

International Painful Bladder Foundation

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

IPBF e-Newsletter and Research Update

Issue 45, May 2017

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

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

- Upcoming ESSIC 2017 Scientific Meeting on IC/BPS, Budapest, 21-23 September
- AUA Meeting Review
- Patient Organization News
- Brain, Mind and Pain Patient-Centred Innovation Grant in Europe
- Summary of the Fibromyalgia Research Symposium 2016 In Nagasaki
- Dutch Guideline on Diagnosis and Treatment of IC/BPS in The Netherlands
- Books
- Calendar of Upcoming Events
- Research Update
- Donations & Sponsoring

UPCOMING ESSIC 2017 SCIENTIFIC MEETING: 21-23 SEPTEMBER 2017, HUNGARIAN ACADEMY OF SCIENCE, BUDAPEST, HUNGARY.

The International Society for the Study of BPS (ESSIC, www.essic.eu) annual scientific meeting, always an important date in the IC/BPS calendar, is to be hosted in the beautiful and historic city of Budapest in Hungary by Professor Sandor Lovasz, 21-23 September 2017. The programme will include in-depth sessions on the GAG layer and urothelium, all aspects of intravesical treatment with interactive discussion of the problems we currently face in the IC/BPS world and what is urgently needed in order to progress.

Abstract submission opened 15 May. For an overview of the preliminary scientific programme, [click here](#).

Other useful links:

For further information and registration: <http://www.essicmeeting.eu>

For contact: essic@defoe.it

MEETING REVIEW

BRIEF LOOK AT IC/BPS RESEARCH HIGHLIGHTS AND UPDATES AT AUA 2017 IN BOSTON

The annual meeting of the American Urological Association held in Boston 12-16 May included several sessions focusing on IC/BPS and chronic pelvic pain. In addition, IC /BPS issues featured in several society and international affiliate meetings.

The meeting programme is available online: <http://www.aur2017.org/common/pdf/publications/Meeting-Program.pdf>

The annual meeting abstracts in the Journal of Urology are open access and can be found at [http://www.jurology.com/issue/S0022-5347\(17\)X0003-7](http://www.jurology.com/issue/S0022-5347(17)X0003-7)

Webcasts at: <http://www.aur2017.org/webcasts/>

Podium Session 01 on Infections/Inflammation/Cystic Disease of the Genitourinary Tract: Interstitial Cystitis I

Pinto et al from Portugal demonstrated that intra-trigonal injection of Onabotulinum toxin A in IC/BPS patients is significantly better than placebo. Adverse events were mild with no cases of urinary retention. McDonnell and colleagues report that there is evidence (in patients and preclinical models) that stress can enhance painful sensations in patients with functional pain syndromes such as interstitial cystitis/bladder pain syndrome (IC/BPS) and their findings suggest increased communication between the sympathetic nervous system and bladder sensory neurons that may play an important role in chronic pain conditions. Tyagi and colleagues presented a novel contrast mixture to improve bladder wall contrast for visualizing IC. Kirk and colleagues looked at the effects of repeat hydrodistension for IC since it is not known whether patients suffer a reduction in bladder capacity due to these multiple procedures or develop ulcerating disease over time. However, they found that repeated hydrodistension did not decrease bladder capacity over time and development of ulceration was rare and therefore concluded that hydrodistension is a safe procedure with low complication rates. Jhang and Kuo from Taiwan investigated the association between the electron microscopic (EM) urothelium characteristics and clinical symptoms severity in patients with interstitial cystitis (IC) and ketamine cystitis (KC), finding that in EM urothelium defects were more severe in KC than IC and that urothelium defects in TEM may be associated with bladder pain severity in KC and IC patients.

PD05: Infections/Inflammation/Cystic Disease of the Genitourinary Tract: Prostate & Genitalia I focused on CP/CPSP in men.

This topic was also addressed by the course on Real Men get Real Pelvic Pain led by Dr Jeannette Potts which looked at symptoms and underlying causes of pelvic pain in men. A further course looked at Managing Male and Female IC/BPS: Comprehensive Multimodal Therapy for Patients with Urologic Pelvic Pain and discussed a multimodal care plan approach taking comorbidities into account. A third course looked at Evaluation and Management of Urogenital Pain.

MP29: Infections/Inflammation/Cystic Disease of the Genitourinary Tract: Interstitial Cystitis II

In this moderated poster session with no fewer than 20 presentations, Lusty and colleagues looked at treatment effectiveness in interstitial cystitis/bladder pain syndrome, asking whether patient perceptions align with efficacy based guidelines? Evidence from clinical treatment trials in IC/BPS is employed to develop treatment guidelines. However, do patients' perceptions of success or failure of those specific therapies align with that of available clinical trial data? The authors report that there is a disconnect between real world patient perceived effectiveness of IC/BPS treatments compared to the efficacy reported from clinical trial data and subsequent guidelines developed from this efficacy data. They emphasize that while optimal therapy must include the best evidence from clinical research, it should also include real life clinical practice implementation and effectiveness.

In a MAPP network study, Lai and colleagues characterized the location and distribution of pain among men and women with a body map and compared urinary symptoms, non-urological factors, and psychosocial measures between UCPPS patients who reported "pelvic pain only," "pelvic pain and beyond," and "widespread body pain", finding that three out of four men and women with urologic chronic pelvic pain syndromes (UCPPS) also reported pain outside the abdomen and pelvis and that widespread body pain was associated with worse quality of life and psychosocial impacts, but not worse urinary symptoms.

Bearing in mind that it is currently hypothesized that IC/BPS patients with Hunner lesions represent a different phenotype than IC/BPS patients without Hunner lesions, Lai and colleagues compared the urologic symptoms (urgency, frequency, nocturia, urologic pain, bladder hypersensitivity, sexual function) and non-urologic features (severity and distribution of systemic pain, co-morbid functional pain syndromes, anxiety, depression) between IC/BPS patients with and without Hunner lesions as seen with cystoscopy without hydrodistension. They found that IC/BPS patients with Hunner lesions did not exhibit urologic and non-urologic features that would easily distinguish them from those without Hunner lesions.

A study by Crane, Lloyd and Shoskes was aimed at improving phenotyping in IC/PBS. While successful in men with chronic pelvic pain syndrome, UPOINT is more limited in patients with IC/PBS. The authors sought to modify UPOINT to be more practical and efficacious for IC/PBS by developing a new phenotype by removing the Urinary

and Organ specific domains from UPOINT and adding a Hunner's Ulcers (U) domain, since these patients benefit from phenotype specific therapies (fulguration, cyclosporine). This results in "INPUT": Infection, Neurologic/Systemic, Psychosocial, Ulcers and Tenderness of Muscles.

(Ed. comment: this is only going to work for those using the term "ulcer". However, a large part of the world has now changed over to using the term Hunner lesion.)

MP31: Urodynamics/Lower Urinary Tract Dysfunction/Female Pelvic Medicine: Non-neurogenic Voiding Dysfunction I

Ackerman and colleagues looked at the considerable symptom overlap between bladder hypersensitivity syndromes such as OAB and IC/PBS. They sought to define the fundamental features of each syndrome and refine diagnostic criteria through retrospective comparison of self-reported symptoms in female patients with a range of clinical presentations and symptom severities. They concluded that the significant overlap of urinary tract symptoms between OAB and IC/PBS suggests common pathological elements.

PATIENT ORGANIZATION NEWS

Bladder Health UK: Reminder new name

A reminder that the former Cystitis and Overactive Bladder Foundation (COBF) in the United Kingdom now has the new name of BLADDER HEALTH UK. More information is available from the website:

<http://bladderhealthuk.org>

BRAIN, MIND AND PAIN PATIENT-CENTRED INNOVATION GRANT IN EUROPE

Researchers and patients brought together by a new Grant offer

Pain Alliance Europe (PAE) and Grünenthal are together introducing an initiative which will encourage patient-centric, patient driven, scientifically robust innovation and research projects, while creating better access to innovative treatments, promoting prevention and self-management approaches, decreasing stigma and finally, working together to improve quality of life for people living with these disabling conditions.

The Brain, Mind, and Pain Patient-Centred Innovation Grant aims to create an environment where patient centricity is the basis for future initiatives. This will contribute towards creating a sense of innovation, with direct impact on patients' needs, and at the same time increasing awareness of chronic pain conditions and neurological disorders.

Several partner organizations are contributing to this project together with PAE and Grünenthal: the European Pain Federation (EFIC), the European Academy of Neurology (EAN), and the European Federation of Neurological Associations (EFNA). The biennial grant provided by Grünenthal is for individual applicants as well as different organizations' initiatives and partnerships. The first BMP Grant Awarding Ceremony will take place in Spring 2018. Interested applicants who meet the eligibility criteria will be able to apply online from the 1st September 2017. [Read more.](#)

More information will be available soon online, at www.bmp-grant.eu

More information about PAE is available at www.pae-eu.eu

SUMMARY OF THE FIBROMYALGIA RESEARCH SYMPOSIUM 2016 IN NAGASAKI

PAIN Reports: [January/February 2017 - Volume 2 - Issue 1 - p e582](#)

If you are looking for an update on fibromyalgia, this summary of the Fibromyalgia Research Symposium in 2016 in Nagasaki is open access. Click on title.

DUTCH GUIDELINE ON DIAGNOSIS AND TREATMENT OF IC/BPS IN THE NETHERLANDS

(Standpunt Kwaliteit Voorwaarden M.B.T. Diagnostiek en Behandeling van het Blaaspijnsyndroom in Nederland)

www.nvu.nl/en-us/kwaliteit/richtlijnen/leidraden.aspx

This new guideline will be useful reading for Dutch/Flemish speakers.

PUBLICATIONS: BOOKS

UROLOGICAL AND GYNAECOLOGICAL CHRONIC PELVIC PAIN: CURRENT THERAPIES.

Ed. Robert M. Moldwin

2017 Springer International Publishing

Hardcover ISBN: 978-3-319-48462-4. 404 pages.

Many well-known names in the field have contributed chapters to this book which is expected to be released at the end of May 2017.

<http://www.springer.com/gp/book/9783319484624>

INCONTINENCE: 6th EDITION 2017

Editors: Paul Abrams, Linda Cardozo, Adrian Wagg, Alan Wein.

Includes a chapter on Bladder Pain Syndrome by Committee 19 of the International Consultation on Incontinence (ICI), chaired by Philip Hanno MD.

