol Urodyn.* 2020 Jan 13. doi: 10.1002/nau.24270. [Epub ahead of print] PMID: 31944369

The underlying mechanism of interstitial cystitis/bladder pain syndrome (IC/BPS) is not well understood and evaluation of current therapeutic interventions has not identified any generally effective treatments. Physical activity has shown beneficial effects on individuals suffering from chronic pain. Anxiety-prone rats exposed to water avoidance stress (WAS) develop urinary frequency and lower bladder sensory thresholds with high face and construct validity for the study of IC/BPS. The aim of this MAPP Network study was to evaluate the role of chronic voluntary exercise on urinary frequency, voiding function, and hyperalgesia in animals exposed to WAS. Twenty-six female Wistar-Kyoto rats were exposed to WAS and thereafter randomized to either voluntary exercise for 3 weeks or sedentary groups. Voiding parameters were assessed at baseline, post-WAS, and weekly for 3 weeks. Before euthanasia, the animals underwent cystometrogram (CMG), external urinary sphincter electromyography, and assessment of visceromotor response (VMR) to isotonic bladder distension (IBD). WAS exposure resulted in adverse changes in voiding parameters. Compared with sedentary animals, animals in the voluntary exercise group had improved voiding parameters during metabolic cage and CMG testing, as well as improved bladder sensory thresholds as determined by VMR during IBD. It was concluded that voluntary exercise in an animal model of chronic stress leads to improvement in voiding function and visceral bladder hyperalgesia.

**HUNNER LESION**

**[THERAPEUTIC ENDOSCOPIC TREATMENT PLUS MAINTENANCE DIMETHYL SULFOXIDE THERAPY PROLONGS RECURRENCE-FREE TIME IN PATIENTS WITH HUNNER TYPE INTERSTITIAL CYSTITIS: A PILOT STUDY.](#)**

Otsuka A, Suzuki T, Matsushita Y, Watanabe H, Tamura K, Motoyama D, Ito T, Sugiyama T, Miyake H. *Int Neurourol J.* 2019 Dec;23(4):327-333. doi: 10.5213/inj.1938110.055. Epub 2019 Dec 31. PMID: 31905280

The purpose of this study from Japan was to evaluate whether hydrodistention with fulguration of Hunner lesions (HD/FUL) plus maintenance dimethyl sulfoxide (DMSO) therapy prolongs the recurrence-free time in patients with Hunner type interstitial cystitis (IC). The study enrolled patients with Hunner type IC who required repeat HD/FUL due to recurrence of IC symptoms after the first HD/FUL. All patients received a second HD/FUL plus maintenance DMSO therapy. The maintenance DMSO therapy was performed every 2 weeks for a total of 8 instillations, and then once every 4 weeks thereafter. The recurrence-free time from HD/FUL to therapeutic failure was estimated using the Kaplan-Meier method. The recurrence-free time between the first HD/FUL and second HD/FUL plus maintenance DMSO therapy was statistically compared using the log-rank test. A total of 21 patients (mean age, 66.3±10.8 years) with Hunner type IC were evaluated. The recurrence-free time for the

second HD/FUL plus maintenance DMSO therapy was significantly longer than that for the first HD/FUL ( $P < 0.0001$ ). The median recurrence-free time for the first HD/FUL was 10.1 months, while that for the second HD/FUL plus maintenance DMSO therapy has yet to be reached. The recurrence-free rate for the first HD/FUL was 81.0% at 6 months, 38.1% at 1 year, 9.5% at 2 years, and 4.8% at 3 years. In contrast, the rate for the second HD/FUL plus maintenance DMSO therapy was 100% at 6 months, 94.7% at 1 year, 82.6% at 2 years, and 82.6% at 3 years. There were no significant differences in efficacy between the first and second HD/FUL. It was concluded that HD/FUL plus maintenance DMSO therapy clearly prolongs the recurrence-free time compared with HD/FUL alone in Hunner type IC.

#### **COMPARISON OF THE EFFICACY BETWEEN TRANSURETHRAL COAGULATION AND TRANSURETHRAL RESECTION OF HUNNER LESION IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PATIENTS: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL.**

*Ko KJ, Cho WJ, Lee YS, Choi J, Byun HJ, Lee KS. Eur Urol. 2020 Jan 17. pii: S0302-2838(20)30002-6. doi: 10.1016/j.eururo.2020.01.002. [Epub ahead of print] PMID: 31959549*

The purpose of this study from Korea was to evaluate the efficacy and safety of transurethral resection (TUR) and transurethral coagulation (TUC) as treatments for Hunner lesion (HL) in IC/BPS. This was a single-center, prospective, randomized controlled trial involving 126 patients with HL in IC/BPS. Primary outcome was recurrence-free time after surgery. Secondary outcomes included change of the number of frequency, nocturia, urgency episodes in voiding diaries, O'Leary-Sant Interstitial Cystitis Symptom Index (ICSI) and Interstitial Cystitis Problem Index (ICPI), pelvic pain and urgency/frequency (PUF) symptom scale, and visual analog scale (VAS) for pain and risk factors for recurrence. There were no differences in the recurrence-free time between treatment groups, a difference of 12.2 mo for TUR, and a difference of 11.5 mo for TUC. No difference was found in decreased mean daytime frequency, nocturia, urgency episodes, ICSI, ICPI, PUF symptom scale, and VAS for pain between both groups over 12 mo. Regardless of treatment types, there were significant improvements in all symptom questionnaires and pain compared with baseline. Treatment type (TUR or TUC), age, sex, previous history of hydrodistension, and number of HLs did not affect recurrence. Incidence of bladder injury was higher in the TUR group (7.9%) than in the TUC group (3.4%). There was no difference in the recurrence-free time and effect on urinary symptoms, including pain between TUC and TUR, for HL. Taking into account procedure-related complications, the surgeon can choose the method with which he/she is most familiar and comfortable.

#### **PATIENT SUMMARY:**

In patients with bladder pain syndrome with Hunner lesions, both endoscopic resection and coagulation of the lesions are effective treatments.

#### **IC/BPS/HSB BASIC SCIENCE, DIAGNOSIS AND TREATMENT**

#### **HOW CAN WE IMPROVE THE DIAGNOSIS AND MANAGEMENT OF BLADDER PAIN SYNDROME? PART 2:ICI-RS 2018.**

*Khullar V, Digesu GA, Veit-Rubin N, Sahai A, Rahnama'i MS, Tarcan T, Chermansky C, Dmochowski R. Neurourol Urodyn. 2019 Dec;38 Suppl 5:S71-S81. doi: 10.1002/nau.24245. PMID: 31821630*

This paper summarises the discussion in a think tank at the International Consultation on Incontinence-Research Society (ICI-RS) 2018 about the treatment of bladder pain syndrome and reviews the treatments of bladder pain syndrome from behavioural treatments to surgical interventions. All guidelines recommend different levels of treatment starting with conservative behavioural treatments then introducing oral treatments followed by intravesical instillations. If these treatments fail then more invasive treatments such as botulinum toxin injections, neuromodulation, or surgery could be suggested. Unfortunately, for all treatments the numbers are limited and therefore the evidence base is not strong. Further suggestions for research are suggested.

#### **PENTOSAN-ASSOCIATED MACULOPATHY: PREVALENCE, SCREENING GUIDELINES, AND SPECTRUM OF FINDINGS BASED ON PROSPECTIVE MULTIMODAL ANALYSIS.**

*Wang D, Au A, Gunnemann F, Hilely A, Scharf J, Tran K, Sun M, Kim JH, Sarraf D. Can J Ophthalmol. 2020 Jan 20. pii: S0008-4182(19)31272-4. doi: 10.1016/j.jcjo.2019.12.001. [Epub ahead of print] PMID: 31973791*

The purpose of this cross-sectional study was to describe the prevalence and spectrum of multimodal imaging findings of pentosan polysulfate sodium (PPS)-associated maculopathy and to recommend dosage-related screening guidelines. Patients previously or currently treated with PPS at University of California, Los Angeles, were randomly ascertained and prospectively screened for PPS-associated maculopathy with multimodal retinal imaging. Daily and cumulative dosages of PPS exposure were calculated for each patient. Images were studied

to identify the characteristic findings of toxicity. The prevalence of PPS-associated maculopathy and screening guidelines were determined. The prevalence of PPS-associated maculopathy in this cohort was 20% (10/50 patients). Both average duration of PPS therapy and average cumulative dosage were significantly lower in the unaffected ( $6.3 \pm 6.6$  years,  $691.7 \pm 706.6$  g) versus the affected groups ( $20.3 \pm 6.6$  years,  $3375.4 \pm 1650.0$  g,  $p < 0.001$ ). Near-infrared reflectance (NIR) illustrated characteristic punctate retinal pigment epithelium (RPE) macular lesions early. Fundus autofluorescence (FAF) showed speckled autofluorescence in the posterior pole with peripapillary extension. Co-localization with optical coherence tomography (OCT) displayed focal RPE thickening and, in more severe cases, RPE atrophy in the macula and even the periphery. A prevalence of 20% in this study cohort suggests a significant risk of macular toxicity for PPS-treated patients. Characteristic alterations are best detected with FAF and NIR. More significant PPS exposure was associated with more severe atrophy. The authors recommend an initial baseline eye examination to include OCT and, most importantly, NIR and FAF with annual retinal imaging thereafter especially with cumulative dosages approaching 500 g. Patients exposed to greater than 1500 g of PPS are at significant risk of retinal toxicity.

#### **ASSOCIATION OF MACULAR DISEASE WITH LONG-TERM USE OF PENTOSAN POLYSULFATE SODIUM: FINDINGS FROM A US COHORT.**

Jain N, Li AL, Yu Y, VanderBeek BL. *Br J Ophthalmol.* 2019 Nov 6. pii: [bjophthalmol-2019-314765](https://doi.org/10.1136/bjophthalmol-2019-314765). doi: [10.1136/bjophthalmol-2019-314765](https://doi.org/10.1136/bjophthalmol-2019-314765). [Epub ahead of print] PMID: 31694837

A series at a single clinical centre recently demonstrated an association between the interstitial cystitis drug pentosan polysulfate sodium (PPS) and a vision-threatening pigmentary maculopathy. The aim of this study was to determine if an association exists between PPS use and macular disease in a large national cohort. A retrospective, matched cohort study using data from a large US medical claims database from 2002 to 2016 was performed. A total of 3012 and 1604 PPS users were compared with 15 060 and 8017 matched controls at 5 and 7 years, respectively. The primary outcome measures included (1) any new diagnosis of a hereditary or secondary pigmentary maculopathy (atypical maculopathy outcome), and (2) any new diagnosis of dry age-related macular degeneration (AMD) or drusen in addition to the aforementioned diagnoses (atypical maculopathy+AMD outcome). At the 5-year and 7-year follow-up, 9 (0.3%) and 10 (0.6%) PPS patients progressed to the atypical maculopathy outcome compared with 32 (0.2%) and 25 (0.3%) control patients, respectively. 103 (3.4%) and 87 (5.4%) PPS patients developed the atypical maculopathy+AMD outcome compared with 440 (2.9%) and 328 (4.1%) control patients at 5 and 7 years, respectively. At 5 years, multivariate analysis showed no significant association. At 7 years, PPS users had significantly increased odds of having the atypical maculopathy+AMD outcome. It was concluded that PPS exposure was associated with a new diagnosis of macular disease at the 7-year follow-up in a large national cohort.