ISBN: 978-9953-493-21-3

<https://www.ics.org/education/icspublications/icibooks/6thicibook>

CALENDAR OF UPCOMING EVENTS

SOCIETAL IMPACT OF PAIN (SIP) SYMPOSIUM 2017

“STRUCTURED CO-OPERATION TO TACKLE THE SOCIETAL IMPACT OF PAIN”,

8-9 JUNE 2017, VALLETTA, MALTA

<https://www.sip-platform.eu>

THE 6TH INTERNATIONAL CONGRESS ON NEUROPATHIC PAIN (NEUPSIG 2017),

5-18 JUNE 2017, GOTHENBURG, SWEDEN

<http://neupsig2017.kenes.com/>

THE 10TH CONGRESS OF THE EUROPEAN PAIN FEDERATION, EFIC® (EFIC 2017),

6-9 SEPTEMBER 2017, COPENHAGEN, DENMARK

<http://www.efic2017.kenes.com/SiteAssets/Top.jpg>

INTERNATIONAL CONTINENCE SOCIETY (ICS) 2017

12-15 SEPTEMBER 2017, FLORENCE, ITALY

www.ics.org

ESSIC 2017 – INTERNATIONAL SOCIETY FOR THE STUDY OF BPS

21-23 SEPTEMBER 2017, HUNGARIAN ACADEMY OF SCIENCE, BUDAPEST, HUNGARY.

www.essic.eu

<http://www.essicmeeting.eu>

essic@defoe.it

3RD WORLD CONGRESS ON ABDOMINAL AND PELVIC PAIN

HOSTED BY THE INTERNATIONAL PELVIC PAIN SOCIETY (IPPS)

OCTOBER 12 - 15, 2017, RENAISSANCE WASHINGTON DC DOWNTOWN, WASHINGTON, DC

<http://pelvicpain.org/meetings/details.aspx?id=114>

SOPATE 2017 - THE SYMPOSIUM ON CLINICAL PAIN TRIALS IN EUROPE

25-26 OCTOBER 2017, HILTON TOWER BRIDGE, LONDON, UK

<http://www.sopate2017.com>

RESEARCH HIGHLIGHTS

A REVIEW OF SELECTED RECENT SCIENTIFIC LITERATURE ON INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME, HYPERSENSITIVE BLADDER, CHRONIC (PELVIC) PAIN AND RELATED DISORDERS

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.

CHARACTERIZATION OF WHOLE BODY PAIN IN UROLOGIC CHRONIC PELVIC PAIN SYNDROME AT BASELINE - A MAPP RESEARCH NETWORK STUDY.

Lai HH, Jemielita T, Sutcliffe S, Bradley CS, Naliboff B, Williams DA, Gereau RW 4th, Kreder K, Clemens JQ, Rodriguez LV, Krieger JN, Farrar JT, Robinson N, Landis JR; [MAPP Research Network](#). *J Urol*. 2017 Mar 31. pii: S0022-5347(17)43848-1. doi: 10.1016/j.juro.2017.03.132. [Epub ahead of print] PMID: 28373134

The authors characterized the location and spatial distribution of whole body pain among patients with urologic chronic pelvic pain syndrome (UCPPS) using a body map. They compared the severity of urinary symptoms, pelvic pain, non-pelvic pain, and psychosocial health among patients with different pain patterns. 233 women and 191 men with UCPPS enrolled in a multi-center, one-year observational study completed a battery of baseline measures, including a body map describing the location of pain during the past week. Participants were categorized as having "pelvic pain only" if they reported pain in the abdomen and pelvis only. Participants who reported pain beyond the pelvis were further divided into two sub-groups based on the number of broader body regions affected by pain: an "intermediate" group (1-2 additional regions outside the pelvis) and a "widespread pain" group (3-7 additional regions). Three-quarters of men and women with UCPPS reported pain outside the pelvis. Widespread pain was associated with greater severity of non-pelvic pain symptoms, poorer psychosocial health and worse quality of life, but not worse pelvic pain or urinary symptoms.

RESTING-STATE FUNCTIONAL CONNECTIVITY PREDICTS LONGITUDINAL PAIN SYMPTOM CHANGE IN UROLOGIC CHRONIC PELVIC PAIN SYNDROME: A MAPP NETWORK STUDY.

Kutch JJ, Labus JS, Harris RE, Martucci KT, Farmer MA, Fenske S, Fling C, Ichesco E, Peltier S, Petre B, Guo W, Hou X, Stephens AJ, Mullins C, Clauw DJ, Mackey SC, Apkarian AV, Landis JR, Mayer EA; [MAPP Research Network](#). *Pain*. 2017 Mar 17. doi: 10.1097/j.pain.0000000000000886. [Epub ahead of print] PMID: 28328579

Chronic pain symptoms often change over time, even in individuals who have had symptoms for years. Studying biological factors that predict trends in symptom change in chronic pain may uncover novel pathophysiological mechanisms and potential therapeutic targets. In this study, the authors investigated whether brain functional connectivity measures obtained from resting-state functional MRI (rs-fMRI) at baseline can predict longitudinal symptom change (3, 6, and 12 months post-scan) in urologic chronic pelvic pain syndrome (UCPPS). They studied 52 individuals with UCPPS (34 female, 18 male) who had baseline neuroimaging followed by symptom tracking every 2 weeks for 1 year as part of the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP)

Research Network study. They found that brain functional connectivity can make a significant prediction of short-term (3 month) pain reduction with 73.1% accuracy (69.2% sensitivity and 75.0% precision). Additionally, they found that the brain regions with greatest contribution to the classification were preferentially aligned with the left frontoparietal network (L-FPN). rs-fMRI measures appeared to be less informative about 6- or 12-month symptom change. This study provides the first evidence that future trends in symptom change in patients in a state of chronic pain may be linked to functional connectivity within specific brain networks.

IDENTIFICATION OF NOVEL NON-INVASIVE BIOMARKERS OF URINARY CHRONIC PELVIC PAIN SYNDROME: FINDINGS FROM THE MULTIDISCIPLINARY APPROACH TO THE STUDY OF CHRONIC PELVIC PAIN (MAPP) RESEARCH NETWORK.

Dagher A, Curatolo A, Sachdev M, Stephens AJ, Mullins C, Landis JR, van Bokhoven A, El-Hayek A, Froehlich JW, Briscoe AC, Roy R, Yang J, Pontari MA, Zurakowski D, Lee RS, Moses MA; MAPP Research Network. BJU Int. 2017 Mar 6. doi: 10.1111/bju.13832. [Epub ahead of print] PMID: 28263447

The purpose of this study was to examine a series of candidate markers for urological chronic pelvic pain syndrome (UCPPS), selected based on their proposed involvement in underlying biological processes so as to provide new insights into pathophysiology and suggest targets for expanded clinical and mechanistic studies. Baseline urine samples from Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network study participants with UCPPS, positive controls (PCs; chronic pain without pelvic pain) and healthy controls (HCs) were analysed for the presence of proteins that are suggested in the literature to be associated with UCPPS. Matrix metalloproteinase (MMP)-2, MMP-9, MMP-9/neutrophil gelatinase-associated lipocalin (NGAL) complex (also known as Lipocalin 2), vascular endothelial growth factor (VEGF), VEGF receptor 1 (VEGF-R1) and NGAL were assayed and quantitated using mono-specific enzyme-linked immunosorbent assays for each protein. Pain severity in women with UCPPS was significantly positively associated with concentrations of all biomarkers except NGAL, and urinary severity with all concentrations except VEGF-R1. The authors found that altered levels of MMP-9, MMP-9/NGAL complex and VEGF-R1 in men, and all biomarkers in women, were associated with clinical symptoms of UCPPS. None of the evaluated candidate markers usefully discriminated UCPPS patients from controls. Elevated VEGF, MMP-9 and VEGF-R1 levels in men and VEGF levels in women may provide potential new insights into the pathophysiology of UCPPS.

IC/BPS/HSB BASIC SCIENCE, DIAGNOSIS AND TREATMENT

UNDERSTANDING PAIN AND COPING IN WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME (IC/BPS).

Katz L, Tripp DA, Carr LK, Mayer R, Moldwin RM, Nickel JC. BJU Int. 2017 Apr 7. doi: 10.1111/bju.13874. [Epub ahead of print] PMID: 28386966.

The purpose of this study from the USA and Canada was to examine a self-regulation and coping model for IC/BPS that may help to understand the pain experience of chronic IC/BPS patients. The model tested illness perceptions, illness-focused coping, emotional regulation, mental health and disability in stepwise method using factor analysis and structural equation modelling. Step 1 explored the underlying constructs. Step 2 confirmed the measurement models to determine the structure/composition of the main constructs. Step 3 evaluated the model fit and specified pathways in the proposed IC-Self Regulation Model. 217 female patients with urologist diagnosed IC/BPS were recruited and diagnosed across tertiary care centres in North America. Data was collected through self-report questionnaires. An IC/BPS self-regulatory model was supported. Physical disability was worsened by patient's negative perception of their illness, attempts to cope using illness-focused coping and poorer emotional regulation. Mental health was supported by perceptions that individuals could do something about their illness, using wellness-focused behavioural strategies, and adaptive emotion regulation. The results clarify the complex and unique process of self-regulation in women suffering from IC/BPS, implicating cognitive and coping targets, and highlighting emotional regulation. This knowledge will help clinicians understand and manage these patients' distress and disability.

ETIOLOGY, PATHOPHYSIOLOGY AND BIOMARKERS OF INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME.

Patnaik SS, Laganà AS, Vitale SG, Buttice S, Noventa M, Gizzo S, Valenti G, Rapisarda AM, La Rosa VL, Magno C, Triolo O, Dandolu V. *Arch Gynecol Obstet.* 2017 Jun;295(6):1341-1359. doi: 10.1007/s00404-017-4364-2. Epub 2017 Apr 8. PMID: 28391486

Interstitial cystitis/painful bladder syndrome (IC/PBS) is a chronic pain syndrome and a chronic inflammatory condition prevalent in women that leads to urgency, sleep disruption, nocturia and pain in the pelvic area, to the detriment of the sufferer's quality of life. The aim of this review from Italy and the USA is to highlight the latest diagnostic strategies and potential therapeutic techniques. A comprehensive literature review was performed on MEDLINE, PubMed, and Cochrane databases gathering all literature about "Interstitial cystitis" and "Painful Bladder Syndrome". Visual analogue scales, epidemiological strategies, pain questionnaires and similar techniques were not included in this literature survey. The etiology, exact diagnosis and epidemiology of IC/PBS are still not clearly understood. To date, its prevalence is estimated to be in the range of 45 per 100,000 women and 8 per 100,000 men, whereas joint prevalence in both sexes is 10.6 cases per 100,000. There are no "gold standards" in the diagnosis or detection of IC/PBS, therefore, several etiological theories were investigated, such as permeability, glycosaminoglycans, mast cell, infection and neuroendocrine theory to find new diagnostic strategies and potential biomarkers. Due to the fact that this disease is of an intricate nature, and that many of its symptoms overlap with other concomitant diseases, the authors suggest that patients could be classified on the basis of the phenotype, as well as their symptom clusters, and that diagnostic and management choices should be tailored according to the observed biomarkers.

[A NEW PLAYER IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: PLATELET-ACTIVATING FACTOR - PAF AND ITS CONNECTION TO SMOKING.](#)

Kullmann FA. *Physiol Rep.* 2017 Apr;5(7). pii: e13235. doi: 10.14814/phy2.13235. PMID: 28408637

Free full text, click on title.

This paper from Pittsburgh highlights platelet-activating factor (PAF) and its associated signalling as novel players in urothelial alterations reported in IC/BPS patients, shines light on a possible mechanism underlying smoking-exacerbated IC/BPS symptoms, and provides potential therapeutic targets to be further explored.

[DIMETHYL SULFOXIDE \(DMSO\) AS INTRAVESICAL THERAPY FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: A REVIEW.](#)

Rawls WF, Cox L, Rovner ES. *NeuroUrol Urodyn.* 2017 Feb 21. doi: 10.1002/nau.23204. [Epub ahead of print] PMID: 28220525

The purpose of this review was to update current understanding of dimethyl sulfoxide (DMSO) and its role in the treatment of interstitial cystitis (IC). Thirteen cohort studies and three randomized-controlled trials were identified. Response rates relying on subjective measurement scores range from 61 to 95%. No increased efficacy was found with "cocktail" DMSO therapy. Great variation existed in diagnostic criteria, DMSO instillation protocols and response measurements. The authors concluded that the current evidence backing DMSO is a constellation of cohort studies and a single randomized-controlled trial versus placebo. The optimal dose, dwell time, type of IC most likely to respond to DMSO, definitions of success/failure and the number of treatments are not universally agreed upon. Improvements in study design, phenotyping patients based on symptoms, as well as the emergence of reliable biomarkers of the disease may better guide the use of DMSO in the future.

[CLINICAL COMPARISON OF INTRAVESICAL HYALURONIC ACID AND CHONDROITIN SULFATE THERAPIES IN THE TREATMENT OF BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.](#)

Gülpinar Ö, Esen B, Kayış A, Gökçe Mİ, Sürer E. *NeuroUrol Urodyn.* 2017 May 8. doi: 10.1002/nau.23284. [Epub ahead of print] PMID: 28480984

Intravesical glucosaminoglycan (GAG) replacement therapies are commonly used in the treatment of bladder pain syndrome (BPS)/interstitial cystitis (IC). Different intravesical glucosaminoglycan products are currently available. In this prospective study from Turkey, clinical efficacy of chondroitin sulfate and hyaluronic acid are compared in patients with BPS/IC. Patients were randomized to CS and HA groups. All patients were evaluated for visual analogue pain scale (VAS), interstitial cystitis symptom index (ICSI), interstitial cystitis problem index (ICPI), voiding diary for frequency/nocturia, and mean urine volume per void at the beginning of the therapy and after 6 months. All patients had a potassium sensitivity test (PST) initially. Wilcoxon and Mann-Whitney U tests were used for statistical analysis. There were 21 patients in both groups. Mean age of patients in CS and HA

groups were 47.10 and 48.90, respectively. Before treatment, Parson's test was positive in 64.3% of patients (27/42) with no difference between groups. VAS of pain, ICSI, ICPI, frequency at 24 h and nocturia results have improved significantly at both treatment arms. Intravesical CS was also found superior to intravesical HA in terms of 24 h frequency, nocturia and ICPI. No severe adverse effects were reported. Noting that data comparing clinical efficiencies of different GAG therapies are very limited, the authors report that in this study intravesical CS was found superior to intravesical HA in terms of 24 h frequency, nocturia and ICPI in patients with BPS/IC in short term follow-up. To provide a definitive conclusion on superiority of one GAG therapy to others, further evaluation with long term follow up is required.

[**A PROSPECTIVE MULTICENTER DOUBLE-BLIND RANDOMIZED TRIAL OF BLADDER INSTILLATION OF LIPOSOME FORMULATION ONABOTULINUMTOXINA FOR INTERSTITIAL CYSTITIS/ BLADDER PAIN SYNDROME.**](#)

Chuang YC, Kuo HC. J Urol. 2017 Feb 12. pii: S0022-5347(17)30228-8. doi: 10.1016/j.juro.2017.02.021. [Epub ahead of print]. PMID: 28202358

Noting that intravesical instillation of liposomal-formulated botulinum toxin A (lipotoxin) has shown therapeutic effects on treatment of refractory overactive bladder without needle injections, Chuang and Kuo from Taiwan assessed lipotoxin for the treatment of refractory interstitial cystitis/bladder pain syndrome (IC/BPS). However, they found that lipotoxin failed to demonstrate a positive proof of concept compared to OnaBoNTA or placebo, although a single intravesical instillation of lipotoxin was associated with a decrease in IC/BPS symptoms compared to baseline in patients with moderate to severe IC/BPS. The authors consider that this effect is likely due to a significant placebo effect.

[**INTRAVESICAL LIPOSOME THERAPY FOR INTERSTITIAL CYSTITIS.**](#)

Tyagi P, Kashyap M, Majima T, Kawamorita N, Yoshizawa T, Yoshimura N. Int J Urol. 2017 Apr;24(4):262-271. doi: 10.1111/iju.13317. Epub 2017 Mar 4. PMID: 28258657

Over the past two decades, there has been lot of interest in the use of liposomes as lipid-based biocompatible carriers for drugs administered by the intravesical route. The lipidic bilayer structure of liposomes facilitates their adherence to the apical membrane surface of luminal cells in the bladder, and their vesicular shape allows them to co-opt the endocytosis machinery for bladder uptake after instillation. Liposomes have been shown to enhance the penetration of both water-soluble and insoluble drugs, toxins, and oligonucleotides across the bladder epithelium. Empty liposomes composed entirely of the endogenous phospholipid, sphingomyelin, could counter mucosal inflammation and promote wound healing in patients suffering from interstitial cystitis. Recent clinical studies have tested multilamellar liposomes composed entirely of sphingomyelin as a novel intravesical therapy for interstitial cystitis. In addition, liposomes have been used as a delivery platform for the instillation of botulinum toxin in overactive bladder patients. The present review from Japan and the USA discusses the properties of liposomes that are important for their intrinsic therapeutic effect, summarizes the recently completed clinical studies with intravesical liposomes and covers the latest developments in this field.

[**FULRANUMAB IN PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: OBSERVATIONS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY.**](#)

Wang H, Russell LJ, Kelly KM, Wang S, Thipphawong J. BMC Urol. 2017 Jan 5;17(1):2. doi: 10.1186/s12894-016-0193-z. PMID: 28056917

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

This study from the USA was designed to evaluate the efficacy and safety of fulranumab, a fully human monoclonal antibody directed against nerve growth factor (NGF), for pain relief in patients with interstitial cystitis/bladder pain syndrome (IC/BPS). However, this study was terminated prematurely based on concerns that this class may be associated with rapidly progressing osteoarthritis or osteonecrosis. Thirty-one patients (of the targeted 70 patients) were randomized, 17 to placebo and 14 to fulranumab, with 15 and 10 patients, respectively, receiving all 3 doses of double-blind treatment. In ANOVA analyses, there was no statistically significant difference between treatment groups for the primary endpoint (LS mean difference [95% CI] vs. placebo, -0.2 [-1.52, 1.10]) or any of the secondary endpoints. Fulranumab was well tolerated, with no patient discontinuing due to an adverse event or experiencing a joint-related serious adverse event over a 26-week follow-up period. No events related to the neurologic or motor systems were reported. Efficacy was not

demonstrated in the present study with the single dose tested and a limited sample size, leading to lack of statistical power. These findings do not exclude the possibility that fulranumab would provide clinical benefit in a larger study and/or specific populations (phenotypes) in this difficult to treat pain condition.

NAFTOPIDIL IMPROVES SYMPTOMS IN A RAT MODEL OF TRANILAST-INDUCED INTERSTITIAL CYSTITIS.

Sugaya K, Nishijima S, Kadekawa K, Ashitomi K, Ueda T, Yamamoto H. Low Urin Tract Symptoms. 2017 May;9(2):107-110. doi: 10.1111/luts.12113. Epub 2015 Sep 26. PMID: 28394500

This study from Japan looked at the effect of naftopidil on symptoms of tranilast-induced interstitial cystitis (IC) was examined in rats. Thirty-two female rats were divided into four groups (control, naftopidil, tranilast, and combination groups). Rats in the control group were fed a standard diet, while rats in the naftopidil, tranilast, and combination groups were fed diets containing naftopidil, tranilast, or naftopidil + tranilast, respectively. After 4 weeks of treatment, locomotor activity was measured and continuous cystometry was performed. During the light period, locomotor activity was lower in the tranilast group than in the control, naftopidil, and combination groups. During the dark period, locomotor activity was higher in the naftopidil group than in the other three groups. The combination group showed higher locomotor activity than the tranilast group, but significantly lower activity than the naftopidil group. Continuous cystometry revealed that the interval between bladder contractions was shorter in the tranilast group than in the other three groups. The combination group also had a shorter interval between contractions than the control group. Sugaya and colleagues found that naftopidil improved the symptoms of tranilast-induced IC, such as reduced locomotor activity due to pelvic pain and a shortened interval between bladder contractions. Therefore, they suggest that naftopidil may be a potential treatment for IC.

DIFFERENTIAL PERTURBATION OF THE INTERSTITIAL CYSTITIS-ASSOCIATED GENES OF BLADDER AND URETHRA IN RAT MODEL.

Choi BH, You S, Park CS, Cho EH, Park TD, Kim S, Kim YJ, Lee T, Kim J. Cell Cycle. 2017 Apr 18;16(8):749-758. doi: 10.1080/15384101.2017.1295184. Epub 2017 Feb 22. PMID: 28278053

Interstitial cystitis (IC) is a chronic bladder dysfunction characterized as urinary frequency, urgency, nocturia, and pelvic pain. The changes in urethra may wind up with the bladder changes in structure and functions, however, the functions of the urethra in IC remains elusive. The aim of this study from the USA and South Korea was to understand the perturbed gene expression in urethra, compared with urinary bladder, associated with the defected urodynamics. Using female IC mimic rats, a comprehensive RNA-sequencing combined with a bioinformatics analysis was performed and revealed that IC-specific genes in bladder or urethra. Gene ontology analysis suggested that the cell adhesion or extracellular matrix regulation, intracellular signalling cascade, cardiac muscle tissue development, and second messenger-mediated signalling might be the most enriched cellular processes in IC context. Further study of the effects of these bladder- or urethra-specific genes may suggest underlying mechanism of lower urinary tract function and novel therapeutic strategies against IC.