#### **PROGRESSIVE MACULOPATHY AFTER DISCONTINUATION OF PENTOSAN POLYSULFATE SODIUM.**

Huckfeldt RM, Vavvas DG. *Ophthalmic Surg Lasers Imaging Retina.* 2019 Oct 1;50(10):656-659. doi: [10.3928/23258160-20191009-10](https://doi.org/10.3928/23258160-20191009-10). PMID: 31671200

A pigmentary maculopathy associated with chronic use of the drug pentosan polysulfate sodium (PPS) was recently described. The authors present a case of PPS-associated maculopathy that continued to progress for 6 years after discontinuation of this medication. [*Ophthalmic Surg Lasers Imaging Retina.* 2019;50:656-659.].

#### **PREVALENCE OF MACULOPATHY ASSOCIATED WITH LONG TERM PENTOSAN POLYSULFATE THERAPY**

Vora RA,, Amar P. Patel AP, Melles R. <https://doi.org/10.1016/j.ophtha.2020.01.017>

A significant number of Kaiser Permanente Northern California patients who had a cumulative exposure to 500 grams or more of pentosan polysulfate sodium (PPS) developed a pigmentary maculopathy.

#### **PENTOSAN POLYSULFATE SODIUM EXPOSURE AND DRUG-INDUCED MACULOPATHY IN COMMERCIALY INSURED PATIENTS IN THE UNITED STATES.**

Ludwig CA, Vail D, Callaway NF, Pasricha MV, Moshfeghi DM. *Ophthalmology.* 2019 Nov 5. pii: [S0161-6420\(19\)32211-0](https://doi.org/10.1016/j.ophtha.2019.10.036). doi: [10.1016/j.ophtha.2019.10.036](https://doi.org/10.1016/j.ophtha.2019.10.036). [Epub ahead of print] PMID: 31899034

The purpose of this article from the Department of Ophthalmology, Byers Eye Institute, Stanford University was to determine the association and cumulative dose-response pattern between pentosan polysulfate sodium (PPS) use for interstitial cystitis (IC) and maculopathy. This concerned a large, multicenter, retrospective cohort study of commercially insured patients in the MarketScan database (Truven Health Analytics, San Jose, CA). Two hundred twenty-seven thousand three hundred twenty-five patients with IC who were enrolled continuously in the MarketScan database participated. Survival models using a binary variable indicating PPS exposure showed no significant associations between PPS exposure and diagnosis of drusen, nonexudative AMD, exudative AMD,

toxic maculopathy, hereditary dystrophy, or an aggregate variable of any maculopathy. Similarly, there was no dose-dependent relationship between PPS exposure and diagnosis of any maculopathy. These findings remained stable in sensitivity analysis models that excluded patients with diabetes mellitus. In this large, commercial claims database analysis, no association was found between PPS exposure and subsequent diagnosis of maculopathy.

#### **IMPROVING THE BARRIER FUNCTION OF DAMAGED CULTURED UROTHELIUM USING CHONDROITIN SULFATE.**

*Rozenberg BB, Janssen DAW, Jansen CFJ, Schalken JA, Heesakkers JPFA. Neurourol Urodyn. 2019 Nov 27. doi: PMID: 31774209*

The aim of this study from the Netherlands was to determine whether glycosaminoglycan (GAG) replenishment is able to improve recovery of a deficient urothelial barrier, chondroitin sulfate (CS) instillations were tested using an in vitro model. Porcine urothelial cells (Ucells) were terminally differentiated in culture conditions to construct a urothelial layer with a functional barrier. This layer was damaged to compromise barrier function to simulate a key characteristic of bladder pain syndrome/interstitial cystitis. The functional effect of subsequent treatment with CS was evaluated. Primary porcine Ucells were isolated and cultured on inserts. Differentiation of cells was evaluated with immunohistochemical analysis for the presence of umbrella cells, tight junctions and CS. Transepithelial electrical resistance (TEER) measurements were performed to evaluate barrier function. Protamine was used to simulate mild urothelial damage. CS 0.2% (vol/vol), a GAG, was subsequently instilled in the treatment group. The recovery of barrier function was further evaluated with TEER measurements. The Student t test was used for the analysis of results. After induction of differentiation, the Ucells expressed barrier markers and a functional barrier was established (measured by high TEER). TEER decreased significantly after instillation with protamine. CS instillation improved recovery of TEER significantly measured after 7 hours (84% vs 22% in controls). However, after 24 hours the TEER was comparable in both experimental groups. It was concluded that CS instillation improves the recovery of the urothelial barrier after damage in vitro. This functional experiment shows that CS improves recovery of damaged urothelial function, which supports the hypothesis behind the mechanism of action of GAG-replenishment therapy.

#### **ASSESSMENT OF LONG-TERM INTRAVESICAL HYALURONIC ACID, CHONDROITIN SULFATE AND COMBINATION THERAPY FOR PATIENTS WITH BLADDER PAIN SYNDROME.**

*Özkıdık M. Cent European J Urol. 2019;72(3):270-275. doi: 10.5173/ceju.2019.0007. Epub 2019 Sep 16. PMID: 31720029*

*Free full article, click on title*

The aim of this prospective, randomized and double-blinded study from Turkey was to evaluate the efficacy, safety and tolerability of intravesical hyaluronic acid (HA), chondroitin sulfate (CS) and combination therapies (HA+CS) for patients with BPS/IC during a 24-month follow-up period. A total of 72 patients were divided into three groups as HA, CS and combination group. Outpatient visits were performed at the beginning of the study and at every 3rd month thereafter. Both objective parameters included in 3 day micturition diary such as number of micturitions per 24 hours, volume voided in each micturition and self-reported questionnaires such as Patient Perception of Bladder Condition Scale, Visual Analog Scale, Pain Urgency Frequency Questionnaire, Interstitial Cystitis Symptom and Problem Index, Health Related Quality of Life (HRQoL) were used to assess the efficacy of three different agents. Safety was defined as any adverse event beginning or worsening in the study and reported in each visit. All groups showed a significant improvement both in the parameters included in the 3-day micturition diary and self-reported questionnaires compared to the baseline values or scores recorded at the beginning of the study. The authors' primary end point was improvement in HRQoL score. The combination therapy was superior to both of the monotherapies in terms of improvement in HRQoL score and the difference was statistically significant. Combination therapy provides better results than the monotherapies to obtain symptomatic relief in patients with BPS/IC. Meta-analysis of different well-designed studies are required for more definitive results.

#### **OPIOID PRESCRIPTION USE IN PATIENTS WITH INTERSTITIAL CYSTITIS.**

*Zillioux J, Clements M, Pike CW, Rapp D. Int Urogynecol J. 2020 Jan 24. doi: 10.1007/s00192-019-04214-2. [Epub ahead of print] PMID: 31980841*

The opioid epidemic is a recent focus of national initiatives to reduce opioid misuse and related addiction. As interstitial cystitis (IC) is a chronic pain state at risk for narcotic use, the authors sought to assess opioid prescription use in patients with IC. Data were accessed from the Virginia All Payers Claims Database. The authors identified female patients diagnosed with IC from 2011 to 2016 using International Classification of Disease codes. A patient identifier was used to link diagnoses with outpatient prescription claims for opioids



using generic product identifiers. They then analyzed opioid prescriptions within 30 days of a claim with a diagnosis of IC. A total of 6,884 patients with an IC diagnosis were identified. The median number of IC claims per patient was 2 (IQR 1 to 4). Mean patient age was 47.8. Twenty-eight percent of patients received at least 1 opioid prescription, with a median of 2 (IQR 1, 4) per patient. Among those receiving opioids, 185 (9.5%) had more than 10 opioid prescriptions, with a maximum of 129. The most common prescriptions were hydrocodone, oxycodone, and tramadol. There was a decline in opioid prescriptions per month for IC, although the rate per IC diagnosis remained stable. It was concluded that a significant number of patients with IC are treated with opioids. Although the overall number of opioid prescriptions associated with IC had declined, the prescription rate per IC diagnosis had not. As part of the national initiative to reduce opioid use, the authors' data suggest that IC treatment strategies should be examined.

#### **HISTAMINE INDUCES PERIPHERAL AND CENTRAL HYPERSENSITIVITY TO BLADDER DISTENSION VIA THE HISTAMINE H1 RECEPTOR AND TRPV1.**

*Grundy L, Caldwell A, Garcia Caraballo S, Erickson A, Schober G, Castro J, Harrington AM, Brierley SM. Am J Physiol Renal Physiol. 2019 Dec 2. doi: 10.1152/ajprenal.00435.2019. [Epub ahead of print] PMID: 31790304*

Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) is a common chronic pelvic disorder with sensory symptoms of urinary urgency, frequency, and pain, indicating a key role for hypersensitivity of bladder-innervating sensory neurons. The inflammatory mast cell mediator histamine has long been implicated in IC/BPS, yet the direct interactions between histamine and bladder afferents remain unclear. Here, Grundy and colleagues from Australia show, using a mouse ex vivo bladder afferent preparation, that intravesical histamine enhanced the mechanosensitivity of sub-populations of afferents to bladder distension. Histamine also recruited 'silent afferents', which were previously unresponsive to bladder distension. Furthermore, in vivo intravesical histamine enhanced activation of dorsal horn neurons within the lumbosacral spinal cord, indicating increased afferent signaling into the central nervous system. qRT-PCR revealed significant expression of histamine receptor subtypes (Hrh1-Hrh3) in mouse lumbosacral dorsal root ganglia (DRG), bladder detrusor smooth muscle, mucosa, and isolated urothelial cells. In DRG, Hrh1 was the most abundantly expressed. Acute histamine exposure evoked calcium influx in select populations of DRG neurons but did not elicit calcium transients in isolated primary urothelial cells. Histamine-induced mechanical hypersensitivity ex vivo was abolished in the presence of the histamine H1 receptor (H1R) antagonist pyrilamine and was not present in preparations from mice lacking the TRPV1 receptor. Together, these results indicate that histamine enhances the sensitivity of bladder afferents to distension via interactions with H1R and TRPV1. This hypersensitivity translates to increased sensory input and activation in the spinal cord, which may underlie the symptoms of bladder hypersensitivity and pain experienced in IC/BPS.