THERAPEUTIC EFFECT OF URINE-DERIVED STEM CELLS FOR PROTAMINE/LIPOPOLYSACCHARIDE-INDUCED INTERSTITIAL CYSTITIS IN A RAT MODEL.

Li J, Luo H, Dong X, Liu Q, Wu C, Zhang T, Hu X, Zhang Y, Song B, Li L. Stem Cell Res Ther. 2017 May 8;8(1):107. doi: 10.1186/s13287-017-0547-9. PMID: 28482861

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Interstitial cystitis (IC) is a chronic inflammation disorder mainly within the submucosal and muscular layers of the bladder. As the cause of IC remains unknown, no effective treatments are currently available. Administration of stem cell provides a potential for treatment of IC. This study from China was conducted using urine-derived stem cells (USCs) for protamine/lipopolysaccharide (PS/LPS)-induced interstitial cystitis in a rodent model. In total, 60 female Sprague-Dawley rats were randomized into three experimental groups: sham controls; IC model alone; and IC animals intravenously treated with USCs (1.2×10^6 suspended in 0.2 ml phosphate-buffered saline (PBS)). The authors report that their data showed that the bladder micturition function was significantly improved in IC animals intravenously treated with USCs compared to those in the IC model alone group. The amount of antioxidants and antiapoptotic protein biomarkers heme oxygenase (HO)-1, NAD(P)H quinone oxidoreductase (NQO)-1, and Bcl-2 within the bladder tissues were significantly higher in IC animals intravenously treated with USCs and lower in the sham controls group as assessed by Western blot and

immunofluorescent staining. In addition, the expression of autophagy-related protein LC3A was significantly higher in the IC model alone group than that in IC animals intravenously treated with USCs. Inflammatory biomarkers and apoptotic biomarkers (interleukin (IL)-6, tumor necrosis factor (TNF) α , nuclear factor (NF)- κ B, caspase 3, and Bax) and the downstream inflammatory and oxidative stress biomarkers (endoplasmic reticulum stress and autophagy-related protein (GRP78, LC3, Beclin1)) in the bladder tissue revealed statistically different results between groups. They concluded that USCs restored the bladder function and histological construction via suppressing oxidative stress, inflammatory reaction, and apoptotic processes in a PS/LPS-induced IC rodent model, which provides potential for treatment of patients with IC.

ESTABLISHMENT OF A NOVEL AUTOIMMUNE EXPERIMENTAL MODEL OF BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS IN C57BL/6 MICE.

Jin XW, Liu BK, Zhang X, Zhao ZH, Shao Y. Inflammation. 2017 Jun;40(3):861-870. doi: 10.1007/s10753-017-0531-7. PMID: 28233078

The aim of this study from China was to identify whether vaccinating twice with bladder homogenate can establish a new model of experimental autoimmune cystitis (EAC) in C57BL/6 strain mice. C57BL/6 mice were vaccinated with bladder homogenate in complete Freund's adjuvant (CFA) and boost immunized with bladder homogenate in incomplete Freund's adjuvant (IFA) after 2 weeks were used as the EAC model. Mice immunized with phosphate-buffered saline (PBS) in CFA or IFA were used as the control. Micturition habits and suprapubic-pelvic pain threshold were measured 4 weeks after primary immunization. Bladder to body weight ratios and expression of inflammatory cytokines and neurokinin 1 receptor (NK1R) were then examined. Histologic and immunohistochemical examination of the bladder was carried out, and IL-1 β , IFN- γ , and TNF- α production by the kidneys, liver, and lungs was also tested. Double-immunized mice were extensively sensitive to pressure applied on the pelvic area. Compared to single-immunized mice or controls, double-immunized mice showed more micturition frequency, lower urine output per micturition, higher bladder to body weight ratio, and significant elevation in the expression of inflammatory cytokines, including IL-1 β , IL-4, IL-6, IL-10, IFN- γ , and TNF- α . NK1R gene expression was significantly increased in double-immunized mice compared to the other three groups. A nonspecific immune response occurred in the liver but was much weaker than bladder inflammation. The authors conclude that their dual immunization EAC model in C57BL/6 mice can effectively mimic the symptoms and pathophysiologic characteristics of BPS/IC and thus can be widely used to investigate the pathogenesis and therapeutic strategies of BPS/IC.

TGF- β /MAPK SIGNALING MEDIATES THE EFFECTS OF BONE MARROW MESENCHYMAL STEM CELLS ON URINARY CONTROL AND INTERSTITIAL CYSTITIS AFTER URINARY BLADDER TRANSPLANTATION.

Xiao Y, Song YJ, Song B, Huang CB, Ling Q, Yu X. Am J Transl Res. 2017 Mar 15;9(3):1193-1202. eCollection 2017. PMID: 28386345

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This study from China aimed to explore the role of the transforming growth factor- β /mitogen activated protein kinase (TGF- β /MAPK) signalling pathway in the effects of bone marrow mesenchymal stem cells (BMSCs) on urinary control and interstitial cystitis in a rat model of urinary bladder transplantation. A urinary bladder transplantation model was established using Sprague-Dawley rats. Rats were assigned to normal (blank control), negative control (phosphate-buffered saline injection), BMSCs (BMSC injection), sp600125 (MAPK inhibitor injection), or protamine sulfate (protamine sulfate injection) groups. Immunohistochemistry, urodynamic testing, hematoxylin-eosin staining, Western blotting, enzyme-linked immunosorbent assay, and MTT assay were used to assess BMSC growth, the kinetics of bladder urinary excretion, pathological changes in bladder tissue, bladder tissue ultrastructure, the expression of TGF- β /MAPK signalling pathway-related proteins, levels of inflammatory cytokines, and the effects of antiproliferative factor on cell proliferation. Compared with normal, negative control, BMSCs, and sp600125 groups, rats in the PS group exhibited decreased discharge volume, maximal micturition volume, contraction interval, and bladder capacity but increased residual urine volume, bladder pressure, bladder peak pressure, expression of TGF- β /MAPK signalling pathway-related proteins, levels of inflammatory cytokines, and growth inhibition rate. Levels of inflammatory cytokines and the growth inhibition rate were positively correlated with the expression of TGF- β /MAPK signalling pathway-related proteins. The authors note that their findings demonstrate that the TGF- β /MAPK signalling pathway mediates the beneficial effects of BMSCs on urinary control and interstitial cystitis.

COMPLETE RESPONSE TO ACUPUNCTURE THERAPY IN FEMALE PATIENTS WITH REFRACTORY INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME.

Sönmez MG, Kozanhan B. Ginekol Pol. 2017;88(2):61-67. doi: 10.5603/GP.a2017.0013. PMID: 28326514

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Interstitial Cystitis/Bladder Pain syndrome (IC/BPS) is a considerable issue in urology and gynecology and unfortunately, the treatment options recommended are not fully efficient. In this study from Turkey, the authors aimed to determine the effectiveness of acupuncture treatment in patients with refractory IC/BPS. 12 refractory IC/BPS female patients received ten sessions of acupuncture twice a week. The visual analog score (VAS), interstitial cystitis symptom index (ICSI), interstitial cystitis problem index (ICPI), O'Leary-Saint symptom score (OSS), Patient Health Questionnaire (PHQ9), Pelvic pain and urgency & frequency patient symptom scale tests (PUF) and maximum voided volume (MVV) was completed in 1st, 3rd, 6th and 12th months following the treatment. There was a statistically significant decrease in all the scores evaluated at first month compared with the baseline. The results of this study suggest that acupuncture appears to be an effective, useful, non-invasive method in IC/BPS patients. It can be used as an appropriate treatment method not only in refractory but also in IC patients since it is rather advantageous compared to other treating agents.

THE ROLE OF RECONSTRUCTIVE SURGERY IN PATIENTS WITH END-STAGE INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: IS CYSTECTOMY NECESSARY?

Redmond EJ, Flood HD. Int Urogynecol J. 2017 Mar 11. doi: 10.1007/s00192-017-3307-6. [Epub ahead of print] PMID: 28283711

Interstitial cystitis is a debilitating condition that has a profound effect on quality of life. Although many approaches to treatment have been explored, no consistently effective treatment has been identified. Reconstructive surgery is offered to patients with refractory IC/BPS; however, expert opinion is divided as to whether simultaneous cystectomy is necessary to achieve symptomatic cure. The aim of this study from Ireland was to report the authors' experience in the surgical management of IC/BPS in a university teaching hospital. The hospital inpatient enquiry (HIPE) system was used to identify patients with IC/BPS who underwent surgery between 1997 and 2013. Medical records were examined and patients were invited to complete three symptom-based questionnaires. Twelve patients were identified (8 female, 4 male). Reconstructive procedures included urinary diversion without cystectomy (9) and augmentation ileocystoplasty (4). One patient failed to have a sustained improvement in symptoms following ileocystoplasty and later underwent successful urinary diversion. All other patients noted a "marked improvement" in overall symptoms on global response assessment (GRA) and the resolution of bladder pain on a visual analogue scale (VAS). There were no persistent symptoms or complications related to the retained bladder following diversion. According to the authors, this study adds to the existing evidence that cystectomy is not necessary to provide symptomatic cure in patients with end-stage IC/BPS. Urinary diversion without cystectomy is a highly effective operation and a successful outcome was achieved in all patients. Ileocystoplasty may be offered in carefully selected cases.

HYDRODISTENSION OF THE BLADDER FOR THE TREATMENT OF BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS (BPS/IC).

Hoke TP, Goldstein H, Saks EK, Vakili B. Neurourol Urodyn. 2017 Mar;36(3):784-786. doi: 10.1002/nau.23024. Epub 2016 Apr 19. PMID: 27092957

The purpose of this study from the USA was to determine whether a transvaginal trigonal block immediately preceding cystoscopy with hydrodistension yields an additional therapeutic benefit compared to cystoscopy with hydrodistension alone for the treatment of bladder pain syndrome/interstitial cystitis (BPS/IC). A retrospective chart review was performed at a single centre. Performance of a trigonal block prior to hydrodistension was at the discretion of the surgeon. A trigonal block consists of injecting 0.25% bupivacaine with 1.0% Xylocaine into the anterior vagina under the trigone under cystoscopic guidance. Procedures between January 1, 2008 and December 31, 2013 were included. The primary outcome compared change in pain score from the baseline to 1-month post-operative. One hundred and eighty-three patients underwent hydrodistension of the bladder. Seventy-seven were excluded and of the 106 patients remaining, 48 received a trigonal block and 58 did not. Both groups had a significant improvement in pain scores. There was no difference in change in pain score from baseline between both groups. Distention time was dichotomized

into 2 and >5 min based on surgeon preference. There was no difference in change in pain score from baseline between both groups. The authors found that hydrodistension of the bladder decreased pain postoperatively regardless of trigonal block or time of distention. A randomized-controlled trial is necessary to determine the benefits of duration of hydrodistension or performance of a block.

PREGNANCY AFTER URINARY DIVERSION AT YOUNG AGES - RISKS AND OUTCOME.

Huck N, Schweizerhof S, Honeck P, Neisius A, Thüroff J, Stein R. Urology. 2017 Feb 13. pii: S0090-4295(17)30136-X. doi: 10.1016/j.urology.2017.01.033. [Epub ahead of print] PMID: 28209547

The purpose of this paper was to assess the urological and obstetric outcomes during and after pregnancy following urinary diversion (UD) performed during childhood or adolescence. Reasons for urinary diversion were neurogenic bladder, exstrophy, trauma, sinus urogenitalis and interstitial cystitis. 17 had continent cutaneous diversion, 4 continent anal diversion and 4 colonic conduit. The authors found that after urinary diversion, pregnancy is possible without major complications. Due to an increased risk of pyelonephritis and dilatation of the upper urinary tract requiring intervention, these pregnancies should be considered high-risk pregnancies. Delivery should be carried out in a centre of expertise with urological stand-by.

THE EFFECT OF SACRAL NEUROMODULATION ON PREGNANCY: A SYSTEMATIC REVIEW.

Mahran A, Soriano A, Safwat AS, Hijaz A, Mahajan ST, Trabuco EC, Siegel SW, El-Nashar SA. Int Urogynecol J. 2017 Feb 3. doi: 10.1007/s00192-017-3272-0. [Epub ahead of print] PMID: 28160010.

The purpose of this study from the USA was to evaluate the effects of sacral neuromodulation (SNM) on pregnancy and the impact of delivery on SNM function. A systematic search was conducted through January 2016. The authors selected studies including women who had SNM and a subsequent pregnancy. Out of 2,316, eight studies were included, comprising 22 patients (26 pregnancies). SNM indications were Fowler's syndrome in 11, urinary retention in 6, fecal incontinence in 1, fecal and urinary urgency in 1, overactive bladder in 1, intractable interstitial cystitis in 1, and myelodysplasia in 1. SNM stayed on in 8 pregnancies. In the remaining 18 pregnancies in which the device was deactivated, 7 had recurrent urinary tract infections, including 1 with pyelonephritis and 2 who requested reactivation owing to recurrent symptoms. Outcomes were reported in 25 pregnancies, 16 had Cesarean section (CS) and 9 had vaginal delivery, including 2 operative deliveries. Out of 25, two infants had pilonidal sinus and motor tic disorder (exhibited at the age of 2 years), both from the same mother. After delivery, SNM was functioning in 15 (60%), 4 required reprogramming, and 3 required replacement (1 had recurrence of fecal incontinence after her operative delivery with evidence of displaced leads and 1 patient reported decreased SNM effects after her two CS), and 3 decided to remove the device (2 out of 3 patients were free of symptoms after SNM deactivation and requested removal). It was concluded that within the current limited evidence, the decision regarding SNM activation or deactivation should be individualized. A registry for those patients is recommended.

TGF- β /MAPK SIGNALING MEDIATES THE EFFECTS OF BONE MARROW MESENCHYMAL STEM CELLS ON URINARY CONTROL AND INTERSTITIAL CYSTITIS AFTER URINARY BLADDER TRANSPLANTATION.

Xiao Y, Song YJ, Song B, Huang CB, Ling Q, Yu X. Am J Transl Res. 2017 Mar 15;9(3):1193-1202. eCollection 2017. PMID: 28386345

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This study from China aimed to explore the role of the transforming growth factor- β /mitogen activated protein kinase (TGF- β /MAPK) signalling pathway in the effects of bone marrow mesenchymal stem cells (BMSCs) on urinary control and interstitial cystitis in a rat model of urinary bladder transplantation. Compared with normal, negative control, BMSCs, and sp600125 groups, rats in the PS group exhibited decreased discharge volume, maximal micturition volume, contraction interval, and bladder capacity but increased residual urine volume, bladder pressure, bladder peak pressure, expression of TGF- β /MAPK signalling pathway-related proteins, levels of inflammatory cytokines, and growth inhibition rate. Levels of inflammatory cytokines and the growth inhibition rate were positively correlated with the expression of TGF- β /MAPK signalling pathway-related proteins. The authors concluded that their findings demonstrate that the TGF- β /MAPK signalling pathway mediates the beneficial effects of BMSCs on urinary control and interstitial cystitis.

CYCLOPHOSPHAMIDE-INDUCED HCN1 CHANNEL UPREGULATION IN INTERSTITIAL CAJAL-LIKE CELLS LEADS TO BLADDER HYPERACTIVITY IN MICE.

Liu Q, Long Z, Dong X, Zhang T, Zhao J, Sun B, Zhu J, Li J, Wang Q, Yang Z, Hu X, Li L. *Exp Mol Med.* 2017 Apr 21;49(4):e319. doi: 10.1038/emm.2017.31. PMID: 28428632

While hyperpolarization-activated cyclic nucleotide-gated (HCN) channels are confirmed to be expressed in bladder interstitial Cajal-like cells (ICC-LCs), little is known about their possible role in cystitis-associated bladder dysfunction. This study from China aimed to determine the functional role of HCN channels in regulating bladder function under inflammatory conditions. Sixty female wild-type C57BL/6J mice and sixty female HCN1-knockout mice were randomly assigned to experimental and control groups, respectively. Cyclophosphamide (CYP)-induced cystitis models were successfully established in these mice. CYP treatment significantly enhanced HCN channel protein expression and Ih density and significantly altered bladder HCN1 channel regulatory proteins. Carbachol (CCH) and forskolin (FSK) exerted significant effects on bladder ICC-LC [Ca²⁺]_i in CYP-treated wild-type (WT) mice, and HCN1 channel ablation significantly decreased the effects of CCH and FSK on bladder ICC-LC [Ca²⁺]_i in both naive and CYP-treated mice. CYP treatment significantly potentiated the spontaneous contractions and CCH (0.001-10 μM)-induced phasic contractions of detrusor strips, and HCN1 channel deletion significantly abated such effects. Finally, they demonstrated that the development of CYP-induced bladder overactivity was reversed in HCN1^{-/-} mice. Taken together, the authors believe that their results suggest that CYP-induced enhancements of HCN1 channel expression and function in bladder ICC-LCs are essential for cystitis-associated bladder hyperactivity development, indicating that the HCN1 channel may be a novel therapeutic target for managing bladder hyperactivity.

THE EFFECT OF INTRAVESICAL LIPOSOME-BASED NGF ANTISENSE THERAPY ON BLADDER OVERACTIVITY AND NOCICEPTION IN A RAT MODEL OF CYSTITIS INDUCED BY HYDROGEN PEROXIDE.

Majima T, Tyagi P, Dogishi K, Kashyap M, Funahashi Y, Gotoh M, Chancellor M, Yoshimura N. *Hum Gene Ther.* 2017 Apr 27. doi: 10.1089/hum.2016.121. [Epub ahead of print] PMID: 28446032

Majima and colleagues from Japan and the USA investigated the effect of intravesical liposome-based NGF antisense therapy on bladder overactivity and nociception in a rat model of cystitis induced by hydrogen peroxide (HP). The authors found that intravesical liposome-based NGF antisense therapy significantly improved bladder overactivity and nociception induced by chemical cystitis in rats. Liposome-based intravesical therapy targeting NGF could be effective as a local treatment of hypersensitive bladder disorders such as bladder pain syndrome/interstitial cystitis.

CLINICAL EFFICACY OF 1-YEAR INTENSIVE SYSTEMATIC DIETARY MANIPULATION AS COMPLEMENTARY AND ALTERNATIVE MEDICINE THERAPIES ON FEMALE INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PATIENTS.

Oh-Oka H. *Urology.* 2017 Apr 20. pii: S0090-4295(17)30375-8. doi: 10.1016/j.urology.2017.02.053. [Epub ahead of print] PMID: 28435032

The purpose of this study from Japan was to evaluate the clinical efficacy of intensive systematic dietary manipulation (ISDM) for female patients with interstitial cystitis/bladder pain syndrome (IC/BPS) in a stable condition who were followed in our hospital. In cooperation with the nutrition control team, the authors created a basic IC/BPS diet menu for 1 month. Data regarding daily food intake and food-related symptoms were collected by detailed interview of each patient, they set meal menu to control IC/BPS symptoms and advised the patients to reduce the intake of specific food items to the maximum possible extent. The following food items were removed from or restricted in the diet of patients: tomatoes, tomato products, soybean, tofu product, spices, excessive potassium, citrus, high-acidity-inducing substances, etc. They evaluated the following factors 3 months and 1 year after the start of the intervention: O'Leary-Sant symptom index, O'Leary-Sant problem index, urgency visual analogue scale score, bladder or pelvic pain visual analogue scale score, and numerical patient-reported quality of life index. ISDM was found to alleviate the symptoms of IC/BPS in almost 3 months and continued clinical efficacy for at least 1 year. ISDM as one of the conservative treatment modality for IC/BPS should be attempted more strictly because of its non-invasiveness, without alterations to the other treatments.

ASSESSMENT OF THERAPEUTIC EFFECT OF HUMAN CHORIOGONADOTROPIN IN A CHEMICAL CYSTITIS MODEL.

Tanik S, Zengin K, Albayrak S, Gurel A, Atar M, Sahin S, Tuzcu N, Tuzcu M, Imamoglu MA, Gurdal M. *Kaohsiung J Med Sci.* 2017 May;33(5):229-235. doi: 10.1016/j.kjms.2017.02.003. Epub 2017 Mar 27. PMID: 28433069

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

In this study from Turkey, female rats induced with chemical cystitis were administered the hormone human choriogonadotropin (HCG), and it was aimed to reveal the usefulness of HCG in the treatment of interstitial cystitis/bladder pain syndrome. The materials for this study were 32 Wistar albino female rats. The study groups were formed as follows: the cystitis group (Group 1), the cystitis + HCG protection group (Group 2), the cystitis + HCG treatment group (Group 3), and the control group (Group 4), with eight rats in each group. In this study, blood and urine samples were taken from the rats, they were euthanized, and their bladders were removed for glutathione, malondialdehyde, tumor necrosis factor alpha, and interferon gamma measurements. It was observed that tissue damage in Group 2 was lower than that in the other two groups. Glutathione levels in Groups 2 and 4 were significantly higher than in Groups 1 and 3 ($p = 0.01$). Malondialdehyde levels of Groups 2 and 4 were significantly lower than the values in Groups 1 and 3 ($p < 0.001$). When the cystitis groups were compared in terms of their interferon gamma and tumor necrosis factor alpha levels, the lowest interferon gamma and tumor necrosis factor alpha levels were detected in Group 3. It was found that HCG has positive effects on experimental cystitis in rats. This study revealed that HCG should be researched as a therapeutic agent and formed a step for studies to be carried out on this subject.