#### **SERUM SPHINGOSINE-1-PHOSPHATE LEVELS IN BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS PATIENTS: COULD IT HELP IN DIAGNOSIS?**

*Asi T, Asci A, Altan M, Gudeloglu A, Ergen A. World J Urol. 2019 Dec 2. doi: 10.1007/s00345-019-03045-6. [Epub ahead of print] PMID: 31792578*

The purpose of this study from Turkey was to find out if there is any potential benefit of serum Sphingosine-1-Phosphate (S1P) level in the diagnosis of BPS/IC. Patients newly or previously diagnosed with BPS/IC between September 2017 and December 2018 were included. Healthy individuals who volunteered to enter the study were included as control group. The measurements of serum S1P in both groups were compared. Multiple regression analysis was conducted to find out the significant factors affecting S1P results. A total of 47 BPS/IC patients and 47 healthy controls were included. BPS/IC patients were older than controls. The female-to-male ratio was 46/1 for patient group and 29/18 for controls. 68.1% (32/47) of BPS/IC patients had previous treatments. 55.3%(26/47) of patient group had accompanying medical or psychiatric disease. The mean serum S1P level was notably elevated in BPS/IC group. Using ROC curve analysis, a value of 165 was a good cut-off point between patient and control groups. On multiple regression analysis, being BPS/IC patient was the only significant predictor of a serum S1P level above the cut-off point documented on ROC analysis. Sphingosine-1-phosphate (S1P) pathway seems to have a potential role in the pathogenesis of BPS/IC. High serum S1P level might support the diagnosis of BPS/IC.

#### **PULSED ELECTROMAGNETIC FIELD THERAPY AS A COMPLEMENTARY ALTERNATIVE FOR CHRONIC PELVIC PAIN MANAGEMENT IN AN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PATIENT.**

*Overholt TL, Ross C, Evans RJ, Walker SJ. Case Rep Urol. 2019 Dec 26;2019:5767568. doi: 10.1155/2019/5767568. eCollection 2019. PMID: 31949970*

Interstitial cystitis/bladder pain syndrome is a chronic pelvic pain condition with no known etiology that affects millions of women and men in the United States. Current management can be aggressive for individuals who are refractory to less invasive options, often resulting in the use of opioid narcotics and/or surgical procedures under general anesthesia, with higher risks and side effects to patients. Pulsed electromagnetic field therapy is a noninvasive therapeutic strategy that is thought to reduce inflammation and pain via alteration of cellular function and microcirculation. This therapy has demonstrated efficacy in management of other chronic pain syndromes including fibromyalgia and chronic low back pain. Here, the authors describe a case of pulsed electromagnetic field therapy for management of interstitial cystitis/bladder pain syndrome that resulted in decreases in pelvic pain, burning with bladder filling, and other nonpelvic pain symptoms. This case provides support for a formal clinical trial to evaluate the efficacy of pulsed electromagnetic field therapy for the management of chronic pelvic pain in interstitial cystitis/bladder pain syndrome.

**PHASE I STUDY OF KRP-116D, A 50% W/W DIMETHYL SULFOXIDE AQUEOUS SOLUTION, ON THE SYSTEMIC ABSORPTION FROM BLADDER BY INTRAVESICAL INSTILLATION IN HEALTHY JAPANESE SUBJECTS.**

*Shimada H, Yono M, Hojo Y, Hamamura Y, Ootsuki A. Low Urin Tract Symptoms. 2019 Nov 6. doi: 10.1111/luts.12295. [Epub ahead of print] PMID: 31696635*

This study from Japan was a single-institution, single-dose, single-arm phase 1 study in healthy adult males to evaluate the safety and absorption of dimethyl sulfoxide (DMSO) from the bladder into the body when KRP-116D (a 50% w/w DMSO solution) was intravesically administered and allowed to remain in the bladder for 15 minutes. Six healthy adult males were enrolled in this study. KRP-116D (50 mL) was instilled directly into the bladder via a catheter where it was allowed to remain for 15 minutes under lidocaine anaesthesia in accordance with the usage of RIMSO-50 (50% w/w DMSO solution) approved in the USA. The residual DMSO solution in the bladder was collected 15 minutes after instillation. The concentrations of DMSO in the plasma and the recovered solution were analysed by a validated high-performance liquid chromatography (HPLC) method. The concentration in the residual DMSO solution was multiplied by the solution volume and divided by the dosage to calculate the recovery rate of DMSO. Plasma DMSO was detected in one of six subjects, and in the remaining five subjects DMSO was not detected (<19.6 µg/mL). The recovery rate of DMSO from the bladder was 60.7% to 93.7%. The only drug-related adverse event was breath odour (garlic-like breath) observed in four of six subjects (66.7%). Absorption of DMSO from the bladder was low (16.3%), and the systemic exposure was limited. Most of the DMSO was recovered from the bladder. KRP-116D 50 mL was well tolerated and safe.

**USING BOTULINUM TOXIN A FOR TREATMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME- POSSIBLE PATHOMECHANISMS AND PRACTICAL ISSUES.**

*Jhang JF. Toxins (Basel). 2019 Nov 4;11(11). pii: E641. doi: 10.3390/toxins11110641. PMID: 31689912*

Treatment for patients with IC/BPS is always challenging for urologists. The main mechanism of the botulinum toxin A (BoNT-A) is inhibition of muscle contraction, but the indirect sensory modulation and anti-inflammatory effect in the bladder also play important roles in treating patients with IC/BPS. Although current guidelines consider BoNT-A injection to be a standard treatment, some practical issues remain debatable. Most clinical evidence of this treatment comes from retrospective uncontrolled studies, and only two randomized placebo-control studies with limited patient numbers have been published. Although 100 U BoNT-A is effective for most patients with IC/BPS, the potential efficacy of 200 U BoNT-A has not been evaluated. Both trigone and diffuse body BoNT-A injections are effective and safe for IC/BPS, although comparison studies are lacking. For IC/BPS patients with Hunner's lesion, the efficacy of BoNT-A injection remains controversial. Most patients with IC/BPS experience symptomatic relapse at six to nine months after a BoNT-A injection, although repeated injections exhibit a persistent therapeutic effect in long-term follow-up. Further randomized placebo-controlled studies with a larger number of patients are needed to support BoNT-A as standard treatment for patients with IC/BPS.

**DIFFERENTIAL EXPRESSION OF HISTAMINE RECEPTORS IN THE BLADDER WALL TISSUES OF PATIENTS WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS - SIGNIFICANCE IN THE RESPONSIVENESS TO ANTIHISTAMINE TREATMENT AND DISEASE SYMPTOMS.**

*Shan H, Zhang EW, Zhang P, Zhang XD, Zhang N, Du P, Yang Y. BMC Urol. 2019 Nov 12;19(1):115. doi: 10.1186/s12894-019-0548-3. PMID: 31718622*

Activation of mast cells plays an important role in the pathogenesis of BPS/IC. Histamine, a mast cell-derived mediators, induced inflammation and hypersensitivity of the bladder. This study from China investigated the expressions of histamine receptors in the bladder wall tissues of patients with BPS/IC, and its association with the effectiveness of antihistamine therapy and disease symptoms. Bladder tissues were collected from 69 BPS/IC patients and 10 control female patients. The expression of H3R in BPS/IC was further examined in an

independent cohort of 10 female patients with BPS/IC and another 10 age-matched female patients. Immunohistochemistry, Western blotting, and quantitative RT-PCR were performed to quantify the expressions of histamine receptors. Statistical analyses of the correlation of histamine receptor expression with antihistamine therapy outcome and severity of disease symptoms were also performed. The expression of four histamine receptors was significantly elevated in BPS/IC. Western blotting revealed that H3R were significantly reduced in the patients, whereas the mRNA levels of H3R were significantly increased. The patients were further divided into antihistamine responders and non-responders. No significant correlation was found in the expression of histamine receptors between responder and non-responder groups. However, significant correlations between OLS and H1R and H3R were found. This study showed that expression of all the 4 histamine receptors were elevated in BPS/IC. There were no statistically significant correlations between the expression levels of the four different histamine receptors and the treatment outcome of antihistamine therapy (amitriptyline or cimetidine).

#### **THERAPEUTIC EFFICACY OF ONABOTULINUMTOXINA DELIVERED USING VARIOUS APPROACHES IN SENSORY BLADDER DISORDER.**

*Chen PY, Lee WC, Wang HJ, Chuang YC. Toxins (Basel). 2020 Jan 23;12(2). pii: E75. doi: 10.3390/toxins12020075. PMID: 31979383*

Cystoscopic onabotulinumtoxinA (onaBoNTA) intradetrusor injection is an efficient and durable modality for treating sensory bladder disorders. However, Chen and colleagues from Taiwan note that the inconvenience of using the cystoscopic technique and anesthesia, and the adverse effects of direct needle injection (e.g., haematuria, pain, and infections) have motivated researchers and clinicians to develop diverse injection-free procedures to improve accessibility and prevent adverse effects. However, determining suitable approaches to transfer onaBoNTA, a large molecular and hydrophilic protein, through the impermeable urothelium to reach therapeutic efficacy remains an unmet medical need. Researchers have provided potential solutions in three categories: To disrupt the barrier of the urothelium (e.g., protamine sulfate), to increase the permeability of the urothelium (e.g., electromotive drug delivery and low-energy shock wave), and to create a carrier for transportation (e.g., liposomes, thermosensitive hydrogel, and hyaluronan-phosphatidylethanolamine). Thus far, most of these novel administration techniques have not been well established in their long-term efficacy; therefore, additional clinical trials are warranted to validate the therapeutic efficacy and durability of these techniques. Finally, researchers may make progress with new combinations or biomaterials to change clinical practices in the future.

#### **EVALUATION OF SEVERAL BOTULINUM TOXINS-A DELIVERING SYSTEMS INTO THE BLADDER IN INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME (IC/PBS).**

*Torkamand F, Mirjavadi SJ, Khatami F, Guitynavard F, Aghamir SMK. Am J Clin Exp Urol. 2019 Oct 25;7(5):346-351. eCollection 2019. PMID: 31763366*

Torkamand and colleagues from Iran note that botulinum toxins were primary suggested for the neurogenic lower urinary tract dysfunction (LUTD) treatment about thirty years ago. The application of BTX-A in LUTD has just developed and the approval of BTX-A injection confirmed in for patients with both overactive bladders (OAB) and neurogenic detrusor overactivity (NDO). Currently, BTX-A medication is not licensed for use in IC/BPS but is under consideration. Despite BTX-A being recommended to treat patients with IC/BPS, its efficacy and safety for IC/BPS is under consideration. One difficulty is related to the toxin delivering systems. It is shown that there is no difference in BTX-A injection to body or trigone but that there is a need for further large-scale studies over this subject. Moreover, Hydrodistention can boost the therapeutic effect of BTX-A for IC/BPS patients. Additional studies should consider the safety and efficacy of BTX-A injection in the treatment of BTX-A.