CHARACTERIZING HEALTH CARE UTILIZATION, DIRECT COSTS, AND COMORBIDITIES ASSOCIATED WITH INTERSTITIAL CYSTITIS: A RETROSPECTIVE CLAIMS ANALYSIS.

Tung A, Hepp Z, Bansal A, Devine EB. *J Manag Care Spec Pharm.* 2017 Apr;23(4):474-482. doi: 10.18553/jmcp.2017.23.4.474. PMID: 28345436

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

Interstitial cystitis (IC) is a debilitating condition that affects up to 5% of the U.S. This condition is characterized by bladder pain, urinary urgency and frequency, nocturia, and, in some patients, bladder lesions called Hunner lesions (HL). IC patients who have HL experience a clinical course that is distinct from those without HL and, as a result, respond differently to existing treatments. Without effective and lasting therapeutic options, IC patients are expected to experience a reduced quality of life and be a significant economic burden. Previous research describing the burden of IC is not only outdated but lacks stratification by HL. The aim of this study was to (a) characterize health care utilization, direct costs, and comorbidities associated with IC and (b) elucidate differences between patients with and without HL. Adults with an incident IC diagnosis between 2009 and 2014 were identified and matched 1:4 to non-IC patients on age, gender, and geographic region. Health care utilization, direct costs, and comorbidities during the first 12 months after diagnosis were compared between the 2 groups, as well as between IC subgroups with and without HL. Associations were evaluated after adjustment for potential confounders using regression models. A total of 24,836 IC patients were identified and matched to 99,344 non-IC patients. Patients were predominantly female (92%), with a mean age of 49.0 (SD = 15.3) years. IC patients used significantly more health care resources across all categories compared with non-IC patients. Findings suggest that patients with IC have significantly higher health care utilization, costs, and comorbidities compared with non-IC patients. This economic burden is further amplified in those with HL.

UROTHELIUM

IS ELECTROLYTE TRANSFER ACROSS THE UROTHELIUM IMPORTANT?: ICI-RS 2015.

McCloskey KD, Vahabi B, Fry CH. *Neurourol Urodyn.* 2017 Apr;36(4):863-868. doi: 10.1002/nau.23085. PMID: 28444701

This article summarizes discussion at the International Consultation on Incontinence Research Society (ICI-RS) 2015 meeting of urine modification in the urinary tract by the urothelium. It considers the literature and proposes pertinent questions that need to be addressed to understand this phenomenon within a physiological context. Following the ICI-RS meeting, publications in PubMed relating to urine modification in the renal pelvis, ureter, and bladder were reviewed. Historically, the urothelium has been simply considered as a passive, impermeable barrier, preventing contact between urine and the underlying cells. In addition to the ability of the

umbrella cells to modify the surface area of the urothelium during bladder filling, the urothelium may also be involved in modifying urine composition. Several lines of evidence support the hypothesis that electrolytes and water can be reabsorbed by the urothelium and that this may have physiological relevance. Firstly, urothelial cells express several types of aquaporins and ion channels; the membrane expression of which is modulated by the extracellular concentration of ions including Na⁺. Secondly, studies of urine composition in the renal pelvis and bladder demonstrate urine modification, indicating that water and/or electrolyte transport has occurred. Thirdly, hibernating mammals, with urothelial and bladder wall histology similar to non-hibernating mammals are known to produce and reabsorb urine daily, during long periods of hibernation. The phenomenon of urine modification by the urothelium may therefore be physiologically important during normal bladder filling. Research should be focused on investigating how this may change in conditions of urinary dysfunction.

KETAMINE CYSTITIS

EFFECTIVE TREATMENT OF KETAMINE-ASSOCIATED CYSTITIS WITH BOTULINUM TOXIN TYPE A INJECTION COMBINED WITH BLADDER HYDRODISTENTION.

Zeng J, Lai H, Zheng D, Zhong L, Huang Z, Wang S, Zou W, Wei L. *J Int Med Res.* 2017 Apr;45(2):792-797. doi: 10.1177/0300060517693956. Epub 2017 Mar 8. PMID: 28415952

Objective Ketamine-associated cystitis (KAC) has been described in a few case reports, but its treatment in a relatively large number of patients has not been documented. This study from China aimed to describe our experience of treatment of 36 patients with KAC. Methods Thirty-six patients (30 males and 6 females, aged 19-38 years) with KAC, who had previously taken a muscarinic receptor blocker and/or antibiotics, but without symptomatic relief, were treated with botulinum toxin A injection combined with bladder hydrodistention. Urodynamic testing, and the O'Leary-Sant interstitial cystitis symptom index (ICSI) and problem index (ICPI) were used to evaluate baseline values and improvement before and after the treatment. Results One month post-treatment, all patients achieved marked relief of symptoms. The nocturia time was markedly reduced, while bladder capacity, the interval between micturition, the void volume, and the maximum flow rate were remarkably increased at 1 month. Additionally, the ICSI and ICPI were significantly improved. Conclusion Botulinum toxin A injection along with bladder hydrodistention is effective for managing KAC.

ACTIVATION OF THE mTOR DEPENDENT SIGNALING PATHWAY UNDERLIES KETAMINE-INDUCED UROPATHY.

Lin CC, Yang AH, Lin AT. *Neurourol Urodyn.* 2017 Feb 21. doi: 10.1002/nau.23234. [Epub ahead of print] PMID: 28220552

The purpose of this study from Taiwan was to investigate the pathogenic role of activation of the mammalian target of the rapamycin (mTOR) in the ketamine induced microvascular injury. Twenty-three patients with ketamine-induced cystitis (KC) and 16 control volunteers were recruited. Bladder tissues were obtained from both groups by cystoscopic biopsies. Phospho-S6 ribosomal protein (p-S6RP), an end product of the mTOR pathway, was stained in the urinary bladder from both groups. Endothelial cells of the urinary bladder (HBdMECs) were examined to investigate the in vitro activation of the mTOR pathway and the co-expression of the endothelial marker (cluster of differentiation 31 [CD31]) and the mesenchymal marker (fibroblast-specific protein 1 [FSP-1]). Expression of p-S6RP increased significantly after ketamine exposure, especially in the vesical microvessels of KC patients. In HBdMECs treated with 100 μM Ketamine, time-dependent activation of the mTOR pathway occurred, with significantly increased levels of the phosphorylated forms of mTOR at 30 min and of S6RP and p70S6 kinase (p70S6K) at 6 h. The increased level of p-S6RP returned to baseline within 2 days after ketamine exposure. The co-expression of CD31 and FSP-1 implied that EndMT was present in HBdMECs at 7 days after ketamine treatment, while TGF-β1 facilitated significant up-regulation of FSP-1 at 1 day after treatment. Furthermore, when the mTOR inhibitor rapamycin was administered with ketamine to the HBdMECs, the expression of FSP-1 decreased significantly. The authors concluded that ketamine induces activation of the mTOR pathway and subsequent mesenchymal phenotypic expression (FSP1) in HBdMECs.

THE PUTATIVE INVOLVEMENT OF ACTIN-BINDING PROTEINS AND CYTOSKELETON PROTEINS IN PATHOLOGICAL MECHANISMS OF KETAMINE CYSTITIS-REVEALED BY A PROSPECTIVE PILOT STUDY USING PROTEOMIC APPROACHES.

Yang HH, Zhai WJ, Kuo HC. *Proteomics Clin Appl.* 2017 Mar;11(3-4). doi: 10.1002/prca.201600085. Epub 2016 Dec 21. PMID: 27863071

Ketamine-induced cystitis (KC) among chronic ketamine young abusers has increased dramatically and it has brought attention for Urologists. The underlying pathophysiological mechanism(s) of KC is still unclear. Therefore, the purpose of this study from Taiwan is to elucidate the possible pathophysiological mechanism(s) of KC through proteomic techniques. Bladder tissues were obtained from seven patients with KC, seven patients with interstitial cystitis/bladder pain syndrome, and five control subjects who underwent video-urodynamic study followed by augmentation enterocystoplasty to increase bladder capacity. 2DE/MS/MS-based approach, functional classifications, and network analyses were used for proteomic and bioinformatics analyses and protein validation was carried out by Western blot analysis. Among the proteins identified, bioinformatics analyses revealed that several actin binding related proteins such as cofilin-1, myosin light polypeptide 9, filamin A, gelsolin, lamin A are involved in the apoptosis. Furthermore, the contractile proteins and cytoskeleton proteins such as myosin light polypeptide 9, filamin A, and calponin are found downregulated in KC bladders. The authors concluded that increased apoptosis in KC might be mediated by actin-binding proteins and a Ca²⁺ - activated protease. Rapid detrusor contraction in KC might be induced by contractile proteins and cytoskeleton proteins.

URINARY MICROBIOME

[THE URINARY MICROBIOME AND ITS CONTRIBUTION TO LOWER URINARY TRACT SYMPTOMS; ICI-RS 2015.](#)

Drake MJ, Morris N, Apostolidis A, Rahnama'i MS, Marchesi JR. *Neurourol Urodyn.* 2017 Apr;36(4):850-853. doi: 10.1002/nau.23006. PMID: 28444712

The microbiome is the term used for the symbiotic microbial colonisation of healthy organs. Studies have found bacterial identifiers within voided urine which is apparently sterile on conventional laboratory culture, and accordingly there may be health and disease implications. The International Consultation on Incontinence Research Society (ICI-RS) established a literature review and expert consensus discussion focused on the increasing awareness of the urinary microbiome, and potential research priorities. The consensus considered the discrepancy between findings of conventional clinical microbiology methods, which generally rely on culture parameters predisposed towards certain "expected" organisms. Discrepancy between selective culture and RNA sequencing to study species-specific 16S ribosomal RNA is increasingly clear, and highlights the possibility that protective or harmful bacteria may be overlooked where microbiological methods are selective. There are now strong signals of the existence of a "core" urinary microbiome for the human urinary tract, particularly emerging with ageing. The consensus reviewed the potential relationship between a patient's microbiome and lower urinary tract dysfunction, whether low-count bacteriuria may be clinically significant and mechanisms which could associate micro-organisms with lower urinary tract symptoms. Key research priorities identified include the need to establish the scope of microbiome across the range of normality and clinical presentations, and gain consensus on testing protocols. Proteomics to study enzymatic and other functions may be necessary, since different bacteria may have overlapping phenotype. Longitudinal studies into risk factors for exposure, cumulative risk, and emergence of disease need to undertaken.