#### **PREDICTIVE FACTORS FOR A SATISFACTORY TREATMENT OUTCOME WITH INTRAVESICAL BOTULINUM TOXIN A INJECTION IN PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.**

*Wang HJ, Yu WR, Ong HL, Kuo HC. Toxins (Basel). 2019 Nov 19;11(11). pii: E676. doi: 10.3390/toxins11110676. PMID: 31752328*

A botulinum toxin A (BoNT-A) intravesical injection can improve the symptoms of interstitial cystitis/bladder pain syndrome (IC/BPS). Patients with IC/BPS have different clinical characteristics, urodynamic features, and cystoscopic findings. This study FROM Taiwan assessed the treatment outcomes of a BoNT-A intravesical injection and aimed to identify the predictive factors of a satisfactory outcome. This retrospective study included IC/BPS patients treated with 100 U BoNT-A. The treatment outcomes were assessed by global response assessment (GRA) at 6 months. The authors classified patients according to different clinical, urodynamic, and cystoscopic characteristics and evaluated the treatment outcomes and predictive factors. A total of 238 patients

were included. Among these patients, 113 (47.5%) had a satisfactory outcome ( $GRA \geq 2$ ) and 125 (52.5%) had an unsatisfactory outcome. Improvements in the IC symptom score, IC problem score, O'Leary-Sant symptom score, and visual analog scale score for pain were significantly greater in patients with a satisfactory outcome than in patients with an unsatisfactory outcome. The IC disease duration and maximal bladder capacity (MBC) were significantly different between patients with and without a satisfactory outcome. Multivariate analysis revealed that only the MBC was a predictor for a satisfactory outcome. Patients with a MBC of  $\geq 760$  mL and glomerulations of 0/1 (58.7%) or glomerulations of 2/3 (75.0%) frequently had a satisfactory outcome. They found that BoNT-A intravesical injection can effectively improve symptoms among patients with IC/BPS, with a remarkable reduction in bladder pain. A MBC of  $\geq 760$  mL is a predictive factor for a satisfactory treatment outcome.

#### **CURRENT AND FUTURE DIRECTIONS OF STEM CELL THERAPY FOR BLADDER DYSFUNCTION.**

*Shin JH, Ryu CM, Yu HY, Shin DM, Choo MS. Stem Cell Rev Rep. 2019 Nov 22. doi: 10.1007/s12015-019-09922-2. [Epub ahead of print] PMID: 31758372*

Stem cells are capable of self-renewal and differentiation into a range of cell types and promote the release of chemokines and progenitor cells necessary for tissue regeneration. Mesenchymal stem cells are multipotent progenitor cells with enhanced proliferation and differentiation capabilities and less tumorigenicity than conventional adult stem cells; these cells are also easier to acquire. Bladder dysfunction is often chronic in nature with limited treatment modalities due to its undetermined pathophysiology. Most treatments focus on symptom alleviation rather than pathognomonic changes repair. The potential of stem cell therapy for bladder dysfunction has been reported in preclinical models for stress urinary incontinence, overactive bladder, detrusor underactivity, and IC/BPS. Despite these findings, however, stem cell therapy is not yet available for clinical use. Only one pilot study on detrusor underactivity and a handful of clinical trials on stress urinary incontinence have reported the effects of stem cell treatment. This limitation may be due to stem cell function loss following ex vivo expansion, poor in vivo engraftment or survival after transplantation, or a lack of understanding of the precise mechanisms of action underlying therapeutic outcomes and in vivo behaviour of stem cells administered to target organs. Efficacy comparisons with existing treatment modalities are also needed for the successful clinical application of stem cell therapies. This review from South Korea describes the current status of stem cell research on treating bladder dysfunction and suggests future directions to facilitate clinical applications of this promising treatment modality, particularly for bladder dysfunction.

#### **VERIFICATION OF MESENCHYMAL STEM CELL INJECTION THERAPY FOR INTERSTITIAL CYSTITIS IN A RAT MODEL.**

*Chung JW, Chun SY, Lee EH, Ha YS, Lee JN, Song PH, Yoo ES, Kwon TG, Chung SK, Kim BS. PLoS One. 2019 Dec 12;14(12):e0226390. doi: 10.1371/journal.pone.0226390. eCollection 2019. PMID: 31830131.*

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

Interstitial cystitis (IC) is a chronic intractable disease. Recently, the potential application of stem cell (SC) therapy was suggested for IC management. This study from South Korea aimed to establish an optimal SC source and verify the efficacy and safety of SC injection therapy in an IC rat model. After IC animal model induction, urine-derived stem cells (USCs), adipose tissue-derived stem cells (ADSCs), bone marrow-derived stem cells (BMSCs) and amniotic fluid-derived stem cells (AFSCs) were injected into the bladder submucosa. The following parameters were analysed: 1) functional improvement of bladder via cystometry, 2) histological changes and 3) inflammatory gene expression and regenerative potential of damaged bladder tissues. Additionally, an optimal method for SC introduction in terms of effective bladder regeneration was analysed. Intercontraction interval was significantly increased and inflammatory reactions and fibrotic changes were decreased in all of the SC-injected groups than in the control group. PCR analysis revealed that inflammatory gene expression significantly decreased in the USC-treated group than in the other groups. To confirm the optimal SC injection route in the IC rat model, group was divided according to the following criteria: 1) direction of SC injection into the bladder submucosa, 2) injection via tail vein, 3) transurethral instillation. In each analysis, the groups in which SCs were injected into the bladder submucosa showed significantly longer intercontraction interval, better morphologic regeneration and inhibition of bladder inflammatory reaction compared with the other groups. Regardless of the cell source, human tissue-derived mesenchymal SCs regenerated damaged bladder tissue, promoted functional recovery and inhibited inflammatory cell accumulation in an IC rat model. In particular, USC had the highest inhibitory effect on inflammation. Additionally, direct USC injection into the bladder submucosa was expected to have the best therapeutic effect, which will be an important factor for clinical applications in the future.

**SYNERGISTIC EFFECTS OF N-ACETYLCYSTEINE AND MESENCHYMAL STEM CELL IN A LIPOPOLYSACCHARIDE-INDUCED INTERSTITIAL CYSTITIS RAT MODEL.**

*Shin JH, Ryu CM, Ju H, Yu HY, Song S, Shin DM, Choo MS. Cells. 2019 Dec 29;9(1). pii: E86. doi: 10.3390/cells9010086. PMID: 31905757*

The purpose of this study from Korea was to reduce the amount of stem cells used in treating preclinical interstitial cystitis (IC model) by investigating the synergistic effects of multipotent mesenchymal stem cells (M-MSCs; human embryonic stem cell-derived) and N-acetylcysteine (NAC). Eight-week-old female Sprague-Dawley rats were divided into seven groups, i.e., sham, lipopolysaccharide/protamine sulfate, LPS/PS + NAC, LPS/PS with 25K MSC, LPS/PS with 50K MSC LPS/PS + 25K MSC + NAC, and LPS/PS + 50K MSC + NAC. To induce the IC rat model, protamine sulfate (10 mg, 45 min) and LPS (750 µg, 30 min) were instilled once a week for five consecutive weeks via a transurethral PE-50 catheter. Phosphate-buffered saline (PBS) was used in the sham group. One week after the final instillation, M-MSCs with two suboptimal dosages (i.e., 2.5 or 5.0 × 10<sup>4</sup> cells) were directly transplanted into the outer-layer of the bladder. Simultaneously, 200 mg/kg of NAC or PBS was intraperitoneally injected daily for five days. The therapeutic outcome was evaluated one week after M-MSC or PBS injection by awake cystometry and histological analysis. Functionally, LPS/PS insult led to irregular micturition, decreased intercontraction intervals, and decreased micturition volume. Both monotherapy and combination therapy significantly increased contraction intervals, increased urination volume, and reduced the residual volume, thereby improving the urination parameters compared to those of the LPS group. In particular, a combination of NAC dramatically reduced the amount of M-MSCs used for significant restoration in histological damage, including inflammation and apoptosis. Both M-MSCs and NAC-based therapy had a beneficial effect on improving voiding dysfunction, regenerating denuded urothelium, and relieving tissue inflammation in the LPS-induced IC/BPS rat model. The combination of M-MSC and NAC was superior to MSC or NAC monotherapy, with therapeutic efficacy that was comparable to that of previously optimized cell dosage (100K) without compromised therapeutic efficacy.

**MICRONIZED PALMITOYLETHANOLAMIDE-POLYDATIN REDUCES THE PAINFUL SYMPTOMATOLOGY IN PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.**

*Cervigni M, Nasta L, Schievano C, Lampropoulou N, Ostardo E. Biomed Res Int. 2019 Nov 11;2019:9828397. doi: 10.1155/2019/9828397. eCollection 2019. PMID: 31828153*

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

The purpose of this study from Italy was to assess the efficacy of a micronized-palmitoylethanolamide-polydatin (m-pea-pol) based product on chronic pelvic pain and severity of other symptoms in interstitial cystitis/bladder pain syndrome patients refractory to conventional therapies. A pilot, open-label bicentric study was carried out involving 32 IC/BPS patients. Chronic, oral m-PEA-Pol treatment lasted 6 months. Bladder pain was evaluated using the visual analog scale, while changes from baseline in other urinary symptoms were evaluated by means of the O'Leary-Sant Interstitial Cystitis Symptom and Problem Index and the Pelvic Pain and Urgency/Frequency (PUF) symptom scale questionnaires. The generalized linear mixed model was used to evaluate significant mean changes across time. A significant and progressive reduction of pain intensity was observed during m-PEA-Pol treatment ( $p < 0.0001$  for reduction over time). The effect was associated with a reduction in severity of patients' symptoms evaluated with the O'Leary-Sant questionnaire and the PUF scale. m-PEA-Pol therapy elicited a significant reduction over time in the urinary frequency evaluated with voiding diary and a small but not significant improvement of bladder capacity. These data highlight the potential benefit of m-PEA-Pol in patients with rare pathology such as IC/BPS and confirm the good safety profile of micronized PEA-based products.