[CLINICAL IMPLICATIONS OF THE MICROBIOME IN URINARY TRACT DISEASES.](#)

Hiergeist A, Gessner A. *Curr Opin Urol.* 2017 Mar;27(2):93-98. doi: 10.1097/MOU.0000000000000367. PMID: 27898455

The purpose of this review from Germany is to outline and evaluate the most recent literature on the role of the microbiome in urinary tract diseases. High throughput molecular DNA sequencing of bacterial 16S rRNA genes enabled the analysis of complex microbial communities inhabiting the human urinary tract. Several recent studies have identified bacterial taxa of the urinary microbiome to impact urinary tract diseases including interstitial cystitis, urgency urinary incontinence or calcium oxalate stone formation. Furthermore, treatment of urinary tract infections by antibiotics globally impacts community profiles of the intestinal microbiota and might indirectly influence human health. Alternative treatment options like application of probiotics for the treatment of urinary tract infections are currently under investigation. The urinary microbiome and its relationship to urinary tract diseases is currently under comprehensive investigation. Further studies are needed to shed light on the role of commensal microbiota for urinary tract infections.

URINARY MICROBIOME AND CYTOKINE LEVELS IN WOMEN WITH INTERSTITIAL CYSTITIS.

Abernethy MG, Rosenfeld A, White JR, Mueller MG, Lewicky-Gaupp C, Kenton K. Obstet Gynecol. 2017 Mar;129(3):500-506. doi: 10.1097/AOG.0000000000001892. PMID: 28178051

The purpose of this study from the USA was to investigate differences in the urinary microbiome and cytokine levels between women with and without interstitial cystitis and to correlate differences with scores on standardized symptom severity scales and depression and anxiety screening tools. This cross-sectional study compared women presenting to a pelvic floor clinic and diagnosed with interstitial cystitis over a 6-month period with age-matched women in a control group from the same institution. Participants provided a catheterized urine sample and completed symptom severity, quality-of-life, depression, and anxiety screening questionnaires. Urinary microbiomes generated through bacterial ribosomal RNA sequencing and cytokine levels were analyzed using a standard immunoassay. Nonparametric analyses were used for all comparisons. The urinary microbiome of participants with interstitial cystitis was less diverse, less likely to contain Lactobacillus species, and associated with higher levels of proinflammatory cytokines. It is unknown whether this represents causality and whether the effect of alterations to the urinary microbiome is mediated through an inflammatory response.

LOWER URINARY TRACT AND SEXUAL FUNCTION

HOW DOES LOWER URINARY TRACT DYSFUNCTION AFFECT SEXUAL FUNCTION IN MEN AND WOMEN? ICI-RS 2015-PART 1.

Rantell A, Apostolidis A, Anding R, Kirschner-Hermanns R, Cardozo L. NeuroUrol Urodyn. 2017 Apr;36(4):949-952. doi: 10.1002/nau.23040. PMID: 28444703

The aim of this ICI-RS paper was to review the literature on the effect of lower urinary tract symptoms (LUTS) on sexual function and dysfunction. At the International Consultation on Incontinence-Research Society (ICI-RS) in 2015, a multidisciplinary group presented a literature search of what is known about the effect of lower urinary tract dysfunction (LUTD) on sexual function (SF) in men and women. Wider discussions regarding knowledge gaps and ideal research methodology ensued. A body of evidence supports associations between LUTS/urinary incontinence on SF in both men and women, but the true prevalence of the impact of LUTD on SF remains largely unknown. There is still reluctance among health care professionals (HCP's) to discuss SF with patients and often patients who are not asked will not volunteer their problems. A significant knowledge gap in this area remains. Education among HCP's on assessment and treatment of sexual dysfunction and communication skills are essential to encourage, and engage patients with HCP's.

HOW DOES LOWER URINARY TRACT DYSFUNCTION (LUTD) AFFECT SEXUAL FUNCTION IN MEN AND WOMEN? ICI-RS 2015-PART 2.

Apostolidis A, Rantell A, Anding R, Kirschner-Hermanns R, Cardozo L. NeuroUrol Urodyn. 2017 Apr;36(4):869-875. doi: 10.1002/nau.23088. PMID:28444704

The aim of this ICI-RS study part 2 was to discuss available data on the links between LUTD and sexual dysfunction, what is still unknown about the causative effect of disease processes on sexual function (SF), and to suggest proposals for further research. At the 2015 International Consultation on Incontinence-Research Society (ICI-RS), a multi-disciplinary group presented a literature search of what is known about the effect of LUTD on SF in men and women. Wider discussions regarding knowledge gaps, and ideal research methodology ensued and are presented. The underlying mechanisms of the impact of LUTD on SF remain largely unknown. Risk factors for the metabolic syndrome may cause both LUTS and ED in men, and their improvement may improve both conditions. In women, neurovascular changes may be common in LUTD and FSD. Successful LUTS management results in FSD improvement, but the mechanisms are ill understood. Gaps in standardization of sexual dysfunction terminology, variations of assessment, and treatment in clinical practice and research make most studies not comparable. The sensitive knowledge and subjective nature of the problem present challenges and often result in neglecting it. Neurovascular and hormonal factors, but also indirect effects may link LUTD to SD in both sexes, but the evidence is not robust and the mechanisms unclear. There is a need for defining the terminology and standardizing outcomes assessed in clinical trials. The multifactorial nature of

SF in both sexes makes trial design challenging and "real world" studies may prove more beneficial for patients' outcomes and clinicians' understanding.

PATIENT REPORTED OUTCOME

CAN A PATIENT REPORTED OUTCOME BE ADEQUATE WITHOUT ASSESSING QUALITY OF LIFE IN LOWER URINARY TRACT DYSFUNCTION?

Cotterill N, Tubaro A. NeuroUrol Urodyn. 2017 Apr;36(4):943-948. doi: 10.1002/nau.23177. PMID: 28444715

A think tank was convened at the sixth ICI-RS meeting held in the United Kingdom on September 2015, to consider the adequacy of patient reported outcome (PRO) measurement if quality of life (QoL) evaluation were excluded. Rigorous methodology is proposed for the development of PROs and much is written about this process but the necessity for QoL inclusion is rarely discussed. The decision was therefore taken to consider what QoL evaluation provides and what these data provide. Discussions highlighted the need to question our aim for including QoL evaluation in clinical practice and research, in order to ensure its necessity for the intended purpose. Improved understanding of the usefulness of QoL data, in particular in relation to important health indicators was also identified as an area of unmet need. The think tank ended with a collaborative research proposal to pool existing QoL databases to explore the correlations with other outcome measures and types of associations present. It was suggested that these findings would enable clinicians and researchers to make more informed decisions regarding PRO selection, use and interpretation.

CHRONIC (PELVIC) PAIN

A COMMON PRO-NOCICEPTIVE PAIN MODULATION PROFILE TYPIFYING SUBGROUPS OF CHRONIC PELVIC PAIN SYNDROMES IS INTERRELATED WITH ENHANCED CLINICAL PAIN.

Keren G, Michal G, Lior L, Liora A, Irit WF. Pain. 2017 Feb 7. doi: 10.1097/j.pain.0000000000000869. [Epub ahead of print] PMID: 28178074

Provoked vestibulodynia (PVD) and painful bladder syndrome (PBS), subgroups of chronic pelvic pain syndromes (CPPS), are considered to share common bio-physiological peripheral mechanisms. In addition, indications of a pro-nociceptive pain profile co-existing with psychological vulnerability suggests common dysfunctional pain processing and pain modulation in these two subgroups of CPPS. Keren and colleagues from Israel therefore aimed at comparing the pain profile and psychological traits of PVD and PBS patients to see whether the pain profile contributes to inter-subject variability of clinical pain symptoms. PVD and PBS patients were compared to healthy controls in their responses to: 1) pain psychophysical tests applied to both referred (supra pubis) and remote (hand) body areas, and 2) pain-related psychological factors (pain catastrophizing, depression, anxiety, and somatization). They found a similar pro-nociceptive pain profile in the two subgroups of CPPS; enhanced facilitation (i.e. hyperalgesia in the referred body area and inefficient inhibition (i.e. reduced conditioned pain modulation that were associated with both enhanced pain ratings evoked during trigger point examination and higher Brief Pain Inventory ratings. The latter was also correlated with pain catastrophizing and depression symptoms. The findings suggest common mechanisms underlying a dysfunctional nociceptive system in both PVD and PBS. The inter-subject variability in the level of dysfunction and its association with disease severity recommends a personalized pain treatment that may alleviate daily pain and dysfunction in CPPS patients.

IRRITABLE BOWEL SYNDROME

IRRITABLE BOWEL SYNDROME: CLINICAL MANIFESTATIONS, DIETARY INFLUENCES, AND MANAGEMENT

Ikechi R, Fischer BD, DeSipio J, Phadtare S. Healthcare (Basel). 2017 Apr 26;5(2). pii: E21. doi: 10.3390/healthcare5020021. PMID: 28445436

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Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder that is characterized by symptoms of chronic abdominal pain and altered bowel habits in the absence of an overtly identifiable cause. It is the most commonly diagnosed functional gastrointestinal disorder, accounting for about one third of gastroenterology visits. It generally presents as a complex of symptoms, including psychological dysfunction. Hypersensitivity to certain foods, especially foods that contain high amounts of fructose, plays a role in the pathophysiology of IBS. Elevated consumption of high-fructose corn syrup (HFCS) has been discussed in this aspect. The treatment

options for IBS are challenging and varied. In addition to dietary restrictions for HFCS-induced IBS, such as low-FODMAP (Fermentable Oligosaccharides, Disaccharide, Monosaccharides, and Polyols) diets, existing drug therapies are administered based on the predominant symptoms and IBS-subtype. Patients with IBS are likely to suffer from issues, such as anxiety, depression, and post-traumatic-stress disorder. Biopsychosocial factors particularly socioeconomic status, sex, and race should, thus, be considered for diagnostic evaluation of patients with IBS.

SYSTEMATIC REVIEW: QUALITY OF TRIALS ON THE SYMPTOMATIC EFFECTS OF THE LOW FODMAP DIET FOR IRRITABLE BOWEL SYNDROME.