**DYSREGULATION OF BLADDER CORTICOTROPIN-RELEASING HORMONE RECEPTOR IN THE PATHOGENESIS OF HUMAN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.**

*Jhang JF1, Birder LA2, Jiang YH1, Hsu YH3, Ho HC4, Kuo HC5. Sci Rep. 2019 Dec 16;9(1):19169. doi: 10.1038/s41598-019-55584-y. PMID: 31844086*

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

Stress is associated with exacerbated symptoms in patients with IC/BPS. To investigate the mechanism of stress implicated on IC/BPS, Jhang and colleagues from Taiwan investigated expression of stress-response receptor corticotropin-releasing hormone receptor (CRHR) in the bladder from IC/BPS patients. Twenty-three IC/BPS patients with Hunner's lesion (HIC), 51 IC/BPS patients without Hunner's lesion (NHIC), and 24 patients with stress urinary incontinence as controls were enrolled. Cystoscopic biopsies of bladder wall including mucosa and submucosa were obtained from all patients. Western blotting was used to investigate the bladder expression of the CRHR1 and CRHR2. Immunochemical staining revealed CRHR1 expression was mainly located in the submucosa while CRHR2 expression was mainly in uroepithelial cells. Compared to control subjects, the CRHR1

expression was significantly higher, while CRHR2 expression was significantly lower in IC/BPS patients. Further analysis of patients with HIC, NHIC, and control subjects showed that bladder in patients with HIC had significantly higher expressions of CRHR1 and significantly lower CRHR2. CRHR2 expression was significantly negatively correlated with O'Leary-Sant score and bladder pain. The authors' results indicate dysregulation of bladder CRHR1 and CRHR2 in patients with IC/BPS and suggest CRH signalling may be associated with IC/BPS symptoms.

#### **EXPERIMENTAL CANNABINOID 2 RECEPTOR ACTIVATION BY PHYTO-DERIVED AND SYNTHETIC CANNABINOID LIGANDS IN LPS-INDUCED INTERSTITIAL CYSTITIS IN MICE.**

*Berger G, Arora N, Burkovskiy I, Xia Y, Chinnadurai A, Westhofen R, Hagn G, Cox A, Kelly M, Zhou J, Lehmann C. Molecules. 2019 Nov 21;24(23). pii: E4239. doi: 10.3390/molecules24234239. PMID: 31766439*

Interstitial cystitis (IC) is a chronic bladder disorder with unclear etiology. The endocannabinoid system has been identified as a key regulator of immune function, with experimental evidence for the involvement of cannabinoid receptors in bladder inflammation. This study from Canada used intravital microscopy (IVM) and behavioral testing in lipopolysaccharide-induced IC, to investigate the anti-inflammatory analgesic effects of a natural dietary sesquiterpenoid, beta-caryophyllene (BCP), which is present in cannabis among other plants, and has reported agonist actions at the cannabinoid 2 receptor (CB2R). BCP's anti-inflammatory actions were compared to the synthetic CB2R-selective cannabinoid, HU308, and to an FDA-approved clinical treatment (dimethyl sulfoxide: DMSO). IVM data revealed that intravesical instillation of BCP and/or HU308 significantly reduces the number of adhering leukocytes in submucosal bladder venules and improves bladder capillary perfusion. The effects of BCP were found to be comparable to that of the selective CB2R synthetic cannabinoid, HU308, and superior to intravesical DMSO treatment. Oral treatment with BCP was also able to reduce bladder inflammation and significantly reduced mechanical allodynia in experimental IC. Based on their findings, the authors believe that CB2R activation may represent a viable therapeutic target for IC, and that drugs that activate CB2R, such as the generally regarded as safe (GRAS) dietary sesquiterpenoid, BCP, may serve as an adjunct and/or alternative treatment option for alleviating symptoms of inflammation and pain in the management of IC.

#### **CANNABINOID RECEPTOR 2 ACTIVATION DECREASES SEVERITY OF CYCLOPHOSPHAMIDE-INDUCED CYSTITIS VIA REGULATING AUTOPHAGY.**

*Liu Q, Wu Z, Liu Y, Chen L, Zhao H, Guo H, Zhu K, Wang W, Chen S, Zhou N, Li Y, Shi B. Neurourol Urodyn. 2019 Nov 14. doi: 10.1002/nau.24205. [Epub ahead of print] PMID: 31729056*

Cannabinoids have been shown to exert analgesic and anti-inflammatory effects, and the effects of cannabinoids are mediated primarily by cannabinoid receptors 1 and 2 (CB1 and CB2). The objective of this study from China was to determine efficacy and mechanism of CB2 activation on cyclophosphamide (CYP)-induced cystitis in vivo. Cystitis was induced by intraperitoneal (IP) injection of CYP in female C57BL/6J mice. Mice were pretreated with CB2 agonist JWH-133 (1 mg/kg, intraperitoneally), CB2 antagonist AM-630 (1 mg/kg, intraperitoneally) or autophagy inhibitor 3-methyladenine (3-MA) (50 mM, intraperitoneally) before IP injection of CYP. Peripheral nociception and spontaneous voiding were investigated in these mice. Bladders were collected, weighed, and processed for real-time polymerase chain reaction, immunoblotting analysis, histological and immunohistochemical analysis. Twenty-four hours after IP injection of CYP, the bladder of CYP-treated mice showed histological evidence of inflammation. The expression of CB2 in bladder was significantly increased in CYP-treated mice. Mechanical sensitivity was significantly increased in CYP-treated mice and CB2 agonist JWH-133 attenuated this effect ( $P < .05$ ). The number of urine spots was significantly increased after CYP treatment and it was decreased in JWH-133 treated mice. Activating CB2 with JWH-133 significantly alleviated bladder tissue inflammatory responses and oxidative stress induced by CYP. Activation of CB2 by JWH-133 increased the expression of LC3-II/LC3-I ratio and decreased the expression of SQSTM1/p62 in the bladder of cystitis mice, whereas AM-630 induced inverse effects. Further study indicated that JWH-133 could promote autophagy and blocking autophagy by 3-MA dismissed the effort of CB2 in alleviating bladder tissue inflammatory responses and oxidative stress injury. Furthermore, treatment with 3-MA decreased the expression of p-AMPK and induced the phosphorylation of mTOR in the presence of JWH-133 stimulation in cystitis model. It was concluded that activation of CB2 decreased severity of CYP-induced cystitis and ameliorated bladder inflammation. CB2 activation is protective in cystitis through the activation of autophagy and AMPK-mTOR pathway may be involved in the initiation of autophagy.

#### **POTASSIUM SENSITIVITY TEST PREDICTS HYDRODISTENSION EFFICACY IN PATIENTS WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.**

Gülpınar Ö, Esen B, Akpınar Ç, Baklacı U, Gökçe Mİ, Süer E, Bedük Y. *Turk J Urol.* 2019 Nov 14. doi: 10.5152/tud.2019.19084. [Epub ahead of print] PMID: 31747364

The purpose of this study from Turkey was to determine the possible role of potassium sensitivity test (PST) in predicting the success of hydrodistention (HD) in patients with bladder pain syndrome/interstitial cystitis (BPS/IC). Patients who underwent PST before diagnostic cystoscopy and HD were evaluated to collect data regarding the visual analog score (VAS) to assess pain, the voiding diary for frequency of urination/nocturia, mean urine volume per void, interstitial cystitis symptom index, and problem index before HD. Patients were requested to provide the VAS of pain at 1 month and 6 months post-HD. A reduction 2 or more on the VAS of pain was considered as a response adequate to be noted. The median age of the patients was 46 years. The PST was positive for 27 patients (27/39; 69.2%). At 1 month post-HD, out of the 27 patients with positive PST, 23 (85.2%) were found to have been responsive to HD and 4 (14.8%) were non-responsive. Of the 12 (12/39; 30.8%) patients who showed a negative PST, 7 (58.3%) were non-responsive and 5 (41.7%) were responsive to HD. A logistic regression analysis revealed that PST ( $p=0.009$ ) was the only parameter that was able to predict HD efficacy at 1 month post-HD. PST was found to be a predictive factor for the short-term efficacy of HD. BPS/IC patients with positive PST are likely to be more susceptible to the damage of mucosal afferent nerve endings, which results in them benefiting from HD to a greater degree.

#### **BDNF PROMOTES ACTIVATION OF ASTROCYTES AND MICROGLIA CONTRIBUTING TO NEUROINFLAMMATION AND MECHANICAL ALLODYNIA IN CYCLOPHOSPHAMIDE-INDUCED CYSTITIS.**

Ding H, Chen J, Su M, Lin Z, Zhan H, Yang F, Li W, Xie J, Huang Y, Liu X, Liu B, Zhou X. *J Neuroinflammation.* 2020 Jan 13;17(1):19. doi: 10.1186/s12974-020-1704-0. PMID: 31931832

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

Patients with IC/BPS often grieve over a low quality of life brought about by chronic pain. In their previous studies, the authors determined that neuroinflammation of the spinal dorsal horn (SDH) was associated with mechanisms of interstitial cystitis. Moreover, it has been shown that brain-derived neurotrophic factor (BDNF) participates in the regulation of neuroinflammation and pathological pain through BDNF-TrkB signaling; however, whether it plays a role in cyclophosphamide (CYP)-induced cystitis remains unclear. This study from China aimed to confirm whether BDNF-TrkB signaling modulates neuroinflammation and mechanical allodynia in CYP-induced cystitis and determine how it occurs. Systemic intraperitoneal injection of CYP was performed to establish a rat cystitis model. BDNF-TrkB signaling was modulated by intraperitoneal injection of the TrkB receptor antagonist, ANA-12, or intrathecal injection of exogenous BDNF. Mechanical allodynia in the suprapubic region was assessed using the von Frey filaments test. The expression of BDNF, TrkB, p-TrkB, Iba1, GFAP, p-p38, p-JNK, IL-1 $\beta$ , and TNF- $\alpha$  in the L6-S1 SDH was measured by Western blotting and immunofluorescence analysis. BDNF-TrkB signaling was upregulated significantly in the SDH after CYP was injected. Similarly, the expressions of Iba1, GFAP, p-p38, p-JNK, IL-1 $\beta$ , and TNF- $\alpha$  in the SDH were all upregulated. Treatment with ANA-12 could attenuate mechanical allodynia, restrain activation of astrocytes and microglia and alleviate neuroinflammation. Besides, the intrathecal injection of exogenous BDNF further decreased the mechanical withdrawal threshold, promoted activation of astrocytes and microglia, and increased the release of TNF- $\alpha$  and IL-1 $\beta$  in the SDH of their CYP-induced cystitis model. In their CYP-induced cystitis model, BDNF promoted the activation of astrocytes and microglia to release TNF- $\alpha$  and IL-1 $\beta$ , aggravating neuroinflammation and leading to mechanical allodynia through BDNF-TrkB-p38/JNK signaling.