Krogsgaard LR, Lyngesen M, Bytzer P. Aliment Pharmacol Ther. 2017 Apr 25. doi: 10.1111/apt.14065. [Epub ahead of print] PMID: 28440580

The low Fermentable Oligo-, Di- Monosaccharides, and Polyoles (FODMAP) diet is a new treatment option for irritable bowel syndrome (IBS). Experts refer to the diet as supported by high level of evidence, but an evaluation of the quality of trials is lacking. The aim of this study from Denmark was to provide a systematic review of the quality of trials on the symptomatic effects of the low FODMAP diet for IBS. Pubmed and EMBASE were searched for randomised controlled trials (RCTs) reporting effect of the low FODMAP diet on IBS symptoms. The quality of trials was evaluated by estimating risk of bias and assessing trial methodology. Nine RCTs were eligible, including 542 patients. The intervention period was from 2 days to 6 weeks and one trial included a 6-month follow-up. Three trials intervened by providing meals, controlling with a diet high in FODMAP content. In six trials, the intervention was instruction by a dietician and a variety of control interventions were used, all with limited established efficacy. Domains with a high risk of bias were identified for all the trials. High risk of bias dominated domains regarding blinding, with only one trial double-blinded. The RCTs on the low FODMAP diet are characterized by high risk of bias. The diet has not been studied in a randomised, controlled setting for more than 6 weeks and trials examining the effect of the important reintroduction period are lacking. There is a risk that the symptomatic effects reported in the trials are driven primarily by a placebo response.

THE FREQUENCY OF PRIMARY SJOGREN'S SYNDROME AND FIBROMYALGIA IN IRRITABLE BOWEL SYNDROME.

Erbasan F, Cekin Y, Coban DT, Karasu U, Suren D, Cekin AH. Pak J Med Sci. 2017 Jan-Feb;33(1):137-141. doi: 10.12669/pjms.331.11168. PMID: 28367187

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The purpose of this study from Turkey was to determine the frequency of sicca complex, Sjogren's Syndrome (SS) and Fibromyalgia (FM) in patients with Irritable Bowel Syndrome (IBS). Seventy seven IBS patients who fulfilled the Rome-III criteria were included in the study. All patients were assessed for FM according to the American College of Rheumatology (ACR) 2010 criteria. After examination for objective evidence of sicca complex by Schirmer test, TBUT and Ocular Staining Score (OSS), serological tests were performed. And the diagnosis of SS was made according to the American College of Rheumatology (ACR) classification criteria for SS - 2012. Thirteen (16.9%) of IBS patients had FM. Dry eye was detected in 20(26.0%), 7(9.1%) and 29(37.7%) patients by OSS, Schirmer test and TBUT, respectively. Of 77 patients with IBS, the diagnosis of SS was established in two patients (2.6%). It was concluded that the frequency of Sjogren's Syndrome among patients with IBS is relatively higher than the general population. All IBS patients should be questioned for dryness of the mouth and eyes, and if necessary, should be evaluated for SS.

FIBROMYALGIA

CONTROVERSIES AND CHALLENGES IN FIBROMYALGIA: A REVIEW AND A PROPOSAL.

Cohen H. Ther Adv Musculoskelet Dis. 2017 May;9(5):115-127. doi: 10.1177/1759720X17699199. Epub 2017 Mar 26. PMID: 28458723

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Fibromyalgia (FM) is the most commonly encountered chronic widespread pain (CWP) condition in rheumatology. In comparison to inflammatory arthritis (IA), it can seem ill defined with no clear understanding of the pathology and therefore no specific targeted treatment. This inevitably raises controversies and challenges. However, this is an outdated view perpetuated by poor teaching of pain at undergraduate and

postgraduate levels, and the perennial problem of advances in relevant cross-speciality knowledge penetrating speciality silos. Research has provided a better understanding of the aetiopathology and FM is now regarded as a centralized pain state. Effective treatment is possible utilizing a multidisciplinary approach combining nonpharmacologic and pharmacologic treatments rooted in a biopsychosocial model. This article will provide a review of the mechanisms, diagnosis and treatment of FM, focus on some ongoing contentious issues and propose a change to the diagnostic terminology.

VULVODYNIA/VULVAL PAIN SYNDROME

PROVOKED VESTIBULODYNIA: DIAGNOSIS, SELF-REPORTED PAIN, AND PRESENTATION DURING GYNAECOLOGICAL EXAMINATIONS.

Dargie EE, Chamberlain SM, Pukall CF. J Obstet Gynaecol Can. 2017 Mar;39(3):145-151. doi: 10.1016/j.jogc.2017.01.001. PMID: 28343555

The purpose of this study from Canada was to explore factors associated with the diagnosis of provoked vestibulodynia (PVD) through (1) self-reported pain characteristics and (2) Friedrich's criteria (vestibular pain during sexual activity/gynaecological examination). Dargie and colleagues also identified cases in which incorrect diagnoses were assigned and explored group differences in gynaecological examination presentation and associations with self-reported pain. Data were extracted from nine studies conducted in their research laboratory. Information obtained during a telephone interview and a standardized gynaecological examination was compiled for 106 participants with vulvar pain and 106 pain-free control participants, matched for age, hormonal contraceptive use, and parity. Their results support the use of a targeted clinical interview and the evaluation of vestibular pain during sexual activity and the gynaecological examination for diagnosing PVD. They note that caution should be exercised when a patient presents with genital pain symptoms other than those typically observed in PVD. Furthermore, the cotton swab test may underestimate the degree of pain regularly experienced.

ALPHA LIPOIC ACID PLUS OMEGA-3 FATTY ACIDS FOR VESTIBULODYNIA ASSOCIATED WITH PAINFUL BLADDER SYNDROME.

Murina F, Graziottin A, Felice R, Gambini D. J Obstet Gynaecol Can. 2017 Mar;39(3):131-137. doi: 10.1016/j.jogc.2016.12.035. PMID: 28343553

This study from Italy assessed the effectiveness of alpha lipoic acid (ALA) plus omega-3 polyunsaturated fatty acids (n-3 PUFAs) in combination with amitriptyline therapy in patients with vestibulodynia/painful bladder syndrome (VBD/PBS). Women with VBD/PBS were randomly assigned to receive amitriptyline or amitriptyline plus a commercially available preparation (ALAnerv Age; Alfa Wassermann, Bologna, Italy) containing, in 2 capsules, ALA 600 mg plus docosahexaenoic acid 250 mg and eicosapentaenoic acid 16.67 mg. Symptoms of burning and pain were assessed using a 10-cm visual analog scale and the short form of the McGill-Melzack Pain Questionnaire. Among 84 women who were randomized, the mean \pm standard deviation dose of amitriptyline was 21.7 ± 6.6 mg/day, without statistical difference between the two groups. Pain, as assessed using both the pain rating index of the visual analog scale and the short-form McGill Pain Questionnaire, decreased significantly in both trial groups, with a greater effect seen with the addition of ALA and n-3 PUFAs. The addition of ALA/n-3 PUFAs to amitriptyline treatment was also associated with improvements in dyspareunia and pelvic floor muscle tone. The overall incidence of adverse events was low, and none led to treatment discontinuation. The authors concluded that the addition of ALA/n-3 PUFAs to amitriptyline treatment in patients with VBD/PBS appears to improve outcomes and may allow for a lower dosage of amitriptyline, which may lead to fewer adverse effects.

SJOGREN'S SYNDROME

IT'S MORE THAN DRYNESS AND FATIGUE: THE PATIENT PERSPECTIVE ON HEALTH-RELATED QUALITY OF LIFE IN PRIMARY SJÖGREN'S SYNDROME - A QUALITATIVE STUDY.

Lackner A, Ficjan A, Stradner MH, Hermann J, Unger J, Stamm T, Stummvoll G, Dür M, Graninger WB, Dejaco C. PLoS One. 2017 Feb 9;12(2):e0172056. doi: 10.1371/journal.pone.0172056. eCollection 2017. PMID: 28182787

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

In Primary Sjögren's Syndrome (PSS), there is an apparent lack of data concerning the perspectives of patients, their needs, preferences and difficulties of daily life. This qualitative study from Austria and Italy was conducted to explore perspectives and needs of patients with PSS that influence health related quality of life (HRQL). Lackner and colleagues recruited 20 PSS patients fulfilling the American-European consensus classification criteria out of the PSS cohort of the Medical University Graz, Austria. In total, 6 focus group sessions (with three to four patients per group) were performed. A modified meaning condensation procedure was used to analyse the data. The interview analysis resulted in 484 meaning units, 254 subconcepts and 86 concepts. The identified concepts were grouped into three dimensions: physical dimension, psychological & emotional challenges and social life & daily living. A dependency between the three categories was identified. The concepts most commonly reported by patients were related to the physical dimension: pain and dryness as well as complaints associated with/provoked by these symptoms. Patients also reported shortness of breath, fatigue and constipation. This qualitative study underpins that HRQL in PSS patients is affected by several factors. The problems are not limited to dryness, pain and fatigue while the complaints secondary to these symptoms are important to patients with PSS significantly affecting physical, psychological and social life components of HRQL. A disease-specific patient related outcome measures for clinical practice and trials should be developed considering the different aspects of HRQL in PSS.

[DEVELOPMENT OF NEW EXTRA-GLANDULAR MANIFESTATIONS OR ASSOCIATED AUTO-IMMUNE DISEASES AFTER ESTABLISHING THE DIAGNOSIS OF PRIMARY SJÖGREN'S SYNDROME : A LONG-TERM STUDY OF THE ANTONIUS NIEUWEGEIN SJÖGREN \(ANS\) COHORT.](#)

Ter Borg EJ, Kelder JC. Rheumatol Int. 2017 Apr 19. doi: 10.1007/s00296-017-3715-4. [Epub ahead of print] PMID: 28424927

The purpose of this long-term study from the Netherlands was to investigate the development of new extra-glandular manifestations (EGM) or associated auto-immune diseases (AID) from 1 year after establishing the diagnosis of primary Sjögren's syndrome (pSS). The primary goal was to examine the frequency and type of these manifestations and to find out which demographic, clinical and serological profile was most at risk. All outpatients diagnosed with primary Sjögren's syndrome were included in a retrospective study, with at least one check-up per year, from June 1991 until August 2015. Patients also fulfilling the criteria for concomitant connective tissue disorders were excluded. Data were collected with respect to the cumulative prevalence of a new EGM or associated AID. 140 patients were included in the final analysis. After 10 years of follow-up, the cumulative incidence of a new EGM or associated AID was 30.7%. The most frequent events were polyneuropathy, interstitial lung disease, (poly)arthritis, discoid lupus erythematosus (LE)/subacute cutaneous LE and Hashimoto's disease. Non-Hodgkin lymphoma was not diagnosed during the follow-up. Patients without chronic benign pain syndrome (CBP), but in particular those with cryoglobulins, developed more events. Age at diagnosis, gender, the presence of ANA, anti-Ro/SSA, anti-La/SSB, IgM-RF, decreased levels of C3 or C4, or hypergammaglobulinaemia did not show any statistically significant differences. The burden of disease in pSS is higher than expected due to the development of EGM or associated AID. Therefore, the authors recommend long-term follow-up of all pSS patients, particularly those with cryoglobulinaemia.

For more information about Sjögren's Syndrome and comorbidities including IC/BPS, [click here](#).

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