#### **[AFFERENT NERVE ACTIVITY IN RELATION TO BLADDER SENSATION].**

[Article in Japanese]

Aizawa N. *Nihon Yakurigaku Zasshi.* 2019;154(5):255-258. doi: 10.1254/fpj.154.255. PMID: 31735754

Bladder afferent nerves are composed by myelinated A $\delta$ - and unmyelinated C-fibers. During the storage phase of urine, distention of the bladder has long been considered to evoke afferent activity via A $\delta$ -fibers connected in series with the smooth muscle fibers. In contrast, a previous study in cats revealed that more than 90% of C-fibers do not respond to normal bladder distension, being so called silent fibers. However, at least in rats, C-fibers can respond to normal bladder distension like A $\delta$ -fibers, although they may also fulfill a potentially different role in the bladder sensory function in response to abnormal stimuli. The symptoms of overactive bladder (OAB) or interstitial cystitis (IC) are believed to be commonly related to the sensory (afferent) function. In addition, it has been suggested that bladder myogenic microcontractions or micromotions may partly contribute to the development of urgency in OAB related to bladder outlet obstruction (BOO), which is one of cause of benign prostatic hyperplasia (BPH). Aizawa and colleagues from Japan investigated the direct effects of drugs (anticholinergics,  $\beta$ 3-adrenoceptor agonists,  $\alpha$ 1-adrenoceptor antagonists, PDE type5 inhibitors, etc.) on

the bladder afferent function in rodents. In their results, almost all drugs may act on the bladder afferent function, and some of drug (e.g. mirabegron) inhibits the afferent activities through the suppression of the bladder myogenic microcontractions in normal or pathophysiological conditions.

#### **BIOINFORMATICS ANALYSIS OF THE HUB GENES AND KEY PATHWAYS OF INTERSTITIAL CYSTITIS PATHOGENESIS.**

*Liu J, Zhang Y, Li S, Sun F, Wang G, Wei D, Yang T, Gu S. NeuroUrol Urodyn. 2020 Jan;39(1):133-143. doi: 10.1002/nau.24196. Epub 2019 Oct 29. PMID: 31663162*

This study from China aimed to identify suitable datasets for reanalysis and then explore potential key genes and related pathways of interstitial cystitis (IC). Liu and colleagues searched the Gene Expression Omnibus database and three expression profile datasets and included 23 lesions of IC and 9 normal tissues in the analysis. Eight urine specimens of patients with IC and five urine specimens of healthy controls were also included. Then, these datasets were reanalyzed to determine the differentially expressed genes (DEGs), which were used to perform Gene Ontology and pathway enrichment analyses. These identified candidate genes were also applied to generate a protein-protein interaction (PPI) network. Forty-two common DEGs were sorted and identified from two datasets, both of which included the samples of bladder lesions. Based on their functions and signaling pathways, these 42 DEGs are mainly classified as cell-surface proteins and are involved in the immune and inflammatory responses. The PPI network included 41 nodes. In this network, they identified 11 genes as central nodes that are involved in the immune system and the inflammatory response. Furthermore, IC with Hunner's lesions shared the same DEGs with IC without Hunner's lesions. In both subgroups (IC with and without Hunner's lesions), they identified some common DEGs shared between bladder lesions and urine samples. They concluded that using bioinformatics they integrated different IC-related datasets and identified potential critical genes involved in IC that may contribute to future research on IC.

#### **PATIENT SURVEYS**

#### **SELF-PERCEPTION OF SYMPTOMS, MEDICAL HELP SEEKING, AND SELF-HELP STRATEGIES OF WOMEN WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME.**

*Chen HC, Liu CY, Liao CH, Tsao LI. Low Urin Tract Symptoms. 2020 Jan 22. doi: 10.1111/luts.12300. [Epub ahead of print] PMID: 31970901*

This study from Taiwan aims to investigate the self-perception of symptoms, medical help seeking, and self-help strategies of women with interstitial cystitis (IC). A mixed method of qualitative and quantitative approaches was employed. The qualitative approach used in-depth interviews about the subjective experience of symptoms, medical help seeking, and self-help strategies for their IC. The quantitative inquiry was conducted by a yes or no response to the question "Did self-perceived severe symptoms of IC interfere with your daily life?" A loglinear model was applied to investigate the associations between possible factors. This study recruited 68 women aged 20 to 69 years, of whom 22 were interviewed for qualitative data. About 72.1% of the women responded that self-perceived severe IC symptoms interfered with their daily life. A significant negative association between employment and self-perceived severe IC symptoms was observed. Qualitative results revealed three important themes: (1) bothersome symptoms-all-day bladder pain and lower urinary tract symptoms and deteriorated quality of life, (2) medical help seeking-exhaustion and frustration, (3) self-help strategies-coexisting with IC or feeling helpless. IC women feel exhausted and frustrated by seeking medical attention for this incurable disease for a long time. IC women have troubled and uneasy daily lives. Being employed or engaging in activities can divert attention to alleviate symptoms. IC patient support groups allow patients to share their self-help experiences with interdisciplinary medical teams to provide physical and psychological treatment.

#### **URINARY MICROBIOME**

#### **URINARY MICROBIOME IN UNCOMPLICATED AND INTERSTITIAL CYSTITIS: IS THERE ANY SIMILARITY?**

*Yildirim S, Shoskes D, Kulkarni S, Laguna P. World J Urol. 2020 Jan 31. doi: 10.1007/s00345-020-03099-x. [Epub ahead of print] PMID: 32006175*

Acute/uncomplicated cystitis is the most common bacterial infection causing inflammation in the bladder tissues and predominantly diagnosed in women. Interstitial cystitis may too, cause inflammation in the bladder but its etiology has been elusive. Even though the site and symptoms of both diseases are largely shared, state of the urinary microbiome in these disorders have not been comparatively evaluated before. The purpose of this review is to assess and qualitatively compare structure and composition of the urinary microbiome in acute/uncomplicated cystitis and interstitial cystitis. The available literature in MEDLINE are extensively



searched using keywords and screened. Pertinent evidence is carefully assessed and synthesized. The authors included the original studies with a cohort of medically stable, non-pregnant women with otherwise functionally normal urinary tract and excluded the original articles if the infection in a patient's cohort is accompanied by urinary syndromes such as incontinence and overactive bladder syndrome. A total of six original papers reporting on the urinary microbiome in acute cystitis and nine papers on the interstitial cystitis met the selection criteria. According to the authors, the evidence they have gleaned from the literature on the urinary microbiome associated with the acute and interstitial cystitis does not point to convergence of microbiome similarities between the two diseases. More studies with direct sampling of the bladder tissues besides sampling bladder surfaces are warranted for accurate comparison of microbiome similarity between the two conditions. Future research on interstitial cystitis microbiome should include stratified cohorts with prospective design.

## URINARY TRACT INFECTIONS

### [HOW CAN WE IMPROVE INVESTIGATION, PREVENTION AND TREATMENT FOR RECURRENT URINARY TRACT INFECTIONS - ICI-RS 2018.](#)

*Harding C, Rantell A, Cardozo L, Jacobson SK, Anding R, Kirschner-Hermanns R, Greenwell T, Swamy S, Malde S, Abrams P. Neurourol Urodyn. 2019 Dec;38 Suppl 5:S90-S97. doi: 10.1002/nau.24021. PMID: 31821632*

Recurrent urinary tract infection (rUTI) is a chronic condition and has a significant impact on health-related quality of life. The commonly used definition for rUTI is greater than three episodes in a year or more than two in 6 months. Current diagnostic methods have been used worldwide for over five decades, despite well evidenced criticism. Enhanced culture techniques demonstrate that the microbiome of the bladder is far more complex than previously thought and begs a reappraisal of our current testing. Treatment of rUTI is based on a small number of antibiotic trials with some evidence showing a reduction in the number of positive cultures, but one must be cautious in interpreting the results and weigh against the risk of generation of antimicrobial resistance (AMR). The International Consultation on Incontinence-Research Society think tank reviewed the literature with a view to improving investigation, prevention and treatment of rUTI. A multidisciplinary team of experts were invited to present evidence regarding the current diagnostic methods, recent advances related to bladder biome mapping and current treatment strategies, including antibiotic and nonantibiotic options. Current guidelines regarding antibiotic stewardship and concerns regarding AMR were discussed. Outcome of the think tank discussions are summarised with a set of recommendations to inform future research. Particular consideration is given to bacterial survival in the bladder after treatment as well as defects in urothelial barrier function which may play a significant part in the failure to eradicate UTI.

### [INHIBITION OF UREASE ACTIVITY IN THE URINARY TRACT PATHOGENS STAPHYLOCOCCUS SAPROPHYTICUS AND PROTEUS MIRABILIS BY DIMETHYLSULFOXIDE \(DMSO\).](#)

*Deutch CE. J Appl Microbiol. 2019 Dec 20. doi: 10.1111/jam.14560. [Epub ahead of print] PMID: 31860153*

Urease is a virulence factor for the urinary tract pathogens *Staphylococcus saprophyticus* and *Proteus mirabilis*. Dimethylsulfoxide (DMSO) is structurally similar to urea, used as a solvent for urease inhibitors, and an effective treatment for interstitial cystitis/bladder pain syndrome (IC/BPS). The aims of this study from the USA were to test DMSO as a urease inhibitor and determine its physiological effects on *S. saprophyticus* and *P. mirabilis*. Urease activity in extracts and whole cells was measured by the formation of ammonium ions. Urease was highly sensitive to noncompetitive inhibition by DMSO ( $K_i$  about 6 mmol l<sup>-1</sup>). DMSO inhibited urease activity in whole cells, limited bacterial growth in media containing urea, and slowed the increase in pH which occurred in artificial urine medium. DMSO should be used with caution as a solvent when testing plant extracts or other potential urease inhibitors. Because it can inhibit bacterial growth and delay an increase in pH, it may be an effective treatment for urinary tract infections. This is the first detailed study of the inhibition of urease by DMSO. Dimethylsulfoxide may be used to treat urinary tract infections that are resistant to antibiotics or herbal remedies.

## SUBSTANCE ABUSE AND THE URINARY TRACT

### [SUBSTANCE ABUSE EFFECTS ON URINARY TRACT: METHAMPHETAMINE AND KETAMINE.](#)

*Yee CH, Ng CF, Hong YL, Lai PT, Tam YH. Hong Kong Med J. 2019 Dec 4;25(6). doi: 10.12809/hkmj198154. [Epub ahead of print] PMID: 31796640*

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

Ketamine is known to cause urinary tract dysfunction. Recently, methamphetamine (MA) abuse has become a growing problem in Asia. Yee and colleagues from Hong Kong investigated the symptomatology and voiding

function in patients who abused MA and ketamine and compared their urinary tract toxicity profiles. In the period of 23 months from 1 October 2016, all consecutive new cases of patients presenting with MA- or ketamine-related urological disorder were recruited into a prospective cohort. Polysubstance abuse patients were excluded. Data were analysed by comparison between patients with ketamine abuse and MA abuse. Basic demographic data and initial symptomatology were recorded, and questionnaires on urinary symptoms and the Montreal Cognitive Assessment (MoCA) were used as assessment tools. Thirty-eight patients were included for analysis. There was a statistically significant difference in mean age between patients with MA and ketamine abuse. Urinary frequency was the most common urological symptom in our cohort of patients. There was a statistically significant difference in the prevalence of dysuria (and a significant trend in the difference in hesitancy). Overall, questionnaires assessing urinary storage symptoms and voiding symptoms did not find a statistically significant difference between the two groups. The MoCA revealed that both groups had cognitive impairment. Abuse of MA caused urinary tract dysfunction, predominantly storage symptoms. Compared with ketamine, MA abuse was not commonly associated with dysuria or pelvic pain.

## COMORBIDITIES – CHRONIC RHEUMATIC DISEASES

### [PAIN WITHOUT INFLAMMATION IN RHEUMATIC DISEASES.](#)

*Lampa J. Best Pract Res Clin Rheumatol. 2019 Jun;33(3):101439. doi: 10.1016/j.berh.2019.101439. Epub 2019 Sep 6. PMID: 31703790*

Chronic pain is a common symptom in rheumatic diseases, and the patient with pain and no signs of inflammation poses a challenge to the physician. Notably, all rheumatic diseases have components of non-inflammatory pain and a higher prevalence of fibromyalgia compared to the overall population. Hypothetically, a chronic pain stimulus may have stronger impact in a chronic inflammatory state, and the process towards a pain condition may be influenced by individual predisposition for development of chronic pain. In addition, the features of peripheral and central pain processing may be exacerbated by inflammation, and disturbed pain processing may be a feature contributing to widespread pain. Lampa and colleagues from Sweden review and describe the prevalence of chronic pain and different pain modalities in the most common rheumatic diseases. In addition, the background mechanisms of non-inflammatory pain in rheumatic diseases are discussed. Finally, they review the current strategies for pain management, with a special focus on non-inflammatory pain. The key message is that pain management should be individualized and based on a thorough pain analysis with investigation of the pain modality, localization and pain intensity. Other factors to consider are the underlying rheumatic disease and treatment, the patient's mental and physical health status and psychological factors.

### [A COMPARATIVE STUDY OF FIBROMYALGIA, RHEUMATOID ARTHRITIS, SPONDYLOARTHRITIS, AND SJÖGREN'S SYNDROME; IMPACT OF THE DISEASE ON QUALITY OF LIFE, PSYCHOLOGICAL ADJUSTMENT, AND USE OF COPING STRATEGIES.](#)

*Bucourt E, Martailé V, Goupille P, Joncker-Vannier I, Huttenberger B, Réveillère C, Mulleman D, Courtois AR. Pain Med. 2019 Nov 9. pii: pnz255. doi: 10.1093/pm/pnz255. [Epub ahead of print] PMID: 31710690*

Fibromyalgia, rheumatoid arthritis, spondyloarthritis, and Sjögren's syndrome are chronic rheumatic diseases with very different clinical characteristics, but which share symptoms such as pain and fatigue. The aim of this study from France was to examine the impact of the disease on psychological adaptation in fibromyalgia compared with other rheumatic diseases (rheumatoid arthritis, spondyloarthritis, and Sjögren's syndrome). In a multicenter study, 165 women with rheumatic diseases (48 with fibromyalgia, 47 with rheumatoid arthritis, 47 with spondyloarthritis, 23 with Sjögren's syndrome) completed the General Health Questionnaire-28 (emotional distress), Fatigue Severity Scale (fatigue), Fibromyalgia Impact Questionnaire (impact of the disease), Coping Strategies Questionnaire (coping), and Mini International Neuropsychiatric Interview (comorbidity with DSM IV axis-I disorders). The authors used the Kruskal-Wallis test, Mann-Whitney U test, and chi<sup>2</sup> test to compare comorbid anxiety and depressive disorders and to compare the impact of the disease on patients' mental well-being and daily life and adjustment (coping strategies). Anxiety and depressive disorders were more common in fibromyalgia patients; they had higher scores on impact of the disease, physical symptoms, pain, and fatigue than rheumatoid arthritis patients and reported more fatigue than patients with spondyloarthritis. Overall, they used more maladaptive coping strategies (less use of distancing from pain than patients with rheumatoid arthritis and spondyloarthritis, less use of ignoring pain sensations, and more use of catastrophizing than those with rheumatoid arthritis). No differences were found between fibromyalgia and Sjögren's syndrome on impact and adjustment. Compared with other rheumatic diseases, fibromyalgia has a greater impact on daily life; patients have more difficulty adjusting to the disease and generally use poorer strategies to cope with pain.

**CLINICAL AND MORPHOLOGICAL EFFECTS OF HYPERBARIC OXYGEN THERAPY IN PATIENTS WITH INTERSTITIAL CYSTITIS ASSOCIATED WITH FIBROMYALGIA.**

*Bosco G, Ostaro E, Rizzato A, Garetto G, Paganini M, Melloni G, Giron G, Pietrosanti L, Martinelli I, Camporesi E. BMC Urol. 2019 Nov 5;19(1):108. doi: 10.1186/s12894-019-0545-6. PMID: 31690286*

Interstitial Cystitis (IC) is a debilitating disorder of the bladder, with a multifactorial and poorly understood origin dealing with microcirculation repeated damage. In addition, Fibromyalgia (FM) is a persistent disorder whose etiology is not completely explained, and its theorized alteration of pain processing can compromise the quality of life. Both these conditions have a high incidence of conventional therapeutic failure, but recent literature suggests a significant beneficial response to Hyperbaric Oxygen Therapy (HBOT). This study from Italy evaluated the effects of HBOT on quality of life, symptoms, urodynamic parameters, and cystoscopic examination of patients suffering from both IC and FM. The authors structured an observational clinical trial design with repeated measures (questionnaires, urodynamic test, and cystoscopy) conducted before and 6 months after a therapeutic protocol with hyperbaric oxygen for the treatment of patients suffering from both IC and FM. Patients were exposed to breathing 100% oxygen at 2 atm absolute (ATA) in a multiplace pressure chamber for 90 min using an oro-nasal mask. Patients undertook a cycle of 20 sessions for 5 days per week, and a second cycle of 20 sessions after 1 week of suspension. Twelve patients completed the protocol. Changes after HBOT were not significant, except for hydrodistension tolerance. A regression of petechiae and Hunner's ulcers was also noted 6 months after completion of HBOT. This study showed no improvement in symptoms, quality of life, and urodynamic parameters, except for hydrodistension, and a slight improvement in cystoscopic pattern. However, to date, the authors could not demonstrate the significance of overall results to justify the use of HBOT alone in patients with IC and FM. This observation suggests that additional studies are needed to better understand if HBOT could treat this subset of patients.

**OAB & IC/BPS IN SJÖGREN'S SYNDROME**

**OVERACTIVE BLADDER AND BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS IN PRIMARY SJÖGREN'S SYNDROME PATIENTS: A NATIONWIDE POPULATION-BASED STUDY.**

*Lee CK, Tsai CP, Liao TL, Huang WN, Chen YH, Lin CH, Chen YM. PLoS One. 2019 Nov 20;14(11):e0225455. doi: 10.1371/journal.pone.0225455. eCollection 2019. PMID: 31747429*

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

The purpose of this study from Taiwan was to investigate the risks of overactive bladder (OAB) and bladder pain syndrome/interstitial cystitis (BPS/IC) in primary Sjögren's syndrome (pSS) patients. A nationwide, population-based cohort study was conducted using data from Taiwan's National Health Insurance Research Database. From 2001 to 2010, participants with newly diagnosed pSS were recognized as the study group. In addition, a comparison cohort of non-pSS participants was matched for age, gender, and initial diagnosis date. Risks of developing OAB and BPS/IC in pSS patients of different age, sex, and various therapeutic strategies were calculated. Hazard ratios (HR) and a 95% confidence interval (CI) were analyzed by Cox proportional hazard model. In total, 11,526 pSS patients were recognized. The HRs of OAB and BPS/IC in pSS patients were 1.68 and 2.34, respectively. The risks of OAB and BPS/IC were significantly increased for pSS patients aged < 65 years (HR: 1.73 and 2.67), female patients (HR: 1.74 and 2.34), and patients requiring treatment for dry eyes and dry mouth (HR: 2.06 and 2.93). pSS patients exhibited an increased risk of OAB and BPS/IC. Female gender, younger age, and severe glandular dysfunction requiring treatments were potential risk factors.

**BLADDER & BOWEL**

**BLADDER-BOWEL INTERACTIONS: DO WE UNDERSTAND PELVIC ORGAN CROSS-SENSITIZATION? INTERNATIONAL CONSULTATION ON INCONTINENCE RESEARCH SOCIETY (ICI-RS) 2018.**

*Panicker JN, Marcelissen T, von Gontard A, Vrijens D, Abrams P, Wyndaele M. NeuroUrol Urodyn. 2019 Dec;38 Suppl 5:S25-S34. doi: 10.1002/nau.24111. PMID: 31821639*

Mounting evidence from experimental animal and human studies suggests that cross-sensitization exists between different organs. Lower urinary tract (LUT) and bowel dysfunction commonly overlap, and the role of cross-sensitization between pelvic visceral organs is uncertain. At the International Consultation on Incontinence Research Society (ICI-RS) meeting in 2018, a panel of clinicians participated in a discussion on bladder and bowel interactions in the context of pelvic organ cross-sensitization. Bladder and bowel problems commonly co-occur in adults and children across different disorders, and the mechanism responsible for overlapping dysfunction is uncertain in most instances. At a neuronal level, cross-sensitization occurs as a result of afferent signalling from the LUT and lower bowel through different central and peripheral mechanisms. Studies in animals and humans

have demonstrated evidence for cross-organ sensitization following experimental inflammation or distension of the lower bowel, affecting the LUT. Nerve stimulation is an effective treatment for different functional LUT and bowel disorders, and whether this treatment may influence cross-organ sensitization remains uncertain. The role of physiologically dormant C-fibers, the bladder-gut-brain axis, and gut microbiome in cross-sensitization are speculative. Recommendations for research were made to explore the role of cross-organ sensitization in the pathogenesis of co-occurring LUT and bowel dysfunction in humans.

#### **CONCURRENT URINARY AND BOWEL DIVERSION: SURGICAL MODIFICATION WITH SIGMOID COLON THAT AVOIDS A BOWEL ANASTOMOSIS.**

*Theva DP, Kuhnen A, Babayan RK, Katz MH. Int Braz J Urol. 2020 Jan-Feb;46(1):108-115. doi: 10.1590/S1677-5538.IBJU.2019.0194. PMID: 31851467*

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

Cystectomy with urinary diversion is the gold standard for muscle invasive bladder cancer. It also may be performed as part of pelvic exenteration for non-urolologic malignancy, neurogenic bladder dysfunction, and chronic conditions that result in a non-functional bladder (e.g., interstitial cystitis, radiation cystitis). The objective of this study from Boston was to describe the surgical technique of urinary diversion using large intestine as a conduit whilst creating an end colostomy, thereby avoiding a primary bowel anastomosis and to show its applicability with respect to urologic conditions. The authors retrospectively reviewed five cases from a single institution that utilized the described method of urinary diversion with large intestine. They describe operative times, hospital length of stay (LOS), and describe post-operative complications. Five patients with a variety of urologic and oncologic pathology underwent the described procedures. Their operative times ranged from 5 hours to 11 hours and one patient experienced a Clavien III complication. The authors describe five patients who underwent this procedure for various medical indications, and describe their outcomes, and believe dual diversion of urinary and gastrointestinal systems with colon as a urinary conduit to be an excellent surgical option for the appropriate surgical candidate.

#### **DYSMENORRHEA AND BLADDER SENSITIVITY**

#### **CLINICAL PROFILE OF COMORBID DYSMENORRHEA AND BLADDER SENSITIVITY: A CROSS-SECTIONAL ANALYSIS.**

*Tu FF, Datta A, Atashroo D, Senapati S, Roth G, Clauw DJ, Hellman KM. Am J Obstet Gynecol. 2019 Dec 20. pii: S0002-9378(19)32767-X. doi: 10.1016/j.ajog.2019.12.010. [Epub ahead of print] PMID: 31870730*

Antecedents of chronic pelvic pain are not well characterized, but pelvic organ visceral sensitivity is a hallmark of these disorders. Recent studies have identified that some dysmenorrhea sufferers are much more likely to exhibit comorbid bladder hypersensitivity. Presumably, these otherwise healthy women may be at higher risk of developing full-blown chronic bladder pain later in life. To encourage early identification of patients harboring potential future risk of chronic pain, the authors describe the clinical profile of women matching this putative pain-risk phenotype. The objectives of the study were to characterize demographic, menstrual, pelvic examination, and psychosocial profiles of young women with comorbid dysmenorrhea and bladder hypersensitivity, defined using a standardized experimental visceral provocation test, contrasted with healthy controls, pure dysmenorrhea sufferers, and women with existing bladder pain syndrome. This prospective cohort study acquired data on participants with moderate to severe dysmenorrhea, healthy controls, and bladder pain syndrome. A subgroup of dysmenorrhea patients was found on screening with noninvasive oral water challenge to report significantly higher bladder pain during experimentally monitored spontaneous bladder filling and separately defined as a group with dysmenorrhea plus bladder pain. Medical/menstrual history and pain history were evaluated with questionnaires. Psychosocial profile and impact were measured with validated self-reported health status Patient Reported Outcomes Measurement Information System short forms and a Brief Symptom Inventory for somatic sensitivity. Pelvic anatomy and sensory sensitivity were examined via a standardized physical examination and a tampon provocation test. In this largely young, single, nulliparous cohort (24 ± 1 years old), approximately a quarter (46 out of 212) of dysmenorrhea sufferers tested positive for the dysmenorrhea plus bladder pain phenotype. Dysmenorrhea-only sufferers were more likely to be African American (24%) than healthy controls. Pelvic examination findings did not differ in the nonchronic pain groups, except for tampon test sensitivity, which was worse in dysmenorrhea plus bladder pain and dysmenorrhea sufferers vs healthy controls. Consistent with heightened pelvic sensitivity, participants with dysmenorrhea plus bladder pain also had more nonmenstrual pain, dysuria, dyschezia, and dyspareunia. Participants with dysmenorrhea plus bladder pain had Patient Reported Outcomes Measurement Information System Global Physical T-scores of 47.7 ± 0.9, lower than in women with dysmenorrhea only (52.3 ± 0.5), and

healthy controls  $56.1 \pm 0.7$ . Similarly, they had lower Patient Reported Outcomes Measurement Information System Global Mental T-score than healthy controls. Similar specific impairments were observed on Patient Reported Outcomes Measurement Information System scales for anxiety, depression, and sleep in participants with dysmenorrhea plus bladder pain vs healthy controls. Women with dysmenorrhea who are unaware they also have bladder sensitivity exhibit broad somatic sensitivity and elevated psychological distress, suggesting combined preclinical visceral sensitivity may be a precursor to chronic pelvic pain. Defining such precursor states is essential to conceptualize and test preventative interventions for chronic pelvic pain emergence. Dysmenorrhea plus bladder pain is also associated with higher self-reported pelvic pain unrelated to menses, suggesting central nervous system changes are present in this potential precursor state.

## **FIBROMYALGIA**

### **IMPROVEMENT IN FIBROMYALGIA SYMPTOMS AND SKIN BIOPSY RESULTS IN PATIENTS WITH FIBROMYALGIA RELATED SMALL FIBER NEUROPATHY.**

*Metyas S, Chen C, Quismorio A, Abdo N, Kamel K. Curr Rheumatol Rev. 2019 Nov 6. doi: 10.2174/1573397115666191106120622. [Epub ahead of print] PMID: 31702528*

Small fiber neuropathy and fibromyalgia are two conditions that share overlapping features. Although various treatments are available for use in fibromyalgia, the response often remains unsatisfactory. Prior studies have shown that in small fiber neuropathy of autoimmune etiology, intravenous immunoglobulin (IVIg) holds promise as an effective treatment. Metyas and colleagues from the USA report the use of IVIg in 7 patients who have both fibromyalgia and small fiber neuropathy. Skin punch biopsy evaluating the nerve fiber density was performed prior to diagnosis and after 6 months of IVIg therapy in each individual. Patient's symptoms were obtained via a fibromyalgia questionnaire pre- and post- treatment. At the end of 6 months therapy, overall patients reported less fibromyalgia symptoms and skin biopsy demonstrated improvements as well. This retrospective pilot study suggests IVIg is a viable potential therapy in a subset of fibromyalgia patients who have small fiber neuropathy.

### **THE FIBROMYALGIA BLADDER INDEX IN 100 CONSECUTIVE WOMEN WITH FIBROMYALGIA.**

*Hamed N, Rida MA, Uthman I, El Taha L, Assad M, Mikhael E, Bazi T. Int Urogynecol J. 2020 Jan 9. doi: 10.1007/s00192-019-04199-y. [Epub ahead of print] PMID: 31919557*

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

### **FIBROMYALGIA INTERFERES WITH DISEASE ACTIVITY AND BIOLOGICAL THERAPY RESPONSE IN INFLAMMATORY RHEUMATIC DISEASES.**

*Coskun Benlidayi I. Rheumatol Int. 2020 Jan 3. doi: 10.1007/s00296-019-04506-2. [Epub ahead of print] PMID: 31900502*

Fibromyalgia is one of the numerous comorbidities that may accompany inflammatory rheumatic diseases. Concomitant fibromyalgia in inflammatory rheumatic conditions can interfere with symptomatology, disease activity and overall management plan. The aim of the present narrative review article from Turkey was to discuss the current evidence on (i) the prevalence/frequency of comorbid fibromyalgia in inflammatory rheumatic conditions, (ii) the role of fibromyalgia on disease activity, (iii) the impact of concomitant fibromyalgia on biological disease-modifying antirheumatic treatment outcomes and (iv) potential effectiveness of biological disease-modifying antirheumatic drugs on fibromyalgia-related symptoms among patients with inflammatory

rheumatic diseases. A literature search was conducted through PubMed/MEDLINE Cochrane and Web of Science databases by using relevant keywords and their combinations. Studies representing different geographical areas of the world revealed that frequency rates of fibromyalgia are higher in inflammatory rheumatic diseases than those in the general population. Comorbid fibromyalgia interferes not only with the disease activity scores but also with the treatment outcomes and management plan. Further evidence is warranted in order to determine the potential benefits of biological disease-modifying antirheumatic drugs on fibromyalgia-related symptoms in patients with inflammatory rheumatic diseases.

## **VULVODYNIA**

### **PAIN, ANXIETY, DEPRESSION, AND QUALITY OF LIFE IN PATIENTS WITH VULVODYNIA.**

*Tribó MJ, Canal C, Baños JE, Robleda G. Dermatology. 2019 Nov 6:1-7. doi: 10.1159/000503321. [Epub ahead of print] PMID: 31694025*

The term vulvodynia refers to vulvar pain of unknown origin lasting at least 3 months. Psychiatric comorbidities are a common feature and, along with pain, may severely affect patients' wellbeing. Tribó and colleagues from Spain aimed to determine the characteristics of pain in vulvodynia, to correlate characteristics with symptoms of anxiety and depression, and to analyse the impact of these factors on patients' quality of life. This cross-sectional observational study analysed pain, anxiety, and depression and the effects of these factors on quality of life. Pain, anxiety, and depression were assessed using validated tools in 110 women. Statistical analyses found correlations between pain and anxiety and between anxiety and worsened quality of life. Patients often reported stinging, burning, pain, itching, and dyspareunia, pointing to the importance of temporal, localisation, punctate pressure, thermal, tactile sensitivity, and emotional tension characteristics. Most patients had severe pain related to psychiatric comorbidities and decreased quality of life. Using descriptors of pain quality and assessing anxiety and depression might help to define subgroups of patients that may benefit from different therapeutic approaches and thus enable treatments to be tailored to individual patients.

## **DONATIONS AND SPONSORING – THE IPBF NEEDS YOUR FINANCIAL HELP TO CONTINUE ITS INTERNATIONAL PATIENT ADVOCACY AND AWARENESS CAMPAIGN AROUND THE GLOBE.**

The voluntary, non-profit IPBF is entirely dependent on sponsoring and donations to be able to continue to carry out its international advocacy, projects and newsletters. In these difficult economic times, it is not easy for us to keep going and ensure continuity. All donations to our international work, however small, will be most gratefully received. The IPBF has fiscal charity status in the Netherlands. If you are thinking of making a donation, please go to this link for bank details: [http://www.painful-bladder.org/donations\\_sponsoring.html](http://www.painful-bladder.org/donations_sponsoring.html)

We would like to take this opportunity of thanking our donors for their greatly appreciated support in the past year for our foundation, projects, patient advocacy, website and newsletters.

## **THE BOARD**

### **INTERNATIONAL PAINFUL BLADDER FOUNDATION (IPBF)**

*The International Painful Bladder Foundation does not engage in the practice of medicine. It is not a medical authority nor does it claim to have medical knowledge. Information provided in IPBF emails, newsletters, patient information and website is not medical advice. The IPBF recommends patients to consult their own physician before undergoing any course of treatment or medication. While the IPBF endeavours to ensure that all information it provides is correct and accurate, it does not accept any liability for errors or inaccuracies.*

***If you do not wish to receive this IPBF e-newsletter or any other communications from the IPBF in future, please notify the International Painful Bladder Foundation: [info@painful-bladder.org](mailto:info@painful-bladder.org) with “unsubscribe” in the subject bar.***